EPILEPSY

A MEDICAL DICTIONARY, BIBLIOGRAPHY,
AND ANNOTATED RESEARCH GUIDE TO
INTERNET REFERENCES

JAMES N. PARKER, M.D.
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FORWARD

In March 2001, the National Institutes of Health issued the following warning: "The number of Web sites offering health-related resources grows every day. Many sites provide valuable information, while others may have information that is unreliable or misleading."[1] Furthermore, because of the rapid increase in Internet-based information, many hours can be wasted searching, selecting, and printing. Since only the smallest fraction of information dealing with epilepsy is indexed in search engines, such as **www.google.com** or others, a non-systematic approach to Internet research can be not only time consuming, but also incomplete. This book was created for medical professionals, students, and members of the general public who want to know as much as possible about epilepsy, using the most advanced research tools available and spending the least amount of time doing so.

In addition to offering a structured and comprehensive bibliography, the pages that follow will tell you where and how to find reliable information covering virtually all topics related to epilepsy, from the essentials to the most advanced areas of research. Public, academic, government, and peer-reviewed research studies are emphasized. Various abstracts are reproduced to give you some of the latest official information available to date on epilepsy. Abundant guidance is given on how to obtain free-of-charge primary research results via the Internet. **While this book focuses on the field of medicine, when some sources provide access to non-medical information relating to epilepsy, these are noted in the text.**

E-book and electronic versions of this book are fully interactive with each of the Internet sites mentioned (clicking on a hyperlink automatically opens your browser to the site indicated). If you are using the hard copy version of this book, you can access a cited Web site by typing the provided Web address directly into your Internet browser. You may find it useful to refer to synonyms or related terms when accessing these Internet databases. **NOTE:** At the time of publication, the Web addresses were functional. However, some links may fail due to URL address changes, which is a common occurrence on the Internet.

For readers unfamiliar with the Internet, detailed instructions are offered on how to access electronic resources. For readers unfamiliar with medical terminology, a comprehensive glossary is provided. For readers without access to Internet resources, a directory of medical libraries, that have or can locate references cited here, is given. We hope these resources will prove useful to the widest possible audience seeking information on epilepsy.

The Editors

[1] From the NIH, National Cancer Institute (NCI): **http://www.cancer.gov/cancerinfo/ten-things-to-know**.

CHAPTER 1. STUDIES ON EPILEPSY

Overview

In this chapter, we will show you how to locate peer-reviewed references and studies on epilepsy.

The Combined Health Information Database

The Combined Health Information Database summarizes studies across numerous federal agencies. To limit your investigation to research studies and epilepsy, you will need to use the advanced search options. First, go to **http://chid.nih.gov/index.html**. From there, select the "Detailed Search" option (or go directly to that page with the following hyperlink: **http://chid.nih.gov/detail/detail.html**). The trick in extracting studies is found in the drop boxes at the bottom of the search page where "You may refine your search by." Select the dates and language you prefer, and the format option "Journal Article." At the top of the search form, select the number of records you would like to see (we recommend 100) and check the box to display "whole records." We recommend that you type "epilepsy" (or synonyms) into the "For these words:" box. Consider using the option "anywhere in record" to make your search as broad as possible. If you want to limit the search to only a particular field, such as the title of the journal, then select this option in the "Search in these fields" drop box. The following is what you can expect from this type of search:

- **Managing Patients Who Have Seizure Disorders: Dental and Medical Issues**

  Source: JADA. Journal of American Dental Association. 126(12): 1641-1647. December 1995.

  Summary: In this article, the authors address concerns that some dental professionals may have about treating patients with seizure disorders. The authors contend that increased knowledge about seizures and how to manage them may make dental professionals more comfortable. They review the various seizure types; discuss commonly used anticonvulsants and their side effects; and outline some special concerns dentists may have in providing care to these patients. 2 figures. 1 table. 18 references. (AA-M).

- **Influence of Epilepsy and Temporal Lobe Resection on Olfactory Function: Review Article**

  Source: Epilepsia. 36(6): 531-542. 1995.

  Summary: Olfactory auras, illusions or hallucinations of smells, accompany some cases of epilepsy. Several aspects of olfactory function, including sensitivity, also may be altered. This article describes the influence of epilepsy and temporal lobe surgery on olfactory function. The authors review the literature on these topics. They conclude that despite several studies, the prevalence of olfactory auras in epilepsy is unknown, with estimates ranging from less than 1 percent to more than 30 percent of the population with epilepsy. Epilepsy appears to cause a generalized decrease in olfactory functioning, although increased sensitivity may occur in some people with epilepsy at some time in the pre-seizure period. Other sensory modalities are also affected by the epileptic process and many of the olfactory deficits previously attributed to temporal lobe resection actually exist preoperatively. Taste and flavor confusion exists in the reporting of taste auras. Unpleasant auras are associated with hyperresponsiveness of neurons, which may explain why most epilepsy-related olfactory auras are described as bad smells. The authors also comment on interesting parallels between the effects of the neuroendocrine system on seizure activity and olfactory functioning. 2 figures. 125 references. (AA-M).

- **Children with Mental Retardation and Epilepsy: Demographics and General Concerns**

  Source: Journal of Dentistry for Children. 67(4): 268-274. July-August 2000.

  Contact: Available from American Society of Dentistry for Children. John Hancock Center, 875 Michigan Avenue, Suite 4040, Chicago, IL 60611-1901. (312) 943-1244.

  Summary: Providing dental care for children with mental retardation can be a challenge and can be complicated by multiple disabilities, family attitudes, and the unavailability of practitioners to provide care. This article reports on demographics and general concerns regarding the provision of dental care to children with mental retardation and epilepsy (the two more frequent types of major neurological impairments in childhood). The authors describe epilepsy, the drugs used to treat epilepsy, the prevalence of epilepsy, attitudes toward children with epileptic seizures, the prevalence of mental retardation, the existence of both conditions in the same child, and the dental practitioner's perspective. The authors offer an appendix in which they outline specific strategies for dental care of youngsters with epilepsy; a second appendix lists the prevalence rate of mental retardation by state (1993 figures). 3 tables. 40 references.

- **Effect of Epilepsy or Diabetes Mellitus on the Risk of Automobile Accidents**

  Source: New England Journal of Medicine. 324(1): 22-26. January 3, 1991.

  Summary: This article reports on a population-based retrospective cohort study of 30,420 subjects (16 to 90 years of age) with and without epilepsy or diabetes mellitus. Standardized rates of moving violations and accidents over a 4 year period (1985 through 1988) were compared in affected and unaffected cohorts. Standardized mishap ratios for subjects with diabetes were 1.14 for all moving violations and 1.32 for accidents; for subjects with epilepsy the ratios were 1.13 for moving violations and 1.33 for accidents. The authors conclude that drivers with epilepsy or diabetes mellitus have slightly increased risk of traffic accidents as compared with unaffected persons. The increases in risk observed in this study were generally smaller than those in previous

studies, and the authors believe that they are not great enough to warrant further restrictions on driving privileges. 6 tables. 13 references. (AA-M).

- **Recent Studies on Colonic Infections, Collagenous and Microscopic Colitis, Short-Chain Fatty Acids, Brown Bowel Syndrome, Abdominal Epilepsy, and Diabetic Diarrhea**

  Source: Current Opinion in Gastroenterology. 7(1): 42-45. February 1991.

  Summary: This article reviews selected articles from the literature over the past eighteen months on a variety of colonic disorders. Case reports of neutropenic colitis, Balantidium coli infestation, amebic colitis, tuberculous colitis, and Listeria infection are included. Eleven reports of collagenous and microscopic colitis are summarized. Two studies dealing with colonic concentrations of short-chain fatty acids are discussed. Other topics include brown bowel syndrome, abdominal epilepsy, asymptomatic ileocolitis, and diabetic diarrhea. 1 figure. 24 annotated references. (AA-M).

- **Developmental Language Disorders and Epilepsy**

  Source: Journal of Paediatrics and Child Health. 33(3): 277-280. June 1997.

  Contact: Available from Blackwell Science Pty Ltd. P.O. Box 378, Carlton, Victoria 3053, Australia. 61 3 9347 0300. Fax 61 3 9349 3016.

  Summary: This article reviews studies connecting developmental language disorders and epilepsy. The association of speech and language disorders with epilepsy is well known in children with acquired epileptic aphasia, involving such entities as Landau-Kleffner syndrome (LKS), continuous spike wave in slow wave sleep (CSWSS) epilepsy, and benign partial epilepsy with centro temporal spikes (BPECTS). The possible association between epilepsy and a subgroup of children with developmental dysphasia is reported less frequently. Lack of controlled prospective studies of sleep electroencephalograms (EEG), and the use of medication, in children with developmental dysphagia, may deny appropriate treatment strategies to children with severe developmental speech and language disorders. The authors recommend that before anti-epileptic medication is tried in individual children, limitations should be discussed with the parents: the treatment duration should be determined; goals should be set for continuation of therapy; pretreatment measures of speech and language should be carried out, including use of video records and standardized tests; the treatment should be at dosage levels used to control seizures; and there should be close monitoring for side effects. 1 table. 38 references.

- **Progressive Myoclonus Epilepsy in Young Adults With Neuropathologic Features of Alzheimer's Disease**

  Source: Neurology. 49: 1732-1733. December 1997.

  Summary: This journal article presents two case reports of progressive myoclonus epilepsy (PME) in young adults with neuropathologic features of Alzheimer's disease (AD). In both cases, the patients became symptomatic around 30 years of age, with rapidly progressing dementia and myoclonus. At autopsy, their brains showed histopathologic changes characteristic of AD. The authors conclude that AD should be considered in addition to possible Kufs' disease and myoclonic epilepsy with ragged red fibers when PME develops in young adults.

Federally Funded Research on Epilepsy

The U.S. Government supports a variety of research studies relating to epilepsy. These studies are tracked by the Office of Extramural Research at the National Institutes of Health.[2] CRISP (Computerized Retrieval of Information on Scientific Projects) is a searchable database of federally funded biomedical research projects conducted at universities, hospitals, and other institutions.

Search the CRISP Web site at **http://crisp.cit.nih.gov/crisp/crisp_query.generate_screen**. You will have the option to perform targeted searches by various criteria, including geography, date, and topics related to epilepsy.

For most of the studies, the agencies reporting into CRISP provide summaries or abstracts. As opposed to clinical trial research using patients, many federally funded studies use animals or simulated models to explore epilepsy. The following is typical of the type of information found when searching the CRISP database for epilepsy:

- **Project Title: 1,2,3-TRIAZOLINES: HIGHLY EFFECTIVE ANTIISCHEMIC AGENTS**

  Principal Investigator & Institution: Kadaba, Pankaja K.; K and K Biosciences, Inc. 2504 Century Ln Chadds Ford, Pa 19317

  Timing: Fiscal Year 2001; Project Start 15-SEP-2001; Project End 31-MAR-2002

  Summary: (provided by applicant): There is strong evidence that the 'excitotoxic' action resulting from the excessive accumulation of L-glutamate plays a prominent role in human **epilepsy** and brain ischemial stroke, leading to neuronal dysfunction and cell death. The triazolines (TRs). One group of novel anticonvulsants discovered in the principal investigator's laboratories, are very effective in the kindling and in the maximal electroshock seizure models of **epilepsy,** the best analogies to human partial seizures, where excitatory amino acids play an important role, and appear to work by impairing glutamate neurotransmission. Thus it is logical to expect that the anticonvulsant TRs may evince beneficial therapeutic potential in cerebral ischemia resulting from stroke. In extensive preliminary studies, the ability of seven TRs to reduce or prevent neuronal damage was assessed in the gerbil model of global ischemia and the MCAO rat model of focal ischemia Out of the seven TRs tested, five afforded protection well over 60 percent, with four of the TRs showing protective effect in the range of 77-96 percent. Testing was done at three doses and in all cases; the protective ability of the TRs was clearly dose dependent. Evaluation of locomotor activity tests indicated no undue toxicity. The most active TR showed significant protective effect in postischemic treatments in the MCAO rat model, up to 50 percent, at a dose of 30 mg/kg x 3, one at the beginning, then 1 hr and 2 hrs of reperfusion. The objectives of Phase I of this Fast Track proposal are to test eight other selected structural analogues and establish antiischemic activity in the TRs as a class. Initially the TRs will be tested in the gerbil model and the most promising compound will be tested further for its protective effects, in both pre- and post-treatment studies, in the MCAO rat model of focal ischemia, a clinically relevant model that mimics human stroke. All compounds will be assessed by behavioral and histopathological tests. Active compounds, including those from the preliminary tests, will be the subject of intense study in the MCAO rat

[2] Healthcare projects are funded by the National Institutes of Health (NIH), Substance Abuse and Mental Health Services (SAMHSA), Health Resources and Services Administration (HRSA), Food and Drug Administration (FDA), Centers for Disease Control and Prevention (CDCP), Agency for Healthcare Research and Quality (AHRQ), and Office of Assistant Secretary of Health (OASH).

model, in both pre- and post-treatments in Phase II. PROPOSED COMMERCIAL APPLICATION: Currently there is a definite need for clinically effective drugs in the treatment of cerebral ischemia/stroke that afflict more than a million Americans annually. The TR anticonvulsants to be evaluated in this proposal are lipid soluble and orally effective with good therapeutic indices and seem to act by impairing the excessive glutamate neurotransmission, the primary cause of neuronal cell death in **epilepsy** and stroke. Thus the TRs have good commercial potential as clinically effective drugs in the management of cerebral ischemia/stroke.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: 1H AND 31P MRSI FOR EPILEPSY LOCALIZATION**

  Principal Investigator & Institution: Laxer, Kenneth D.; Professor of Clinical Medicine and Neuro; Neurology; University of California San Francisco 500 Parnassus Ave San Francisco, Ca 94122

  Timing: Fiscal Year 2001; Project Start 01-MAY-1994; Project End 31-MAR-2004

  Summary: The long term goal of this application is to improve the outcome of seizure surgery by better presurgical localization of medically refractory **epilepsy** using a combination of neuroimaging techniques including magnetic resonance imaging (MRI), 1H and 31P MR spectroscopic imaging (MRSI), and 18F-PET. These techniques will be directed at three groups with medically refractory **epilepsy** who are being evaluated for seizure surgery (numbers for 5 years): 1)patients with medial temporal lobe **epilepsy** in whom MRI is non-concordant i.e., MRI shows no abnormality, or an abnormality contralateral to the EEG-defined seizure focus (NC-mTLE, n=75), 2) patients with non-lesional neocortical **epilepsy** (NE, n=100), and 3) children with Infantile Spasms (IS, n=100). NC-mTLE and NE patients frequently require invasive EEG recording, have less than a 50 percent probability of becoming seizure free with surgery, and are often not considered for surgery. Post-operative surgical outcome will be analyzed in relation to the pre-operative neuroimaging findings. Hypotheses: 1) NC-mTLE -Patients with medically refractory mTLE without MRI concordance, who have 1H and 31P MRSI measures concordant with the EEG localization (i.e., lobe and side), will have a significantly better post surgical outcome than patients without MRSI concordance. 2a) NE - NE patients without lesions on MRI, will have 1H and 31P MRSI concordant with the EEG localization (i.e., lobe and side), and this concordance will be greater than that provided by 18FDG-PET. 2b) NE - NE patients, who have 1H and 31P MRSI measures concordant with the EEG localization will have a significantly better post surgical outcome than patients without MRSI concordance. 3a) IS - Children with medically refractory Infantile Spasms will have 1H and 31P MRSI concordant with the seizure focus determined by a combination of two or more studies (VET, 18FDG-PET, and/or MRI) and this concordance will be greater than that provided by MRI or 18FDG-PET. 3b) IS - IS children, who have 1H and 31P MRSI concordant with the localization provided by the other clinical and imaging studies will have a significantly better post surgical outcome than patients without such concordance. These studies are expected to lead to improved surgical outcome, and to reduce unnecessary surgery, in patients with intractable **epilepsy.**

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: A MULTI-CENTER STUDY OF EPILEPSY SURGERY**

  Principal Investigator & Institution: Spencer, Susan S.; Professor; Neurology; Yale University 47 College Street, Suite 203 New Haven, Ct 065208047

Timing: Fiscal Year 2001; Project Start 04-APR-1996; Project End 31-MAY-2006

Summary: (Applicant's Abstract): Nearly one percent of the United States population has **epilepsy.** By some estimates more than 20% of those patients are inadequately treated despite a growing number of anti-epileptic medications. Resective surgery is increasingly used to treat this population, despite its high costs. Outcome with regard to seizures following **epilepsy** surgery has rarely been systematically or prospectively assessed in large samples, and quality-of-life, cognitive, neurologic, and psychiatric status following **epilepsy** surgery in the long or short-term are largely unexplored. Over the past 5 years we enrolled a 400 patient cohort in the first multi-center study of **epilepsy** surgery. Evaluation and treatment of these patients incorporated uniformity and technological advances, as well as reliable and validated baseline and follow-up measures of psychiatric status, cognitive function, quality-of-life, seizure severity and frequency, productive activities, and family dynamic. We propose to complete two-year follow-up on the full cohort, and extend follow-up to 5 years. We seek to define the occurrence and predictors of seizure remission, as well as improvements in quality-of-life, and stability or improvement in psychiatric, cognitive and neurologic status, based on factors in the preoperative profile and postoperative observations. We also propose to define relapse and continued remission off all medications and the predictors for successful medications withdrawal, an important yet unstudied aspect of **epilepsy** surgery. Our primary goals are: 1. to study the probability of achieving 1, 2, and 5 year seizure remission after **epilepsy** surgery, and the probability of relapse after remission over a total 5 year follow-up, as well as the prognostic significance of specified preoperative and postoperative factors; 2. to determine the probability of relapse and prediction of relapse in patients who discontinue medications after 2 year remission, and prognostic factors for successful outcome; 3. to assess self reported quality-of-life and employment status yearly for 5 years after resective **epilepsy** surgery, and to determine the magnitude and time course of change, and the extent to which seizure response and medication changes are associated with alterations in self-perceived health and employment; 4. to identify the nature and magnitude of changes in cognitive and neurologic status after resective **epilepsy** surgery, the factors that predict changes, and their resilience and functional impact over 5 years of follow-up; and 5. to prospectively assess changes in behavior and psychiatric profile yearly for 5 years and examine predictive factors in long-term prognosis of depression, anxiety and other psychiatric diagnoses, as well as family dynamics. The proposed study represents a unique multi-center effort that will result in the largest systematic study of **epilepsy** surgery to date, and will provide definitive answers to key questions regarding the outcomes of **epilepsy** surgery, their measurement, and their prediction in a contemporary patient population.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: ADRENERGIC MODULATION OF SEIZURES AND NEURODEGENERATION**

  Principal Investigator & Institution: Carr, Patrick A.; University of North Dakota 264 Centennial Drive Grand Forks, Nd 58202

  Timing: Fiscal Year 2002; Project Start 15-SEP-2002; Project End 31-AUG-2007

  Summary: (provided by applicant): The broad, long-term objective of this research is to find a better therapeutic strategy for preventing neurodegeneration (neuronal damage and cell death) associated with recurring uncontrolled seizures or **epilepsy.** The immediate goal of this project is to characterize the effects of alpha-1 adrenergic receptor (alpha1AR) activation on interneurons. Many of the currently employed antiepileptic

drugs (AEDs) enhance gamma- aminobutyric acid (GABA)-mediated inhibition. The major source of GABA, the predominant inhibitory neurotransmitter in the brain, is a small population of inhibitory cells known as interneurons. Many of the traditional AEDs (e.g., phenobarbital) do not target interneurons, but rather potentiate actions of GABA at the level of the GABAA receptor. Several of the new, more effective second generation AEDs (e.g., gabapentin) appear to act by increasing the amount of GABA available, either by enhancing its synthesis or by inhibiting its catabolism or reuptake. However, none of these AEDs directly activate interneurons. Several lines of evidence indicate that alpha1AR activation is potently antiepileptogenic. The mechanism underlying this effect is unknown. Preliminary studies suggest that alpha1AR activation excites a subpopulation of interneurons leading to enhanced GABA release. This finding may be very important and suggests that selective alpha1AR activation of inhibitory GABAergic interneurons may provide a novel therapeutic strategy for the prophylaxis of seizures and neurodegeneration. This study will test this hypothesis. Using a cross-disciplinary approach combining electrophysiological, molecular biological, and neuroimaging techniques, this project will address these specific aims: 1) characterize the effects of alpha1AR activation on discrete populations of interneurons; 2) identify the particular subtype of alpha1AR mediating these responses; 3) ascertain the connectivity, neurochemistry and synaptological profile of alpha1AR-activated interneurons; and 4) examine the functional consequences of alpha1AR activation on neuronal excitability. The information derived from this research not only will yield important insights into the anatomy, physiology and pharmacology of interneurons, but also may lead to the development of a new class of AEDs with improved neuroprotective actions and enhanced efficacy for treating **epilepsy.**

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: AN IMPLANTABLE DEVICE TO PREDICT AND PREVENT SEIZURES**

  Principal Investigator & Institution: Dichter, Marc A.; Professor; Neurology; University of Pennsylvania 3451 Walnut Street Philadelphia, Pa 19104

  Timing: Fiscal Year 2001; Project Start 15-AUG-2001; Project End 31-JUL-2006

  Summary: Epilepsy affects 50 million people worldwide, and 2.5 million in the United States alone. Fully 25 percent of those with recurrent seizures cannot be controlled by current medical or surgical treatment, and must resort to high doses of sedating medications or experimental therapy. Even when seizures are controlled, patients bear a significant burden of neurological and medication side effects. We propose to assemble an ensemble of accomplished investigators from the University of Pennsylvania, Georgia Institute of Technology, Children's Hospital of Philadelphia and IntelliMedix, a small start-up company through the GIT and Penn, in an intensive five to ten year effort to create a novel therapy for refractory epilepsy: an implantable closed loop system capable of predicting epileptic seizures prior to electrical and behavioral onset and triggering intervention to abort them before clinical expression. This diverse group of investigators represents multiple disciplines and areas of expertise including bioengineering, computer science, computational modeling of neuronal networks, image processing, clinical adult and pediatric **epilepsy,** cellular and molecular neuroscience, neurophysiology and neuropharmacology. The work will have three major thrusts: (1) Seizure Prediction: Developing and refining seizure prediction algorithms derived from data obtained from implanted biosensors in adults, children and in animal models of human **epilepsy,** capable of predicting seizures hours to minutes prior to electrical and clinical onset, (2) Mechanisms of ictogenesis: Unraveling

the cellular, molecular, neurophysiologic and neuronal network mechanisms underlying the observed signal changes identified by these algorithms through in-vitro and in-vivo experiments in animals, recordings in human candidates for **epilepsy** surgery, and modeling these findings via computer simulations in order to refine predictive and intervention strategies, (3) Therapeutics: Developing strategies aimed at specific points in the "ictogenic" process, as discovered above, consisting of electrophysiological and pharmacological interventions to disrupt the cascade of events which lead to seizures, in ways which do not interfere with normal brain function. This work will directly give rise to commercially viable intellectual property including: implantable biosensors, miniaturized biocompatible electrical stimulation and drug infusion hardware, stimulation paradigms, customized pharmacologic agents, customized software/hardware interfaces for signal acquisition, processing and synchronization with algorithms for driving therapeutic interventions. It is hoped that a closed loop seizure prediction and prevention device will be implementable in a 5-10 year period and will significantly improve the quality of life of individuals with **epilepsy.**

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: ANALYSIS & CONTROL OF NONSYNAPTIC EPILEPTIFORM ACTIVITY**

  Principal Investigator & Institution: Durand, Dominique M.; Professor; Biomedical Engineering; Case Western Reserve University 10900 Euclid Ave Cleveland, Oh 44106

  Timing: Fiscal Year 2001; Project Start 04-SEP-2001; Project End 31-AUG-2005

  Summary: (provided by applicant): **Epilepsy** is characterized by the abnormal synchronization of large numbers of neurons. The synchronization and propagation of epileptic seizures are thought to rely on synaptic transmission. However, non-synaptic mechanisms such as neuronal swelling, electric field effects, potassium diffusion, gap junctions and glial cell function also contribute to the generation and spread of epileptiform activity. Non-synaptic **epilepsy** is generated by lowering calcium in the extracellular space thereby eliminating synaptic transmission. As a result, the clinical relevance of non-synaptic mechanisms has been questioned. We have recently generated novel models of non-synaptic activity in the presence of normal calcium and normal synaptic transmission. We propose to analyze the role of non-synaptic mechanisms in neuronal synchronization in order to understand and potentially develop novel therapies to prevent abnormal neural activity. We have recently shown that the frequency, amplitude and duration of non-synaptic epileptiform events can be controlled independently suggesting that different mechanisms are responsible. In particular, preliminary experiments show that gap junctions are not responsible for the propagation of non-synaptic events generated in zero-calcium medium, but that potassium diffusion (potentially mediated by the activity of glial cells) plays a crucial role. The goal of this proposal is to analyze and control non-synaptic epileptiform activity. Specifically, we propose to 1) determine the common mechanisms underlying three models of non-synaptic **epilepsy,** 2) establish the conditions sufficient for the generation of non-synaptic epileptogenesis, 3) analyze the mechanisms underlying the propagation of non-synaptic epileptiform activity, 4) develop a computer model of non-synaptic propagation to test hypotheses not directly testable by experimentation, and 5) develop methods for controlling epileptiform activity. Multi-disciplinary experimental approaches such as computer simulation and fluorescence imaging will be combined with pharmacology and in-vitro slice electrophysiology to achieve these goals. Current therapeutic agents are not capable of controlling seizure activity in 25 percent of all epileptic patients. The results of our studies should provide valuable insight into

mechanisms underlying epileptogenesis as well as new tools for the control and suppression of epileptic seizures.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: AP3 IN NEUROLOGICAL DISORDERS**

  Principal Investigator & Institution: Burmeister, Margit M.; Associate Professor of Genetics in Psych; Psychiatry; University of Michigan at Ann Arbor 3003 South State, Room 1040 Ann Arbor, Mi 481091274

  Timing: Fiscal Year 2001; Project Start 01-APR-1994; Project End 31-MAY-2003

  Summary: (Adapted from investigator's abstract) The P.I. has recently identified the mutant gene in mocha mice as the delta subunit of the adapter-related complex AP-3. They have also found that the ZnT-3 transporter is not transported correctly to synaptic vesicles, resulting in a lack of zinc in cortex and hippocampus. In this application, the P.I. proposes to genetically map all subunits of the AP-3 complex to determine if other mutants with a similar phenotype are caused by mutations in these AP-3 subunit genes, and test for interaction between mocha locus and pale-ear, the mouse homologue of HPS, the gene most commonly mutated in human Hermansky-Pudlak syndrome (HPS). They will focus on the neurological phenotype of mocha, and determine if mocha may be a mouse model for **epilepsy,** ADHD, autism or other neurological disorders. Mocha mutant mice have an HPS-like phenotype as well as neurological deficits (seizures, hyperactivity, spike-wave discharges, a hypersynchronized electrocortigram, increased auditory gating). In contrast, pearl mice have HPS but none of these neurological phenotypes, which they postulate is because pearl mice miss the non-neuronal form of the beta subunit, Ap3b1, but not the neuronal form of AP-3 beta, Ap3b2, whereas the delta subunit mutated in mocha is ubiquitously expressed. Dr. Burmeister postulates that inactivation of the neuronal form of AP-3 beta will result in a mouse with the neurological defects of mocha without the HPS-like phenotypes and higher fertility and viability than mocha mice. They will prepare a LoxP construct to knock out Ap3b2 in such a way that they can not only generate a complete knockout in ES cells, but also, by mating to mice in which Cre is under region-specific promoters, mice in which the AP-3 complex is missing only in specific brain regions. The P.I. will characterize the behavior of mocha, mh-2J, ZnT-3 deficient mice as well as the proposed knockout mice for the nature of hyperactivity (is it generally more active, has increased startle, or stereotypic behavior), seizure propensity, anxiety, learning and memory and electrophysiological parameters. To determine if AP3B2 plays a role in human neurological disorders, Dr. Burmeister will isolate and characterize the human AP3B2 gene and search for mutations or polymorphisms that may be present in the normal population or in patients. Given the mocha phenotype, it is anticipated that this gene may be involved in human neurological disorders characterized by increased seizure frequency and hyperactivity (e.g. autism, OCD, ADHD and epilepsy). Such polymorphisms will be made available for the scientific community to test as a candidate gene for other neurological or psychiatric disorders if justified by the results of the behavior tests.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: AXONAL SPROUTING AND EPILEPSY AFTER TRAUMATIC CNS INJURY**

  Principal Investigator & Institution: Thompson, Scott M.; Associate Professor; Physiology; University of Maryland Balt Prof School Baltimore, Md 21201

  Timing: Fiscal Year 2002; Project Start 01-APR-2002; Project End 31-MAR-2006

Summary: The Problem: **Epilepsy** is a common consequence of traumatic head injury. Its cause is unknown. The Hypotheses: 1) The release of neurotrophins after traumatic CNS injury triggers axonal sprouting by pyramidal cells. 2) The glutamate sensitivity and excitability of postsynaptic target cells increase as a consequence of partial denervation. 3) Injury-induced presynaptic axonal sprouting and increased postsynaptic excitability combine synergistically to cause posttraumatic **epilepsy.** The Model: After Schaffer collateral transection, CA3 cells in hippocampal slice cultures sprout new axon collaterals and CA1 cells become supersensitive to glutamate. These phenomena may account for the lesion-induced hyperexcitability. This model provides an experimentally tractable and informative approach for studying pre- and postsynaptic mechanisms of posttraumatic **epilepsy.** The genesis of hyperexcitability after axonal injury in this model will therefore be investigated using neuroanatomical, cell biological, and electrophysiological techniques. AIM 1: Determine the presynaptic mechanisms underlying injury- induced hyperexcitability. TrkB immunoadhesins, biolistic transfection with full length and dominant negative neurotrophin receptor constructs, and cultures derived from trk receptor knockout mice will be used to test the hypothesis that activation of trk receptors is required for injury-induced axonal sprouting. The hypothesis predicts that lesion-induced sprouting will not occur in the presence of trkB immunoadhesin, in cells transfected with dominant negative irk receptors or in cultures made from trk receptor knock-out mice. Lack of axonal sprouting is predicted to eliminate injury-induced hyperexcitability. AIM 2: Determine the postsynaptic mechanisms underlying injury- induced hyperexcitability. Using whole-cell voltage-clamp and laser microphotolysis of caged neurotransmitters targeted to individual distal dendrites, we will test the hypotheses that glutamate supersensitivity and intrinsic hyperexcitability occur in CA1 cells after denervation. The hypothesis predicts that changes in the levels of expression of neurotransmitter receptors and/or changes in intrinsic voltage-dependent ionic conductances underlie the potentiation of dendritic glutamate responses observed previously after Schaffer collateral transection. The Goal: to better understand the causes of posttraumatic **epilepsy** and, ultimately, to offer new and improved prophylactic therapeutic strategies to cure this disease.

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- **Project Title: AXONAL SPROUTING OF GABAERGIC NEURONS IN EPILEPTOGENESIS**

  Principal Investigator & Institution: Bausch, Suzanne B.; Henry M. Jackson Fdn for the Adv Mil/Med Rockville, Md 20852

  Timing: Fiscal Year 2002; Project Start 01-FEB-2002; Project End 31-JAN-2005

  Summary: Epileptogenesis, the process by which a normal brain become chronically prone to seizures, is poorly understood. Many CNS insults (i.e. stroke, trauma, neurodegenerative disease) can induce epileptogenesis, yet no therapies currently exist to arrest this process. Although neuronal reorganization and alterations in brain physiology are associated with epileptogenesis, the functional consequences and relative importance of these changes to epileptogenesis, the functional consequences and relative importance of these changes to epileptogenesis and seizure genesis remain unknown. Many of the molecular, cellular and genetic mechanisms underlying neuronal reorganization and physiological alterations are likewise unknown. This information is crucial in providing a rational basis for the development of new therapies designed to disrupt epileptogenesis. Our hypothesis are that during epileptogenesis 1) GABAergic neurons undergo seizure- induced axonal sprouting, 2) the incidence of reciprocal granule cell- GABAergic interneuron synapses is increased, but individual mossy fiber

synaptic inputs onto interneurons are weaker or less reliable and 3) different neuronal populations express unique gene expression patterns for axon guidance molecules associated with synaptic rearrangements. We will test these hypothesis at multiple time points during epileptogenesis using two different models of temporal lobe **epilepsy.** A combination of anatomical, electrophysiological, molecular biological and genetic approaches will be used. Results from these experiments will document morphological changes in GABAergic interneurons during epileptogenesis, identify and physiologically characterize novel aberrant excitatory inputs onto GABAergic interneurons in the epileptic dentate gyrus, and define genetic programs that encode the critical guidance cues regulating the synaptic reorganization associated with **epilepsy.** Results from the proposed study will contribute to a more detailed understanding of the regulation of the synaptic circuitry involved in **epilepsy,** memory and information processing in the hippocampus and provide insight for development of novel therapies to arrest epileptogenesis before chronic seizures develop.

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- **Project Title: BIOIMAGING AND INTERVENTION IN NEOCORTICAL EPILEPSY**

  Principal Investigator & Institution: Duncan, James S.; Diagnostic Radiology; Yale University 47 College Street, Suite 203 New Haven, Ct 065208047

  Timing: Fiscal Year 2002; Project Start 15-APR-2002; Project End 31-MAR-2007

  Summary: Description (provided by application): Magnetic resonance functional and spectroscopic imaging (fMRI, MRS) of the brain provides tremendous opportunities in the study and treatment of **epilepsy.** In neocortical **epilepsy,** where the epileptogenic region is highly variable in size, structure and location, deeper insight into the biochemical and functional characteristics of the region and surrounding tissue may provide critical data to assist the neurosurgeon and neurologist in localization and treatment. To fully utilize the multiple forms of information (MR and EEG), these data must be transformed into a common space and integrated into the intraoperative environment. We will develop high resolution MRS and fMRI at 4T and advanced analysis and integration methods to better define the epileptogenic tissue and surrounding regions, and enhance our understanding of the biochemical mechanisms underlying the dysfunction in neocortical **epilepsy.** We will validate these measurements against the gold standard of intracranial electrical recording. These goals will be achieved in this bioengineering research partnership (BRP) by bringing together six partners from 3 academic institutions (Yale (lead institution), Albert Einstein and the Univ. of Minnesota) and 1 industrial partner (Medtronics SNT) to carry out four integrated programs of scientific investigation and bioengineering development in the area of bioimaging and intervention: 1) development of high resolution fMRI and MRS at 4T for the study of **epilepsy;** 2) investigation with MRS of the relationship between neuronal damage or loss through the measurement of N-acetylaspartate (NAA), alterations in neurotransmitter metabolism through the measurement of gamma amino butyric acid (GABA) and glutamate, and abnormalities in electrical activity in the epileptogenic region and surrounding tissue; 3) investigation of the relationship between fMRI activation amplitude and the cognitive task, underlying cortical structure, cortical metabolic state, and physiology, and the impact of **epilepsy** on these factors; 4) development of integration methodologies for fusing multimodal structural and functional (image- and electrode-derived) information for the study and treatment of **epilepsy.** We anticipate that by developing and integrating these high resolution functional and metabolic images of neocortical **epilepsy,** we will improve our understanding and treatment of this difficult disorder. The first year's effort will include

high resolution coil and integrated software platform design and development, as well as the acquisition of normal control studies. In years 2 through 5, the coils will be incorporated into the MR imaging platforms, the software platform will be fully developed and hypotheses related to the biochemical makeup of neocortical epileptogenic tissue and its relation to brain function will be evaluated.

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- **Project Title: CASPASES MEDIATE SEIZURE-INDUCED BRAIN INJURY**

  Principal Investigator & Institution: Henshall, David C.; Emanuel Hospital and Health Center 2801 N Gantenbein Ave Portland, or 97227

  Timing: Fiscal Year 2001; Project Start 01-AUG-2001; Project End 31-JUL-2005

  Summary: Progressive hippocampal atrophy has been demonstrated in humans with **epilepsy.** Such SEIZURE-induced neurodegeneration may be under the control of the CASPASE family of cell death regulating enzymes, as our recent studies in brains of patients with intractable **epilepsy** showed the presence and activation of the programmed cell death/apoptosis pathway. INITIATOR caspases begin the cell death process: following activation of surface- expressed death receptors - the EXTRINSIC pathway, or following mitochondrion-based events within the cell - the INTRINSIC pathway. Subsequently these caspases activate downstream EFFECTOR caspases, which carry out the execution and disassembly of the cell. Intervention in this cell death cascade has considerable implications for the therapeutic treatment of neurodegenerative diseases to which **epilepsy** may now be added. Therefore the broad, long-term goals of this proposal are to characterize the contribution of the caspase family of cell death-controlling enzymes in mediating seizure-induced brain injury. They hypotheses to be tested are (A) Neuronal death occurs following seizures and is initiated by caspases 2, 8 and/or 10 of the extrinsic death receptor pathway. (B) Caspase 2, 8 and/or 10 activation requires recruitment to death receptors by adaptor proteins in response to death ligands. (C) Activation of the intrinsic, mitochondrion-dependent caspase-9 pathway is co- dependent on the death receptor pathway via the cytochrome c releasing factor Bid. (D) Novel effector caspases 6 and 7 are activated by seizures via these extrinsic and intrinsic pathways and contribute to neuronal death. The specific aims are: 1) Characterize the expression, processing and consequences of activation of the extrinsic death-signaling pathway caspases 2, 8 and 10 using an in vivo rat model of brief limbic seizures. 2) Characterize the expression and functional interaction of death receptors with their adaptor protein(s) in the signal transduction and recruitment of caspases 2, 8 and 10 following seizures. 3) Characterize the expression, processing and consequences of activation of the intrinsic caspase-9-dependent pathway in seizure-induced brain injury. 4) Characterize the activation of the novel death effector caspases 6 and 7 in response to the extrinsic and/or intrinsic initiator pathways following seizures. 5) Characterize the involvement of extrinsic, intrinsic and death effector caspases mediating apoptosis induced by seizure-like activity in neuronal cultures in vitro. Elucidation of the molecular control of seizure-induced cell death will further our understanding of brain injury processes and take a significant step toward therapeutic approaches to reduce brain injury in **epilepsy.**

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- **Project Title: CENTRAL NICOTINIC RECEPTORS AND EPILEPTIC SEIZURES**

  Principal Investigator & Institution: Cohen, Bruce N.; Research Associate; None; California Institute of Technology Mail Code 201-15 Pasadena, Ca 91125

Timing: Fiscal Year 2001; Project Start 04-SEP-2001; Project End 31-AUG-2005

Summary: Genetic defects cause 20-40 percent of all epilepsies. Several types of inherited **epilepsy** appear to be linked to nicotinic receptors. However, autosomal dominant nocturnal frontal lobe **epilepsy** (ADNFLE) is the only one that has been linked to specific nicotinic mutations -alpha4(S248F), alpha4(777ins3), and alpha4(S252L). These mutations produce brief, repetitive seizures that occur primarily during phase 2 sleep. The mechanism of seizure generation has not been established. We hypothesize that a reduction in Ca2+-induced potentiation of the acetylcholine (ACH) response causes ADNFLE seizures. Our preliminary data show that all three presently identified ADNFLE mutations reduce Ca2+ potentiation of the ACH response. However, previous studies show that the alpha4(S248F) mutation also reduces the Ca2+ permeability of the receptor relative to Na+ (Pca/PNa) and, that the alpha4(S248F) and alpha4(777ins3) mutations enhance ACh-induced receptor desensitization. Aim 1 is to determine whether reduced Ca2+ potentiation is the only common functional effect of the ADNFLE mutations. We will express rat versions (S252F, +L264, S256L) of the human ADNFLE mutations with wild-type (WT) rat beta2 subunits in Xenopus oocytes and examine their effects on desensitization, surface expression, receptor turnover, and choline potentiation of the ACH response. Aim 2 is to determine whether all three ADNFLE mutations reduce the Pca/PNa and Ca2+ influx through the receptors. Aim 3 is to demonstrate that the ADNFLE mutations reduce Ca2+ potentiation by enhancing Ca2+ block of the receptor rather than by reducing Ca2+ potentiation per se. Aim 4 is to characterize the mechanism of mutant-induced reductions in Ca2+ potentiation at the single-channel level. Our results should elucidate the connection between central nicotinic receptors and epileptic seizures.

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- **Project Title: CHILDHOOD ABSENCE EPILEPSY: COORDINATING CENTER**

  Principal Investigator & Institution: Cnaan, Avital; Associate Professor of Biostatistics; Children's Hospital of Philadelphia 34Th St and Civic Ctr Blvd Philadelphia, Pa 19104

  Timing: Fiscal Year 2003; Project Start 30-SEP-2003; Project End 31-MAY-2008

  Summary: (provided by the applicant): Treatment for Childhood Absence **Epilepsy** (CAE) is largely empiric. Although there are three efficacious antiepileptic drugs (AEDs) - ethosuximide (ETX), lamotrigine (LTG), valproic acid (VPA) - each has variable success in seizure control, as well as treatment-limiting toxicities. This project is being resubmitted as two linked R01 applications. The clinical proposal, "Childhood Absence **Epilepsy** - Rx, PK/PK, Genetics," (PI: T. Glauser, Co-PI: P. Adamson) is being resubmitted by the Cincinnati Children's Hospital. The objectives of the clinical trial are twofold: a) identify the optimal initial AED in terms of seizure control and lowest toxicity incidence; and b) to determine the clinical, pharmacokinetic and pharmacogenetic factors underlying the inter-individual variation in AED response and toxicity. This linked R01 proposal will establish the Childhood Absence **Epilepsy** Coordinating Center [CHAECC] at The Children's Hospital of Philadelphia to support this broad, integrated plan to study CAE. A strong and efficient coordinating center is needed in a project of this magnitude and complexity to ensure that the scientific goals are achieved in a timely manner and to a high standard of scientific excellence and data integrity as well as subject safety. The Children's Hospital of Philadelphia (CHOP) has established a highly experienced team to provide this coordinating center function. The aims of the CHAECC are to provide: 1) operational support to implement the protocol; 2) data base and data management for the protocol and the Core's data; 3) biostatistical analyses of the project aims. To meet these goals, the CHAECC will perform start-up

activities to implement the project, coordinate all communication activities, oversee adherence to Good Clinical Practice and HIPPA guidelines in protocol implementation, and will work closely with the Scientific Leadership of the study. The CHAECC will develop procedures for data collection, transference, and storage in a secure relational database. The CHAECC will coordinate receipt of video EEG's by Core readers and meetings to achieve consensus in interpretations. It will conduct all statistical analyses and support preparation of reports, manuscripts and presentations.

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- **Project Title: CHRONOBIOLOGY OF PARTIAL EPILEPSY**

  Principal Investigator & Institution: Quigg, Mark S.; Assistant Professor; Neurology; University of Virginia Charlottesville Box 400195 Charlottesville, Va 22904

  Timing: Fiscal Year 2001; Project Start 30-SEP-1997; Project End 31-MAY-2003

  Summary: (provided by applicant): Mesial temporal lobe **epilepsy** (MTLE), the most common partial **epilepsy,** accounts for the majority of patients with uncontrolled seizures. Seizures in MTLE do not strike randomly but occur in daily patterns. Possible influences on the timing of seizures include those factors that underlie circadian oscillation and that facilitate or inhibit seizures. Influences provided by the hypothalamicpituitaryadrenal axis (HPAA) are logical candidates to modulate seizures and will be the focus of the proposed experiments. This proposal examines the temporal distribution of spontaneous, limbic seizures in a unique animal model of partial epileps~ that shares clinical, electrographic, histological, and timing similarities with MTLE. The specific aim of this proposal is to evaluate the role of endogenous rhythmicity of the HPAA in the circadian modulation of experimental limbic **epilepsy.** Hypothesis 1. Rhythmicity of the HPAA is intact in experimental **epilepsy.** Hypothesis 2. Corticosterone releasing hormone (CRH) is differentially affected within the hypothalamus and limbic system by lesions at different levels of the clockHPAA system. Our data suggests that circadian mechanisms continue to function in the epileptic rat and that neuronal density in regions important in HPAA regulation is normal. We will evaluate whether CRH expression remains rhythmic in intact animals as well as in animals that have lesions of the clock or of the HPAA. Hypothesis 3. The normal variations of CRH and corticosterone are necessary for circadian recurrence of limbic seizures. We predict that alterations of inputs into the HPAA will cause changes in the circadian distribution of seizures. Previous results show that seizures occur in an endogenously mediated circadian rhythm. In summary, these studies will provide insight into the chronoblological factors that facilitate partial seizure expression and may provide new perspectives into treatments for poorly controlled partial **epilepsy.**

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- **Project Title: CLINICAL RESEARCH PROGRAM FOR THE PARTIAL EPILEPSIES**

  Principal Investigator & Institution: Engel, Jerome J.; Professor; Neurology; University of California Los Angeles 10920 Wilshire Blvd., Suite 1200 Los Angeles, Ca 90024

  Timing: Fiscal Year 2001; Project Start 01-JAN-1985; Project End 31-AUG-2005

  Summary: The UCLA clinical neurophysiology program project (CNP) is composed of tightly-coordinated, interactive, multi-disciplinary investigations into the fundamental mechanisms of human temporal lobe **epilepsy** by the collaborative efforts of a team for clinical and basic neuroscientists who have been working together for a number of years. The CNP is currently in its 38th year of NIH funding, and has continued to take advantage of the unique opportunities offered by an **epilepsy** surgery facility to carry

out invasive research on patients with **epilepsy.** Emphasis was placed initially on clinical research, but by 1981 the program project became devoted entirely to basic research on normal and abnormal function of the human temporal lobe. Beginning with our last renewal, we further narrowed our focus to investigate only epileptic mechanisms of the hippocampus, particularly hippocampal sclerosis, and also began to include experimental animal models of human temporal lobe **epilepsy.** With this application, all subprojects integrate studies of temporal lobe **epilepsy** in patients, with parallel studies in the intra-hippocampal kainate rat model, which morphologically, electrophysiologically, and behaviorally resembles human mesial temporal lobe **epilepsy** with hippocampal sclerosis. Experimental protocols include in vivo electrophysiology and microdialysis, as ell as in vitro neurochemistry and molecular microanatomy, molecular and cellular physiology, and local circuit physiology, in patients and animals, with a particular emphasis on elucidating the role of the dentate gyrus in the epileptogenic properties of sclerotic hippocampus. We propose three subjects to investigate: i) molecular alterations in glutamate receptors on interneurons and their functional correlates; ii) changes in cellular excitability resulting from altered intracellular neurochemistry, neurotransmitter receptor function, and network characteristics; and iii) the neuroanatomical and neurochemical substrates of unique interictal and ictal epileptiform electrophysiological events recorded from the intact brain. We anticipate that elucidation of fundamental mechanisms underlying epileptic abnormalities of mesial temporal lobe **epilepsy,** the most common, and most refractory, form of human **epilepsy,** will ultimately result in new approaches to diagnosis, therapy and prevention of **epilepsy,** and its adverse biological consequences.

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- **Project Title: CONSEQUENCES OF PROLONGED FEBRILE SEIZURES IN CHILDHOOD**

  Principal Investigator & Institution: Shinnar, Shlomo; Professor; Montefiore Medical Center (Bronx, Ny) Bronx, Ny 104672490

  Timing: Fiscal Year 2003; Project Start 01-FEB-2003; Project End 31-JAN-2008

  Summary: (provided by the applicant): Temporal Lobe **Epilepsy** (TLE) is often associated with Mesial Temporal Sclerosis (MTS). The relationship between Febrile Seizures (FSs) and MTS remains controversial. Retrospective data suggest that prolonged FSs cause MTS, but epidemiological studies have not found this association. Recent data from MRIs performed immediately after FSs provide preliminary evidence that very prolonged FSs (i.e. febrile Status Epilepticus (SE)) sometimes produce acute hippocampal injury that evolves into MTS. Identification of children at high risk to develop MTS is necessary prior to designing interventions aimed at prevention. This study will examine the consequences of febrile SE, and clarify the relationship between febrile SE, MTS, and subsequent **epilepsy** and cognitive impairment. Short-term consequences will be examined using a cohort of 200 children with febrile SE, who will be recruited at 5 centers. All children will have MRIs within 72 hours of their SE and at one year, as well as viral studies, psychological testing, EEGs and clinical follow-up. Intermediate term outcomes (5-9 years) will be ascertained using a cohort of 40 children recruited between 1995 and 200, all of whom had MRIs within 72 hours of the episode of febrile SE. They will have a follow-up MRI, EEG and psychological testing >5 years later. Long-term (10-20 years) outcomes will be examined using an established epidemiologic cohort of 163 children with febrile SE, prospectively identified between 1984 and 1996. These children will receive an MRI, EEG and psychological testing >10 years later. In those who develop **epilepsy,** we will characterize seizure types and

epilepsy syndromes, and correlate them with the presence or absence of MTS. The following hypotheses will be tested: 1) Hippocampal T2 signal and/or volume abnormalities will be seen on 30-40% of acute MRIs. The occurrence and severity of these abnormalities will correlate with total seizure duration and seizure lateralization, the presence of pre-existing brain abnormalities and febrile SE in the context of human herpes virus 6 or 7 infection; 2) The severity of acute MRI hippocampal abnormalities will predict subsequent MTS; 3) Children developing TLE will have MRI evidence of MTS.; 4) Subjects with MTS will have impaired memory, whether or not they have **epilepsy.**

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- **Project Title: CONTRIBUTIONS OF MEG TO THE SURGICAL MGMT OF EPILEPSY**

  Principal Investigator & Institution: Papanicolaou, Andrew C.; Professor and Director; Neurosurgery; University of Texas Hlth Sci Ctr Houston Box 20036 Houston, Tx 77225

  Timing: Fiscal Year 2001; Project Start 15-FEB-2000; Project End 31-DEC-2003

  Summary: (Verbatim from the Applicant's Abstract) The purpose of this project is to evaluate the contributions of Magnetoencephalography (MEG) to the surgical management of **epilepsy.** Specifically, we propose the following: First, to estimate the relative accuracy of MEG, as compared to that of surface and invasive electrophysiology, in identifying epileptogenic zones to be resected in patients with focal **epilepsy.** Second, to explore the possibility that identification of epileptogenic zones based on MEG data combined with data from other standard non-invasive diagnostic procedures and data from the Wada procedure may, in some cases, be sufficiently accurate to obviate the need for invasive electrophysiology. In addition, we propose to examine whether judgements of differential hemispheric involvement in language and memory derived from MEG data concur with those routinely derived from Wada procedure. Finally, incidental to addressing the above main questions, we will also address the question as to whether MEG influences the planning of invasive electrophysiological procedures and we will explore alternative ways of improving its diagnostic accuracy by considering alternative, not yet standardized modes of MEG data collection and analysis.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: CORTICAL EXCITABILITY AFTER TRAUMATIC BRAIN INJURY**

  Principal Investigator & Institution: Golarai, Golijeh; Neurosciences; University of New Mexico Albuquerque Controller's Office Albuquerque, Nm 87131

  Timing: Fiscal Year 2002; Project Start 01-APR-1999; Project End 31-MAR-2004

  Summary: (Applicant's abstract) Traumatic brain injury (TBI) leads to severe and lasting disabilities in sensorimotor and cognitive functions in 30,000 to 50,000 people in the United States each year. Approximately one third of individuals with serious head injuries eventually develop **epilepsy.** As TBI largely afflicts young people, health care and lost income are more costly than for stroke or degenerative diseases that typically affect the elderly. Clearly, interventions to prevent **epilepsy,** while promoting recovery from primary deficits after TBI, would be of great social value. Accordingly, this proposal examines the development of epileptogenic cellular physiology in rat sensorimotor cortex after a controlled injury, using a combination of extra-and intracellular electrophysiolgy, voltage- and calcium imaging, and histological methods. The experiments will also include an examination of the neuromodulatory role of

noradrenaline (NA) after TBI for two reasons. First, NA plays a complex role in both suppressing and promoting epileptogenesis. Second, NA with physical therapy (NA/PT) is the only pharmacotherapy that has enhanced functional recovery in double-blind studies of patients with well-established brain injury. This proposal represents a synthesis of my ongoing interest in basic mechanisms of **epilepsy** (which I have explored in hippocampus) and my career goal of expanding my area of research to include the neocortex, intracellular electro-and calcium physiology, and pathophysiology of head trauma. This project, including the mentorship of J.A. Connor and the collaboration of D.M. Feeney and R.C. S. Lin, will allow me to establish myself in these new areas, wile drawing on my experience with the kindling and kainate models of **epilepsy,** with various histological methods, with electrophysiolgy in vivo, and with the voltage-imaging techniques that I have learned with J.A. Connor. I will work with three senior scientists who have made major contributions to the fields of neuronal calcium and electrophysiology (Connor), TBI and NA/PT (Feeney) and anatomical correlates of neuopathophysiology (Lin). This rare interdisciplinary research opportunity will allow me to contribute to the understanding of post-traumatic **epilepsy** while increasing my breadth and depth as a scientist.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: CORTICAL LOCALIZATION IN TEMPORAL LOBE EPILEPSY**

  Principal Investigator & Institution: Hamberger, Marla J.; Neurology; Columbia University Health Sciences New York, Ny 10032

  Timing: Fiscal Year 2003; Project Start 01-DEC-1996; Project End 31-AUG-2008

  Summary: (provided by applicant): It is well established that the temporal lobe plays a critical role in language mediation. Yet, the functional-anatomical organization of language within the temporal lobe region is not well understood. This is a significant concern for temporal lobe **epilepsy** patients who elect surgical treatment for seizure control, because a substantial portion of temporal cortex is removed with this procedure. To preserve verbal abilities, cortical language mapping is often performed to identify "essential" language cortex and spare these areas from resection. Nonetheless, many patients decline post-operatively despite such mapping, primarily with respect to word finding. Although most surgery programs rely on visual object naming to identify 'essential' language cortex, the addition of auditory naming revealed a distinct region in anterior temporal cortex where stimulation impaired auditory but not visual naming. Preliminary follow-up testing suggests that sparing these auditory naming sites preserves word finding whereas resecting these sites results in decline (without affecting seizure outcome). Interestingly, a number of patients declined on both auditory and visual naming, despite the fact that only "pure auditory" sites were resected, and that all visual naming sites were spared. In the proposed studies, psycholinguistic tasks will be used before and after temporal lobe resection to study the role of anterior temporal cortex in the access of words and their meaning. Similar tasks will be used during mapping to delineate language-related structure-function relations at a level of analysis that is not attainable with other methods. Continued post-operative follow-up will assess the reliability of the preliminary findings, and determine whether deficits persist. Seizure outcome will be monitored as well. Primary goals are: 1) To determine how often, and in which patients, removing auditory naming sites results in word finding decline; 2) To determine the extent to which processes involved in word selection and access to word meaning are anatomically distinct, and where these process are represented neuroanatomically, 3) Determine why resection of cortex that appears to support modality-specific (auditory) naming can result in general word finding decline;

4) Determine whether sparing auditory naming sites from resection affects seizure outcome. Results promise deeper understanding of the neuro-functional organization of language, potentially offering improved treatment and preservation of language skills, not only to **epilepsy** surgery patients, but also to individuals with other neurologically based language disorders.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: DEPRESSION AND HEALTH OUTCOMES IN REFRACTORY EPILEPSY**

  Principal Investigator & Institution: Gilliam, Frank G.; Neurology; Washington University Lindell and Skinker Blvd St. Louis, Mo 63130

  Timing: Fiscal Year 2001; Project Start 24-AUG-2001; Project End 31-JUL-2006

  Summary: (provided by applicant): **Epilepsy** is the most prevalent disabling neurologic illness, and depression is the most frequent comorbid condition associated with **epilepsy.** The prevalence of depression is 20-50 percent in patients with uncontrolled seizures. This combination affects between 250,000 and 450,000 people in the United States. Our recent clinical studies have shown that depression is a strong predictor of function and health outcomes in **epilepsy.** Despite the marked adverse effects and high prevalence of depression in **epilepsy,** most affected patients are not treated. This complacency toward treatment may result from insufficient use of diagnostic screening, the widespread belief that antidepressants lower the seizure threshold, or lack of demonstrated efficacy in the only controlled trial of antidepressant medications in **epilepsy.** The broad aims of this study are to define the benefits of antidepressant treatment on mood, compliance, and health outcomes in **epilepsy** patients with comorbid major depression. Based on our prior clinical and research experience, we hypothesize that 1) pharmacotherapy or psychotherapy will reduce depression and improve health-related quality of life in patients with refractory **epilepsy,** 2) antiepileptic medication compliance will improve after reduction of depression, 3) seizure frequency will not significantly increase during treatment with a selective seratonin reuptake inhibitor compared to psychotherapy, and 4) depression and antiepileptic medication toxicity are stronger predictors of health-related quality of life than seizure frequency or severity in patients with refractory **epilepsy.** The hypotheses will be tested through a randomized trial comparing the efficacy of sertraline (n=127) to cognitive behavior therapy (n=127) for mood and health outcomes in patients with refractory **epilepsy** and depression. Reliable and valid measures will be used to assess depression and health-related quality of life. Electronic, computer-assisted monitoring will determine compliance. Multivariate repeated-measures analyses will be used to determine the interrelationships of treatment, mood, antiepileptic medication toxicity, seizure frequency and severity, compliance and health-related quality of life. We anticipate that dissemination of the results of a positive study will support the modification of the current model of intervention for **epilepsy** from predominantly seizure reduction to a more comprehensive approach that includes assessment and treatment of depression

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: DEPRESSION IN TEMPORAL LOBE EPILEPSY**

  Principal Investigator & Institution: Jones, Jana E.; Neurology; University of Wisconsin Madison 750 University Ave Madison, Wi 53706

  Timing: Fiscal Year 2003; Project Start 01-JUN-2003; Project End 31-MAY-2006

Summary: (provided by applicant): The proposed study would be the first controlled prospective investigation of the incidence and predictors of depressive disorders in individuals with chronic temporal lobe **epilepsy** (TLE). Beginning four years ago, a large cohort of individuals with TLE and healthy controls underwent a baseline psychiatric interview, MRI, cognitive testing, and assessment of quality of life. For this project, a consecutive series of individuals with TLE and controls (n = 118) will be seen four years later in order to: 1) determine the prospective incidence and relative risk of DSM-IV major depression and other depressive disorders in chronic TLE compared to controls; 2) identify the psychiatric, stressful life events, MRI, and clinical **epilepsy** variables predictive of prospective episodes of major depression and other depressive disorders over the interval; 3) identify the incidence of depressive episodes which meet the DSM-IV-TR criteria for minor depressive disorder and recurrent brief depressive disorder. The methodology will include: l) a comprehensive standardized psychiatric re-interview of DSM-IV Axis I disorders (SCID); 2) identification of stressful life events that occurred over the interval; and 3) review of medical records with participant interview to determine change in interval regarding seizure frequency and treatment. This study will make a significant contribution to understanding a major psychiatric complication in **epilepsy** and will integrate psychosocial, neurobiological, and clinical factors to provide a more comprehensive understanding of depressive episodes in **epilepsy.**

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- **Project Title: DEVELOPING APPROACHES TO REDUCING STIGMA OF EPILEPSY**

  Principal Investigator & Institution: Jacoby, Ann; University of Liverpool Box 147 Liverpool,

  Timing: Fiscal Year 2003; Project Start 30-SEP-2003; Project End 31-AUG-2005

  Summary: (provided by applicant): **Epilepsy** is the world's most common brain disorder, affecting some 50 million people worldwide. There is general agreement that stigma and exclusion are common features of **epilepsy** in both the developed and developing countries and a major contributor to the burden associated with the condition. Reducing the stigma of **epilepsy** is therefore key to reducing its impact and so improving quality of life. In order for effective health policy initiatives to be implemented to reduce the stigma of **epilepsy,** a number of issues first need to be addressed. These include addressing cultural variations in the meaning attached to having **epilepsy** and hence the way in which stigma is played out; and defining appropriate outcomes and methods for assessing them. This project will address these issues and so inform development of culturally appropriate approaches to reducing stigma and discrimination. The project will involve ethnographic studies to explore prevailing beliefs and attitudes to **epilepsy** in two developing countries, China and Vietnam. It will define theoretical models of stigma and its link to disease burden. It will develop validated and culturally specific measures of outcome for use in future intervention studies. Through its implementation, the project will enhance social science research capacity in these two countries and facilitate development of strong collaborations for future related research activities.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: DEVELOPMENT OF LOW FREQUENCY MEG HARDWARE AND SOFTWARE**

  Principal Investigator & Institution: Tepley, Norman; Professor; Neurology; Case Western Reserve Univ-Henry Ford Hsc Research Administraion Cfp-046 Detroit, Mi 48202

  Timing: Fiscal Year 2001; Project Start 01-JAN-1993; Project End 31-MAY-2003

  Summary: The ongoing objective of our research has been to develop hardware, software, and techniques to expand the utility of Magnetoencephalography (MEG), both as a clinical diagnostic tool, and as a modality for basic studies in the neurosciences. With a large array, whole head neuromagnetometer now available in our lab, and such systems becoming more generally available, but at quite high prices, the demonstration of added utility for MEG becomes even more significant. Sophisticated mathematical analytical techniques develooped in this lab, finite difference field mapping (FDFM) and two dimensional inverse imaging (2DII), as well as several commercial software packages, will be applied to clinical data gathered from potential **epilepsy** surgery patients, for presurgical mapping and source localization. The results of these techniques will be systematically compared to the standard equivalent current dipole (ECD) analysis, carried out at a number of institutions. A second method of source location utilizing the pseudo-DC magnetic fields arising post- ictally in temporal lobe **epilepsy** patients will also be studied using **epilepsy** surgery candidates. DC MEG techniques will be utilized for a continuing study of migraine and stroke patients. During the next grant period the physiological differences and similarities between migraine with aura and migraine without aura (classic and common migraine) will be studied using MEG signals essentially identical to signals measured from spreading cortical depression in animal models. Methods for using MEG measurements for determining rehabilitation and recovery in stroke patients will be developed. In all of the foregoing studies, the nature of the MEG signals detected in humans will be validated using the MEG signals arising from well-established animal models of the same conditions. These studies will be conducted in three species with progressively more complex cortexes, rat, rabbit, and swine. The use of dynamic period analysis (DPA) to produce whole head mapping of the changes in cortical activity accompanying arousal changes and sleep will be studied. 2DII imaging will be used to define active discrete and extended source activity associated with sleep. The spatial and temporal resolution of MEG will be utilized to study dyslexic subjects, and to localize regions of abnormal activity. A series of visual/auditory stimuli involving word, picture, and shape recognition will be used. If successful with young adult dyslexics, the study will be extended the study to children and individuals with other learning disabilities.

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- **Project Title: DEVELOPMENT OF POSITIVE FEEDBACK DURING EPILEPTOGENESIS**

  Principal Investigator & Institution: Staley, Kevin J.; Associate Professor; Neurology; University of Colorado Hlth Sciences Ctr P.O. Box 6508, Grants and Contracts Aurora, Co 800450508

  Timing: Fiscal Year 2001; Project Start 01-DEC-1996; Project End 31-JUL-2005

  Summary: (provided by applicant): Excitation spreads through a neural network via positive feedback connections between the neurons. The amount of positive feedback in the network is determined by the number and strength of these excitatory synaptic connections, as well as the degree to which these connections are masked by pre and

postsynaptic inhibition. The proposed research will test the hypothesis that the amount of positive feedback in a neural network is correlated with the probability that the network will initiate a seizure. To test this hypothesis, we have developed two noninvasive methods. The first method quantifies the amount of positive feedback based on the temporal pattern of interictal spikes on the electroencephalogram (EEG). The second method modifies the amount of positive feedback by selective long-term depression (LTD) of the strength of recurrent excitatory synapses. Using a well-characterized rat kainate model of chronic **epilepsy,** the amount of positive feedback measured from the EEG will be correlated with seizure probability during epileptogenesis. As an additional test of the hypothesis, the amount of positive feedback in the epileptic networks will be decreased by LTD of the recurrent synapses, and the seizure probability will be compared to EEG measures of positive feedback before and after LTD. These experiments may provide two important tools for treating **epilepsy.** The first is the ability to estimate seizure probability from the pattern of interictal spike activity on the EEG, which would make possible the prospective evaluation of the risk of seizures and the efficacy of anticonvulsant therapy. The second is the induction of long-term decreases in seizure probability by synapse-specific LTD of recurrent excitatory synapses in the epileptic network, which may prove to be a very useful anticonvulsant strategy.

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- **Project Title: EFFECT OF TEMPORAL LOBECTOMY ON SENSORY DEFICITS IN TLE**

  Principal Investigator & Institution: Grant, Arthur C.; Neurology; University of California Irvine Irvine, Ca 926977600

  Timing: Fiscal Year 2003; Project Start 30-SEP-2003; Project End 31-MAY-2008

  Summary: (provided by applicant): This application is for a Mentored Patient-Oriented RCDA (K23). The candidate is trained in clinical neurology and neurophysiology, and completed a Ph.D. thesis in basic visual neurophysiology. He is a tenure track Assistant Professor of Neurology at UC Irvine, and Associate Director of the UCI comprehensive **epilepsy** program. The candidate's long-term career goal is to study cortical network function and dysfunction using psychophysical, imaging, and electrophysiologic techniques, initially using temporal lobe **epilepsy** (TLE) as a model system. This grant application represents the first step in that process, by proposing to characterize psychophysically early or "low-lever' perceptual impairments in three sensory modalities in patients with medically intractable (mi) TLE, and to determine if such impaired cortical processing normalizes after surgical removal of the epileptogenic zone. The training portion of the proposal emphasizes three areas: 1) Network theory and its application to human sensory systems, 2) clinical experimental design and biostatistics, and 3) methodology and application of psychophysical perceptual tasks. UC Irvine has a proven reputation in basic, clinical and cognitive neuroscience. It also has developed a busy surgical clinical **epilepsy** program, and is thus ideally suited to the candidate's career goals. There is limited but compelling evidence that TLE is a network disease, not isolated pathologicallyto the epileptogenic focus. In this view, interictal cerebral function within the network is affected by the seizure focus, even in the absence of frequent seizures. Clinical implications of this theory are significant, and include the possibility that such cerebral dysfunction may normalize with surgical treatment. Outside the domains of language and memory, little is known of cognitive impairments in TLE. It is hypothesized that multi-modal perceptual dysfunction is present in mi TLE, that it may result from transient disruption of normal cerebral

processes by interictal "spiking" originating in the epileptogenic zone, and that it will normalize after surgical removal of the seizure focus. Forty subjects with mi TLE will undergo a battery of auditory, tactile and visual psychophysical tasks, and their performance compared to normal controls. Tasks were chosen to: 1) Determine the effect of stimulus duration on task performance. This should be a critical factor if interictal spiking is responsible for performance deficits, 2) test two analogous abilities (primary tasks) in all three sensory modalities, and 3) test early cortical sensory processes. Subjects will perform a subset of the tasks after anti-epileptic medication (AED) withdrawal during clinically indicated continuous video-EEG monitoring to assess the effect of AEDs on task performance. Subjects will then be retested on all tasks 6 months after surgery, or 6 months after initial testing for those who do not qualify for surgical treatment. If performance improves after surgery and is unchanged without surgery, as is hypothesized, these results would strongly support the notion of TLE as a network disease whose disruption of cortical processes could be reversed with surgical, but not medical treatment.

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- **Project Title: EFFECTS OF TREATING OBSTRUCTIVE SLEEP APNEA IN EPILEPSY**

  Principal Investigator & Institution: Malow, Beth A.; Associate Professor; Neurology; University of Michigan at Ann Arbor 3003 South State, Room 1040 Ann Arbor, Mi 481091274

  Timing: Fiscal Year 2002; Project Start 15-SEP-2002; Project End 31-JUL-2003

  Summary: (provided by applicant): **Epilepsy** affects approximately 2.5 million Americans, resulting in substantial disability. Because up to 30% of patients with **epilepsy** continue to have seizures despite appropriate treatment with antiepileptic medications, additional interventions to improve seizure control are needed. One approach to improving seizure control is to treat coexisting sleep disorders, such as obstructive sleep apnea. Obstructive sleep apnea (OSA) may exacerbate seizures via sleep fragmentation, sleep deprivation, or other pathophysiological processes that have not yet been determined. The investigators recently documented that OSA is common in **epilepsy** patients with seizures refractory to medical treatment. In addition, preliminary data in the form of retrospective case series by the investigators and others have suggested that treatment of OSA may improve seizure control. However, no prospective studies have been done to verify these findings. Proof that treating OSA is effective in reducing seizure frequency will require a multicenter Randomized Clinical Trial (RCT). This large RCT will test the hypothesis that treatment of OSA in patients with **epilepsy** refractory to medical treatment will reduce seizure frequency. In addition, the RCT will assess the impact of treating OSA on health-related quality of life and on daytime sleepiness, common concerns in **epilepsy** patients that are often attributable to antiepileptic medications or to frequent seizures rather than to a coexisting sleep disorder. The proposed aims of the Pilot Clinical Trial (PCT) are to determine critical information for the design of the RCT to allow for the testing of the above hypotheses in the RCT. In the PCT subjects 18 years and older with 4 or more seizures per month who meet survey criteria for OSA and other study criteria will be recruited at 3 different sites from **epilepsy** patients seen in clinical settings. A total of 60 subjects will be observed longitudinally through PSG confirmation and treatment of OSA and randomized to either therapeutic continuous positive airway pressure (CPAP) or sub-therapeutic (placebo or sham) CPAP in order to determine tolerability. Rates of adherence to therapeutic and sham CPAP and dropout rates due to antiepileptic drug changes during the treatment phase will be estimated. Specifically, the proposed PCT will: 1. Evaluate

screening ranges on the Sleep Apnea scale of the Sleep Disorders Questionnaire (DA/SDQ), a survey instrument that is used to determine whether subjects are eligible for inclusion into the RCT. 2. Determine the necessity of performing two nights of PSG in patients with **epilepsy.** A second night of study increases the cost and may decrease recruitment in the RCT, but may be important to include given the night-to-night variability in the PSG and the potential for seizure occurrence during recordings. The working hypothesis is that one night of PSG will be sufficient for the RCT. 3. Determine rates of adherence to therapeutic and sham CPAP, dropout rates due to antiepileptic drug changes, and response rates will provide valuable data for planning the RCT. 4. Develop quality control measures to ensure accurate and consistent data collection among sites in the RCT, including aspects related to remote data entry and standardization of performance and interpretation of PSG studies across sites.

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- **Project Title: EPILEPSY AND CHILDBIRTH: PK/PD MODELING OF AEDS**

  Principal Investigator & Institution: Pennell, Page; Emory University 1784 North Decatur Road Atlanta, Ga 30322

  Timing: Fiscal Year 2002; Project Start 01-SEP-2002; Project End 31-AUG-2007

  Summary: Approximately 1.1 million women with **epilepsy** are of childbearing age in the United States and give birth to over 20,000 babies each year. Pregnancy in women with **epilepsy** is accompanied by increased adverse neonatal outcomes, and approximately 28% of women will experience increased seizures. Serum concentrations of most of the AEDs decline during pregnancy, but findings from previous studies are too inconsistent to provide guidelines for management of AEDs during pregnancy. The primary objectives of Project 1 are: 1) pharmacokinetic/pharmacodynamic (PK/PD) modeling of antiepileptic drugs (AEDs) during pregnancy and lactation in women with **epilepsy** to define fetal/neonatal exposure; 2) identifying the predictors of seizure worsening during pregnancy and postpartum. Given that both AEDs and maternal seizures have been identified as having deleterious effects on the developing fetus and neonate, the PK/PD modeling combined with the course and predictors of illness will provide the foundation to propose guidelines to reduce exposure to both seizure activity and medication. PK/PD modeling of each of the AEDs encountered will be performed in Core A. Both a traditional, two-stage approach and population PK modeling will be employed. The influence of gestational age and other demographic, genetic, and environmental factors (covariates) will be analyzed. Frequency of seizures by type will be documented throughout pregnancy and first postpartum year and compared to each woman's preconception baseline. Worsening of seizure frequency will be correlated with potential predictors, including change in serum AED concentrations, hormonal status, stress, and altered sleep patterns.

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- **Project Title: EPILEPSY AND ELECTRICAL STIMULATION OF THE STN**

  Principal Investigator & Institution: Lado, Fred A.; Neurology; Yeshiva University 500 W 185Th St New York, Ny 10033

  Timing: Fiscal Year 2001; Project Start 01-AUG-2001; Project End 31-JUL-2006

  Summary: (provided by applicant): This application is for a Mentored Clinical Scientist Development Award (K08) for Fred Lado, MD PhD. Dr. Lado obtained clinical training in neurology at the Cornell University Medical College and subsequently completed a fellowship in Clinical Neurophysiologywith emphasis in EEG and **Epilepsy** at the

Albert Einstein College of Medicine. His current faculty appointment in the Department of Neurology at the Albert Einstein College of Medicine began in 1999. He previously received a PhD for his investigation of human subjects using magnetoencepahalography, but he is currently learning in vivo experimental methods using animals, as these are best suited to his longterm career goals. His goals are to study subcortical structures that regulate and propagate seizure activity, and to develop therapies targeting these regions in order to control human **epilepsy.** The Albert Einstein College of Medicine and the Montefiore Medical Center, the main teaching hospital of the College, offer broad strengths in basic neuroscience and clinical epileptology. Laboratory space, equipment, office space and access to established scientists across multiple disciplines are readily available. Opportunities for didactic instruction are also available through the medical college and through specialized summer courses. The environment and support available to the candidate are ideally suited to promoting and fostering Dr. Lado's longterm professional goals. Dr. Lado proposes to investigate the anticonvulsant effects of electrical stimulation of the subthalamic nucleus. The goals of these investigations are fourfold. (1) To investigate a novel treatment of seizures of adults using deep brain electrical stimulation of the subthalamic nucleus (STN). (2) To investigate the mechanisms of anticonvulsant action of STN stimulation and further development of our basic understanding of intrinsic anticonvulsant networks in the brain. (3) To determine whether anticonvulsant deep brain stimulation produces detrimental effects. And (4), to determine whether deep brain stimulation at the STN has an antiepileptogenic or neuroprotective effect. In the course of the proposed work, Dr. Lado will learn methods of intracranial injection, induction of chemical and electrical seizures, in vivo electrophysiology to record single unit and population activity, 2deoxyglucose autoradiography to map metabolic activation, neuroanatomical methods to detect synaptic reorganization and neuronal injury, and biostatistics. The proposed studies are designed to translate the insights and results obtained from animal research into improved treatments of human **epilepsy.** Moreover, the work described in this proposal will provide the investigator with an opportunity to acquire the necessary intellectual and technical skills be an independent investigator in translational i **epilepsy** research.

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- **Project Title: EPILEPSY OUTCOMES IN YOUTH--NEUROLOGICAL/FAMILY FACTORS**

  Principal Investigator & Institution: Austin, Joan K.; Distinguished Professor; None; Indiana Univ-Purdue Univ at Indianapolis 620 Union Drive, Room 618 Indianapolis, in 462025167

  Timing: Fiscal Year 2001; Project Start 01-SEP-1997; Project End 31-MAY-2004

  Summary: (Adapted from the Investigator's Abstract): **Epilepsy** is one of the most common neurological disorders in childhood. Children with **epilepsy** have been found to have high rates of adaptation problems, especially mental health and academic achievement problems. Factors accounting for these problems, however, have not been identified. The goal of this study is to identify factors that are related to these problems over time. The sample will be 160 youth (80 girls and 80 boys) ages 9-14 years, who have been diagnosed and treated for **epilepsy** for at least 6 months. Data will be collected three times over a 2-year period: baseline, 1 year, and 2 years. The primary aim is to identify a predictive model for child adaptation (behavior problems, self-concept, depression, psychiatric syndrome, and academic achievement) over time based on selected neurological, seizure condition, family, and child variables. Neurological

variables include brain structure and neuropsychological functioning (e.g., intelligence, memory, attention, learning, and executive function). Seizure condition variables include age at onset, type, syndrome, frequency, severity, and anti-epilepsy medication and side effects. Family variables include demographics (socioeconomic status and parent education); parent responses (perceptions of stigma and coping responses); family environment (stressors, resources, and adaptation); and parent psychosocial care needs. Child variables include demographics (age, gender, and pubertal status); response (attitudes, coping, and learned helplessness); and psychosocial care needs. Data analyses will include repeated measures regression and structural equation modeling. We will determine the extent to which neurological, seizure, family and child variables are related to child mental health and academic achievement over time. In addition, we will elaborate the above model by identifying how by exploring whether selected variables serve as mediating (e.g. child responses) or moderating (e.g., intelligence) variables in the model.

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- **Project Title: EPILEPTOGENIC EFFECT OF PERINATAL HYPOXIA**

  Principal Investigator & Institution: Jensen, Frances E.; Professor; Children's Hospital (Boston) Boston, Ma 021155737

  Timing: Fiscal Year 2001; Project Start 01-AUG-1992; Project End 31-MAY-2002

  Summary: (Adapted from Applicant's Abstract): Perinatal hypoxia is the single most common cause of seizures in the neonatal period. A subset of infants with seizures due to hypoxic encephalopathy develop chronic **epilepsy.** Several major questions regarding the pathophysiology of hypoxia-induced neonatal seizures remain unanswered. First, it is not clear why the immature brain is so susceptible to the epileptogenic effects of hypoxia, because seizures much less commonly complicate hypoxia/ischemia in the adult. Second, seizures complicating hypoxic encephalopathy con be refractory to anticonvulsant therapy that is effective in adult **seizure disorders,** indicating that the mechanism underlying perinatal hypoxia-induced seizures may be age-dependent. Third, it is not known how the acute perinatal seizures relate to later **epilepsy,** and whether the two phenomena share a common mechanism. The investigators have developed a unique model of perinatal hypoxia in the rat which exhibits both acute and chronic epileptogenic effects of hypoxia. Hypoxia induces seizure only during a critical developmental window of 10-12 days of age in the rat, and these animals have lowered seizure susceptibility as adults. Hippocampal slices removed acutely after hypoxia or in adulthood show enhanced excitability. Their recent studies indicate that hypoxia downregulates gene and protein expression for the GluR2 AMPA subunit and also results in a decreased in cells stained with the GABA synthetic enzyme, GAD. Here they propose to characterized the cellular and molecular effects of perinatal hypoxia in the hippocampus with respect to these new findings. Specific Aims: 1) To identify alterations in synaptic currents which underlie the acute and chronic epileptogenic effects of perinatal hypoxia. 2) To characterize changes in gene and protein expression of AMPA and NMDA subunits following perinatal hypoxia. 3) To evaluate the developmental distribution of AMPA subunit mRNAs and proteins in non hypoxic rats at different age intervals before, during and after the window of vulnerability for the epileptogenic effect of hypoxia. 4) To determine whether the observed decreased in interneurons stained with GAD-67 in adult CA1 after perinatal hypoxia is due to selective cell death or to a downregulation of GAD activity in surviving cells. Using this multidisciplinary approach, we aim to characterize the cellular and molecular effects of perinatal hypoxia in the hippocampus and to begin to assess the impact of

pharmacological therapies on these effects. The long term goal of this proposal is to define age-specific therapeutic strategies for the treatment of epileptogenesis in the developing brain.

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- **Project Title: ESTROGEN INDUCED HIPPOCAMPAL SEIZURE SUSCEPTIBILITY**

  Principal Investigator & Institution: Woolley, Catherine S.; Assistant Professor; Neurobiology and Physiology; Northwestern University 633 Clark St Evanston, Il 60208

  Timing: Fiscal Year 2001; Project Start 30-SEP-1998; Project End 31-JUL-2003

  Summary: A significant proportion of women with **epilepsy** experience increased seizure frequency during phases of the menstrual cycle in which estradiol levels are elevated. This is termed catemenial **epilepsy.** Animal models of **epilepsy** also demonstrate that estradiol increases seizure susceptibility. Previous work in the adult female rat has shown that estradiol induces new dendritic spines and axospinous synapses on CA1 pyramidal cells in the hippocampus, a key brain structure in the generation and propagation of seizure activity. Furthermore, estradiol-induced dendritic spines and synapses are correlated with increased excitability of hippocampal neurons and decreased hippocampal seizure threshold. This correlation suggests that estradiol-induced seizure susceptibility in women with catamenial **epilepsy** may be due, at least in part, to hormone-mediated alterations in hippocampal synaptic connectivity. The studies in this proposal will use the adult female rat to test the hypothesis that estradiol facilitates seizure activity through alteration of hippocampal synaptic structure and physiology. The proposed experiments will use light and electron microscopy, electrophysiological recording from hippocampal slices and behavioral seizure testing to better understand how estradiol-induced changes in synaptic connectivity affect hippocampal neuronal excitability and behavioral seizure susceptibility. Three hypotheses will be tested: 1) Estradiol up-regulates a subpopulation of NMDA receptor-specific excitatory synapses; 2) Estradiol up-regulates GABAA receptor-mediated inhibition; 3)Estradiol-induced changes in hippocampal synaptic structure/function are necessary for estradiol-induced seizure facilitation. These studies will further understanding of estradiol's effects on hippocampal synaptic structure and function. In women with catamenial **epilepsy,** estradiol-induced changes in hippocampal synaptic connectivity could provide a structural mechanism for the increased seizure frequency seen with elevated estradiol during certain phases of the menstrual cycle. As such, this proposal will lend insight into a mechanism of catamenial **epilepsy** and suggest a novel role for hormone-mediated structural plasticity in control of seizure susceptibility.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: FUNCTIONAL MRI FOR NEUROSURGICAL PLANNING IN EPILEPSY**

  Principal Investigator & Institution: Constable, Robert T.; Diagnostic Radiology; Yale University 47 College Street, Suite 203 New Haven, Ct 065208047

  Timing: Fiscal Year 2002; Project Start 01-APR-1999; Project End 31-MAR-2007

  Description (provided by applicant): **Epilepsy** patients who are candidates for surgical resection of a brain lesion must have some form of functional mapping to determine if the lesion can be removed without creating a functional deficit. The current procedures for mapping language in these patients are spatially limited (e.g. hemispheric mapping with Wada testing) or highly invasive (cortical stimulation using subdural electrodes).

Functional MR imaging (fMRI) has the potential to replace, or significantly enhance, the current methods used in Neurosurgical planning. It is noninvasive and has been shown to be able to localize cortical activity. However, the standard echo planar imaging fMR1 methods, based on the BOLD activation response, suffer from low spatial resolution, and sensitivity to static Bo magnetic field inhomogeneities which lead to image distortions and low signal intensity. These problems severely limit the ability of fMRI to localize brain activity for Neurosurgical planning. This project has 3 aims. First, it is designed to improve fMRI methodology. Our earlier work has identified the need to develop single shot approaches to maximize statistical power in fMRI studies, and thus the methodology developments will focus on single shot approaches to image distortion and signal loss, including the investigation of asymmetric spin echo EPI and dynamic shimming. This innovative program will allow for highly robust functional localization required for surgical planning, but the methods to be developed may be applied to any fMRI study. Secondly, we will continue our work on validating the fMRI activation detected through comparison with Wada testing and cortical stimulation. A battery of fMRI language paradigms, parallel to out-of-magnet behavioral studies, have been designed to address the specific deficits obtained in temporal lobe **epilepsy** patients and these will be applied to both control subjects and patients with intractable **epilepsy** who are candidates for surgery. Patients will be imaged and tested behaviorally both pre and post- surgery. Through such studies the ability of fMRI to predict surgical outcome will be evaluated. Finally, we will examine the relationship between disease states (mesial temporal sclerosis, cortical malformations, and tumors) and language reorganization both acutely (pre- and post- surgery) and chronically by relating the language organization and performance prior to surgery, to the type, location, and age at onset of **epilepsy.** Such a study will provide evidence not only of language reorganization but also of the specific cortical regions that reorganize, and the impact this reorganization has on performance and surgical outcome.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: FUNCTIONAL MRI FOR NEUROSURGICAL PLANNING IN EPILEPSY**

  Principal Investigator & Institution: Constable, R. Todd.; Director, Mri Research; Diagnostic Radiology; Yale University 47 College Street, Suite 203 New Haven, Ct 065208047

  Timing: Fiscal Year 2001; Project Start 01-APR-1999; Project End 31-MAR-2002

  Summary: Epilepsy patients who are candidates for surgical resection of a brain lesion must have some form of functional mapping to determine if the lesion can be removed without creating a functional deficit. The current procedures for mapping language functional areas in these patients are either spatially limited (hemispheric mapping with the Wada test for example) or highly invasive (cortical stimulation using subdural electrodes). Functional MR imaging (fMRI) has the potential to replace the current methods used in Neurosurgical planning. It is completely noninvasive and has been shown to be able to detect functional brain regions. However, the standard echo planar imaging fMRI methods, based on the BOLD activation response, suffer from low spatial resolution, and a sensitivity to static Bomicron magnetic field inhomogeneities which lead to geometric image distortions and low signal intensity. These problems severely limit the ability of fMRI to localize brain activity for Neurosurgical planning. This project is designed to improve fMRI methodology and to perform a thorough comparison between fMRI language mapping and the current gold standard cortical stimulation in patients. This study will determine the ability of fMRI to predict surgical

outcome. The patients will have language areas mapped using cortical stimulation and fMRI, and they will undergo behavioral studies pre- and post- surgery in order to measure any deficits that may arise post-surgery. The methodology development will specifically focus on novel techniques we have designed to reduce image distortion in echo planar fMRI, while increasing spatial resolution, and while producing highly robust activation maps even in the presence of field inhomogeneities. Our approach includes modifications to image acquisition strategies in conjunction with new post-processing algorithms. This innovative program will allow for highly robust localization of functional brain regions needed for surgical planning. While the emphasis is on the development and validation of fMRI methodology for Neurosurgical planning in **epilepsy,** the technical developments will be general and can be applied to any functional MR imaging study. Successful completion of this project may allow fMRI to be used as the primary source of functional localization in the brain for Neurosurgical planning reducing the need for invasive mapping techniques.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: FUNCTIONAL PLASTICITY IN CHILDREN WITH HEMISPHERECTOMIES**

  Principal Investigator & Institution: Asarnow, Robert F.; Professor; None; University of California Los Angeles 10920 Wilshire Blvd., Suite 1200 Los Angeles, Ca 90024

  Timing: Fiscal Year 2001; Project Start 01-SEP-2000; Project End 31-AUG-2005

  Summary: This revised application addresses hypotheses developed from work that the investigators carried out in the initial UCLA **Epilepsy** Surgery Program concerning the extent and nature of functional plasticity in young children following early hemispherectomies. The proposed project addresses key questions concerning the capacity of the human brain for functional plasticity. The investigators will test hypotheses about the functional plasticity of language, certain cognitive functions, and social communication in a unique cohort of children who have received left or right hemispherectomies for medially intractable **epilepsy** prior to 10 years of age. They will attempt to better define the temporal "window" for functional plasticity. They will determine if age at seizure onset and age at surgery predict the extent to which children show functional plasticity for specific linguistic, cognitive, and social communication function. The effect of seizure etiology on functional plasticity will be examined by comparing 1) children with and without evidence of cortical dysphasia in the resected hemisphere and 2) children with Rasmussen encephalitis to children with cerebral infarcts within the non-cortical dysplasia groups. This project represents a singular opportunity to more fully integrate the work conducted in their respective laboratories in order to examine the interrelation between language, cognition, and social communication in the isolated right and left hemispheres of children receiving early hemispherectomies. These questions will be addressed at two, five and ten years of age in the UCLA Pediatric **Epilepsy** Surgery Program. The investigators are currently following almost 50 children starting from pre-surgical evaluation to follow-up intervals ranging from 1 to 12 years. During the follow-up evaluations, children will be administered a careful selected set of tasks which have been demonstrated in prior research to tap linguistic, cognitive and social communication function normally lateralized to either the left or right hemisphere. This will provide the investigators the opportunity to determine the extent to which an isolated left or right hemisphere can support functions normally supported by the resected hemisphere.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: GABA-A RECEPTOR GENE TRANSFER TO PREVENT EPILEPTOGENESIS**

  Principal Investigator & Institution: Russek, Shelley J.; Pharmacol & Exper Therapeutics; Boston University Medical Campus 715 Albany St, 560 Boston, Ma 02118

  Timing: Fiscal Year 2002; Project Start 01-FEB-2002; Project End 31-JAN-2005

  Summary: Destabilization of the delicate balance between inhibition and excitation in the nervous system may underlie many neurological disorders, including temporal lobe **epilepsy** (TLE). Gamma-aminobutyric acid (GABA) is the major transmitter at inhibitory chemical synapses in the central nervous system. Alteration in type A GABA receptor (GABA/AR) function due to change in subunit composition has been hypothesized to be a critical component of epileptogenesis. Little is known, however, about the genetic mechanisms that regulate granule cells of adult rats following pilocarpine-induced status epilepticus (SE), it has yet to be demonstrated that these changes are either necessary or sufficient for the development of **epilepsy.** The presence of an alpha4 subunit (GABRA4) and the lack of an alpha1 subunit (GABRA) in the GABAalphaR complex has been associated with a decrease in benzodiazepine sensitivity and a heightened sensitivity to blockade by zinc. Both of these features are also seen in adult rats with TLE following pilocarpine-induced SE. The broad objective of this project is to test the hypothesis that alterations in GABAA4 subunit gene expression play a critical role in the process of epileptogenesis by re- establishing normal levels of GABRA4 and GABRA1 following pilocarpine-induced SE and determining whether development of spontaneous seizures is subsequently prevented. To accomplish this objective we will further characterize the 5'flanking region of the GABRA4 gene to identify the boundaries of the promoter and its regulatory sequences that are critical for transcriptional activity in primary cultures of dentate granule cells. Adeno-associated parvovirus (AAV) vectors will then be designed to contain the GABRA4 promoter driving the transcription of GABRA1 transgene to up-regulate alpha1 subunit levels, or a GABRA4 antisense RNA, to down-regulate alpha4 levels. GABA/AR subunit levels will be examined following viral delivery of these vectors to dentate granule cells in culture and in vivo. An alternative strategy of decoy oligonucleotides containing regulatory sequences found in the GABRA4 promoter will also be tested in vitro and in vivo for its ability to down-regulate endogenous GABRA4 promoter will also be tested in vitro and in vivo for its ability to down- regulate sequences found in the GABRA4 promoter will also be tested in vitro and in vivo for its ability to down-regulate endogenous GABRA4 gene expression. These vectors will then be introduced into dentate granule cells of pilocarpine-treated rats to determine whether GABA/AR alpha-subunit expression can be normalized, and if so whether subsequent development of **epilepsy** can be prevented. Results of these studies should enhance our understanding of GABA/AR subunit gene regulation, establish if subunit changes are a necessary component of epileptogenesis and provide a basis for novel therapeutic strategies for the prevention or cure of **epilepsy.**

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- **Project Title: GABAERGIC INHIBITION AND THE KETOGENIC DIET**

  Principal Investigator & Institution: Rho, Jong M.; Assistant Professor; Pediatrics; University of California Irvine Irvine, Ca 926977600

  Timing: Fiscal Year 2003; Project Start 01-FEB-2003; Project End 31-JAN-2008

  Summary: (provided by applicant): This application is for an Independent Scientist Award (K02). The candidate is a pediatric neurologist with a specialty interest in

childhood **epilepsy,** and is currently in the final year of K08 (MCSDA) funding. He recently relocated to the University of California at Irvine (UCI). UCI hosts an internationally recognized basic neuroscience research community, and is well suited to the career development needs of the candidate, especially at this critical time when he has just established an independent laboratory. During the early period of K08 funding, the candidate performed detailed studies of a developmental animal model of **epilepsy,** the Kv1.1 potassium channel knockout mouse (i.e., the Kcna1-null mutant). Later, the applicant pursued research into the mechanisms underlying the anticonvulsant efficacy of the ketogenic diet (KD), an established but still poorly understood treatment for intractable **epilepsy.** The KD is a high-fat, low carbohydrate and low-protein diet designed to mimic the early biochemical changes seen upon fasting. The hallmark feature of the KD is the production of the ketone bodies by the liver. The fundamental goal of the proposed studies is to assess the potential role of the GABAergic system in contributing to seizure control by the KD, and in the process establish and validate a clinically relevant animal model of the KD. As a secondary goal, it will be determined whether chronic ketone body exposure can enhance GABAergic inhibition in the brain. Further, the question of whether the KD can exert a lasting antiepileptic effect, beyond the duration of therapy, will be addressed, thereby setting the stage for future studies aimed at determining a mechanistic basis for an anti-epileptogenic effect of the KD. Toward these goals, the effects of the KD on the Kcna1-null mutant will be investigated. In addition, the long-term impact of ketone bodies in hippocampal organotypic slice cultures prepared from these mice will be studied. Neuroanatomical (i.e., histological, immunocytochemical, in situ hybridization) and functional (i.e., video-EEG monitoring, cellular electrophysiological) techniques will be employed in the proposed studies. It is expected that the results of these investigations will shed light on the potential role of the KD in epileptogenesis, especially as it relates to effects on GABAergic inhibition

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- **Project Title: GENETIC DISSECTION OF GLUTAMATE RECEPTOR FUNCTION**

  Principal Investigator & Institution: Heinemann, Stephen F.; Professor; Salk Institute for Biological Studies 10010 N Torrey Pines Rd San Diego, Ca 92037

  Timing: Fiscal Year 2001; Project Start 01-JUL-1990; Project End 31-MAY-2003

  Summary: Most theories of nervous system function depend heavily on the properties of the synapse and for this reason the synapse has been a focus of neuroscience research for many decades. The synapse is also the focus of medical and pharmaceutical research because in general the drugs that have proven useful for the treatment of mental illness and neurological disease act on various aspects of synaptic function, i.e. transmitter uptake and metabolism, ion channels and receptors. It is also likely that synaptic changes underlie the long term or permanent changes that take place in memory formation and learning. Recently there are suggestions that similar long term changes in synaptic transmission take place as part of the mechanism of many neurological diseases such as **epilepsy,** drug addiction and long term intractable pain. Long term alterations in synaptic function may explain the symptoms of withdrawal experienced by addicts when drug administration is terminated. Inappropriate activation of glutamate receptors is thought to contribute to the nerve cell death which occurs after brain injury due to stroke, **epilepsy,** head trauma and perhaps other neurological diseases such as ALS, Parkinson's and Alzheimer's disease. Little is known about the function of the kainate glutamate receptor subtype which is a major focus of this grant application made possible by the recent cloning of the kainate receptor genes. The structure of the glutamate binding site will be studied. A search for glutamate receptor

modulatory and accessory proteins will be undertaken using a new molecular genetic approach. The calcium permeability and function of the glutamate receptors are regulated by a novel mechanism of RNA editing which will be studied and altered in mutant mice. The role of kainate receptors will be studied making use of a battery of mutant mice that we have engineered to alter the kainate receptor system and synaptic transmission. Results from these studies will provide insight into the role that specific glutamate receptor subtypes play in the nervous system. This should make it possible by using recombinant DNA technology to develop new drugs and therapies to treat **epilepsy,** pain, stroke, mental illness, degenerative diseases and drug addiction.

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- **Project Title: GLUTAMATE NMDA RECEPTORS IN EPILEPTIC CORTEX**

  Principal Investigator & Institution: Babb, Thomas L.; Professor; Pediatrics; Wayne State University 656 W. Kirby Detroit, Mi 48202

  Timing: Fiscal Year 2002; Project Start 01-AUG-1999; Project End 31-JAN-2004

  Summary: (Verbatim from the Applicant's Abstract) This project is designed to identify and quantify the molecular mechanisms of NMDA receptor proteins and their subunit coassemblies that are necessary and/or sufficient for hyperexcitability of physiologically-verified (EEG) epileptic human cortical seizures. The most frequent drug-resistant neocortical seizures occur in human epileptics with cortical dysplasia. This serious **seizure disorder** occurs in approximately 20% OF all epileptics and is associated with the most severe social and educational retardations compared to the other focal or generalized epilepsies. Most of these cortical dysplasias can be surgically removed and in some cases seizures are reduced or eliminated. Surgical success however cannot be predicted from routine histopathologic analysis of the resected cortex. Continued seizures requiring medication occur in about 50% of cases. By contrast, sophisticated immunocytochemistry on NMDA receptors has now revealed upregulation of the NR2 subunits, and their coexpression with NR1 subunits in epileptic but not non-epileptic cortex. This proposal is designed to uncover the mechanisms by which NMDA receptors generate hyperexcitability by examining freshly resected epileptic cortex (documented by preoperative cortical recordings of the EEG seizure onset). Quantitative comparisons will be made in each patient's "epileptic" and "non-epileptic" cortex (no EEG seizure onsets). These parallel studies will uncover differences in NMDA receptor composition and function in: 1) NMDA receptor protein subunit gene products NR2A, B and their coassemblies with NR1 A-H)splice variants); 2) double-labeled NR1-NR2 immunofluorescence on single dysplastic neurons; 3) coimmunoprecipitation blots for NR1-NR2 antibodies; 4) Northern blots (with mRNA hybridization tests for NR2A, B, and NR1 splice variants A-H; 5) quantitative in situ hybridization to confirm Northern blot mRNAs; and 6) in vitro slice and dissociated neuron electrophysiology with field potential, patch clamp recordings, and selective pharmacologic blockade of NMDA receptor subunits. These multidisciplinary protein, molecular, and pharmaco-physiologic analyses will provide new information about the mechanisms of **epilepsy** and may suggest novel approaches to designing new drugs. These drugs should selectively act on hyperexcitable dysplastic neurons that have unique heteromeric coassemblies of NR2 and NR1 subunits not found on "non-epileptic" cortical neurons. Specific receptor-targeted drugs would avoid general nervous system depression and should provide more effective management of **epilepsy** in cortical dysplasia.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: HEREDITARY DEFECTS IN HUMAN SODIUM CHANNELS**

  Principal Investigator & Institution: George, Alfred L.; Director, Division of Genetic Medicine a; Medicine; Vanderbilt University 3319 West End Ave. Nashville, Tn 372036917

  Timing: Fiscal Year 2003; Project Start 01-JAN-1994; Project End 31-DEC-2006

  Summary: (provided by applicant): Voltage-gated sodium channels are heteromultimeric integral membrane proteins that are responsible for the initial phase of the action potential in most excitable cells. A variety of inherited disorders affecting skeletal muscle contraction (hyperkalemic periodic paralysis, paramyotonia congenita, K+-aggravated myotonia), cardiac excitability (congenital long QT syndrome, idiopathic ventricular fibrillation, familial conduction system disease) and certain forms of **epilepsy** have been associated with mutations in various human sodium channel genes. This proposal is a competing renewal of R01-NS32387 that for 8 years has funded our efforts to elucidate the molecular genetic, physiologic and pharmacologic mechanisms of human sodium "channelopathies". We have recently shifted our focus from studies of the two striated muscle sodium channel genes (SCN4A, SCN5A) to investigations of brain sodium channel genes and their role in inherited epilepsies. We propose to perform a series of carefully integrated experiments employing molecular genetic, recombinant DNA and cellular electrophysiological approaches to elucidate the molecular defects responsible for **seizure disorders** linked to three distinct neuronal sodium channel genes (SCN1B, SCNIA, SCN2A). In Specific Aim 1, we propose to perform molecular genetic screening in a large cohort of families segregating seizure phenotypes consistent with generalized **epilepsy** with febrile seizures plus (GEFS+), severe myoelonic **epilepsy** of infancy (SMEI) and other less well characterized disorders that may be associated with mutations in brain sodium channels. In Specific Aim 2, we plan to perform biophysical and pharmacological characterization of epilepsy-associated mutations using recombinant human neuronal sodium channels expressed heterologously in mammalian cells. Our laboratory is uniquely qualified to elucidate the molecular mechanism of SCN1A-associated **epilepsy** using recombinant human SCN1A, a reagent that we have recently developed. Finally in Specific Aim 3, we will elucidate the molecular mechanisms responsible for dysfunction of the human sodium channel [31 subunit in some forms of familial **epilepsy.** Altogether, this work is designed to establish important correlations between genotype, clinical phenotype and biophysical properties of mutant sodium channels in human epilepsies and will have important pathophysiologic and therapeutic implications for hereditary disorders of sodium channels.

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- **Project Title: HERPES SIMPLEX VIRUS, EARLY BRAIN INJURY AND EPILEPSY**

  Principal Investigator & Institution: Eid, Tore; Neurosurgery; Yale University 47 College Street, Suite 203 New Haven, Ct 065208047

  Timing: Fiscal Year 2002; Project Start 01-AUG-2002; Project End 31-JUL-2005

  Summary: (provided by applicant): Herpes simplex virus type 1 (HSV-1) is a common cause of acute and recurrent disease in humans. After the primary infection, which usually occurs in childhood, HSV-1 remains dormant in the nervous system. This proposal is aimed at exploring a novel hypothesis that early infection with HSV-1 plays a critical role in the genesis of temporal lobe **epilepsy** (TLE). The virus may contribute to this by creating a specialized brain focus involving alterations in neural circuitry and formation of a unique glial/microvascular substrate that promotes epileptogenesis and

maintenance of seizures. Several observations suggest that HSV-1 may cause TLE. For example, survivors of HSV-1 encephalitis frequently develop **epilepsy.** HSV-1, when causing encephalitis, preferentially invades and lesions limbic structures, including the hippocampus, which also shows neuropathological changes in TLE. Moreover, patients with medically intractable TLE have a ten times higher rate of latent HSV-1 infection in their hippocampus than control subjects. To evaluate our hypothesis two approaches are proposed. (1) To critically explore the connection between HSV-1 and TLE by assessing the presence of viral DNA (by polymerase chain reaction) and virions (by immunohistochemistry) in surgically resected hippocampi from TLE patients, and correlating these with the specific neuropathological characteristics of TLE, i.e. (a) loss of hilar interneurons, (b) gliosis, and (c) vascular proliferation. (2) To assess the causal relationship of HSV-1 to the development of chronic seizures and neuropathology in TLE, rat models of HSV-1 infection will be studied and experimental modifiers of infection such as (a) viral strain, (b) age, (c) fever/febrile seizures, and (d) acute seizures, will be evaluated. The cellular/molecular mechanisms of viral-induced neuropathology and seizures will be explored by investigating the pattern and time-course of viral invasion during the infection. If a viral causation of TLE is established, then this would not only open new avenues for prevention and control of this disorder, but also improve our understanding of viral-induced brain injury.

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- **Project Title: HILAR GRANULE CELLS & SYNAPTIC REMODELING AFTER SEIZURE**

  Principal Investigator & Institution: Pierce, Joseph P.; Neurology and Neuroscience; Weill Medical College of Cornell Univ New York, Ny 10021

  Timing: Fiscal Year 2002; Project Start 01-FEB-2002; Project End 31-JAN-2006

  Summary: Temporal lobe **epilepsy** (TLE) is often associated with a pattern of neuropathology within the dentate gyrus (DG) that is strikingly similar to changes observed in several models of **epilepsy.** Granule cells (GCs, the principal cells of the DG) disperse, and their axons undergo extensive restructuring, sprouting into new terminal fields. Recent findings also indicate that after seizures, the neurogenesis of GCs increases, and some can migrate to the hilar/CA3 border (ectopic GCs). Determining how GC synaptic circuitry is altered is critical to understanding how hippocampal seizures could develop in TLE, since the DG is normally able to prevent electrographic seizures from spreading into the rest of the hippocampal formation. The proposed studies will test the hypothesis that following seizures, there is a selective strengthening of the pattern of synaptic connectivity among cells that could support recurrent excitation in the ventral DG (which is particularly excitable), thus promoting subsequent seizures. Tissue from control and experimental animals will be examined anatomically and physiologically four months after pilocarpine treatment, when spontaneous seizures have appeared. Aim I will ascertain if the synaptic input to, and output from, ectopic GCs is consistent with a role in a novel recurrent excitatory pathway. Dual electron microscopic (EM) immunolabeling techniques will be applied to characterize synaptic input to ectopic GCs in experimental tissue. Additionally, physiologically-identified and intracellularly-labeled ectopic GC axons in slices will be reconstructed at light and EM levels, after immunolabeling to identify neurons that receive output from ectopic GCs. Aim II will examine whether GC axons strengthen (in terms of synapse number and size) their innervation of hilar neurons that could support recurrent excitation (surviving mossy cells and ectopic GCs). This analysis will be conducted both across the whole population of terminals (by combining dual EM immunolabeling with

stereological techniques), and within individual axons (by examining physiologically-identified and labeled axons from GCs in the GC layer). Since these fibers also contact interneuron subpopulations involved in recurrent inhibition, even small shifts in the balance of synaptic input could have a large impact on the excitability of the DG. The results of these studies will elucidate mechanisms underlying increased excitability in the DG, advancing our understanding of the pathophysiology of TLE.

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- **Project Title: HIPPOCAMPAL NETWORK STRUCTURE AND FUNCTION IN EPILEPSY**

  Principal Investigator & Institution: Sloviter, Robert S.; Professor; Pharmacology; University of Arizona P O Box 3308 Tucson, Az 857223308

  Timing: Fiscal Year 2003; Project Start 01-DEC-1984; Project End 31-JUL-2007

  Summary: (provided by applicant): Temporal lobe **epilepsy** is a common and devastating neurological disorder that is often resistant to treatment. Although spontaneous epileptic seizures are believed to arise from an altered circuit within the temporal lobe, the nature of the causal network defect remains unidentified. The proposed experimental studies have been designed to elucidate the normal functional and structural organization of the hippocampus, with particular emphasis on the lamellar organization of this epileptogenic brain region. One hypothesis suggests that hippocampal segments are functionally separated from adjacent segments by translamellar inhibitory mechanisms, and that the breakdown of inhibitory barriers causes the formation of hyperexcitable "supersegments." This hypothesis will be addressed in a series of studies designed to demonstrate translamellar inhibition electrophysiologically, to identify the neurons that form the longitudinal projections that establish and maintain translamellar inhibition, and to determine whether loss of vulnerable interneurons causes translamellar disinhibition. Other studies will address the role of septal neurons in establishing lamellar hippocampal function. A second hypothesis predicts that synaptic reorganization forms abnormal connections between normally unconnected excitatory hippocampal neurons and that these interconnections give rise to hippocampal seizure discharges. A series of parallel electrophysiological studies in awake, chronically implanted animals will describe for the first time whether spontaneous epileptic seizures arise from the hippocampus, and will utilize a molecular marker of excitation to identify the neurons that are discharging in the most commonly used **epilepsy** models. Continuous electrophysiological monitoring will also determine the behavior of hippocampal neuron populations before and after injury, before and after injury-induced synaptic reorganization, and before and after the development of spontaneous seizures. New preliminary data indicating that human patients may have a pre-existing region of focal disinhibition will be used to develop several new models of temporal lobe **epilepsy.** These studies, which utilize a newly developed neurotoxin that selectively removes inhibitory interneurons in a highly focal region, will address the possibility that new animal models that may more closely approximate the human condition may be useful for detecting new pharmacological treatments for what remains a frequently drug-resistant neurological disorder.

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- **Project Title: HUMAN EPILEPTIC FOCI: HIDDEN CORTICAL RELATIONSHIPS**

  Principal Investigator & Institution: Towle, Vernon L.; Neurology; University of Chicago 5801 S Ellis Ave Chicago, Il 60637

Timing: Fiscal Year 2001; Project Start 04-SEP-2001; Project End 31-AUG-2005

Summary: This is a proposal to analyze electrophysiologic recordings taken directly from the cerebral cortex of **epilepsy** patients to test our hypothesis that seizures arise from a pathological epileptic system. We will develop and apply coherence analysis to EEG recordings that are obtained from arrays of electrodes that are implanted over the cortex of **epilepsy** patients as part of their work-ups for determining the source of their intractable **epilepsy.** Current techniques employed for the evaluation of seizure foci are subjective, imprecise, and ineffective a large portion of the time, leaving many of these patients postoperatively unable to work or otherwise carry on a normal life style. We plan to take recordings from 75 **epilepsy** patients and 25 control patients over a four-year period with the goal of determining the optimal analysis strategy to identify areas of cortex that have become part of the epileptic system, and differentiate them from normal and eloquent cortex. This will involve comparing standard clinical evaluation techniques to our new measures of lateral coherence, which should increase our understanding of the spread of epileptic seizures and the underlying neuropathology associated with seizure activity. At the time of surgery the coherence patterns will be interactively displayed directly on the cortical surface in real-time by means of intra-operative digitized video images. This technique should also make it possible to reduce the surgical morbidity associated with **epilepsy** surgery and increase its efficacy, thereby allowing a greater proportion of intractable **epilepsy** patients to realize self-sufficient and productive lives.

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- **Project Title: IMAGING TRYPTOPHAN METABOLISM IN CHILDREN WITH EPILEPSY**

  Principal Investigator & Institution: Chugani, Diane C.; Associate Professor; Pediatrics; Wayne State University 656 W. Kirby Detroit, Mi 48202

  Timing: Fiscal Year 2004; Project Start 01-JAN-2004; Project End 31-DEC-2007

  Summary: (provided by applicant): Approximately 0.5% to 1.0% of the population suffers from **epilepsy.** Fifteen to 20% of these individuals have seizures which cannot be controlled with anticonvulsants. **Epilepsy** is particularly devastating in children, in whom recurrent prolonged seizures may result in impaired cognitive development. The major goal of this proposal is to provide improved preoperative localization of epileptogenic brain tissue in children with medically uncontrolled neocortical **epilepsy** who are being treated with surgical resection of the epileptic focus. The central hypothesis of this proposal is that abnormalities in brain tryptophan metabolism via the serotonin and/or kynurenine pathways contribute to the pathophysiology and localization of neocortical **epilepsy.** Brain tryptophan metabolism will be measured in vivo in drug-resistant **epilepsy** patients using the tracer alpha [C-11]methyl-L-tryptophan (AMT) with positron emission tomography (PET). Our preliminary data show increased AMT accumulation in epileptogenic cortex in approximately one-half of patients assessed for **epilepsy** surgery. The focus of increased AMT uptake is typically much smaller than the large areas of hypometabolism seen on glucose metabolism PET scanning. In the present grant application, we propose to confirm and extend these findings by comparing AMT PET results to quantitative electrophysiological measures obtained during presurgical evaluation. In order to better understand the pathophysiology underlying altered AMT uptake by epileptic brain tissue, we will perform biochemical measurements in the tissue which is surgically resected for control of intractable **epilepsy.** Three specific aims will be addressed: 1. To determine the extent to which AMT PET and glucose metabolism PET regions of abnormality localize

neocortical epileptogenic regions defined by subdural electrode recordings in both lesional and nonlesional neocortical **epilepsy.** 2. To determine whether resection of cortex with increased AMT uptake is related to outcome of **epilepsy** surgery. 3. To determine the underlying biochemical mechanism for the observed focal increases in cortical AMT uptake in patients with **epilepsy.** Our research will contribute to a better understanding of the pathophysiology and improve localization of focal **epilepsy.**

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- **Project Title: IMPACT OF SEIZURE CLUSTERING ON ADULT EPILESPY**

  Principal Investigator & Institution: Haut, Sheryl; Assistant Professor of Neurology; Montefiore Medical Center (Bronx, Ny) Bronx, Ny 104672490

  Timing: Fiscal Year 2001; Project Start 21-SEP-2000; Project End 31-AUG-2005

  Summary: This application is for a Mentored Patient-oriented RCDA (K23). The candidate is trained in clinical neurology and neurophysiology, and is currently on the faculty at the Albert Einstein College of Medicine (AECOM). The ma interests of the candidate are neurophysiologic, epidemiologic, and outcome issues in **epilepsy,** with a special f on seizure patterns and precipitants. The long term goals of the candidate are to develop the research sophistication and techniques to allow for high quality clinical research in the field of **epilepsy** or other neurologic disorders. career development proposal includes completion of a Masters of Science in the AECOM Clinical Research Training Program, followed by the design, implementation and analysis of the proposed research project on seizure clusting at Montefiore Medical Center/AECOM, which is a site of extensive, successful clinical research, and is ideally for the candidate's long term goals. Seizure clustering may affect treatment and outcome of **epilepsy,** but has not been widely studied. We aim recruit a cohort of 300 adult, predominantly inner-city patients with **epilepsy,** and follow them prospectively for months. We will define seizure clustering as three or more seizures occurring within 24 hours. We plan to examine the incidence, risk factors and precipitants for clustered seizures, as well as the impact of clustering on various **epilepsy** outcomes. We hypothesize that the incidence of clustering will be high ,that seizure clustering will be associated with localization-related factors and risk factors for status epilepticus (SE), and that patients with club will be at increased risk for SE. Identifying patients at risk for clustering may improve their treatment, especial they are at an increased risk of SE. Furthermore, we hypothesize that we will identify potentially modifiable precipitating factors for seizure clustering, and specifically, seizure clustering which requires emergency intervention. This may allow for a reduction in the incidence of clustering and a decrease in resultant morbidity. Finally, we examine outcome measures of **epilepsy** in our cohort, including response to medical therapy, quality of life, an of care, and examine the impact of seizure clustering on these outcome measures. If outcome of **epilepsy** is demonstrated to be worse in patients with clustered seizures, development of a specialized **epilepsy** care program these patients, including more aggressive medical therapy and earlier psychosocial intervention, may be appropriate. We anticipate that this study will both define the role of seizure clustering in adult **epilepsy,** and increase o appreciation of the medical, social and financial impact of **epilepsy** in a large cohort of inner city adult patients.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: IN VIVO OPTICAL MAPPING OF RODENT NEOCORTICAL EPILEPSY**

  Principal Investigator & Institution: Schwartz, Theodore H.; Neurology and Neuroscience; Weill Medical College of Cornell Univ New York, Ny 10021

  Timing: Fiscal Year 2001; Project Start 01-SEP-2001; Project End 31-AUG-2006

  Summary: Epilepsy is a disease affecting 1-2% of the population. Electrical recordings from chronic animal models and human neocortical epileptic foci indicate that the population of neurons underlying each interictal epileptiform discharge varies over time. The spatial relationship between interictal events and the ictal onset zone, thought to be the critical area of epileptogenesis, is not well understood and critical to the surgical treatment of **epilepsy.** Electrophysiological recording methods, although currently the "gold standard", are inadequate to address these questions based on restrictions due to volume conduction or sampling limitations, many of which can be overcome with optical recording techniques. The PI is a fellowship trained **epilepsy** surgeon at UMDNJ with extensive laboratory experience in optical recording of neuronal activity, both in vitro and in vivo. In a second post-doctoral fellowship, the PI demonstrated that in vivo optical recording of intrinsic signals can be used to generate high-resolution, real-time maps of the population of neurons participating in an epileptiform event. The goal of the current study is to examine the shifting spatio-temporal dynamics of the epileptogenic aggregate in both acute and chronic experimental models of in vivo rodent **epilepsy.** In the laboratory of mentor Gyorgy Buzsaki, a world-renowned expert in electrophysiological mapping of rodent **epilepsy** at Rutgers and part of the joint UMDNJ-Rutgers Graduate Center m Newark-Program in Neurosciences, we will first determine the precise relationship between the optical signal and the interictal and ictal epileptiform events using well-established acute and chronic in vivo rodent models. Optical **epilepsy** maps will be correlated with maps derived from electrophysiological recordings from a grid of surface electrodes, multicontact silicon probes, as well as c fos hybridization. Additional technical support in optical recording and data analysis will be provided by collaborator Ralph Siegel, also a member of the UMDNJ- Rutgers Graduate Center in Newark-Program in Neurosciences. As a related goal, optically-guided surgical resections of epileptogenic cortex will ascertain the required volume of epileptogenic tissue which must be removed to eliminate seizures. The results of these investigations will not only be important in understanding the pathophysiology of neocortical **epilepsy** but also critical in optimizing surgical treatment of human clinical **epilepsy.** Following the period of mentorship, the PI will be able to combine independent basic science research in a separate laboratory at UMDNJ with clinical optical recordings in the operating room during the neurosurgical treatment of **epilepsy.**

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- **Project Title: INVESTIGATING A ROLE FOR GLUTAMATE TRANSPORT IN EPILEPSY**

  Principal Investigator & Institution: Sutherland, Margaret L,.; Assistant Professor; Pharmacology; George Washington University 2121 I St Nw Washington, Dc 20052

  Timing: Fiscal Year 2002; Project Start 01-JUN-2002; Project End 31-MAY-2007

  Summary: (provided by applicant): Our long term goal is to characterize the cellular and molecular mechanisms regulated by glutamate transport activity under both normal and pathophysiological conditions. Glutamate is the major excitatory neurotransmitter in the mammalian central nervous system, and as such plays a key role in neurological

diseases involving hyperexcitability and excitotoxic cell death. Glutamate transport maintains extracellular glutamate concentrations below neurotoxic levels and loss of transporter protein is associated with several neurodegenerative disorders. We have tested the hypothesis that glutamate transporters play a key role in preventing cell death in limbic seizures, by generating a transgenic mouse model of astrocytic EAAT2 (Glt-1) overexpression. The EAAT2 protein is tagged with GFP (green fluorescent protein) and expression is driven by the astrocyte-specific GFAP promoter. Overexpression of the EAAT2 transgenic protein results in a 2-3 fold increase in hippocampal and cerebrocortical synaptosomal D-aspartate uptake. In a kainic acid (KA) model of temporal lobe **epilepsy,** increased glutamate transport results in an 80 percent decrease in hippocampal cell death compared to the level of cell death following KA-induced seizures in a wild-type age-matched animals. Surprisingly, we also found that increased glutamate uptake in the EAAT2 transgenic blunted network excitability and immediate early gene responses. These data, taken together with recent findings from other investigators, indicate that in addition to maintaining low steady-state concentrations of glutamate around the synaptic cleft, transporters may mediate a more rapid control of synaptic efficacy. Since glutamate is the major excitatory neurotransmitter in the CNS, we hypothesize that increased glutamate transport will blunt network excitability in most, if not all, CNS models of seizure-related hyperexcitability. To test this central hypothesis, we will use three models of status epilepticus (KA, pilocarpine and kindling). To extend our preliminary studies we will examine the acute actions of the glutamate analogue kainic acid using two in vitro slice preparations (hippocampal and piriform cortex) to determine if increased glutamate transport alters the threshold, frequency or duration of epileptiform activity. We will also inject KA, NMDA or AMPA into the hippocampus and record EEG activity to elucidate differences in seizure onset, frequency and duration in the presence of increased glutamate uptake (Specific Aim 1). To determine if the effects of increased glutamate transporter expression are generalized or limited to convulsants acting directly through a glutamate receptor pathway, we will use pilocarpine, that acts through muscarinic receptors, to generate seizure activity in vivo and in an in vitro hippocampal slice preparation to compare wild-type to EAAT2 transgenic responses (Specific Aim 2). Finally we will use two kindling models of status epilepticus to determine if increased glutamate transport activity lowers the threshold, rate of kindling acquisition, molecular plasticity or degree of cell death in PAAT2 transgenic mice compared with age-matched wild-type animals Specific Aim 3).

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- **Project Title: LOCALIZATION OF EPILEPTIC FOCI WITH PET IN CHILDREN**

  Principal Investigator & Institution: Chugani, Harry T.; Rosalie and Bruce Rosen Chair in Neurolo; Pediatrics; Wayne State University 656 W. Kirby Detroit, Mi 48202

  Timing: Fiscal Year 2001; Project Start 01-DEC-1996; Project End 31-AUG-2006

  Summary: (Verbatim from the Applicant's Abstract) Approximately 0.5 percent to 1.0 percent of the population suffer from some sort of **epilepsy,** and in 15 percent -20 percent of cases the seizure are refractory to medical treatment with anticonvulsants. Eplepsy is particularly devastating in the pediatric age group. Infants and children whose seizures are recurrent, difficult to control with anticonvulsants, and prolonged tend to have the worst prognosis in terms or cognitive development. When seizures cannot be controlled with medication, surgical treatment may be considered. The outcome of **epilepsy** surgery varies depending upon the type of operation performed. Of the various types of cortical resections performed, the worst results are reported in patients without MRI lesions who undergo extratemporal lobe resection; seizure free

outcome is achieverd in only approximately one-half of this group of patients despite the used of invasive intracranial electrographic monitoring. Even when an extratemporal lobe lesion is present on the MRI, surgical success remains far less thatn that of temporal lobectomy. The major goal of this proposal is to provide improve noninvasive preoperative localization of epileptogenic brain tissue in children with medically uncontrolled extratemporal lobe **epilepsy** who are being treated with surgical resection of the epileptic focus. We will evaluate the utility of positron emission tomotgraphy (PET) imaging of the GABA/benzodiazepine receptor complex with [11C]flumazenil (FMZ) and glucose metabolism with 2-deoxy-2 [18F} fluoro-D-glucose (FDG) to provide optimum identification of epileptogenic tissue. Three specific aims are to be addressed in this proposal: 1) To determine the extent to which FMZ and/or FDG PET foci or abnormality accurately identify brain regions of seizure onset, immediate seizure spread, frequent interictal, spiking and background slowing defined by the rating of subdural electrode recordings in both lesional and non lesional extratemporal lobe **epilepsy.** 2) To determine if FMZ and/or FDG PET contribute to improved surgical outcome in nonlesional extratemporal lobe **epilepsy.** 3) To identify patterns of FMZ abnormalities outside the primary epileptic focus which are associated with poor outcome or which are associated with good seizure control following removal of the primary epiletic focus. The overall goal of our research is to improve the success rates of extratemporal lobe resections and to increase understanding of the basic mechanisms of epileptogenesis.

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- **Project Title: MAGNETOENCEPHALOGRAM IN EPILEPSY**

  Principal Investigator & Institution: Sutherling, William W.; Medical Director; Huntington Medical Research Institutes 734 Fairmount Ave Pasadena, Ca 91105

  Timing: Fiscal Year 2002; Project Start 01-MAY-1993; Project End 31-MAR-2006

  Summary: (Verbatim from applicant's abstract) We will measure simultaneous MEG and chronic ECoG co-registered in MRI in pre-surgical patients with intractable partial **epilepsy** during afterdischarges, inter-ictal spikes, and, in some patients, seizures. We will use our newly installed whole cortex 68-channel neuromagnetometer and 64 EEG channels. We will compare the localization specificity and detection sensitivity of the two fields and investigate new methods of improving the MEG by studying the same event from the cortex. We will apply realistic models of the source and of the volume conductor in BrainStorm and Curry in collaboration with Drs. Mosher, Leahy, and Baillet. We will compare these new models to the standard single dipole model used clinically. We will study MEG and EEG and attempt their fusion. We will study the characteristics of live skull. We will test if realistic models add useful additional information. We will test how MEG and source analysis can enhance present noninvasive standard **epilepsy** pre-surgical evaluations to localize the epileptogenic zone. We will map the outer borders of hand cortex to allow more precise maps of essential areas for surgical planning. We purchased the neuromagnetometer with a shared instrumentation grant and we will make our results and lab available to several other collaborators, to enhance their research in, for instance, language and to ensure maximum utility from this costly NIH equipment.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: MAPPING IDIOPATHIC EPILEPSY GENES IN CANINE MODELS**

  Principal Investigator & Institution: Patterson, Edward E.; Small Animal Clinical Sciences; University of Minnesota Twin Cities 200 Oak Street Se Minneapolis, Mn 554552070

  Timing: Fiscal Year 2001; Project Start 30-SEP-2000; Project End 31-AUG-2005

  Summary: (Adapted from the Applicant's Abstract): Idiopathic **epilepsy** (IE) is a common condition in human patients as well as the domestic dog (Canis familiaris). In both species, genetic factors are believed to be a significant factor in conferring susceptibility to seizures. The most common forms of human IE are known to be polygenic, and consequently dissecting out individual **epilepsy** susceptibility genes has been difficult. Dogs have been strongly inbred over the last 100 years, and therefore many of their inherited diseases are caused by a "founder" effect similar to that found in isolated human populations. We hypothesize that idiopathic **epilepsy** in some dog breeds has a simple mode of inheritance (monogenic or oligogenic), and consequently it will be possible to efficiently map the genetic loci and eventually identify causative mutations. The causative mutation(s) could be used as candidate genes for IE's of human patients, and as a basis for experimental studies of neuronal hyperexcitability. The overall objective of this proposal is to locate chromosomal loci linked to idiopathic **epilepsy** in dogs, as a major step towards identifying susceptibility genes and developing a model for human idiopathic **epilepsy.** Dr. Edward (Ned) Patterson received his D.V.M. in 1996. He is nearing completion of his residency in small animal internal medicine with an emphasis in medical neurology, and is working towards a Ph.D. in the Veterinary Medicine Graduate Program at the University of Minnesota. He has chosen a thesis project and a research career in comparative neurogenetics using a canine model. During the initial two years of support for this award, Dr. Patterson will be working under the direct supervision of the sponsor, Dr. James Mickelson. He will have frequent meetings with the co-sponsors Drs. Laura Ranum and Yang Da. During this time, while he completes the Ph.D. thesis, 75% effort will be placed on the proposed research, and 25% on clinical and teaching duties. Dr. Mickelson has trained successful scientists in the past and is a well-known and respected scientist in the field of animal neuromuscular genetics. Dr. Ranum is a respected scientist in field of human neuroscience and genetics. Dr. Da is an accomplished statistical animal geneticist. Upon completion of his Ph.D, Dr. Patterson will be appointed to an Assistant Professorship. At this time, 75% effort will be placed on the proposed research, while other time will be utilized teaching and in clinical services. The advisory committee, composed of individuals who are all active in the areas of veterinary medicine and/or genetics, will meet quarterly to discuss research and future directions. Upon completion of the five-year plan, Dr. Patterson will have fully developed into an independent investigator who can bridge the gap from characterizing clinical inherited neuromuscular disorders to identifying the causative molecular pathobiology.

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- **Project Title: MEDICAL COLLEGE OF VIRGINIA EPILEPSY RESEARCH CENTER**

  Principal Investigator & Institution: Delorenzo, Robert J.; Professor and Chairman; Neurology; Virginia Commonwealth University Richmond, Va 232980568

  Timing: Fiscal Year 2001; Project Start 01-JAN-1989; Project End 31-JAN-2005

  Summary: Status epilepticus (SE) is a major medical emergency, causing more than 35,000 deaths each year in the United States. The four research projects of this **Epilepsy** Research Center (ERC) at the Medical College of Virginia of Virginia Commonwealth

University are focused on the CENTRAL THEME of studying SE. These projects compliment each other and the interaction of multi-disciplined investigators around a common theme greatly enhances the development of new insights and research productivity. The four projects will test specific hypotheses developed to investigate clinical aspects and basic mechanisms of SE are: SE: A Clinical and Epidemiological Study; Pathophysiology and Mortality of SE; Genetic Preponderance of SE in Twin Kindreds; and SE Duration- Dependent Modulation of GABAA Receptor Function. The clinical projects will offer important new insights into the epidemiology of SE in the elderly, the neonatal period, the young child, and different ethnic groups. This research will also produce a SE Outcome Scale for identifying high risk patients that can be used for clinical assessment and future therapeutic interventions. The intensive cardiac and central nervous system (CNS) physiological monitoring will test preliminary evidence that persistent CNS excitability predicts HIGH RISK patients for cardiac abnormalities that may ultimately lead to death in SE. In addition, this research effort has identified non-convulsive SE as a major cause of morbidity and mortality and has developed a prospective data base to evaluate this under recognized form of SE in the comatose patient. Utilizing one of the largest twin registries in the world, studies are proposed that provide the first direct evidence that the development of SE in man is controlled in part by a genetic predisposition. Animal models of SE demonstrate that there is a modulation of the GABAA receptor function that underlies the development of SE intractability and resistance to treatment. Studies indicate that alterations in the gamma amino butyric acid (GABA) receptor function play a major role in the pathogenesis of SE. The accomplishments of this research program are enhanced by the collaboration between committed investigators and research projects. The results from this study will ultimately develop new strategies to offer insights into the pathophysiology of SE and improve the diagnosis and treatment of this severe neurological condition.

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- **Project Title: MOLECULAR MECHANISMS OF NEURONAL MIGRATION**

  Principal Investigator & Institution: Gleeson, Joseph G.; Assistant Professor; Neurosciences; University of California San Diego 9500 Gilman Dr, Dept. 0934 La Jolla, Ca 92093

  Timing: Fiscal Year 2002; Project Start 15-JAN-2002; Project End 31-DEC-2006

  Summary: (provided by applicant): Almost nothing is known about how neurons migrate, or about the molecular mechanism regulating this migration. Understanding these mechanisms is critical for our understanding of childhood **epilepsy** and mental retardation, as defects in neuronal migration frequently underlie these disorders. Additionally, one of the major hurdles in neuronal transplantation or regeneration following damage is poor neuronal migration into target areas, which may be overcome through approaches derived from a better understanding of how neurons migrate. One common inherited cause of severe mental retardation and **epilepsy** in humans is classical lissencephaly, defined by a lack of cortical gyri and sulci formation and due to a failure of neurons to properly migrate. Mutations in either of two genes, doublecortin (DCX) or lissencephalyI (LIS1), leads to severe generalized defects in neuronal migration and produces nearly identical lissencephaly in humans. A mutation in the cdk5 gene in mouse also leads to a defect in neuronal migration that is strikingly similar to human lissencephaly. The central hypothesis of this application is that these common mutant phenotypes suggest that there may be interactions between the encoded proteins. The predicted DCX and LIS1 proteins are entirely novel, suggesting they may help define novel molecular mechanisms of neuronal migration, and both were previously shown to

function as microtubuleassociated proteins that are localized around the nucleus. The cdk5 gene is a serinethreonine kinase that phosphorylates some cytoskeletal proteins. However, the role of DCX, LIS1 and cdk5 in neuronal migration is unknown. Additionally, despite the very similar mutant phenotypes, it is untested whether these proteins interact directly to mediate their effect or even act in a common pathway. Therefore the Specific Aims of this proposal are to determine whether: 1) There are genetic or physical interactions between DCX and LIS1. 2) DCX and LIS1 function to regulate nuclear movement during neuronal migration. 3) DCX is regulated by cdk5 during neuronal migration.

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- **Project Title: MRS LOCALIZATION OF ADULTS/PEDIATRIC EPILEPTIC FOCI**

  Principal Investigator & Institution: Ng, Thian C.; Professor of Medicine; Medicine; University of Alabama at Birmingham Uab Station Birmingham, Al 35294

  Timing: Fiscal Year 2001; Project Start 03-APR-1998; Project End 31-MAR-2004

  Summary: (Adapted from Applicant's Abstract): The proposal is designed to use proton magnetic resonance spectroscopic imaging (MRSI) in patients with drug-refractory surgically treatable focal temporal lobe **epilepsy** (TLE) to determine if MRSI spectra of localized abnormal brain metabolites are associated with: 1) the site(s) of maximal electroencephalographic (EEG) epileptiform activity, as determined by video-EEG monitoring of conventional scalp-sphenoidal or by depth-electrode recordings, 2) post-resection histopathologic tissue abnormalities in the MRSI abnormal region of interest (ROI); and 3) post-resection measurement of seizure control as predicted by the locations and extents of qualified anomalies in MSRI metabolites; 4) baseline of functional status of memory and the degree of post-surgery memory loss as determined by IAP and neuropsychological measures; 5) the study of the mechanism of correlations of MRS metabolite disturbances in hippocampal formation (HF) to the HF neuron cell loss (by histopathology) and HF atrophy (by MRI-volumetry). There is a history of using brain imaging in focal **epilepsy,** to lateralize temporal lobe **epilepsy** by fluoro-deoxyglucose positron emission tomography (18F-PET), and gross anatomic pathologies by magnetic resonance imaging (MRI). However, no imaging technique has yet actually tested if more subtle but well-established abnormalities in an epileptic focus can be reliably imaged, such as alterations in various neurochemicals and changes in their concentrations (e.g. glucose-lactate production, high-energy substrate creatine, or membrane substrate choline). Pediatric and adult patients with temporal lobe **epilepsy** (TLE) will be imaged interictally and early postictally by MRSI and MRS. Simultaneous acquisitions of two-dimensional double-spin echo (echo-time 135 msec.) MRSI and conventional MRI (T1, T2 and thin-slice Turbo-Flash) will provide feasibility of in situ metabolic maps for correlation to EEG seizure-onset profiles, and to the surgical regions, and pathoanatomic region(s) studied. Concentrations of and ratios between N-acetyl-aspertate (NAA), choline, (Cho), Creatine (Cr), and Lactate (Lac) will allow multivariate statistical tests with other variables to determine when MSRI of certain chemical substrates may be characteristic of epileptogenic areas of hippocampal sclerosis (neuronal loss and gliosis) and ultimately of seizure control after resection. This research is of great importance to the development of reliable and sensitive diagnostic methods for isolating surgically treatable focal epilepsies as well as the more difficult surgical treatment of childhood focal **epilepsy,** both of which afflict about 1% of Americans.

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- **Project Title: NEURAL NETWORK MODEL OF EPILEPTIFORM ACTIVITY**

  Principal Investigator & Institution: Franaszczuk, Piotr J.; Neurology; Johns Hopkins University 3400 N Charles St Baltimore, Md 21218

  Timing: Fiscal Year 2002; Project Start 01-JUL-1999; Project End 31-AUG-2006

  Summary: (provided by applicant): Epileptic seizures represent abnormal periods of increased excitation and synchronized bursting of large networks of neurons. While various in vitro models for **epilepsy** have provided important insights into cellular, synaptic, and local network behavior, additional models are needed to understand recurrent bursting in more characteristic large neural networks. Unfortunately intact animal models have significant limitations for these studies. In contrast, model neural networks offer a number of distinct advantages for studies of large network behavior, including the ability to exactly model and monitor specific neuronal assemblies with known structure, connectivity and membrane properties. Such model neural networks are now being developed and utilized to study recurrent bursting and seizure propagation. Using reduced compartment neurons based on modified Av-Ron Rinzel equations, networks can be assembled that can simulate recurrent bursting behavior and seizure propagation. Modeling is greatly facilitated by distributed computing with computer clusters, allowing for studies on network arrays of 10 6 or more neurons. Since recurrent seizures produce changes in intrinsic neuronal connectivity, the influences of these changes will be studied through specific models with varying connectivity. The ability to disrupt or terminate this bursting behavior with external excitatory stimuli will be modeled and characterized. The importance of feedback loops in burst termination and the specific parameters of external stimulation that optimize burst termination or disruption will be defined. Both discrete external excitatory pulses and low level external excitatory stimulation will be studied. Brain stimulation for the amelioration or control of epileptic seizures in humans is attracting considerable and growing interest. Unfortunately the optimal parameters for favorable modulation by external excitatory stimulation are not well understood and the applications at present use somewhat arbitrary parameters. The studies proposed here may provide important insights into the important criteria responsible for burst generating in large neuronal arrays. From these results the parameters for application of excitatory stimulation for reduction of repetitive bursting in these models networks can be addressed. Hopefully these insights can be applied to devices useful to patients with uncontrolled **epilepsy.**

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- **Project Title: NEURONAL INJURY AND NEUROPROTECTION IN EPILEPSY**

  Principal Investigator & Institution: Cole, Andrew J.; Massachusetts General Hospital 55 Fruit St Boston, Ma 02114

  Timing: Fiscal Year 2001; Project Start 01-APR-1998; Project End 31-MAR-2004

  Summary: Repeated or prolonged seizures may result in a striking behavioral syndrome comprised of cognitive decline and selective impairment of declarative memory. This consequence of seizures is a major cause of long-term morbidity in patients with **epilepsy** and with isolated convulsions that occur in the setting of metabolic disturbances. Elegant neuropsychological studies have implicated the hippocampus and related structures in the pathophysiology of this acquired behavioral disorder. Human neuropathological studies and animal models of **epilepsy** have repeatedly demonstrated evidence of selective neuronal vulnerability in hippocampus and other limbic structures after seizures. Nonetheless, the molecular and biochemical mechanisms of neuronal injury with subsequent behavioral disturbance following

seizures remain unclear. In preliminary studies using an assay for neuronal injury in an animal model that can be measured and quantitated with cellular resolution, the applicant has demonstrated selective neuroprotective effects of nerve growth factor following kainate-induced seizures. While the trophic properties of NGF appear to require interaction with its high affinity receptor tyrosine kinase, TrkA, NGF also interacts with a low affinity receptor, p75, that is shared with other neurotrophins but whose function is unknown. The mechanisms of trophic factor-mediated neuroprotection remain poorly understood. The proposed studies are designed to understand the mechanism of NGF-mediated neuroprotection in a seizure model, and specifically to examine the hypothesis that NGF neuroprotection in the kainate seizure model is receptor-mediated. The applicant will use anatomic and biochemical assays to examine the neuroprotective properties of several trophic factors, and the distribution and regulation of their respective receptors. As all neurotrophins appear to interact with the low affinity receptor, but each reacts only with a specific high affinity receptor, comparison of protective properties should provide insight as to which, if any, receptor components are necessary. The applicant will also use a transgenic mouse with a defective NGF binding domain and an immunotoxin that selectively lesions p75-bearing neurons to specifically examine the role of the low affinity p75 receptor in neuroprotection.

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- **Project Title: NEURONAL INTERACTIONS IN EPILEPSY/DYSPLASIA**

  Principal Investigator & Institution: Schwartzkroin, Philip A.; Professor; Neurological Surgery; University of California Davis Sponsored Programs, 118 Everson Hall Davis, Ca 95616

  Timing: Fiscal Year 2001; Project Start 01-JAN-1983; Project End 31-AUG-2005

  Summary: (Verbatim from the Applicant's Abstract) Cortical dysplasia is thought to arise from abnormalities in brain cell proliferation, migration, and/or differentiation. Advances in biomedical technology - medical genetics and brain imaging - have confirmed that a high proportion of early-onset epilepsies is associated with such structural abnormalities. Despite this high correlation, we still do not understand what features of dysplasia lead to **epilepsy** - the cause and effect relationship between structural and and functional abnormalities. To gain some insight into the epileptogenic components of dysplastic brain tissue, we propose to analyze animal models in which dysplastic abnormalities are or are not associated with seizure activity. We will test two general hypotheses. First, disruption of normal cortical organization (as seen in models of heterotopia) leads to epileptigenicity by virtue of subsequent reorganization. In such cases, we propose that heterotopic cell regions are rarely the site of seizures initiation, but serves to distribute epileptic discharge generated by surrounding brain regions. To test this hypothesis, we will characterize heterotopic dysplasia seen in the methylazoxymethanol (MAM) rat and in the p35 mouse knockout models of neuronal migration disorder. Second, we hypothesize that disruption of differentiation programs as seen in syndromes such as tuberous sclerosis gives rise to cells with aberrant electrical activity. properties that can trigger epileptic discharges. In such cases we propose that the ''tuber'' containing the aberrant cells serves as an initiator zone. We will explore this hypothesis in the Eker rat model of tuberous sclerosis (heterozygous mutation of the TSC2 gene). Finally, key characteristics obtained from animal model studies will be compared to morphological and electrophysiological properties of human cortical tissue resected from patients with cortical dysplasia and medically-intractable **epilepsy.** By identifying the critical features that are essential for epileptic activity, we will be able to

develop more effective treatments that target seizure-causing aberrations in brain structure and function.

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- **Project Title: NEUROPHYCHOLOGICAL PROGRESSION IN NEW ONSET EPILEPSY**

  Principal Investigator & Institution: Hermann, Bruce P.; Professor; Neurology; University of Wisconsin Madison 750 University Ave Madison, Wi 53706

  Timing: Fiscal Year 2003; Project Start 01-APR-2003; Project End 31-MAR-2008

  Summary: (provided by applicant): Our prior investigation of adults with chronic localization-related (temporal lobe) **epilepsy** and healthy controls has shown childhood onset **epilepsy** to be associated with a generalized adverse neurodevelopmental impact on brain structure and cognitive function (NS-37738). The purpose of this proposal is to directly characterize the timing, cause and consequences of this adverse neurodevelopmental impact. Using a combined cross-sectional and longitudinal design, 75 children (age 8-18) with new onset localization-related **epilepsy** will be compared to 75 age and gender matched controls. Cross-sectional and two-year longitudinal assessment of neuropsychological status and neuroimaging (quantitative MRI, diffusion tensor imaging, and magnetization transfer imaging) will be integrated with information regarding neurodevelopmental history, clinical **epilepsy** characteristics and psychiatric morbidity in order to clarify the timing, etiology and consequences of evident abnormalities in brain structure and cognition. We hypothesize the following: (1) children with new onset localization-related **epilepsy** will exhibit generalized cognitive impairment, generalized reduction in total brain tissue volumes (especially cerebral white matter volumes), and microstructural abnormalities in cerebral white matter compared to controls, (2) frequency of preexisting neurodevelopmental abnormalities will be significantly increased in children with new onset **epilepsy** compared to controls and will be associated with neuroimaging and cognitive abnormalities at **epilepsy** onset, (3) ongoing childhood onset **epilepsy** will be associated with lags in normal cognitive and brain development (especially cerebral white matter) and increased psychiatric morbidity compared to controls, and (4) earlier age of **epilepsy** onset will be the strongest predictor of lags in brain growth and cognitive development while seizure severity will be most strongly associated with increased psychiatric morbidity.

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- **Project Title: NEW STRATEGIES FOR NEOCORTICAL EPILEPSY**

  Principal Investigator & Institution: Rothman, Steven M.; Director of Pediatric Neurology; Neurology; Washington University Lindell and Skinker Blvd St. Louis, Mo 63130

  Timing: Fiscal Year 2003; Project Start 01-APR-2003; Project End 31-MAR-2008

  Summary: (provided by applicant): The treatment of many human epileptic syndromes remains unsatisfactory. While anticonvulsant medications allow about 75% of epileptics to achieve excellent seizure control, the remaining 25% of patients suffer from a combination of continued seizures and medication toxicity. It is unlikely that a single medical breakthrough will provide a cure for all of these refractory patients. Focal neocortical epilepsies have proven particularly difficult to manage. While some respond to anticonvulsants, a large fraction remains intractable to medical therapy. This group can respond to cortical resection, but surgical management is problematic. Exact

identification of the epileptogenic focus can be complicated and there is a risk of unanticipated, irreversible neurological deficits after resection. Focal cortical cooling has the potential to improve the evaluation and treatment of this epileptic subgroup. The aims of the experiments described in this application are to investigate the potential of focal cooling with thermoelectric (Peltier) chips to rapidly terminate chronic seizure discharges, determine the degree of cooling required to stop these seizures, determine whether cooling can prevent seizures, and develop computer programs that recognize and anticipate seizures in "real time". In addition, the potential pathological consequences of cortical cooling will be determined. These experiments represent a necessary first step toward utilizing these techniques for the therapy of human **epilepsy.** These experiments will utilize models of acute and chronic rodent neocortical seizures and small Peltier devices developed for the microelectronics industry. If Peltier devices can control focal seizures in our models, they will be refined for future experiments to investigate their potential role in mapping and controlling epileptogenic neocortex in man.

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- **Project Title: NON-RADIAL CELL MIGRATION IN CNS DEVELOPMENT**

  Principal Investigator & Institution: Golden, Jeffrey A.; Associate Professor of Pathology; Children's Hospital of Philadelphia 34Th St and Civic Ctr Blvd Philadelphia, Pa 19104

  Timing: Fiscal Year 2003; Project Start 15-FEB-2003; Project End 31-DEC-2007

  Summary: (provided by applicant): **Epilepsy,** mental retardation and structural anomalies of the brain often have a genetic etiology. Although they affect 3-5% of all children, the underlying pathogeneses for these disorders is poorly understood in most cases. Cell migration is a central component of normal central nervous system (CNS) development and disruptions in this process have been implicated in the development of multiple disorders such as Fukuyama Muscular dystrophy, Miller-Dieker Syndrome, Walker-Warburg Syndrome, and the Muscle-Eye-Brain syndrome to name just a few. Two primary patterns of cell migration are recognized during CNS development, radial and non-radial. While the cellular and molecular bases of radial cell migration, long considered the predominant mode of cell migration, have begun to be defined, the mechanisms of guidance for non-radial cell migration remain largely unexplored. Using lineage analysis, we have defined the developmental time and location where non-radial cell migration begins in the chick forebrain. Based on these data we have developed a model to explain the cellular and molecular mechanisms of non-radial cell migration. Our model is based on the hypotheses that cell surface molecules, secreted molecules, and extracellular matrix molecules guide non-radially migrating cells. This proposal will begin to address our hypothesis by 1) directly testing several components of our model, and 2) generate a mammalian model to further study one of the molecules we have identified as a component of non-radial cell migration in the chick. These data will certainly enhance our understanding of normal CNS development. Furthermore, we anticipate the data from these studies will provide insight into the pathogenesis of a variety of inherited and non-inherited conditions that afflict children such as **epilepsy,** mental retardation and structural malformations of the brain. This may ultimately lead to improvements in the diagnosis, management, and prevention of neurological diseases where abnormal cell migration has a pathogenetic role.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: NONVESICULAR GABA RELEASE VIA GABA TRANSPORTER REVERSAL**

  Principal Investigator & Institution: Richerson, George B.; Associate Professor; Neurology; Yale University 47 College Street, Suite 203 New Haven, Ct 065208047

  Timing: Fiscal Year 2002; Project Start 01-APR-2002; Project End 31-MAR-2006

  Summary: As one of the most common neurological diseases in this country, **epilepsy** affects approximately 2.5 million Americans. Drugs used to treat **epilepsy** often target neurotransmission, and their design and use would be advanced by a better understanding of the mechanisms of neurotransmission. It is commonly assumed that neurotransmitters are only released by synaptic vesicle fusion. However, our recent studies suggest that GABA transporters reverse during seizures, resulting in GABA efflux. This "nonvesicular" GABA release inhibits neurons, and is also the target of a new class of anticonvulsants, including gabapentin and vigabatrin. The current proposal extends this work by using rat neurons to address the following unanswered questions. What is the source of nonvesicular GABA release: neurons or glia? This will be examined using neuronal vs. glial specific GABA transporter antagonists in pure neuron, pure glia or mixed cultures. How do changes in cytosolic [GABA] affect vesicular GABA release? The effect on vesicular and nonvesicular GABA release of increasing or decreasing cytosolic [GABA] will be compared. How commonly is nonvesicular GABA release modulated by anticonvulsants? The effects on nonvesicular GABA release of pregabalin, topiramate, levetiracetam, and tiagabine will be studied. How ubiquitous is nonvesicular GABA release? The role of nonvesicular GABA release will be studied in brain slices from the hippocampus, neocortex, striatum, cerebellum and medulla. Does the glutamate transporter reverse as easily as the GABA transporter? The threshold for nonvesicular glutamate release will be determined. We propose that the GABA transporter reverses as part of a fail-safe negative feedback system. If the glutamate transporter reversed so easily, it would lead to runaway excitotoxicity. The proposed experiments are designed to answer fundamental questions about the newly recognized role of the GABA transporter in inhibition of seizures, and the mechanism of action of anticonvulsants. A complete description of GABA transporter function should help define the pathophysiology of **epilepsy,** and lead to a better understanding of how and when the new anticonvulsants should be used.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: NOVEL AMPA RECEPTOR ANTAGONIST FOR TREATMENT OF EPILEPSY**

  Principal Investigator & Institution: Pei, Xue-Feng; Annovis, Inc. 34 Mt. Pleasant Dr Aston, Pa 19014

  Timing: Fiscal Year 2001; Project Start 30-SEP-1997; Project End 31-JUL-2003

  Summary: adapted from applicant's abstract): Bearsden Bio Inc. has developed novel compounds that selectively regulate glutamate receptor subtypes. In Phase I we synthesized a large number of AMPA receptor allosteric antagonists and tested them for inhibition of APA and kainate induced calcium influx into cortical cells. We were able to group the over 50 compounds into categories and determine their structure/activity profile. We also tested the activity of some promising compounds against MES induced seizures and compared it to their sedative effect on the rotarod. Our structure activity program from Phase I produced ligands that exhibit good affinity for AMPA receptors and promising separation between the desired anticonvulsant response and the major side effect, the drop in performance on the rotarod. We continued to synthesize new

analogs to better understand the structure activity relation of the compounds and we have, to date, identified several more compounds with promising in vitro activity. We are seeking Phase II funding to better understand the mechanism of action of these novel AMPA antagonists including their subtype specificity and efficacy animal models of **epilepsy** to determine the best compound for further development we will select an allosteric AMPA antagonist as lead candidate for the treatment of **epilepsy.** The preclinical studies about Phase II will include pharmacokinetics, metabolism and toxicity. At the same time we will be preparing alternative candidates for use as back-ups in the event our lead should not have the requisite properties of a clinical candidate for the treatment of **epilepsy.** PROPOSED COMMERCIAL APPLICATION: Not Available

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: NPY DEPRESSION OF HIPPOCAMPAL EPILEPSY**

  Principal Investigator & Institution: Van Den Pol, Anthony N.; Professor; Neurosurgery; Yale University 47 College Street, Suite 203 New Haven, Ct 065208047

  Timing: Fiscal Year 2001; Project Start 15-APR-1999; Project End 31-MAR-2003

  Summary: (Applicant's abstract) Hippocampal **epilepsy** is characterized by synchronized hyperexcitable neurons. Many of the neurons in the hippocampus release the excitatory transmitter glutamate which contributes to the excitation. The general hypothesis that endogenous neuromodulators may influence levels of excitability in the hippocampus will be examined. Specifically, we will focus on neuropeptide Y (NPY) inhibition of excitatory neurons in the epileptic human hippocampus, and in a rat model of **epilepsy.** NPY is found throughout the hippocampus in both neurons and in presynaptic axons. It has been suggested as one of the brain's natural anti-seizure transmitters, and its expression and distribution appears to change with **epilepsy.** The presynaptic role of NPY in reducing glutamate actions will be studied with whole cell recordings in slices of the human hippocampus. Using a simplified model of hyperexcitability consisting of a single self-innervating rat hippocampal neuron, we will examine the effect of NPY and specific receptor agonists to test the hypothesis that NPY acts by a presynaptic mechanism via Y2 and Y5 receptors to reduce glutamate release in neurons showing epileptiform activity. In parallel we will directly test the hypothesis that NPY blocks glutamate release presynaptically by using the dye FM1-43 to study transmitter vesicle exocytosis in glutamatergic neurons. The hypothesis that NPY is found in GABAergic neurons will be tested with dual ultrastructural immunocytochemistry. The hypothesis that changes in neuronal activity mediated by glutamate will alter levels of expression of NPY and NPY receptor Y1-Y5 mRNA will be tested with cDNA-PCR and Northern blot analyses in parallel studies of different regions of the epileptic human and rat hippocampus and in a tissue culture model of hyperexcitable rat hippocampal neurons. NPY is potentially of great interest because its primary action in the normal hippocampus appears to be one of depressing hyperexcited neurons, without a substantial effect on normal neurotransmission.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: OPTICAL INTRINSIC SIGNAL IMAGING OF SEIZURE**

  Principal Investigator & Institution: Chen, James Wy.; Neurology; University of California Los Angeles 10920 Wilshire Blvd., Suite 1200 Los Angeles, Ca 90024

  Timing: Fiscal Year 2002; Project Start 01-APR-2002; Project End 31-MAR-2007

Summary: (provided by applicant): The development of both structural and functional neuroimaging has progressed significantly in the last decade. However, clinical application of functional neuroimaging techniques in **epilepsy** has been complicated by their unsatisfactory temporal and spatial resolution. Optical imaging of intrinsic signals (OIS) is a functional neuroimaging technique that measures cortical reflectance changes with millisecond temporal resolution and micron spatial resolution. These optical images are correlated with neuronal activity and are due to changes in cerebral blood volume, light scattering, and in hemoglobin and cytochrome oxidation state. In the preliminary studies, OIS was recorded from the somatosensory cortex of rats at, near infrared frequency (850 nm). OIS was shown to correlate well with seizure activities, in a recoverable and reproducible fashion. It was also noted that OIS changes could precede the initial EEG spikes for up to I minute. The goal of this project is to correlate multiplewavelength optical signals with both electrophysiological and immunohistochemical markers, and to establish a primary foundation of interpreting OIS seizure data. The results of this project can be applied in the future in various **epilepsy** models, such as in a cortical kindling model for the study of neuronal network behaviors during kindling process. OIS imaging might hold a promising potential of better understanding of epileptogenesis, seizure induction, cessation and propagation pathways. Additional application of OIS imaging during **epilepsy** surgery in defining the eloquent cortex and confirming the seizure focus should be explored thoroughly in the future. The candidate, Dr. Chen, is a neurologist and a cellular electrophysiologist who has the expertise of using patch clamp technique. His career goal is to elucidate the basic mechanisms of **epilepsy** by integrating all the research skills that he has learned or will learn in electrophysiology, optical imaging, neurochemistry and computer simulation. This project will be conducted at the UCLA School of Medicine under Drs. Toga and Wasterlain's guidance. Both mentors are internationally known authorities in their respective fields of research.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: PHARMACOGENOMIC STUDY OF ANTICONVULSANT THERAPY**

  Principal Investigator & Institution: Ferraro, Thomas N.; Associate Professor; Psychiatry; University of Pennsylvania 3451 Walnut Street Philadelphia, Pa 19104

  Timing: Fiscal Year 2001; Project Start 29-JAN-2001; Project End 31-DEC-2003

  Summary: (adapted from applicant's abstract): Many patients with **epilepsy** are resistant to standard anticonvulsant drug (ACD) treatments. This proposal seeks to elucidate the origin of the genetic factors that affect individual response to ACDs by mapping the location of genes that influence these responses in mice. There are 2 phases to this proposal. Phase 1 involves identifying mouse strains best suited for dissecting the genetic influences which control response to specific ACDs. Phase 2 involves mapping these genetic influences to defined regions of the genome. In phase 1, strain-specific maximal electroshock seizure threshold (MEST) will be characterized. Strains with similar mean MESTs will be considered equivalently seizure-sensitive and such pairs of strains will be used for subesequent anticonvulsant drug (ACD) testing. ACD testing will involve dose-reponse studies with a panel of clinically relevant ACDs: phenytoin, carbamazepine, vaiproic acid and gamma-vinyl GABA. The quantitatve endpoint will be the absolute MEST determined in the presence of drug. Strains will be selected for quantitative trait loci (QTL) analyses based on their strain-specific response such that pairs of strains exhibiting the largest differential effects on MEST for a given drug (the strains showing the largest and smallest anticonvulsant effects) will be used for QTL studies. Brain levels of ACDs will be determined in parental strains in order to address

one possible major co-phenotype in correlation with the anticonvulsant MEST response. In phase 2, QTL mapping studies will be conducted using mouse strains suggested by phase 1 phenotype studies. Mapping will utilize segregating F2 (intercross) populations for each strain pair. Quantitative phenotype for mapping will be MEST in individual F2 mice pretreated with a specific ACD. Brain ACD levels will be determined in F2 animals and used as a second quantitative phenotype for mapping. In order to distinguish ACD response QTLs from seizure sensitivity QTLs which may segregate in the cross, a parallel QTL study will be conducted for each ACD using an independent F2 population tested for MEST following saline rather than ACD pretreatement. QTL genotype and mapping experiments will combine a 15-20 cM genome scan with comprehensive statistical analyses including both parametric and non-parametric single and multilocus models. Results will lead to the direct localization of genes that influence anticonvulsant responses in mice with future directions involving the identification of these genes. The described studies build directly from the foundation of work in the investigator's lab on mapping mouse loci involved in differential sensitivity to chemically- and electrically-induced seizures and ultimately will lead to a focused strategy for investigating genetic influences on response to anticonvulsant drugs in humans with **epilepsy.** The association of human anticonvulsant response with specific genomic variants will lead to more rational decisions regarding the choice of drug for individual patients and will lead to greater success in treating seizures disorders in general.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: PHENOTYPE DEFINITION IN THE GENETICS OF EPILEPSY**

  Principal Investigator & Institution: Winawer, Melodie; Gertrude H Sergievsky Center; Columbia University Health Sciences New York, Ny 10032

  Timing: Fiscal Year 2001; Project Start 30-SEP-2000; Project End 31-AUG-2005

  Summary: (Adapted From The Applicant's Abstract): Previous studies have shown that genetic factors influence not only the risk of **epilepsy** but also its clinical features. However, it remains unclear which individual clinical features have an inherited basis and how these characteristics might cluster as a result of a common genetic cause. We propose to systematically examine which clinical features of **epilepsy** best reflect differences in susceptibility, and therefore could be used to divide the epilepsies into subgroups appropriate for linkage analysis. Although some EEG abnormalities have been shown to have a genetic component, the genetic relationship between these EEG abnormalities and clinically manifest **epilepsy** needs further exploration. The applicant will examine the way in which generalized EEG abnormalities aggregate in families concordant or discordant for generalized or focal **epilepsy** to investigate how these abnormalities should best be used to define families or an individual's disease status for linkage analysis. The applicant will address the problem of phenotype definition in **epilepsy** in approximately 130 families containing multiple individuals with idiopathic/cryptogenic **epilepsy** ascertained in the **Epilepsy** Family Study of Columbia University. The applicants will conduct semi-structured telephone interviews and EEGs on a subgroup of these families. Their aims are to: (1) evaluate the consistency of clinical features within families, classifying by seizure type, syndrome type, specific seizure symptoms, and age at onset; (2) evaluate EEG abnormalities within families concordant and discordant for seizure type; and (3) develop an instrument to assess **epilepsy** severity and use this instrument to evaluate the consistency of **epilepsy** severity as a clinical feature within families. This applicant is trained as an academic clinical neurologist with specialization in epilepsy/clinical neurophysiology and neuroepidemiology. This grant will enable her to develop an academic career in

neurology and genetic epidemiology by allowing her to (1) collaborate with neurologists and genetic epidemiologists in the Sergievsky Center, (2) learn methods of genetic epidemiology, statistical genetics, laboratory and computational techniques in molecular genetics and (3) gain independence as a clinical investigator, through the combined responsibilities of formal coursework, conferences and research. Drs. R. Ottman, W.A. Hauser, S. Hodge, T. C. Gilliam and M. Morrell will provide guidance in these endeavors.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: PHOTOTHROMBOTIC BRAIN INFARCTION AND EPILEPTOGENESIS**

  Principal Investigator & Institution: Kelly, Kevin M.; Associate Professor of Neurology; Allegheny-Singer Research Institute 320 E North Ave Pittsburgh, Pa 15212

  Timing: Fiscal Year 2003; Project Start 30-SEP-2003; Project End 31-MAY-2006

  Summary: (provided by applicant): Poststroke seizures and **epilepsy** have been described in numerous clinical and population studies. In contrast, the pathophysiological events of injured brain that establish poststroke epileptogenesis are not well understood because animal modelinq has had limited development (Kelly, 2002). In the elderly, stroke is the dominant cause of **epilepsy** yet the modeling of poststroke **epilepsy** in aged animals has had only preliminary study (Kelly et al., 2001a). Recent studies in our laboratory have indicated that the technique of cortical photothrombosis and brain infarction can result in poststroke **epilepsy** in young adult rats characterized electrically by seizures originating in the peri-infarct area and behaviorally by motor arrest of the animal (Kelly et al., 2001a, Kharlamov et al., submitted). In contrast, mid-aged and aged animals demonstrated behavioral seizures characterized by brief but relatively intense rhythmic body jerking associated with focal features (Kelly et al., 2001a). We hypothesize that poststroke epileptogenesis is expressed differentially in an aging-related manner and propose to more appropriately model poststroke **epilepsy** in the elderly by using photothrombosis and an aging paradigm. Specific Aim #1 will characterize, compare, and contrast the electroencephalographic, behavioral, and neuroanatomical properties of 4 and 20 mo old F344 rats during epileptogenesis and the epileptic state. During photothrombosis, NMDA receptor-mediated events have been implicated in establishing subsequent cortical hyperexcitability, which could lead to the development of epileptic seizures. We hypothesize that neuroprotection limiting glutamate-mediated excitotoxicity associated with photothrombosis will prevent poststroke epileptogenesis. Specific Aim #2 will determine whether MK-801, a non-competitive NMDA receptor antagonist, is capable of preventing poststroke epileptogenesis and whether animal age is a critical variable. The short-term goals of these studies are to establish a reliable animal model of poststroke **epilepsy** in the elderly and to begin neuroprotection studies designed to prevent or limit poststroke epileptogenesis. The long-term goal of these studies is to advance understanding of the progressive anatomic and physiologic changes of aged brain during poststroke epileptogenesis so that the focus of therapeutic strategies can shift from control of symptoms (seizures) to prevention and cure.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: PHYSIOLOGIC ANALYSIS OF TWO GABAR GAMMA2-SUBUNIT DOMAINS**

  Principal Investigator & Institution: Gallagher, Martin J.; Neurology; Vanderbilt University 3319 West End Ave. Nashville, Tn 372036917

Timing: Fiscal Year 2002; Project Start 01-AUG-2002; Project End 31-MAY-2007

Summary: (provided by applicant): This proposal describes a 5-year-training program for the development of an academic career in neurology and **epilepsy.** The principal investigator has completed residency training in neurology at Washington University in St. Louis and will complete a clinical **epilepsy** fellowship at Washington University in June 2002. He will then expand upon his scientific skills as an Assistant Professor of Neurology in the **Epilepsy** Division at Vanderbilt University Medical School. This program will promote the command of electro physiology, as applied to **epilepsy.** Robert L. Macdonald, MD, PhD will mentor the principal investigator's scientific development. Dr. Macdonald is a recognized leader in the field of electro physiology. He is the Chair of Neurology and has trained numerous K08 recipients, post-doctoral fellows and graduate students. In addition, close interaction with faculty in the Department of Neuroscience will provide additional scientific and career advice. Research will focus on the physiology and pharmacology of the gamma amino butyric acid receptor type A (GABAAR), the main fast inhibitory ion channel in the central nervous system. The GABAAR is the target of several anti-epileptic drugs, is associated with point mutations in at least two forms of human familial **epilepsy,** and is hypothesized will have an altered modulation by zinc in temporal lobe **epilepsy.** The proposed experiments entail construction of mutant and chimeric GABAARs, expressing the recombinant receptors in cultured cells, and determining their physiological kinetic parameters by rapid-application of drugs to macropatches and by analysis of single channel currents. The Specific Aims include: 1) evaluating the physiology GABAAR containing the point mutations found in human **epilepsy,** 2) determining the effect of allosteric modulators on the same GABAAR mutants, 3) determining the binding domains of zinc, and 4) determining the effect of GABAAR modulators on zinc inhibition. The Neurology Department at Vanderbilt University provides an ideal setting for training physician-scientists by incorporating expertise from diverse resources into customized programs. Such an environment maximizes the probability that the principal investigator will establish a scientific niche and embark upon a successful independent academic career.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: PHYSIOLOGY OF THALAMOCORTICAL RHYTHMICITY IN VITRO**

  Principal Investigator & Institution: Coulter, Douglas A.; Associate Professor; Children's Hospital of Philadelphia 34Th St and Civic Ctr Blvd Philadelphia, Pa 19104

  Timing: Fiscal Year 2001; Project Start 01-JUL-1992; Project End 31-MAY-2003

  Summary: GABAergic inhibition plays an atypical "pro-oscillatory" role in the thalamocortical (TC) system. Unlike most other brain areas, where inhibition checks excessive synchronous activation, in the TC system, inhibition synchronizes and drives rhythmic oscillatory behavior involving the tightly interconnected synaptic circuit comprised of thalamus, nucleus reticularis thalami (NRT), and neocortex. Within this circuit, the GABAergic NRT neurons are pacemakers, synchronizing TC rhythms via their powerful inhibitory connections onto neighboring thalamic neurons. TC oscillations normally occur during slow wave sleep, and pathological variants of these rhythms include the spike wave discharges of Generalized Absence **epilepsy,** and generalized tonic clonic seizures characteristic of most convulsive forms of **epilepsy.** In these normal and pathological TC oscillations, the nature of cellular activity is fundamentally dissimilar, and these differences may reflect the added contributions of the neocortex to pathological rhythms. The central hypothesis underlying the research to be conducted in this proposal is that mechanisms involved in determining these distinct

patterns of activity in pathological and nonpathological TC oscillations fundamentally depend on the cellular and regional properties of GABAergic inhibition within the TC system. Studies proposed in this application are designed to investigate and test this hypothesis through research centered on 3 specific aims: 1. Characterize inhibitory synaptic activity recorded under normal and pathological conditions in thalamic and NRT neurons; 2. Determine how intrinsic thalamic interneurons contribute to generation of TC rhythms; and 3. Investigate how chronic epilepsy-associated alterations in GABAergic inhibition in the TC system contribute to enhanced seizure susceptibility. Results of this research could provide important insight at cellular, synaptic, and molecular levels into mechanisms critically involved in GABAergic regulation of normal and pathological TC rhythmicity. This provides new directions to exploit in therapeutic intervention to control epileptic TC oscillations, as well as new insight into processes potentially altered in genetic forms of **epilepsy** involving pathological function of the TC system.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: PILOT TRIAL OF THALAMIC STIMULATION FOR EPILEPSY**

  Principal Investigator & Institution: Fisher, Robert S.; Neurology & Neurological Scis; Stanford University Stanford, Ca 94305

  Timing: Fiscal Year 2001; Project Start 30-SEP-2001; Project End 31-JUL-2002

  Summary: (Applicant's Abstract): This application proposes a clinical pilot study of anterior nucleus thalamic stimulation (ANTS) as a treatment for intractable **epilepsy,** in order to lay the groundwork for a larger randomized, controlled clinical trial. Studies by the principal investigator and others have suggested that thalamic stimulation is useful for treatment of seizures in animal models and potentially in patients. **Epilepsy** affects about 1% of the U.S. population, and approximately 25% are not helped by existing therapies. Therefore, the need for new therapies is great. Study subjects will have partial **epilepsy** with or without secondarily generalized seizures, at least 10 per month, and not responsive to standard medical or surgical therapies. Stimulating electrodes will be implanted bilaterally in the anterior nucleus of thalamus and connected subcutaneously to subclavicular stimulators. A combination of physiological and anatomical techniques will be used to verify proper electrode placements. Stimulation will be delivered continuously as 90 microsecond pulses at 100/s, for one minute on and five minutes off, at five Volts amplitude. A blinded lead-in design will be used to establish safety and a preliminary evaluation of efficacy of this therapy. Specific aims of the pilot trial will be to establish that ANTS targeting can be accomplished in the operating room with accuracy of 5 mm or better. The pilot will show that it is possible to develop a suitable double-blind test protocol. The study will establish that a high level of stimulation at 5 V, 90 us, 100 Hz is as well-tolerated as is a low level of stimulation at 1 V, 90 us, 100 Hz, thereby allowing future trials to use high levels of stimulation. Sub-projects to be done at selected study sites will determine whether PET scans can provide metabolic maps of brain sites activated by thalamic stimulation, whether EEG spikes and seizures can be recorded from ANT, whether unit recording increases accuracy of electrode placement, and whether ANTS affects neuropsychologic testing. The pilot study will serve to develop a group of investigators experienced with ANTS for future trials, to identify institutions at which the protocol successfully can be completed, and to provide an accurate sample size estimate for a definitive trial. A consortium of centers experienced in **epilepsy** research will collaborate on this project, which will move brain stimulation for **epilepsy** into the realm of a testable new therapy for intractable seizures.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: PLASTICITY OF GABAERGIC INHIBITION FOLLOWING HEAD INJURY**

  Principal Investigator & Institution: Soltesz, Ivan; Assistant Professorr; Anatomy and Neurobiology; University of California Irvine Irvine, Ca 926977600

  Timing: Fiscal Year 2001; Project Start 01-JUN-1997; Project End 31-MAY-2002

  Summary: Two million people suffer traumatic brain injury in the US every year, and among young adults head injury is the leading cause of death and disability. Of head injury survivors, 10 percent-15 percent develop post-traumatic **epilepsy,** and following penetrating head injuries this number increases to 53 percent, presenting an enormous social and medical problem. However, the mechanisms by which head injury gives rise to **epilepsy** are poorly understood. The dentate gyrus of the hippocampal formation plays a central role in the regulation of excitability in the epilepsy-prone cortico-limbic system. The inhibitory control of dentate granule cells, the principal output neurons of the dentate gyrus, is provided by local gamma-aminobutyric acid-releasing (GABAergic) interneurons. The goal of this study is to test the overall hypothesis that head injury results in a severe, long-lasting disturbance of the GABAergic control of dentate granule cells. The hypothesis will be tested using the lateral fluid percussion model of head trauma in rodents, and the assessment will be carried out with immunocytochemical and electrophysiological methods ar various time points after surgery. Our preliminary data indicate that head injury affects the survival of a crucially important GABAergic interneuronal class (the parvalbumin-immunoreactive basket and axo-axonic cells in the dentate hilus), which provide the perisomatic inhibitory control of granule cells. Furthermore, our data also indicate that head injury results in the appearance of novel GABAA receptor properties, and paradoxically increases the excitatory innervation of the surviving interneurons. The experiments of this proposal are designed to specifically target cellular-synaptic mechanisms underlying trauma-induced hyperexcitability. It is anticipated that defining the functional effects of head trauma on neurons, especially those in epilepsy-prone brain regions such as the hippocampal formation, will help the future development of novel anti-epileptic treatment strategies.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: PLASTICITY OF LANGUAGE NETWORKS IN CHILDHOOD EPILEPSY**

  Principal Investigator & Institution: Gaillard, William D.; Associate Professor; Children's National Medical Center Washington, D.C., Dc 20010

  Timing: Fiscal Year 2002; Project Start 01-SEP-2002; Project End 31-JUL-2007

  Summary: (provided by applicant): This study will examine the effects of seizures on the functional anatomy of language skills in children with both early onset and chronic **epilepsy.** This population provides an opportunity to gain insight into the effect of chronic neuronal dysfunction on the development of human language abilities and their brain representation. We hypothesize that seizures cause neuronal injury and force reorganization of the representation of essential cognitive skills, such as language. Patients with early **epilepsy** onset are expected to have greater variation in fMRI language activation patterns than those with later onset; these changes are expected to occur only after several years of **epilepsy.** Children will be evaluated with high resolution structural 1.5 Tesla MR.1, and functional MRI. Image data will also be transformed into a standard brain atlas to facilitate intra-subject regional comparison, as well as to account for inter-subject variability of language activation patterns. Three

groups will be compared: 1) children within one year after localization related seizure onset 2) children with chronic localization related **epilepsy** (>3 years duration) 3) a normal control population. As a result of this study a greater understanding of the anatomic organization of language during critical periods of cognitive development and neuronal plasticity will be gained. We will determine whether seizures themselves or a common brain pathology is the driving force behind brain plasticity. Such information is important to plan intervention strategies to mitigate the sequelae of **epilepsy** at disease onset and in the most vulnerable children to its effects. Unlike acute and limited neuronal insults, such as head trauma and stroke, **epilepsy** is a chronic process with continuing but paroxysmal neuronal sequelae. Furthermore, patients may be identified and evaluated at the outset of the disease process so that the neuronal response and degree of plasticity may be assessed and monitored.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: PRESYNAPTIC TRANSPORT OF GLUTAMATE FOR GABA SYNTHESIS**

  Principal Investigator & Institution: Mathews, Gregory C.; Neurology; Vanderbilt University 3319 West End Ave. Nashville, Tn 372036917

  Timing: Fiscal Year 2003; Project Start 15-AUG-2003; Project End 31-JUL-2008

  Summary: (provided by applicant): The research and training plan will be conducted jointly at the NIH and Johns Hopkins University. The proposed plan contributes to a long term research interest in the physiology of inhibitory synaptic transmission and how it is altered during epileptogenesis, and a long term career goal of building an independent research and clinical program where basic mechanisms of synaptic transmission are applied to the study of **epilepsy** and the development of new treatment strategies. The ability of inhibitory synapses to maintain their strength and to adapt in response to increased demands will be a central issue in understanding the causes and the treatment of **epilepsy.** The central hypothesis is that GABA synthesis by inhibitory neurons is regulated by the transport of its precursor, glutamate, into their synaptic terminals, and, as a result, inhibitory transmission is regulated by the release of glutamate from excitatory terminals. The Specific Aims are to investigate the contribution of neuronal glutamate transporters and other sources of glutamate for GABA synthesis for inhibitory synapses, to examine whether the amount of GABA packaged into vesicles is regulated due to the modulation of glutamate transporters, and to demonstrate whether released glutamate is used to augment GABA release in response to increased or excessive excitation, such as during seizures. It is our expectation that by revealing mechanisms by which GABA synthesis and release are maintained and regulated, we can identify what alterations might contribute to epileptogenesis and where therapeutic interventions could be targeted. To advance the research goals, I will spend 2 years to become skilled in the techniques of synaptic electrophysiology and data analysis with Dr. Jeffrey S. Diamond, an NIH investigator with expertise in the role glutamate transporters in synaptic transmission. In the later years, while continuing my interaction with Dr. Diamond, I will also establish an electrophysiology laboratory at Hopkins. The oversight of my research and career development by Dr. Jeffrey D. Rothstein, who is an expert on the biology glutamate transporters and their role in neurologic disease, will become increasingly important as I make this transition. During the entire time, I will continue to develop my clinical expertise in the treatment of **epilepsy** at Johns Hopkins, among a group of faculty members with whom I have already worked for several years.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: PROTON MR SPECTROSCOPIC IMAGING OF EPILEPSY**

  Principal Investigator & Institution: Maudsley, Andrew A.; Professor; Northern California Institute Res & Educ San Francisco, Ca 941211545

  Timing: Fiscal Year 2001; Project Start 15-AUG-2001; Project End 31-JUL-2002

  Summary: Proton MR Spectroscopic Imaging (MRSI) enables non- invasive measurement of tissue metabolite distributions and offers considerable potential as a diagnostic imaging technique for localization of **epilepsy,** a devastating condition that affects thousands of children and adults. The proposed technique development is aimed at improving the effectiveness of these techniques for presurgical evaluation of **epilepsy.** The measurement of metabolite distributions in human brain is possible with only modest spatial resolution, for which conventional Fourier reconstruction methods result in errors associated with the truncated sampling. To improve the quality of the metabolite images, new reconstruction methods will be developed that do not suffer from these limitations and which enable improved spatial resolution for reconstruction of stronger metabolite signals. This will be achieved by using a Bayesian framework to incorporate known spatial and spectral information into an optimization reconstruction procedure. Although computationally intensive, these new methods can now be practically applied with the availability of low-cost multiprocessor computers. A second aim of this proposal is to develop methods for measurement of brain pH distributions using proton MR observation, which will provide additional diagnostic information as well as improving understanding of metabolic changes associated with **epilepsy.** This will be achieved by using a signal enhancement technique based on the administration of histidine and development of specialized parametric spectral analysis procedures. This measurement will offer increased sensitivity over previously used phosphorus measurements, as well as providing the capability for pH measurement on standard clinical MRI instrumentation. The developed MRSI techniques will be evaluated for detection of focal metabolic abnormalities associated with **epilepsy.** The improved metabolite image reconstruction and regional pH measurement techniques also have potential clinical applications in other areas, such as cancer, stroke, and brain trauma.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: QUALITY OF LIFE IN NEWLY DIAGNOSED EPILEPSY AND SEIZURES**

  Principal Investigator & Institution: Ficker, David M.; Assistant Professor; Neurology; University of Cincinnati 2624 Clifton Ave Cincinnati, Oh 45221

  Timing: Fiscal Year 2001; Project Start 05-APR-2000; Project End 31-MAR-2005

  Summary: (Adapted From The Applicant's Abstract): This proposal is for a Mentored Patient-Oriented Research Career Development Award. The candidate's immediate goal during this award is to gain expertise in the design, implementation and analysis of epidemiologic studies in the field of **epilepsy.** The long-term career goals are to develop a large-scale **epilepsy** epidemiology program in an urban population that will serve as a basis for studies on incidence of **epilepsy, epilepsy** prognosis (including predictors of response to treatment), mortality, morbidity, genetics and economic costs of **epilepsy.** In order to attain these goals there are two major areas of focus for this award. The first area of focus is a formal program in epidemiology and biostatistics in the Environmental Health Department of the University of Cincinnati College of Medicine. The candidate will take formal coursework in epidemiology and biostatistics with the anticipation that a Masters degree in epidemiology will be obtained. The second area of focus is the development of a research project in **epilepsy** epidemiology. The research portion of

this award will examine health related quality of life (HRQOQ issues in patients with newly diagnosed **epilepsy** and single seizures. **Epilepsy** is a chronic neurologic condition that may affect HRQOL by interfering with employment or driving. Patients take a daily dose of medication that may produce adverse effects. Patients with a new diagnosis of **epilepsy** or a single seizure may have a greater impact on HRQOL because of important changes in lifestyle that need to be made after the diagnosis is made. Prior HRQOL studies have been performed in patients with intractable seizures. The specific aims of the project are to: 1) Assess initial HRQOL measures in a cohort of patients with newly diagnosed single seizures or a new diagnosis of **epilepsy** using a specific HRQOL in **epilepsy** inventory (QOLIE-89). 2) Prospectively examine for subsequent changes in HRQOL in this cohort of patients. 3) Examine for potential mechanisms that may be responsible for changes in HRQOL. 4) Determine if seizure recurrence negatively impacts HRQOL. This study will prospectively gather HRQOL data and neurologic histories and examinations in the cohort every four months for a minimum of two years. Mentors for this project are Drs. Joseph Broderick and Michael Privitera. Dr. Broderick has significant experience in developing stroke epidemiology projects and will provide the candidate the necessary guidance and support to develop his own research program. Dr. Privitera has led the **epilepsy** program at the University of Cincinnati since 1987 and will serve as a resource for clinical **epilepsy.** After the completion of this award, it is anticipated that the candidate will develop larger scale projects in the area of the epidemiology of **epilepsy.**

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: RISK AND PREDICTORS OF INTRACTABLE EPILEPSY IN CHILDREN**

  Principal Investigator & Institution: Berg, Anne T.; Professor; None; Northern Illinois University De Kalb, Il 60115

  Timing: Fiscal Year 2001; Project Start 15-JAN-1993; Project End 31-DEC-2001

  Summary: (Adapted from the Applicant's Abstract). This application is to continue an ongoing community-based study of the risks and predictors of intractable **epilepsy** in a prospectively identified cohort of children with newly diagnosed **epilepsy,** recruited from offices of child neurologists in Connecticut. Information comes from medical record review, interviews and follow-up calls. The primary goals are to determine the probability and to identify predictors of intractable **epilepsy** and of remission. **Epilepsy** is a common disorder. Through the 1980's the estimated cumulative risk of childhood and adolescent **epilepsy** was about 1.0% with remission occurring to 70% to 80%. Despite overall high remission rates, a substantial minority, 10-20%, develop intractable **epilepsy,** a severe, chronic, disabling condition. There is almost no information about the risk or predictors of intractability children. This is especially important with the increasing use of **epilepsy** surgery in children which has occurred in the nearly complete absence of any information about prevention, prediction, and eventual remission (without surgery) of intractability. Very recent (1993-1994), population-based studies have reported 40-50% decreases in the incidence of childhood **epilepsy,** possibly secondary to changes in causes of **epilepsy** and also improvements in diagnosis with correct recognition of events that are often mistaken for, but which are not **epilepsy.** Consequently, what is diagnosed as **epilepsy** today may differ substantially from that in the past, and earlier studies may no longer be fully informative about **epilepsy** today. This study is unique because it has a primary focus on intractable **epilepsy,** and it will provide information about remission of childhood onset **epilepsy** at it is currently diagnosed and treated. Such information can be used to plan treatment strategies,

identify high risk patients in whom aggressive approaches may be taken and who may be good candidates for clinical trials, to educate and counsel families, and to provide information to guide future research into causes, mechanisms, treatment, and ultimately even the prevention of some forms of **epilepsy.**

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: RNA BINDING PROTEINS IN EPILEPSY AND NEUROLOGIC DISEASE**

  Principal Investigator & Institution: Toth, Miklos; Associate Professor; Pharmacology; Weill Medical College of Cornell Univ New York, Ny 10021

  Timing: Fiscal Year 2001; Project Start 13-DEC-1995; Project End 31-MAY-2003

  Summary: (from applicant's abstract): This is a competing continuation proposal of a grant funded to study the novel Jerky protein and its role in **epilepsy.** The mouse line defective in the jerky gene shows epileptic seizures and our work has shown that consistent with its mutant phenotype, jerky is transcribed at a relatively high level in neurons of the central nervous system and that Jerky binds mRNA. We also showed that antibodies recognizing Jerky are present in sera of patients suffering of a certain from of autoimmune neuronal degeneration (paraneoplastic disorders, PND). Other studies suggested that the human jerky gene is a candidate for childhood absence **epilepsy** (CAE). We now understand Jerky to be a prototypic member of an evolutionarily conserved family of RNA binding proteins (RNPs) containing a novel RNA binding motif. RNPs are trans-acting factors mediating posttranscriptional processing of mRNAs and pre-mRNAs, including splicing, polyadenylation, transport, targeting, stability and translation. We hypothesize that lack of Jerky in mutant mice leads to a deficiency in the processing of certain mRNAs compromising neuronal functions that results in seizures. We also show that lack of FMRP (Fragile X Mental Retardation Protein), another RNP whose inactivation causes fragile X syndrome and which is believed to be involved in mRNA processing, also results in seizures in mice. This finding is consistent with the high incidence of seizures in fragile X patients. Since FMRP-deficient animals represent a second example of a situation in which abnormalities in an RNP result in seizures, we suggest that RNP dysfunction may be more general disease mechanism in **epilepsy.** Due to the potential importance of RNPs in **epilepsy,** the focus of our current grant application is to study the cellular role of Jerky, Jerky-like proteins, and FMRP. We propose I) to analyze the RNA binding properties of the human JERKY protein and a similar human protein HHJRK, II) to identify the cellular binding targets of JERKY and FMRP (by a method recently developed in our laboratory) and to assign functions for these targets, and 3) to employ Jerky autoantibodies as tool to study Jerky-RNA complexes. These proposed experiments will establish the jerky family as a distinct group of RNPs with a novel RNA binding motif. Also, specifying targets for JERKY and FMRP will allow us to link these targets to cellular pathways and ascertain how these pathways contribute to the overall function of these proteins. Finally, these experiments will aid in our understanding of certain aspects of the pathogenesis of **epilepsy** and autoimmune diseases.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: ROLE OF FDG-PET, 1H-MRSI, AND MSI IN EPILEPSY SURGERY**

  Principal Investigator & Institution: Knowlton, Robert C.; Neurology; University of Alabama at Birmingham Uab Station Birmingham, Al 35294

  Timing: Fiscal Year 2001; Project Start 06-SEP-2001; Project End 31-AUG-2006

Summary: (provided by applicant): Candidate: The candidate specifically came to UAB to pursue a longstanding career interest in **epilepsy** imaging research. His immediate goals are: 1) to establish routine use of multimodality image coregistration in the presurgical **epilepsy** evaluation at UAB, 2) to set up and establish the UAB Magnetic Source Imaging Laboratory for presurgical **epilepsy** and brain mapping evaluations, and 3) to complete manuscripts for publication from two ongoing projects at UAB and the University of California, San Francisco. This proposal is designed to address the candidates longterm career goals1) to produce research that elucidates the role and impact of developing and established functional imaging modalities in the presurgical evaluation, 2) to demonstrate the applicability of image coregistration to improve routine functional brain image interpretation, and 3) to design and test a completely noninvasive **epilepsy** localization algorithm that includes cortical brain mapping with functional imaging. Environment: UAB offers a unique combination of support, mentorship, and equipment resources to foster the candidate's career development. The Department of Neurology and The **Epilepsy** Center are both academically strong and economically sound. Dr. Kuzniecky (applicant's mentor) is a leading expert in the field of **epilepsy** imaging. Dr. George Howard (applicant's cosponsor) is Chairman of Biostatistics and an expert in clinical research design and biostatistical analysis. Uniquely available at UAB are all structural and functional **epilepsy** imaging modalities necessary for comparative studies. Research: **Epilepsy** surgery candidates without identifiable focal epileptogenic lesions on MRI present a particularly difficult problem. These patients who represent approximately 40% of the total **epilepsy** surgery population in the U.S. typically require expensive and invasive intracranial electroencephalography (ICEEG) to help localize the volume of brain tissue necessary and sufficient for the generation of seizures (epileptogenic zone). Functional **epilepsy** imaging tests offer the possibility to noninvasively identify abnormalities of brain function associated with the epileptogenic zone; however, the clinical role and prognostic value of these tests is not known. The main goal of this proposal is to gain descriptive information on the predictive and prognostic value of FDGPET, HMRSI, and MSI as compared to ICEEG and seizure control outcome from surgery. The primary hypothesis is that noninvasive functional imaging modalities, either alone or in combination with image coregistration, can predict localization of nonlesional partial **epilepsy** as indicated by ICEEG. The secondary hypothesis is that discordant imaging tests provide additional predictive information as indicated by surgical outcome. The specific aims are: (1) to determine the relative predictive value of FDGPET, HMRSI, and MSI (and various combinations of these tests using image coregistration) to replace or supplement the information provided by ICEEG, and (2) to determine the degree of image localization redundancy between functional imaging tests. Toward a longterm goal, it is expected that this study will provide the information needed to mount a welldesigned and efficient trial to evaluate the clinical impact of each of these functional imaging tests on the use of ICEEG and surgical outcome.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: ROLE OF SOMATOSTATIN IN NORMAL AND EPILEPTIC BRAIN**

  Principal Investigator & Institution: Tallent, Melanie K.; Assistant Professor; Scripps Research Institute Tpc7 La Jolla, Ca 92037

  Timing: Fiscal Year 2001; Project Start 30-SEP-1999; Project End 31-JUL-2002

  Summary: The objective of this study is to determine the actions and mechanisms of the peptide somatostatin (SST) in normal and epileptic neurotransmission. SST has long been speculated to play a role in **epilepsy,** however its function is unknown. Our

planned studies are based on the following: 1) We have shown that SST strongly reduces epileptiform activity in both CA1 and CA3 regions of hippocampus. SST acts on both evoked and spontaneous epileptiform events, suggesting that this peptide may act to limit the spread of seizures through the hippocampus and to other limbic structures. 2) SST appears to specifically reduce recurrent excitatory feedforward neurotransmission which is critical to the generation of epileptiform events. Recurrent excitatory synapses are increased in epileptic tissue. 3) One of the most consistent findings in eplieptic hippocampus is the selective loss of SST-containing neurons in the hilus of the dentate gyrus. The functional consequence of this loss is unknown, nor has the action of SST in the dentate been characterized. 4) Transgenic mice have been developed with null mutations (knockouts) for the SST peptide gene or for selective SST receptor subtype genes. These mice provide a unique tool for studying the function of endogenous SST in the brain. Our preliminary data suggests SST has inhibitory actions in the dentate. Therefore the specific aims of this proposal are: 1) Examine the effects of SST on neurotransmission in the dentate, which acts as a gate through which seizure events enter the hippocampus. 2) Examine the effects of SST in hippocampus which has undergone the synaptic remodeling characteristic of epileptic tissue. 3) Begin studies to examine hyperexcitabilty and SST effects in SST or SST receptor knockout mice. We will perform these studies using intracellular, extracellular, and whole-cell patch clamp techniques. These studies will help determine the function of SST in normal and epileptic brain, and could have therapeutic implications in the treatment of **epilepsy** and other neurological disorders.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: SEMANTIC MEMORY AND MRI VOLUMETRICS IN EPILEPSY**

  Principal Investigator & Institution: Bell, Brian D.; Neurology; University of Wisconsin Madison 750 University Ave Madison, Wi 53706

  Timing: Fiscal Year 2001; Project Start 06-SEP-2001; Project End 31-AUG-2006

  Summary: (provided by applicant): Early onset temporal lobe **epilepsy** (TLE) typically is associated with cognitive deficits and quantitative volumetric magnetic resonance imaging (MRI) abnormalities. Impairment of episodic memory, or new learning, and hippocampal atrophy are the best characterized of these cognitive and structural deficits. In contrast, abnormalities of semantic memory, or factual knowledge, have been studied much less systematically, and the neuroanatomic correlates of impaired semantic memory in TLE have yet to be reported. In this application for a Mentored PatientOriented Research Career Development Award, the candidate proposes an organized program of training and supervised research focusing on semantic memory and its neural substrate in TLE. While the applicant has experience in clinical neuropsychology, the proposal provides for additional training in research ethics, experimental cognitive neuropsychology, quantitative volumetric MRI processing, MRI diagnostics, clinical **epilepsy,** language development, and advanced statistical analysis. This training will be integrated with a research project that will: 1) Compare TLE patients and healthy controls on a comprehensive battery of semantic memory measures, 2) quantify MRI volumetric abnormalities in sub-regions of the temporal lobe, and 3) determine the relationship between the cognitive measures and lateral versus mesial (i.e., hippocampal) temporal lobe volumetrics. These findings will lead to improved detection of semantic knowledge deficits in clinical neuropsychological assessment and an advance understanding of the neural substrate of semantic memory. Finally, this award would provide the applicant with the background and training for an independent research career dedicated to elucidating the relationships in TLE

patients among semantic memory, other cognitive abilities, and brain structure, and characterizing the implications of these relationships for social, educational, and occupational functioning.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: THE MAPK CASCADE IN EPILEPSY**

  Principal Investigator & Institution: Anderson, Anne; Assistant Professor; Pediatrics; Baylor College of Medicine 1 Baylor Plaza Houston, Tx 77030

  Timing: Fiscal Year 2001; Project Start 30-SEP-2000; Project End 31-AUG-2005

  Summary: (Adapted from the Applicant's Abstract): **Epilepsy** is a common neurological disorder. Basic research in the field of **epilepsy** has focused on understanding the cellular and molecular mechanisms that underlie the disorder. The goal of this proposal is to evaluate the role that the mitogen-activated protein kinase (MAPK) signaling cascade plays in **epilepsy.** We have shown that MAPK regulates K channel activity and synaptic plasticity. Furthermore MAPK activation leads to long-lasting changes in the hippocampus through regulation of gene transcription. Recent studies have demonstrated MAPK activation in animal models of **epilepsy,** although the downstream targets of MAPK in **epilepsy** are unknown. We propose that the MAPK cascade plays a critical role in the genesis of the acute and chronic phases of **epilepsy** through regulation of K channel activity and gene transcription. Regulation of K channel activity could impact membrane excitability, and recent studies have shown that humans and genetic mouse models with K channel mutations have an **epilepsy** phenotype. MAPK regulation of transcription factors such as cyclic AMP response element binding protein (CREB) could contribute to the chronic changes seen in **epilepsy** (i.e. hippocampal sclerosis). Our preliminary results show hippocampal MAPK activation, an increase in NLAPK phosphorylation of a dendritic K channel subunit, Kv4.2, and increases in CREB phosphorylation in the kainate model of **epilepsy.** To further support a role for the MAPK cascade in **epilepsy** we have pilot studies showing that inhibition of the MAPK cascade blocks the expression of kainate-induced limbic motor seizures. In this proposal we wish to test the hypotheses that: 1) the MAPK cascade is activated in hippocampus following kainate-induced status epilepticus and is necessary for kainate-induced epileptogenesis; 2) the K channel subunit, Kv4.2, is an effector of MAPK in the kainate model of **epilepsy;** and 3) the transcription factor, CREB, is an effector of MAPK in the kainate model of **epilepsy.** By further defining the role of the MAPK signaling cascade in **epilepsy** we hope to gain insight into the basic mechanisms contributing to this disorder. Thus these studies may lead to the development of new treatments for **epilepsy.**

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: THOUGHT DISORDER: A DEVELOPMENTAL DISABILITY IN EPILEPSY**

  Principal Investigator & Institution: Caplan, Rochelle; Associate Professor; None; University of California Los Angeles 10920 Wilshire Blvd., Suite 1200 Los Angeles, Ca 90024

  Timing: Fiscal Year 2001; Project Start 30-SEP-1999; Project End 31-JUL-2004

  Summary: This prospective study will determine if uncontrolled seizures over time impair development by comparing measures of morphometry, cognition, thought disorder, and psychopathology in 6 - 18 year old children with complex partial **seizure disorder** (CPS), primary generalized **epilepsy** with absences (PGE), and normal children

at baseline and 2 years later. By including nonepileptic siblings of the CPS, PGE, and normal subjects, the project will ascertain if the hypothesized developmental abnormalities in the patients are epilepsy-related rather than familial. Specific Aims: The study will test 3 main hypotheses: (a) CPS and PGE patients with an increase in seizure frequency from baseline through the 2 year follow-up will have a drop in IQ and an associated increase in thought disorder and psychopathology compared to patients with a decrease in seizure frequency and the normal subjects. (b) The patients with an increase in seizure frequency will have a smaller age-related increase in mesial temporal lobe (i.e., hippocampus, amygdala) and frontal lobe white matter volumes than the patients with a decrease in seizure frequency and the normal subjects. (c) The smaller age-related increase in mesial temporal lobe and frontal lobe white matter volumes will be associated with the predicted drop in IQ, and increase in thought disorder and psychopathology in the patients with uncontrolled seizures. Significance: By addressing the on-going debate "Do seizures impair development?" the study's findings will delineate neurobiologic mechanisms of impaired cognition, thought disorder, and psychopathology in middle childhood **epilepsy.** They will underscore the importance of medical control of seizures to promote optimal development of cognition, communication, and behavior in these children. They will highlight the potential use of MRI for identifying children at risk for thought disorder and pave the way for future studies on treatment and prevention of thought disorder and psychopathology in pediatric CPS and PGE. Research Design and Methods: The study mill recruit 40 CPS, 40 PGE, and 40 normal children matched on age, gender, ethnicity, and socioeconomic status. Twenty-five siblings of the CPS, PGE, and normal subjects will also participate in the study. Each subject will undergo an MRI, as well as cognitive, thought disorder, behavioral, and linguistic testing at baseline and 2 years later. Weekly seizure frequency data will be obtained on a monthly basis from the parent during the 2 years.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: TREATMENT OF ADHD IN PEDIATRIC PATIENTS WITH EPILEPSY**

  Principal Investigator & Institution: Gonzalez-Heydrich, Joseph M.; Children's Hospital (Boston) Boston, Ma 021155737

  Timing: Fiscal Year 2003; Project Start 01-FEB-2003; Project End 31-JAN-2008

  Summary: (provided by applicant): **Epilepsy** is highly prevalent and associated with increased risk for psychiatric disorders. Patients with chronic recurrent seizures are excluded from most pharmacological trials establishing standard treatments in pediatric psychiatry. Finding safe and effective treatments for psychiatric disorders in pediatric patients with **epilepsy** is of pressing public health importance. The purpose of this Mentored Patient-Oriented Research Development Award (K23) is for the candidate to become an independent clinical researcher in the psychopharmacologic treatment of psychiatric disorders in children and adolescents facing **epilepsy.** The proposal focuses on patients with comorbid ADHD and **epilepsy.** The project will be conducted at Children's Hospital Boston (CHB), which serves a large population of patients with **epilepsy.** Joseph Biederman, MD, with expertise in clinical trials in pediatric psychopharmacology will serve as the primary mentor. William R. Beardslee, MD, Chairman of Psychiatry at CHB will serve as the sponsor. Blaise Bourgeois, MD, Chairman of the Division of **Epilepsy** and Clinical Neurophysiology at CHB is the principal **epilepsy** consultant. Research plan: The aims are: 1) To perform a randomized placcbo controlled crossover trial of extended release methylphenidate (Concerta) in pediatric patients with comorbid ADHD and **epilepsy;** 2) To establish methods of assuring the safety of children with **epilepsy** in psychopharmacological clinical trials.

Career development plan: The training will emphasize skills necessary for conducting randomized controlled clinical trials in youth with **epilepsy** comorbid with psychiatric disorders and to explore the neurobiological mechanisms underlying their increased risk for psychopathology. Didactic work in intervention research design, statistics, developmental psychopathology, and assessment methodologies for psychopathology and treatment response will complement supervision by the program consultants. The long-term goals of the candidate are to develop and evaluate treatments for children with comorbid psychiatric disorders and **epilepsy** as well as to investigate neurobiological correlates of the risk and response to treatment of these disorders.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: VIRAL NEUROPATHOLOGY NEUROPEPTIDES AND EPILEPSY**

  Principal Investigator & Institution: Solbrig, Marylou V.; Neurology; University of California Irvine Irvine, Ca 926977600

  Timing: Fiscal Year 2003; Project Start 01-APR-2003; Project End 31-MAR-2006

  Summary: (provided by applicant): **Epilepsy,** or recurrent seizures, is a neurologic disease of all age groups and affects approximately 1% of Americans. Twenty to 25% of patients respond poorly to existing medications, and, as a group, patients with seizures secondary to CNS infections have been the most medically refractory. Persistence, tropism of virus for epileptogenic areas, and immaturity of the nervous system at the time of exposure are each predictive of poor **epilepsy** control. In this proposal, the overall hypothesis that reduced dynorphin expression in the dentate gyrus of the hippocampus due to periadolescent virus exposure leads to epileptic-like responses will be tested. The generality of the hypothesis, the mechanism of effect, and treatments will be studied. Borna Disease virus, a neurotropic virus causing hippocampal degeneration in many mamma an species, is a rare cause of hippocampal sclerosis in man. The Borna Disease virus infected rat (BD rat), is a biologically plausible animal model of periadolescent viral injury and seizures: it has an epileptic phenotype, predictable neuropathologic outcome with consistent hippocampal lesions, and reproduces a neurochemical change, dynorphin deficit, now recognized as a risk factor in human temporal lobe **epilepsy.** The hypothesis that viral injury in young subjects conveys a vulnerability to epileptic activity that is mediated by decreased dynorphin in the hippocampus will be tested in the BD rat for Specific Aim 1 using specific neuropharmacologic agents, electroencephalographic recording, immediate early gene labeling for localization, and histologic probes. A mechanism of dynorphin deficit during infection, failure of maturation of dynorphin-expressing granule cells of the hippocampus, will be examined using histologic probes to track neurogenesis and cell development over time. Herpes simplex virus is a significant human pathogen, with undisputed links to viral epilepies. The hypothesis that viruses other than Borna viruses convey vulnerability to epileptic-like responses will be tested for herpes simplex virus in rats and vesicular stomatitis virus in rats for Specific Aim 2 using specific neuropharmacologic agents and histologic probes. This work will enhance our understanding of viral interaction with the immature nervous system and provide a heuristic basis for exploring individual differences in vulnerability to **epilepsy** both from an environmental and genetic perspective.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: YALE EPILEPSY RESEARCH CENTER**

  Principal Investigator & Institution: Mattson, Richard H.; Neurology; Yale University 47 College Street, Suite 203 New Haven, Ct 065208047

Timing: Fiscal Year 2001; Project Start 01-SEP-1986; Project End 31-MAR-2003

Summary: The Yale **Epilepsy** Research Center Program Project is organized as a widely based investigational effort into mechanisms of epileptic seizures and their control. A consortium of 25 scientists from various disciplines have joined together to study experimental and clinical aspects of **epilepsy.** The ultimate aim of these studies is to discern factors responsible for the occurrence, frequency, and effects of seizures, and how they can be controlled. Animal experimental, human clinical and neuropathological studies are oriented toward an understanding of basic physiological and neurochemical alterations responsible for seizures as well as a development of pharmacological and surgical methods effective for treatment and control of seizures. The specific scientific components of this research program are: - Cellular Actions of Antiepileptic Drugs on Hippocampal Neurons - Microdialysis of Intracerebral Extracellular Fluid in **Epilepsy** Patients - Pharmacology of Antiepileptic Drugs Using Microdialysis in **Epilepsy** Patients - Evaluation of SPECT Benzodiazepine Receptor Imaging and MRI to Localize a Seizure Focus - Molecular Neuroanatomic Analyses of Epileptiform Human Temporal Lobe Tissue - Neurophysiological Studies of Human Epileptic Hippocampus - NMR Spectroscopic Analyses of Human Cerebrum and Synaptosomes - Extracellular pH Responses in Mammalian CNS

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

E-Journals: PubMed Central[3]

PubMed Central (PMC) is a digital archive of life sciences journal literature developed and managed by the National Center for Biotechnology Information (NCBI) at the U.S. National Library of Medicine (NLM).[4] Access to this growing archive of e-journals is free and unrestricted.[5] To search, go to **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Pmc**, and type "epilepsy" (or synonyms) into the search box. This search gives you access to full-text articles. The following is a sample of items found for epilepsy in the PubMed Central database:

- **A Nerve Growth Factor Peptide Retards Seizure Development and Inhibits Neuronal Sprouting in a Rat Model of Epilepsy.** by Rashid K, van der Zee CE, Ross GM, Chapman CA, Stanisz J, Riopelle RJ, Racine RJ, Fahnestock M.; 1995 Oct 10; http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&rendertype=abstract&artid=40828
- **A 'real puzzle': the views of patients with epilepsy about the organisation of care.** by Elwyn G, Todd S, Hibbs R, Thapar A, Edwards P, Webb A, Wilkinson C, Kerr M.; 2003; http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=161791
- **Colocalization and coassembly of two human brain M-type potassium channel subunits that are mutated in epilepsy.** by Cooper EC, Aldape KD, Abosch A, Barbaro NM, Berger MS, Peacock WS, Jan YN, Jan LY.; 2000 Apr 25; http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=18332

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[3] Adapted from the National Library of Medicine: **http://www.pubmedcentral.nih.gov/about/intro.html**.

[4] With PubMed Central, NCBI is taking the lead in preservation and maintenance of open access to electronic literature, just as NLM has done for decades with printed biomedical literature. PubMed Central aims to become a world-class library of the digital age.

[5] The value of PubMed Central, in addition to its role as an archive, lies in the availability of data from diverse sources stored in a common format in a single repository. Many journals already have online publishing operations, and there is a growing tendency to publish material online only, to the exclusion of print.

- **Comparative Analysis of Epilepsy Abstracts and a MEDLARS Bibliography.** by Goode DJ, Penry JK.; 1970 Jan;
  http://www.pubmedcentral.gov/picrender.fcgi?tool=pmcentrez&action=stream&blobtype=pdf&artid=197401
- **Development and persistence of kindling epilepsy are impaired in mice lacking glial cell line-derived neurotrophic factor family receptor [alpha]2.** by Nanobashvili A, Airaksinen MS, Kokaia M, Rossi J, Asztely F, Olofsdotter K, Mohapel P, Saarma M, Lindvall O, Kokaia Z.; 2000 Oct 24;
  http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=17338
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  http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&rendertype=external&artid=143552
- **Enhanced GABAergic Inhibition Preserves Hippocampal Structure and Function in a Model of Epilepsy.** by Ylinen AM, Miettinen R, Pitkanen A, Gulyas AI, Freund TF, Riekkinen PJ.; 1991 Sep 1;
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- **Epilepsy Abstracts Retrieval System (EARS): A New Concept for Medical Literature Storage and Retrieval.** by Porter RJ, Penry JK.; 1971 Jul;
  http://www.pubmedcentral.gov/picrender.fcgi?tool=pmcentrez&action=stream&blobtype=pdf&artid=197610
- **Epilepsy Abstracts: Its Role in Disseminating Scientific Information.** by Caponio JF.; 1970 Jan;
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- **Epilepsy in mice deficient in the 65-kDa isoform of glutamic acid decarboxylase.** by Kash SF, Johnson RS, Tecott LH, Noebels JL, Mayfield RD, Hanahan D, Baekkeskov S.; 1997 Dec 9;
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- **Grafts of adenosine-releasing cells suppress seizures in kindling epilepsy.** by Huber A, Padrun V, Deglon N, Aebischer P, Mohler H, Boison D.; 2001 Jun 19;
  http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=34716
- **Health-related quality of life in childhood epilepsy: Moving beyond 'seizure control with minimal adverse effects'.** by Ronen GM, Streiner DL, Rosenbaum P.; 2003;
  http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=201010
- **In vitro analysis of mutations causing myoclonus epilepsy with ragged-red fibers in the mitochondrial tRNA(Lys)gene: two genotypes produce similar phenotypes.** by Masucci JP, Davidson M, Koga Y, Schon EA, King MP.; 1995 May;
  http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&rendertype=abstract&artid=230518
- **Limbic Epilepsy in Transgenic Mice Carrying a Ca2+/Calmodulin-Dependent Kinase II [alpha]-Subunit Mutation.** by Butler LS, Silva AJ, Abeliovich A, Watanabe Y, Tonegawa S, McNamara JO.; 1995 Jul 18;
  http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&rendertype=abstract&artid=41427

- **Localization of a Gene for Progressive Myoclonus Epilepsy to Chromosome 21q22.** by Lehesjoki A, Koskiniemi M, Sistonen P, Miao J, Hastbacka J, Norio R, de la Chapelle A.; 1991 May 1; http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&rendertype=abstract&artid=51519
- **Long-Lasting Reduction of Inhibitory Function and [gamma]-Aminobutyric Acid Type A Receptor Subunit mRNA Expression in a Model of Temporal Lobe Epilepsy.** by Rice A, Rafiq A, Shapiro SM, Jakoi ER, Coulter DA, DeLorenzo RJ.; 1996 Sep 3; http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&rendertype=abstract&artid=38486
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- **Mefloquine: contraindicated in patients with mood, psychotic or seizure disorders.** by Wooltorton E.; 2002 Nov 12; http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=134297
- **Mice devoid of [gamma]-aminobutyrate type A receptor [beta]3 subunit have epilepsy, cleft palate, and hypersensitive behavior.** by Homanics GE, DeLorey TM, Firestone LL, Quinlan JJ, Handforth A, Harrison NL, Krasowski MD, Rick CE, Korpi ER, Makela R, Brilliant MH, Hagiwara N, Ferguson C, Snyder K, Olsen RW.; 1997 Apr 15; http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=20582
- **Myokymia and neonatal epilepsy caused by a mutation in the voltage sensor of the KCNQ2 K + channel.** by Dedek K, Kunath B, Kananura C, Reuner U, Jentsch TJ, Steinlein OK.; 2001 Oct 9; http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=59804
- **Operative GABAergic inhibition in hippocampal CA1 pyramidal neurons in experimental epilepsy.** by Esclapez M, Hirsch JC, Khazipov R, Ben-Ari Y, Bernard C.; 1997 Oct 28; http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=23733
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The National Library of Medicine: PubMed

One of the quickest and most comprehensive ways to find academic studies in both English and other languages is to use PubMed, maintained by the National Library of Medicine.[6] The advantage of PubMed over previously mentioned sources is that it covers a greater number of domestic and foreign references. It is also free to use. If the publisher has a Web site that offers full text of its journals, PubMed will provide links to that site, as well as to sites offering other related data. User registration, a subscription fee, or some other type of fee may be required to access the full text of articles in some journals.

To generate your own bibliography of studies dealing with epilepsy, simply go to the PubMed Web site at **http://www.ncbi.nlm.nih.gov/pubmed**. Type "epilepsy" (or synonyms) into the search box, and click "Go." The following is the type of output you can expect from PubMed for epilepsy (hyperlinks lead to article summaries):

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[6] PubMed was developed by the National Center for Biotechnology Information (NCBI) at the National Library of Medicine (NLM) at the National Institutes of Health (NIH). The PubMed database was developed in conjunction with publishers of biomedical literature as a search tool for accessing literature citations and linking to full-text journal articles at Web sites of participating publishers. Publishers that participate in PubMed supply NLM with their citations electronically prior to or at the time of publication.

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  Source: Seizure : the Journal of the British Epilepsy Association. 2003 September; 12(6): 373-8.
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CHAPTER 2. NUTRITION AND EPILEPSY

Overview

In this chapter, we will show you how to find studies dedicated specifically to nutrition and epilepsy.

Finding Nutrition Studies on Epilepsy

The National Institutes of Health's Office of Dietary Supplements (ODS) offers a searchable bibliographic database called the IBIDS (International Bibliographic Information on Dietary Supplements; National Institutes of Health, Building 31, Room 1B29, 31 Center Drive, MSC 2086, Bethesda, Maryland 20892-2086, Tel: 301-435-2920, Fax: 301-480-1845, E-mail: ods@nih.gov). The IBIDS contains over 460,000 scientific citations and summaries about dietary supplements and nutrition as well as references to published international, scientific literature on dietary supplements such as vitamins, minerals, and botanicals.[7] The IBIDS includes references and citations to both human and animal research studies.

As a service of the ODS, access to the IBIDS database is available free of charge at the following Web address: **http://ods.od.nih.gov/databases/ibids.html**. After entering the search area, you have three choices: (1) IBIDS Consumer Database, (2) Full IBIDS Database, or (3) Peer Reviewed Citations Only.

Now that you have selected a database, click on the "Advanced" tab. An advanced search allows you to retrieve up to 100 fully explained references in a comprehensive format. Type "epilepsy" (or synonyms) into the search box, and click "Go." To narrow the search, you can also select the "Title" field.

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[7] Adapted from **http://ods.od.nih.gov**. IBIDS is produced by the Office of Dietary Supplements (ODS) at the National Institutes of Health to assist the public, healthcare providers, educators, and researchers in locating credible, scientific information on dietary supplements. IBIDS was developed and will be maintained through an interagency partnership with the Food and Nutrition Information Center of the National Agricultural Library, U.S. Department of Agriculture.

The following information is typical of that found when using the "Full IBIDS Database" to search for "epilepsy" (or a synonym):

- **A study of the relationship between metabolism using 1H-MRS and function using several neuropsychological tests in temporal lobe epilepsy.**
  Author(s): Department of Neuropsychiatry, Gunma University School of Medicine, 3-39-15, Shouwa-machi, Maebashi-shi, 371-8511, Japan. skikuchi@showa.gunma-u.ac.jp
  Source: Kikuchi, S Kubota, F Hattori, S Oya, N Mikuni, M Seizure. 2001 April; 10(3): 188-93 1059-1311
- **Animal models of drug-resistant epilepsy.**
  Author(s): Department of Pharmacology, Toxicology, and Pharmacy, School of Veterinary Medicine, Hanover, Germany.
  Source: Loscher, W Novartis-Found-Sympage 2002; 243: 149-59; discussion 159-66, 180-5
- **Atypical benign partial epilepsy of childhood (pseudo-Lennox syndrome): report of two brothers.**
  Author(s): Department of Pediatrics, Division of Pediatric Neurology, Ankara University, Faculty of Medicine, Ankara, Turkey. gulhisdeda@hotmail.com
  Source: Deda, G Caksen, H Neurol-India. 2002 September; 50(3): 337-9 0028-3886
- **Basic pharmacology of valproate: a review after 35 years of clinical use for the treatment of epilepsy.**
  Author(s): Department of Pharmacology, School of Veterinary Medicine, Toxicology and Pharmacy, Hannover, Germany. wolfgang.loescher@tiho-hannover.de
  Source: Loscher, W CNS-Drugs. 2002; 16(10): 669-94 1172-7047
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  Author(s): Department of Neurosurgery, Asahikawa Medical College, Asahikawa, Japan. tanakat@asahikawa-med.ac.jp
  Source: Tanaka, T Hashizume, K Sawamura, A Yoshida, K Tsuda, H Hodozuka, A Nakai, H Stereotact-Funct-Neurosurg. 2001; 77(1-4): 239-44 1011-6125
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  Author(s): Division of Statistics and Operational Research, Department of Mathematical Sciences, University of Liverpool, Mathematics & Oceanography Building, Peach Street, Liverpool, UK, L69 7ZL. cat1@liverpool.ac.uk
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  Author(s): Department of Cell and Neurobiology, Institute of Anatomy, Charite, Berlin, Germany.
  Source: Deisz, R A Novartis-Found-Sympage 2002; 243: 186-99; discussion 199-206, 231-5
- **Clinical expression and EEG features of patients with juvenile myoclonic epilepsy (JME) from North India.**
  Author(s): Department of Neurology, G.B. Pant Hospital, New Delhi, India. mmehndi@vsnl.acom
  Source: Mehndiratta, M M Aggarwal, P Seizure. 2002 October; 11(7): 431-6 1059-1311
- **Detection of antibodies to Taenia solium in sera of patient with epilepsy using ELISA.**
  Author(s): National Institute of Communicable Diseases, 22-Sham Nath Marg, Delhi-110054, India.
  Source: Mittal, V Singh, V K Ichhpujani, R L J-Commun-Dis. 2001 March; 33(1): 23-7 0019-5138

- **Epilepsy and women's issues: an update.**
  Author(s): Neuology Clinic, Katonsspital St Gallen, Switzerland.
  Source: Tettenborn, B Genton, P Polson, D Epileptic-Disord. 2002 October; 4 Suppl 2: S23-31 1294-9361

- **Evidence of neuronal injury outside the medial temporal lobe in temporal lobe epilepsy: N-acetylaspartate concentration reductions detected with multisection proton MR spectroscopic imaging--initial experience.**
  Author(s): MR Unit, Department of Veterans Affairs Medical Center, University of California, San Francisco, USA. peter.vermathen@insel.ch
  Source: Vermathen, P Laxer, K D Schuff, N Matson, G B Weiner, M W Radiology. 2003 January; 226(1): 195-202 0033-8419

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  Author(s): Departments of Pharmacolgy, Maulana Azad Medical College and G.B. Pant Hospital, New Delhi - 110 002, India.
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  Author(s): Department of Clinical Pharmacology, Jichi Medical School, Minamikawachi-machi, Tochigi 329-0498, Japan. kodama@kiko.go.jp
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  Author(s): Epilepsy Research Laboratory, Department of Neurological Surgery and The Graduate Program in Neuroscience, University of California, San Francisco, San Francisco, California 94143, USA.
  Source: Calcagnotto, M E Paredes, M F Baraban, S C J-Neurosci. 2002 September 1; 22(17): 7596-605 1529-2401

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  Author(s): Charite, Campus-Virchow-Klinikum, Department of Neurology, Augustenburger Platz 1, 13353 Berlin, Germany. tamara.schmidt@charite.de
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  Author(s): Department of Radiology, Chang Gung Memorial Hospital and Chang Gung University, Taipei.
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  Author(s): Department of Epileptology, University of Bonn, Germany, Dr Willmar Schwabe GmbH, Karlsruhe, Germany.
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  Author(s): First Department of Neurology, Aristotle University of Thessaloniki, AHEPA General Hospital, 1, Stilponos Kyriakidi Street, 54636 Thessaloniki, Greece. koniaris@vergina.eng.auth.gr
  Source: Karlovassitou Koniari, A Alexiou, D Angelopoulos, P Armentsoudis, P Dimitrakoudi, E Delithanasis, I Hamlatzis, P Baloyannis, S J-Neurol. 2002 April; 249(4): 396-9 0340-5354

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  Author(s): Department of Veterans Affairs Medical Center, Magnetic Resonance Spectroscopy Unit, University of California, San Francisco, USA.
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  Author(s): Child Neurology Unit & Epilepsy Service, Rambam Medical Center, Rappaport School of Medicine, Haifa, Israel. e_shahar@rambam.health.gov.il
  Source: Shahar, E Andraus, J J-Clin-Neurosci. 2002 September; 9(5): 605-7 0967-5868

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  Author(s): Neurosciences Research Institute, School of Life and Health Sciences, Aston University, Birmingham, UK. s.l.hosking@aston.ac.uk
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  Author(s): Biology Department, Bradley University, Peoria, IL 61625, USA. kurtz@bradley.edu
  Source: Kurtz, B S Lehman, J Garlick, P Amberg, J Mishra, P K Dailey, J W Weber, R Jobe, P C J-Neurogenet. 2001; 15(3-4): 233-44 0167-7063

- **Pharmacokinetic and pharmacodynamic effects of clonazepam in children with epilepsy treated with valproate: a preliminary study.**
  Author(s): Pediatric Neurology, Peking University First Hospital, Beijing, China. wangli54@yahoo.com
  Source: Wang, L Wang, X D Ther-Drug-Monit. 2002 August; 24(4): 532-6 0163-4356

- **Phenytoin-induced choreoathetosis in patients with severe myoclonic epilepsy in infancy.**
  Author(s): Department of Pediatrics, Tokyo Women's Medical University, Shinjuku-ku, Tokyo, Japan. saitoyo@tmin.ac.jp
  Source: Saito, Y Oguni, H Awaya, Y Hayashi, K Osawa, M Neuropediatrics. 2001 October; 32(5): 231-5 0174-304X

- **Polycystic ovaries, obesity and insulin resistance in women with epilepsy. A comparative study of carbamazepine and valproic acid in 105 women.**
  Author(s): Department of Neurology, University Hospital Innsbruck, Anichstrasse 35, Austria. gerhard.luef@uibk.ac.at
  Source: Luef, G Abraham, I Haslinger, M Trinka, E Seppi, K Unterberger, I Alge, A Windisch, J Lechleitner, M Bauer, G J-Neurol. 2002 July; 249(7): 835-41 0340-5354
- **Protective effect of copper-rutin complex in animals with experimental epilepsy.**
  Author(s): Biological Faculty, Belorussian State University, Minsk.
  Source: Tsaryuk, V V Potapovich, A I Kostyuk, V A Bull-Exp-Biol-Med. 2002 April; 133(4): 334-5 0007-4888
- **Serum concentrations of topiramate in patients with epilepsy: influence of dose, age, and comedication.**
  Author(s): Department of Biochemistry, Gesellschaft fur Epilepsieforschung, Maraweg 13, D-33546 Bielefeld, Germany. may_gfe@t-online.de
  Source: May, T W Rambeck, B Jurgens, U Ther-Drug-Monit. 2002 June; 24(3): 366-74 0163-4356
- **St. John's wort (Hypericum perforatum L.) and kindling epilepsy in rabbit.**
  Author(s): Department of Physiology, Medical Faculty, University of Novi Sad, Yugoslavia.
  Source: Ivetic, V Popovic, M Mimica Dukic, N Barak, O Pilija, V Phytomedicine. 2002 September; 9(6): 496-9 0944-7113
- **Sudden unexplained death in epilepsy (SUDEP) following previous seizure-related pulmonary oedema: case report and review of possible preventative treatment.**
  Author(s): The Welsh Epilepsy Unit, University Hospital of Wales, Heath Park, Cardiff CF14 4XW, UK.
  Source: Swallow, R A Hillier, C E Smith, P E Seizure. 2002 October; 11(7): 446-8 1059-1311
- **The treatment gap and primary health care for people with epilepsy in rural Gambia.**
  Author(s): Medical Research Council Laboratories, Banjul, The Gambia. rosalind_coleman@hotmail.com
  Source: Coleman, Rosalind Loppy, Louie Walraven, Gijs Bull-World-Health-Organ. 2002; 80(5): 378-83 0042-9686
- **Topiramate add-on for drug-resistant partial epilepsy.**
  Author(s): Neurology, Ottawa Hospital - General Campus, 501 Smyth Road, Ottawa, Canada, K1H 8L6. n.jette@sympatico.ca
  Source: Jette, N J Marson, A G Hutton, J L Cochrane-Database-Syst-Revolume 2002; (3): CD001417 1469-493X
- **Topiramate therapeutic monitoring in patients with epilepsy: effect of concomitant antiepileptic drugs.**
  Author(s): Laboratory of Clinical Neuropharmacology, Department of Neurological Sciences, University of Bologna, Via Foscolo 7, 40123 Bologna, Italy. contin@neuro.unibo.it
  Source: Contin, M Riva, R Albani, F Avoni, P Baruzzi, A Ther-Drug-Monit. 2002 June; 24(3): 332-7 0163-4356
- **Treatment and long-term prognosis of myoclonic-astatic epilepsy of early childhood.**
  Author(s): Department of Pediatrics, Tokyo Women's Medical University, Tokyo, Japan. hoguni@ped.twmu.ac.jp

Source: Oguni, H Tanaka, T Hayashi, K Funatsuka, M Sakauchi, M Shirakawa, S Osawa, M Neuropediatrics. 2002 June; 33(3): 122-32 0174-304X

- **Visual field constriction in epilepsy patients treated with vigabatrin and other antiepileptic drugs: a prospective study.**
  Author(s): Charite, Campus-Virchow-Klinikum, Department of Neurology, Augustenburger Platz 1, 13353 Berlin, Germany. bettina.schmitz@charite.de
  Source: Schmitz, B Schmidt, T Jokiel, B Pfeiffer, S Tiel Wilck, K Ruther, K J-Neurol. 2002 April; 249(4): 469-75 0340-5354
- **Visual functions in epilepsy patients on valproate monotherapy.**
  Author(s): Faculty of Medicine, Department of Neurology, University of Harran, Sanliurfa, Turkey. bulgurler@hotmail.com
  Source: Ozkul, Y Gurler, B Uckardes, A Bozlar, S J-Clin-Neurosci. 2002 May; 9(3): 247-50 0967-5868

Federal Resources on Nutrition

In addition to the IBIDS, the United States Department of Health and Human Services (HHS) and the United States Department of Agriculture (USDA) provide many sources of information on general nutrition and health. Recommended resources include:

- healthfinder®, HHS's gateway to health information, including diet and nutrition: **http://www.healthfinder.gov/scripts/SearchContext.asp?topic=238&page=0**
- The United States Department of Agriculture's Web site dedicated to nutrition information: **www.nutrition.gov**
- The Food and Drug Administration's Web site for federal food safety information: **www.foodsafety.gov**
- The National Action Plan on Overweight and Obesity sponsored by the United States Surgeon General: **http://www.surgeongeneral.gov/topics/obesity/**
- The Center for Food Safety and Applied Nutrition has an Internet site sponsored by the Food and Drug Administration and the Department of Health and Human Services: **http://vm.cfsan.fda.gov/**
- Center for Nutrition Policy and Promotion sponsored by the United States Department of Agriculture: **http://www.usda.gov/cnpp/**
- Food and Nutrition Information Center, National Agricultural Library sponsored by the United States Department of Agriculture: **http://www.nal.usda.gov/fnic/**
- Food and Nutrition Service sponsored by the United States Department of Agriculture: **http://www.fns.usda.gov/fns/**

Additional Web Resources

A number of additional Web sites offer encyclopedic information covering food and nutrition. The following is a representative sample:

- AOL: **http://search.aol.com/cat.adp?id=174&layer=&from=subcats**
- Family Village: **http://www.familyvillage.wisc.edu/med_nutrition.html**

- Google: **http://directory.google.com/Top/Health/Nutrition/**
- Healthnotes: **http://www.healthnotes.com/**
- Open Directory Project: **http://dmoz.org/Health/Nutrition/**
- Yahoo.com: **http://dir.yahoo.com/Health/Nutrition/**
- WebMD®Health: **http://my.webmd.com/nutrition**
- WholeHealthMD.com: **http://www.wholehealthmd.com/reflib/0,1529,00.html**

The following is a specific Web list relating to epilepsy; please note that any particular subject below may indicate either a therapeutic use, or a contraindication (potential danger), and does not reflect an official recommendation:

- **Vitamins**

  Folic Acid
  Source: Healthnotes, Inc.; www.healthnotes.com

  Folic Acid
  Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
  Hyperlink:
  http://www.wholehealthmd.com/refshelf/substances_view/0,1525,887,00.html

  Vitamin B
  Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
  Hyperlink:
  http://www.wholehealthmd.com/refshelf/substances_view/0,1525,10067,00.html

  Vitamin B Complex
  Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
  Hyperlink:
  http://www.wholehealthmd.com/refshelf/substances_view/0,1525,962,00.html

  Vitamin B1
  Source: Prima Communications, Inc.www.personalhealthzone.com

  Vitamin B6
  Source: Healthnotes, Inc.; www.healthnotes.com

  Vitamin E
  Source: Healthnotes, Inc.; www.healthnotes.com

  Vitamin K
  Alternative names: Menadione, Menaphthone, Menaquinone, Phylloquinone
  Source: Integrative Medicine Communications; www.drkoop.com

- **Minerals**

  Calcium/Magnesium
  Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
  Hyperlink:
  http://www.wholehealthmd.com/refshelf/substances_view/0,1525,937,00.html

  Carnitine (l-carnitine)
  Source: Integrative Medicine Communications; www.drkoop.com

  Folate
  Source: Prima Communications, Inc.www.personalhealthzone.com

  Gabapentin
  Source: Healthnotes, Inc.; www.healthnotes.com

  L-carnitine
  Source: Integrative Medicine Communications; www.drkoop.com

  Manganese
  Source: Integrative Medicine Communications; www.drkoop.com

  Manganese
  Source: Prima Communications, Inc.www.personalhealthzone.com

CHAPTER 3. ALTERNATIVE MEDICINE AND EPILEPSY

Overview

In this chapter, we will begin by introducing you to official information sources on complementary and alternative medicine (CAM) relating to epilepsy. At the conclusion of this chapter, we will provide additional sources.

National Center for Complementary and Alternative Medicine

The National Center for Complementary and Alternative Medicine (NCCAM) of the National Institutes of Health (**http://nccam.nih.gov/**) has created a link to the National Library of Medicine's databases to facilitate research for articles that specifically relate to epilepsy and complementary medicine. To search the database, go to the following Web site: **http://www.nlm.nih.gov/nccam/camonpubmed.html**. Select "CAM on PubMed." Enter "epilepsy" (or synonyms) into the search box. Click "Go." The following references provide information on particular aspects of complementary and alternative medicine that are related to epilepsy:

- **"The moon" and "the blood": two emblematic symbols in headache and epilepsy according to scientific traditions of the Salerno Medical school and popular medicine in southern Italy.**
  Author(s): Cassano D, Colucci d'Amato C.
  Source: Journal of the History of the Neurosciences. 1992 April; 1(2): 97-110.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11618427&dopt=Abstract

- **(18)F-FDG PET in localization of frontal lobe epilepsy: comparison of visual and SPM analysis.**
  Author(s): Kim YK, Lee DS, Lee SK, Chung CK, Chung JK, Lee MC.
  Source: Journal of Nuclear Medicine : Official Publication, Society of Nuclear Medicine. 2002 September; 43(9): 1167-74.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12215554&dopt=Abstract

- **A kindling model of pharmacoresistant temporal lobe epilepsy in Sprague-Dawley rats induced by Coriaria lactone and its possible mechanism.**
  Author(s): Wang Y, Zhou D, Wang B, Li H, Chai H, Zhou Q, Zhang S, Stefan H.
  Source: Epilepsia. 2003 April; 44(4): 475-88.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12680996&dopt=Abstract

- **Alcohol and marijuana: effects on epilepsy and use by patients with epilepsy.**
  Author(s): Gordon E, Devinsky O.
  Source: Epilepsia. 2001 October; 42(10): 1266-72. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11737161&dopt=Abstract

- **All seizures are not epilepsy: many have a cardiovascular cause.**
  Author(s): Akhtar MJ.
  Source: J Pak Med Assoc. 2002 March; 52(3): 116-20.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12071066&dopt=Abstract

- **Alternative Medicine Use by Patients with Epilepsy.**
  Author(s): Peebles CT, McAuley JW, Roach J, Moore JL, Reeves AL.
  Source: Epilepsy & Behavior : E&B. 2000 February; 1(1): 74-77.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12609128&dopt=Abstract

- **Assessment and cost comparison of sleep-deprived EEG, MRI and PET in the prediction of surgical treatment for epilepsy.**
  Author(s): DellaBadia J Jr, Bell WL, Keyes JW Jr, Mathews VP, Glazier SS.
  Source: Seizure : the Journal of the British Epilepsy Association. 2002 July; 11(5): 303-9.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12076102&dopt=Abstract

- **Bathing epilepsy.**
  Author(s): Seneviratne U.
  Source: Seizure : the Journal of the British Epilepsy Association. 2001 October; 10(7): 516-7.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11749110&dopt=Abstract

- **Betel nut indulgence as a cause of epilepsy.**
  Author(s): Huang Z, Xiao B, Wang X, Li Y, Deng H.
  Source: Seizure : the Journal of the British Epilepsy Association. 2003 September; 12(6): 406-8.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12915088&dopt=Abstract

- **Brain histamine XE "Histamine" in the WAG/RIJ rat, an animal model of absence epilepsy.** Author(s): Midzyanovskaya IS, Kuznetsova GD, Tuomisto L.

Source: Inflammation Research : Official Journal of the European Histamine Research Society. [et Al.]. 2002 April; 51 Suppl 1: S49-50.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12013406&dopt=Abstract

- **Clinical care of pregnant women with epilepsy: neural tube defects and folic acid supplementation.**
  Author(s): Yerby MS.
  Source: Epilepsia. 2003; 44 Suppl 3: 33-40. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12790884&dopt=Abstract

- **Clinical observation on 930 child epilepsy cases treated with anti-epilepsy capsules.**
  Author(s): Ma R, Li S, Li X, Hu S, Sun X, Liu Y, Zhang X, Li X, Ma X.
  Source: J Tradit Chin Med. 2003 June; 23(2): 109-12.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12875066&dopt=Abstract

- **Comparative utility of technetium-99m hexamethylpropylenamine oxime single photon emission computed tomography (SPECT) with anatomic neuroimaging and electroencephalography (EEG) in childhood intractable epilepsy.**
  Author(s): Kalra V, Gulati S, Rana KS, Bal CS, Bhatia M.
  Source: Journal of Child Neurology. 2001 April; 16(4): 257-63.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11332460&dopt=Abstract

- **Comparison of fluorine-18 deoxyglucose and O-15 water PET in temporal lobe epilepsy.**
  Author(s): Tatlidil R, Luther S, West A, Jadvar H, Kingman T.
  Source: Acta Neurol Belg. 2000 December; 100(4): 214-20.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11233675&dopt=Abstract

- **Contribution of SISCOM imaging in the presurgical evaluation of temporal lobe epilepsy related to dysembryoplastic neuroepithelial tumors.**
  Author(s): Valenti MP, Froelich S, Armspach JP, Chenard MP, Dietemann JL, Kerhli P, Marescaux C, Hirsch E, Namer IJ.
  Source: Epilepsia. 2002 March; 43(3): 270-6.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11906512&dopt=Abstract

- **Corrections to: Clinical Care of Pregnant Women with Epilepsy: Neural Tube Defects and Folic Acid Supplementation.**
  Author(s): Yerby MS.
  Source: Epilepsia. 2003 November; 44(11): 1465.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=14636360&dopt=Abstract

- **Correlation between GABA(A) receptor density and vagus nerve stimulation in individuals with drug-resistant partial epilepsy.**
  Author(s): Marrosu F, Serra A, Maleci A, Puligheddu M, Biggio G, Piga M.
  Source: Epilepsy Research. 2003 June-July; 55(1-2): 59-70.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12948617&dopt=Abstract

- **Correlation of hippocampal glucose oxidation capacity and interictal FDG-PET in temporal lobe epilepsy.**
  Author(s): Vielhaber S, Von Oertzen JH, Kudin AF, Schoenfeld A, Menzel C, Biersack HJ, Kral T, Elger CE, Kunz WS.
  Source: Epilepsia. 2003 February; 44(2): 193-9.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12558573&dopt=Abstract

- **Correlation of SPECT with pathology and seizure outcome in children undergoing epilepsy surgery.**
  Author(s): Hartley LM, Gordon I, Harkness W, Harding B, Neville BG, Cross JH.
  Source: Developmental Medicine and Child Neurology. 2002 October; 44(10): 676-80.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12418792&dopt=Abstract

- **Cross-cultural differences in levels of knowledge about epilepsy.**
  Author(s): Doughty J, Baker GA, Jacoby A, Lavaud V.
  Source: Epilepsia. 2003 January; 44(1): 115-23.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12581238&dopt=Abstract

- **Detection of mesial temporal lobe hypoperfusion in patients with temporal lobe epilepsy by use of arterial spin labeled perfusion MR imaging.**
  Author(s): Wolf RL, Alsop DC, Levy-Reis I, Meyer PT, Maldjian JA, Gonzalez-Atavales J, French JA, Alavi A, Detre JA.
  Source: Ajnr. American Journal of Neuroradiology. 2001 August; 22(7): 1334-41.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11498422&dopt=Abstract

- **Devices in the treatment of epilepsy.**
  Author(s): Karceski S.
  Source: Seminars in Neurology. 2002 September; 22(3): 259-68. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12528051&dopt=Abstract

- **Did Ezekiel have temporal lobe epilepsy?**
  Author(s): Altschuler EL.
  Source: Archives of General Psychiatry. 2002 June; 59(6): 561-2.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12044200&dopt=Abstract

- **Diet enriched with omega-3 fatty acids alleviates convulsion symptoms in epilepsy patients.**
  Author(s): Schlanger S, Shinitzky M, Yam D.
  Source: Epilepsia. 2002 January; 43(1): 103-4.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11879394&dopt=Abstract

- **Digital photography and 3D MRI-based multimodal imaging for individualized planning of resective neocortical epilepsy surgery.**
  Author(s): Wellmer J, von Oertzen J, Schaller C, Urbach H, Konig R, Widman G, Van Roost D, Elger CE.
  Source: Epilepsia. 2002 December; 43(12): 1543-50.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12460257&dopt=Abstract

- **EEG and evoked potential recording from the subthalamic nucleus for deep brain stimulation of intractable epilepsy.**
  Author(s): Dinner DS, Neme S, Nair D, Montgomery EB Jr, Baker KB, Rezai A, Luders HO.
  Source: Clinical Neurophysiology : Official Journal of the International Federation of Clinical Neurophysiology. 2002 September; 113(9): 1391-402.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12169320&dopt=Abstract

- **Electrical resection: new concept in management of focal epilepsy.**
  Author(s): Jaseja H.
  Source: Medical Hypotheses. 2002 November; 59(5): 498-500.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12376070&dopt=Abstract

- **Electrical stimulation for epilepsy: stimulation of hippocampal foci.**
  Author(s): Velasco F, Velasco M, Velasco AL, Menez D, Rocha L.
  Source: Stereotactic and Functional Neurosurgery. 2001; 77(1-4): 223-7.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12378080&dopt=Abstract

- **Epilepsy and all that jazz.**
  Author(s): Puranam RS, McNamara JO.
  Source: Nature Medicine. 2001 October; 7(10): 1103-5.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11590427&dopt=Abstract

- **Epilepsy and seizure disorders: a review of literature relative to chiropractic care of children.**
  Author(s): Pistolese RA.
  Source: Journal of Manipulative and Physiological Therapeutics. 2001 March-April; 24(3): 199-205. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11313616&dopt=Abstract

- **Epilepsy and surgical mapping.**
  Author(s): Richardson MP.
  Source: British Medical Bulletin. 2003; 65: 179-92. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12697625&dopt=Abstract

- **Epilepsy and the ancient world: from the magic beliefs of the Babylonians to the Hippocratic scientific thinking.**
  Author(s): Daras M, Papakostas G, Tuchman AI.
  Source: Journal of the History of the Neurosciences. 1994 October; 3(4): 233-6.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11618824&dopt=Abstract

- **Epilepsy in Chinese culture.**
  Author(s): Lee TM, Yang SH, Ng PK.
  Source: The American Journal of Chinese Medicine. 2001; 29(1): 181-4. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11321477&dopt=Abstract

- **Epilepsy surgery in childhood.**
  Author(s): Cross JH.
  Source: Epilepsia. 2002; 43 Suppl 3: 65-70. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12060008&dopt=Abstract

- **Epilepsy surgery in infancy. A review of four cases.**
  Author(s): Olavarria G, Petronio JA.
  Source: Pediatric Neurosurgery. 2003 July; 39(1): 44-9.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12784078&dopt=Abstract

- **Epilepsy surgery, delays and referral patterns-are all your epilepsy patients controlled?**
  Author(s): Benbadis SR, Heriaud L, Tatum WO, Vale FL.
  Source: Seizure : the Journal of the British Epilepsy Association. 2003 April; 12(3): 167-70.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12651083&dopt=Abstract

- **Epilepsy surgery. Presurgical evaluation.**
  Author(s): Sheth RD.
  Source: Neurologic Clinics. 2002 November; 20(4): 1195-215. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12616688&dopt=Abstract

- **Epilepsy with auditory features: a LGI1 gene mutation suggests a loss-of-function mechanism.**
  Author(s): Pizzuti A, Flex E, Di Bonaventura C, Dottorini T, Egeo G, Manfredi M, Dallapiccola B, Giallonardo AT.

Source: Annals of Neurology. 2003 March; 53(3): 396-9. Erratum In: Ann Neurol. 2003 July; 54(1): 137.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12601709&dopt=Abstract

- **Epilepsy.**
  Author(s): Marson A, Ramaratnam S.
  Source: Clin Evid. 2002 June; (7): 1153-68. Review. No Abstract Available.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12230734&dopt=Abstract

- **Epileptic activity influences the speech organization in medial temporal lobe epilepsy.**
  Author(s): Janszky J, Jokeit H, Heinemann D, Schulz R, Woermann FG, Ebner A.
  Source: Brain; a Journal of Neurology. 2003 September; 126(Pt 9): 2043-51. Epub 2003 June 23.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12821521&dopt=Abstract

- **Evidence-based prescribing in adults with learning disability and epilepsy.**
  Author(s): Kerr M, Bowley C.
  Source: Epilepsia. 2001; 42 Suppl 1: 44-5; Discussion 50-1.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11422357&dopt=Abstract

- **FDG-PET images quantified by probabilistic atlas of brain and surgical prognosis of temporal lobe epilepsy.**
  Author(s): Lee SK, Lee DS, Yeo JS, Lee JS, Kim YK, Jang MJ, Kim KK, Kim SK, Oh JB, Chung CK.
  Source: Epilepsia. 2002 September; 43(9): 1032-8.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12199728&dopt=Abstract

- **Felbamate, gabapentin and topiramate as adjuvant antiepileptic drugs in experimental models of epilepsy.**
  Author(s): Czuczwar SJ, Przesmycki K.
  Source: Polish Journal of Pharmacology. 2001 January-February; 53(1): 65-8.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11785915&dopt=Abstract

- **Focal functional deficits in temporal lobe epilepsy on PET scans and the intracarotid amobarbital procedure: comparison of patients with unitemporal epilepsy with those requiring intracranial recordings.**
  Author(s): Salanova V, Markand O, Worth R.
  Source: Epilepsia. 2001 February; 42(2): 198-203.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11240589&dopt=Abstract

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- **Suprathreshold 0.3 Hz repetitive TMS prolongs the cortical silent period: potential implications for therapeutic trials in epilepsy.**
Author(s): Cincotta M, Borgheresi A, Gambetti C, Balestrieri F, Rossi L, Zaccara G, Ulivelli M, Rossi S, Civardi C, Cantello R.
Source: Clinical Neurophysiology : Official Journal of the International Federation of Clinical Neurophysiology. 2003 October; 114(10): 1827-33.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=14499744&dopt=Abstract

- **Tc-99m ethyl cysteinate dimer brain perfusion spect in presurgical evaluation for intractable partial epilepsy in a young infant.**
Author(s): Friberg J, Choquet P, De Saint-Martin A, Christmann D, Joanny-Flinnois O, Sainte-Rose C, Hirsch E, Fischbach M, Namer I, Constantinesco A.
Source: Clinical Nuclear Medicine. 2001 June; 26(6): 557-8.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11353312&dopt=Abstract

- **Temporal lobe epilepsy and corpora amylacea in the hippocampus: clinicopathologic correlation.**
Author(s): Kawamura T, Morioka T, Nishio S, Fukui K, Fukui M.
Source: Neurological Research. 2002 September; 24(6): 563-9.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12238621&dopt=Abstract

- **Temporal pole MRI abnormalities in temporal lobe epilepsy.**
Author(s): Ryvlin P, Coste S, Hermier M, Mauguiere F.

Source: Epileptic Disord. 2002 September; 4 Suppl 1: S33-9.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12424089&dopt=Abstract

- **The current status of neuroimaging for epilepsy: editorial review.**
Author(s): Duncan J.
Source: Current Opinion in Neurology. 2003 April; 16(2): 163-4. Review.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12644743&dopt=Abstract

- **The role of nonpharmaceutic conservative interventions in the treatment and secondary prevention of epilepsy.**
Author(s): Wolf P.
Source: Epilepsia. 2002; 43 Suppl 9: 2-5.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12383271&dopt=Abstract

- **The Terry Parker case: marijuana for epilepsy -- and soon for HIV/AIDS?**
Author(s): Riley D, Oscapella E.
Source: Can Hiv Aids Policy Law Newsl. 1997-98 Winter; 3-4(4-1): 20-3.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11365283&dopt=Abstract

- **The treatment gap and primary health care for people with epilepsy in rural Gambia.**
Author(s): Coleman R, Loppy L, Walraven G.
Source: Bulletin of the World Health Organization. 2002; 80(5): 378-83.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12077613&dopt=Abstract

- **The use of stereotactic radiosurgery to treat intractable childhood partial epilepsy.**
Author(s): Dunoyer C, Ragheb J, Resnick T, Alvarez L, Jayakar P, Altman N, Wolf A, Duchowny M.
Source: Epilepsia. 2002 March; 43(3): 292-300.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11906515&dopt=Abstract

- **The usefulness of subtraction ictal SPECT coregistered to MRI in single- and dual-headed SPECT cameras in partial epilepsy.**
Author(s): Kaiboriboon K, Lowe VJ, Chantarujikapong SI, Hogan RE.
Source: Epilepsia. 2002 April; 43(4): 408-14.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11952772&dopt=Abstract

- **The utility of a 3-dimensional, large-field-of-view, sodium iodide crystal--based PET scanner in the presurgical evaluation of partial epilepsy.**
Author(s): O'Brien TJ, Hicks RJ, Ware R, Binns DS, Murphy M, Cook MJ.

Source: Journal of Nuclear Medicine : Official Publication, Society of Nuclear Medicine. 2001 August; 42(8): 1158-65.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11483674&dopt=Abstract

- **Transcranial magnetic stimulation and epilepsy.**
  Author(s): Tassinari CA, Cincotta M, Zaccara G, Michelucci R.
  Source: Clinical Neurophysiology : Official Journal of the International Federation of Clinical Neurophysiology. 2003 May; 114(5): 777-98. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12738425&dopt=Abstract

- **Transcranial magnetic stimulation and epilepsy.**
  Author(s): Macdonell RA, Curatolo JM, Berkovic SF.
  Source: Journal of Clinical Neurophysiology : Official Publication of the American Electroencephalographic Society. 2002 August; 19(4): 294-306. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12436086&dopt=Abstract

- **Treatment of depression in patients with epilepsy: problems, pitfalls, and some solutions.**
  Author(s): Krishnamoorthy ES.
  Source: Epilepsy & Behavior : E&B. 2003 October; 4 Suppl 3: S46-54.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=14592640&dopt=Abstract

- **Treatment of memory disorders in epilepsy.**
  Author(s): Shulman MB, Barr W.
  Source: Epilepsy & Behavior : E&B. 2002 October; 3(5S): 30-34.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12609318&dopt=Abstract

- **Use of aromatherapy (with or without hypnosis) in the treatment of intractable epilepsy-a two-year follow-up study.**
  Author(s): BETTS T.
  Source: Seizure : the Journal of the British Epilepsy Association. 2003 December; 12(8): 534-538.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=14630489&dopt=Abstract

- **Use of complementary medicine in children with attention deficit hyperactivity disorder and epilepsy.**
  Author(s): Gross-Tsur V, Lahad A, Shalev RS.
  Source: Pediatric Neurology. 2003 July; 29(1): 53-5.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=13679122&dopt=Abstract

- **Vagus nerve stimulation reduces daytime sleepiness in epilepsy patients.**
  Author(s): Malow BA, Edwards J, Marzec M, Sagher O, Ross D, Fromes G.

Source: Neurology. 2001 September 11; 57(5): 879-84.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11552020&dopt=Abstract

- **Visual activation positron emission tomography for presurgical evaluation of occipital lobe epilepsy--case report.**
Author(s): Nakama H, Ohtomo S, Otsuki T, Kaneko Y, Ohnishi T, Matsuda H.
Source: Neurol Med Chir (Tokyo). 2002 August; 42(8): 356-60.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12206492&dopt=Abstract

- **VNS in patients with previous unsuccessful resective epilepsy surgery: antiepileptic and psychotropic effects.**
Author(s): Koutroumanidis M, Binnie CD, Hennessy MJ, Alarcon G, Elwes RD, Toone BK, Chandler C, Selway R, Polkey CE, O'Connor SA.
Source: Acta Neurologica Scandinavica. 2003 February; 107(2): 117-21.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12580861&dopt=Abstract

- **Zinc, magnesium and copper profiles in three experimental models of epilepsy.**
Author(s): Doretto MC, Simoes S, Paiva AM, Osorio-Neto E.
Source: Brain Research. 2002 November 22; 956(1): 166-72.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12426059&dopt=Abstract

Additional Web Resources

A number of additional Web sites offer encyclopedic information covering CAM and related topics. The following is a representative sample:

- Alternative Medicine Foundation, Inc.: **http://www.herbmed.org/**
- AOL: **http://search.aol.com/cat.adp?id=169&layer=&from=subcats**
- Chinese Medicine: **http://www.newcenturynutrition.com/**
- drkoop.com®: **http://www.drkoop.com/InteractiveMedicine/IndexC.html**
- Family Village: **http://www.familyvillage.wisc.edu/med_altn.htm**
- Google: **http://directory.google.com/Top/Health/Alternative/**
- Healthnotes: **http://www.healthnotes.com/**
- MedWebPlus: **http://medwebplus.com/subject/Alternative_and_Complementary_Medicine**
- Open Directory Project: **http://dmoz.org/Health/Alternative/**
- HealthGate: **http://www.tnp.com/**
- WebMD®Health: **http://my.webmd.com/drugs_and_herbs**
- WholeHealthMD.com: **http://www.wholehealthmd.com/reflib/0,1529,00.html**
- Yahoo.com: **http://dir.yahoo.com/Health/Alternative_Medicine/**

The following is a specific Web list relating to epilepsy; please note that any particular subject below may indicate either a therapeutic use, or a contraindication (potential danger), and does not reflect an official recommendation:

- **General Overview**

  Bone Loss
  Source: Integrative Medicine Communications; www.drkoop.com

  Diabetes
  Source: Prima Communications, Inc.www.personalhealthzone.com

  Epilepsy
  Source: Healthnotes, Inc.; www.healthnotes.com

  Epilepsy
  Source: Integrative Medicine Communications; www.drkoop.com

  Migraine Headaches
  Source: Healthnotes, Inc.; www.healthnotes.com

  Obesity
  Source: Integrative Medicine Communications; www.drkoop.com

  Osteoporosis
  Source: Integrative Medicine Communications; www.drkoop.com

  Osteoporosis
  Source: Prima Communications, Inc.www.personalhealthzone.com

  Seizure Disorders
  Source: Integrative Medicine Communications; www.drkoop.com

- **Alternative Therapy**

  Biofeedback
  Source: Integrative Medicine Communications; www.drkoop.com

  Biofeedback
  Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
  Hyperlink:
  http://www.wholehealthmd.com/refshelf/substances_view/0,1525,675,00.html

  Color Therapy
  Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
  Hyperlink:
  http://www.wholehealthmd.com/refshelf/substances_view/0,1525,683,00.html

  Fasting
  Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com

Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,694,00.html

Magnet Therapy
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,715,00.html

- **Chinese Medicine**

Baifan
Alternative names: Alum; Baifan (Bai Fan); Alumen
Source: Chinese Materia Medica

Dannanxing
Alternative names: Bile Arisaema; Dannanxing (Dan Nan Xing); Arisaema Cum Bile
Source: Chinese Materia Medica

Hujiao
Alternative names: Pepper Fruit; Fructus Piperis
Source: Chinese Materia Medica

Jinmengshi
Alternative names: Mica-schist; Lapis Micas Aureus
Source: Chinese Materia Medica

Lingyangjiao
Alternative names: Antelope Horn; Cornu Saigae Tataricae
Source: Chinese Materia Medica

Niuhuang
Alternative names: Cow-bezoar; Calculus Bovis
Source: Chinese Materia Medica

Niuhuang Qingxin Wan
Alternative names: Niuhuang Qingxin Pills
Source: Pharmacopoeia Commission of the Ministry of Health, People's Republic of China

Qingmengshi
Alternative names: Chlorite Schist; Lapis Chloriti
Source: Chinese Materia Medica

Shichangpu
Alternative names: Grassleaf Sweetflag Rhizome; Rhizoma Acori Talarinowii
Source: Chinese Materia Medica

Suhexiang
Alternative names: Storax; Styrax
Source: Chinese Materia Medica

Tianma
Alternative names: Tall Gastrodia Tuber; Rhizoma Gastrodiae
Source: Chinese Materia Medica

Tiannanxing
Alternative names: Jackinthepulpit Tuber; Rhizoma Arisaematis
Source: Chinese Materia Medica

Yujin
Alternative names: Turmeric Root Tuber; Radix Curcumae
Source: Chinese Materia Medica

Zhenzhu
Alternative names: Nacre; Zhenzhumu; Concha Margaritifera Usta
Source: Chinese Materia Medica

Zhusha
Alternative names: Cinnabar; Cinnabaris
Source: Chinese Materia Medica

Zhuyazao
Alternative names: Chinese Honeylocust Abnormal Fruit; Fructus Gleditsiae Abnormalis
Source: Chinese Materia Medica

- **Herbs and Supplements**

American Scullcap
Alternative names: Scutellaria lateriflora
Source: Healthnotes, Inc.; www.healthnotes.com

Amino Acids Overview
Source: Healthnotes, Inc.; www.healthnotes.com

Anticonvulsants
Source: Healthnotes, Inc.; www.healthnotes.com

Asian Ginseng
Alternative names: Panax ginseng
Source: Healthnotes, Inc.; www.healthnotes.com

Barbiturates
Source: Healthnotes, Inc.; www.healthnotes.com

Benzodiazepines
Source: Healthnotes, Inc.; www.healthnotes.com

Beta-carotene
Source: Prima Communications, Inc.www.personalhealthzone.com

Blue Vervain
Source: The Canadian Internet Directory for Holistic Help, WellNet, Health and Wellness Network; www.wellnet.ca

Bupleurum
Alternative names: Bupleurum chinense, Bupleurum falcatum
Source: Healthnotes, Inc.; www.healthnotes.com

Carbamazepine
Alternative names: Atretol, Carbatrol, Epitol, Tegretol, Tegretol XR
Source: Prima Communications, Inc.www.personalhealthzone.com

Chinese Scullcap
Alternative names: Scutellaria baicalensis
Source: Healthnotes, Inc.; www.healthnotes.com

Coleus Forskohlii
Source: Prima Communications, Inc.www.personalhealthzone.com

DMAE
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,10023,00.html

Fiber
Source: Integrative Medicine Communications; www.drkoop.com

GABA
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,10027,00.html

GABA (Gamma-Amino Butyric Acid)
Source: Healthnotes, Inc.; www.healthnotes.com

Ginger
Alternative names: Zingiber officinale
Source: Healthnotes, Inc.; www.healthnotes.com

GLA (Gamma-Linolenic Acid)
Source: Prima Communications, Inc.www.personalhealthzone.com

Glutamic Acid
Source: Healthnotes, Inc.; www.healthnotes.com

Glutamine
Source: Integrative Medicine Communications; www.drkoop.com

Glutamine
Source: Prima Communications, Inc.www.personalhealthzone.com

Hydantoin Derivatives
Source: Integrative Medicine Communications; www.drkoop.com

Hyssop
Alternative names: Hyssopus officinalis
Source: Healthnotes, Inc.; www.healthnotes.com

Hyssop
Source: The Canadian Internet Directory for Holistic Help, WellNet, Health and Wellness Network; www.wellnet.ca

Ipriflavone
Source: Prima Communications, Inc.www.personalhealthzone.com

Ispaghula
Alternative names: Psyllium
Source: Integrative Medicine Communications; www.drkoop.com

Kava
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,798,00.html

Licorice
Alternative names: Glycyrrhiza glabra, Glycyrrhiza uralensis
Source: Healthnotes, Inc.; www.healthnotes.com

Lobelia
Source: The Canadian Internet Directory for Holistic Help, WellNet, Health and Wellness Network; www.wellnet.ca

Medium-Chain Triglycerides
Source: Prima Communications, Inc.www.personalhealthzone.com

Melatonin
Source: Healthnotes, Inc.; www.healthnotes.com

Melatonin
Source: Integrative Medicine Communications; www.drkoop.com

Melatonin
Source: Prima Communications, Inc.www.personalhealthzone.com

Melatonin
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,804,00.html

Menadione
Source: Integrative Medicine Communications; www.drkoop.com

Menaphthone
Source: Integrative Medicine Communications; www.drkoop.com

Menaquinone
Source: Integrative Medicine Communications; www.drkoop.com

Mistletoe
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,10109,00.html

N-Acetyl Cysteine
Source: Healthnotes, Inc.; www.healthnotes.com

Phenobarbital
Source: Healthnotes, Inc.; www.healthnotes.com

Phylloquinone
Source: Integrative Medicine Communications; www.drkoop.com

Piper Nigrum
Alternative names: Black Pepper
Source: Alternative Medicine Foundation, Inc.; www.amfoundation.org

Plantago Isphagula
Alternative names: Psyllium
Source: Integrative Medicine Communications; www.drkoop.com

Primidone
Alternative names: Mysoline
Source: Prima Communications, Inc.www.personalhealthzone.com

Psyllium
Alternative names: Ispaghula
Source: Integrative Medicine Communications; www.drkoop.com

Skullcap
Source: Prima Communications, Inc.www.personalhealthzone.com

Skullcap
Source: The Canadian Internet Directory for Holistic Help, WellNet, Health and Wellness Network; www.wellnet.ca

Taurine
Source: Healthnotes, Inc.; www.healthnotes.com

Taurine
Source: Prima Communications, Inc.www.personalhealthzone.com

Valproic Acid
Source: Healthnotes, Inc.; www.healthnotes.com

Valproic Acid
Source: Prima Communications, Inc.www.personalhealthzone.com

Valproic Acid Derivatives
Source: Integrative Medicine Communications; www.drkoop.com

General References

A good place to find general background information on CAM is the National Library of Medicine. It has prepared within the MEDLINEplus system an information topic page dedicated to complementary and alternative medicine. To access this page, go to the MEDLINEplus site at **http://www.nlm.nih.gov/medlineplus/alternativemedicine.html**. This Web site provides a general overview of various topics and can lead to a number of general sources.

CHAPTER 4. DISSERTATIONS ON EPILEPSY

Overview

In this chapter, we will give you a bibliography on recent dissertations relating to epilepsy. We will also provide you with information on how to use the Internet to stay current on dissertations. **IMPORTANT NOTE:** When following the search strategy described below, you may discover non-medical dissertations that use the generic term "epilepsy" (or a synonym) in their titles. To accurately reflect the results that you might find while conducting research on epilepsy, we have not necessarily excluded non-medical dissertations in this bibliography.

Dissertations on Epilepsy

ProQuest Digital Dissertations, the largest archive of academic dissertations available, is located at the following Web address: **http://wwwlib.umi.com/dissertations**. From this archive, we have compiled the following list covering dissertations devoted to epilepsy. You will see that the information provided includes the dissertation's title, its author, and the institution with which the author is associated. The following covers recent dissertations found when using this search procedure:

- **A Phenomenology of Epilepsy: Graphic Illustrations of Epileptics' Perception of Their Worlds (Thematic Clustering, Common Sentiments, Assessment)** by De La Rosa, Maria L., PhD from The Union for Experimenting Colleges and Universities, 1985, 400 pages
  http://wwwlib.umi.com/dissertations/fullcit/8605929
- **A Qualitative Analysis of Figural Memory Performance in Persons with Epilepsy** by Hoffnung, Deborah Schrager; PhD from Louisiana State University and Agricultural & Mechanical College, 2002, 85 pages
  http://wwwlib.umi.com/dissertations/fullcit/3063055
- **A Study of Subjective Symptoms Associated with Seizure Disorders in Adolescents** by Fletcher-Janzen, Elaine, EDD from The College of William and Mary, 1993, 115 pages
  http://wwwlib.umi.com/dissertations/fullcit/9414206

- **An Analysis of Gender Differences on the Washington Psychosocial Seizure Inventory among Surgical Candidates with Temporal Lobe Epilepsy** by Decosta, James Russell; PhD from Alliant International University, Fresno, 2002, 97 pages
http://wwwlib.umi.com/dissertations/fullcit/3062705
- **An Empirical Test of the Labor Market Discrimination Hypothesis for People with Epilepsy** by Famulari, Melissa, PhD from University of Washington, 1987, 199 pages
http://wwwlib.umi.com/dissertations/fullcit/8802227
- **An Investigation of Variables Related to Epilepsy and Performance on Cognitive and Achievement Tasks** by Dasher, Tanis King, PhD from Howard University, 1987, 120 pages
http://wwwlib.umi.com/dissertations/fullcit/8809208
- **An Iowa Survey of Employment Related Factors among Persons with Epilepsy.** by Sheridan, Richard Ludeman, PhD from The University of Iowa, 1978, 219 pages
http://wwwlib.umi.com/dissertations/fullcit/7912899
- **Assessment of Dietary Compliance, Growth, and Seizure Reduction in Children Using the Ketogenic Diet As a Treatment for Intractable Epilepsy** by Peterson, Sarah Jean; MS from Rush University, 2002, 311 pages
http://wwwlib.umi.com/dissertations/fullcit/1409776
- **Assessment of Human Service Needs of Persons with Epilepsy and Cerebral Palsy.** by Bruyere, Susanne Marie, PhD from The University of Wisconsin - Madison, 1975, 219 pages
http://wwwlib.umi.com/dissertations/fullcit/7528788
- **Attention Performance in Children Affected with Absence Epilepsy and Their First Degree Relatives (Familial Markers, Neuropsychology)** by Levav, Maria L., PhD from University of Maryland College Park, 1991, 157 pages
http://wwwlib.umi.com/dissertations/fullcit/9222717
- **Attitude Change toward Epilepsy As a Function of Viewing a Seizure Episode** by Sorensen, David Allen, PhD from The University of Connecticut, 1973, 47 pages
http://wwwlib.umi.com/dissertations/fullcit/7309844
- **Attitudes of In-Service Elementary School Teachers in the San Diego Public Schools Regarding Persons with Epilepsy.** by Dillon, Stephen Lawrence, PhD from United States International University, 1977, 124 pages
http://wwwlib.umi.com/dissertations/fullcit/7909538
- **Attitudes toward Epilepsy in Higher Education** by Milan, Leo Francis, PhD from University of Denver, 1967, 194 pages
http://wwwlib.umi.com/dissertations/fullcit/6710330
- **Behavioral Characteristics of Children with Partial Complex and Generalized Epilepsy** by Town, Patricia Anne, PhD from University of Georgia, 1988, 119 pages
http://wwwlib.umi.com/dissertations/fullcit/8910474
- **Beliefs about Folk Medicine As Related to Compliance with Drug Instructions among Latinos with Epilepsy (Medical Anthropology)** by Power, Ann Marie, PhD from United States International University, 1991, 345 pages
http://wwwlib.umi.com/dissertations/fullcit/9209754

- **Cardiopulmonary Hemodynamic Consequences of Motor Seizure Activity in the Kainic Acid Model of Temporal Lobe Epilepsy** by Rhodes, Jann; PhD from Colorado State University, 2002, 220 pages
  http://wwwlib.umi.com/dissertations/fullcit/3053446
- **Characteristics and Attitudes of and Guidelines for Counselors Working with Persons with Epilepsy.** by Biel, Marcia Anne, PhD from University of Missouri - Kansas City, 1978, 120 pages
  http://wwwlib.umi.com/dissertations/fullcit/7900001
- **Clinical and Molecular Genetic Analysis of Familial Idiopathic Epilepsy: Linkage to Chromosome 19Q and Investigation of Candidate Genes** by McKee, Shane Alexander; MD from Queen's University of Belfast (northern Ireland), 2002, 180 pages
  http://wwwlib.umi.com/dissertations/fullcit/f364913
- **Cytoarchitectural, Neurochemical and Circuitry Reorganization in Kainate-Induced Epilepsy: a Model for Human Temporal Lobe Epilepsy with Hippocampal Sclerosis** by Siddiqui, Adnan Hussain; PhD from The University of Rochester, 2003, 433 pages
  http://wwwlib.umi.com/dissertations/fullcit/3092244
- **Design of a Medical Image Data Warehouse for Epilepsy Diagnosis and Research** by Soo Hoo, Kent, Jr.; PhD from Univ. of Calif., San Francisco with the Univ. of Calif., Berkeley, 2002, 125 pages
  http://wwwlib.umi.com/dissertations/fullcit/3051031
- **Development and Characterization of Adenosine Releasing Cellular Grafts for an Ex Vivo Gene Therapy of Focal Epilepsy** by Huber, Alexander Felix; DRSCNAT from Eidgenoessische Technische Hochschule Zuerich (Switzerland), 2002, 111 pages
  http://wwwlib.umi.com/dissertations/fullcit/f364353
- **Emx1 Null Mutant Mouse Phenotype: Potential Implications for Human Epilepsy** by Sofia, Francesca; PhD from Open University (United Kingdom), 2002
  http://wwwlib.umi.com/dissertations/fullcit/f352113
- **Epilepsy and Fair Employment.** by Hauck, Vern Edward, PhD from The University of Iowa, 1974, 244 pages
  http://wwwlib.umi.com/dissertations/fullcit/7513760
- **Epilepsy and Holy Orders in the Canonical Practice of the Western Church** by Churchwell, Stephen T., JCD from The Catholic University of America, 1982, 221 pages
  http://wwwlib.umi.com/dissertations/fullcit/8226674
- **Epilepsy and Reading Skills in Children** by Antonello, Judy Lee, PhD from University of Minnesota, 1999, 1207 pages
  http://wwwlib.umi.com/dissertations/fullcit/9921420
- **Epilepsy and Synaptic Reorganization in Models of Status Epilepticus and Hypoxia-ischemia** by Williams, Philip Andrew; PhD from Colorado State University, 2002, 181 pages
  http://wwwlib.umi.com/dissertations/fullcit/3053459
- **Epilepsy As a Pharmakon in Dostoevsky's Fiction (Russia)** by Gedney, Curtis Lester, PhD from The University of Arizona, 1992, 201 pages
  http://wwwlib.umi.com/dissertations/fullcit/9234896
- **Epilepsy Self-Help Groups, Stigma, and Social Support** by Droge, David Allen, PhD from Northwestern University, 1983, 328 pages
  http://wwwlib.umi.com/dissertations/fullcit/8400664

- **Evaluation of Short-Term Training for Rehabilitation Counselors: Effectiveness of an Institute on Epilepsy** by Stude, Everett Wilson, Jr., EDD from University of Southern California, 1972, 189 pages
  http://wwwlib.umi.com/dissertations/fullcit/7217517
- **Experiments in the Automation and Quantification of Eeg Interpretation : Localized Brain Lesions and Epilepsy** by Gotman, Jean; PhD from McGill University (Canada), 1976
  http://wwwlib.umi.com/dissertations/fullcit/NK31781
- **Focal Epilepsy and Related Disorders: Genetic, Metabolic and Prognostic Studies** by Andermann, Eva; PhD from McGill University (Canada), 1972
  http://wwwlib.umi.com/dissertations/fullcit/NK14401
- **Glutamate Injury-Induced Epileptogenesis in Cultured Hippocampal Neurons: an in Vitro Model of Stroke-Induced Epilepsy** by Sun, David Antonio; PhD from Virginia Commonwealth University, 2002, 218 pages
  http://wwwlib.umi.com/dissertations/fullcit/3041398
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CHAPTER 5. CLINICAL TRIALS AND EPILEPSY

Overview

In this chapter, we will show you how to keep informed of the latest clinical trials concerning epilepsy.

Recent Trials on Epilepsy

The following is a list of recent trials dedicated to epilepsy.[8] Further information on a trial is available at the Web site indicated.

- **Activating Effects of Sleep Deprivation On Synchronized MEF-EEG Recordings Of Epilepsy Patients with Non-Diagnostic EEG**

  Condition(s): Epilepsy

  Study Status: This study is currently recruiting patients.

  Sponsor(s): National Institute of Neurological Disorders and Stroke (NINDS)

  Purpose - Excerpt: Objective: We would like to evaluate the activating effects of complete sleep deprivation (SD) on synchronized MEG-EEG recordings, and on each of the components singly, in relation to the degree of alertness during recording (awake vs. sleep) and the subjective degree of sleepiness as assessed by standardized scales. We postulate that acute SD will increase the diagnostic yield of synchronized MEG-EEG and activate both modalities (MEG, EEG) to the same degree. The increased diagnostic utility of MEG could improve the epilepsy surgery evaluation procedure for many patients by rendering invasive studies less necessary. The medical and economic utilization of such expensive resources as MEG could thus be rationalized. Population: Participants of this study will be epilepsy patients whose last routine interictal EEG (performed at least two weeks earlier), subsequent pre-screening EEG and screening MEG-EEG show no interictal epileptiform discharges (IEDs), and are therefore considered non-diagnostic. Study Design/Methods: We will use a 275-channel Whole-head MEG System (CTF Systems 2001 Inc.). Patients will have a screening, non-SD and SD MEG-EEG after their degree of sleepiness is assessed using the Epworth, Stanford and Karnolinska sleepiness scales. Starting one day after the MEG-EEG, SD and non-

[8] These are listed at **www.ClinicalTrials.gov**.

SDMEG-EEG will be performed in random order within 14-21 days of each other. This will ensure an equal amount of sampling effect in SD and non-SD data sets. The MEG-EEG session will last 90 to 180 minutes. Patients may take a break after at least 10 minutes a scanner. We will attempt to record a comparable amount of awake and sleep data. At least thirty minutes of artifact-free baseline, non-SD and SD MEG-EEG will be analyzed. For the purpose of blinding, each modality will be read independently by two readers, each of whom will be blinded to the relationship of the MEG-EEG data to sleep deprivation, results obtained by the other modality and subjective degree of sleepiness. Only interpretations of each modality agreed upon by both readers will be accepted. When there is no agreement, a third independent reader will resolve the disagreement. Outcomes: The primary outcome measure will be the proportion of seizure foci detected and delineated after SD on synchronized MEG-EEG recordings. Comparisons will also be made for each recording modality and between them, according to the state of alertness during recording and subjective feeling of sleepiness before each recording.

Study Type: Observational

Contact(s): see Web site below

Web Site: http://clinicaltrials.gov/ct/show/NCT00071370

- **Brain Infusion of Muscimol to Treat Epilepsy**

  Condition(s): Epilepsy

  Study Status: This study is currently recruiting patients.

  Sponsor(s): National Institute of Neurological Disorders and Stroke (NINDS)

  Purpose - Excerpt: This study will examine the safety and effectiveness of infusing a chemical called muscimol into the brain to control seizures in patients with intractable epilepsy (frequent seizures that persist despite therapy). Muscimol, which is similar to a naturally occurring brain chemical called GABA, has been shown to reduce seizures in rats. After the infusion study, patients will undergo a standard surgical procedure for controlling seizures. Patients 18 years of age or older with intractable epilepsy may be eligible for this study. Candidates will be screened under protocol (75-N-0124 - Monitoring of Seizures, EEG and Serum Antiepileptic Drug Concentrations in Patients with Uncontrolled Epilepsy) with a medical history, physical and neurologic examination, chest X-ray, electrocardiogram, blood and urine tests, electroencephalographic (EEG) monitoring and magnetic resonance imaging (MRI) of the head. Patients enrolled in this study will have the following procedures: 1. Computerized tomography (CT) and magnetic resonance imaging (MRI) of the head to guide catheter/electrode placement (see #2). 2. Depth catheter/electrode placement into the presumed or possible location of the seizure focus (the part of the brain where the seizures originate) - Small holes are drilled through the skull. Electrodes with a hole in the center of the tubing that holds them are passed through the brain into the structures usually involved in intractable epilepsy. MRI will be done to check electrode placement. Video-EEG monitoring will continue for 5 days in patients in whom the location of the seizure focus is known but longer (up to 33 days) in patients in whom the seizure focus is difficult to locate. Patients will be tested for their ability to understand and produce speech, see normally, move their arms and legs, distinguish sharp and dull objects, and put pegs in a pegboard. They will be questioned about headache, weakness, numbness or sleepiness. The electrodes will be left in place for muscimol infusion (see #3), except in patients in whom a seizure focus cannot be located. Patients in whom a seizure focus cannot be located will not receive muscimol infusion or undergo surgery. 3. Muscimol infusion - Into the seizure focus, patients will be given two infusions-one of saline (salt

water) alone and one of muscimol diluted in saline. Each infusion will be given over a period of 5 1/2 days, infused at the rate of 0.1 ml (1/50th of a teaspoon) per hour. During the infusions video-EEG recordings will continue and patients will be interviewed and examined as described in #2 above). 4. Blood testing - About 2 tablespoons of blood will be drawn daily during the testing period and for the first 2 days after surgery (see #5). 5. Surgery - Temporal lobectomy or topectomy (removal of a small, specific area of brain tissue) is the standard surgical treatment for medically intractable epilepsy whose seizure focus is not in a critical brain region, such as an area that controls language, movement, or sensation. If the patient's seizures arise from one of these areas, an alternative procedure called multiple subpial transection will be offered. In this procedure, vertical cuts are made in the seizure focus to prevent neurons (nerve cells that transmit electrical impulses) in the focus from spreading the seizure to the rest of the brain. 6. Surgery follow-up - Patients will be monitored in the surgical intensive care unit for 24 to 48 hours and then in the NINDS nursing unit for 4 to 8 days before being discharged to home. Another visit in the NINDS outpatient clinic will be scheduled for 6-12 weeks after surgery.

Phase(s): Phase I

Study Type: Interventional

Contact(s): see Web site below

Web Site: http://clinicaltrials.gov/ct/show/NCT00005925

- **Depression and Health Outcomes in Refractory Epilepsy**

  Condition(s): Depression; Epilepsy

  Study Status: This study is currently recruiting patients.

  Sponsor(s): National Institute of Neurological Disorders and Stroke (NINDS)

  Purpose - Excerpt: To define the benefits of antidepressant treatment or cognitive behavior therapy on mood, function, and quality of life in patients with depression or refractory epilepsy.

  Phase(s): Phase III

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00026637

- **Developmental Effects On Children Of Women Who Take Antiepileptic Drugs During Pregnancy**

  Condition(s): Epilepsy; Seizure; Cognition Disorders

  Study Status: This study is currently recruiting patients.

  Sponsor(s): National Institute of Neurological Disorders and Stroke (NINDS)

  Purpose - Excerpt: To determine if antiepileptic drugs (AEDs) differ in their neurodevelopmental effects. Specifically, do the children of the women with **epilepsy** differ in their behavioral and cognitive development depending on which AED their mother takes during pregnancy?

  Study Type: Observational

  Contact(s): see Web site below

Web Site: http://clinicaltrials.gov/ct/show/NCT00021866

- **Dose Response Study of Zonegran in Patients With Newly Diagnosed Epilepsy**

  Condition(s): Epilepsy, Complex Partial

  Study Status: This study is currently recruiting patients.

  Sponsor(s): Elan Pharmaceuticals

  Purpose - Excerpt: The purpose of this study is to determine whether zonisamide alone is effective as a treatment for epilepsy in newly diagnosed cases.

  Phase(s): Phase III

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00056576

- **Double-blind, placebo-controlled trial of vitamin E as add-on therapy for children with epilepsy**

  Condition(s): Epilepsy

  Study Status: This study is currently recruiting patients.

  Sponsor(s): National Center for Research Resources (NCRR)

  Purpose - Excerpt: This is a study to see if vitamin E helps children with epilepsy have fewer seizures. About 20-30% of children with epilepsy do not have adequate seizure control with established antiepileptic drugs (AEDs). Other options for patients with uncontrolled epilepsy are newer antiepileptic medications, ketogenic diet and surgery. However, a small percentage of patients are candidates for these options. Therefore, additional treatments are needed to improve seizure control in patients with uncontrolled epilepsy. Animal studies have shown an association between vitamin E supplementation and seizure reduction. A study in children also showed that vitamin E helped reduce seizures. However, a similar study in adults did not show a reduction in seizures with vitamin E supplementation. Therefore, this research study is being done to help define vitamin E's usefulness and safety as a treatment for epilepsy. Fifty patients will be recruited from the Children's Epilepsy Program at The Children's Hospital in Denver, Colorado. Qualifying patients will have a confirmed diagnosis of epilepsy that is currently uncontrolled with standard AEDs. The study period is 6 months and includes the following: Baseline period (1 month), Arm I (2 months), Wash-out period (1 month), and Arm II (2 months). Patients must have been on the same AEDs for 2 months before enrollment. All medications and complementary therapies must remain constant throughout the study. If at any point the physician feels it is not best for the patient to continue the study they will be discontinued. Before the study starts, study participants will be asked about seizure activity, what they eat and about any complementary and/or alternative medicine they may use. The study is two phases. Study participants will be given either vitamin E or placebo (fake pill/liquid) in each phase of the study. They will receive both vitamin E and placebo during the study. Which phase they receive vitamin E and placebo will be decided by chance (similar to rolling dice). Study participants will take liquid vitamin E or placebo two times per day. The study participants and study doctors will not know who is taking vitamin E and who is taking placebo. Study participants will come to the hospital for 3 outpatient and 2 inpatient visits. Health-related quality of life questionnaires will be filled out and blood will be drawn at three of the visits. Seizure diaries will be maintained throughout the study.

Phase(s): Phase IV

Study Type: Interventional

Contact(s): see Web site below

Web Site: http://clinicaltrials.gov/ct/show/NCT00004637

- **Early Surgical Intervention to Treat Epilepsy**

  Condition(s): Epilepsy; Epilepsy, Temporal Lobe; Seizures

  Study Status: This study is currently recruiting patients.

  Sponsor(s): National Institute of Neurological Disorders and Stroke (NINDS)

  Purpose - Excerpt: The purpose of this trial is to compare the effectiveness of early surgical intervention for mesial temporal lobe epilepsy to continued treatment with antiepileptic drugs.

  Phase(s): Phase III

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00040326

- **Effects of Treating Obstructive Sleep Apnea in Epilepsy**

  Condition(s): Epilepsy; Sleep Apnea; Obstructive Sleep Apnea

  Study Status: This study is currently recruiting patients.

  Sponsor(s): National Institute of Neurological Disorders and Stroke (NINDS)

  Purpose - Excerpt: The purpose of this trial is to determine whether treating sleep-related breathing disorders in people with epilepsy results in improvement in seizure control or an improvement in alertness during the day.

  Phase(s): Phase II

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00047463

- **Evaluation and Treatment of Patients with Epilepsy**

  Condition(s): Epilepsy

  Study Status: This study is currently recruiting patients.

  Sponsor(s): National Institute of Neurological Disorders and Stroke (NINDS)

  Purpose - Excerpt: This protocol has three purposes: 1) to screen patients with seizures for participation in research studies of NINDS's Clinical Epilepsy Section (CES), 2) to follow the natural course of seizure disorders, and 3) to train CES fellows in evaluating and treating epilepsy. Only standard diagnostic tests and treatments will be used in this study. Patients of any age with seizures who are referred to CES may participate in this study. At the end of the study, patients may be discharged to the care of their referring physician, offered participation in another NINDS research protocol, or followed for teaching purposes. Participants will undergo standard diagnostic procedures used to determine the type of their seizures, what part of the brain they are coming from, what

is causing them, and whether standard drug treatments can help them. These may include some or all of the following: - Physical and neurological examination - Neuropsychological tests - tests of learning and memory - Electroencephalography (EEG) - brain wave recording - Evoked potentials - tests of nerve reactions to lights and sounds - Polysomnography - simultaneous recordings of brain waves, breathing and eye movements - Video-EEG monitoring - simultaneous recording of seizures using a video camera and brain waves - Video-EEG monitoring with extra electrodes to record muscle activity, breathing and eye movements for analyzing sleep patterns - Imaging studies, such as magnetic resonance imaging (MRI) and positron emission tomography (PET) scans to examine the structure and function of the brain - Frequent blood tests to measure blood levels of anti-seizure drugs

Study Type: Observational

Contact(s): see Web site below

Web Site: http://clinicaltrials.gov/ct/show/NCT00013845

- **Functional Coupling of Cortico-Cortical and Cortico-Muscular Connections during Motor Movements: An Electrocorticographic Study of Ipsilateral Motor Control**

  Condition(s): Epilepsy

  Study Status: This study is currently recruiting patients.

  Sponsor(s): National Institute of Neurological Disorders and Stroke (NINDS)

  Purpose - Excerpt: This study examines the relationship between a cerebral hemisphere and control of muscles on the same side of the body (ipsilateral control). One good way to study this relationship is to record electroencephalogram (EEG) activity directly from the cortical surface. Because patients with **epilepsy** who are surgical candidates are already undergoing monitoring with subdural and/or depth electrodes, they present an opportunity to study ipsilateral control. Studying the electrocorticographic (ECoG) activity associated with simple voluntary movement in such patients would not disturb ongoing monitoring of nearby areas of the brain, nor would it endanger the patients. Ten patients, who may be children or adults, will be recruited for this study. Brain activity will be measured while they move the corner of their mouth and their fingers, wrists, arms, and feet. The baseline measurements will be done with scalp electrodes. Once subdural electrodes have been placed, a second set of measurements will be done. Surface EMG electrodes will be placed on the muscles whose movements are being tested. The tests will be done on no more than 3 separate days, in sessions no longer than 2 hours, for each patient.

  Study Type: Observational

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00036595

- **Genetic Study of Familial Epilepsy**

  Condition(s): Epilepsy

  Study Status: This study is currently recruiting patients.

  Sponsor(s): National Center for Research Resources (NCRR); Columbia University

  Purpose - Excerpt: Objectives: I. Determine the chromosomal regions that contain genes that raise the risk of epilepsy in families by performing genetic linkage analysis of idiopathic/cryptogenic epilepsy.

Study Type: Observational

Contact(s): see Web site below

Web Site: http://clinicaltrials.gov/ct/show/NCT00006059

- **Human Epilepsy Genetics--Neuronal Migration Disorders Study**

  Condition(s): Epilepsy; Seizures; Cognition Disorders; Neuronal Migration Disorders

  Study Status: This study is currently recruiting patients.

  Sponsor(s): National Institute of Neurological Disorders and Stroke (NINDS)

  Purpose - Excerpt: The purpose of this study is to identify genes responsible for epilepsy and disorders of human cognition.

  Study Type: Observational

  Contact(s): Adria Bodell, MS, CGC 617-667-8035 abodell@caregroup.harvard.edu; Kira Apse, ScM 617-667-8044 kapse@bidmc.harvard.edu

  Web Site: http://clinicaltrials.gov/ct/show/NCT00041600

- **Light Scattering Spectroscopy to Determine Brain Tumors**

  Condition(s): Epilepsy, Temporal Lobe; Temporal Lobe

  Study Status: This study is currently recruiting patients.

  Sponsor(s): National Institute of Neurological Disorders and Stroke (NINDS)

  Purpose - Excerpt: This study will use light scattering spectroscopy (LSS) to analyze brain tissue removed from patients during brain surgery to determine if this new technology can be used to differentiate between normal and cancerous cells. LSS focuses light on cells or tissues, and the way that light is reflected back from the tissues provides information about the size of cells and the density of the cell nuclei (the part of the cell that contains the genes). Patients between 18 and 75 years of age with a known or suspected brain tumor and patients with temporal lobe **epilepsy** that does not respond to medication may be eligible for this study. (Examination of tissue from patients with **epilepsy** will allow comparison of tumor and non-tumor brain cells.) All patients must require surgery to treat their condition. Participants will be admitted to the Clinical Center for 3 to 10 days for physical and neurological examinations, blood and urine tests, and other tests needed to prepare for surgery. They will then undergo surgery. A small amount of tissue removed during surgery for pathological review will be collected for use in this study. Half of the tissue will be examined using LSS to help determine the size of the cell and its nucleus. Studies will be done to measure how many of the cells are actively dividing and which proteins are expressed more often in tumor cells compared with normal cells. This information may shed light on how tumor cells are different from normal cells. Participants may be contacted for up to 3 years to follow their health status.

  Study Type: Observational

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00067418

- **MRI in Autosomal Dominant Partial Epilepsy with Auditory Features**

  Study Status: This study is currently recruiting patients.

Sponsor(s): National Institute of Neurological Disorders and Stroke (NINDS)

Purpose - Excerpt: Objectives: to study potential structural and functional abnormalities in patients with an inherited form of epilepsy. Study Population: Patients with autosomal dominant partial epilepsy with auditory features, a newly described syndrome, asymptomatic family members who are gene carriers, and unaffected family members, and normal volunteers. Design: magnetic resonance imaging, electroencephalography, and magnetoencephalography. Outcome measures: detection of structural lesions; regional activation patterns on fMRI. MEDLINEplus consumer health information

Study Type: Observational

Contact(s): see Web site below

Web Site: http://clinicaltrials.gov/ct/show/NCT00072813

- **Multicenter trial for adults with partial seizures**

  Condition(s): Epilepsy

  Study Status: This study is currently recruiting patients.

  Sponsor(s): IVAX Research

  Purpose - Excerpt: This study is to see if talampanel helps and is safe to use on adults with partial seizures.

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00034814

- **Non-Invasive Seizure Localization in Patients with Medically Refractory Localization Related Epilepsy: Synchronized MEG-EEG Recordings**

  Condition(s): Epilepsy

  Study Status: This study is currently recruiting patients.

  Sponsor(s): National Institute of Neurological Disorders and Stroke (NINDS)

  Purpose - Excerpt: Objective: We will use magnetoencephalography (MEG) alone, and in combination with EEG (MEG-EEG), to study the contribution of each method and their combination to the localizing yield of the non-invasive pre-surgical evaluation as compared to the invasive method. We will also correlate seizure origin and localizing data with surgical outcome, and, in retrospect, calculate the proportion of patients in whom invasive monitoring could have been avoided. Study Population: Participants in this study will be patients with medically refractory localization-related epilepsy who will be undergoing epilepsy surgery as part of their standard clinical care. Study Design/Methods: We will use a 275-channel whole-head MEG System (CTF Systems 2001 Inc). Patients will undergo a supine resting MEG-EEG recording prior to any surgical procedure. The resulting data will be integrated with the data obtained during the patient's standard pre-surgical evaluation, and compared with the invasive data obtained during chronic invasive monitoring (if clinically indicated), and/or intra-operative electrocorticography (all patients-standard of care). When analyzing the data, readers will be blinded to the results of the other modality (MEG vs. EEG, non-invasive vs. invasive). The patients will be followed in the outpatient clinic at 1-, 3-, 6- and 12-month intervals. Surgical outcomes will be graded according to the Engel and International League Against Epilepsy (ILAE) outcome scales. The findings from this

protocol will not in themselves indicate or lead to epilepsy surgery. Outcomes: The primary outcome measure will be the proportion of seizure foci detected and delineated both non-invasively and invasively. The secondary outcome measures will be the proportion of patients with seizure foci co-localized invasively and non-invasively, the correlation of the obtained localizing data from both modalities with surgical outcome, and the correlation between the anatomical location of the epileptogenic zone and surgical outcome.

Study Type: Observational

Contact(s): see Web site below

Web Site: http://clinicaltrials.gov/ct/show/NCT00071305

- **Pediatric Epilepsy Study**

  Condition(s): Epilepsy

  Study Status: This study is currently recruiting patients.

  Sponsor(s): (Sponsor Name Pending)

  Purpose - Excerpt: This study will evaluate the safety of an investigational medication to treat pediatric patients 1-24 months old with partial seizures. Patients must have previously taken part in previous sponsored study.

  Phase(s): Phase II

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00044278

- **Phenotype and Etiology of Pallister-Hall Syndrome**

  Condition(s): Epilepsy; Hamartoma; Multiple Abnormalies; Syndactyly

  Study Status: This study is currently recruiting patients.

  Sponsor(s): National Human Genome Research Institute (NHGRI)

  Purpose - Excerpt: We aim to delineate the range of severity, natural history, molecular etiology, and pathophysiology of Pallister-Hall syndrome (PHS), Greig cephalopolysyndactyly syndrome (GCPS), McKusick-Kaufman syndrome (MKS), Bardet-Biedl syndrome (BBS), Oro-facial digital syndromes (OFDs), and other overlapping phenotypes. These disorders comprise a syndrome community of overlapping manifestations and we hypothesize that this is a reflection of a common mechanistic pathway. This hypothesis be addressed by a combined clinical-molecular approach where we bring up to 50-100 patients with each disorder to the NIH clinical center for a comprehensive clinical evaluation with follow-up at a frequency appropriate to the disorder. Specimens will be collected and evaluated in the laboratory by linkage analysis, physical mapping, candidate gene characterization, mutation screening, and cell biologic studies of normal mutant proteins.

  Study Type: Observational

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00001404

- **Progesterone vs Placebo Therapy for Women with Epilepsy**

  Condition(s): Epilepsy

  Study Status: This study is currently recruiting patients.

  Sponsor(s): Beth Israel Deaconess Medical Center

  Purpose - Excerpt: There is considerable evidence to suggest that natural progesterone has anti-seizure properties. The purpose of this study is to determine if progesterone supplement during the second half of the menstrual cycle lessens seizure frequency in women with epilepsy.

  Phase(s): Phase II

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00029536

- **Reducing Seizure Frequency Using Cooling of the Head and Neck**

  Condition(s): Epilepsy; Seizures

  Study Status: This study is currently recruiting patients.

  Sponsor(s): National Institute of Neurological Disorders and Stroke (NINDS)

  Purpose - Excerpt: Doctors use cooling of the brain to help stop seizures. This procedure is usually accomplished through surgery. Cooling of the face and scalp may also cool the brain, avoiding the need for surgery. The purpose of this study is to assess a head-neck cooling device that the patient can wear. Researchers will determine whether the device can change the frequency of seizures in people with **epilepsy.** Study participants must be 21 years of age or older and must experience seizures that occur once a week on a regular basis. Participants will be asked to keep a detailed seizure diary for a 12-week period before the date of the first cooling session. For each of the four cooling sessions, participants will be admitted to the hospital overnight. They will undergo a physical and neurological exam and an EEG (electroencephalogram). They will also swallow a temperature-sensor pill. Participants will have one 60-minute cooling session once a week for 4 weeks. Investigators will paste temperature-sensing electrodes on the scalp, forearm, abdomen, and leg. Participants will then be fitted with the cooling unit and the session will begin.

  Phase(s): Phase II

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00067210

- **Role of Hormones in Susceptibility to Seizures in Women with Epilepsy**

  Condition(s): Epilepsy

  Study Status: This study is currently recruiting patients.

  Sponsor(s): National Institute of Neurological Disorders and Stroke (NINDS)

  Purpose - Excerpt: This study will measure and compare hormone levels in women with catamenial epilepsy (epilepsy in which seizures are more frequent during menstrual periods), women with seizures not related to their menstrual cycle, and normal control subjects. It will determine whether there are differences among the three groups in their

hormone levels or in how fast the levels change. It will also examine what relationship, if any, exists between hormone changes and seizures in women with catamenial epilepsy. The hormones under study include the gonadal hormones estrone, estradiol and progesterone, and the neuroactive steroids allopregnanolone, pregnenolone, and dehydroepiandrosterone. Women who meet the following criteria may be eligible for this 3-month study: - Between 18 and 45 years of age, with catamenial epilepsy - Between 18 and 45 years of age, with seizures, but not catamenial epilepsy - Between 18 and 45 years of age, without seizures All participants will have a physical examination at the beginning of the study, at each clinic visit, and at completion or withdrawal from the study. In addition, they will undergo the following procedures: Baseline Monitoring For the first 2 months, all participants will keep a diary of their temperature and onset of menses. Women with epilepsy will also record their seizures. Electroencephalography (EEG) Healthy volunteers will have a 45-minute EEG (recording of the electrical activity of the brain) at the beginning of each menstrual cycle and each day during the menses. Women with epilepsy will have continuous EEG monitoring for 8 days, beginning 5 days before their menstrual period is expected. The continuous monitoring can be done on an outpatient basis, using a portable EEG recording device, or as an inpatient, with admission to the hospital for the 8 days of recording. Blood Sampling All participants will have a small blood sample (2 teaspoons) drawn once a day on days 10, 14, 17, 19 and 21 of their menstrual cycle and three times a day on day 6 and for a period of 8 days, starting 5 days before the expected menses and continuing for 3 days of the next cycle. For the days with three blood draws, a small needle that can stay in place for up to 72 hours will be placed in the arm to avoid the discomfort of multiple needle sticks.

Study Type: Observational

Contact(s): see Web site below

Web Site: http://clinicaltrials.gov/ct/show/NCT00044252

- **Search for Genes Influencing Childhood Absence Epilepsy Study**

  Condition(s): Childhood Absence Epilepsy; Epilepsy; Seizures

  Study Status: This study is currently recruiting patients.

  Sponsor(s): National Institute of Neurological Disorders and Stroke (NINDS)

  Purpose - Excerpt: The purpose of our study is to identify gene(s) involved in the cause of childhood absence epilepsy (CAE).

  Study Type: Observational

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00041951

- **Serotonin Receptors in Seizure Disorders**

  Condition(s): Partial Epilepsy

  Study Status: This study is currently recruiting patients.

  Sponsor(s): National Institute of Neurological Disorders and Stroke (NINDS)

  Purpose - Excerpt: Patients in this study will undergo PET scans (a type of nuclear imaging test) to look for abnormalities in certain brain proteins associated with seizures. Studies in animals have shown that serotonin-a chemical messenger produced by the body-attaches to proteins on brain cells called 5HT1A receptors and changes them in some way that may help control seizures. There is little information on these changes,

however. A new compound that is highly sensitive to 5HT1A, will be used in PET imaging to measure the level of activity of these receptors and try to detect abnormalities. Changes in receptor activity may help determine where in the brain the seizures are originating. Additional PET scans will be done to measure the amount of blood flow to the brain and the rate at which the brain uses glucose-a sugar that is the brain's main fuel. Blood flow measurement is used to calculate the distribution of serotonin receptors, and glucose use helps determine how seizures affect brain function. The information gained from the study will be used to try to help guide the patient's therapy and determine if surgery might be beneficial in controlling the patient's seizures.

Study Type: Observational

Contact(s): see Web site below

Web Site: http://clinicaltrials.gov/ct/show/NCT00001932

- **Study of Specimens Obtained during Epilepsy Surgery**

  Condition(s): Epilepsy

  Study Status: This study is currently recruiting patients.

  Sponsor(s): National Institute of Neurological Disorders and Stroke (NINDS)

  Purpose - Excerpt: This study will collect brain tissue samples for research purposes from patients undergoing surgery to treat epilepsy. The standard surgical procedure for medically intractable epilepsy-i.e., epilepsy that cannot be controlled with medicine-requires removal of more brain tissue than is needed for diagnostic study. This extra tissue, which would otherwise be discarded, will be used for research purposes. In addition, a blood vessel in the scalp, called the superficial temporal artery, is also normally cut during surgery, and a piece of this vessel will be taken for research use. Patients 4 years of age or older who undergo surgery for medically intractable epilepsy may be eligible for this study. Brain tissue collected under this protocol will be used for studies of brain cells in other diseases and of serotonin receptors. Any remaining brain tissue will be frozen for use in future research. The superficial temporal artery will be used for comparison with carotid arteries (a neck artery that supplies the brain) from patients with blockage of this blood vessel.

  Study Type: Observational

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00025714

- **Transcranial Magnetic Stimulation to Treat Epilepsy**

  Condition(s): Epilepsy

  Study Status: This study is currently recruiting patients.

  Sponsor(s): National Institute of Neurological Disorders and Stroke (NINDS)

  Purpose - Excerpt: This study will use transcranial magnetic stimulation, or TMS (described below), to treat epilepsy in certain patients whose seizures persist despite optimum medical treatment. TMS used in this study is intended to lessen the number of seizures a patient has by decreasing excitability of the brain in the region where the seizures originate. Patients between 5 and 65 years of age who have had epilepsy for two or more years and have had at least one seizure a week for at least 6 months may be eligible for this 18-week study. Their seizures must come from a neocortical focus-that

is, near the surface of the brain. Candidates will be selected from the NIH Epilepsy clinic and will be screened with an electroencephalogram (EEG), magnetic resonance imaging (MRI) scans, and blood tests. Participants will keep a diary of the seizures they experience over an 8-week period. After the 8 weeks, they will come to the NIH outpatient clinic for 6 consecutive days for the following procedures: - Day 1: A regular clinic visit, plus 6 hours of video-EEG recording (described below) - Days 2 through 5: Video-EEG monitoring and TMS as follows: 8:00 - 11: 00 a.m. 3 hours video-EEG monitoring 11:00 - 12:30 p.m. TMS (includes set-up time; actual stimulation time lasts 30 minutes) 12:30 - 3:00 p.m. Lunch + rest 3:00 - 4:30 p.m. TMS 4:30 - 7:30 p.m. 3 hours video-EEG monitoring (On the fifth day, subjects will have 6 hours of video-EEG monitoring in the afternoon instead of 3 hours.) Participants will be randomly assigned to one of two TMS groups. One group will have TMS delivered in a way that is thought to have a chance of reducing seizures; the other will have sham, or placebo, stimulation. When the TMS sessions are completed, participants will keep a diary of their seizures for another 8 weeks. Transcranial Magnetic Stimulation For TMS, an insulated wire coil is placed on the subject's scalp. A brief electrical current passes through the coil, creating a magnetic pulse that travels through the scalp and skull and causes small electrical currents in the cortex, or outer part of the brain. The stimulation may cause muscle, hand or arm twitching, or may cause twitches or temporary tingling in the forearm, head, or face muscles. During the stimulation, electrical activity of muscles is recorded with a computer or other recording device, using electrodes attached to the skin with tape. Some TMS sessions may be videotaped. Video-EEG Recordings The EEG recording device is housed in a small pouchlike container that is worn below the shoulder, attached to a belt worn around the waist.

Phase(s): Phase II

Study Type: Interventional

Contact(s): see Web site below

Web Site: http://clinicaltrials.gov/ct/show/NCT00048490

- **Treatment Of Primary Generalized Tonic-Clonic Seizures With An Investigational New Drug**

  Condition(s): Epilepsy

  Study Status: This study is currently recruiting patients.

  Sponsor(s): (Sponsor Name Pending)

  Purpose - Excerpt: The purpose of this study is to evaluate the effectiveness and safety of an investigational new drug for supplemental therapy in subjects with primary generalized tonic-clonic seizures.

  Phase(s): Phase IV

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00043901

- **Hormone Replacement in Menopausal Women with Epilepsy**

  Condition(s): Menopause; Epilepsy

  Study Status: This study is no longer recruiting patients.

  Sponsor(s): National Institute of Neurological Disorders and Stroke (NINDS)

Purpose - Excerpt: The goal of this study is to evaluate the effect of synthetic hormone replacement therapy on anti-seizure medication levels, menopausal symptom relief, and seizure frequency and safety in menopausal women with epilepsy.

Phase(s): Phase II

Study Type: Interventional

Contact(s): see Web site below

Web Site: http://clinicaltrials.gov/ct/show/NCT00027209

- **Ketogenic Diet for Child Epilepsy and Seizure Control**

  Condition(s): Epilepsy; Seizures; Lennox-Gastaut Syndrome

  Study Status: This study is no longer recruiting patients.

  Sponsor(s): National Institute of Neurological Disorders and Stroke (NINDS)

  Purpose - Excerpt: Twenty to thirty percent of children with epilepsy continue to suffer from seizures, even when treated with currently available anticonvulsant medications. Children with Lennox-Gastaut Syndrome (LGS) are particularly handicapped by atonic-myoclonic seizures. Preliminary data suggest that even when other medications have failed, these seizures may respond rapidly and dramatically to a high-fat-low-carbohydrate ketogenic diet. The purpose of the study is to assess if the classic ketogenic diet is efficacious in reducing seizure frequency, medication toxicity, and improves quality of life.

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00004729

- **Measurement Of Serum Levels Of Two Antiepileptic Drugs During Conversion In Patients With Epilepsy.**

  Condition(s): Epilepsy

  Study Status: This study is no longer recruiting patients.

  Sponsor(s): (Sponsor Name Pending)

  Purpose - Excerpt: This study includes patients 16 years of age or older with a confident diagnosis of epilespy who are currently treated with an antiepileptic drug (AED) monotherapy but require a change in therapy due to inadequate seizure control and/or unacceptable side effects.

  Phase(s): Phase IV

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00043914

- **Metabolic Abnormalities in Children with Epilepsy**

  Condition(s): Generalized Epilepsy; Infantile Spasms; Metabolic Disease; Partial Epilepsy; Seizures

  Study Status: This study is no longer recruiting patients.

  Sponsor(s): National Institute of Neurological Disorders and Stroke (NINDS)

Purpose - Excerpt: This study is designed to use positron emission tomography to measure brain energy use. Positron Emission Tomography (PET) is a technique used to investigate the functional activity of the brain. The PET technique allows doctors to study the normal processes of the brain (central nervous system) of normal individuals and patients with neurologic illnesses without physical / structural damage to the brain. When a region of the brain is active, it uses more fuel in the form of oxygen and sugar (glucose). As the brain uses more fuel it produces more waste products, carbon dioxide and water. Blood carries fuel to the brain and waste products away from the brain. As brain activity increases blood flow to and from the area of activity increases also. Researchers can label a sugar with a small radioactive molecule called FDG (fluorodeoxyglucose). As areas of the brain use more sugar the PET scan will detect the FDG and show the areas of the brain that are active. By using this technique researchers hope to answer the following questions; 4. Are changes in brain energy use (metabolism) present early in the course of epilepsy 5. Do changes in brain metabolism match the severity of patient's seizures 6. Do changes in metabolism occur over time or in response to drug therapy

Study Type: Observational

Contact(s): see Web site below

Web Site: http://clinicaltrials.gov/ct/show/NCT00001325

- **Pediatric Epilepsy Trial**

  Condition(s): Epilepsy

  Study Status: This study is no longer recruiting patients.

  Sponsor(s): (Sponsor Name Pending)

  Purpose - Excerpt: This study is to evaluate the effectiveness and safety of an investigational medication to treat pediatric patients age 1-24 months old with partial seizures. The medication used in this study has been approved by FDA for use in patients 2 years and older.

  Phase(s): Phase II

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00043875

- **Randomized Study of Albendazole in Patients with Epilepsy Due to Neurocysticercosis**

  Condition(s): Epilepsy; Cysticercosis

  Study Status: This study is no longer recruiting patients.

  Sponsor(s): FDA Office of Orphan Products Development; Johns Hopkins University

  Purpose - Excerpt: Objectives: I. Determine the effect of antiparasitic treatment with albendazole on the severity and duration of epilepsy due to neurocysticercosis. II. Determine the effect of a short course of albendazole on Taenia solium cysts present in the brain. III. Determine the natural regression of cerebral T. solium cysts in patients given placebo and their response to treatment at the end of the study.

  Study Type: Interventional

  Contact(s): see Web site below

Web Site: http://clinicaltrials.gov/ct/show/NCT00004403

- **Brain Blood Flow Studies of Language and Memory**

  Condition(s): Cerebrovascular Disorder; Epilepsy

  Study Status: This study is completed.

  Sponsor(s): National Institute of Neurological Disorders and Stroke (NINDS)

  Purpose - Excerpt: Positron Emission Tomography (PET) is a technique used to investigate the functional activity of the brain. The PET technique allows doctors to study the normal processes of the brain (central nervous system) of normal individuals and patients with neurologic illnesses without physical / structural damage to the brain. When a region of the brain is active, it uses more fuel in the form of oxygen and sugar (glucose). As the brain uses more fuel it produces more waste products, carbon dioxide and water. Blood carries fuel to the brain and waste products away from the brain. As brain activity increases blood flow to and from the area of activity increases also. Knowing these facts, researchers can use radioactive water (H215O) and PET scans to observe what areas of the brain are receiving more blood flow. This study is designed to use positron emission tomography (PET) with radioactive water (H215O) to determine the areas of the brain associated with memory and language. Patients participating in the study will be made up of normal volunteers, patients with **epilepsy,** and patients with other abnormalities related to the surface of the brain (non-epileptic focal cortical dysfunctions).

  Study Type: Observational

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00001288

- **Effect of Levetiracetam on Brain Excitability**

  Condition(s): Healthy; Myoclonic Epilepsy

  Study Status: This study is completed.

  Sponsor(s): National Institute of Neurological Disorders and Stroke (NINDS)

  Purpose - Excerpt: This study will examine the effect of the newly developed anti-epileptic drug, levetiracetam, on excitability of the cortex (surface layer) of the brain. Levetiracetam works differently from other anti-seizure drugs, but its mechanism is not well understood. This study may provide insight into a new protection mechanism against seizures as well as the effect of the drug on cortical excitability. Healthy normal volunteers 18 years of age and older may be eligible for this study. Candidates will have a medical history taken and undergo physical and neurological examinations. Participants will undergo two different procedures in four separate sessions. One procedure (cortical excitability) involves taking either levetiracetam or placebo (a look-alike inactive substance) and having transcranial magnetic stimulation (TMS). The other procedure (pinch-training related changes) involves taking levetiracetam or placebo, doing a motor exercise called pinch training, and having transcranial magnetic stimulation. For TMS, a very brief electrical current is passed through an insulated coil wire placed on the scalp. The magnetic pulse travels through the scalp and skull, causing small electrical currents in the cortex that may cause muscle, hand, or arm twitching or it may affect movements or reflexes. During the study, subjects may be asked to make movements, do simple tasks or tense muscles. Electrical activity of the muscles will be recorded using electrodes taped to the skin over the muscle. For the

pinch training, the subject makes a brief, brisk pinch after each beat of a metronome every two seconds and then completely relaxes the hand until the next beat. Subjects will be tested on four different days at least 72 hours apart. Each session will last about 3 to 4 hours. Approximate schedule for cortical excitability testing: TMS (study 1) Take levetiracetam or placebo TMS (study 2) < 60 minutes after drug or placebo TMS (study 3) < 120 minutes after drug or placebo Approximate schedule for pinch-training related changes: Take levetiracetam or placebo TMS and pinch power measurement < 60 minutes after drug or placebo Pinch training for 30 minutes TMS and pinch power measurement Sample schedule: Session 1 < LTC and cortical excitability testing Session 2 < Placebo and cortical excitability testing Session 3 < LTC and pinch-training related changes Session 4 < Placebo and pinch-training related changes

Study Type: Observational

Contact(s): see Web site below

Web Site: http://clinicaltrials.gov/ct/show/NCT00006191

- **Effect of Vigabatrin on Brain Blood Flow and Glucose Metabolism**

  Condition(s): Epilepsy; Epilepsy, Complex Partial

  Study Status: This study is completed.

  Sponsor(s): National Institute of Neurological Disorders and Stroke (NINDS)

  Purpose - Excerpt: This study is designed to test the effects of vigabatrin (gamma-vinyl-GABA) an experimental drug used for the treatment of **epilepsy.** The study will use positron emission tomography (PET scan) to detect areas of the brain receiving increased blood flow and using increased amounts of glucose. Increases in blood flow and glucose use are good indicators of brain activity. Researchers are interested in determining the effects of Vigabatrin on brain blood flow and glucose use.

  Study Type: Observational

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00001489

- **Infrared Camera for Brain Mapping During Surgery**

  Condition(s): Epilepsy; Neurologic Manifestations

  Study Status: This study is completed.

  Sponsor(s): National Institute of Neurological Disorders and Stroke (NINDS)

  Purpose - Excerpt: It is extremely important to identify and distinguish healthy brain tissue from diseased brain tissue during neurosurgery. If normal tissue is damaged during neurosurgery it can result in long term neurological problems for the patient. The brain tissue as it appears prior to the operation on CT scan and MRI is occasionally very different from how it appears during the actual operation. Therefore, it is necessary to develop diagnostic procedures that can be used during the operation Presently, the techniques used for intraoperative mapping of the brain are not reliable in all cases in which they are used. Researchers in this study have developed a new approach that may allow diseased brain tissue to be located during an operation with little risk. This new approach uses nfrared technology to locate the diseased tissue and identify healthy brain tissue. The goal of this study is to investigate the clinical use of intraoperative infrared (IR) neuroimaging to locate diseased tissue and distinguish it from normal functioning tissue during the operation.

Phase(s): Phase I

Study Type: Interventional

Contact(s): see Web site below

Web Site: http://clinicaltrials.gov/ct/show/NCT00001554

- **Language Localization Using Repetitive Transcranial Magnetic Stimulation (rTMS) in Patients with Epilepsy**

  Condition(s): Epilepsy, Temporal Lobe

  Study Status: This study is completed.

  Sponsor(s): National Institute of Neurological Disorders and Stroke (NINDS)

  Purpose - Excerpt: Repetitive transcranial magnetic stimulation (rTMS) may be able to provide a moderately detailed localization of language functions in the brain. We propose to test the ability of rTMS to locate the substrate of visual naming to a limited area of the temporal lobe in patients with temporal lobe epilepsy before and after surgical resections. The study is expected to yield information on the organization of language in the temporal lobes and how unilateral temporal lobe lesions and lobectomy cause relocation of language mechanisms in the lesioned and in the other hemisphere. It will also be a preliminary step in the development of a clinically useful procedure for locating critical language areas in potential surgical candidates.

  Study Type: Observational

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00001672

- **Mapping the Areas of the Brain Associated with Language in Children with Epilepsy**

  Condition(s): Epilepsy; Seizures

  Study Status: This study is completed.

  Sponsor(s): National Institute of Neurological Disorders and Stroke (NINDS)

  Purpose - Excerpt: Researchers are interested in studying if magnetic resonance imaging (MRI) is practical for locating the areas of the brain associated with language in children with epilepsy. When a region of the brain is active, it uses more fuel in the form of oxygen and sugar (glucose). As the brain uses more fuel it produces more waste products, carbon dioxide and water. Blood carries fuel to the brain and waste products away from the brain. As brain activity increases blood flow to and from the area of activity increases also. Patients participating in the study will be asked to perform tasks designed to test language skills while undergoing an MRI to detect areas of the brain using oxygen and receiving blood flow.

  Study Type: Observational

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00001366

- **Monitoring Patients with Uncontrolled Epilepsy**

  Condition(s): Epilepsy; Seizures

  Study Status: This study is completed.

Sponsor(s): National Institute of Neurological Disorders and Stroke (NINDS)

Purpose - Excerpt: This study is designed to evaluate patients with uncontrolled seizures. Seizures can be associated with and monitored by abnormal electrical activity in the brain. In this study researchers will use video-electroencephalography (EEG) to monitor patients with uncontrolled or suspected seizures. EEG works by measuring electrical activity in different areas of the brain. The video-EEG allows researchers to examine changes in the EEG along with the clinical features of seizures as they occur. In addition to monitoring electrical activity of the brain, researchers will take frequent antiepileptic drug blood levels. These measures will allow researchers to learn more about how each drug is absorbed and metabolized in the body. The information collected in the study will be used to place patients into other scientific studies testing new therapies for epilepsy.

Study Type: Observational

Contact(s): see Web site below

Web Site: http://clinicaltrials.gov/ct/show/NCT00001149

- **Phase II Randomized Study of Early Surgery vs Multiple Sequential Antiepileptic Drug Therapy for Infantile Spasms Refractory to Standard Treatment**

  Condition(s): Spasms, Infantile; Epilepsy

  Study Status: This study is completed.

  Sponsor(s): National Center for Research Resources (NCRR); National Institute of Neurological Disorders and Stroke (NINDS); University of California, Los Angeles

  Purpose - Excerpt: Objectives: I. Evaluate the efficacy of surgical resection of an identifiable zone of cortical abnormality versus multiple drug therapy in children with infantile spasms refractory to standard therapy. II. Assess how infantile spasms interfere with development and whether this is partially reversible. III. Determine the predictors of good surgical outcome and whether surgery permanently controls seizures and improves development.

  Phase(s): Phase II

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00004758

- **Phase III Double Blind Trial of Valproate Sodium for Prophylaxis of Post Traumatic Seizures**

  Condition(s): Post-Traumatic Seizure Disorder; Head Injuries

  Study Status: This study is completed.

  Sponsor(s): National Institute of Neurological Disorders and Stroke (NINDS); Harborview Medical Center

  Purpose - Excerpt: Objectives: I. Determine whether treating head injured patients with valproate sodium will reduce the risk of developing seizures as a result of the head injury. II. Determine the safety of valproate, the appropriate dose, and the effect valproate may have on the recovery of the brain's ability to compute numbers, solve problems, remember information, and control the movement of limbs after head injury.

  Phase(s): Phase III

Study Type: Interventional

Contact(s): see Web site below

Web Site: http://clinicaltrials.gov/ct/show/NCT00004817

- **Transcranial Magnetic Stimulation for the Treatment of Poorly Controlled Partial Epilepsy**

  Condition(s): Partial Epilepsy; Seizures

  Study Status: This study is completed.

  Sponsor(s): National Institute of Neurological Disorders and Stroke (NINDS)

  Purpose - Excerpt: Transcranial Magnetic Stimulation (TMS) is a non-invasive technique that can be used to stimulate brain activity and gather information about brain function. It is very useful when studying the areas of the brain related to motor activity (motor cortex, corticospinal tract, and corpus callosum). Epilepsy is a condition associated with seizures as a result of an over excitable cerebral cortex. Despite the introduction of several new antiepileptic medications, less than half of the patients diagnosed with partial epilepsy are well controlled. However, studies have shown that non-invasive stimulation of the brain can decrease the excitability of the cerebral cortex. Researchers are interested in the potential therapeutic effects of TMS on patients with epilepsy that have responded poorly to standard medication. This study will use TMS to decrease the excitability of the areas of the brain responsible for seizures.

  Study Type: Observational

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00001666

Keeping Current on Clinical Trials

The U.S. National Institutes of Health, through the National Library of Medicine, has developed ClinicalTrials.gov to provide current information about clinical research across the broadest number of diseases and conditions.

The site was launched in February 2000 and currently contains approximately 5,700 clinical studies in over 59,000 locations worldwide, with most studies being conducted in the United States. ClinicalTrials.gov receives about 2 million hits per month and hosts approximately 5,400 visitors daily. To access this database, simply go to the Web site at **http://www.clinicaltrials.gov/** and search by "epilepsy" (or synonyms).

While ClinicalTrials.gov is the most comprehensive listing of NIH-supported clinical trials available, not all trials are in the database. The database is updated regularly, so clinical trials are continually being added. The following is a list of specialty databases affiliated with the National Institutes of Health that offer additional information on trials:

- For clinical studies at the Warren Grant Magnuson Clinical Center located in Bethesda, Maryland, visit their Web site: **http://clinicalstudies.info.nih.gov/**
- For clinical studies conducted at the Bayview Campus in Baltimore, Maryland, visit their Web site: **http://www.jhbmc.jhu.edu/studies/index.html**
- For cancer trials, visit the National Cancer Institute: **http://cancertrials.nci.nih.gov/**

- For eye-related trials, visit and search the Web page of the National Eye Institute: **http://www.nei.nih.gov/neitrials/index.htm**
- For heart, lung and blood trials, visit the Web page of the National Heart, Lung and Blood Institute: **http://www.nhlbi.nih.gov/studies/index.htm**
- For trials on aging, visit and search the Web site of the National Institute on Aging: **http://www.grc.nia.nih.gov/studies/index.htm**
- For rare diseases, visit and search the Web site sponsored by the Office of Rare Diseases: **http://ord.aspensys.com/asp/resources/rsch_trials.asp**
- For alcoholism, visit the National Institute on Alcohol Abuse and Alcoholism: **http://www.niaaa.nih.gov/intramural/Web_dicbr_hp/particip.htm**
- For trials on infectious, immune, and allergic diseases, visit the site of the National Institute of Allergy and Infectious Diseases: **http://www.niaid.nih.gov/clintrials/**
- For trials on arthritis, musculoskeletal and skin diseases, visit newly revised site of the National Institute of Arthritis and Musculoskeletal and Skin Diseases of the National Institutes of Health: **http://www.niams.nih.gov/hi/studies/index.htm**
- For hearing-related trials, visit the National Institute on Deafness and Other Communication Disorders: **http://www.nidcd.nih.gov/health/clinical/index.htm**
- For trials on diseases of the digestive system and kidneys, and diabetes, visit the National Institute of Diabetes and Digestive and Kidney Diseases: **http://www.niddk.nih.gov/patient/patient.htm**
- For drug abuse trials, visit and search the Web site sponsored by the National Institute on Drug Abuse: **http://www.nida.nih.gov/CTN/Index.htm**
- For trials on mental disorders, visit and search the Web site of the National Institute of Mental Health: **http://www.nimh.nih.gov/studies/index.cfm**
- For trials on neurological disorders and stroke, visit and search the Web site sponsored by the National Institute of Neurological Disorders and Stroke of the NIH: **http://www.ninds.nih.gov/funding/funding_opportunities.htm#Clinical_Trials**

CHAPTER 6. PATENTS ON EPILEPSY

Overview

Patents can be physical innovations (e.g. chemicals, pharmaceuticals, medical equipment) or processes (e.g. treatments or diagnostic procedures). The United States Patent and Trademark Office defines a patent as a grant of a property right to the inventor, issued by the Patent and Trademark Office.[9] Patents, therefore, are intellectual property. For the United States, the term of a new patent is 20 years from the date when the patent application was filed. If the inventor wishes to receive economic benefits, it is likely that the invention will become commercially available within 20 years of the initial filing. It is important to understand, therefore, that an inventor's patent does not indicate that a product or service is or will be commercially available. The patent implies only that the inventor has "the right to exclude others from making, using, offering for sale, or selling" the invention in the United States. While this relates to U.S. patents, similar rules govern foreign patents.

In this chapter, we show you how to locate information on patents and their inventors. If you find a patent that is particularly interesting to you, contact the inventor or the assignee for further information. **IMPORTANT NOTE:** When following the search strategy described below, you may discover non-medical patents that use the generic term "epilepsy" (or a synonym) in their titles. To accurately reflect the results that you might find while conducting research on epilepsy, we have not necessarily excluded non-medical patents in this bibliography.

Patents on Epilepsy

By performing a patent search focusing on epilepsy, you can obtain information such as the title of the invention, the names of the inventor(s), the assignee(s) or the company that owns or controls the patent, a short abstract that summarizes the patent, and a few excerpts from the description of the patent. The abstract of a patent tends to be more technical in nature, while the description is often written for the public. Full patent descriptions contain much more information than is presented here (e.g. claims, references, figures, diagrams, etc.). We

[9]Adapted from the United States Patent and Trademark Office: **http://www.uspto.gov/web/offices/pac/doc/general/whatis.htm**.

will tell you how to obtain this information later in the chapter. The following is an example of the type of information that you can expect to obtain from a patent search on epilepsy:

- **.DELTA.9 Tetrahydrocannabinol (.DELTA.9 THC) solution metered dose inhaler**

  Inventor(s): Byron; Peter R. (Richmond, VA), Lichtman; Aron H. (Richmond, VA), Martin; Billy R. (Richmond, VA), Peart; Joanne (Richmond, VA)

  Assignee(s): Virginia Commonwealth University (Richmond, VA)

  Patent Number: 6,509,005

  Date filed: March 22, 1999

  Abstract: The present invention provides therapeutic formulations for solutions of.DELTA.sup.9 -tetrahydrocannabinol (.DELTA.sup.9 THC) to be delivered by metered dose inhalers. The formulations, which utilize non-CFC propellants, provide a stable aerosol-deliverable source of.DELTA.sup.9 THC for the treatment of various medical conditions, such as: nausea and vomiting associated with chemotherapy; muscle spasticity; pain; anorexia associated with AIDS wasting syndrome; **epilepsy;** glaucoma; bronchial asthma; and mood disorders.

  Excerpt(s): The invention is generally related to the therapeutic use of.DELTA.sup.9 Tetrahydrocannabinol (.DELTA.sup.9 THC). In particular, the invention provides a metered dose inhaler (MDI) for the aerosol administration of.DELTA.sup.9 THC to patients suffering from nausea and vomiting associated with cancer chemotherapy, muscle spasticity, pain, anorexia associated with AIDS wasting syndrome, **epilepsy,** glaucoma, bronchial asthma, mood disorders, and the like. When marijuana is used illegally as a recreational psychoactive drug, the active ingredient.DELTA.sup.9 THC is usually delivered to the lungs as an impure non-pharmaceutical aerosol in the form of marijuana smoke. Aerosolized.DELTA.sup.9 THC in the inhaled smoke is absorbed within seconds and delivered to the brain efficiently. Table 2 and references 19-20 describe the pharmacokinetics of the administration of.DELTA.sup.9 THC. As can be seen, inhalation is the preferred route of delivery for.DELTA.sup.9 THC. When compared to oral delivery, inhalation provides a more rapid onset of pharmacological action and peak plasma levels. The effects achieved via inhalation are comparable to those achieved when the drug is administered intravenously, but inhalation is a much less invasive technique. Currently, the sources of.DELTA.sup.9 THC for patients who could benefit from the drug are very limited. An oral form of.DELTA.sup.9 THC (MARINOL) is marketed as a treatment for nausea and vomiting related to cancer chemotherapy, and as an appetite stimulant in patients suffering from AIDS wasting syndrome. In MARINOL, pharmaceutical grade.DELTA.sup.9 THC is dissolved in sesame oil, encapsulated in gelatin capsules and delivered orally. However, when the drug is taken orally, the absorption is slower and more variable than when inhaled, with an onset of action between 30 minutes and 2 hours (Table 2). Alternatively, some cancer patients do manage to obtain and smoke marijuana in order to alleviate such conditions as nausea and vomiting due to chemotherapy. This is, however, technically illegal and is thus obviously a less than ideal treatment protocol. There is no currently available pharmaceutically acceptable aerosol form of.DELTA.sup.9 THC.

  Web site: http://www.delphion.com/details?pn=US06509005__

- **1-substituted-1-aminomethyl-cycloalkane derivatives (=gabapentin analogues), their preparation and their use in the treatment of neurological disorders**

  Inventor(s): Bryans; Justin Stephen (Balsham, GB), Capiris; Thomas (Plymouth, MI), Horwell; David Christopher (Cambridge, GB), Kneen; Clare Octavia (Essex, GB), Wustrow; David Juergen (Ann Arbor, MI)

  Assignee(s): Pfizer, Inc. (Ann Arbor, MI)

  Patent Number: 6,518,289

  Date filed: April 3, 2000

  Abstract: Novel amines of formulas (1), (1C), (1F), (1G) and (1H) or a pharmaceutical acceptable salt thereof wherein n is an integer of from 0 to 2; m is an integer of from 0 to 3; R is sulfonamide, amide, phosphonic acid, heterocycle, sulfonic acid, or hydroxamic acid; A' is a bridged ring selected from (1), (2), (3), (4), (5) wherein is the point of attachment; Z.sub.1 to Z.sub.4 are each independently selected from hydrogen and methyl; o is an integer of from 1 to 4; and p is an integer of from 0 to 2. In formula (1) above R cannot be sulfonic acid when m is 2 and n is 1 are disclosed and are useful as agents in the treatment of **epilepsy,** faintness attacks, hypokinesia, cranial disorders, neurodegenerative disorders, depression, anxiety, panic, pain, neuropathological disorders, especially irritable bowel syndrome.

  Excerpt(s): wherein R.sub.1 is a straight or branched alkyl group having from 1 to 6 carbon atoms, phenyl, or cycloalkyl having from 3 to 6 carbon atoms; R.sub.2 is hydrogen or methyl; and R.sub.3 is hydrogen, methyl, or carboxyl are known in U.S. Pat. No. 5,563,175 and various divisionals. These patents are hereby incorporated by reference. The compounds of the instant invention are novel amines and their pharmaceutically acceptable salts useful in a variety of disorders. The disorders include: **epilepsy,** faintness attacks, hypokinesia, cranial disorders, neurodegenerative disorders, depression, anxiety, panic, pain, neuropathological disorders, inflammatory diseases, and gastrointestinal disorders, especially irritable bowel syndrome. The compounds of the invention are those of formulas 1, 1C, 1F, 1G, and 1H below.

  Web site: http://www.delphion.com/details?pn=US06518289__

- **Aminoadamantane derivatives as therapeutic agents**

  Inventor(s): Larrick; James W. (Woodside, CA), Lipton; Stuart A. (Rancho Santa Fe, CA), Stemler; Jonathan S. (Chapel Hill, NC), Wang; Yuqiang (Mountain View, CA), Ye; Wenqing (Fremont, CA)

  Assignee(s): NeuroMolecular, Inc. (Mill Valley, CA)

  Patent Number: 6,444,702

  Date filed: February 22, 2000

  Abstract: The present invention provides novel aminoadamantane derivatives, methods of making the derivatives, compositions including the novel aminoadamantane derivatives, and methods for the treatment and prevention of neurological diseases using the derivatives and compositions. There are a variety of neurological disorders that can be treated using the present invention, including, for example, the following: neurological disorders arising from trauma, ischemic or hypoxic conditions that can be treated include stroke, hypoglycemia, cerebral ischemia, cardiac arrest, spinal cord trauma, head trauma, perinatal hypoxia, cardiac arrest and hypoglycemic neuronal

damage; neurodegenerative disorders such as **epilepsy,** Alzheimer's disease, Huntington's disease Parkinsonism, and amyotrophic lateral sclerosis; other diseases or disorders such as convulsion, pain, depression, anxiety, schizophrenia, muscle spasms, migraine headaches, urinary incontinence, nicotine withdrawal, opiate tolerance and withdrawal, emesis, brain edema, tardive dyskinesia, AIDS-induced dementia, ocular damage, retinopathy, cognitive disorders, and neuronal injury associated with HIV-infection such as dysfunction in cognition, movement and sensation.

Excerpt(s): Certain adamantane derivatives have been used to treat illnesses. Rimantadine (1-(1-aminoethyl)adamantane) is used for the prophylaxis and treatment of influenza in humans. Amantadine has been used for the treatment of both influenza and Parkinson's disease (Schwab et al., J. Am. Med. Assoc. (1969) 208:1168). Another derivative, memantine, is currently under clinical investigation for the treatment of various neurodegenerative diseases and has been licensed for the treatment of Parkinson's associated spasticity in Germany (Schneider et al., Dtsch. Med. Wschr. (1984) 109:987). Memantine protects cortical and retinal neuron cultures from the toxicity of glutamate, NMDA and the HIV-1 coat protein gp120 (Dreyer et al., Science (1990) 248:364). Recent studies demonstrate that it prevents quinolinic acid-induced hippocampal damage in rats (Kelhoff and Wolf., Eur. J. Pharmacol. (1992) 219:451). Memantine demonstrates antiphypoxic properties in vitro and in vivo. It is thought that memantine exerts a neuroprotective effect because it is a micromolar antagonist of the NMDA receptor (Bormann J., Eur. J. Pharmacol. (1989) 166:591). While memantine is being used to treat neurological disorders, the variety and severity of neurological diseases presents a need for other neuroprotective agents. The present invention provides novel compounds, compositions and methods for the treatment of neurological diseases. The present invention also provides methods of making the novel compounds.

Web site: http://www.delphion.com/details?pn=US06444702__

- **Anticonvulsant and central nervous system-depressing bis(fluorophenyl)alkylamides and their uses**

  Inventor(s): Artman; Linda D. (Salt Lake City, UT), Balandrin; Manuel F. (Sandy, UT), Moe; Scott T. (Salt Lake City, UT), Mueller; Alan L. (Salt Lake City, UT), Smith; Daryl (Salt Lake City, UT), VanWagenen; Bradford C. (Salt Lake City, UT)

  Assignee(s): NPS Pharmaceuticals, Inc. (Salt Lake City, UT)

  Patent Number: 6,617,358

  Date filed: June 2, 2000

  Abstract: Bis(Fluorophenyl)alkylamides have been chemically synthesized which possess beneficial pharmacological properties (e.g., anticonvulsant activity) useful for the treatment of neurological diseases or disorders, such as, for example, **epilepsy,** convulsions, and **seizure disorders.** The preferred compounds of the invention also cause little sedation and have high therapeutic and protective indices in animal models of **epilepsy.** These compounds further possess long pharmacological half-lives, which, in practical clinical therapeutic application, should translate into once-a-day dosing, of great benefit to patients suffering from these diseases and/or disorders. These compounds may also be of further clinical utility in the treatment of other diseases and disorders of the central and peripheral nervous systems, or diseases or disorders affected by them, including, but not limited to, spasticity, skeletal muscle spasms and pain, restless leg syndrome, anxiety and stress, and bipolar disorder.

Excerpt(s): The present invention relates to compounds useful in treating pathological conditions, such as convulsions and spasticity, without producing undesirable excessive sedation or muscle weakness in animal subjects, including humans. More particularly, the invention relates to the preparation, biological activities, and therapeutic uses of 3,3-bis(3-fluorophenyl)propionamide and related compounds in patients suffering from pathologies of this nature. The following is a description of relevant art, none of which is admitted to be prior art to the claims. A number of pathological states, diseases, and disorders are characterized by a profound aberration in the normal function of the central nervous system (CNS). Such conditions include multiple sclereosis, strokes, spinal cord injuries, chronic neurodegenerative disorders and diseases such as Parkinson's and Huntington's diseases, Alzheimers disease, amyotrophic lateral sclerosis (ALS; Lou Gehrig disease), and **epilepsy.** At the clinical level, these states usually only respond to pharmacologic intervention with compounds or substances that possess significant activity at the level of the CNS.

Web site: http://www.delphion.com/details?pn=US06617358__

- **Bisarylamines as potassium channel openers**

  Inventor(s): Amato; George Salvatore (Cary, NC), McNaughton-Smith; Grant Andrew (Morrisville, NC)

  Assignee(s): ICAgen, Inc. (Durham, NC)

  Patent Number: 6,593,349

  Date filed: March 11, 2002

  Abstract: Compounds, compositions and methods are provided which are useful in the treatment of diseases through the modulation of potassium ion flux through voltage-dependent potassium channels. More particularly, the invention provides bisarylamines, compositions and methods that are useful in the treatment of central or peripheral nervous system disorders (e.g., migraine, ataxia, Parkinson's disease, bipolar disorders, trigeminal neuralgia, spasticity, mood disorders, brain tumors, psychotic disorders, myokymia, seizures, **epilepsy,** hearing and vision loss, Alzheimer's disease, age-related memory loss, learning deficiencies, anxiety and motor neuron diseases) and as neuroprotective agents (e.g., to prevent stroke and the like) by opening potassium channels associated with the onset or recurrence of the indicated conditions.

  Excerpt(s): This invention relates to the use of certain bisarylamines as potassium channel openers and to the treatment of diseases modulated by potassium channel opening. Additionally, this invention relates to novel compounds that are useful as potassium channel openers. Ion channels are cellular proteins that regulate the flow of ions, including calcium, potassium, sodium and chloride, into and out of cells. These channels are present in all human cells and affect such processes as nerve transmission, muscle contraction and cellular secretion. Among the ion channels, potassium channels are the most ubiquitous and diverse, being found in a variety of animal cells such as nervous, muscular, glandular, immune, reproductive, and epithelial tissue. These channels allow the flow of potassium in and/or out of the cell under certain conditions. For example, the outward flow of potassium ions upon opening of these channels makes the interior of the cell more negative, counteracting depolarizing voltages applied to the cell. These channels are regulated, e.g., by calcium sensitivity, voltage-gating, second messengers, extracellular ligands, and ATP-sensitivity. Potassium channels have now been associated with a number of physiological processes, including regulation of heartbeat, dilation of arteries, release of insulin, excitability of nerve cells, and regulation

of renal electrolyte transport. Potassium channels are made by alpha subunits that fall into at least 8 families, based on predicted structural and functional similarities (Wei et al., Neuropharmacology 35(7): 805-829 (1997)). Three of these families (Kv, eag-related, and KQT) share a common motif of six transmembrane domains and are primarily gated by voltage. Two other families, CNG and SK/IK, also contain this motif but are gated by cyclic nucleotides and calcium, respectively. The three other families of potassium channel alpha subunits have distinct patterns of transmembrane domains. Slo family potassium channels, or BK channels have seven transmembrane domains (Meera et al., Proc. Natl. Acad. Sci. U.S.A. 94(25): 14066-71 (1997)) and are gated by both voltage and calcium or pH (Schreiber et al., J. Biol. Chem. 273: 3509-16 (1998)). Another family, the inward rectifier potassium channels (Kir), belongs to a structural family containing two transmembrane domains, and an eighth functionally diverse family (TP, or "two-pore") contains two tandem repeats of this inward rectifier motif.

Web site: http://www.delphion.com/details?pn=US06593349__

- **Brain fluid ion concentration modification for treating neurological disorders**

  Inventor(s): Gielen; Frans L. H. (Eckelrade, NL), Gijsbers; Johan F. M. (Munstergeleen, NL)

  Assignee(s): Medtronic, Inc. (Minneapolis, MN)

  Patent Number: 6,447,500

  Date filed: April 28, 2000

  Abstract: Epilepsy and other neurological disorders that are affected by the electrical potential difference between intracellular fluid and extra-cellular fluid and therefore the cell membrane potentials, and therefore the thresholds for the communication between brain cells can be controlled by re-circulating extra-cellular brain fluid after the fluid has been treated to alter its ion concentrations. A computer-controlled pump can precisely control the extraction and delivery of brain fluid after the ion concentration of the fluid is appropriately adjusted, e.g. guided by the Goldmann equation. Well-known techniques for modifying ion concentrations can be used to raise or lower ion concentrations as needed.

  Excerpt(s): This invention relates to methods of treating medical disorders. In particular, this invention relates to a method of treating the cause of **epilepsy,** which is rooted in the basic concepts described by the Goldman equation. This equation describes the relation between the cell rest membrane potential and the concentration of ions inside and outside the cells in e.g. nervous and muscle tissue. This implies that cell excitability can be modified and therefore the physiological inter-connectivity between cells. This interconnectivity is a major factor in the generation of e.g. **epilepsy.** The key concept of this invention is that if cell rest membrane electrical potentials are modified, **epilepsy,** and perhaps other neurological disorders might be effectively controlled. Epilepsy is a debilitating neurological disorder. Functional control of many or all body functions can be lost and further permanent brain damage results from each generalized epileptic attack. It is known that an epileptic seizure is manifested by an uncontrolled propagation of nerve impulses throughout the nerve cells in certain, areas of the brain. The nerve impulses of an epileptic seizure are characterized by many synchronized discharges, which may involve the whole brain. As a consequence the control of many body functions is lost. During epileptic seizures, the normal physiological interconnectivity between brain cells is greatly altered, resulting in a synchronized highly pathological brain activity.

Web site: http://www.delphion.com/details?pn=US06447500__

- **Controlled release formulation of divalproex sodium**

  Inventor(s): Bollinger; J. Daniel (Libertyville, IL), Cheskin; Howard S. (Glencoe, IL), Engh; Robert K. (Kenosha, WI), Poska; Paul Richard (Mundelein, IL), Qiu; Yihong (Gurnee, IL)

  Assignee(s): Abbott Laboratories (Abbott Park, IL)

  Patent Number: 6,528,091

  Date filed: May 10, 2002

  Abstract: A controlled release tablet formulation which permits once daily dosing in the treatment of **epilepsy** comprises from about 50 weight percent to about 55 weight percent of an active ingredient selected from the group consisting of valproic acid, a pharmaceutically acceptable salt or ester of valproic acid, divalproex sodium, and valpromide; from about 20 weight percent to about 40 weight percent hydroxypropyl methylcellulose; from about 5 weight percent to about 15 weight percent lactose, from about 4 weight percent to about 6 weight percent microcrystalline cellulose, and from about 1 weight percent to about 5 weight percent silicon dioxide having an average particle size ranging between about 1 micron and about 10 microns; all weight percentages based upon the total weight of the tablet dosage form. Also disclosed are pre-tableting granular formulations, methods of making the granular formulations and tablets, and a method of treating **epilepsy** employing the controlled release tablet formulations of the invention.

  Excerpt(s): The present invention relates to pharmaceutical formulations. More particularly, the present invention concerns a formulation comprising valproic acid, a pharmaceutically acceptable salt, ester, or amide thereof or divalproex sodium, in a controlled release tablet formulation. 2-Propylpentanoic acid, more commonly known as valproic acid (VPA), its amide, valpromide (VPO), and certain salts and esters of the acid are effective in the treatment of epileptic seizures or as antipsychotic agents. U.S. Pat. No. 4,988,731 to Meade discloses an oligomer having a 1:1 molar ratio of sodium valproate and valproic acid containing 4 units, and U.S. Pat. No. 5,212,326 to Meade discloses a stable, non-hygroscopic solid form of valproic acid which comprises an oligomer having 1:1 molar ratio of sodium valproate and valproic acid and containing four to six units. Divalproex sodium (sodium hydrogen divalproate) is one of the most widely accepted antiepileptic agents currently available. However, despite its efficacy in the treatment of **epilepsy,** valproic acid has been shown to exhibit an elimination half-life which is shorter than other commonly used antiepileptic agents. Half-lives for the drug of between six and seventeen hours in adults and between four and fourteen hours in children have been reported. This leads to substantial fluctuations in the plasma concentration of the drug, especially in chronic administration. To maintain reasonably stable plasma concentrations, it is necessary to resort to frequent dosing, and the resulting inconvenience to the patient often results in lowered compliance with the prescribed dosing regimen. Moreover, widely fluctuating plasma concentrations of the drug may result in administration of less than therapeutic amounts of the drug in a conservative dosing regimen, or amounts too large for the particular patient in an aggressive dosing regimen.

  Web site: http://www.delphion.com/details?pn=US06528091__

- **Extradural leads, neurostimulator assemblies, and processes of using them for somatosensory and brain stimulation**

  Inventor(s): Greene; David A. (Ft. Wayne, IN)

  Assignee(s): NeuroPace, Inc. (Mountain View, CA)

  Patent Number: 6,529,774

  Date filed: November 9, 2000

  Abstract: This is directed to a neurostimulator assembly that is preferably implantable and is suitable for treating **epilepsy** and other neurological disorders. The assembly includes inventive leads that are suitable both for providing electrical somatosensory stimulation, extradurally applied, as well as electrical stimulation that is applied to the central nervous system. The leads are preferably also suitable for sensing electrical signals in the brain. The invention includes processes of using the neurostimulator and its leads. The neurostimulator may independently provide a variety of different electrical stimulation, e.g., non-responsive electrical stimulation signals applied to the central nervous system to reduce the likelihood of a seizure or other undesirable neurological even from occurring, electrical stimulation signals applied to the central nervous system when the neurostimulator determines that epileptiform waveforms are impending or extant, and extradural electrical somatosensory stimulation signals. The responsive electrical stimulation signal or signals are intended to terminate epileptiform activity, e.g., to desynchronize abnormally synchronous brain electrical activity.

  Excerpt(s): This invention is directed to a neurostimulator that is preferably implantable and is suitable for treating **epilepsy** and other neurological disorders. The invention includes inventive leads that are suitable both for providing electrical somatosensory stimulation, extradurally applied, as well as electrical stimulation that is applied to the central nervous system. The leads are preferably also suitable for sensing electrical signals in the brain. The invention includes processes of using the neurostimulator and its leads. The neurostimulator may independently provide a variety of different electrical stimulation, e.g., non-responsive electrical stimulation signals applied to the central nervous system to reduce the likelihood of a seizure or other undesirable neurological even from occurring, electrical stimulation signals applied to the central nervous system when the neurostimulator determines that epileptiform waveforms are impending or extant, and extradural electrical somatosensory stimulation signals. The responsive electrical stimulation signal or signals are intended to terminate epileptiform activity, e.g., to desynchronize abnormally synchronous brain electrical activity.

  Web site: http://www.delphion.com/details?pn=US06529774__

- **Felbamate derived compounds**

  Inventor(s): Dieckhaus; Christine M. (North Wales, PA), MacDonald; Timothy L. (Charlottesville, VA), Miller; Thomas A. (New York, NY), Thompson; Charles D. (Stow, MA)

  Assignee(s): University of Virginia Patent Foundation (Charlottesville, VA)

  Patent Number: 6,538,024

  Date filed: August 9, 2001

  Abstract: The present invention relates to novel felbamate derivatives and their use to treat neurological diseases such as **epilepsy** and to treat tissue damage resulting form

ischemic events. The felbamate derivatives are modified to prevent the formation of metabolites that are believed responsible for the toxicity associated with felbamate therapy.

Excerpt(s): The present invention is directed to novel derivatives of 2-phenyl-1,3-propanediol dicarbamate (felbamate), and the use of such derivatives as therapeutic agents. More particularly, compositions comprising the present felbamate derivatives can be administered for reducing the incidence and severity of epileptic seizures and for preventing and treating hypoxic damage resulting from an ischemic event. Felbamate (2-phenyl-1,3-propanediol dicarbamate) is a known pharmaceutical compound having been described in U.S. Pat. Nos. 2,884,444 and 4,868,327, the disclosures of which are expressly incorporated herein. Felbamate is a modulator of NMDA (N-methyl-D-aspartate) receptor function, and a glycine site antagonist but also has other reported mechanisms of actions. Felbamate has also been reported to interact at the AMPA/kainate receptor, facilitate the function of the GABA receptor, and modulate Na.sup.+ channel conductance. Felbamate has also been demonstrated to decrease delayed neuronal cell death after kainic acid induced status epilepticus in animals. Glycine or d-serine were able to functionally reverse the anticonvulsant and ischemic protective effect of felbamate.

Web site: http://www.delphion.com/details?pn=US06538024__

- **Gamma amino butyric and acid analogs**

  Inventor(s): Belliotti; Thomas Richard (Saline, MI), Wustrow; David Juergen (Ann Arbor, MI)

  Assignee(s): Pfizer Inc (New York, NY)

  Patent Number: 6,627,771

  Date filed: April 13, 2001

  Abstract: The instant invention is improved gamma amino butyric acid analogs, processes for their preparation, and methods of using them as agents for treating **epilepsy** and other neurodegenerative disorders, depression, anxiety, panic, pain, neuropathological disorders, gastrointestinal damage, and inflammation.

  Excerpt(s): wherein R.sub.1 is hydrogen or a lower alkyl radical and n is 4, 5, or 6 are known in U.S. Pat. No. 4,024,175 and its divisional U.S. Pat. No. 4,087,544. The uses disclosed are: protective effect against cramp induced by thiosemicarbazide; protective action against cardiazole cramp; the cerebral diseases, **epilepsy,** faintness attacks, hypokinesia, and cranial traumas; and improvement in cerebral functions. The compounds are useful in geriatric patients. The patents are hereby incorporated by reference. wherein R.sub.1 is a straight or branched alkyl group having from 1 to 6 carbon atoms, phenyl, or cycloalkyl having from 3 to 6 carbon atoms; R.sub.2 is hydrogen or methyl; and R.sub.3 is hydrogen, methyl, or carboxyl are known in U.S. Pat. No. 5,563,175 and various divisionals. These patents are hereby incorporated by reference. are known in U.S. Pat. Application No. 60/059900 filed Sep. 24, 1997, now abandoned and PCT/US97/17997 filed Oct. 7, 1997. This is also incorporated by reference.

  Web site: http://www.delphion.com/details?pn=US06627771__

- **Lipophilic diesters of chelating agents**

  Inventor(s): Kozak; Alexander (Rehovot, IL), Shapiro; Israel (Ramla, IL)

  Assignee(s): D-Pharm Ltd. (Rehovot, IL)

  Patent Number: 6,458,837

  Date filed: March 27, 2000

  Abstract: The invention discloses stable diesters of chelating agents of divalent metal ions, processes for their preparation and pharmaceutical compositions thereof. Most preferred compounds according to the present invention are stable lipophilic diesters comprising a covalent conjugate of a BAPTA and a pharmaceutically acceptable alcohol. The diesters are useful in a method for treating a condition or disease related to an excess of divalent metal ions, and in particular for the treatment of a condition or disease related to elevated levels of intracellular calcium ions, such as in brain or cardiac ischemia, stroke, **epilepsy,** Alzheimer's disease or cardiac arrhythmia and in open heart surgery.

  Excerpt(s): The present invention relates to lipophilic diesters of a chelating agent, to processes of synthesizing these agents, to pharmaceutical compositions thereof and to their use in treating a condition or disease related to abnormal levels of divalent metal ions, in particular to elevated levels of intracellular calcium ions. More particularly the invention relates to diesters of 1,2-bis(2 aminophenoxy)ethane-N,N,N',N'-tetraacetic acid denoted herein as BAPTA which are stable lipophilic derivatives of divalent metal ions chelator. Metal ions such as calcium, manganese, magnesium, copper, zinc and ferrous ions play a pivotal role in biological systems by regulating protein structure, enzyme activity and cellular signaling. Various diseases or pathological states including brain and cardiac ischemia, stroke, myocardial infarction, **epilepsy,** chronic neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease and acute inflammation are all believed to be related to the phenomenon of abnormally elevated intracellular calcium levels. Other diseases associated with neuronal and muscular hyperactivity such as urinary incontinence, prostatic hypertrophy, muscular spasm, arterial hypertension, asthma, irritable bowel syndrome, have all been related to elevated levels of intracellular divalent ions such as calcium and zinc. Intracellular calcium is an important determinant for cell death, irrespective of the initial insult sustained by the cell. It may be involved in cell death in lymphocyte and killer cell mediated damage of target cells, in organ damage during transplantation, and in other types of tissue damage including ischemic insults. Calcium channel blockers or cell membrane permeable forms of calcium chelators have been suggested to protect against tissue injury or to decrease tissue damage.

  Web site: http://www.delphion.com/details?pn=US06458837__

- **Method of treating, preventing or inhibiting central nervous system injuries and diseases**

  Inventor(s): Koenig; Michael L. (Silver Spring, MD), Meyerhoff; James L. (Silver Spring, MD), Yourick; Debra L. (Linthicum Heights, MD)

  Assignee(s): The United States of America as represented by the Secretary of the Army (Washington, DC)

  Patent Number: 6,469,049

  Date filed: April 20, 2001

Abstract: Methods of preventing, treating, or both preventing and treating CNS injury, disease, neurotoxicity or memory deficit in a subject by the administration of at least one lipoic acid compound to the subject are disclosed. Examples of CNS injuries or disease include traumatic brain injury (TBI), posttraumatic **epilepsy** (PTE), stroke, cerebral ischemia, neurodegenerative diseases of the brain such as Parkinson's disease, Dementia Pugilistica, Huntington's disease and Alzheimer's disease, brain injuries secondary to seizures which are induced by radiation, exposure to ionizing or iron plasma, nerve agents, cyanide, toxic concentrations of oxygen, neurotoxicity due to CNS malaria or treatment with anti-malaria agents, and other CNS traumas. Examples of lipoic acid compounds include alpha-lipoic acid (ALA), dihydrolipoic acid (DHLA), 2-(N,N-dimethylamine) ethylamido lipoate-HCL (LA-plus), the oxidized or reduced R- or S-isomers thereof, the metabolites of alpha-lipoic acid such as 6,8-bisnorlipoic acid and tetranorlipoic acid and analogs thereof. Also disclosed are pharmaceutical compositions and kits comprising at least one lipoic acid compound.

Excerpt(s): The invention relates to a method of treating, preventing or inhibiting central nervous system (CNS) injuries and diseases. In particular, the invention relates to a method of treating, preventing or inhibiting a CNS injury or disease in a subject by the administration of at least one lipoic acid compound to the subject. Traumatic brain injury (TBI) can initiate a cascade of events which may lead to dramatic elevation of intracranial pressure (ICP), cerebral edema, ischemia, intracranial hemorrhage and dysfunction of cerebrovascular regulatory mechanisms essential for survival. Deficits in memory, attention, and perception, emotional disorders, social behavioral problems, seizures (including non-convulsive seizures), paralysis, aphasia, post-traumatic **epilepsy** (PTE), and oxidative stress-induced neurotoxicity may result from TBI. In several studies of severely head-injured patients, over 80% had ischemic damage in the hippocampus. See McIntosh, T. K., et al., (1996) Laboratory Investigation 74(2):315-342. The hippocampal damage may explain the prevalence of memory defects in survivors of TBI. Generally, the two main stages in the development of TBI are (1) primary, including contusion, laceration, intracranial hemorrhage and diffuse axonal injury; and (2) secondary, including delayed effects such as seizures, ischemia, edema, and biochemical reactions, which lead to necrosis and apoptosis.

Web site: http://www.delphion.com/details?pn=US06469049__

- **Methods and compositions for treating conditions of the central and peripheral nervous systems using non-synaptic mechanisms**

  Inventor(s): Hochman; Daryl W. (Seattle, WA)

  Assignee(s): Cytoscan Sciences LLC (Seattle, WA)

  Patent Number: 6,495,601

  Date filed: December 22, 1999

  Excerpt(s): The present invention relates to methods and compositions for treating selected conditions of the central and peripheral nervous systems employing non-synaptic mechanisms. More specifically, one aspect of the present invention relates to methods and materials for treating seizures and **seizure disorders, epilepsy,** status epilepticus, migraine headache, cortical spreading depression, intracranial hypertension, neuropsychiatric disorders, central nervous system edema; for treating or protecting from the pathophysiological effects of toxic agents such as ethanol and certain infectious agents; for treating the pathophysiological effects of head trauma, stroke, ischemia and hypoxia; and for improving certain brain functions, such as cognition, learning and

memory by administering agents that modulate ionic concentrations and ionic balances in the central nervous system. Specific treatment compositions, including loop diuretics, analogs and derivatives of such compositions, as well as combinations of such compositions with other agents for modulating ionic concentrations and gradients, and for treating various conditions, are disclosed. Materials and methods for treating pain by administering agents that modulate ionic concentrations and gradients in the peripheral nervous system are also disclosed. Methods and systems for screening drug candidate compounds for desired activities using in vitro and in vivo systems are described. Conventional treatments for neuronal disorders, such as **seizure disorders, epilepsy,** and the like, target synaptic mechanisms that affect excitatory pathways, such as by modulating the release or activity of neurotransmitters or inhibitors. Conventional treatment agents and regimen for **seizure disorders** diminish neuronal excitability and inhibit synaptic firing. One serious drawback of this approach is that while seizures are generally localized, the treatment affects (diminishes) neuronal activity indiscriminately. For this reason, there are serious side effects and repeated use of conventional medications may result in unintended deficiencies in normal and desirable brain functions, such as cognition, learning and memory. More detailed information concerning particular disorders of interest is provided below. Epilepsy is characterized by abnormal discharges of cerebral neurons and typically manifested as various types of seizures. Epileptiform activity is identified with spontaneously occurring synchronized discharges of neuronal populations that can be measured using electrophysiological techniques. This synchronized activity, which distinguishes epileptiform from non-epileptiform activity, is referred to as "hypersynchronization" because it describes the state in which individual neurons become increasingly likely to discharge in a time-locked manner with one another.

Web site: http://www.delphion.com/details?pn=US06495601__

- **Methods for responsively treating neurological disorders**

  Inventor(s): Fischell; David R. (Fair Haven, NJ), Fischell; Robert E. (Dayton, MD), Upton; Adrian R. M. (Hamilton, CA)

  Assignee(s): NeuroPace, Inc. (Sunnyvale, CA)

  Patent Number: 6,459,936

  Date filed: August 17, 2001

  Abstract: Disclosed is a multiple electrode, closed-loop, responsive system for the treatment of certain neurological diseases such as **epilepsy,** migraine headaches and Parkinson's disease. Brain electrodes would be placed in close proximity to the brain or deep within brain tissue. When a neurological event such as the onset of an epileptic seizure occurs, EEG signals from the electrodes are processed by signal conditioning means in a control module that can be placed beneath the patient's scalp, within the patient's chest, or situated externally on the patient. Neurological event detection means in the control module will then cause a response to be generated for stopping the neurological event. The response could be an electrical signal to brain electrodes or to electrodes located remotely in the patient's body. The response could also be the release of medication or the application of a sensory input such as sound, light or mechanical vibration or electrical stimulation of the skin. The response to the neurological event can originate from devices either internal or external to the patient. The system also has the capability for multi-channel recording of EEG related signals that occur both before and after the detection of a neurological event. Programmability of many different operating

parameters of the system by means of external equipment provides adaptability for treating patients who manifest different symptoms and who respond differently to the response generated by the system.

Excerpt(s): This invention is in the field of devices for the treatment of neurological disorders in human subjects, particularly those disorders that originate in the brain. The current state of the art in treating neurological disorders such as **epilepsy** or Parkinson's disease involves either drugs or the open-loop electrical stimulation of neurologic tissue. Drug therapy has been shown to have significant short and long term side effects and is often ineffective. In U.S. Pat. No. 3,850,161, Liss describes a continuous closed-loop feedback system which will always feedback part of the brain EEG signal to separate electrodes so that if a large EEG signal occurs it will be fed back in an attempt to cancel out the original signal. This system does not take advantage of recently developed digital signal processing and microcomputer technology by which feedback signals can be activated only when a neurological event occurs, nor does it provide a practical means to recognize and intervene during early stages in the evolution of a neurological event. In addition, the Liss device is not programmable and it does not provide a means to record EEG signals. Examples of a "neurological event" are the occurrence of an epileptic seizure or the occurrence of a migraine headache. A "neurological event" is defined herein as either the precursor of an event such as an epileptic seizure, or the epileptic seizure itself. Maurer and Sorenson in U.S. Pat. No. 4,019,518 describe a combined internal/external system for electrical stimulation of the body with biphasic pulses but do not describe any means of detecting neurological events. Fischell in U.S. Pat. No. 4,373,527 describes a programmable medication infusion system but does not anticipate its use in response to a detected neurological event.

Web site: http://www.delphion.com/details?pn=US06459936__

- **Methods for treating vascular dementia**

  Inventor(s): Pratt; Raymond (Leonia, NJ)

  Assignee(s): Eisai Co., Ltd. (Tokyo, JP)

  Patent Number: 6,458,807

  Date filed: September 4, 2001

  Excerpt(s): The invention describes novel methods for treating and preventing dementia caused by vascular diseases; dementia associated with Parkinson's disease; Lewy Body dementia; AIDS dementia; mild cognitive impairments; age-associated memory impairments; cognitive impairments and/or dementia associated with neurologic and/or psychiatric conditions, including **epilepsy,** brain tumors, brain lesions, multiple sclerosis, Down's syndrome, Rett's syndrome, progressive supranuclear palsy, frontal lobe syndrome, and schizophrenia and related psychiatric disorders; cognitive impairments caused by traumatic brain injury, post coronary artery by-pass graft surgery, electroconvulsive shock therapy, and chemotherapy, by administering a therapeutically effective amount of at least one of the cholinesterase inhibitor compounds described herein. The invention also describes novel methods for treating and preventing delirium, Tourette's syndrome, myasthenia gravis, attention deficit hyperactivity disorder, autism, dyslexia, mania, depression, apathy, and myopathy associated with or caused by diabetes by administering a therapeutically effective amount of at least one of the cholinesterase inhibitor compounds described herein. The invention also describes novel methods for delaying the onset of Alzheimer's disease, for enhancing cognitive functions, for treating and preventing sleep apnea, for

alleviating tobacco withdrawal syndrome, and for treating the dysfunctions of Huntington's Disease by administering a therapeutically effective amount of at least one of the cholinesterase inhibitor compounds described herein. A preferred cholinesterase inhibitor for use in the methods of the invention is donepezil hydrochloride or ARICEPT.RTM. Novel cholinesterase inhibitors are described in U.S. Pat. No. 4,895,841 and WO 98/39000, the disclosures of which are incorporated by reference herein in their entirety. The cholinesterase inhibitors described in U.S. Pat. No. 4,895,841 include donepezil hydrochloride or ARICEPT.RTM., which has proven to be a highly successful drug for the treatment of Alzheimer's disease. There is a need in the art for new and improved treatments for other diseases, disorders, and syndromes that are characterized by symptoms of dementia and/or cognitive impairments. The invention is directed to these, as well as other, important ends.

Web site: http://www.delphion.com/details?pn=US06458807__

- **Multimodal neurostimulator and process of using it**

  Inventor(s): Pless; Benjamin D. (Atherton, CA)

  Assignee(s): Neuropace, Inc. (Sunnyvale, CA)

  Patent Number: 6,466,822

  Date filed: April 5, 2000

  Abstract: This is directed to an implantable multimodal neurostimulator having improved efficacy in treating **epilepsy** and other neurological disorders and to processes of using that neurostimulator. The neurostimulator itself generally has two modes of electrical stimulation: the first involves delivering a non-responsive electrical stimulation signal which is applied to the central nervous system to reduce the likelihood of a seizure or other undesirable neurological even from occurring, and a second mode that involves delivering electrical stimulation signal or signals when epileptiform waveforms are impending or extant. The responsive electrical stimulation signal or signals are intended to terminate epileptiform activity, e.g., to desynchronize abnormally synchronous brain electrical activity. Alternatively, the second mode may be used to deliver sensory stimulation, e.g., a scalp or sound stimulation, to the patient rather than deliver electrical stimulation to the patient. Finally, the implanted neurostimulator may be used by a physician to induce epileptiform activity and then verify the effectiveness of the parameters of the first and second neurostimulation signal or signals.

  Excerpt(s): This invention is directed to an implantable neurostimulator having improved efficacy in treating **epilepsy** and other neurological disorders and to processes of using that neurostimulator. The neurostimulator itself generally involves two modes of electrical stimulation: the first involves delivering a non-responsive electrical stimulation signal which is applied to the central nervous system to reduce the likelihood of a seizure or other undesirable neurological even from occurring, and a second mode that involves delivering electrical stimulation signal or signals when epileptiform waveforms are impending or extant. The responsive electrical stimulation signal or signals are intended to terminate epileptiform activity, e.g., to desynchronize abnormally synchronous brain electrical activity. Alternatively, the second mode may be used to deliver sensory stimulation, e.g., a scalp or sound stimulation, to the patient rather than deliver electrical stimulation to the patient.

  Web site: http://www.delphion.com/details?pn=US06466822__

- **Neurological disease model**

  Inventor(s): Van der Putten; Petrus Herman Maria (Binningen, CH)

  Assignee(s): Novartis AG (Basel, CH)

  Patent Number: 6,566,580

  Date filed: March 8, 1999

  Abstract: The use of a metabotropic glutamate receptor mGluR7 agonist for the facilitation of neurotransmitter release from a nerve ending and the treatment of neurological conditions, including **epilepsy.** Transgenic knockout non-human mammals are provided which lack the mGluR7 gene, suitable for studying mGluR7 and modulators thereof as well as **epilepsy.** Specifically provided is a transgenic mouse homozygous for an inactivated endogenous mGlu7 gene which exhibits symptoms of epileptic seizures.

  Excerpt(s): This is a national stage of International Application Ser. No. PCT/EP97/04985, filed Sep. 11, 1997. The present invention relates to metabotropic glutamate receptors (mGluRs). In particular, the invention relates to the mGlu.sub.7 receptor and novel applications thereof in models for neurological disease and as a target for neuroactive drugs. L-glutamate is the major excitatory neurotransmitter in the central nervous system (CNS). Two major classes of glutamatergic receptors exist. The first class, the ionotropic receptors, which consists of NMDA, AMPA and kainate receptors, is responsible for fast synaptic transmission in the mammalian CNS. The second class, the metabotropic glutamate receptors (mGluR), exert actions on neurotransmission, synaptic plasticity and cellular excitation that are less well characterised.

  Web site: http://www.delphion.com/details?pn=US06566580__

- **Neurological event detection procedure using processed display channel based algorithms and devices incorporating these procedures**

  Inventor(s): Fischell; David R. (Fair Haven, NJ), Harwood; Jonathan (Rumson, NJ), Pless; Benjamin D. (Atherton, CA)

  Assignee(s): Neuropace, Inc. (Sunnyvale, CA)

  Patent Number: 6,473,639

  Date filed: March 2, 2000

  Abstract: This invention relates generally to information processing techniques used in the treatment of **epilepsy** and to devices for using these techniques.

  Excerpt(s): The current state-of-the-art in workstations for processing EEG signals allow for the viewing of either monopole or bipolar montages of electrode inputs. A bipolar EEG signal represents the voltage difference between two spatially separated electrodes. Existing workstations generally do not have the capability to process and display signals produced by summing two or more monopole or bipolar EEG signals. Epileptiform activity detection software, such as that by Gotman, processes individual electroencephalogram (hereinafter "EEG") channels rather than a pre-processed aggregation of selected EEG channels. In U.S. Pat. No. 6,016,449, Fischell et. al. describe an implantable system for the processing of EEG signals. Fischell et al. further describe the use of a physician's workstation for programming a separate implantable device. Physician's Workstations may also be used independently for patient diagnosis,

treatment evaluation, and pre-implantation patient testing. Although an implantable device for detecting and stopping a neurological event, such as those described in the Fischell et al. patent, may be the final patient treatment, it is highly desirable first to determine the appropriate modality of treatment and to evaluate its potential for working with an external system. It is also highly desirable that the epileptiform activity algorithms created during patient testing and evaluation then be programmable into the implantable electrical stimulation therapy device itself. In U.S. Pat. No. 5,311,876, Olsen et al. describe detection of seizures in a patient-independent manner by use of standardization techniques. Olsen et al. do not disclose patient-specific detection customization as part of a treatment based on electrical stimulation. Systems such as those described by Olsen et al. typically are used by neurologists to accelerate the analysis of patient EEGs by identifying spikes and other abnormal EEG waveforms.

Web site: http://www.delphion.com/details?pn=US06473639__

- **NMDA receptor agonist pharmaceutical compositions**

  Inventor(s): Hong; Jinyang (Stonington, CT), Kim; Yesook (Branford, CT)

  Assignee(s): Pfizer Inc (New York, NY)

  Patent Number: 6,635,270

  Date filed: December 5, 2001

  Abstract: This invention relates to stable pharmaceutical compositions of the NMDA receptor agonist, (1S,2S)-1-(4-hydroxyphenyl)-2-(4-hydroxy-4-phenylpiperidin-1-yl)-1-propano l], methods of preparing such pharmaceutical compositions and methods of treating stroke, spinal cord trauma, traumatic brain injury, multiinfarct dementia, CNS degenerative diseases such as Alzheimer's disease, senile dementia of the Alzheimer's type, Huntington's disease, Parkinson's disease, **epilepsy,** amyotrophic lateral sclerosis, pain, AIDS dementia, psychotic conditions, drug addictions, migraine, hypoglycemia, anxiolytic conditions, urinary incontinence and an ischemic event arising from CNS surgery, open heart surgery or any procedure during which the function of the cardiovascular system is compromised using the pharmaceutical compositions.

  Excerpt(s): This invention provides stable pharmaceutical compositions of the N-methyl-D-aspartic acid (NMDA) receptor antagonist, (1S,2S)-1-(4-hydroxyphenyl)-2-(4-hydroxy-4-phenylpiperidin-1-yl)-1-propano l, methods of preparing such pharmaceutical compositions and methods of treating stroke, spinal cord trauma, traumatic brain injury, multiinfarct dementia, CNS degenerative diseases such as Alzheimer's disease, senile dementia of the Alzheimer's type, Huntington's disease, Parkinson's disease, **epilepsy,** amyotrophic lateral sclerosis, pain, AIDS dementia, psychotic conditions, drug addictions, migraine, hypoglycemia, anxiolytic conditions, urinary incontinence and an ischemic event arising from CNS surgery, open heart surgery or any procedure during which the function of the cardiovascular system is compromised, using the pharmaceutical compositions of this invention. (1S,2S)-1-(4-Hydroxyphenyl)-2-(4-hydroxy-4-phenylpiperidin-1-yl)-1-propanol (hereafter referred to as the "Compound") is a neuroprotecting agent that is useful for the treatment of stroke, spinal cord trauma, traumatic brain injury, multiinfarct dementia, CNS degenerative diseases such as Alzheimer's disease, senile dementia of the Alzheimer's type, Huntington's disease, Parkinson's disease, **epilepsy,** amyotrophic lateral sclerosis, pain, AIDS dementia, psychotic conditions, drug addictions, migraine, hypoglycemia, anxiolytic conditions, urinary incontinence and an ischemic event arising from CNS surgery, open heart surgery or any procedure during which the function of the

cardiovascular system is compromised. The Compound exhibits activity as an NMDA receptor antagonist. NMDA is an excitatory amino acid involved in excitatory neurotransmission in the central nervous system. NMDA antagonists are compounds that block the NMDA receptor by interacting with the receptor's binding site. Antagonists of neurotransmission at NMDA receptors are useful therapeutic agents for the treatment of neurological disorders. U.S. Pat. No. 4,902,695 is directed to series of competitive NMDA antagonists useful for the treatment of neurological disorders, including **epilepsy,** stroke, anxiety, cerebral ischemia, muscular spasms, and neurodegenerative disorders such as Alzheimer's disease and Huntington's disease. U.S. Pat. No. 4,968,878 is directed to a second series of competitive NMDA receptor antagonists useful for the treatment of similar neurological disorders and neurodegenerative disorders. U.S. Pat. No. 5,192,751 discloses a method of treating urinary incontinence in a mammal, which comprises administering an effective amount of a competitive NMDA antagonist.

Web site: http://www.delphion.com/details?pn=US06635270__

- **Stimulation method for the sphenopalatine ganglia, sphenopalatine nerve, or vidian nerve for treatment of medical conditions**

  Inventor(s): Ansarinia; Mehdi M. (349 Condon Ct., Santa Clara, CA 95050)

  Assignee(s): none reported

  Patent Number: 6,526,318

  Date filed: June 16, 2000

  Abstract: A method is provided for the suppression or prevention of pain, movement disorders, **epilepsy,** cerebrovascular diseases, autoimmune diseases, sleep disorders, autonomic disorders, urinary bladder disorders, abnormal metabolic states, disorders of the muscular system, and neuropsychiatric disorders in a patient. The method comprises positioning at least one electrode on or proximate to at least one of the patient's sphenopalatine ganglia ("SPG"), sphenopalatine nerves ("SPN"), or vidian nerves ("VN"), and activating the at least one electrode to apply an electrical signal to at least one of the SPG, SPN, or VN. In a further embodiment of the invention used to treat the same conditions, the electrode used is capable of dispensing a medication solution or analgesic which is applied via an electrode to at least one of the SPG, SPN, or VN. A method is also provided for surgically implanting an electrode on or proximate to at least one of the SPG, SPN, or VN of a patient.

  Excerpt(s): The present invention relates generally to methods for suppressing or preventing medical conditions such as pain, movement disorders, sleep disorders, autonomic disorders, gastrointestinal disorders, and abnormal metabolic states arising from signals generated by or transmitted through the sphenopalatine ganglia, the sphenopalatine nerve, or vidian nerve. Headaches are one of the most common ailments, and afflict millions of individuals. The specific etiology of headaches may be difficult to pinpoint. Known sources of headache pain include trauma and vascular, autoimmune, degenerative, infectious, drug and medication-induced, inflammatory (sarcoid), neoplastic (primary or metastatic), metabolic-endocrine, iatrogenic (such as post-surgical), muscloskelatal and myofascial causes. Even if the condition underlying the headache pain is identified and treated, headache pain may persist. Diagnosis of headache pain will typically include an identification of one or more categories of headaches. There are a variety of different headaches with different features. Migraine headaches, as defined by the International Headache Society (IHS) Classification, are

typically unilateral, throbbing headaches lasting from four to seventy-two hours. Migraines are often accompanied by nausea, vomiting, light sensitivity and/or noise sensitivity. Females suffer from migraines more than males by an approximate ratio of 3:1. Migraine headaches can be further subdivided and sub-classified into a number of different categories, such as, for example, migraine with aura, migraine without aura, and retinal migraine.

Web site: http://www.delphion.com/details?pn=US06526318__

- **System and method for controlling epileptic seizures with spatially separated detection and stimulation electrodes**

  Inventor(s): Fischell; David R. (Fair Haven, NJ), Fischell; Robert E. (Dayton, MD), Pless; Benjamin D. (Atherton, CA)

  Assignee(s): NeuroPace, Inc. (Mountain View, CA)

  Patent Number: 6,597,954

  Date filed: November 28, 2000

  Abstract: A system and method for controlling **epilepsy** and other neurological disorders by providing electrical stimulation to a patient's brain in response to detected neurological conditions. An implantable device includes a stimulation subsystem coupled to a stimulation electrode to provide responsive electrical brain stimulation in response to an event detected via an on-board processor's analysis of data received from a detection subsystem coupled to a detection electrode located in a different portion of the patient's brain.

  Excerpt(s): The invention relates to systems and methods for treating neurological disorders, and more particularly to a system and method employing an electronic device for sensing and detecting neurological dysfunction, specifically neuronal activity characteristic of epileptic seizures, in one region of a patient's brain, and applying treatment in response thereto in another region of the patient's brain. Because **epilepsy** is characterized by seizures, its sufferers are frequently limited in the kinds of activities they may participate in. **Epilepsy** can prevent people from driving, working, or otherwise participating in much of what society has to offer. Some **epilepsy** sufferers have serious seizures so frequently that they are effectively incapacitated. Furthermore, **epilepsy** is often progressive and can be associated with degenerative disorders and conditions. Over time, epileptic seizures often become more frequent and more serious, and in particularly severe cases, are likely to lead to deterioration of other brain functions (including cognitive function) as well as physical impairments.

  Web site: http://www.delphion.com/details?pn=US06597954__

- **Use of morphine derivatives as medicaments for the treatment of neuropathic problems**

  Inventor(s): Buschmann; Helmut (Aachen, DE), Krueger; Thomas (Langerwehe-Schlich, DE), Reiss-Mueller; Elke (Bielefeld, DE), Strassburger; Wolfgang (Wuerselen, DE), Wnendt; Stephan (Aachen, DE)

  Assignee(s): Gruenenthal GmbH (Aachen, DE)

  Patent Number: 6,476,044

  Date filed: February 15, 2002

  Abstract: A method for agonizing or antagonizing the ORL1 (opioid receptor-like) receptor of the nociceptin/orphanin FQ ligand ORL1 receptor system using a morphinan compound of the general formula I or derivatives thereof. Also disclosed are methods for treating neuropathic pain and/or anxiolysis and/or depression and/or diuresis and/or urinary incontinence and/or hypotension and or hypertension and/or senile dementia and/or Alzheimer's disease and/or general cognitive disfunctions an/or tinnitus and/or impaired hearing and/or **epilepsy** and/or obesity and/or cachexia.

  Excerpt(s): The present invention relates to the use of morphinan derivatives as well as their bases or salts of physiologically compatible acids as regulators for the nociceptin/orphanin FQ ligand ORL1 receptor system and for the production of a medicament. The heptadecapeptide nociceptin/orphanin FQ is an endogenous ligand of the ORL1 (opioid receptor-like) receptor (Meunier et al., Nature 377, 1995, pp. 532-535) that belongs to the family of opioid receptors and can be found in many regions of the brain and spinal cord (Mollereau et al., FEBS Letters, 341, 1994, pp. 33-38, Darland et al., Trends in Neurosciences, 21, 1998, pp. 215-221). The peptide is characterised by a high affinity, with a Kd value of around 56 pM (Ardati et al., Mol. Pharmacol. 51, pp. 816-824), and by a high selectivity for the ORL1 receptor. The ORL1 receptor is homologous to the.mu.,.kappa. and.delta. opioid receptors, and the amino acid sequence of the nociceptin/orphanin FQ peptide has a strong similarity to those of the known opioid peptides. The activation of the receptor induced by nociceptin/orphanin FQ leads via the coupling with G.sub.i/o proteins to an inhibition of adenylate cyclase (Meunier et al., Nature 377, 1995, pp. 532-535). Also, at the cellular level there are functional similarities between the.mu.,.kappa. and.delta. opioid receptors and the ORL1 receptor as regards the activation of the potassium channel (Matthes et al., Mo. Pharmacol. 50, 1996, pp. 447-450; Vaughan et al., Br. J. Pharmacol. 117, 1996, pp. 1609-1611) and the inhibition of the L, N and P/Q type calcium channels (Conner et al., Br. J. Pharmacol. 118, 1996, pp. 205-207; Knoflach et al., J. Neuroscience 16, 1996, pp. 6657-6664). The nociceptin/orphanin FQ peptide exhibits after intercerebroventricular application a pronociceptive and hyperalgesic activity in various animal models (Reinscheid et al., Science 270, 1995, pp. 792-794; Hara et al., Br. J. Pharmacol. 121, 1997, pp. 401-408). These results may be explained as inhibition of stress-induced analgesia (Mogil et al., Neurosci. Letters 214, 1996, pp. 131-134, as well as Neuroscience 75, 1996, pp. 333-337). In this connection an anxiolytic activity of the nociceptin/orphanin FQ peptide was also detected (Jenck et al., Proc. Natl. Acad. Sci. USA 94, 1997, 14854-14858).

  Web site: http://www.delphion.com/details?pn=US06476044__

Patent Applications on Epilepsy

As of December 2000, U.S. patent applications are open to public viewing.[10] Applications are patent requests which have yet to be granted. (The process to achieve a patent can take several years.) The following patent applications have been filed since December 2000 relating to epilepsy:

- **2,5-Dihydro-pyrazolo[3,4-d]pyrimidin-4-ones with an anticonsulsive action and methods for producing the same**

  Inventor(s): Arnold, Thomas; (Radebeul, DE), Bernoster, Katrin; (Radebeul, JP), Dost, Rita; (Dresden, JP), Gasparic, Antje; (Coswig, JP), Lankau, Hans-Joachim; (Weinbohla, DE), Rundfeldt, Chris; (Coswig, DE), Tober, Christine; (Weinbohla, DE), Unverferth, Klaus; (Dresden, DE)

  Correspondence: FULBRIGHT & JAWORSKI, LLP; 666 FIFTH AVE; NEW YORK; NY; 10103-3198; US

  Patent Application Number: 20030186997

  Date filed: February 18, 2003

  Abstract: The invention relates to 2,5-dihydropyrazolo[3,4-d]pyrimidin-4-ones and their tautomers which contain in the 5-position an ar(alkyl) radical and in the 2-position a hydrogen or an ar(alkyl) radical, processes for their preparation and their use as medicaments, in particular for the treatment of **epilepsy** of various forms.

  Excerpt(s): The invention relates to 2,5-dihydropyrazolo-[3,4-d]pyrimidin-4-one- s and their tautomers which contain an ar(alkyl) radical in the 5-position and a hydrogen or an ar(alkyl) radical in the 2-position, processes for their preparation and their use as medicaments, in particular for the treatment of **epilepsy** of various forms. On account of the structural similarities to adenine, pyrazolo[3,4-d]pyrimidines are compounds of pharmacological interest. Hitherto, only 5-benzyl-2,5-dihydropyrazolo[3,4-d]pyrimidin-4-one and 5-phenethyl-2,5-dihydropyrazolo[3,4-d]pyrimidin-4-one have been described [Sochneva, E. O.; Solov'eva, N. P.; Granik, V. G., Khim. Geterotsikl. Soedin. 1978, (12), 1671-6; Granik, V. G.; Sochneva, E. O.; Solov'eva, N. P.; Shvarts, G. Ya.; Syubaev, R. D.; Mashkovskii, M. D., Khim.-Farm. Zh. 1980, 14(6), 36-40]. These compounds were investigated for antiinflammatory action; an anticonvulsant action is not mentioned or suggested. 5-Arylmetyl-2,5-dihydropyrazolo[3,4-d]pyrimidin-4-ones [sic] which have a further substituent in the pyrazole ring are not known.

  Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **2-oxo-1-pyrrolidine derivatives, processes for preparing them and their uses**

  Inventor(s): Differding, Edmond; (Louvain-la-Neuve, BE), Kenda, Benoit; (Emines, BE), Lallemand, Benedicte; (Waimes, BE), Matagne, Alain; (Gerpinnes, BE), Michel, Philippe; (Beersel, BE), Pasau, Patrick; (Chastre, BE), Talaga, Patrice; (Watermael-Boitsfort, BE)

  Correspondence: WENDEROTH, LIND & PONACK, L.L.P.; 2033 K STREET N. W.; SUITE 800; WASHINGTON; DC; 20006-1021; US

  Patent Application Number: 20030120080

  Date filed: August 20, 2002

[10] This has been a common practice outside the United States prior to December 2000.

Abstract: The invention concerns 2-oxo-1-pyrrolidine derivatives of formula (I) wherein the substituents are as defined in the specification, as well as their use as pharmaceuticals. The compounds of the invention are particularly suited for treating neurological disorders such as **epilepsy.**

Excerpt(s): The present invention concerns 2-oxo-1-pyrrolidine derivatives, processes for preparing them, pharmaceutical compositions containing them and their use as pharmaceuticals. European Patent No. 0 162 036 B1 discloses the compound (S)-.alpha.-ethyl-2-oxo-1-pyrrolidine acetamide, which is known under the International Nonproprietary Name of levetiracetam. Levetiracetam, a laevorotary compound, is disclosed as a protective agent for the treatment and prevention of hypoxic and ischemic type aggressions of the central nervous system. This compound is also effective in the treatment of **epilepsy,** a therapeutic indication for which it has been demonstrated that its dextrorotatory enantiomer (R)-.alpha.-ethyl-2-oxo-1-pyrrolidine acetamide, also known from European Patent No. 0 165 919 B1, completely lacks activity (A. J. GOWER et al., Eur. J. Pharmacol., 222, (1992), 193-203).

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **3,7-dihydro-purine-2,6-dione derivatives as CRF receptor ligands**

  Inventor(s): Hartz, Richard A.; (Kennett Square, PA)

  Correspondence: STEPHEN B. DAVIS; BRISTOL-MYERS SQUIBB COMPANY; PATENT DEPARTMENT; P O BOX 4000; PRINCETON; NJ; 08543-4000; US

  Patent Application Number: 20030119831

  Date filed: November 7, 2002

  Abstract: Compounds provided herein are 3,7-dihydro-purine-2,6-dione derivatives of Formula (I): 1Such compounds are particularly useful as CRF receptor ligands, and hence, in the treatment of various neurologically-related disorders such as affective disorder, anxiety and depression, headache, irritable bowel syndrome, post-traumatic stress disorder, supranuclear palsy, immune suppression, Alzheimer's disease, gastrointestinal diseases, anorexia nervosa or other feeding disorder, drug addiction, drug or alcohol withdrawal symptoms, inflammatory diseases, cardiovascular or heart-related diseases, fertility problems, human immunodeficiency virus infections, hemorrhagic stress, obesity, infertility, head and spinal cord traumas, **epilepsy,** stroke, ulcers, amyotrophic lateral sclerosis or hypoglycemia.

  Excerpt(s): This application claims the priority benefit of U.S. Provisional Appl No. 60/331,829, filed Nov. 20, 2001, the disclosure of which is incorporated herein by reference in its entirety. This invention relates to 3,7-dihydro-purine-2,6-dione derivatives as CRF antagonists, pharmaceutical compositions containing the same, and methods of using the same in the treatment of psychiatric disorders and neurological diseases including affective disorder, anxiety related disorders, depression, headache, post-traumatic stress disorder, supranuclear palsy, Alzheimer's disease, head and spinal cord traumas, anorexia nervosa or other feeding disorders, as well as treatment of irritable bowel syndrome, gastrointestinal diseases, cardiovascular or heart-related diseases, immune supression, human immunodeficiency virus infections, fertility problems, or a disorder the treatment of which can be effected or facilitated by antagonizing CRF, including but not limited to disorders induced or facilitated by CRF. Corticotropin releasing factor (herein referred to as CRF), a 41 amino acid peptide, is the primary physiological regulator of proopiomelanocortin (POMC)-derived peptide

secretion from the anterior pituitary gland [J. Rivier et al., Proc. Nat. Acad. Sci. (USA) 80:4851 (1983); W. Vale et al., Science 213:1394 (1981)]. In addition to its endocrine role at the pituitary gland, immunohistochemical localization of CRF has demonstrated that the hormone has a broad extrahypothalamic distribution in the central nervous system and produces a wide spectrum of autonomic, electrophysiological and behavioral effects consistent with a neurotransmitter or neuromodulator role in brain [W. Vale et al., Rec. Prog. Horm. Res. 39:245 (1983); G. F. Koob, Persp. Behav. Med. 2:39 (1985); E. B. De Souza et al., J. Neurosci. 5:3189 (1985)]. There is also evidence that CRF plays a significant role in integrating the response of the immune system to physiological, psychological, and immunological stressors [J. E. Blalock, Physiological Reviews 69:1 (1989); J. E. Morley, Life Sci. 41:527 (1987)].

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Adaptive electric field modulation of neural systems**

  Inventor(s): Gluckman, Bruce J.; (Arlington, VA), Schiff, Steven J.; (Chevy Chase, MD)

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  Patent Application Number: 20030114886

  Date filed: October 11, 2002

  Abstract: The present invention relates to devices and methods of modifying the neuronal activity of a neural system comprising neurons, comprising, one or more of the following steps, measuring the neuronal activity of a neural system; and applying an oriented electric field to said neural system effective to modify the neuronal activity of the neural system, wherein the magnitude and polarity of said applied electric field is changed in response to the measured neuronal activity. The present invention also relates to devices and methods for treating brain disorders, such as **epilepsy** and Parkinson's disease, comprising, one or more of the following steps, applying a sub-threshold and oriented electric field in situ to the brain of a patient having such a disorder in an amount effective to reduce the abnormal activity of the brain, wherein the electric field is applied through field electrodes in contact with the brain. The present invention also relates to methods and devices for restoring or repairing a brain function, such as sensation (e.g., taste, or smell), somatic activity, auditory activity, visual activity, or motor activity. It can also be used for testing drugs, pharmacological agents, and other modulators of neuronal function.

  Excerpt(s): This application is a continuation-in-part of U.S. Ser. No. 09/729,929, filed Dec. 6, 2000, which claims the benefit of provisional application Serial No. 60/169,280, filed Dec. 7, 1999, which are hereby incorporated by reference in their entirety. Numerous attempts have been made to suppress epileptic seizures in human patients with indirect electrical stimulation at sites remote from the epileptic focus, including cerebellum (Cooper et al., 1976; Van Buren et al., 1978), thalamus (Cooper et al., 1985; Fisher et al., 1992), and vagal nerve (Murphy et al., 1995; McLachlin, 1997). Surprisingly, there has been far less investigation of the technology required to directly control an epileptic focus electrically. It has been shown that direct current injection into tissue could suppress evoked (Kayyali and Durand, 1991) or spontaneous (Nakagawa and Durand, 1991; Warren and Durand, 1998) epileptiform activity in brain slices. Even simple periodic pacing of a neuronal network with direct electrical stimulation (Kerger and Schiff, 1995) can reduce seizure-like events. In addition, there is some evidence that nonlinear control schemes might be useful in manipulating epileptiform activity (Schiff

et al., 1994). In each of these cases, the stimulation was applied in the form of short current pulses directly into the tissue that evoke neuronal firing. Recently, it was demonstrated that steady state (DC) electric fields oriented parallel to pyramidal cells were capable of suppressing epileptic seizure activity in in vitro hippocampal brain slices (Gluckman et al., 1996a). Such field application led to nearly complete suppression of neuronal activity, yet due to a combination of polarization effects (electrode and tissue) and neuronal adaptation, this effect was transient. FIGS. 1(A and B). (A) is a top view schematic drawing of a perfusion chamber used to adaptively modulate the neuronal activity of an isolated neural system. (B) is a side view schematic of the same chamber. The brain slices rest on a nylon mesh just below the upper surface of the perfusate of artificial cerebrospinal fluid (ACSF), and the atmosphere above the perfusate is warmed to the bath temperature of 35.degree. C. and saturated with 95% O.sub.2-5% CO.sub.2. An electric field is imposed on the slice by a set of Ag--AgCl electrodes embedded in the floor of the chamber. The potential difference applied between parallel plate electrodes F1 and F2 is feedback controlled so that the average field measured at sensing electrodes S1 and S2 is proportional to a program voltage. An additional pair of electrodes, G, are used as recording ground.

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Alkyl amino acid derivatives useful as pharmaceutical agents**

  Inventor(s): Blakemore, David Clive; (Cambridge, GB), Bryans, Justin Stephen; (Balsham, GB), Williams, Sophie Caroline; (Cambridge, GB)

  Correspondence: David R. Kurlandsky; Warner-Lambert Company; 2800 Plymouth Road; Ann Arbor; MI; 48105; US

  Patent Application Number: 20030144214

  Date filed: November 21, 2002

  Abstract: GABA-related pro-drugs of the formula (III) are provided that when administered to humans or other mammals provide an increased duration of active compound in the plasma compared to compounds of corresponding structure in which labile groups are not present. The compounds are of the formula (III) 1In the above formula:P represents hydrogen or methyl;Q represents a labile amine- or amide-forming organic group that becomes removed in the human or animal body;R.sup.1 represents straight or branched C.sub.2-C.sub.6 alkyl, C.sub.3-C.sub.6 cycloalkyl or phenyl;R.sup.2 represents hydrogen or methyl; andR.sup.3 represents hydrogen, methyl or carboxyl; andR.sup.4 represents hydrogen or a labile ester-forming group selected from substituted and unsubstituted C.sub.1-C.sub.6 alkyl, benzyl and phenyl groups that become removed in the human or animal body. In the above formula when R.sup.1 is phenyl, R.sup.2, R.sup.3 and R.sup.4 are not simultaneously hydrogen. Pharmaceutically acceptable salts of any salt-forming compound within the above class are also included. The compounds may be used to treat a range of neurological conditions, e.g. **epilepsy** and pain.

  Excerpt(s): This invention relates to novel alkyl amino acid derivatives useful as pharmaceutical agents, to processes for their production, to pharmaceutical compositions containing them, and to their use for the treatment of the neurological conditions set out below. R.sup.3 represents hydrogen, methyl or carboxyl. That compound is variously called 4-amino-3-(2-methylpropyl)butanoi- c acid, 3-(aminomethyl)-5-methylhexanoic acid,.beta.-isobutyl-.gamma.-ami- nobutyric acid, isobutyl-GABA, isobutylgaba and pregabalin.

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Aminoalkyl substituted 5,6,7,8-tetrahydro-9H-pyridino[2,3-b]indole and 5,6,7,8-tetrahydro-9H-pyrimidino[4,5-b]indole derivatives: CRF1 specific ligands**

  Inventor(s): Darrow, James W.; (Wallingford, CT), Horvath, Raymond F.; (North Branford, CT), Maynard, George D.; (Clinton, CT)

  Correspondence: Steven J. Sarussi; McDonnell Boehnen Hulbert & Berghoff; 32nd Floor; 300 S. Wacker Drive; Chicago; IL; 60606; US

  Patent Application Number: 20030105117

  Date filed: August 27, 2002

  Abstract: Disclosed are compounds of the formula: 1whereinAr, R.sup.1, W, X and m are substituents as defined herein.These compounds are modulators of CRF receptors and are therefore useful for treating affective disorder, anxiety, depression, headache, irritable bowel syndrome, post-traumatic stress disorder, supranuclear palsy, immune suppression, Alzheimer's disease, gastrointestinal diseases, anorexia nervosa or other feeding disorder, drug addiction, drug or alcohol withdrawal symptoms, inflammatory diseases, cardiovascular or heart-related diseases, fertility problems, human immunodeficiency virus infections, hemorrhagic stress, obesity, infertility, head and spinal cord traumas, **epilepsy,** stroke, ulcers, amyotrophic lateral sclerosis, hypoglycemia or a disorder the treatment of which can be effected or facilitated by antagonizing CRF, including but not limited to disorders induced or facilitated by CRF, in mammals, comprising: administering to the mammal a therapeutically effective amount of a compound of Formula I.

  Excerpt(s): The present invention relates to aminoalkyl substituted 5,6,7,8-tetrahydro-9H-pyridino[2,3-b]indole and 5,6,7,8-tetrahydro-9H-pyr- imidino[4,5-b]indole derivatives, pharmaceutical compositions containing such compounds and their use in treating psychiatric disorders, neurological diseases, immunological, cardiovascular or heart-related diseases and colonic hypersensitivity associated with psychopathological disturbance and stress. Corticotropin releasing factor (herein referred to as CRF), a 41 amino acid peptide, is the primary physiological regulator of proopiomelanocortin (POMC) derived peptide secretion from the anterior pituitary gland [J. Rivier et al., Proc. Nat. Acad. Sci. (USA) 80:4851 (1983); W. Vale et al., Science 213:1394 (1981)]. In addition to its endocrine role at the pituitary gland, immunohistochemical localization of CRF has demonstrated that the hormone has a broad extrahypothalamic distribution in the central nervous system and produces a wide spectrum of autonomic, electrophysiological and behavioral effects consistent with a neurotransmitter or neuromodulator role in brain [W. Vale et al., Rec. Prog. Horm. Res. 39:245 (1983); G. F. Koob, Persp. Behav. Med. 2:39 (1985); E. B. De Souza et al., J. Neurosci. 5:3189 (1985)]. There is also evidence that CRF plays a significant role in integrating the response of the immune system to physiological, psychological, and immunological stressors [J. E. Blalock, Physiological Reviews 69:1 (1989); J. E. Morley, Life Sci. 41:527 (1987)]. Clinical data provide evidence that CRF has a role in psychiatric disorders and neurological diseases including depression, anxiety-related disorders and feeding disorders. A role for CRF has also been postulated in the etiology and pathophysiology of Alzheimer's disease, Parkinson's disease, Huntington's disease, progressive supranuclear palsy and amyotrophic lateral sclerosis as they relate to the dysfunction of CRF neurons in the central nervous system [for review see E. B. De Souza, Hosp. Practice 23:59 (1988)].

  Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Aminomethyl-phenyl-cyclohexanone derivatives**

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  Patent Application Number: 20030096811

  Date filed: July 5, 2002

  Abstract: Aminomethyl-phenyl-cyclohexanone derivatives of formula I or Ia, 1their diastereomers, enantiomers and salts formed with a physiologically tolerated acid. Also disclosed are processes for preparing the same, pharmaceutical compositions comprising the same, and methods of using the same for the treatment of pain, inflammatory reaction, allergic reactions, depression, drug abuse, alcohol abuse, gastritis, cardiovascular disease, respiratory tract disease, coughing, mental illness, **epilepsy,** urinary incontinence, itching, and diarrhoea.

  Excerpt(s): The present application is a continuation of international patent application no. PCT/EP00/13282, filed Dec. 27, 2000, designating the United States of America, the entire disclosure of which is incorporated herein by reference. Priority is claimed based on Federal Republic of Germany patent application no. 100 00 311.7, filed Jan. 5, 2000. The present invention relates to aminomethyl-phenyl-cyclohexanone derivatives and processes for their preparation, the use of aminomethyl-phenyl-cyclohexanone derivatives for the preparation of medicaments and medicaments comprising aminomethyl-phenyl-cyclohexanone derivatives. Treatment of chronic and non-chronic states of pain is of great importance in medicine. There is a worldwide need for pain treatments with a good action for target-orientated treatment of chronic and non-chronic states of pain appropriate for the patient, by which is to be understood successful and satisfactory pain treatment for the patient. This manifests itself in the large number of scientific works which have been published in the field of applied analgesia and basic research in nociception in recent years.

  Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Anticonvulsant and central nervous system-depressing bis (fluorophenyl) alkylamides and their uses**

  Inventor(s): Artman, Linda D.; (Salt Lake City, UT), Balandrin, Manuel F.; (Sandy, UT), Moe, Scott T.; (Boston, MA), Mueller, Alan L.; (Salt Lake City, UT), Smith, Daryl; (Salt Lake City, UT), VanWagenen, Bradford C.; (Salt Lake City, UT)

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  Patent Application Number: 20030199589

  Date filed: May 2, 2003

  Abstract: Bis(Fluorophenyl)alkylamides have been chemically synthesized which possess beneficial pharmacological properties (e.g., anticonvulsant activity) useful for the treatment of neurological diseases or disorders, such as, for example, **epilepsy,** convulsions, and **seizure disorders.** The preferred compounds of the invention also cause little sedation and have high therapeutic and protective indices in animal models of **epilepsy.** These compounds further possess long pharmacologic half-lives, which, in

practical clinical therapeutic application, should translate into once-a-day dosing, of great benefit to patients suffering from these diseases and/or disorders. These compounds may also be of further clinical utility in the treatment of other diseases and disorders of the central and peripheral nervous systems, or diseases or disorders affected by them, including, but not limited to, spasticity, skeletal muscle spasms and pain, restless leg syndrome, anxiety and stress, and bipolar disorder.

Excerpt(s): This application is a Continuation of International Application No. PCT/US98/26315, filed Dec. 9, 1998 which claims the benefit of Provisional Application No. 60/069,005, filed Dec. 10, 1997. The present invention relates to compounds useful in treating pathological conditions, such as convulsions and spasticity, without producing undesirable excessive sedation or muscle weakness in animal subjects, including humans. More particularly, the invention relates to the preparation, biological activities, and therapeutic uses of 3,3-bis(3-fluorophenyl)propionamide and related compounds in patients suffering from pathologies of this nature. The following is a description of relevant art, none of which is admitted to be prior art to the claims.

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Arylpiperidinol and arylpiperidine derivatives and pharmaceuticals containing the same**

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Correspondence: Ronald L. Grudziecki; BURNS, DOANE, SWECKER & MATHIS, L.L.P.; P.O. Box 1404; Alexandria; VA; 22313-1404; US

Patent Application Number: 20030130312

Date filed: July 17, 2002

Abstract: A pharmaceutical composition, especially a pharmaceutical composition for the alleviation or treatment of symptoms due to ischemic diseases and symptoms derived from seizures, **epilepsy,** and migraine, and a Ca.sup.2+ overload suppressant, containing an arylpiperidinol or arylpiperidine derivative having the formula (I): 1wherein, R is H, an optionally substituted phenyl, an optionally substituted phenoxy, or an optionally substituted benzoyl, A is a connecting bond, a cycloalkylene, or an alkenylene optionally substituted with a lower alkyl, B is an alkylene optionally substituted with OH or an alkoxy or --NHCO(CH.sub.2).sub.n-- where n is an integer of 1 to 5, E is a connecting bond, O, or a methylene, X is OH or H provided that when E is O or a methylene, X is not H, and Y and Z are independently H, a halogen, an alkoxy, or an alkyl optionally substituted with a halogen.

Excerpt(s): The present invention relates to a pharmaceutical composition for the alleviation or treatment of symptoms due to ischemic diseases, for example, cerebral infarction, intracerebral hemorrhage, transient ischemic attack, subarachnoid hemorrhage, head trauma, after effects of brain surgery, after effects of cerebral arteriosclerosis, and other cerebrovascular disorders, or variant angina, unstable angina, myocardial infarction, cardiovascular system disorders accompanying surgery for revascularization by PTCA (percutaneous transluminal coronary angioplasty)/PTCR (percutaneous transluminal coronary revascularization)/CABG (coronary artery bypass grafting) etc., malignant arrhythmia and myocardial ischemia-reperfusion injury, and further disorders of transplanted organs at the time of organ transplants and temporary blockage of the blood flow in organs at the time of surgery, and also symptoms derived

from seizures, **epilepsy,** migraine, etc. and Ca.sup.2+ overload suppressants. The present invention further relates to a novel arylpiperidinol and arylpiperidine derivatives having an action in suppressing Ca.sup.2+ overload and useful for the alleviation or treatment of symptoms due to the above ischemic diseases and also symptoms derived from seizures, **epilepsy,** migraine, etc., their pharmaceutically acceptable salts, and synthetic intermediates for the preparation of the aforementioned compounds. In cellular disorders caused by advanced ischemia, the depletion of ATP, the fall in the pH in the cells, and the destruction of the mechanism for maintenance of the energy-dependent ion homeostasis inside and outside the cell cause the accumulation of a large amount of intracellular divalent Ca ions (Ca.sup.2+). It is believed that the Ca.sup.2+ overload causes functional disorders in the mitochondria and randomly activates various enzyme reactions and invites further Ca.sup.2+ overload to cause a repeated vicious cycle and in the end causes irreparable damage to the cell wall and cell death [F. B. Meyer: Brain Res. Rev., 14, 227 (1989); E. Boddeke et al.: Trends Pharmacol. Sci., 10,397 (1989)]. Pharmaceuticals which suppress cytotoxic Ca.sup.2+ overload are considered to be these for the alleviation or treatment of various ischemic diseases, for example, cerebral infarction, intracerebral hemorrhage, transient ischemic attack, subarachnoid hemorrhage, head trauma, after effects of brain surgery, after effects of cerebral arteriosclerosis, and other cerebrovascular disorders, or variant angina, unstable angina, myocardial infarction, cardiovascular system disorders accompanying surgery for revascularization by PTCA/PTCR/CABG etc., malignant arrhythmia and myocardial ischemia-reperfusion injury, and further disorders of transplanted organs at the time of organ transplants and temporary blockage of the blood flow in organs at the time of surgery.

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- **Arylsulphonyl substituted-tetrahydro- and hexahydro-carbazoles**

  Inventor(s): Fu, Jian-Min; (Kalamazoo, MI)

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  Patent Application Number: 20030100596

  Date filed: October 8, 2002

  Abstract: The invention provides compounds of formula I for use in treating conditions in which 5-HT.sub.6 receptors are involved such as in anxiety, depression, schizophrenia, Alzheimer's disease, stress-related disease, panic, a phobia, obsessive compulsive disorder, obesity, post-traumatic stress syndrome, **epilepsy,** and other CNS disorders. 1

  Excerpt(s): This application claims the benefit of U.S. provisional application Serial No. 60/327,876 and U.S. provisional application Serial No. 60/327,875, both filed on Oct. 9, 2001, under 35 USC 119(e)(i), which are incorporated herein by reference in their entirety. The present invention relates to substituted 6-arylsulphonyl tetrahydro- and hexahydro-carbazoles which are serotonin receptor, 5-HT.sub.6, ligands and are useful for treating anxiety, depression, schizophrenia, Alzheimer's disease, stress-related disease, panic, a phobia, obsessive compulsive disorder, obesity, post-traumatic stress syndrome, **epilepsy,** and other central nervous system (CNS) disorders in humans and animals. Serotonin has been implicated in a number of diseases, disorders, and conditions that originate in the CNS. Serotonin also plays an important role in

peripheral systems, such as the gastrointestinal system, where it has been found to mediate a variety of contractile, secretory, and electrophysiological effects.

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Brain selective transmembrane receptor gene**

  Inventor(s): Fan, Wufang; (Germantown, MD), Jay, Gilbert; (North Bethesda, MD), Shu, Youmin; (Potomac, MD)

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  Patent Application Number: 20030082548

  Date filed: August 31, 2001

  Abstract: The present invention relates to all facets of novel polynucleotides, the polypeptides they encode, antibodies and specific binding partners thereto, and their applications to research, diagnosis, drug discovery, therapy, clinical medicine, forensic science and medicine, etc. The polynucleotides are expressed in thalamus and testes and are therefore useful in variety of ways, including, but not limited to, as molecular markers, as drug targets, and for detecting, diagnosing, staging, monitoring, prognosticating, preventing or treating, determining predisposition to, etc., diseases and conditions, such as Parkinsonian manifestations (e.g., tremor), neurogenic pain, depression, tinnitis, **epilepsy,** obsessive-compulsive disorder, dystonia, and spasticity, especially relating to thalamus and testes.

  Excerpt(s): SEQ ID NOS 1 and 2 show the nucleotide sequences of human GPCR150. SEQ ID NOS 3 and 4 show polynucleotides sequences which can be used to specifically detect human GPCR150. SEQ ID NOS 5 and 6 show polynucleotide sequences of mouse GPCR150. SEQ ID NOS 7-9 show promoter sequences for human GPCR150. Polyadenylated mRNA was isolated from tissue samples, and used as a template for first-strand cDNA synthesis. The resulting cDNA samples were normalized using beta-actin as a standard. For the normalization procedure, PCR was performed on aliquots of the first-strand cDNA using beta-actin specific primers. The PCR products were visualized on an ethidium bromide stained agarose gel to estimate the quantity of beta-actin cDNA present in each sample. Based on these estimates, each sample was diluted with buffer until each contained the same quantity of beta-actin cDNA per unit volume. To detect gene expression, PCR was carried out on aliquots of the normalized tissue samples using gene-specific bases, CTACCGCTTCAAGCAGGGCTTCC (SEQ IS NO 3) and CATCGTGCTGGACTTCTCCCCAG (SEQ ID NO 4). The reaction products were loaded on to an agarose (e.g., 1.5-2%) gel and separated electrophoretically. The lane at the far left of each panel contains molecular weight standards.

  Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Compounds of use in the treatment of epilepsy, seizure, and electroconvulsive disorders**

  Inventor(s): Bence, Aimee Karis; (Indianapolis, IN), Crooks, Peter A.; (Nichozasville, KY), Worthern, David Robert; (Lexington, KY)

  Correspondence: MCDERMOTT, WILL & EMERY; 600 13th Street, N.W.; Washington; DC; 20005-3096; US

  Patent Application Number: 20030186942

  Date filed: January 16, 2003

  Abstract: The present invention provides pharmaceutical preparations and the uses thereof for preventing and/or treating seizures and other electroconvulsive disorders by administering a pharmaceutically effective amount of a therapeutic compound having the following formula (I): 1Embodiments include administering an effective amount of 4,4'-thiodianiline, 4,4'-diaminobenzophenone, 4,4'-methylenedianiline, 4,4'-diaminodiphenyl ether, or (3-aminophenyl)-(4-aminophenyl) amine, an analog, or a pharmaceutically accepted salt or complex thereof to a mammal in need of treatment or prevention of **epilepsy,** seizure, or other electroconvulsive disorder.

  Excerpt(s): This application claims the benefit of U.S. Provisional Patent Application No. 60/348,366 filed Jan. 16, 2002, which is incorporated herein by reference. The present invention relates to bridged dianilino compounds and pharmaceutical compositions and method of use thereof for the prevention and treatment of epilepsies, seizures, and other electroconvulsive disorders. Specifically, this invention relates to the use of 4,4'-thiodianiline, 4,4'-diaminobenzophenone, 4,4'-methylenedianiline, 4,4'-diaminodiphenyl ether, or (3-aminophenyl)-(4-aminophenyl) amine and related compounds, and preparations thereof, for the prevention, palliation and/or treatment of seizures, conduction disturbances and electroconvulsive disorders of all types, manifestations and origins, in humans and in animals. Epilepsy is a general term describing a group of central nervous system disorders that are characterized by recurrent seizures that are the outward manifestation of excessive and/or hyper-synchronous abnormal electrical activity of neurons of the cerebral cortex and other regions of the brain. This abnormal electrical activity can be manifested as motor, convulsion, sensory, autonomic, or psychic symptoms.

  Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Compounds, compositions and methods for preventing neurodegeneration in acute and chronic injuries in the central nervous system**

  Inventor(s): Gwag, Byoung Joo; (Seocho-ku, KR), Lee, Young Ae; (Suwon-si, KR), Moon, Ho Sang; (Suwon-si, KR), Ryu, Bo Rum; (Suwon-si, KR), Yoon, Sung Hwa; (Suwon-si, KR)

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  Patent Application Number: 20030097018

  Date filed: July 29, 2002

  Abstract: The present invention provides compositions and methods for prevention and prophylaxis of neurological diseases accompanied by neuronal death. The invention includes synthesis of 5-benzylamino salicylic acid (BAS) and its derivatives. BAS and its

derivatives protect cortical neurons from toxic insults by N-methyl-D-aspartate, Zn.sup.2+, and reactive oxygen species. Thus, the present invention provides compositions and methods for treating stroke, traumatic brain and spinal cord injury, **epilepsy,** and neurodegenerative diseases that are accompanied by severe neuronal loss via excitotoxicity, Zn.sup.2+ neurotoxicity, and free radical neurotoxicity.

Excerpt(s): The present invention is related to novel salicylic compounds, compositions and methods for prevention and prophylaxis of neurological diseases accompanied by neuronal death. Excess activation of ionotropic glutamate receptors sensitive to N-methyl-D-aspartate (NMDA receptors) produces neuronal death and has been known to mediate various neurological diseases [Choi, Neuron 1:623-634 (1988)]. Glutamate, the excitatory neurotransmitter, is massively accumulated in brain subjected to hypoxic-ischemic injuries, which activates ionotropic glutamate receptors permeable to Ca.sub.2+and Na.sup.+ and then causes neuronal death [Choi and Rothman, Annu Rev Neurosci 13:171-182 (1990)]. Antagonists of NMDA receptors remarkably attenuate brain injury following hypoglycemia, hypoxia, or hypoxic-ischemia [Simon, Swan, Griffiths, and Meldrum. Science 226:850-852 (1984); Park, Nehls, Graham, Teasdale, and McCulloch, Ann Neurol 24:543-551 (1988).; Wieloch, Science 230:681-683 (1985); Kass, Chambers, and Cottrell, Exp.Neurol 103:116-122 (1989); Weiss, Goldberg, and Choi, Brain Res. 380:186-190 (1986)]. Thus, NMDA receptor antagonists possess therapeutic potentials to protect brain against hypoglycemia, hypoxia, and hypoxic-ischemic injuries. Excitotoxicity appears to contribute to neuronal degeneration following traumatic brain injury (TBI). Levels of quinolinic acid, an endogenous agonist of NMDA receptors, was increased 5- to 50-fold in human patients with TBI [E. H. Sinz, P. M. Kochanek, M. P. Heyes, S. R. Wisniewski, M. J. Bell, R. S. Clark, S. T. DeKosky, A. R. Blight, and D. W. Marion]. Quinolinic acid is increased in the cerebrospinal fluid and associated with mortality after TBI in humans [J. Cereb.Blood Flow Metab. 18:610-615, (1998)]. In animal models of brain trauma, levels of glutamate and aspartate were markedly increased [Faden, Demediuk, Panter, and Vink, Science 244:798-800 (1989)]. Glutamate release was also observed in rat spinal cord following impact trauma [Demediuk, Daly, and Faden. J Neurochem J. Neurochem. 52 :1529-1536 (1989)]. NMDA receptor antagonists attenuate neuronal death following traumatic brain or spinal cord injuries [Faden, Lemke, Simon, and Noble. J.Neurotrauma. 5:33-45(1988); Okiyama, Smith, White, Richter, and McIntosh. J.Neurotrauma. 14:211-222 (1997)].

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Conformationally constrained compounds as pharmaceutical agents**

  Inventor(s): Bryans, Justin Stephen; (Balsham, GB), Horwell, David Christopher; (Cambridge, GB), Receveur, Jean-Marie; (Cambridge, GB)

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  Patent Application Number: 20030119858

  Date filed: October 22, 2002

  Abstract: Novel substituted amino acids of formula 1are disclosed and are useful as agents in the treatment of **epilepsy,** faintness attacks, hypokinesia, cranial disorders, neurodegenerative disorders, depression, anxiety, panic, pain, and neuropathological disorders. Processes for the preparation and intermediates useful in the preparation are also disclosed.

Excerpt(s): wherein R.sub.1 is hydrogen or a lower alkyl radical and n is 4, 5, or 6 are known in U.S. Pat. No. 4,024,175 and its divisional U.S. Pat. No. 4,087,544. The uses disclosed are: protective effect against cramp induced by thiosemicarbazide; protective action against cardiazole cramp; the cerebral diseases, **epilepsy,** faintness attacks, hypokinesia, and cranial traumas; and improvement in cerebral functions. The compounds are useful in geriatric patients. The patents are hereby incorporated by reference. The compounds, prodrugs, and pharmaceutically acceptable salts are useful in a variety of disorders. The disorders include: **epilepsy,** faintness attacks, hypokinesia, cranial disorders, neurodegenerative disorders, depression, anxiety, panic, pain, and neuropathological disorders. u is an integer of from 0 to 1.

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Cyclic amino acid derivatives useful as pharmaceutical agents**

  Inventor(s): Blakemore, David Clive; (Kent, GB), Bryans, Justin Stephen; (Kent, GB), Williams, Sophie Caroline; (Cambridgeshire, GB)

  Correspondence: Mehdi Ganjeizadeh; Warner-Lambert Company; 2800 Plymouth Road; Ann Arbor; MI; 48105; US

  Patent Application Number: 20030216469

  Date filed: April 14, 2003

  Abstract: Pro-drug compounds of the formula (I) or (II) and compositions containing them are provided that when administered to humans or other mammals provide an increased duration of active compound in the plasma compared to compounds of corresponding structure in which labile groups are not present. In the above formulae n, P, Q, R.sup.1, R.sup.2; and R.sup.3; are as defined in the specification. The compounds may be used to treat a range of neurological conditions. e.g. **epilepsy** or pain.

  Excerpt(s): This invention relates to novel cyclic amino derivatives useful as pharmaceutical agents, to processes for their production, to pharmaceutical compositions containing them, and to their use for the prevention or treatment of the neurological conditions set out below. in which R.sub.1 is hydrogen or a lower alkyl radical and n is 4, 5, or 6. These compounds are described U.S. Pat. No. 4,024,175 and its divisional U.S. Pat. No. 4,087,544. Their disclosed uses are: protective effect against cramp induced by thiosemicarbazide; protective action against cardiazole cramp; the cerebral diseases, **epilepsy,** faintness attacks, hypokinesia, and cranial traumas; and improvement in cerebral functions. The compounds are useful in geriatric patients. The disclosures of the above two patents are hereby incorporated by reference. in which R.sup.1 to R.sup.10 are each independently selected from straight or branched chain C.sup.1-C.sup.6 alkyl, substituted or unsubstituted benzyl or phenyl which substituents are selected from halogen, alkoxy, alkyl, hydroxy, carboxy, carboalkoxy, trifluoromethyl and nitro, any of R.sup.1 to R.sup.10 which is not one of the above being hydrogen. They are useful in the prevention or treatment of **epilepsy,** faintness attacks, hypokinesia, cranial disorders, neurodegenerative disorders, depression, anxiety, panic, pain and neuropathological disorders.

  Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Cyclic amino acids and derivatives thereof useful as pharmaceutical agents**

  Inventor(s): Bryans, Justin Stephen; (Balsham, GB), Horwell, David Christopher; (Cambridge, GB), Thorpe, Andrew John; (Ann Arbor, MI), Wustrow, David Juergen; (Ann Arbor, MI), Yuen, Po-Wai; (Ann Arbor, MI)

  Correspondence: WARNER-LAMBERT COMPANY; 2800 PLYMOUTH RD; ANN ARBOR; MI; 48105; US

  Patent Application Number: 20030220397

  Date filed: May 30, 2003

  Abstract: The invention is a novel series of cyclic amino acids which are useful in the treatment of **epilepsy,** faintness attacks, neurodegenerative disorders, depression, anxiety, panic, pain, neuropathological disorders, gastrointestinal disorders such as irritable bowel syndrome (IBS), and inflammation, especially arthritis. A pharmaceutical composition containing a compound of the invention as well as methods of preparing the compounds and novel intermediates useful in the preparation of the final compounds are included.

  Excerpt(s): This is a continuation of Ser. No. 09/485,382 filed Feb. 8, 2000, which is a 371 filing of PCT/US98/19876 filed Sep. 23, 1998, which claims priority to U.S. Provisional Serial No. 60/063,644 filed Oct. 27, 1997, and U.S. Provisional Serial No. 60/097,685 filed Aug. 24, 1998. wherein R.sub.1 is hydrogen or a lower alkyl radical and n is 4, 5, or 6 are known in U.S. Pat. No. 4,024,175 and its divisional U.S. Pat. No. 4,087,544. The uses disclosed are: protective effect against cramp induced by thiosemicarbazide; protective action against cardiazole cramp; the cerebral diseases, **epilepsy,** faintness attacks, hypokinesia, and cranial traumas; and improvement in cerebral functions. The compounds are useful in geriatric patients. The patents are hereby incorporated by reference. wherein R to R.sup.14 are as defined below.

  Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Diagnositc methods for determining susceptibility to convulsive conditions**

  Inventor(s): Campbell, Allyson J.; (Kingston, CA), Carran, John R.; (Kingston, CA), Lyon, Angela P.; (Kingston, CA), Weaver, Donald F.; (Halifax, CA)

  Correspondence: LAHIVE & COCKFIELD; 28 STATE STREET; BOSTON; MA; 02109; US

  Patent Application Number: 20030077833

  Date filed: August 16, 2002

  Abstract: The present invention exploits the discovery that amounts of uracil and thymine metabolites, especially.beta.-aminoisobutyric acid, in various bodily fluids, especially urine, are correlated with the occurrence of **epilepsy** when compared to matched control subjects. Analytical and diagnostic protocols, including a novel high performance liquid chromatography system, for use in the invention are disclosed.

  Excerpt(s): This application claims the priority of U.S. provisional patent application No. 60/318,139, filed Sep. 7, 2001, and U.S. provisional patent application No. 60/378,781, filed May 7, 2002. The contents of each of these aforementioned applications are hereby incorporated herein by reference. A variety of clinical methods exist by which a physician is directed to a diagnosis of the cause of apparent seizures in a patient as either **epilepsy** or otherwise. For example, routine blood studies including electrolyte

and glucose measurements, complete blood counts, and toxin screens may be carried out to assist a physician in determining a cause of seizures in a patient. Medical imaging, including CT and MRI, as well as EEG examinations may also yield valuable clinical information in this regard. There are, however, no routinely used prospective or predictive clinical tests which a physician may perform which indicate whether or not a patient is at risk of developing seizures in the future. Retrospective studies have revealed that several factors are associated with an increased risk of seizure, for example, a familial history of seizures, meningitis, or a recent head trauma. An individual's susceptibility to seizure is determined additionally by the individual's brain chemistry, and consequently a head trauma of equal magnitude, e.g., may precipitate seizures in one individual, but not another. Presently, there is no predictive test to distinguish between these two hypothetical individuals.

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Dihydroimidazo[2,1-b]thiazole and dihydro-5h-thiazolo[3,2-A]pyrimidines as antidepressant agents**

  Inventor(s): Doyle, Kevin James; (Nottingham, GB), Kerrigan, Frank; (Nottingham, GB), Watts, John Paul; (Nottingham, GB)

  Correspondence: BROMBERG & SUNSTEIN LLP; 125 SUMMER STREET; BOSTON; MA; 02110-1618; US

  Patent Application Number: 20030166628

  Date filed: January 16, 2003

  Abstract: The present invention relates to certain novel substituted dihydroimidazo[2,1-b]thiazole and dihydro-5H-thiazolo[3,2-a]pyrimidine compounds of Formula (I) including pharmaceutically acceptable salts thereof in which have affinity for 5-HT.sub.1A receptors and which inhibits neuronal reuptake of 5-hydroxytryptamine and/or noradrenaline, to processes for their preparation, to pharmaceutical compositions containing them and to their use in the treatment of depression, anxiety, psychoses (for example schizophrenia), tardive dyskinesia, obesity, drug addiction, drug abuse, cognitive disorders, Alzheimer's disease, obsessive-compulsive behaviour, panic attacks, social phobias, eating disorders such as bulimia, anorexia, snacking and binge eating, non-insulin dependent diabetes mellitus, hyperglycaemia, hyperlipidaemia, stress, as an aid to smoking cessation and in the treatment and/or prophylaxis of seizures, neurological disorders such as **epilepsy** and/or in which there is neurological damage such as stroke, brain trauma, cerebral ischaemia, head injuries and haemorrhage.

  Excerpt(s): The present invention relates to certain novel substituted dihydroimidazo[2,1-b]thiazole and dihydro-5H-thiazolo[3,2-a]pyrimidine compounds which have affinity for 5-HT.sub.1A receptors and which inhibit neuronal reuptake of 5-hydroxytryptamine and/or noradrenaline, to processes for their preparation, to pharmaceutical compositions containing them and to their use in the treatment of depression, anxiety, psychoses (for example schizophrenia), tardive dyskinesia, obesity, drug addiction, drug abuse, cognitive disorders, Alzheimer's disease, obsessive-compulsive behaviour, panic attacks, social phobias, eating disorders such as bulimia, anorexia, snacking and binge eating, non-insulin dependent diabetes mellitus, hyperglycaemia, hyperlipidaemia, stress, as an aid to smoking cessation and in the treatment and/or prophylaxis of seizures, neurological disorders such as **epilepsy** and/or conditions in which there is neurological damage such as stroke, brain trauma,

cerebral ischaemia, head injuries and haemorrhage. are useful in the treatment of depression, anxiety, Parkinson's disease, obesity, cognitive disorders, seizures, neurological disorders such as **epilepsy,** and as neuroprotective agents to protect against conditions such as stroke. The compounds of the present invention are not disclosed or suggested in this document. Sharpe C. J and Shadbolt R. S. (Journal of Medicinal Chemistry, 1971, Vol 14 No.10, p977-982) disclose certain dihydroimidazo[2,1-b]thiaz- ole compounds having antidepressant activity. However, the document also states that these compounds were generally less active and more toxic than the imidazolines also disclosed in the document. The compounds of the present invention are not disclosed or suggested in this document.

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Fused bicyclic or tricyclic amino acids**

  Inventor(s): Blakemore, David Clive; (Sandwich, GB), Bryans, Justin Stephen; (Sandwich, GB), Williams, Sophie Caroline; (Sandwich, GB)

  Correspondence: PFIZER INC; 150 EAST 42ND STREET; 5TH FLOOR - STOP 49; NEW YORK; NY; 10017-5612; US

  Patent Application Number: 20030078300

  Date filed: April 16, 2002

  Abstract: The compounds of the instant invention are bicyclic or tricyclic amino acids useful in the treatment of **epilepsy,** faintness attacks, hypokinesia, cranial disorders, neurodegenerative disorders, depression, anxiety, panic, pain, arthritis, neuropathological disorders, sleep disorders, visceral pain disorders, and gastrointestinal disorders. Processes for the preparation of the final products and intermediates useful in the process are included. Pharmaceutical compositions containing one or more of the compounds are also included.

  Excerpt(s): This invention relates to novel cyclic amino derivatives useful as pharmaceutical agents, to processes for their production, to pharmaceutical compositions containing them, and to their use for the treatment of the conditions set out below. It also relates to bicyclic and tricyclic ketones useful as intermediates in the production of the aforesaid compounds. in which R.sub.1 is hydrogen or a lower alkyl radical and n is 4, 5, or 6. These compounds are described U.S. Pat. No. 4,024,175 and its divisional U.S. Pat. No. 4,087,544. Their disclosed uses are: protection against thiosemicarbazide-induced cramp; protection against cardiazole cramp; the cerebral diseases, **epilepsy,** faintness attacks, hypokinesia, and cranial traumas; and improvement in cerebral functions. The compounds are useful in geriatric patients. The disclosures of the above two patents are hereby incorporated by reference. and salts thereof, in which: R is hydrogen or a lower alkyl; and R.sup.1 to R.sup.8 are each independently selected from hydrogen, straight or branched alkyl of from 1 to 6 carbons, phenyl, benzyl, fluorine, chlorine, bromine, hydroxy, hydroxymethyl, amino, aminomethyl, trifluoromethyl, --CO.sub.2H, --CO.sub.2R, --CH.sub.2CO.sub.2H, --CH.sub.2CO.sub.2R.sup.15, --OR.sup.15 wherein R.sup.is a straight or branched alkyl of from 1 to 6 carbons, phenyl, or benzyl, R.sup.1 to R.sup.8 not being simultaneously hydrogen.

  Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Human potassium channel 1 and 2 proteins**

  Inventor(s): Adams, Mark D.; (Rockville, MD), Li, Yi; (Sunnyvale, CA), White, Owen R.; (Rockville, MD)

  Correspondence: HUMAN GENOME SCIENCES INC; 9410 KEY WEST AVENUE; ROCKVILLE; MD; 20850

  Patent Application Number: 20030092895

  Date filed: December 23, 2002

  Abstract: Disclosed are human K.sup.+ channel polypeptides and DNA (RNA) encoding such K.sup.+ channel polypeptides. Also provided is a procedure for producing such polypeptides by recombinant techniques. Agonists for such K.sup.+ channel polypeptides are also disclosed. Such agonists may be used to treat **epilepsy,** stroke, hypertension, asthma, Parkinson's disease, schizophrenia, anxiety, depression and neurodegeneration. Also disclosed are antagonists against such polypeptides which may be used to treat AIDS, SLE, diabetes, multiple sclerosis and cancer. Also disclosed are diagnostic assays for detecting mutations in the polynucleotide sequences of the present invention.

  Excerpt(s): This invention relates to newly identified polynucleotides, polypeptides encoded by such polynucleotides, the use of such polynucleotides and polypeptides, as well as the production of such polynucleotides and polypeptides. More particularly, the polypeptides of the present invention are human potassium channel proteins sometimes hereinafter referred to as a "K.sup.+ channel 1 and 2 polypeptides." The invention also relates to inhibiting the action of such polypeptides. Potassium channels probably form the most diverse group of ion channels, and are essential to the control of the excitability of nerve and muscle. Some potassium channels open in response to a depolarization of the membrane, others to a hyperpolarization or an increase in intracellular calcium. Some can also be regulated by the binding of a transmitter and by intracellular kinases, GTP-binding proteins or other second messengers. Potassium channels are a heterogeneous group of ion channels that are similar in their ability to select for potassium over other ions, but differ in details of activation, inactivation and kinetics (Latorre, R. and Miller, C., J. Memb. Biol., 7:11-30, (1983)). They contribute significantly to several physiological functions, for example, action potential repolarization, cardiac pacemaking, neuron bursting, and possibly learning and memory (Hodgkin, A. L. and Huxley, A. F., J. Physiol. 117:500-544 (1952)).

  Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Intracranial botulinum toxin therapy for focal epilepsy**

  Inventor(s): Donovan, Stephen; (Capistrano Beach, CA), Francis, Joseph; (Aliso Viejo, CA)

  Correspondence: STEPHEN DONOVAN; ALLERGAN, INC.; 2525 Dupont Drive, T2-7H; Irvine; CA; 92612; US

  Patent Application Number: 20030202990

  Date filed: April 22, 2003

  Abstract: Methods for treating and/or curing **epilepsy** by intracranial administration of a botulinum toxin.

Excerpt(s): This application is a continuation in part of Ser. No. 09/903,849, filed Jul. 12, 2001, which is a divisional of Ser. No. 09/596,306, filed Jun. 14, 2000, now U.S. Pat. No. 6,306,403, which prior patent application and patent are incorporated herein by reference in their entireties. The present invention relates to methods for treating movement disorders. In particular, the present invention relates to methods for treating **epilepsy** by intracranial administration of a botulinum toxin. A major impediment to therapeutic treatment of a neurodegenerative disease, such as various movement disorders, is the blood-brain barrier which significantly limits penetration of the brain by even small molecules from the bloodstream upon peripheral administration of a pharmaceutical. To circumvent the blood-brain barrier direct infusion of various bioactive substances has been carried out. Most clinical experience is with intraventricular (i.e. into a cerebral-spinal fluid [CSF] filled ventricle of the brain) drug delivery. Thus, ventricular infections have been treated by direct infusion of antibiotic. Additionally, intraventricular infusion: of baclofen to treat spasticity; various chemotherapeutics, radiolabelled antibodies, and cytokines to treat brain tumors; cholinergic agonists and Nerve Growth Factor (NGF) to treat Alzheimer's disease, and; dopamine to treat Parkinson's disease is known. Unfortunately, there is a brain-CSF barrier such that penetration of drugs into brain tissue from CSF is suboptimal. Intraventricular drug delivery has therefore been met with limited success in the treatment of, for example, solid tumors, neurodegenerative diseases (such as movement disorders) and other intraparenchymal pathology.

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **KCNQ2 and KCNQ3 - potassium channel genes which are mutated in benign familial neonatal convulsions (BFNC) and other epilepsies**

  Inventor(s): Charlier, Carole; (Sprimont, BE), Leppert, Mark F.; (Salt Lake City, UT), Singh, Nanda A.; (Heber City, UT)

  Correspondence: ROTHWELL, FIGG, ERNST & MANBECK, P.C.; 1425 K STREET, N.W.; SUITE 800; WASHINGTON; DC; 20005; US

  Patent Application Number: 20030165874

  Date filed: March 14, 2002

  Abstract: Generalized idiopathic epilepsies (IGE) cause 40% of all seizures and commonly have a genetic basis. One type of IGE is Benign Familial Neonatal Convulsions (BFNC), a dominantly inherited disorder of newborns. A submicroscopic deletion of chromosome 20q13.3 which co-segregates with seizures in a BFNC family has been identified. Characterization of cDNAs spanning the deleted region identified a novel voltage-gated potassium channel, KCNQ2, which belongs to a new KCNQ1-like class of potassium channels. Nine other BFNC probands were shown to have KCNQ2 mutations including three missense mutations, three frameshifts, two nonsense mutations, and one splice site mutation. A second gene, KCNQ3, was found in a separate BFNC family in which the mutation had been localized to chromosome 8. A missense mutation was found in this gene in perfect cosegregation with the BFNC phenotype in this latter family. This demonstrates that defects in potassium channels can cause **epilepsy.** Furthermore, some members of one of the BFNC families with a mutation in KCNQ2 also exhibited rolandic **epilepsy** and one individual with juvenile myoclonic **epilepsy** has a mutation in an alternative exon of KCNQ3.

  Excerpt(s): This application is a divisional of U.S. patent application Ser. No. 09/177,650 filed Oct. 23, 1998. This application is further related to U.S. provisional patent

application Serial No. 60/063,147, filed Oct. 24, 1997, to which priority is claimed under 35 USC.sctn.119(e) and which is incorporated herein by reference. This application was made with Government support under Grant Nos. R01-NS32666 funded by the National Institutes of Health, Bethesda, Md. Epileptic disorders affect about 20 to 40 million people worldwide. Generalized idiopathic epilepsies (IGE) cause 40% of all epileptic disorders and commonly have a genetic basis (Plouin, 1994). Most of the IGEs that are inherited are complex, non-monogenic diseases. One type of IGE is Benign Familial Neonatal Convulsions (BFNC), a dominantly inherited disorder of newborns (Ronen et al., 1993; Hauser and Kurland, 1975). BFNC (OMIM 121200) is an autosomal dominantly inherited **epilepsy** of the newborn infant. This idiopathic, generalized **epilepsy** typically has an onset of seizures on day two to four of life. Spontaneous remission of the seizures occurs between two to fifteen weeks (Ronen et al., 1993; Plouin, 1994; Hauser and Kurland, 1975). Seizures typically start with a tonic posture, ocular symptoms and other autonomic features which then often progress to clonic movements and motor automatisms. These neonates thrive normally between the seizures, and their neurologic examinations and later development indicate normal brain functioning (Ronen et al., 1993; Plouin, 1994; Hauser and Kurland, 1975). However, in spite of normal neurologic development, seizures recur later in life in approximately 16% of BFNC cases compared with a 2% cumulative lifetime risk of **epilepsy** in the general population (Ronen et al., 1993; Plouin, 1994; Hauser and Kurland, 1975).

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Methanocarba cycloakyl nucleoside analogues**

  Inventor(s): Jacobson, kenneth A; (Silver Spring, MD), Marquez, Victor E; (Montgomery, MD)

  Correspondence: LEYDIG VOIT & MAYER, LTD; 700 THIRTEENTH ST. NW; SUITE 300; WASHINGTON; DC; 20005-3960; US

  Patent Application Number: 20030216412

  Date filed: July 12, 2002

  Abstract: The present invention provides novel nucleoside and nucleotide derivatives that are useful agonists or antagonists of P1 or P2 receptors. For example, the present invention provides a compound of formula A-M, wherein A is modified adenine or uracil and M is a constrained cycloalkyl group. The adenine or uracil is bonded to the constrained cycloakyl group. The compounds of the present invention are useful in the treatment or prevention of various diseases including airway diseases (through A.sub.2B, A.sub.3, P2Y.sub.2 receptors), cancer (through A.sub.3, P2 receptors), cardiac arrhythmias (through A.sub.1 receptors), cardiac ischemia (through A.sub.1, A.sub.3 receptors), **epilepsy** (through A.sub.1, P2X receptors), and Huntington's Disease (through A.sub.2A receptors).

  Excerpt(s): This application claims the benefit of U.S. provisional application No. 60/176,373, filed Jan. 14, 2000, the disclosure of which is incorporated herein by reference. This invention pertains to a novel class of receptor ligands for P1 and P2 receptors and their therapeutic use. More specifically, the invention pertains to nucleoside derivatives in which the sugar moiety is replaced with a cycloalkyl group that is conformationally constrained by fusion to a second cycloalkyl group. Purines such as adenosine have been shown to play a wide array of roles in biological systems. For example, physiological roles played by adenosine include, inter alia, modulator of vasodilation and hypotension, muscle relaxant, central depressant, inhibitor of platelet

aggregation, regulator of energy supply/demand, responder to oxygen availability, neurotransmitter, and neuromodulator. (Bruns, Nucleosides & Nucleotides, 10(5), 931-934 (1991)). Because of its potent actions on many organs and systems, adenosine and its receptors have been the subject of considerable drug-development research (Daly, J. Med. Chem., 25, 197 (1982)). Potential therapeutic applications for agonists include, for instance, the prevention of reperfusion injury after cardiac ischemia or stroke, and treatment of hypertension and **epilepsy** (Jacobson, et al., J. Med. Chem., 35, 407-422 (1992)). Adenosine itself has recently been approved for the treatment of paroxysmal supra ventricular tachycardia (Pantely, et al., Circulation, 82, 1854 (1990)). Adenosine receptor agonists also find use as anti-arrhythmics, antinociceptives, anti-lipolytics, cerebroprotectives, and antipsychotics.

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Method and apparatus for electrically stimulating cells implanted in the nervous system**

  Inventor(s): Blazer, Jeffrey; (Allison Park, PA), Firlik, Andrew D.; (Ridgefield, CT), Gliner, Bradford Evan; (Sammamish, WA), Levy, Alan J.; (Bellevue, WA), Sheffield, W. Douglas; (Loveland, OH)

  Correspondence: PERKINS COIE LLP; PATENT-SEA; P.O. BOX 1247; SEATTLE; WA; 98111-1247; US

  Patent Application Number: 20030088274

  Date filed: September 30, 2002

  Abstract: The following disclosure describes several methods and apparatus for stimulating cells implanted in the regions of nervous system, such as the brain, spinal cord or peripheral nerves. Accordingly, the functionality of the cells can be improved, for example, by differentiating undifferentiated or partially undifferentiated cells into neurons or other cells having action potentials. The method can also include promoting directional growth and connectivity of fully differentiated neural cells implanted in a patient's nervous system through electrical enhancement, for example, electrical stimulation via an anode and cathode. Methods in accordance with the invention can be used to treat brain damage (e.g., stroke, trauma, etc.), brain disease (e.g., Alzheimer's, Pick's, Parkinson's, etc.), and/or brain disorders (e.g., **epilepsy,** depression, etc.). The methods in accordance with the invention can also be used to enhance neural-function of normal, healthy brains (e.g., learning, memory, etc.), or to control sensory functions (e.g., pain).

  Excerpt(s): This application claims the benefit of U.S. application Ser. No. 09/802,808, filed Mar. 8, 2001, which claims the benefit of U.S. Provisional Application No. 60/217,981, filed Jul. 31, 2000, both of which are incorporated herein in their entireties by reference. This application also claims the benefit of U.S. Provisional Application No. 60/325,830, filed Sep. 28, 2001 and incorporated herein in its entirety by reference. Several embodiments of methods and apparatus in accordance with the invention are related to electrically stimulating cells before and/or after being implanted in the nervous system of a patient to enhance the ability of cells to achieve increased functionality. A wide variety of mental and physical processes are known to be controlled or are influenced by neural activity in particular regions of the brain.

  Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Methods of treatment using a gastric retained gabapentin dosage**

  Inventor(s): Berner, Bret; (El Granada, CA), Gusler, Gloria M.; (Cupertino, CA), Hou, Sui Yuen Eddie; (Foster City, CA)

  Correspondence: COOLEY GODWARD, LLP; 3000 EL CAMINO REAL; 5 PALO ALTO SQUARE; PALO ALTO; CA; 94306; US

  Patent Application Number: 20030100611

  Date filed: January 22, 2003

  Abstract: A method of treatment for **epilepsy** and other disease states is described, which comprises the delivery of gabapentin in a gastric retained dosage form.

  Excerpt(s): The present invention relates to the use of gabapentin in a gastric retained dosage form. More specifically, the invention relates to the use of such dosage form to treat **epilepsy** and other disease states. Gabapentin (1-(aminomethyl)cyclohexaneacetic acid) is an anti-epileptic drug that is currently available in 100 mg, 300 mg and 400 mg hard shell capsule as well as 600 mg and 800 mg tablet dosage forms, with recommended dosing of 900 mg to 1800 mg total daily dose in three divided dosages. The oral bioavailability is dose-dependent, with approximately 60% bioavailability for a dose in the range of 300-400 mg, but with only 35% bioavailability for a dose of 1600 mg (Bourgeois, Epilepsia 36 (Suppl. 5):S1-S7 (1995); Gram, Epilepsia 37 (Suppl. 6):S12-S16 (1996)). The decrease in bioavailability with dose has been attributed to carrier-mediated absorption (Stewart, et al., Pharmaceutical Research 10(2):276-281 (1993). In early work with rats, Vollmer, et al., Arzneim-Forsch/Drug Research 36(1, Nr. 5):781-892 (1986) found that the absorption site for gabapentin was the duodenum. The absorption of gabapentin occurs relatively slowly with the peak plasma concentration occurring approximately 2-6 hours after dosing (Bourgeois, supra). The elimination of gabapentin is exclusively through renal pathways (Chadwick; The Lancet 343:89-91 (1994); Vollmer, supra; Thomson, et al., Clin. Pharmacokinet. 23(3):216-230 (1992); and Riva, et al., Clin. Pharmacokinet. 31(6):470-493 (1996)) with reported half-lives of 5-7 hours (Chadwick, supra) and 6-7 hours (Gram, supra).

  Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Mono-and disubstituted 3-propyl gamma-aminobutyric acids**

  Inventor(s): Wise, Lawrence David; (Ann Arbor, MI), Wustrow, David Juergen; (Ann Arbor, MI), Yuen, Po-Wai; (Ann Arbor, MI), Belliotti, Thomas Richard; (Saline, MI), Bryans, Justin Stephen; (Balsham, GB), Ekhato, Ihoezo Victor; (West Chester, PA), Osuma, Augustine Tobi; (Canton, MI), Schelkun, Robert Michael; (Milan, MI), Schwarz, Jacob Bradley; (Ann Arbor, MI), Thorpe, Andrew John; (Ann Arbor, MI)

  Correspondence: Mehdi Ganjeizadeh; Warner-Lambert Company; 2800 Plymouth Road; Ann Arbor; MI; 48105; US

  Patent Application Number: 20030181523

  Date filed: December 20, 2002

  Abstract: The instant invention is a series of novel mono- and disubstituted 3-propyl gamma aminobutyric acids of Formula I 1The compounds are useful as therapeutic agents in the treatment of **epilepsy,** faintness attacks, hypokinesia, cranial disorders, neurodegenerative disorders, depression, anxiety, panic, pain, neuropathological

disorders, arthritis, sleep disorders, IBS, and gastric damage. Methods of preparing the compounds and useful intermediates are also part of the invention.

Excerpt(s): wherein R.sub.1 is hydrogen or a lower alkyl radical and n is 4, 5, or 6 are known in U.S. Pat. No. 4,024,175 and its divisional U.S. Pat. No. 4,087,544. The uses disclosed are: protective effect against cramp induced by thiosemicarbazide; protective action against cardiazole cramp; the cerebral diseases, **epilepsy,** faintness attacks, hypokinesia, and cranial traumas; and improvement in cerebral functions. The compounds are useful in geriatric patients. The patents are hereby incorporated by reference. or a pharmaceutically acceptable salt thereof wherein R.sub.1 is a straight or branched alkyl group having from 1 to 6 carbon atoms, phenyl or cycloalkyl having from 3 to 6 carbon atoms; R.sub.2 is hydrogen or methyl; and R.sub.3 is hydrogen, or carboxyl are known in U.S. Pat. No. 5,563,175 and its various divisionals. These patents are hereby incorporated by reference. R.sup.1 is straight or branched alkyl of from 1 to 6 carbon atoms or phenyl when R.sup.2 is methyl.

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Novel anticonvulsant derivative salts**

  Inventor(s): Abdel-Magid, Ahmed; (Ambler, PA), Maryanoff, Cynthia; (Forest Grove, PA)

  Correspondence: AUDLEY A. CIAMPORCERO JR.; JOHNSON & JOHNSON; ONE JOHNSON & JOHNSON PLAZA; NEW BRUNSWICK; NJ; 08933-7003; US

  Patent Application Number: 20030176362

  Date filed: January 3, 2003

  Abstract: The invention relates to novel pharmaceutically acceptable salts of anticonvulsant derivatives, processes for preparation of and pharmaceutical compositions containing said salts, useful in the treatment of **epilepsy.**

  Excerpt(s): This application is a continuation in part of U.S. non-provisional application Ser. No. 10/188,924 filed Jul. 3, 2002 which claims priority from U.S. provisional application Serial No. 60/303,962 filed Jul. 9, 2001, the contents of which are hereby incorporated by reference. The present invention relates to novel pharmaceutically acceptable salts of anticonvulsant derivatives, processes for preparation of and pharmaceutical compositions containing said salts. U.S. Pat. No. 4,513,006, which is hereby incorporated by reference, discloses a class of novel anti-epileptic compounds. One of these compounds, 2,3,4,5-bis-O-(1-methylethylidene)-.beta.-D-fructopyranose sulfamate, known as topiramate, has been demonstrated in clinical trials of human **epilepsy** to be effective as adjunctive therapy or as monotherapy in treating simple and complex partial seizure and secondarily generalized seizures (E. Faught, B. J. Wilder, R. E. Ramsey, R. A. Reife, L. D. Kramer, G. Pledger, R. M. Karim, et al., Epilepsia, 36 (S4) 33, (1995); S. K. Sachdeo, R. C. Sachdeo, R. A. Reife, P. Lim and G. Pledger, Epilepsia, 36 (S4) 33, (1995)). U.S. Pat. No. 4,513,006, No. 5,242,942, and No. 5,384,327, which are hereby incorporated by reference, disclose processes for the preparation of these novel anti-epileptic compounds.

  Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Novel dicarboxylic acid derivatives**

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  Patent Application Number: 20030134902

  Date filed: December 6, 2002

  Abstract: The present invention relates to 2-amino-6-fluorobicyclo[3.1.0]hexane-2,6--dicarboxylic acid derivatives represented by the formula: 1the pharmaceutically acceptable salts thereof, or the hydrates thereof. The compounds of the present invention are useful as a medicament, and in particular, are useful as modulators acting on group 2 metabotropic glutamate receptors, having effects for treating and/or preventing psychiatric disorders such as schizophrenia, anxiety and its associated diseases, depression, bipolar disorder, and **epilepsy;** and/or neurological diseases such as drug dependence, cognitive disorders, Alzheimer's disease, Huntington's chorea, Parkinson's disease, dyskinesia associated with muscular stiffness, cerebral ischemia, cerebral failure, myelopathy, and head trauma.

  Excerpt(s): The present invention relates to 2-amino-6-fluorobicyclo[3.1.0]hexa- ne-2,6-dicarboxylic acid derivatives that are useful as a medicament. In particular, it relates to novel 2-amino-6-fluorobicyclo[3.1.0]hexane-2,6-- dicarboxylic acid derivatives which exhibit treatment effects and/or prevention effects on psychiatric disorders such as schizophrenia, anxiety and its associated diseases, depression, bipolar disorder, and **epilepsy;** and/or on neurological diseases such as drug dependence, cognitive disorders, Alzheimer's disease, Huntington's chorea, Parkinson's disease, dyskinesia associated with muscular stiffness, cerebral ischemia, cerebral failure, myelopathy, and head trauma. In recent years, with the repeated cloning of glutamate receptor genes, it has become clear that there are surprisingly many subtypes of glutamate receptors. At present, glutamate receptors are roughly classified into two types: the "ionotropic type", in which the receptor has an ion channel type structure, and the "metabotropic type", in which the receptor is coupled to G-proteins (Science, 258, 597-603, 1992). In addition, ionotropic receptors are classified pharmacologically into three types: NMDA,.alpha.-amino-3-hydroxy-5-methyl isoxazole-4-propionate (AMPA), and kainate (Science, 258, 597-603, 1992). Metabotropic receptors are classified into eight types, type 1 through type 8 (J. Neurosci., 13, 1372-1378, 1993; and Neuropharmacol., 34, 1-26, 1995). The metabotropic glutamate receptors are classified pharmacologically into three groups. Of these, group 2 (mGluR2/mGluR3) bind with adenylcyclase, and inhibit the accumulation of the Forskolin stimulation of cyclic adenosine monophosphate (cAMP) (Trends Pharmacol. Sci., 14, 13 (1993)), and for this reason, it is suggested that the compounds acting on group 2 metabotropic glutamate receptors should be useful for the treatment or prevention of acute and chronic psychiatric disorders and neurological diseases.

  Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Novel imidazonline compounds**

  Inventor(s): Fukami, Takehiro; (Tsukuba-shi, JP), Ishihara, Akane; (Tsukuba-shi, JP), Ishii, Yasuyuki; (Tsukuba-shi, JP), Jitsuoka, Makoto; (Tsukuba-shi, JP), Kanatani, Akio; (Tsukuba-shi, JP), Nagai, Keita; (Tsukuba-shi, JP), Okamoto, Osamu; (Tsukuba-shi, JP), Sato, Nagaaki; (Tsukuba-shi, JP)

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  Patent Application Number: 20030158418

  Date filed: September 25, 2002

  Abstract: Compounds represented by the general formula (I): 1wherein Ar.sup.1 and Ar.sup.2 are each aryl or heteroaryl; R.sup.1 is lower cycloalkyl, --Ar.sup.3, or a group of the general formula (a), (b) or (c): 2and R.sup.2 and R.sup.3 are each hydrogen, lower cycloalkyl, lower alkenyl, or optionally substituted lower alkyl (with the proviso that when R.sup.2 and R.sup.3 are simultaneously hydrogen, Ar.sup.1, Ar.sup.2 and R.sup.1 do not simultaneously represent unsubstituted phenyl). The compounds are useful as treating agents for various NPY-related diseases, for example, circulatory diseases including hypertension, kidney diseases, cardiac diseases, vasospasm and arteriosclerosis; central nervous system diseases including hyperphagia, depression, anxiety, convulsion, **epilepsy,** dementia, pain, alcohol dependence, and withdrawal symptoms due to abstinence from drugs; metabolic diseases including obesity, diabetes, hormonal disorders, hypercholesterolemia, and hyperlipidemia; sexual dysfunction and reproductive function disorders; digestive diseases including enterokinetic disorders; respiratory diseases; inflammation; or glaucoma.

  Excerpt(s): The present invention is useful in medical fields. In more detail, novel imidazoline compounds of this invention are useful as neuropeptide Y receptor antagonists and as agents for the treatment of various kinds of cardiovascular disorders, central nervous system disorders, metabolic diseases, or the like. Neuropeptide Y (hereinafter referred to as NPY), a peptide consisting of 36 amino acids, was first isolated from porcine brain by Tatemoto et al. in 1982 (Nature, 296: 659(1982)). NPY is widely distributed in the central nervous system and the peripheral nervous system and plays various roles as one of the most abundant peptide in the nervous system. That is, NPY acts as an orexigenic substance in the central nervous system and markedly promotes fat accumulation via the secretion of various hormones or the action of the nervous system. It is known that the continuous intracerebroventricular administration of NPY induces obesity and insulin resistance based on these actions (International Journal of Obesity, vol.19:517(1995); Endocrinology, vol.133: 1753(1993)). It is also known that NPY has central effects, such as depression, anxiety, schizophrenia, pain, dementia, or the like (Drugs, vol.52: 371(1996)). Further, in the periphery, NPY coexists with norepinephrine in sympathetic nerve ending and is involved in the tonicity of the sympathetic nervous system. It is known that peripheral administration of NPY causes vasoconstriction and enhances the effects of other vasoconstrictive substances such as norepinephrine (British Journal of Pharmacology, vol.95: 419(1988)). It is also reported that NPY is involved in the enhancement of cardiac hypertrophy as a result of the acceleration of sympathetic nervous system (Proceeding National Academic Science USA, vol. 97: 1595(2000)). Further, it is reported that NPY is also involved in the secretory function of sexual hormones and growth hormone, sexual and reproductive function, gastrointestinal motility, bronchoconstriction, inflammation and alcohol preference (Life Science, vol. 55: 551(1994); The Journal of Allergy and Immunology, vol. 101: S345(1998); Nature, vol.396: 366(1998)).

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Novel spiro compounds**

  Inventor(s): Fukami, Takehiro; (Tsukuba-shi, JP), Haga, Yuji; (Tsukuba-shi, JP), Ishihara, Akane; (Tsukuba-shi, JP), Ishii, Yasuyuki; (Tsukuba-shi, JP), Itoh, Takahiro; (Okazaki-shi, JP), Kanatani, Akio; (Tsukuba-shi, JP), Sakamoto, Toshihiro; (Tsukuba-shi, JP), Takahashi, Toshiyuki; (Tsukuba-shi, JP)

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  Patent Application Number: 20030220499

  Date filed: June 4, 2003

  Abstract: Compounds of the general formula (I): 1(wherein Ar.sup.1 represents optionally substituted aryl or heteroaryl;n represents 0 or 1;T, U, V and W represent independently nitrogen atom or optionally substituted methine group, where at least two of them represent the said methine group;X represents methine or nitrogen;Y represents optionally substituted imino or oxygen atom) exhibit NPY antagonistic activities and are useful as agents for the treatment of various diseases related to NPY, for example, cardiovascular disorders such as hypertension, nephropathy, heart disease, vasospasm, arteriosclerosis and the like, central nervous system disorders such as bulimia, depression, anxiety, seizure, **epilepsy,** dementia, pain, alcoholism, drug withdrawal and the like, metabolic diseases such as obesity, diabetes, hormone abnormality, hypercholesterolemia, hyperlipidemia and the like, sexual and reproductive dysfunction, gastrointestinal disorder, respiratory disorder, inflammation or glaucoma, and the like.

  Excerpt(s): The present invention is useful in medical fields. In more detail, novel spiro compounds of this invention are useful as neuropeptide Y receptor antagonists and as agents for the treatment of various kinds of cardiovascular disorders, central nervous system disorders, metabolic diseases, and the like. Neuropeptide Y (hereinafter referred to as NPY), a peptide consisting of 36 amino acids, was first Isolated from porcine brain by Tatemoto et al. in 1982 [Nature, 296: 659 (1982)]. NPY is widely distributed in central nervous system and peripheral nervous system and plays various roles as one of the most abundant peptide in the nervous system. That is, NPY acts as an orexigenic substance in the central nervous system and markedly promotes fat accumulation via the mediation of the secretion of various hormones or the action of the nervous system. It is known that the continuous intracerebroventricular administration of NPY induces obesity and insulin resistance based on these actions (International Journal of Obesity, vol.19: 517 (1995); Endocrinology, vol.133: 1753 (1993)). It is also known that NPY has central effects, such as depression, anxiety, schizophrenia, pain, dementia and the like (Drugs, vol.52, 371(1996). Further, in the periphery, NPY coexists with norepinephrine in sympathetic ending and is involved in the tonicity of the sympathetic nervous system. It is known that peripheral administration of NPY causes vasoconstriction and enhances the activities of other vasoconstrictive substances such as norepinephrine (British Journal of Pharmacology, vol.95: 419 (1988)). It is also reported that NPY could participate in the development of cardiac hypertrophy as a result of the sympathic stimulation (Proceeding National Academic Science USA, Vol. 97, 1595(2000)). On the other hand, it is reported that NPY is also involved in the secretory function of sexual hormones and growth hormone, sexual behavior and reproductive function, gastro-intestinal motility, bronchoconstriction, inflammation and alcohol preference (Life

Science, vol. 55, 551(1994); The Journal of Allergy and Immunology, vol. 101, S345(1998); Nature, vol. 396, 366(1998)).

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Pharmaceutically active pyrrolidine derivatives as bax inhibitors**

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  Patent Application Number: 20030171309

  Date filed: April 28, 2003

  Abstract: The present invention is related to new substituted pyrrolidine derivatives of formula (I). Said compounds are preferably for use as pharmaceutically active compounds. Specifically, pyrrolidine derivatives of formula (I) are useful in the treatment and/or prevention of neurodegenerative disorders, diseases associated with polygultamine tracts, **epilepsy,** ischemia, infertility, cardiovascular disorders renal hypoxia, hepatitis and AIDS. Said pyrrolidine derivatives display a modulatory and most notably a down-regulating-up to an inhibitory-activity with respect to the cellular death agonist Bax and/or the activation pathways leading to Bax and allows therefore to block the release of cytochrome (c). The present invention is furthermore related to novel pharmaceutically activity substituted pyrrolidine derivatives as well as to methods of their preparation, wherein X is selected from the group consisting of O, S, CR<6>R<7>, NOR<6>, NNR<6>R<7>; A is selected from the group consisting of --(C.dbd.O)--, --(C.dbd.O)--O--, --C(.dbd.NH)--, --(C.dbd.O)--NH--, --(C.dbd.S)--NH, --SO2-, --SO2NH--; --CH2-; B is either a group --(C.dbd.O)--NR<8>R<9> or represents a heterocyclic residue having the formula (II) wherein Q is NR<10>, O or S; n is an integer selected of 0, 1 or 2; Y, Z and E form together with the 2 carbons to which they are attached a 5-6 membered aryl or heteroaryl ring.

  Excerpt(s): The present invention is related to new substituted pyrrolidine derivatives of formula I. Said compounds are preferably for use as pharmaceutically active compounds. Specifically, pyrrolidine derivatives of formula I are useful in the treatment and/or prevention of neurodegenerative disorders, diseases associated with polyglutamine tracts, **epilepsy,** ischemia, infertility, cardiovascular disorders, renal hypoxia, hepatitis and AIDS. Said pyrrolidine derivatives display a modulatory and most notably a down-regulating--up to an inhibitory--activity with respect to the cellular death agonist Bax and/or the activation pathways leading to Bax and allows therefore to block the release of cytochrome c. The present invention is furthermore related to novel pharmaceutically active substituted pyrrolidine derivatives as well as to methods of their preparation. The cell surface begins to bleb and expresses pro-phagocytic signals. The whole apoptotic cell then fragments into membrane-bound vesicles that are rapidly and neatly disposed of by phagocytosis, so that there is minimal damage to the surrounding tissue. The cell then separates from its neighbors.

  Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Photodynamic therapy for the treatment of epilepsy**

  Inventor(s): Zusman, Edie; (Piedmont, CA)

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  Patent Application Number: 20030125314

  Date filed: December 3, 2002

  Abstract: The present invention is based on the discovery that cells associated with seizure have selective intake of photoactive compounds. The present invention provides methods of triggering cell death in cells associated with seizure conditions by exposing such cells to photoactive compounds and irradiating the photoactive compounds contained within the cells. The present invention also provides methods of labeling cells associated with seizure conditions by exposing such cells with photoactive compounds. In addition, the present invention provides model systems useful for studying seizure conditions.

  Excerpt(s): The present application claims priority under 35 U.S.C.sctn.119(e) from provisional application No. 60/336,955, filed Dec. 3, 2001. This invention relates generally to the field of photodynamic therapy, and more specifically to the use of photodynamic therapy to treat a seizure condition. In addition, the present invention relates to the use of photoactive compounds to label cells associated with a seizure condition. For more than 2,000,000 people with **epilepsy** the daily life challenges are well known--decreased school and work performance, medication side effects, difficulty or inability to obtain a driver's license, psychosocial problems and fear of injury or sudden death. Today surgery is usually the only known "cure" for **epilepsy.** Some patients are candidates for restrictive surgery, however in most cases, the epileptic focus cannot be clearly localized or visualized. Although the use of subdural electrodes and intraoperative EEG can approximate the location of the epileptic focus, the surgery still has many side effects, e.g., the operation can removes tissues that are not specific to the epileptic process while significant for maintaining normal human functions.

  Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Polymorphisms associated with ion-channel disease**

  Inventor(s): Curran, Mark Edward; (Newark, CA), Guida, Marco; (San Diego, CA), Rienhoff, Hugh Y. JR.; (San Carlos, CA), Sotos, John G.; (Palo Alto, CA)

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  Patent Application Number: 20030162192

  Date filed: August 20, 2002

  Abstract: The present invention provides methods and materials to identify genetic abnormalities that predispose an individual to ion-channel diseases. The invention provides four polymorphic sites in the KCNQ1 gene that cause reduced conductance of the associated potassium ion channel current and a variant form of the KCNE1 gene which causes decreased conductance though the channel. The variant form of KCNE1 also acts synergistically with variants of KCNQ1 to cause further decreased conductance than either variant alone. The invention further provides polymorphisms in ion channel genes showing a higher frequency in populations afflicted with ion channel diseases or

within control groups. The detection of these polymorphic sites that produce the potassium ion channel protein variants in either heterozygous or homozygous form in a subject indicates that the subject has, or is susceptible to, ion channel diseases such as congenital or acquired cardiac arrhythmia, LQT syndrome, SIDS, **epilepsy,** or hearing loss.

Excerpt(s): This application claims benefit under 35 USC.sctn.119(e) of U.S. Provisional Application No. 60/314,331, filed Aug. 20, 2001, and U.S. Provisional Application No. 60/378,521, filed May 6, 2002, which are incorporated herein in their entirety by this reference. The invention lies in the field of genetic changes associated with ion channel diseases and methods of identifying and detecting these changes in individuals having or suspected of having an ion channel disease. Electrical functions in complex living organisms depend on a specialized class of molecules called "ion channels." Ion channels are protein molecules that regulate the flow of electrically charged atoms (ions) across membranes. Complex organisms have a plurality of ion channel proteins which allow them to precisely control the timing, direction, and magnitude of ion flux (Hille, B. (1984). Ionic Channels of Excitable Membranes, pp. 99-116, Sinauer. Variations in ion flux and/or ion channel structure have been associated with several disease states, collectively referred to as "ion channel diseases." (Schulze-Bahr, Z Kardiol 89 Suppl 4:IV12-22 (2000); Noebels News Physiol Sci. October; 13:255-256 (1998); Bockenhauer, Curr Opin Pediatr. April 2001; 13(2):142-9.; Schofield, Clin Exp Pharmacol Physiol.28(1-2):84-8. (2001)).

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Pyrimidine compounds as anti-ictogenic and/or anti-epileptogenic agents**

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  Patent Application Number: 20030153584

  Date filed: April 11, 2002

  Abstract: Methods and compounds useful for the inhibition of convulsive disorders, including **epilepsy,** are disclosed. The methods and compounds of the invention inhibit or prevent ictogenesis and/or epileptogenesis. Methods for preparing the compounds of the invention are also described. Particularly preferred compounds of the invention include: 1

  Excerpt(s): This application claims the priority of U.S. provisional patent application No. 60/282,987 (attorney docket no. NCI-109-1), filed Apr. 11, 2001, entitled "Anti-Epileptogenic Agents," U.S. provisional patent application No. 60/285,940 (attorney docket no. NCI-109-2), filed Apr. 23, 2001, entitled "Pyrimidine Compounds as Anti-Seizure Agents," and U.S. provisional patent application No. 60/310,748 (attorney docket no. NCI-109-3), filed Aug. 7, 2001, entitled "Pyrimidine Compounds as Anti-Ictogenic and/or Anti-Epileptogenic Agents," and U.S. patent application Ser. No. 10/099,934 (attorney docket no. NCI-006CP), filed Mar. 13, 2002, entitled "Anti-Epileptogenic Agents," the entire contents of each of which are incorporated herein by reference. Epilepsy is a serious neurological condition, associated with seizures, that affects hundreds of thousands of people worldwide. Clinically, a seizure results from a sudden electrical discharge from a collection of neurons in the brain. The resulting nerve

cell activity is manifested by symptoms such as uncontrollable movements. A seizure is a single discrete clinical event caused by an excessive electrical discharge from a collection of neurons through a process termed "ictogenesis." As such, a seizure is merely the symptom of **epilepsy. Epilepsy** is a dynamic and often progressive process characterized by an underlying sequence of pathological transformations whereby normal brain is altered, becoming susceptible to recurrent seizures through a process termed "epileptogenesis." While it is believed that ictogenesis and epileptogenesis have certain biochemical pathways in common, the two processes are not identical. Ictogenesis (the initiation and propagation of a seizure in time and space) is a rapid and definitive electrical/chemical event occurring over seconds or minutes. Epileptogenesis (the gradual process whereby normal brain is transformed into a state susceptible to spontaneous, episodic, time-limited, recurrent seizures, through the initiation and maturation of an "epileptogenic focus") is a slow biochemical and/or histological process which generally occurs over months to years. Epileptogenesis is a two phase process. Phase 1 epileptogenesis is the initiation of the epileptogenic process prior to the first seizure, and is often the result of stroke, disease (e.g., meningitis), or trauma, such as an accidental blow to the head or a surgical procedure performed on the brain. Phase 2 epileptogenesis refers to the process during which an individual already susceptible to seizures, becomes still more susceptible to seizures of increasing frequency and/or severity. While the processes involved in epileptogenesis have not been definitively identified, some researchers believe that upregulation of excitatory coupling between neurons, mediated by N-methyl-D-aspartate (NMDA) receptors, is involved. Other researchers implicate downregulation of inhibitory coupling between neurons, mediated by gamma-amino-butyric acid (GABA) receptors.

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Regulated gene in the pathophysiology of ischemic stroke**

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  Patent Application Number: 20030190653

  Date filed: January 10, 2003

  Abstract: The present invention identifies the K11 gene, whose gene products can be modulated to provide a protective effect against stroke, especially ischemic stroke, **epilepsy** and neurodegenerative disorders and enhancement of memory function. Further, the invention provides methods for diagnosing or assessing an individual's susceptibility to a stroke. Also provided are therapeutic methods for treating a stroke patient or methods for prophylactically treating an individual susceptible to stroke. Additionally, the invention describes screening methods for identifying agents that can be administered to treat individuals that have suffered a stroke or that are at risk for stroke.

  Excerpt(s): Neurodegenerative diseases are characterized by the dysfunction and death of neurons, leading to the loss of neurologic functions mediated by the brain, spinal cord and the peripheral nervous system. These disorders have a major impact on society. For example, approximately 4 to 5 million Americans are afflicted with the chronic neurodegenerative disease known as Alzheimer's disease. Other examples of chronic neurodegenerative diseases include diabetic peripheral neuropathy, multiple sclerosis,

amyotrophic lateral sclerosis, Huntington's disease and Parkinson's disease. Normal brain aging is also associated with loss of normal neuronal function and may entail the depletion of certain neurons. Though the mechanisms responsible for the dysfunction and death of neurons in neurodegenerative disorders are not well understood, a common theme is that loss of neurons results in both the loss of normal functions and the onset of adverse behavioral symptoms. Therapeutic agents that have been developed to retard loss of neuronal activity and survival has been largely ineffective. Some have toxic side effects that limit their usefulness. Other promising therapies, such as neurotrophic factors, are prevented from reaching their target site because of their inability to cross the blood-brain barrier. Stroke is the third ranking cause of death in the United States, and accounts for half of neurology inpatients. Depending on the area of the brain that is damaged, a stroke can cause coma, paralysis, speech problems and dementia. The five major causes of cerebral infarction are vascular thrombosis, cerebral embolism, hypotension, hypertensive hemorrhage, and anoxia/hypoxia.

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Regulation of human glur5 -like receptor**

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  Patent Application Number: 20030099982

  Date filed: September 18, 2002

  Abstract: Reagents and methods for regulating the high affinity binding of GluR5-like receptor (GR5LR) to kainate are provided. Such reagents and methods can be used inter alia, to treat or prevent urinary incontinence, **epilepsy,** schizophrenia and other mood disorders, neurodegenerative diseases such as Huntington's disease and Alzheimer's disease, ischemia, and pain.

  Excerpt(s): The invention relates to the area of regulation of glutamate-gated ion channel receptors. More particularly, the invention relates to the regulation of human GluR5-like receptors to increase or decrease excitatory neurotransmission at synapses. L-glutamate is the major excitatory neurotransmitter in the vertebrate central nervous system (CNS). L-glutamate opens cation channels that mediate fast excitatory synaptic responses and establish and maintain synaptic plasticity underlying learning and memory. These cation channels also mediate cell death resulting from excessive glutamate release in the CNS due to acute injury or environmental excitotoxins. Thus, glutamate receptors are involved in the developmental plasticity processes and long term potentiation. Further, the continuous activation of glutamate receptors can contribute to the pathogenesis of diseases such as ischemia, pain, **epilepsy,** schizophrenia, Huntington's disease, Parkinson's disease and Alzheimer's disease. There are distinct ionotropic glutamate receptor subtypes: NMDA, AMPA-low affinity kainate, and high affinity kainate receptors. The AMPA-low affinity kainate and high affinity kainate receptors are referred to as non-NMDA receptors. GluR5 is a high affinity kainate glutamate receptor. GluR5 has a high affinity for domoate and kainate and is capable of forming homomeric channels that can be gated by domoate, kainate, L-glutamate, and AMPA. See Sommer et al., EMBO J. 11, 1651-1656, 1992; Bettler et al., Neuron. 5, 583-595, 1990.

  Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Salts of bicyclic, N-acylated imidazo-3-amines and imidazo-5-amines**

  Inventor(s): Gerlach, Matthias; (Brachttal, DE), Sundermann, Corinna; (Aachen, DE)

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  Patent Application Number: 20030119842

  Date filed: October 18, 2002

  Abstract: Salts of a bicyclic, N-acylated imidazo-3-amine or an imidazo-5-amine of the formula: 1addition products thereof with acids, and methods for preparing the salts and addition products. Also disclosed are pharmaceutical compositions comprising the same and methods using the pharmaceutical compositions for the treatment or prophylaxis of pain, drug or alcohol abuse, diarrhoea, gastritis, ulcers, urinary incontinence, depression, narcolepsy, overweight, asthma, glaucoma, tinnitus, itching, hyperkinetic syndrome, **epilepsy,** or schizophrenia, for inducing anesthesia, and for anxiolysis.

  Excerpt(s): The present application is a continuation of international patent application no. PCT/EP01/03772, filed Apr. 3, 2001, designating the United States of America, and published in German as WO 01/81344, the entire disclosure of which is incorporated herein by reference. Priority is claimed based on Federal Republic of Germany patent application no. 100 19 714.0, filed Apr. 20, 2000. The present invention relates to salts of bicyclic, N-acylated imidazo-3-amines and imidazo-5-amines, to a process for producing them, to their use for producing pharmaceutical compositions and to pharmaceutical compositions containing these compounds. Individual compounds from the category of non-acylated bicyclic imidazo-3-amines and imidazo-5-amines which form the basis of the compounds according to the present invention are known to have interesting pharmacological properties. Thus, certain imidazo[1,2-a]pyridines are described as blood pressure-reducing active ingredients (GB-B-1,135,893), as anthelmintics and antimycotics (J. Med. Chem. 1972, 15, 982-985) and as anti-secretory active ingredients for the treatment of inflammatory diseases (EP-A-0 068 378). EP-A-0 266 890 and J. Med. Chem. 1987, 30, 2031-2046 also describe an effect of individual imidazopyridines against inflammatory diseases, in particular of the stomach. Further pharmacological effects described for individual representatives of the category of non-acylated imidazo-3-amines and imidazo-5-amines are antibacterial properties (Chem. Pharm. Bull. 1992, 40, 1170), antiviral properties (J. Med. Chem. 1998, 41 5108-5112) and the effect as benzodiazepine-receptor antagonist (J. Heterocyclic Chem. 1998, 35, 1205-1217).

  Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Signal analysis, heat flow management, and stimulation techniques to treat medical disorders**

  Inventor(s): Lesser, Ronald P.; (Baltimore, MD), Webber, W. R.S.; (Ellicott City, MD)

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  Patent Application Number: 20030171685

  Date filed: April 15, 2003

  Abstract: Analytical methods and devices for analyzing biological signals, for example, electrical signals from the brain to determine whether an abnormal condition caused by a medical condition exists. In one embodiment, the medical disorder may be **epilepsy.**

The analytical methods include wavelet analysis and neighbor cross-correlation count, which is a frequency specific measure of the degree of correlation of a single channel of data with respect to its neighbors. The devices according to the invention are programmed to include the analytical methods and to administer treatment regimens such as electrical stimulation, heating, cooling and medication as needed.

Excerpt(s): This is a continuation-in-part of U.S. application Ser. No. 09/691,051, filed Oct. 19, 2000, which, in turn, claims priority to U.S. Provisional Application No. 60/160,328, filed Oct. 19, 1999, and No. 60/201,188 filed May 2, 2000. Those applications are incorporated herein by reference in their entireties. The invention relates to methods for biomedical signal analysis, heat flow management, and stimulation techniques to treat medical disorders. Biological signal processing and analysis can be used in a variety of contexts, ranging from purely scientific applications to patient diagnosis and treatment. Virtually any biological signal can be analyzed to yield scientifically or medically useful information, although bioelectrical signals, particularly from the nervous system, heart, and muscles, are very often analyzed in scientific and clinical contexts. During patient diagnosis and treatment, biological signal processing may be coupled to a treatment regimen, such as electrical stimulation or administration of medication.

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Substituted imidazoles as cannabinoid receptor modulators**

Inventor(s): Finke, Paul E.; (Milltown, NJ), Mills, Sander G.; (Scotch Plains, NJ), Plummer, Christopher W.; (Keasbey, NJ), Shah, Shrenik K.; (Metuchen, NJ), Truong, Quang T.; (Edison, NJ)

Correspondence: MERCK AND CO INC; P O BOX 2000; RAHWAY; NJ; 070650907

Patent Application Number: 20030114495

Date filed: July 17, 2002

Abstract: The use of compounds of the present invention as antagonists and/or inverse agonists of the Cannabinoid-1 (CB1) receptor particularly in the treatment, prevention and suppression of diseases mediated by the Cannabinoid-1 (CB1) receptor. The invention is concerned with the use of these novel compounds to selectively antagonize the Cannabinoid-1 (CB1) receptor. As such, compounds of the present invention are useful as psychotropic drugs in the treatment of psychosis, memory deficits, cognitive disorders, migraine, neuropathy, neuro-inflammatory disorders including multiple sclerosis and Guillain-Barre syndrome and the inflammatory sequelae of viral encephalitis, cerebral vascular accidents, and head trauma, anxiety disorders, stress, **epilepsy,** Parkinson's disease, and schizophrenia. The compounds are also useful for the treatment of substance abuse disorders, particularly to opiates, alcohol, and nicotine. The compounds are also useful for the treatment of obesity or eating disorders associated with excessive food intake and complications associated therewith. Novel compounds of structural formula (I) are also claimed.

Excerpt(s): The present application claims priority of U.S. provisional application Serial No. 60/307,224, filed Jul. 20, 2001. and pharmaceutically acceptable salts thereof which are antagonists and/or inverse agonists of the Cannabinoid-1 (CB1) receptor and are useful in the treatment, prevention and suppression of diseases mediated by the Cannabinoid-1 (CB1) receptor. The invention is concerned with the use of these novel compounds to selectively antagonize the Cannabinoid-1 (CB1) receptor. As such,

compounds of the present invention are useful as psychotropic drugs in the treatment of psychosis, memory deficits, cognitive disorders, migraine, neuropathy, neuro-inflammatory disorders including multiple sclerosis and Guillain-Barre syndrome and the inflammatory sequelae of viral encephalitis, cerebral vascular accidents, and head trauma, anxiety disorders, stress, **epilepsy,** Parkinson's disease, and schizophrenia. The compounds are also useful for the treatment of substance abuse disorders, particularly to opiates, alcohol, and nicotine. The compounds are also useful for the treatment of obesity or eating disorders associated with excessive food intake and complications associated therewith. The present invention is also concerned with treatment of these conditions, and the use of compounds of the present invention for manufacture of a medicament useful in treating these conditions.

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Technical field**

  Inventor(s): Teuber, Lene; (Vaerloese, DK), Watjen, Frank; (Herlev, DK)

  Correspondence: BIRCH STEWART KOLASCH & BIRCH; PO BOX 747; FALLS CHURCH; VA; 22040-0747; US

  Patent Application Number: 20030166638

  Date filed: November 20, 2002

  Abstract: Chemical compounds of the formula 1as well as pharmaceutical compositions containing them and methods for their use in the treatment of disorders and diseases responsive to modulation of the GABA.sub.A receptor complex of the central nervous system, such disorders and diseases including anxiety, sleep disorders, anesthesia, memory disorders, and **epilepsy** and other convulsive disorders.

  Excerpt(s): The present invention relates to novel benzimidazole compounds, pharmaceutical compositions containing these compounds, methods of treating therewith, and to method of preparing such benzimidazole compounds. The novel compounds of the invention are useful in the treatment of central nervous system diseases and disorders, which are responsive to modulation of the GABA.sub.A receptor complex, such as for example anxiety, sleep disorders, anaestesia, memory disorders, and epilepsia or other convulsive disorders. GABA.sub.A receptors for.gamma.-aminobutyric acid (GABA) are the most abundant inhibitory receptors in the mammalian brain. The GABA.sub.A receptors are structurally constituted as macromolecular heteropentameric assemblies (combinations of.alpha.,.beta., and.gamma./.delta. protein subunits). Several subtypes of such GABA.sub.A receptors have been described by techniques of modern molecular biology. Each GABA.sub.A receptor complex comprises a chloride ion channel that controls chloride flux across the neuronal membrane, and multiple recognition sites for small modulatory molecules such as benzodiazepines, barbiturates, picrotoxin, and certain steroids. When GABA interacts with its receptor, the ion channel is opened, chloride influx is enhanced, the membrane is hyperpolarized and the cell becomes less responsive to excitatory stimuli. This GABA induced ion current can be regulated by diverse agents, including agents that interact with the benzodiazepine receptor or recognition site.

  Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Thyrotropin releasing hormone receptor disruptions, compositions and methods relating thereto**

  Inventor(s): Allen, Keith D.; (Cary, NC), Brennan, Thomas J.; (Saratoga, CA)

  Correspondence: DELTAGEN, INC.; 740 Bay Road; Redwood City; CA; 94063; US

  Patent Application Number: 20030115617

  Date filed: September 23, 2002

  Abstract: The present invention relates to compositions and methods relating to the characterization and function of the TRH receptor. Specifically, the present invention provides transgenic animals comprising disruptions in a TRH receptor gene and methods of treating diseases conditions, such as diabetes related disorders, anxiety, pain and **epilepsy.** The present invention further relates to agents that modulate the TRH receptor and methods of screening for agents that modulate TRH receptor for the treatment of diseases and conditions such as diabetes related disorders, anxiety, pain and **epilepsy.**

  Excerpt(s): This application claims priority to U.S. Provisional Application No. 60/324,561, filed Sep. 24, 2001, and U.S. Provisional Application No. 60/391,222, filed Jun. 24, 2002, the entire contents of which are incorporated herein by reference. The present invention relates to transgenic animals, compositions and methods relating to the characterization of gene function. Many medically significant biological processes are mediated by proteins participating in signal transduction pathways that involve G-proteins and/or second messengers such as cAMP. The membrane protein gene superfamily of G-protein coupled receptors (GPCRs) include a wide range of biologically active receptors, such as hormone, viral, growth factor and neuroreceptors. GPCRs have been characterized as having seven putative transmembrane domains (designated TM1, TM2, TM3, TM4, TM5, TM6, and TM7), which are believed to represent transmembrane.alpha.-helices connected by extracellular or cytoplasmic loops. Most G-protein coupled receptors have single conserved cysteine residues in each of the first two extracellular loops which form disulfide bonds that are believed to stabilize functional protein structure. G-protein coupled receptors can be intracellularly coupled by heterotrimeric G-proteins to various intracellular enzymes, ion channels and transporters. Different G-protein.alpha.-subunits preferentially stimulate particular effectors to modulate various biological functions in a cell.

  Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **TIMM8b-related protein**

  Inventor(s): Hillman, Jennifer L.; (Mountain View, CA)

  Correspondence: INCYTE CORPORATION (formerly known as Incyte; Genomics, Inc.); 3160 PORTER DRIVE; PALO ALTO; CA; 94304; US

  Patent Application Number: 20030166041

  Date filed: February 8, 2001

  Abstract: The invention provides a cDNA which encodes TIMM8 b-related protein. It also provides for the use of the cDNA, fragments, complements, and variants thereof and of the encoded protein, portions thereof and antibodies thereto for diagnosis and treatment of cancer, particularly breast cancer, ovarian cancer, and kidney cancer; and neurodegenerative disorders, particularly Mohr-Tranebjaerg syndrome, **epilepsy,**

spasticity, and dystonia. The invention additionally provides expression vectors and host cells for the production of the protein and a transgenic model system.

Excerpt(s): This invention relates to a cDNA which encodes TIMM8b-related protein and to the use of the cDNA and the encoded protein in the diagnosis and treatment of cancer and neurodegenerative disorders. Phylogenetic relationships among organisms have been demonstrated many times, and studies from a diversity of prokaryotic and eukaryotic organisms suggest a more or less gradual evolution of molecules, biochemical and physiological mechanisms, and metabolic pathways. Despite different evolutionary pressures, the proteins of nematode, fly, rat, and man have common chemical and structural features and generally perform the same cellular function. Comparisons of the nucleic acid and protein sequences from organisms where structure and/or function are known accelerate the investigation of human sequences and allow the development of model systems for testing diagnostic and therapeutic agents for human conditions, diseases, and disorders. The neurodegenerative disorder DFN-1, which is also known as Mohr-Tranebjaerg syndrome is caused by defects in a gene that encodes deafness/dystonia peptide (DDP) (Wallace and Murdock (1999) Proc Natl Acad Sci 96:1817-1819). Human deafness dystonia syndrome is associated with progressive sensorineural deafness, cortical blindness, dystonia, dysphagia, and paranoia. Human DDP shows sequence similarity to a family of zinc-binding proteins in yeast, referred to as TIM proteins, that are involved in mitochondrial import. This family of proteins is characterized by the presence of a zinc-binding motif, CX.sub.3CX.sub.11-17CX.sub.3C(Jin et al. (1999) Genomics 61:259-267). Mitochondrial import, in yeast, involves cytosolic chaperones, a TOM complex (translocase of the outer membrane), and a TIM complex (translocase of the inner membrane). Mitochondrial proteins with an N-terminal signal sequence are targeted to the TOM complex. The TOM complex interacts with TIM complexes to transport proteins across the intermembrane space. Two TIM complexes are present in the inner mitochondrial membrane, TIM23 and TIM22, which import different substrates. TIM23 imports molecules with a matrix targeting signal into the matrix space and into the inner membrane. TIM22 imports members of the mitochondrial carrier family and other integral inner membrane proteins that lack a matrix targeting signal.

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Treatment of convulsive states**

  Inventor(s): Craig, Fiona; (Kent, GB), Davidson, Elizabeth Janina; (Herts, GB)

  Correspondence: SALIWANCHIK LLOYD & SALIWANCHIK; A PROFESSIONAL ASSOCIATION; 2421 N.W. 41ST STREET; SUITE A-1; GAINESVILLE; FL; 326066669

  Patent Application Number: 20030162810

  Date filed: December 9, 2002

  Abstract: Single enantiomer-threo-methylphenidate is useful in the therapy of a convulsant state, e.g. **epilepsy,** a bipolar disorder or narcolepsy. It may be administered topically.

  Excerpt(s): This invention relates to the treatment of **epilepsy** and other convulsive states, bipolar disorder and narcolepsy. Existing therapies for **epilepsy** have a variety of associated problems. For example, Epilim.RTM. (sodium valproate) is associated with liver dysfunction, including hepatic failure which has resulted in death, and has been found to interact with other drugs such as monoamine oxidase inhibitors. Drowsiness

and sedation are among the side-effects on the CNS that have been noted for Epanutin.RTM. (phenytoin) and the benzodiazepine Valium.RTM. (diazepam). Drugs with the capacity to inhibit hepatic enzymes, such as cimetidine and omeprazole, have been found to reduce the clearance of benzodiazepines and can potentiate their action. A further issue with existing anti-epilepsy treatments is patient compliance. Most of the oral treatments require repeated dosing within the day and it is not uncommon for doses to be omitted in error or inadvertently for logistical reasons.

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Use of crf receptor agonists for the treatment or prophylaxis of diseases, for example neurodegenerative diseases**

  Inventor(s): Facci, Laura; (Harlow Essex, GB), Skaper, Stephen Drake; (Harlow, GB), Strijbos, Paul Johannes Leonardus Maria; (Harlow Essex, GB)

  Correspondence: SMITHKLINE BEECHAM CORPORATION; CORPORATE INTELLECTUAL PROPERTY-US, UW2220; P. O. BOX 1539; KING OF PRUSSIA; PA; 19406-0939; US

  Patent Application Number: 20030186867

  Date filed: September 30, 2002

  Abstract: CRF receptor agonists, especially CRF receptor-1 agonists such as CRF, urocortin, sauvagine or urotensin 1, can be used for the prevention or inhibition of neuronal cell death in a mammal suffering from or susceptible to chronic neurodegenerative disease (e.g. Alzheimer's disease, Parkinson's disease or Huntington's disease), traumatic (mechanical) neuronal injury, epilepsy-associated neuronal loss, paralysis, or spinal chord injury. CRF receptor-1 agonists can also be administered to aid the prevention or inhibition of neuronal cell death in a mammal suffering from or susceptible to cerebral ischaemia (stroke). Also, where neuronal cell death is potentiated by inhibition or suppression of the PI 3-kinase signalling pathway, a treatment comprises administering to the mammal an effective amount of a CRF receptor agonist.

  Excerpt(s): The present invention relates to the uses of CRF receptor agonists for the treatment or prophylaxis of certain diseases, to methods of treatment of those diseases using CRF receptor agonists, and to CRF receptor agonists for use in the treatment of these diseases. Corticotropin-releasing factor (CRF) is a 41 amino-acid peptide distributed broadly within the central nervous system (CNS) including the cerebellum, where its receptors have also been described. CRF is secreted by the hypothalamus in response to stress and stimulates the corticotrope cells of the anterior pituitary to release the hormone corticotropin (or adrenocorticotropic hormone, ACTH). ACTH binds to receptors in the adrenal cortex and activates the release of glucocorticoid hormones. CRF from ovine hypothalamus was first isolated and disclosed in U.S. Pat. No. 4,415,558 (Salk Institute) and in W. Vale et al., Science, 213, 1394-1397, 1981, and CRF from rat hypothalamus was disclosed in U.S. Pat. No. 4,489,163 (Salk Institute); potential uses of CRF in elevating levels of ACTH or.beta.-endorphin, lowering blood pressure, elevating mood, and improving memory and learning are also suggested. The cognition-enhancing effects of CRF in rats were confirmed in Behan et al., Nature, 378, 284-287, 1995, but the use of a CRF receptor agonist for the treatment of the cognitive deficits seen in Alzheimer's disease was discouraged owing to its perceived associated side effects (the doses of CRF which produced increases in learning and memory also produced anxiety in rats). CRF stimulates cAMP production (Battaglia, G., et al, Synapse

(1987) 1:572-581). CRF receptors characterised so far are encoded by two distinct genes and differ in their anatomical distribution and affinities for CRF and other peptide CRF analogues. The Type 1 CRF receptor (CRF receptor-1 or CRF-R1) was isolated from rat/human pituitary/brain (R. Chen et al., Proc. Natl. Acad. Sci USA, 90, 8967-8971, 1993 (human brain); N. Vita et al., FEBS Lett., 335, 1-5, 1993 (human brain and mouse pituitary); M. H. Perrin et al., Endocrinology, 133, 3058-3061, 1993; C. Chang et al., Neuron, 11, 1187-1195, 1993) and appears to be concentrated in neocortical, cerebellar and sensory relay structures in rat brain (WO 95/34651, Neurocrine Biosciences, Inc.). CRF-R1 deficient mice have been disclosed (WO 99/50657).

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **USE OF SERINE PROTEASE INHIBITORS TO INHIBIT PATHOPHYSIOLOGY AND NEUROPATHOLOGY IN A HOST**

  Inventor(s): HOFFMAN, KEITH B; (SAN DIEGO, CA), LYNCH, GARY; (IRVINE, CA)

  Correspondence: BOZICEVIC, FIELD & FRANCIS LLP; 200 MIDDLEFIELD RD; SUITE 200; MENLO PARK; CA; 94025; US

  Patent Application Number: 20030144212

  Date filed: July 6, 2000

  Abstract: Methods are provided for inhibiting cell adhesion molecule cleavage in brain tissue of a host. In the subject methods, an effective amount of a protease inhibitor, particularly serine protease inhibitors, such as those that inhibit tPA and related proteases, is administered to the host. The subject methods find use in the treatment and prevention of pathophysiology and neuropathology in a host, such as the treatment of a variety of pathological conditions resulting from pathophysiology and/or excitotoxicity. Specific pathological conditions in which the subject methods find use include **epilepsy** (and related seizure states) and neuronal damage associated with excessive glutamate activity, e.g. resulting from an acute event such as hypoxia, head trauma or stroke.

  Excerpt(s): The field of the invention is methods of treating seizures and related neurological disorders. Synaptic plasticity is natural physiological process that is associated with memory and learning. See Wang et al., J. Clin. Neurophysiology (July 1997) 14: 264-293. It has been found that activity-dependent short- and long-term changes in the strength of synaptic transmission, such as long-term potentiation, are important for memory processes, and that such changes can result from synaptic plasticity. Thus, some synaptic plasticity is normal and does not lead to neuropathological conditions. However, where the magnitude of synaptic plasticity deviates from that required for normal physiological purposes, such as memory and learning, neuropathological conditions or diseases can arise. For example, synaptic plasticity can lead to the consolidation of excessive long-term potentiation and a concomitant increase in neuronal excitability. Ben Ari & Represa, Trends in Neuroscience (August 1990) 13:312-318. Such changes can, in turn, render the host more susceptible to seizures.

  Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Vagal nerve stimulation techniques for treatment of epileptic seizures**

  Inventor(s): Frei, Mark G.; (Lawrence, KS), Osorio, Ivan; (Leawood, KS)

  Correspondence: BANNER & WITCOFF, LTD.; TEN SOUTH WACKER DRIVE; SUITE 3000; CHICAGO; IL; 60606; US

  Patent Application Number: 20030195574

  Date filed: May 12, 2003

  Abstract: The present invention uses electrical stimulation of the vagus nerve to treat **epilepsy** with minimized or no effect on the heart. Treatment is carried out by an implantable signal generator, one or more implantable electrodes for electrically stimulating a predetermined stimulation site of the vagus nerve, and a sensor for sensing characteristics of the heart such as heart rate. The heart rate information from the sensor can be used to determine whether the vagus nerve stimulation is adversely affecting the heart. Once threshold parameters are met, the vagus nerve stimulation may be stopped or adjusted. In an alternative embodiment, the invention may include a modified pacemaker to maintain the heart in desired conditions during the vagus nerve stimulation. In yet another embodiment, the invention may be simply a modified pacemaker having circuitry that determines whether a vagus nerve is being stimulated. In the event that the vagus nerve is being stimulated, the modified pacemaker may control the heart to maintain it within desired conditions during the vagus nerve stimulation.

  Excerpt(s): This patent application is a continuation of U.S. patent application Ser. No. 10/047,179, filed Nov. 9, 2001, which is a divisional of U.S. patent application Ser. No. 09/302,516, filed Apr. 30, 1999, now U.S. Pat. No. 6,341,236 for which priority is claimed. These parent applications are incorporated herein by reference in their entireties. This invention relates to neural tissue stimulation techniques, and more particularly relates to techniques for providing more effective vagus nerve stimulation and for controlling or preventing epileptic seizures with minimized effect on the heart. Epileptic seizures are the outward manifestation of excessive and/or hypersynchronous abnormal activity of neurons in the cerebral cortex. Many types of seizures occur. The behavioral features of a seizure reflect function of the portion of the cortex where the hyper activity is occurring. Seizures can be generalized and appearing to involve the entire brain simultaneously. Generalized seizures can result in the loss of conscious awareness only and are then called absence seizures (previously referred to as "petit mal"). Alternatively, the generalized seizure may result in a convulsion with tonic-clonic contractions of the muscles ("grand mal" seizure). Some types of seizures, partial seizures, begin in one part of the brain and remain local. The person may remain conscious throughout the seizure. If the person loses awareness, the seizure is referred to as a complex partial seizure.

  Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

Keeping Current

In order to stay informed about patents and patent applications dealing with epilepsy, you can access the U.S. Patent Office archive via the Internet at the following Web address: **http://www.uspto.gov/patft/index.html**. You will see two broad options: (1) Issued Patent, and (2) Published Applications. To see a list of issued patents, perform the following steps:

Under "Issued Patents," click "Quick Search." Then, type "epilepsy" (or synonyms) into the "Term 1" box. After clicking on the search button, scroll down to see the various patents which have been granted to date on epilepsy.

You can also use this procedure to view pending patent applications concerning epilepsy. Simply go back to **http://www.uspto.gov/patft/index.html**. Select "Quick Search" under "Published Applications." Then proceed with the steps listed above.

CHAPTER 7. BOOKS ON EPILEPSY

Overview

This chapter provides bibliographic book references relating to epilepsy. In addition to online booksellers such as **www.amazon.com** and **www.bn.com**, excellent sources for book titles on epilepsy include the Combined Health Information Database and the National Library of Medicine. Your local medical library also may have these titles available for loan.

Book Summaries: Federal Agencies

The Combined Health Information Database collects various book abstracts from a variety of healthcare institutions and federal agencies. To access these summaries, go directly to the following hyperlink: **http://chid.nih.gov/detail/detail.html**. You will need to use the "Detailed Search" option. To find book summaries, use the drop boxes at the bottom of the search page where "You may refine your search by." Select the dates and language you prefer. For the format option, select "Monograph/Book." Now type "epilepsy" (or synonyms) into the "For these words:" box. You should check back periodically with this database which is updated every three months. The following is a typical result when searching for books on epilepsy:

- **Brain Facts: A Primer on the Brain and Nervous System**

  Source: Washington, DC: Society for Neuroscience. 1993. 52 p.

  Contact: Society for Neuroscience. 11 Dupont Circle, NW, Suite 500, Washington, DC 20036. (202) 462-6688. PRICE: $6.00.

  Summary: This book briefly describes what is known about the brain and nervous system, brain disorders, and avenues of research that promise new therapies for many of the most devastating neurological and psychiatric diseases. Topics include brain development; what a neuron is and its function; and the brain's involvement in sensation and perception, learning and memory, movement, sleep, stress, and aging. This book examines advances in research on Parkinson's disease, pain, **epilepsy,** major depression, and manic-depressive illness in addition to neurological disorders such as addiction, Alzheimer's disease, Down syndrome, Gilles de la Tourette's syndrome, brain tumors, and multiple sclerosis. It explores recent advances in diagnostic methods such

as positron emission tomography, magnetic resonance imaging, magnetic source imaging, and gene diagnosis; and discusses potential therapies using drugs and transplants.

- **Dementias: Crossroads Between Neurology and Psychiatry**

  Source: St. Louis, MO: Warren H. Green, Inc. 1992. 187 p.

  Contact: Available from Warren H. Green, Inc. 8356 Olive Boulevard, St. Louis, MO 63132. (314) 991-1335 or (800) 537-0655. PRICE: $27.50 plus $2.00 for shipping and handling. ISBN: 875273505.

  Summary: This book discusses neurobiological research in brain disorders such as dementia. The book focuses on research in cell biology and biochemistry, with a particular emphasis on acetylcholine and the amino acid neurotransmitters. These excitatory neurotransmitters have been implicated in the etiology of affective disorders, limbic **epilepsy,** and the degenerative disorders of the brain. The book is particularly concerned with the neurotransmitter function of glutamate, its possible role in neuropsychiatric disorders, and the use of kainic acid as a tool in neurobiological research. One chapter includes a discussion of neurotoxic amino acids in Alzheimer's disease. Another chapter is devoted to the role of the cholinergic system in Alzheimer's disease, the effects of cholinergic and anticholinergic drugs on learning and memory, and treatment with the acetylcholinesterase inhibitors physostigmine and THA. 367 references.

- **Dementia**

  Source: Philadelphia, PA: F.A. Davis Co. 1993. 465 p.

  Contact: Available from F.A. Davis Co. 1915 Arch Street, Philadelphia, PA 19103. (215) 568-2270 or (800) 523-4049 or FAX (215) 568-5065. PRICE: $90.00. ISBN: 803692714.

  Summary: This book includes 15 chapters, each designed to be an intensive review, that address many aspects of dementia. The book intends to offer a broad overview of the biologic, psychological, and societal challenges of dementia. The first part reviews the role of different disciplines, including epidemiology, genetics, neurobiology, clinical neurology, and neuropsychology, in the study of dementia, addressing general principles as well as specific examples of particular approaches. The second part presents discussions of the major categories of dementia: degenerative dementia, including Alzheimer's disease, Pick's disease, Huntington's disease, Parkinson's disease, and other forms; vascular dementias, including multi-infarct dementia and Binswanger's disease; viral dementias, including types of encephalitis; bacterial, fungal, and parasitic causes of dementia; metabolic dementia; miscellaneous causes of dementia, including hydrocephalus, trauma, neoplasia, multiple sclerosis, and **epilepsy;** and cognitive impairment as a manifestation of psychiatric syndromes. The third part discusses management and treatment of dementia, from three perspectives: biologic therapies for Alzheimer's disease, including drug therapy; management of the patient, the environment, and the family; and legal and financial decision making. An epilogue presents the challenges that lie ahead in research and patient care. References are included at the end of each chapter.

- **Young People and Chronic Illness: True Stories, Help and Hope**

  Source: Minneapolis, MN: Free Spirit Publishing. 1998. 199 p.

Contact: Available from Free Spirit Publishing. 400 First Avenue North, Suite 616, Minneapolis, MN 55401-1724. (612) 338-2068. Fax (612) 337-5050. E-mail: help4kids@freespirit.com. Website: www.freespirit.com. PRICE: $14.95 plus shipping and handling. ISBN: 1575420414.

Summary: This book offers information and advice about coping with a chronic illness during adolescence and young adulthood. Part one profiles 10 adolescents and young adults who are learning to balance their chronic illness and their active lives. Illnesses include diabetes, juvenile rheumatoid arthritis, asthma, leukemia, a congenital heart defect, **epilepsy,** hemophilia, lupus, and Crohn's disease. These young men and women share their stories and advice from discovery and diagnosis to management of day-to-day medical decisions, symptoms, family, friends, and school. Each story is followed by a question and answer section that provides more information about each illness, as well as a list of resources. Part two presents steps for managing the illness, ways to develop a good patient-doctor relationship, tips on telling friends and classmates about the illness, advice on communicating with family, strategies for coping with school, and suggestions on handling a fear of hospitals. It also provides information on support groups and national organizations.

- **Person to person: A guide for professionals working with people with disabilities. (3rd ed.)**

  Source: Baltimore, MD: Paul H. Brookes Publishing Company. 1997. 371 pp.

  Contact: Available from Paul H. Brookes Publishing Company, P.O. Box 10624, Baltimore, MD 21285-0624. Telephone: (800) 638-3775 or (410) 337-9580 / fax: (410) 337-8539 / e-mail: custserv@pbrookes.com. $39.00 includes shipping and handling.

  Summary: This book presents information about people with disabilities in Australia. Chapters discuss the nature of different disabilities, and issues in living with the disability (personal adjustment, sexuality, parenting, lifestyle, family, community living, education, and employment). The book covers the following specific disabilities: acquired brain injury, amputation, arthritis, cerebral palsy, diabetes mellitus, **epilepsy,** hearing impairment and deafness, spinal cord impairment, intellectual disability, mental illness, multiple sclerosis, muscular dystrophies, short stature, and severe vision impairment and blindness. The chapters incorporate personal comments from persons with particular disabilities. They give suggestions for interaction with people with specific disabilities and lists of further resources.

- **Effects of Drugs on Communication Disorders. 2nd ed**

  Source: San Diego, CA: Singular Publishing Group. 1999. 238 p.

  Contact: Available from Singular Publishing Group, Inc. 401 West 'A' Street, Suite 325, San Diego, CA 92101-7904. (800) 347-7707. Fax (800) 774-8398. E-mail: info@delmar.com. Website: www.singpub.com. PRICE: $49.95 plus shipping and handling. ISBN: 1565939964.

  Summary: This handbook gives communication specialists information about prescription drugs and their use with patients who suffer neurogenic or psychogenic communication disorders. The book was designed for communication specialists who work in medical centers, rehabilitation clinics, private practice, public schools, or any setting in which drug therapy may influence a client's communication. Chapter 1 is a discussion of why and how drugs work, the scientific basis of neuropharmacology. Chapter 2 contains general information about drug related issues, including how drugs

are administered and arrive at their destination in the body, the procedures for drug approval by the Food and Drug Administration (FDA), the influence of age on drug effectiveness, how to evaluate the effectiveness of a drug, and a discussion of dietary supplements and naturally occurring remedies. The authors next discuss the underlying neurologic and psychiatric diseases and conditions most likely to be encountered by speech language pathologists, along with the medicines currently and most commonly used to treat the disorders. Disorders covered include Parkinson disease, myasthenia gravis, amyotrophic lateral sclerosis (ALS), multiple sclerosis, Wilson's disease, cerebral palsy, Huntington's disease, Tourette's syndrome, stroke, **epilepsy,** neoplasm (brain tumors), dementia, Alzheimer disease, traumatic brain injury (TBI), depression, mania, bipolar disorder, generalized anxiety disorder, schizophrenia, autism, attention deficit hyperactivity disorder (ADHD), stuttering, spasmodic dysphonia, and dysphagia (swallowing disorders). The handbook concludes with a glossary of terms related to medical conditions and management, an appendix of abbreviations and definitions of terms associated with medical management, an appendix of drugs that affect the ear and hearing, and a subject index.

- **Disability etiquette: Tips on interacting with people with disabilities**

  Source: Buffalo, NY: Eastern Paralyzed Veterans Association. [1998]. 51 pp.

  Contact: Available from Eastern Paralyzed Veterans Association, 75-20 Astoria Boulevard, Jackson Heights, NY 11370. Telephone: (718) 803-3782 / fax: (718) 803-0414 / e-mail: info@epva.org / Web site: http://www.epva.org. Available from the Web site at no charge.

  Summary: This illustrated booklet is for anyone-with or without a disability- who wants to interact more effectively with people with disabilities. Topics include sensitivity in offering assistance, physical contact, general conversation, and the Americans with Disabilities Act. Chapters offer tips unique to the type of disability encountered; blind/visually impaired; deaf/hard of hearing; speech disabilities; short stature; cerebral palsy; Tourette syndrome; multiple chemical sensitivity; **epilepsy;** HIV and AIDS; psychiatric disabilities; cognitive disabilities; and emergency evacuation procedures. Additional information is provided about print, Web, and other special resources.

- **Developmental disabilities and child welfare**

  Source: Washington, DC: Child Welfare League of America. 1998. 134 pp.

  Contact: Available from CWLA c/o PMDS, Child Welfare League of America, P.O. Box 2019, Annapolis Junction, MD 20701-2019. Telephone: (800) 407-6273 or (301) 617-7825 / e-mail: cwla@pmds.com. $12.95.

  Summary: This monograph, reproduced from the comprehensive Field Guide to Child Welfare by the authors of this book, addresses common misconceptions about developmental disabilities, describes the conditions child welfare workers are most likely to see, provides examples of effective interventions, and stresses the importance of early intervention to promote health development. The chapters discuss cerebral palsy, **epilepsy,** mental retardation, spina bifida, autism, and other pervasive developmental disorders, attention-deficit/hyperactive disorder and learning disabilities, and prenatal exposure to alcohol and other drugs.

Book Summaries: Online Booksellers

Commercial Internet-based booksellers, such as Amazon.com and Barnes&Noble.com, offer summaries which have been supplied by each title's publisher. Some summaries also include customer reviews. Your local bookseller may have access to in-house and commercial databases that index all published books (e.g. Books in Print®). **IMPORTANT NOTE:** Online booksellers typically produce search results for medical and non-medical books. When searching for "epilepsy" at online booksellers' Web sites, you may discover non-medical books that use the generic term "epilepsy" (or a synonym) in their titles. The following is indicative of the results you might find when searching for "epilepsy" (sorted alphabetically by title; follow the hyperlink to view more details at Amazon.com):

- **Abnormal Cortical Development and Epilepsy: From Basic to Clinical Science Ed by Roberto Spreafico** by Spreafico (1999); ISBN: 0861965795; http://www.amazon.com/exec/obidos/ASIN/0861965795/icongroupinterna
- **Brain Development and Epilepsy** by Philip A. Schwartzkroin, et al (1995); ISBN: 0195078462; http://www.amazon.com/exec/obidos/ASIN/0195078462/icongroupinterna
- **Brain Disorders Sourcebook: Basic Consumer Health Information About Strokes, Epilepsy, Amyotrophic Lateral Sclerosis (Als/Lou Gehrig's Disease) Parkinson's Disease, Brain Tumors** by Karen Bellenir (Editor) (1999); ISBN: 0780802292; http://www.amazon.com/exec/obidos/ASIN/0780802292/icongroupinterna
- **Brain Imaging in Epilepsy** by David D. Maudgil (2001); ISBN: 1901346242; http://www.amazon.com/exec/obidos/ASIN/1901346242/icongroupinterna
- **Brainquake: In the Grip of Epilepsy** by Amy S. Morris (2003); ISBN: 1401071457; http://www.amazon.com/exec/obidos/ASIN/1401071457/icongroupinterna
- **Brainstorms-Epilepsy in Our Words: Personal Accounts of Living With Seizures (Brainstorms Series, 1)** by Steven C. Schachter (Editor) (1993); ISBN: 0881679976; http://www.amazon.com/exec/obidos/ASIN/0881679976/icongroupinterna
- **Challenge of Epilepsy: New Antiepileptic Drugs** by H. Stefan, et al (1998); ISBN: 3894123850; http://www.amazon.com/exec/obidos/ASIN/3894123850/icongroupinterna
- **Childhood Epilepsy : Language, Learning and Emotional Complications** by William Svoboda (Author) (2003); ISBN: 0521823382; http://www.amazon.com/exec/obidos/ASIN/0521823382/icongroupinterna
- **Chronic Encephalitis and Epilepsy** (1991); ISBN: 0409901857; http://www.amazon.com/exec/obidos/ASIN/0409901857/icongroupinterna
- **Chronic Encephalitis and Epilepsy: Rasmussen's Syndrome** by Frederick Andermann, Theodore Rasmussen (Editor) (1991); ISBN: 0750690097; http://www.amazon.com/exec/obidos/ASIN/0750690097/icongroupinterna
- **Coping with Epilepsy** by Fiona Marshall, Pamela Crawford (2001); ISBN: 0859698246; http://www.amazon.com/exec/obidos/ASIN/0859698246/icongroupinterna
- **Deep Brain Stimulation and Epilepsy** by Hans Luders, Hans Lsders (2003); ISBN: 1841842591; http://www.amazon.com/exec/obidos/ASIN/1841842591/icongroupinterna

- **Dotty the Dalmatian Has Epilepsy (Dr. Wellbook, 3)** by Tim Peters (1996); ISBN: 1879874350;
  http://www.amazon.com/exec/obidos/ASIN/1879874350/icongroupinterna
- **Drug Trials in Epilepsy: a physicians guide** by Dieter Schmidt (1998); ISBN: 1853176338;
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- **Dysplasias of Cerebral Cortex & Epilepsy** by Renzo Guerrini (1991); ISBN: 0397517564;
  http://www.amazon.com/exec/obidos/ASIN/0397517564/icongroupinterna
- **Economic Evaluation of Epilepsy Management** by Pachlatko, et al (1996); ISBN: 0861965566;
  http://www.amazon.com/exec/obidos/ASIN/0861965566/icongroupinterna
- **Epilepsy** by Judith Peacock (2000); ISBN: 0736802789;
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  http://www.amazon.com/exec/obidos/ASIN/1560067012/icongroupinterna
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  http://www.amazon.com/exec/obidos/ASIN/1899541276/icongroupinterna
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  http://www.amazon.com/exec/obidos/ASIN/1403446016/icongroupinterna
- **Epilepsy (Understanding Illness (Mankato, Minn.).)** by Sue Vander Hook, Sue Vander Hook (2000); ISBN: 1583400257;
  http://www.amazon.com/exec/obidos/ASIN/1583400257/icongroupinterna
- **Epilepsy : Models, Mechanisms and Concepts** by Philip A. Schwartzkroin (Editor) (1993); ISBN: 0521392985;
  http://www.amazon.com/exec/obidos/ASIN/0521392985/icongroupinterna
- **Epilepsy and Movement Disorders** by Renzo Guerrini (Editor), et al (2002); ISBN: 0521771102;
  http://www.amazon.com/exec/obidos/ASIN/0521771102/icongroupinterna
- **Epilepsy and the Family: A New Guide** by Richard Lechtenberg (1999); ISBN: 0674258975;
  http://www.amazon.com/exec/obidos/ASIN/0674258975/icongroupinterna
- **Epilepsy Explained** by Lennart Gram, Dam (1995); ISBN: 8716113608;
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- **Epilepsy in Babylonia (Cuneiform Monographs, 2)** by M. Stol (1993); ISBN: 9072371631;
  http://www.amazon.com/exec/obidos/ASIN/9072371631/icongroupinterna
- **Epilepsy in Children** by Sheila J. Wallace, Kevin Farrell (2004); ISBN: 0340808144;
  http://www.amazon.com/exec/obidos/ASIN/0340808144/icongroupinterna
- **Epilepsy in Elderly People - pocketbook** (1995); ISBN: 1853172448;
  http://www.amazon.com/exec/obidos/ASIN/1853172448/icongroupinterna
- **Epilepsy in the Elderly: Clinical Aspects and Pharmacotherapy** by Kraemer (2000); ISBN: 0865778965;
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- **Epilepsy You're Not Alone** by Stacey Chillemi (2001); ISBN: 0595195261; http://www.amazon.com/exec/obidos/ASIN/0595195261/icongroupinterna
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- **Epilepsy, Infantile Spasms, and Developmental Encephalopathy** by Rho Jong (Editor), et al (2002); ISBN: 0123668492; http://www.amazon.com/exec/obidos/ASIN/0123668492/icongroupinterna
- **Epilepsy, Pregnancy and the Child** by Sibylle Ried, et al (1997); ISBN: 0632041641; http://www.amazon.com/exec/obidos/ASIN/0632041641/icongroupinterna
- **Epilepsy, Psychiatry and Learning Difficulty** by Tim Betts (1997); ISBN: 1853174041; http://www.amazon.com/exec/obidos/ASIN/1853174041/icongroupinterna
- **Epilepsy, Sleep and Sleep Deprivation (Epilepsy Research Supplement, No 2)** by Rolf Degan, Ernst Rodin MD (Editor) (1991); ISBN: 0444813365; http://www.amazon.com/exec/obidos/ASIN/0444813365/icongroupinterna
- **Epilepsy: 199 Answers a Doctor Responds to His Patients' Questions** by Andrew N., Md. Wilner (2003); ISBN: 1888799706; http://www.amazon.com/exec/obidos/ASIN/1888799706/icongroupinterna
- **Epilepsy: A New Approach** by Adrienne Richard, Joel Reiter (1995); ISBN: 0802774652; http://www.amazon.com/exec/obidos/ASIN/0802774652/icongroupinterna
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- **Epilepsy: Questions and Answers** by J. W. Sander, et al (1998); ISBN: 1873413807; http://www.amazon.com/exec/obidos/ASIN/1873413807/icongroupinterna
- **Epilepsy: The Facts (Facts Series)** by Anthony Hopkins, et al (1996); ISBN: 0192625489; http://www.amazon.com/exec/obidos/ASIN/0192625489/icongroupinterna
- **Epilepsy: The Ultimate Teen Guide** by Kathlyn Gay, Sean McGarrahan (2003); ISBN: 0810843390; http://www.amazon.com/exec/obidos/ASIN/0810843390/icongroupinterna
- **Focal Epilepsy: Clinical Use of Emission Tomography: Proceedings of the International Symposium on Focal Epilepsy: Clinical Use of Emission Tomogr** by M. Baldy-Moulinier, et al (1991); ISBN: 0861962060; http://www.amazon.com/exec/obidos/ASIN/0861962060/icongroupinterna
- **Forced Normalization and Alternative Psychoses of Epilepsy** by Michael R. Trimble (Editor), Bettina Schmitz (Editor) (1998); ISBN: 1871816378; http://www.amazon.com/exec/obidos/ASIN/1871816378/icongroupinterna
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- **Genetics of Focal Epilepsy, Clinical Aspects and Molecular Biology** by S. F. Berkovic (Editor), et al (1999); ISBN: 0861965698; http://www.amazon.com/exec/obidos/ASIN/0861965698/icongroupinterna
- **Getting on with Epilepsy (Books Beyond Words)** by Sheila Hollins, et al (1999); ISBN: 1901242390; http://www.amazon.com/exec/obidos/ASIN/1901242390/icongroupinterna
- **Growing Up With Epilepsy: A Practical Guide for Parents** by Lynn Bennett, Ph.D. Blackburn (2003); ISBN: 1888799749; http://www.amazon.com/exec/obidos/ASIN/1888799749/icongroupinterna
- **Hand Trembling, Frenzy Witchcraft, and Moth Madness: A Study of Navajo Seizure Disorders** by Jerrold E. Levy, et al (1995); ISBN: 0816515727; http://www.amazon.com/exec/obidos/ASIN/0816515727/icongroupinterna
- **Handbook of Epilepsy** by Thomas R., Md. Browne, Gregory L., Md. Holmes (2004); ISBN: 0781743524; http://www.amazon.com/exec/obidos/ASIN/0781743524/icongroupinterna
- **Has Epilepsy** by Anna Levene (2003); ISBN: 1932333282; http://www.amazon.com/exec/obidos/ASIN/1932333282/icongroupinterna
- **Herpin's Contribution to the Knowledge of Epilepsy: A Translation of an Early French Epileptologist's 19th Century** by Herpin (2001); ISBN: 0861966090; http://www.amazon.com/exec/obidos/ASIN/0861966090/icongroupinterna
- **Imitators of Epilepsy** by Peter W. Kaplan (Editor) (2004); ISBN: 1888799838; http://www.amazon.com/exec/obidos/ASIN/1888799838/icongroupinterna
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- **In Bad Taste: The Msg Symptom Complex: How Monosodium Glutamate Is a Major Cause of Treatable and Preventable Illnesses, Such As Headaches, Asthma, Epilepsy, heart** by George R., Md. Schwartz, Kathleen A. Schwartz (1999); ISBN: 0929173309; http://www.amazon.com/exec/obidos/ASIN/0929173309/icongroupinterna
- **Intractable Epilepsy** by S. I. Johannessen (Editor), et al (1995); ISBN: 1871816289; http://www.amazon.com/exec/obidos/ASIN/1871816289/icongroupinterna
- **Issues and Answers: Exploring Your Possibilities a Guide for Teens and Young Adults With Epilepsy.** (1992); ISBN: 9993212571; http://www.amazon.com/exec/obidos/ASIN/9993212571/icongroupinterna
- **Issues in Epilepsy** by Gordon Mallarkey (1999); ISBN: 0864710542; http://www.amazon.com/exec/obidos/ASIN/0864710542/icongroupinterna
- **Juvenile Myoclonic Epilepsy: The Janz Syndrome** by Bettina Schmitz (Editor), Thomas Sander (Editor) (2000); ISBN: 1871816424; http://www.amazon.com/exec/obidos/ASIN/1871816424/icongroupinterna
- **Legal Rights of Persons With Epilepsy an Overview of Legal Issues Federal Laws and State Laws Affecting Persons With Epilepsy** (1992); ISBN: 9992613874; http://www.amazon.com/exec/obidos/ASIN/9992613874/icongroupinterna
- **Lipid Mediators in Ischemic Brain Damage and Experimental Epilepsy (New Trends in Lipid Mediators Research, Vol 4)** by Nicolas G. Bazan (Editor) (1990); ISBN: 3805550685; http://www.amazon.com/exec/obidos/ASIN/3805550685/icongroupinterna

- **Living Well With Epilepsy** by Robert J. Gumnit, et al (1997); ISBN: 1888799110; http://www.amazon.com/exec/obidos/ASIN/1888799110/icongroupinterna
- **Living With Epilepsy** by Shirley Wimbish Gray, Serge Bloch (2002); ISBN: 1567661033; http://www.amazon.com/exec/obidos/ASIN/1567661033/icongroupinterna
- **Living With Epilepsy** by Patsy Westcott, Raintree Steck-Vaughn Publishers (1999); ISBN: 0817255788; http://www.amazon.com/exec/obidos/ASIN/0817255788/icongroupinterna
- **Mechanisms of Drug Resistance in Epilepsy - No. 243 : Lessons from Oncology** by Novartis Foundation Symposium (Author) (2002); ISBN: 047084146X; http://www.amazon.com/exec/obidos/ASIN/047084146X/icongroupinterna
- **Neuronal Substrates of Sleep and Epilepsy** by Mircea Steriade (Author) (2003); ISBN: 0521817072; http://www.amazon.com/exec/obidos/ASIN/0521817072/icongroupinterna
- **Neuropharmacology of Epilepsy: Pathophysiology and Drug Mechanisms** by Robert A. Gross (Editor), et al (2004); ISBN: 0896035220; http://www.amazon.com/exec/obidos/ASIN/0896035220/icongroupinterna
- **Panayiotopoulos Syndrome: A Common and Benign Childhood Epileptic Syndrome (Current Problems in Epilepsy)** by C.P. Panayiotopoulos (2001); ISBN: 0861966198; http://www.amazon.com/exec/obidos/ASIN/0861966198/icongroupinterna
- **Photosensitive Epilepsy : New and Expanded Edition** by Graham F. A. Harding (Author), Peter M. Jeavons (Author) (1995); ISBN: 1898683026; http://www.amazon.com/exec/obidos/ASIN/1898683026/icongroupinterna
- **Psychological Disturbances in Epilepsy** by J. Chris Sackellares (Editor), Stanley Berent (Editor) (1997); ISBN: 0750696052; http://www.amazon.com/exec/obidos/ASIN/0750696052/icongroupinterna
- **Quantitative Assessment in Epilepsy Care (NATO Asi Series A: Life Sciences, Vol 255)** by Harry Meinardi, Joyce A. Cramer (1993); ISBN: 0306446200; http://www.amazon.com/exec/obidos/ASIN/0306446200/icongroupinterna
- **Recent Advances in Epilepsy Research** by Devin K. Binder (Editor), Helen E. Scharfman (Editor) (2003); ISBN: 0306478609; http://www.amazon.com/exec/obidos/ASIN/0306478609/icongroupinterna
- **Seizing Control: Live with Epilepsy** by Tim Betts (1994); ISBN: 0719038146; http://www.amazon.com/exec/obidos/ASIN/0719038146/icongroupinterna
- **Seizure Free : From Epilepsy to Brain Surgery, I Survived, and You Can, Too!** by Leanne Chilton (2000); ISBN: 0966381904; http://www.amazon.com/exec/obidos/ASIN/0966381904/icongroupinterna
- **Seizures and Epilepsy in Childhood: A Guide** by John M. Freeman, et al (2003); ISBN: 0801870518; http://www.amazon.com/exec/obidos/ASIN/0801870518/icongroupinterna
- **Seizures and Epilepsy in the Elderly** by R. Eugene Ramsay, A. James Rowan (1997); ISBN: 0750696222; http://www.amazon.com/exec/obidos/ASIN/0750696222/icongroupinterna
- **Surgical Treatment of Epilepsy** by Josef Zentner (Editor), Wolfgang Seeger (Editor) (2003); ISBN: 3211837701; http://www.amazon.com/exec/obidos/ASIN/3211837701/icongroupinterna

- **The Assessment of Cognitive Function in Epilepsy** by W. Edwin Dodson, et al (1992); ISBN: 0939957450; http://www.amazon.com/exec/obidos/ASIN/0939957450/icongroupinterna
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- **The Clinical Psychologist's Handbook of Epilepsy: Assessment and Management** by Christine Cull (Editor), Laura H. Goldstein (Editor) (1997); ISBN: 0415130514; http://www.amazon.com/exec/obidos/ASIN/0415130514/icongroupinterna
- **The Educator's Guide to Students With Epilepsy** by Robert J. Michael (1997); ISBN: 0398065381; http://www.amazon.com/exec/obidos/ASIN/0398065381/icongroupinterna
- **The Falling Sickness: A History of Epilepsy from the Greeks to the Beginnings of Modern Neurology (Softshell Books)** by Owsei Temkin (1994); ISBN: 0801848490; http://www.amazon.com/exec/obidos/ASIN/0801848490/icongroupinterna
- **The History of Modern Epilepsy: The Beginning, 1865-1914 (Contributions in Medical Studies)** by Walter J. Friedlander (Author) (2001); ISBN: 0313315892; http://www.amazon.com/exec/obidos/ASIN/0313315892/icongroupinterna
- **The Illustrated Encyclopedia of Epilepsy** by David Chadwick (1997); ISBN: 0948270659; http://www.amazon.com/exec/obidos/ASIN/0948270659/icongroupinterna
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- **The Medical Treatment of Epilepsy** by Stanley R., Jr. Resor, Henn Kutt (Editor) (1992); ISBN: 0824785495; http://www.amazon.com/exec/obidos/ASIN/0824785495/icongroupinterna
- **The Neuropsychology of Epilepsy (Critical Issues in Neuropsychology)** by Thomas L. Bennett (Editor) (1995); ISBN: 0306439484; http://www.amazon.com/exec/obidos/ASIN/0306439484/icongroupinterna
- **The Official Patient's Sourcebook on Seizures and Epilepsy: A Revised and Updated Directory for the Internet Age** by Icon Health Publications (2003); ISBN: 0597835357; http://www.amazon.com/exec/obidos/ASIN/0597835357/icongroupinterna
- **The Treatment of Epilepsy** by Shorvon Shorvon (Editor), et al (1996); ISBN: 0632037822; http://www.amazon.com/exec/obidos/ASIN/0632037822/icongroupinterna

- **Understanding Epilepsy Chart** by Anatomical Chart (2003); ISBN: 1587793350; http://www.amazon.com/exec/obidos/ASIN/1587793350/icongroupinterna
- **Valproate: A Drug for Epilepsy, Psychiatry and Beyond** by Wolfgang Loscher (Editor) (1999); ISBN: 376435836X; http://www.amazon.com/exec/obidos/ASIN/376435836X/icongroupinterna
- **Visions: Artists Living with Epilepsy** by Steven C. Schachter (Author) (2003); ISBN: 0126213577; http://www.amazon.com/exec/obidos/ASIN/0126213577/icongroupinterna
- **Visual Diagnosis Self Tests in Epilepsy** by A. Guberman (1997); ISBN: 1873413262; http://www.amazon.com/exec/obidos/ASIN/1873413262/icongroupinterna
- **Women and Epilepsy** by T. A. Betts, Pam Crawford (1998); ISBN: 1853176443; http://www.amazon.com/exec/obidos/ASIN/1853176443/icongroupinterna
- **Women with Epilepsy : A Handbook of Health and Treatment Issues** by Martha J. Morrell (Editor), Kerry L. Flynn (Editor) (2003); ISBN: 0521655412; http://www.amazon.com/exec/obidos/ASIN/0521655412/icongroupinterna
- **Your Child's Epilepsy: A Parent's Guide (Your Child's Health)** by Richard E. Appleton, et al (1997); ISBN: 1872362613; http://www.amazon.com/exec/obidos/ASIN/1872362613/icongroupinterna

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The National Library of Medicine at the National Institutes of Health has a massive database of books published on healthcare and biomedicine. Go to the following Internet site, **http://locatorplus.gov/**, and then select "Search LOCATORplus." Once you are in the search area, simply type "epilepsy" (or synonyms) into the search box, and select "books only." From there, results can be sorted by publication date, author, or relevance. The following was recently catalogued by the National Library of Medicine:[11]

- **A study of epilepsy in its clinical, social, and genetic aspects.** Author: Alström, Carl Henry,; Year: 1962; Stockholm [Munksgaard] 1950
- **About epilepsy.** Author: Scott, Donald F.; Year: 1965; London, Duckworth [1969]
- **Abstracts. Themes: technical progress in neurological diagnostics; the need for neurological service; steroid treatment of neurological disease; epilepsy. Ed. by Olof Gilland [and] Kurt Boman.** Author: Gilland, Olof.; Year: 1955; [Göteborg, 1964]
- **Annotated bibliography on epilepsy; social, psychological and behavioral literature from 1955 through 1965, by George N. Wright and James C. Jacks.** Author: Wright, George N. (George Nelson); Year: 1964; Washington,

[11] In addition to LOCATORPlus, in collaboration with authors and publishers, the National Center for Biotechnology Information (NCBI) is currently adapting biomedical books for the Web. The books may be accessed in two ways: (1) by searching directly using any search term or phrase (in the same way as the bibliographic database PubMed), or (2) by following the links to PubMed abstracts. Each PubMed abstract has a "Books" button that displays a facsimile of the abstract in which some phrases are hypertext links. These phrases are also found in the books available at NCBI. Click on hyperlinked results in the list of books in which the phrase is found. Currently, the majority of the links are between the books and PubMed. In the future, more links will be created between the books and other types of information, such as gene and protein sequences and macromolecular structures. See **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Books**.

- **Biological factors in temporal lobe epilepsy, by Christopher Ounsted [et al.].** Author: Ounsted, Christopher.; Year: 1935; London, Pub. by the Spastics Society Medical Education and Information Unit in Association with Heinemann Medical Books, 1966
- **Comparative and cellular pathophysiology of epilepsy; proceedings of a symposium held in Liblice, near Prague, September 20-24, 1965.** Author: Servít, Zdenek.; Year: 1932; Prague, Pub. House of the Czechoslovak Academy of Sciences; Amsterdam, New York, Excerpta Medica Foundation, 1966
- **Drug therapy for epilepsy. Anticonvulsant drugs; usage, metabolism and untoward reactions (prevention, detection and management) by Samuel Livingston, assisted by Irving M. Pruce.** Author: Livingston, Samuel,; Year: 1964; Springfield, Ill., Thomas [c1966]
- **Epilepsy - today's encouraging outlook, by Harry Sands and Jacqueline Seaver.** Author: Sands, Harry.; Year: 1965; New York, Public Affairs Committee, c1966]
- **Epilepsy [by] Richard Penrose Schmidt and B. Joe Wilder.** Author: Schmidt, Richard Penrose.; Year: 1964; Philadelphia, Davis [c1968]
- **Epilepsy and the law; a report on legal reform in the light of medical progress [by] Roscoe L. Barrow [and] Howard D. Fabing.** Author: Barrow, Roscoe L.; Year: 1965; New York, Hoeber [1966]
- **Epilepsy; a review of basic and clinical research. Prepared for the National Institute of Neurological Diseases and Blindness.** Author: Robb, James Preston,; Year: 1948; [Washington] National Institute of Neurological Diseases and Blindness, 1965
- **Experimental epilepsy.** Author: Kreindler, A. (Arthur); Year: 1936; Amsterdam, Elsevier, 1965
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- **Local anaesthetics as anticonvulsants; a study on experimental and clinical epilepsy, by Carl Gustaf Bernhard and Einar Bohm.** Author: Bernhard, Carl Gustaf.; Year: 1965; Stockholm, Almqvist; Wiksell [1965]
- **Mental symptoms in temporal lobe epilepsy and temporal lobe gliomas, with special reference to laterality of lesion and the relationship between handedness and brainedness. A study of 90 cases of temporal lobe epilepsy and 253 cases of temporal lobe glioma.** Author: Bingley, Torsten.; Year: 1964; København, Munksgaard, 1958
- **Summaries of articles on juvenile epilepsy.** Author: Epilepsy Foundation.; Year: 1965; Washington [c1967]
- **The clinical neurophysiology of epilepsy: a survey of current research.** Author: Wilder, B. J. (Buna Joe),; Year: 1964; Bethesda, Md., National Institutes of Health; [for sale by the Supt. of Docs., U. S. Govt. Print. Off., Washington, 1968]
- **The medical care of epilepsy in Scotland; report of a Sub-Committee of the Standing Medical Advisory Committee.** Author: Scotland. Standing Medical Advisory Committee.; Year: 1962; Edinburgh, H. M. Stationery Off., 1968
- **Total protein, globulin and albumin in lumbar fluid in cryptogenic epilepsy; a clinical methodological study.** Author: Eeg-Olofsson, Richard,; Year: 1961; Stockholm, 1948
- **Treatment of epilepsy; guest editor: Russell N. DeJong. Treatment of arthritis; guest editor: Carl M. Pearson.** Author: DeJong, Russell N.; Year: 1958; [New York] Harper; Row, 1964

- **Vocabulary changes in mental deterioration; the relationship of vocabulary functioning as measured by a variety of word meaning and usage tests to clinically estimated degrees of mental deterioration in 'idiopathic' epilepsy, by Harry Marcellus Capps.** Author: Capps, Harry Marcellus.; Year: 1964; New York, 1939
- **What are the effects of medication on epilepsy?** Author: Fosha, Karen.; Year: 1964; [Rockford, Ill., 1968]

Chapters on Epilepsy

In order to find chapters that specifically relate to epilepsy, an excellent source of abstracts is the Combined Health Information Database. You will need to limit your search to book chapters and epilepsy using the "Detailed Search" option. Go to the following hyperlink: **http://chid.nih.gov/detail/detail.html**. To find book chapters, use the drop boxes at the bottom of the search page where "You may refine your search by." Select the dates and language you prefer, and the format option "Book Chapter." Type "epilepsy" (or synonyms) into the "For these words:" box. The following is a typical result when searching for book chapters on epilepsy:

- **Neurologic Disorders**

  Source: in Little, J.W., et al. Dental Management of the Medically Compromised Patient. 5th ed. St. Louis, MO: Mosby, Inc. 1997. p. 373-386.

  Contact: Available from Harcourt Health Sciences. 11830 Westline Industrial Drive, St. Louis, MO 63146. (800) 325-4177. Fax (800) 874-6418. Website: www.harcourthealth.com. PRICE: $48.00 plus shipping and handling. ISBN: 0815156340.

  Summary: A working knowledge of the multitude of compromised health states is essential for dental professionals, as the majority of medically compromised patients need or want oral health care. This chapter on neurologic disorders is from a text that provides the dental practitioner with an up to date reference work describing the dental management of patients with selected medical problems. The authors focus on two of the more common and significant neurologic disorders: **epilepsy** and stroke (cerebrovascular accident). **Epilepsy** is a term that describes a group of disorders characterized by chronic, recurrent, paroxysmal changes in neurologic function (seizures) that are caused by abnormal and spontaneous electrical activity in the brain. Stroke is a general term used to refer to a neurologic deficit caused by sudden interruption of oxygenated blood to the brain. The authors discuss incidence and prevalence of each condition, its etiology (including genetics), pathophysiology and complications, signs and symptoms (clinical presentation and laboratory findings), the medical management of patients with neurologic disorders, and the dental management of this population, including common oral complications for each type of disorder. 6 figures. 6 tables. 21 references.

- **Neurological Disorders**

  Source: in Scully, C. and Cawson, R.A. Medical Problems in Dentistry. 4th ed. Woburn, MA: Butterworth-Heinemann. 1998. p. 336-373.

  Contact: Available from Butterworth-Heinemann. 225 Wildwood Avenue, Woburn, MA 01801-2041. (800) 366-2665 or (781) 904-2500. Fax (800) 446-6520 or (781) 933-6333. E-mail: orders@bhusa.com. Website: www.bh.com. PRICE: $110.00. ISBN: 0723610568.

Summary: Dental staff should be able to recognize abnormalities involving the cranial nerves, especially the trigeminal, facial, glossopharyngeal, vagal and hypoglossal nerves. This chapter on neurologic disorders is from a text that covers the general medical and surgical conditions relevant to the oral health care sciences. Topics include congenital neurological disorders, including cerebral palsy (CP), neural tube defects (spina bifida), syringomyelia, Huntington's chorea, and Friedreich's ataxia; acquired neurological disorders, including the examination and lesions of the cranial nerves, facial sensory loss (facial pain is covered in a separate chapter), facial paralysis, Bell's palsy, trigeminal motor neuropathy, abnormal facial movements (dystonias, dyskinesias, facial tics, Tourette syndrome), multiple cranial nerve palsies, blindness and visual impairment, deafness and hearing impairment, Meniere's disease, autonomic dysfunction, **epilepsy,** syncope (fainting), raised intracranial pressure, hypoxic encephalopathy, infections of the nervous system (including HIV and syphilis), cerebrovascular accidents (stroke), Parkinson's disease, multiple sclerosis, Guillain-Barre syndrome (infective or idiopathic polyneuritis), motor neurone disease, mercury intoxication, tumors of the central nervous system (CNS), myasthenia gravis, patients with respiratory paralysis, and peripheral neuropathies. For each condition, the authors discuss general aspects, diagnosis and management issues, dental aspects, and patient care strategies. The chapter includes a summary of the points covered. 1 appendix. 4 figures. 15 tables. 52 references.

- **Neurofibrillary Degeneration in Alzheimer's Disease: A Discussion With a Contribution to Aluminum Pathology in Man**

  Source: in Bes, A., et al. Senile Dementias: Early Detection. London, England: John Libbey and Company Limited. 1986. p. 191-201.

  Contact: Available from John Libbey and Company Limited. 80/84 Bondway, London SW8 1SF, ENGLAND. (01) 582-5266. ISBN: 0861960947. PRICE: $90.00.

  Summary: This book chapter surveys arguments for the specificity of neurofibrillary degeneration (NFD) in relation to Alzheimer's disease (AD). Particular consideration is given to aspects of morphology, illustrated with a detailed case report, and to immunohistochemical aspects of paired helical filaments, morphologically associated with modified neurofibrils in the brain of demented subjects. The case report describes how the accidental implantation of metallic aluminum in the brain of a 14-year-old boy apparently produced focal and generalized ingravescent **epilepsy** after 15 years, and, about 2 years later, a decline in mental efficiency. This was characterized more by slowness of response than by memory loss and was more clinically similar to epileptic dementia than to AD. Photomicrographs are included. 48 references.

- **Developmental Disabilities**

  Source: in Roe, S.N., ed. Dietician's Patient Education Manual. Frederick, MD: Aspen Publishing Company. 1991. p. 20:1-20:60.

  Contact: Available from Aspen Publishing Company. 7201 McKinney Circle, Frederick, MD 21701. (800) 234-1660 or (301) 698-7140. PRICE: $255.00 plus shipping and handling. ISBN: 0834201968.

  Summary: This book chapter, from a dietitian's patient education manual, discusses developmental disabilities. The author presents a definition and rationale for treatment, considerations for diet counseling, details of food intake, and strategies for patient education and compliance. Specific topics covered include abnormal oral-motor development; weight problems; vomiting and diarrhea; poor fluid intake; drug and food

interactions; dental problems; patient assessment; strategies for cerebral palsy, **epilepsy,** Prader-Willi syndrome, and spina bifida; determining energy requirements for specific developmental disabilities, including Down syndrome; weight management; problems with constipation; breast-feeding and bottle-feeding; mealtime behavior; dental health; and poison control tips. The manual contains numerous charts and short sidebars for photocopying and incorporation into a patient education program. The chapter concludes with a few recipes and a list of related publications and resource organizations.

- **Nutrition Concerns for Individuals with Mental Retardation and Other Developmental Disabilities**

  Source: in Fenton, S.J.; Perlman, S.; Turner, H., eds. Oral Health Care for People with Special Needs: Guidelines for Comprehensive Care. River Edge, NJ: Exceptional Parent, Psy-Ed Corp. 2003. p. 28,46.

  Contact: Available as part of a monograph from Exceptional Parent, Psy-Ed Corp. 65 East Route 4, River Edge, NJ 07661. (800) EPARENT or (800) 372-7368. E-mail: epedit@aol.com. Website: www.eparent.com. PRICE: Contact publisher.

  Summary: This brief article is from a monograph that offers guidelines for comprehensive oral health care for people with special needs. The monograph is designed to help oral health care providers embrace more fully all the members of their communities, while being respectful of a variety of special needs. In this article, the author considers nutrition concerns for individuals with mental retardation and other developmental disabilities. Topics include the risks of poor nutrition, prevention of early childhood caries (ECC, cavities), the goal of nutrition services, and general nutrition guidance. One table highlights the nutrition problems that are common to selected disabilities, including cerebral palsy, **epilepsy,** muscular dystrophy, melomeningocele, Down syndrome, Prader-Willi syndrome, mental retardation, and autism. 1 table. 4 references.

- **Central and Vascular Vestibular Disorders**

  Source: in Blakley, B.W.; Siegel, M.E. Feeling Dizzy: Understanding and Treating Dizziness, Vertigo, and Other Balancing Disorders. New York, NY: Macmillan Publishing. 1995. p. 117-128.

  Contact: Available from Macmillan Publishing. 201 West 103rd Street, Indianapolis, IN 46290. (800) 428-5331; Fax (800) 882-8583. PRICE: $21.95 plus shipping and handling. ISBN: 0028600096.

  Summary: This chapter is from a layperson's guide to vertigo, imbalance, fainting, and other balance disorders. This chapter describes central and vascular vestibular disorders. Topics covered include acoustic neuroma, other brain tumors, cerebral atrophy, disorders of the blood supply, transient ischemic attacks, stroke, migraine, **epilepsy,** and multiple sclerosis. For each type of vestibular disorder discussed, the authors consider symptoms, diagnosis, etiology, natural course, and treatment options. The authors also share the experiences of patients who have each of these types of disorders.

- **Classification, Etiology and Epidemiology**

  Source: in Andreasen, J.O.; Andreasen, F.M., eds. Textbook and Color Atlas of Traumatic Injuries to the Teeth. 3rd ed. Copenhagen, Denmark: Munksgaard International Publishers Ltd. 1994. p. 151-180.

  Contact: Available from Munksgaard International Publishers Ltd. 35 Norre Sogade, P.O. Box 2148, DK-1016 Copenhagen K, Denmark. Phone +45 33 12 70 30; Fax +45 33 12 93 87; E-mail: headoffice@mail.munksgaard.dk; http://www.munksgaard.dk. PRICE: $224.00 plus shipping and handling. ISBN: 8716106377.

  Summary: This chapter is from a medical textbook and color atlas that explores the treatment of traumatic injuries to the teeth. The authors address classification, etiology, and epidemiology issues. They describe a classification system based on the World Health Organization's (WHO) system; the classification includes injuries to the teeth, supporting structures, gingiva, and oral mucosa and is based on anatomical, therapeutic, and prognostic considerations. The classification can be applied to both the permanent and the primary dentitions. Etiology discussed includes iatrogenic injuries in newborns, falls in infancy, child physical abuse, falls and collisions, sports injuries, horseback riding injuries, bicycle injuries, automobile injuries, assaults, torture, mental retardation, **epilepsy,** drug-related injuries, and dentinogenesis imperfecta. Epidemiological factors discussed include sex and age distribution, prevalence of dental injuries according to sex, location of injuries, type of dental injuries, and seasonal variations. Extensive graphics, black and white photographs and radiographs, and full color photographs illustrate the chapter. 36 figures. 4 tables. 199 references. (AA-M).

- **Brain Damage in Aphasia**

  Source: in Benson, D.F.; Ardila, A. Aphasia: A Clinical Perspective. New York, NY: Oxford University Press, Inc. 1996. p. 61-87.

  Contact: Available from Oxford University Press, Inc. 200 Madison Avenue, New York, NY 10016. (800) 334-4249 or (212) 679-7300. PRICE: $49.95 plus shipping and handling. ISBN: 0195089340.

  Summary: This chapter on brain damage in aphasia is from a book that presents an integrated analysis of the language disturbances associated with brain pathology. The authors note that the underlying disease process must be recognized and treated along with the language problem; both the type of language therapy offered and the patient's prognosis depend on the basic pathology. The authors discuss some of the more common brain disorders associated with aphasia, including vascular disorders (thrombosis, embolism, hemorrhage), trauma, intracranial neoplasms, infections (including intracranial abscess), and miscellaneous causes of aphasia, including multiple sclerosis, **epilepsy,** Alzheimer's disease, Jakob-Creutzfeldt disease, and progressive aphasia. The authors continue by discussing localization techniques (to locate the neuroanatomical site of brain damage in cases of aphasia), neuropathology, neurosurgery, posttrauma skull defects, the neurologic examination, and brain-imaging studies. The authors conclude that the localization of aphasia-producing lesions has advanced tremendously in the past several decades, particularly with the advent of noninvasive techniques that can produce accurate anatomical localizations. 10 figures. 2 tables. (AA-M).

- **Communication-Other Disabilities: Scholarships, Fellowships-Grants, Loans, Grants-in-Aid, Awards**

  Source: in Schlachter, G.A.; Weber, R.D. Financial Aid for the Disabled and Their Families. 1996-1998. El Dorado Hills, CA: Reference Service Press. 1996. p. 199-207.

  Contact: Available from Reference Service Press. 5000 Windplay Drive, Suite 4, El Dorado Hills, CA 95762. (916) 939-9620; Fax (916) 939-9626. PRICE: $39.50 plus shipping and handling. ISBN: 0918276365.

  Summary: This chapter on communication and other disabilities is from a Directory that provides comprehensive information about more than 800 resources set aside for persons with disabilities or for members of their family. This chapter describes 30 programs open to individuals who have a communication disorder (such as stuttering or voice impairment), have a learning disability (including such conditions as brain injury and dyslexia), are emotionally disturbed, or have other chronic or acute health problems, such as heart condition, tuberculosis, **epilepsy,** or hemophilia. Included are scholarships, fellowships or grants, loans, grants-in-aid, and awards. Entries list program title, sponsoring organization, purpose of the program, eligibility, financial data, duration and renewal, special features, limitations, number awarded, and deadline.

- **Language-Specific Neurologic Disorders**

  Source: in Vogel, D.; Carter, J.E.; Carter, P.B. Effects of Drugs on Communication Disorders. 2nd ed. San Diego, CA: Singular Publishing Group, Inc. 1999. p. 103-123.

  Contact: Available from Singular Publishing Group, Inc. 401 West 'A' Street, Suite 325, San Diego, CA 92101-7904. (800) 347-7707. Fax (800) 774-8398. E-mail: info@delmar.com. Website: www.singpub.com. PRICE: $49.95 plus shipping and handling. ISBN: 1565939964.

  Summary: This chapter on language specific neurologic disorders is from a handbook that gives communication specialists information about prescription drugs and their use with patients who suffer neurogenic or psychogenic communication disorders. The book was designed for communication specialists who work in medical centers, rehabilitation clinics, private practice, public schools, or any setting in which drug therapy may influence a client's communication. This chapter covers neurologic disorders that may affect language. For each disorder, the authors provide a definition and cause; discuss the general features, symptoms, and signs; describe the features, symptoms, and signs of language impairment associated with each disorder; list pharmacologic (drug) treatment for each disorder; and discuss the influence that drug treatment may have on communication. Each section also lists references for additional information. Disorders covered are stroke, **epilepsy** (seizure disorder), and neoplasm (brain tumors). 1 table. 21 references.

- **People with Learning Disabilities**

  Source: in Griffiths, J. and Boyle, S. Colour Guide to Holistic Oral Care: A Practical Approach. Mosby-Year Book Europe. 1993. p. 151-161.

  Contact: Available from Mosby-Year Book Europe. Lynton House, 7-12 Tavistock Square, London WC1H 9LB, England. Telephone 0171-391 4471. Fax 0171-391 6598. ISBN: 0723417792.

Summary: This chapter, from a textbook that outlines the role of the nurse in oral health care, discusses oral care for people with learning disabilities. The authors use the term 'learning disabilities' to refer to people with mental disabilities. Topics covered include barriers to dental care; oral and dental health; risk factors; Down syndrome; cerebral palsy; **epilepsy;** autism; oral self-mutilation; medicines and drugs; and preventive measures. The authors stress that caregivers, whether family, professional, or volunteer, need to know the risks to oral health and to know about various preventive techniques, so that their charges' oral health and dignity can be maintained. 4 tables. 14 references. (AA-M).

- **Patients' Experiences with Their Disease: Learning from the Differences and Sharing the Common Problems**

  Source: in Assal, J., Golay, A., and Visser, A.P., eds. New Trends in Patient Education: A Trans-Cultural and Inter-Disease Approach. Amsterdam, The Netherlands: Elsevier Science B.V. 1995. p. 301-312.

  Contact: Available from Elsevier Science. Regional Sales Office, Customer Support Department, 655 Avenue of the Americas, New York, NY 10010. (212) 633-3730. Fax (212) 633-3680. E-mail: usinfo-f@elsevier.com. PRICE: $209.50. ISBN: 0444822348.

  Summary: This chapter, from the proceedings of an international patient education conference, presents patients' experiences and views about the psychological, professional, family, cognitive, and financial costs of several chronic diseases. Diseases covered include arterial hypertension, autonomous dialysis, back pain, bronchial asthma, chronic obstructive pulmonary disease, colostomy, diabetes mellitus, **epilepsy,** laryngectomy, and Parkinson's disease. (AA-M).

Directories

In addition to the references and resources discussed earlier in this chapter, a number of directories relating to epilepsy have been published that consolidate information across various sources. The Combined Health Information Database lists the following, which you may wish to consult in your local medical library:[12]

- **Resources for People with Disabilities and Chronic Conditions**

  Source: Lexington, MA: Resources for Rehabilitation. 1996. 288 p.

  Contact: Available from Resources for Rehabilitation. 33 Bedford Street, Suite 19A, Lexington, MA 02173. (617) 862-6455; Fax (617) 861-7517. PRICE: $49.95 plus shipping and handling. ISBN: 0929718178.

  Summary: This book is a resource guide covering many common conditions, including spinal cord injury, low back pain, diabetes, multiple sclerosis, hearing and speech impairments, visual impairment and blindness, and **epilepsy.** Each chapter includes information about the disease or condition, psychological aspects of the condition, professional service providers, environmental adaptations, assistive devices, and

[12] You will need to limit your search to "Directory" and "diseasex" using the "Detailed Search" option. Go directly to the following hyperlink: **http://chid.nih.gov/detail/detail.html**. To find directories, use the drop boxes at the bottom of the search page where "You may refine your search by." For publication date, select "All Years." Select your preferred language and the format option "Directory." Type "diseasex" (or synonyms) into the "For these words:" box. You should check back periodically with this database as it is updated every three months.

descriptions of related organizations and publications. Also included is information on rehabilitation services, independent living, self-help, laws that affect people with disabilities, making everyday life easier, children with disabilities, computer bulletin boards, and resources on the Internet. The book concludes with an organization name index. (AA-M).

CHAPTER 8. MULTIMEDIA ON EPILEPSY

Overview

In this chapter, we show you how to keep current on multimedia sources of information on epilepsy. We start with sources that have been summarized by federal agencies, and then show you how to find bibliographic information catalogued by the National Library of Medicine.

Video Recordings

An excellent source of multimedia information on epilepsy is the Combined Health Information Database. You will need to limit your search to "Videorecording" and "epilepsy" using the "Detailed Search" option. Go directly to the following hyperlink: **http://chid.nih.gov/detail/detail.html**. To find video productions, use the drop boxes at the bottom of the search page where "You may refine your search by." Select the dates and language you prefer, and the format option "Videorecording (videotape, videocassette, etc.)." Type "epilepsy" (or synonyms) into the "For these words:" box. The following is a typical result when searching for video recordings on epilepsy:

- **Meniere's Disease: An Inner Ear Disorder**

  Source: Englewood, CO: International Meniere's Disease Research Institute (IMDRI). 1993. (Videocassette).

  Contact: Available from International Meniere's Disease Research Institute (IMDRI). 300 East Hampden Avenue, Suite 401, Englewood, CO 80110. Voice (303) 781-7223 or (303) 788-4235; Fax (303) 788-4234. PRICE: $5.00 donation appreciated.

  Summary: This videotape presents an overview of information about Meniere's disease. The narrator discusses the symptoms of Meniere's, likening them to the dizziness experienced following some carnival rides. The discovery that Vincent Van Gogh suffered from Meniere's, rather than from **epilepsy** and madness, is discussed in some detail. Other topics include the work of the International Meniere's Disease Research Institute (IMDRI) at the Ear Center; treatment options, including diet, drug therapy, and surgery; the anatomy and physiology of the ear and hearing; and possible causes of Meniere's disease. Two patients recount their own experiences with Meniere's, and their

struggle with misdiagnosis. The program concludes with a discussion of the Ear Center's research and educational activities and a listing of available publications.

- **Autism: Diagnosis, Causes, and Treatments**

  Source: Films for the Humanities and Sciences. Princeton, NJ. 2002.

  Contact: Available from Films for the Humanities and Sciences. P.O. Box 2053, Princeton, NJ 08543-2053. Voice (800) 257-5126; (609) 275-1400, 8:00am to 5:30pm EST. Fax (609) 275-3767. E-mail: custserv@films.com. Web site: http://www.films.com. PRICE: $149.95 plus shipping.

  Summary: What is it like for people with autism, living among others, yet in a sense, always living alone? How do their parents cope as they care for them? Built around several case studies, this video program distinguishes between high- and low-functioning autism; illustrates structural and functional differences between autistic and non-autistic brains; considers genetics, neurological diseases, and immune system anomalies as possible contributory factors, and discusses associated conditions such as mental retardation, **epilepsy,** and echolalia. Applied behavior analysis, the TEACCH system, multisensory stimulation, and dietary interventions also mentioned. 52 minutes, color video.

Bibliography: Multimedia on Epilepsy

The National Library of Medicine is a rich source of information on healthcare-related multimedia productions including slides, computer software, and databases. To access the multimedia database, go to the following Web site: **http://locatorplus.gov/**. Select "Search LOCATORplus." Once in the search area, simply type in epilepsy (or synonyms). Then, in the option box provided below the search box, select "Audiovisuals and Computer Files." From there, you can choose to sort results by publication date, author, or relevance. The following multimedia has been indexed on epilepsy:

- **As if by stroke of lightning [videorecording]: a program about epilepsy** Source: presented by the Louisiana Epilepsy Association Employment Program; produced by the LSU School of Medicine in New Orleans; Year: 1981; Format: Videorecording; [Louisiana]: The Association, c1981
- **Complex partial seizures [motion picture]: temporal lobe or psychomotor epilepsy** Source: Geigy Pharmaceuticals; Year: 1976; Format: Motion picture; [Summit, N. J.: Geigy, 1976]
- **Comprehensive epilepsy program [videorecording]** Source: [University of Virginia]; Year: 1976; Format: Videorecording; [Charlottesville: The University: for loan or sale by its Medical Center Audiovisual Center, 1976]
- **Doctors talk about epilepsy [motion picture]** Source: Epilepsy Foundation of America; [produced by] Interkal; Year: 1975; Format: Motion picture; [Ardsley, N. Y.: Geigy Pharmaceuticals, 1975]
- **Epilepsy [videorecording]** Source: Emory University School of Medicine; Year: 1974; Format: Videorecording; Atlanta: Georgia Regional Medical Television Network: [for loan or sale by A. W. Calhoun Medical Library, 1974]
- **Modern concepts of epilepsy [motion picture]** Source: presented by Ayerst Laboratories; produced by Sturgis-Grant Productions, Inc; Year: 1956; Format: Motion picture; United States: Ayerst, c1956

- **Nurses talk about epilepsy [motion picture]** Source: Epilepsy Foundation of America; produced by Interkal; Year: 1975; Format: Motion picture; [Ardsley, N. Y.: Geigy Pharmaceuticals, 1975]
- **People who have epilepsy [videorecording]** Source: Martha Stuart Communications; Year: 1979; Format: Videorecording; New York: MS Comms, c1979
- **Petit mal epilepsy [videorecording]** Source: Anis Racy, author; Year: 1978; Format: Videorecording; [Washington]: George Washington University, c1978
- **Seizure disorders in children [slide]: pharmacological management of behavior** Source: produced by Child Evaluation and Treatment Program, University of North Dakota Medical Center Rehabilitation Hospital; Year: 1981; Format: Slide; Grand Forks, ND: CETP, c1981
- **Seizure disorders in children [videorecording]: a report** Source: Robert C. Vannucci; [made by] Penn Sate Television; Year: 1976; Format: Videorecording; University Park, Pa.: Pennsylvania State University: [for loan or sale by its Audio-Visual Services], c1976

CHAPTER 9. PERIODICALS AND NEWS ON EPILEPSY

Overview

In this chapter, we suggest a number of news sources and present various periodicals that cover epilepsy.

News Services and Press Releases

One of the simplest ways of tracking press releases on epilepsy is to search the news wires. In the following sample of sources, we will briefly describe how to access each service. These services only post recent news intended for public viewing.

PR Newswire

To access the PR Newswire archive, simply go to **http://www.prnewswire.com/**. Select your country. Type "epilepsy" (or synonyms) into the search box. You will automatically receive information on relevant news releases posted within the last 30 days. The search results are shown by order of relevance.

Reuters Health

The Reuters' Medical News and Health eLine databases can be very useful in exploring news archives relating to epilepsy. While some of the listed articles are free to view, others are available for purchase for a nominal fee. To access this archive, go to **http://www.reutershealth.com/en/index.html** and search by "epilepsy" (or synonyms). The following was recently listed in this archive for epilepsy:

- **Ivax wins tentative OK for generic epilepsy drug**
  Source: Reuters Industry Breifing
  Date: November 25, 2003
- **NICE backs limited use of new epilepsy drugs**
  Source: Reuters Industry Breifing
  Date: November 06, 2003

- **Teva gets tentative approval for epilepsy drug**
  Source: Reuters Industry Breifing
  Date: October 20, 2003
- **Alpharma says FDA approves generic epilepsy drug**
  Source: Reuters Industry Breifing
  Date: September 15, 2003
- **FDA approves once-daily Abbott epilepsy drug**
  Source: Reuters Industry Breifing
  Date: September 09, 2003
- **Epilepsy trial will compare brain surgery to drugs**
  Source: Reuters Health eLine
  Date: September 03, 2003
- **UK epilepsy group criticises drug discontinuation**
  Source: Reuters Health eLine
  Date: August 14, 2003
- **U.K. epilepsy group criticises AstraZeneca over Mysoline discontinuation**
  Source: Reuters Industry Breifing
  Date: August 14, 2003
- **Novartis wins U.S. OK for new epilepsy drug use**
  Source: Reuters Industry Breifing
  Date: August 07, 2003
- **Australia to subsidise UCB's epilepsy drug**
  Source: Reuters Industry Breifing
  Date: July 31, 2003
- **Gene therapy attenuates focal seizure disorder in rats**
  Source: Reuters Medical News
  Date: July 14, 2003
- **Adjunctive levetiracetam helpful for refractory pediatric epilepsy**
  Source: Reuters Industry Breifing
  Date: June 12, 2003
- **Epilepsy myths persist in Britain: survey**
  Source: Reuters Health eLine
  Date: May 19, 2003
- **Epilepsy drug may help alcoholics curb drinking**
  Source: Reuters Health eLine
  Date: May 16, 2003
- **Many in China untreated for epilepsy: report**
  Source: Reuters Health eLine
  Date: May 12, 2003
- **Genetic polymorphism linked to multidrug resistant epilepsy**
  Source: Reuters Industry Breifing
  Date: April 09, 2003
- **UCB epilepsy drug a cost-effective add-on: study**
  Source: Reuters Industry Breifing
  Date: April 04, 2003

- **Levetiracetam is cost-effective add-on drug for refractory epilepsy**
  Source: Reuters Medical News
  Date: April 04, 2003
- **Tiagabine therapy not linked to vision problems in epilepsy patients**
  Source: Reuters Industry Breifing
  Date: March 21, 2003
- **UK doctors compare ketogenic diets for epilepsy**
  Source: Reuters Medical News
  Date: March 10, 2003
- **Neurosearch starts phase II study on epilepsy drug**
  Source: Reuters Industry Breifing
  Date: February 19, 2003
- **Not all kids need epilepsy drugs after seizure**
  Source: Reuters Health eLine
  Date: January 27, 2003
- **FDA OKs Glaxo's epilepsy drug use for children**
  Source: Reuters Health eLine
  Date: January 21, 2003
- **Glaxo epilepsy drug gets FDA approval for treatment of children**
  Source: Reuters Industry Breifing
  Date: January 20, 2003
- **Epilepsy patients often miss medication doses**
  Source: Reuters Health eLine
  Date: January 01, 2003
- **Valproate may increase ovulatory failure in women with epilepsy**
  Source: Reuters Medical News
  Date: December 30, 2002
- **Abbott once-daily epilepsy drug approved in US**
  Source: Reuters Health eLine
  Date: December 23, 2002
- **Alpharma says court backs epilepsy-drug filing**
  Source: Reuters Industry Breifing
  Date: December 17, 2002
- **Exercise improves quality of life of epilepsy patients**
  Source: Reuters Medical News
  Date: December 11, 2002
- **Epilepsy remains misunderstood among older adults**
  Source: Reuters Health eLine
  Date: December 11, 2002
- **Epilepsy may worsen in some women taking estrogen**
  Source: Reuters Health eLine
  Date: December 11, 2002
- **Prevalence of depression high in patients with epilepsy**
  Source: Reuters Medical News
  Date: December 10, 2002

- **Levetiracetam appears safe, sometimes effective in pediatric epilepsy**
  Source: Reuters Industry Breifing
  Date: December 10, 2002
- **Epilepsy drug may help restless legs syndrome**
  Source: Reuters Health eLine
  Date: November 25, 2002
- **Study ties epilepsy to social, economic deprivation**
  Source: Reuters Health eLine
  Date: November 01, 2002
- **Johnson Johnson seeks to market epilepsy drug in US as stand-alone therapy**
  Source: Reuters Industry Breifing
  Date: November 01, 2002
- **Epilepsy linked to social deprivation**
  Source: Reuters Medical News
  Date: November 01, 2002
- **Attorneys general probe Pfizer's marketing of epilepsy drug**
  Source: Reuters Industry Breifing
  Date: October 18, 2002
- **Ketogenic diet helpful in "intractable" epilepsy in adults**
  Source: Reuters Medical News
  Date: October 16, 2002
- **Nanogen, Bionomics to collaborate on molecular test for epilepsy**
  Source: Reuters Industry Breifing
  Date: October 01, 2002
- **Second epilepsy drug shows promise against migraine**
  Source: Reuters Health eLine
  Date: September 25, 2002
- **Epilepsy drug could help prevent migraines: study**
  Source: Reuters Health eLine
  Date: September 23, 2002
- **Pfizer to delay epilepsy drug application**
  Source: Reuters Industry Breifing
  Date: September 06, 2002
- **Glaxo files Lamictal epilepsy drug for manic depression**
  Source: Reuters Industry Breifing
  Date: August 29, 2002
- **Epilepsy drug linked to high rate of eye problems**
  Source: Reuters Health eLine
  Date: August 22, 2002
- **Elan epilepsy drug gets bolded warnings, shares continue to slide**
  Source: Reuters Industry Breifing
  Date: July 15, 2002
- **Seizure worsening may not be due to epilepsy drugs**
  Source: Reuters Health eLine
  Date: July 12, 2002

- **Seizure worsening may not be due to addition of new epilepsy drug**
  Source: Reuters Medical News
  Date: July 12, 2002
- **Study links complex partial epilepsy to creativity**
  Source: Reuters Health eLine
  Date: June 25, 2002
- **Treatable form of epilepsy often not diagnosed**
  Source: Reuters Health eLine
  Date: June 24, 2002

The NIH

Within MEDLINEplus, the NIH has made an agreement with the New York Times Syndicate, the AP News Service, and Reuters to deliver news that can be browsed by the public. Search news releases at **http://www.nlm.nih.gov/medlineplus/alphanews_a.html**. MEDLINEplus allows you to browse across an alphabetical index. Or you can search by date at the following Web page: **http://www.nlm.nih.gov/medlineplus/newsbydate.html**. Often, news items are indexed by MEDLINEplus within its search engine.

Business Wire

Business Wire is similar to PR Newswire. To access this archive, simply go to **http://www.businesswire.com/**. You can scan the news by industry category or company name.

Market Wire

Market Wire is more focused on technology than the other wires. To browse the latest press releases by topic, such as alternative medicine, biotechnology, fitness, healthcare, legal, nutrition, and pharmaceuticals, access Market Wire's Medical/Health channel at **http://www.marketwire.com/mw/release_index?channel=MedicalHealth**. Or simply go to Market Wire's home page at **http://www.marketwire.com/mw/home**, type "epilepsy" (or synonyms) into the search box, and click on "Search News." As this service is technology oriented, you may wish to use it when searching for press releases covering diagnostic procedures or tests.

Search Engines

Medical news is also available in the news sections of commercial Internet search engines. See the health news page at Yahoo (**http://dir.yahoo.com/Health/News_and_Media/**), or you can use this Web site's general news search page at **http://news.yahoo.com/**. Type in "epilepsy" (or synonyms). If you know the name of a company that is relevant to epilepsy, you can go to any stock trading Web site (such as **http://www.etrade.com/**) and search for the company name there. News items across various news sources are reported on indicated hyperlinks. Google offers a similar service at **http://news.google.com/**.

BBC

Covering news from a more European perspective, the British Broadcasting Corporation (BBC) allows the public free access to their news archive located at **http://www.bbc.co.uk/**. Search by "epilepsy" (or synonyms).

Newsletter Articles

Use the Combined Health Information Database, and limit your search criteria to "newsletter articles." Again, you will need to use the "Detailed Search" option. Go directly to the following hyperlink: **http://chid.nih.gov/detail/detail.html**. Go to the bottom of the search page where "You may refine your search by." Select the dates and language that you prefer. For the format option, select "Newsletter Article." Type "epilepsy" (or synonyms) into the "For these words:" box. You should check back periodically with this database as it is updated every three months. The following is a typical result when searching for newsletter articles on epilepsy:

- **Headaches in Ehlers-Danlos Syndrome**

  Source: Loose Connections. XV(3): 1,4-8. September-October 2000.

  Contact: Available from Ehlers-Danlos National Foundation. 6399 Wilshire Blvd., Suite 510, Los Angeles, CA 90048. (323) 651-3038.

  Summary: This newsletter article provides health professionals and people who have Ehlers-Danlos syndrome (EDS) with information on a study that investigated the occurrence of chronic headaches in this complex hereditary connective tissue disorder. Data were obtained from 18 patients with EDS and chronic headaches. All of the patients were seen in a rural practice setting and were followed for a minimum of 2 years. Procedures included clinical history taking, neurologic examination, computerized tomography of the head, magnetic resonance imaging of the brain, and electroencephalogram (EEG). Headaches were classified according to the International Headache Society. The study found that four patients had migraine with aura, four had migraine without aura, four had tension headaches, four had a combination of migraine and tension headaches, and two had posttraumatic headaches. Nine patients exhibited blepharoclonus, but none had a history of seizures and their EEGs were normal, ruling out eye closure **epilepsy.** Although one patient had a small right frontal angioma, a second had Arnold Chiari malformation type I, and a third had an old stroke, headaches did not clinically correlate with their central nervous system (CNS) lesions. The article concludes that chronic recurrent headaches may constitute the neurologic presentation of EDS in the absence of structural, congenital, or acquired CNS lesions that correlate with their symptoms. People who have EDS may be prone to migraine due to an inherent disorder of cerebrovascular reactivity or cortical excitability. Additional studies are needed to elucidate the pathogenesis of headaches in EDS. 1 table and 5 references. (AA-M).

Academic Periodicals covering Epilepsy

Numerous periodicals are currently indexed within the National Library of Medicine's PubMed database that are known to publish articles relating to epilepsy. In addition to these

sources, you can search for articles covering epilepsy that have been published by any of the periodicals listed in previous chapters. To find the latest studies published, go to **http://www.ncbi.nlm.nih.gov/pubmed**, type the name of the periodical into the search box, and click "Go."

If you want complete details about the historical contents of a journal, you can also visit the following Web site: **http://www.ncbi.nlm.nih.gov/entrez/jrbrowser.cgi**. Here, type in the name of the journal or its abbreviation, and you will receive an index of published articles. At **http://locatorplus.gov/**, you can retrieve more indexing information on medical periodicals (e.g. the name of the publisher). Select the button "Search LOCATORplus." Then type in the name of the journal and select the advanced search option "Journal Title Search."

CHAPTER 10. RESEARCHING MEDICATIONS

Overview

While a number of hard copy or CD-ROM resources are available for researching medications, a more flexible method is to use Internet-based databases. Broadly speaking, there are two sources of information on approved medications: public sources and private sources. We will emphasize free-to-use public sources.

U.S. Pharmacopeia

Because of historical investments by various organizations and the emergence of the Internet, it has become rather simple to learn about the medications recommended for epilepsy. One such source is the United States Pharmacopeia. In 1820, eleven physicians met in Washington, D.C. to establish the first compendium of standard drugs for the United States. They called this compendium the U.S. Pharmacopeia (USP). Today, the USP is a non-profit organization consisting of 800 volunteer scientists, eleven elected officials, and 400 representatives of state associations and colleges of medicine and pharmacy. The USP is located in Rockville, Maryland, and its home page is located at **http://www.usp.org/**. The USP currently provides standards for over 3,700 medications. The resulting USP DI® Advice for the Patient® can be accessed through the National Library of Medicine of the National Institutes of Health. The database is partially derived from lists of federally approved medications in the Food and Drug Administration's (FDA) Drug Approvals database, located at **http://www.fda.gov/cder/da/da.htm**.

While the FDA database is rather large and difficult to navigate, the Phamacopeia is both user-friendly and free to use. It covers more than 9,000 prescription and over-the-counter medications. To access this database, simply type the following hyperlink into your Web browser: **http://www.nlm.nih.gov/medlineplus/druginformation.html**. To view examples of a given medication (brand names, category, description, preparation, proper use, precautions, side effects, etc.), simply follow the hyperlinks indicated within the United States Pharmacopeia (USP).

Below, we have compiled a list of medications associated with epilepsy. If you would like more information on a particular medication, the provided hyperlinks will direct you to ample documentation (e.g. typical dosage, side effects, drug-interaction risks, etc.). The

following drugs have been mentioned in the Pharmacopeia and other sources as being potentially applicable to epilepsy:

Anesthetics, General

- **Systemic - U.S. Brands:** Amidate; Brevital; Diprivan; Ethrane; Fluothane; Forane; Ketalar; Penthrane; Pentothal
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/203043.html

Anticonvulsants, Hydantoin

- **Systemic - U.S. Brands:** Cerebyx; Dilantin; Dilantin Infatabs; Dilantin Kapseals; Dilantin-125; Mesantoin; Peganone; Phenytex
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202052.html

Anticonvulsants, Succinimide

- **Systemic - U.S. Brands:** Celontin; Zarontin
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202053.html

Benzodiazepines

- **Systemic - U.S. Brands:** Alprazolam Intensol; Ativan; Dalmane; Diastat; Diazepam Intensol; Dizac; Doral; Halcion; Klonopin; Librium; Lorazepam Intensol; Paxipam; ProSom; Restoril; Serax; Tranxene T-Tab; Tranxene-SD; Tranxene-SD Half Strength; Valium; Xanax
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202084.html

Carbamazepine

- **Systemic - U.S. Brands:** Atretol; Carbatrol; Epitol; Tegretol; Tegretol-XR
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202111.html

Carbonic Anhydrase Inhibitors

- **Systemic - U.S. Brands:** Ak-Zol; Daranide; Dazamide; Diamox; Diamox Sequels; MZM; Neptazane; Storzolamide
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202114.html

http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202911.html

- **Systemic - U.S. Brands:** Tetramune
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202911.html

Felbamate

- **Systemic - U.S. Brands:** Felbatol
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202711.html

Gabapentin

- **Systemic - U.S. Brands:** Neurontin
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202732.html

Lamotrigine

- **Systemic - U.S. Brands:** Lamictal
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202786.html

Levetiracetam

- **Systemic - U.S. Brands:** Keppra
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/500101.html

Oxcarbazepine

- **Systemic - U.S. Brands:** Trileptal
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/500111.html

Primidone

- **Systemic - U.S. Brands:** Myidone; Mysoline
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202479.html

Tiagabine

- **Systemic - U.S. Brands:** Gabitril
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/203392.html

Topiramate

- **Systemic - U.S. Brands:** Topamax
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/203085.html

Valproic Acid

- **Systemic - U.S. Brands:** Depacon; Depakene; Depakote; Depakote Sprinkle
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202588.html

Zonisamide

- **Systemic - U.S. Brands:** Zonegran
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/500137.html

Commercial Databases

In addition to the medications listed in the USP above, a number of commercial sites are available by subscription to physicians and their institutions. Or, you may be able to access these sources from your local medical library.

Mosby's Drug Consult™

Mosby's Drug Consult™ database (also available on CD-ROM and book format) covers 45,000 drug products including generics and international brands. It provides prescribing information, drug interactions, and patient information. Subscription information is available at the following hyperlink: **http://www.mosbysdrugconsult.com/**.

PDR*health*

The PDR*health* database is a free-to-use, drug information search engine that has been written for the public in layman's terms. It contains FDA-approved drug information adapted from the Physicians' Desk Reference (PDR) database. PDR*health* can be searched by

brand name, generic name, or indication. It features multiple drug interactions reports. Search PDR*health* at **http://www.pdrhealth.com/drug_info/index.html**.

Other Web Sites

Drugs.com (**www.drugs.com**) reproduces the information in the Pharmacopeia as well as commercial information. You may also want to consider the Web site of the Medical Letter, Inc. (**http://www.medletter.com/**) which allows users to download articles on various drugs and therapeutics for a nominal fee.

Researching Orphan Drugs

Although the list of orphan drugs is revised on a daily basis, you can quickly research orphan drugs that might be applicable to epilepsy by using the database managed by the National Organization for Rare Disorders, Inc. (NORD), at **http://www.rarediseases.org/**. Scroll down the page, and on the left toolbar, click on "Orphan Drug Designation Database." On this page (**http://www.rarediseases.org/search/noddsearch.html**), type "epilepsy" (or synonyms) into the search box, and click "Submit Query." When you receive your results, note that not all of the drugs may be relevant, as some may have been withdrawn from orphan status. Write down or print out the name of each drug and the relevant contact information. From there, visit the Pharmacopeia Web site and type the name of each orphan drug into the search box at **http://www.nlm.nih.gov/medlineplus/druginformation.html**. You may need to contact the sponsor or NORD for further information.

NORD conducts "early access programs for investigational new drugs (IND) under the Food and Drug Administration's (FDA's) approval 'Treatment INDs' programs which allow for a limited number of individuals to receive investigational drugs before FDA marketing approval." If the orphan product about which you are seeking information is approved for marketing, information on side effects can be found on the product's label. If the product is not approved, you may need to contact the sponsor.

The following is a list of orphan drugs currently listed in the NORD Orphan Drug Designation Database for epilepsy:

- **Diazepam viscous solution for rectal administration**
  http://www.rarediseases.org/nord/search/nodd_full?code=489
- **Albendazole (trade name: Albenza)**
  http://www.rarediseases.org/nord/search/nodd_full?code=515
- **Antiepilepsirine**
  http://www.rarediseases.org/nord/search/nodd_full?code=561

If you have any questions about a medical treatment, the FDA may have an office near you. Look for their number in the blue pages of the phone book. You can also contact the FDA through its toll-free number, 1-888-INFO-FDA (1-888-463-6332), or on the World Wide Web at **www.fda.gov**.

APPENDICES

APPENDIX A. PHYSICIAN RESOURCES

Overview

In this chapter, we focus on databases and Internet-based guidelines and information resources created or written for a professional audience.

NIH Guidelines

Commonly referred to as "clinical" or "professional" guidelines, the National Institutes of Health publish physician guidelines for the most common diseases. Publications are available at the following by relevant Institute[13]:

- Office of the Director (OD); guidelines consolidated across agencies available at **http://www.nih.gov/health/consumer/conkey.htm**
- National Institute of General Medical Sciences (NIGMS); fact sheets available at **http://www.nigms.nih.gov/news/facts/**
- National Library of Medicine (NLM); extensive encyclopedia (A.D.A.M., Inc.) with guidelines: **http://www.nlm.nih.gov/medlineplus/healthtopics.html**
- National Cancer Institute (NCI); guidelines available at **http://www.cancer.gov/cancerinfo/list.aspx?viewid=5f35036e-5497-4d86-8c2c-714a9f7c8d25**
- National Eye Institute (NEI); guidelines available at **http://www.nei.nih.gov/order/index.htm**
- National Heart, Lung, and Blood Institute (NHLBI); guidelines available at **http://www.nhlbi.nih.gov/guidelines/index.htm**
- National Human Genome Research Institute (NHGRI); research available at **http://www.genome.gov/page.cfm?pageID=10000375**
- National Institute on Aging (NIA); guidelines available at **http://www.nia.nih.gov/health/**

[13] These publications are typically written by one or more of the various NIH Institutes.

- National Institute on Alcohol Abuse and Alcoholism (NIAAA); guidelines available at **http://www.niaaa.nih.gov/publications/publications.htm**
- National Institute of Allergy and Infectious Diseases (NIAID); guidelines available at **http://www.niaid.nih.gov/publications/**
- National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS); fact sheets and guidelines available at **http://www.niams.nih.gov/hi/index.htm**
- National Institute of Child Health and Human Development (NICHD); guidelines available at **http://www.nichd.nih.gov/publications/pubskey.cfm**
- National Institute on Deafness and Other Communication Disorders (NIDCD); fact sheets and guidelines at **http://www.nidcd.nih.gov/health/**
- National Institute of Dental and Craniofacial Research (NIDCR); guidelines available at **http://www.nidr.nih.gov/health/**
- National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK); guidelines available at **http://www.niddk.nih.gov/health/health.htm**
- National Institute on Drug Abuse (NIDA); guidelines available at **http://www.nida.nih.gov/DrugAbuse.html**
- National Institute of Environmental Health Sciences (NIEHS); environmental health information available at **http://www.niehs.nih.gov/external/facts.htm**
- National Institute of Mental Health (NIMH); guidelines available at **http://www.nimh.nih.gov/practitioners/index.cfm**
- National Institute of Neurological Disorders and Stroke (NINDS); neurological disorder information pages available at **http://www.ninds.nih.gov/health_and_medical/disorder_index.htm**
- National Institute of Nursing Research (NINR); publications on selected illnesses at **http://www.nih.gov/ninr/news-info/publications.html**
- National Institute of Biomedical Imaging and Bioengineering; general information at **http://grants.nih.gov/grants/becon/becon_info.htm**
- Center for Information Technology (CIT); referrals to other agencies based on keyword searches available at **http://kb.nih.gov/www_query_main.asp**
- National Center for Complementary and Alternative Medicine (NCCAM); health information available at **http://nccam.nih.gov/health/**
- National Center for Research Resources (NCRR); various information directories available at **http://www.ncrr.nih.gov/publications.asp**
- Office of Rare Diseases; various fact sheets available at **http://rarediseases.info.nih.gov/html/resources/rep_pubs.html**
- Centers for Disease Control and Prevention; various fact sheets on infectious diseases available at **http://www.cdc.gov/publications.htm**

NIH Databases

In addition to the various Institutes of Health that publish professional guidelines, the NIH has designed a number of databases for professionals.[14] Physician-oriented resources provide a wide variety of information related to the biomedical and health sciences, both past and present. The format of these resources varies. Searchable databases, bibliographic citations, full-text articles (when available), archival collections, and images are all available. The following are referenced by the National Library of Medicine:[15]

- **Bioethics:** Access to published literature on the ethical, legal, and public policy issues surrounding healthcare and biomedical research. This information is provided in conjunction with the Kennedy Institute of Ethics located at Georgetown University, Washington, D.C.: **http://www.nlm.nih.gov/databases/databases_bioethics.html**
- **HIV/AIDS Resources:** Describes various links and databases dedicated to HIV/AIDS research: **http://www.nlm.nih.gov/pubs/factsheets/aidsinfs.html**
- **NLM Online Exhibitions:** Describes "Exhibitions in the History of Medicine": **http://www.nlm.nih.gov/exhibition/exhibition.html**. Additional resources for historical scholarship in medicine: **http://www.nlm.nih.gov/hmd/hmd.html**
- **Biotechnology Information:** Access to public databases. The National Center for Biotechnology Information conducts research in computational biology, develops software tools for analyzing genome data, and disseminates biomedical information for the better understanding of molecular processes affecting human health and disease: **http://www.ncbi.nlm.nih.gov/**
- **Population Information:** The National Library of Medicine provides access to worldwide coverage of population, family planning, and related health issues, including family planning technology and programs, fertility, and population law and policy: **http://www.nlm.nih.gov/databases/databases_population.html**
- **Cancer Information:** Access to cancer-oriented databases: **http://www.nlm.nih.gov/databases/databases_cancer.html**
- **Profiles in Science:** Offering the archival collections of prominent twentieth-century biomedical scientists to the public through modern digital technology: **http://www.profiles.nlm.nih.gov/**
- **Chemical Information:** Provides links to various chemical databases and references: **http://sis.nlm.nih.gov/Chem/ChemMain.html**
- **Clinical Alerts:** Reports the release of findings from the NIH-funded clinical trials where such release could significantly affect morbidity and mortality: **http://www.nlm.nih.gov/databases/alerts/clinical_alerts.html**
- **Space Life Sciences:** Provides links and information to space-based research (including NASA): **http://www.nlm.nih.gov/databases/databases_space.html**
- **MEDLINE:** Bibliographic database covering the fields of medicine, nursing, dentistry, veterinary medicine, the healthcare system, and the pre-clinical sciences: **http://www.nlm.nih.gov/databases/databases_medline.html**

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[14] Remember, for the general public, the National Library of Medicine recommends the databases referenced in MEDLINE*plus* (**http://medlineplus.gov/** or **http://www.nlm.nih.gov/medlineplus/databases.html**).

[15] See **http://www.nlm.nih.gov/databases/databases.html**.

- **Toxicology and Environmental Health Information (TOXNET):** Databases covering toxicology and environmental health: **http://sis.nlm.nih.gov/Tox/ToxMain.html**
- **Visible Human Interface:** Anatomically detailed, three-dimensional representations of normal male and female human bodies: **http://www.nlm.nih.gov/research/visible/visible_human.html**

The Combined Health Information Database

A comprehensive source of information on clinical guidelines written for professionals is the Combined Health Information Database. You will need to limit your search to one of the following: Brochure/Pamphlet, Fact Sheet, or Information Package, and "epilepsy" using the "Detailed Search" option. Go directly to the following hyperlink: **http://chid.nih.gov/detail/detail.html**. To find associations, use the drop boxes at the bottom of the search page where "You may refine your search by." For the publication date, select "All Years." Select your preferred language and the format option "Fact Sheet." Type "epilepsy" (or synonyms) into the "For these words:" box. The following is a sample result:

- **Progress and Promise, 1992: A Status Report on the NINDS Implementation Plan for the Decade of the Brain**

  Source: Bethesda, MD: National Institute of Neurological Disorders and Stroke. 1992. 50 p.

  Contact: National Institute of Neurological Disorders and Stroke. Information Office Building 31, 9000 Rockville Pike, Bethesda, MD 20892. (800) 352-9424.

  Summary: This status report reviews the National Advisory Neurological Disorders and Stroke Council's implementation plan and summarizes progress made in basic and clinical research on neurological disorders. It discusses the major areas of research opportunity, recommendations to the National Institute of Neurological Disorders and Stroke for research objectives in the Decade of the Brain, and resources needed to initiate and fully implement these efforts over the next several years. Future plans and budgets are presented for study in inherited disorders; cerebral palsy and other developmental disorders; **epilepsy;** traumatic brain and spinal cord injury; stroke and cerebrovascular disease; brain tumors; and various diseases that cause the brain to fail such as Alzheimer's disease, multiple sclerosis, and Parkinson's disease. Other topics include the effects of alcohol and drugs on the brain, pain control, and restoring and repairing brain function. Recommendations for research are presented for each of the areas discussed, including increases in funding and total operating budgets required.

The NLM Gateway[16]

The NLM (National Library of Medicine) Gateway is a Web-based system that lets users search simultaneously in multiple retrieval systems at the U.S. National Library of Medicine (NLM). It allows users of NLM services to initiate searches from one Web interface, providing one-stop searching for many of NLM's information resources or databases.[17] To use the NLM Gateway, simply go to the search site at **http://gateway.nlm.nih.gov/gw/Cmd**.

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[16] Adapted from NLM: **http://gateway.nlm.nih.gov/gw/Cmd?Overview.x**.

[17] The NLM Gateway is currently being developed by the Lister Hill National Center for Biomedical Communications (LHNCBC) at the National Library of Medicine (NLM) of the National Institutes of Health (NIH).

Type "epilepsy" (or synonyms) into the search box and click "Search." The results will be presented in a tabular form, indicating the number of references in each database category.

Results Summary

Category	Items Found
Journal Articles	76981
Books / Periodicals / Audio Visual	1984
Consumer Health	248
Meeting Abstracts	41
Other Collections	5
Total	79259

HSTAT[18]

HSTAT is a free, Web-based resource that provides access to full-text documents used in healthcare decision-making.[19] These documents include clinical practice guidelines, quick-reference guides for clinicians, consumer health brochures, evidence reports and technology assessments from the Agency for Healthcare Research and Quality (AHRQ), as well as AHRQ's Put Prevention Into Practice.[20] Simply search by "epilepsy" (or synonyms) at the following Web site: **http://text.nlm.nih.gov**.

Coffee Break: Tutorials for Biologists[21]

Coffee Break is a general healthcare site that takes a scientific view of the news and covers recent breakthroughs in biology that may one day assist physicians in developing treatments. Here you will find a collection of short reports on recent biological discoveries. Each report incorporates interactive tutorials that demonstrate how bioinformatics tools are used as a part of the research process. Currently, all Coffee Breaks are written by NCBI staff.[22] Each report is about 400 words and is usually based on a discovery reported in one or more articles from recently published, peer-reviewed literature.[23] This site has new articles every few weeks, so it can be considered an online magazine of sorts. It is intended for general background information. You can access the Coffee Break Web site at the following hyperlink: **http://www.ncbi.nlm.nih.gov/Coffeebreak/**.

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[18] Adapted from HSTAT: **http://www.nlm.nih.gov/pubs/factsheets/hstat.html**.

[19] The HSTAT URL is **http://hstat.nlm.nih.gov/**.

[20] Other important documents in HSTAT include: the National Institutes of Health (NIH) Consensus Conference Reports and Technology Assessment Reports; the HIV/AIDS Treatment Information Service (ATIS) resource documents; the Substance Abuse and Mental Health Services Administration's Center for Substance Abuse Treatment (SAMHSA/CSAT) Treatment Improvement Protocols (TIP) and Center for Substance Abuse Prevention (SAMHSA/CSAP) Prevention Enhancement Protocols System (PEPS); the Public Health Service (PHS) Preventive Services Task Force's *Guide to Clinical Preventive Services*; the independent, nonfederal Task Force on Community Services' *Guide to Community Preventive Services*; and the Health Technology Advisory Committee (HTAC) of the Minnesota Health Care Commission (MHCC) health technology evaluations.

[21] Adapted from **http://www.ncbi.nlm.nih.gov/Coffeebreak/Archive/FAQ.html**.

[22] The figure that accompanies each article is frequently supplied by an expert external to NCBI, in which case the source of the figure is cited. The result is an interactive tutorial that tells a biological story.

[23] After a brief introduction that sets the work described into a broader context, the report focuses on how a molecular understanding can provide explanations of observed biology and lead to therapies for diseases. Each vignette is accompanied by a figure and hypertext links that lead to a series of pages that interactively show how NCBI tools and resources are used in the research process.

Other Commercial Databases

In addition to resources maintained by official agencies, other databases exist that are commercial ventures addressing medical professionals. Here are some examples that may interest you:

- **CliniWeb International:** Index and table of contents to selected clinical information on the Internet; see **http://www.ohsu.edu/cliniweb/**.
- **Medical World Search:** Searches full text from thousands of selected medical sites on the Internet; see **http://www.mwsearch.com/**.

The Genome Project and Epilepsy

In the following section, we will discuss databases and references which relate to the Genome Project and epilepsy.

Online Mendelian Inheritance in Man (OMIM)

The Online Mendelian Inheritance in Man (OMIM) database is a catalog of human genes and genetic disorders authored and edited by Dr. Victor A. McKusick and his colleagues at Johns Hopkins and elsewhere. OMIM was developed for the World Wide Web by the National Center for Biotechnology Information (NCBI).[24] The database contains textual information, pictures, and reference information. It also contains copious links to NCBI's Entrez database of MEDLINE articles and sequence information.

To search the database, go to **http://www.ncbi.nlm.nih.gov/Omim/searchomim.html**. Type "epilepsy" (or synonyms) into the search box, and click "Submit Search." If too many results appear, you can narrow the search by adding the word "clinical." Each report will have additional links to related research and databases. In particular, the option "Database Links" will search across technical databases that offer an abundance of information. The following is an example of the results you can obtain from the OMIM for epilepsy:

- **Alopecia, Psychomotor Epilepsy, Pyorrhea, and Mental Subnormality**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?104130
- **Alopecia-epilepsy-oligophrenia Syndrome of Moynahan**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?203600
- **Ataxia with Myoclonic Epilepsy and Presenile Dementia**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?208700
- **Centralopathic Epilepsy**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?117100
- **Deafness, Congenital, and Familial Myoclonic Epilepsy**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?220300

[24] Adapted from **http://www.ncbi.nlm.nih.gov/**. Established in 1988 as a national resource for molecular biology information, NCBI creates public databases, conducts research in computational biology, develops software tools for analyzing genome data, and disseminates biomedical information--all for the better understanding of molecular processes affecting human health and disease.

- **Epilepsy and Yellow Teeth**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?226750
- **Epilepsy with Bilateral Occipital Calcifications**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?226810
- **Epilepsy with Grand Mal Seizures on Awakening**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?607628
- **Epilepsy, Benign Neonatal, 1**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?121200
- **Epilepsy, Benign Neonatal, 2**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?121201
- **Epilepsy, Benign Neonatal, 3**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?608217
- **Epilepsy, Benign Neonatal, Autosomal Recessive**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?269720
- **Epilepsy, Benign Neonatal-infantile**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?607745
- **Epilepsy, Benign Occipital**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?132090
- **Epilepsy, Childhood Absence, 1**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?600131
- **Epilepsy, Childhood Absence, 2**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?607681
- **Epilepsy, Childhood Absence, 3**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?607682
- **Epilepsy, Familial Temporal Lobe**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?608096
- **Epilepsy, Female Restricted, with Mental Retardation**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?300088
- **Epilepsy, Idiopathic Generalized**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?600669
- **Epilepsy, Idiopathic Generalized, Susceptibility To, Locus on Chromosome 14**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?606972
- **Epilepsy, Idiopathic Generalized, Susceptibility To, Locus on Chromosome 8**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?606970
- **Epilepsy, Juvenile Absence**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?607631
- **Epilepsy, Juvenile Myoclonic**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?606904
- **Epilepsy, Lateral Temporal Lobe, Autosomal Dominant**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?600512
- **Epilepsy, Myoclonic, Benign Adult Familial, Type 1**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?601068

- **Epilepsy, Myoclonic, Benign Adult Familial, Type 2**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?607876
- **Epilepsy, Myoclonic, X-linked, with Mental Retardation and Spasticity**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?300432
- **Epilepsy, Nocturnal Frontal Lobe, Type 1**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?600513
- **Epilepsy, Nocturnal Frontal Lobe, Type 2**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?603204
- **Epilepsy, Nocturnal Frontal Lobe, Type 3**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?605375
- **Epilepsy, Partial, with Pericentral Spikes**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?607221
- **Epilepsy, Partial, with Variable Foci**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?604364
- **Epilepsy, Photogenic**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?132100
- **Epilepsy, Photogenic, with Spastic Diplegia and Mental Retardation**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?226800
- **Epilepsy, Pyridoxine-dependent**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?266100
- **Epilepsy, Reading**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?132300
- **Epilepsy, Rolandic, with Paroxysmal Exercise-induced Dystonia and Writer's Cramp**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?608105
- **Epilepsy-Telangiectasia**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?226850
- **Generalized Epilepsy with Febrile Seizures Plus**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?604233
- **Kifafa Seizure Disorder**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?245180
- **Mental Retardation with Epilepsy and Characteristic Facies**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?606155
- **Mental Retardation, Microcephaly, Epilepsy, and Coarse Face**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?601352
- **Mental Retardation, X-linked, with Epilepsy**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?300423
- **Myoclonic Epilepsy Associated with Ragged-red Fibers**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?545000
- **Myoclonic Epilepsy of Lafora**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?254780
- **Myoclonic Epilepsy of Unverricht and Lundborg**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?254800

- **Myoclonic Epilepsy, Congenital Deafness, Macular Dystrophy, and Psychiatric Disorders**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?604363
- **Myoclonic Epilepsy, Hartung Type**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?159600
- **Myoclonic Epilepsy, Infantile**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?605021
- **Myoclonic Epilepsy, Juvenile, 1**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?254770
- **Myoclonic Epilepsy, Juvenile, 2**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?604827
- **Myoclonic Epilepsy, Progressive**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?310370
- **Myokymia with Neonatal Epilepsy**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?606437
- **Retinal Degeneration and Epilepsy**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?267740
- **Rolandic Epilepsy and Speech Dyspraxia**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?601085
- **Severe Myoclonic Epilepsy of Infancy**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?607208
- **Spastic Paraplegia with Myoclonic Epilepsy**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?270805
- **Spastic Paraplegia, Epilepsy, and Mental Retardation**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?182610

Genes and Disease (NCBI - Map)

The Genes and Disease database is produced by the National Center for Biotechnology Information of the National Library of Medicine at the National Institutes of Health. This Web site categorizes each disorder by system of the body. Go to **http://www.ncbi.nlm.nih.gov/disease/**, and browse the system pages to have a full view of important conditions linked to human genes. Since this site is regularly updated, you may wish to revisit it from time to time. The following systems and associated disorders are addressed:

- **Cancer:** Uncontrolled cell division.
  Examples: Breast and ovarian cancer, Burkitt lymphoma, chronic myeloid leukemia, colon cancer, lung cancer, malignant melanoma, multiple endocrine neoplasia, neurofibromatosis, p53 tumor suppressor, pancreatic cancer, prostate cancer, Ras oncogene, RB: retinoblastoma, von Hippel-Lindau syndrome.
  Web site: **http://www.ncbi.nlm.nih.gov/disease/Cancer.html**
- **Immune System:** Fights invaders.
  Examples: Asthma, autoimmune polyglandular syndrome, Crohn's disease, DiGeorge syndrome, familial Mediterranean fever, immunodeficiency with Hyper-IgM, severe

combined immunodeficiency.
Web site: **http://www.ncbi.nlm.nih.gov/disease/Immune.html**

- **Metabolism:** Food and energy.
  Examples: Adreno-leukodystrophy, atherosclerosis, Best disease, Gaucher disease, glucose galactose malabsorption, gyrate atrophy, juvenile-onset diabetes, obesity, paroxysmal nocturnal hemoglobinuria, phenylketonuria, Refsum disease, Tangier disease, Tay-Sachs disease.
  Web site: **http://www.ncbi.nlm.nih.gov/disease/Metabolism.html**
- **Muscle and Bone:** Movement and growth.
  Examples: Duchenne muscular dystrophy, Ellis-van Creveld syndrome, Marfan syndrome, myotonic dystrophy, spinal muscular atrophy.
  Web site: **http://www.ncbi.nlm.nih.gov/disease/Muscle.html**
- **Nervous System:** Mind and body.
  Examples: Alzheimer disease, amyotrophic lateral sclerosis, Angelman syndrome, Charcot-Marie-Tooth disease, epilepsy, essential tremor, fragile X syndrome, Friedreich's ataxia, Huntington disease, Niemann-Pick disease, Parkinson disease, Prader-Willi syndrome, Rett syndrome, spinocerebellar atrophy, Williams syndrome.
  Web site: **http://www.ncbi.nlm.nih.gov/disease/Brain.html**
- **Signals:** Cellular messages.
  Examples: Ataxia telangiectasia, Cockayne syndrome, glaucoma, male-patterned baldness, SRY: sex determination, tuberous sclerosis, Waardenburg syndrome, Werner syndrome.
  Web site: **http://www.ncbi.nlm.nih.gov/disease/Signals.html**
- **Transporters:** Pumps and channels.
  Examples: Cystic fibrosis, deafness, diastrophic dysplasia, Hemophilia A, long-QT syndrome, Menkes syndrome, Pendred syndrome, polycystic kidney disease, sickle cell anemia, Wilson's disease, Zellweger syndrome.
  Web site: **http://www.ncbi.nlm.nih.gov/disease/Transporters.html**

Entrez

Entrez is a search and retrieval system that integrates several linked databases at the National Center for Biotechnology Information (NCBI). These databases include nucleotide sequences, protein sequences, macromolecular structures, whole genomes, and MEDLINE through PubMed. Entrez provides access to the following databases:

- **3D Domains:** Domains from Entrez Structure,
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=geo**
- **Books:** Online books,
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=books**
- **Genome:** Complete genome assemblies,
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Genome**
- **NCBI's Protein Sequence Information Survey Results:**
  Web site: **http://www.ncbi.nlm.nih.gov/About/proteinsurvey/**
- **Nucleotide Sequence Database (Genbank):**
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Nucleotide**

- **OMIM:** Online Mendelian Inheritance in Man,
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=OMIM**
- **PopSet:** Population study data sets,
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Popset**
- **ProbeSet:** Gene Expression Omnibus (GEO),
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=geo**
- **Protein Sequence Database:**
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Protein**
- **PubMed:** Biomedical literature (PubMed),
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=PubMed**
- **Structure:** Three-dimensional macromolecular structures,
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Structure**
- **Taxonomy:** Organisms in GenBank,
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Taxonomy**

To access the Entrez system at the National Center for Biotechnology Information, go to **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?CMD=search&DB=genome**, and then select the database that you would like to search. The databases available are listed in the drop box next to "Search." Enter "epilepsy" (or synonyms) into the search box and click "Go."

Jablonski's Multiple Congenital Anomaly/Mental Retardation (MCA/MR) Syndromes Database[25]

This online resource has been developed to facilitate the identification and differentiation of syndromic entities. Special attention is given to the type of information that is usually limited or completely omitted in existing reference sources due to space limitations of the printed form.

At **http://www.nlm.nih.gov/mesh/jablonski/syndrome_toc/toc_a.html**, you can search across syndromes using an alphabetical index**.** Search by keywords at **http://www.nlm.nih.gov/mesh/jablonski/syndrome_db.html**.

The Genome Database[26]

Established at Johns Hopkins University in Baltimore, Maryland in 1990, the Genome Database (GDB) is the official central repository for genomic mapping data resulting from the Human Genome Initiative. In the spring of 1999, the Bioinformatics Supercomputing Centre (BiSC) at the Hospital for Sick Children in Toronto, Ontario assumed the management of GDB. The Human Genome Initiative is a worldwide research effort focusing on structural analysis of human DNA to determine the location and sequence of the estimated 100,000 human genes. In support of this project, GDB stores and curates data generated by researchers worldwide who are engaged in the mapping effort of the Human

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[25] Adapted from the National Library of Medicine:
http://www.nlm.nih.gov/mesh/jablonski/about_syndrome.html.

[26] Adapted from the Genome Database: **http://gdbwww.gdb.org/gdb/aboutGDB.html - mission**.

Genome Project (HGP). GDB's mission is to provide scientists with an encyclopedia of the human genome which is continually revised and updated to reflect the current state of scientific knowledge. Although GDB has historically focused on gene mapping, its focus will broaden as the Genome Project moves from mapping to sequence, and finally, to functional analysis.

To access the GDB, simply go to the following hyperlink: **http://www.gdb.org/**. Search "All Biological Data" by "Keyword." Type "epilepsy" (or synonyms) into the search box, and review the results. If more than one word is used in the search box, then separate each one with the word "and" or "or" (using "or" might be useful when using synonyms).

APPENDIX B. PATIENT RESOURCES

Overview

Official agencies, as well as federally funded institutions supported by national grants, frequently publish a variety of guidelines written with the patient in mind. These are typically called "Fact Sheets" or "Guidelines." They can take the form of a brochure, information kit, pamphlet, or flyer. Often they are only a few pages in length. Since new guidelines on epilepsy can appear at any moment and be published by a number of sources, the best approach to finding guidelines is to systematically scan the Internet-based services that post them.

Patient Guideline Sources

The remainder of this chapter directs you to sources which either publish or can help you find additional guidelines on topics related to epilepsy. Due to space limitations, these sources are listed in a concise manner. Do not hesitate to consult the following sources by either using the Internet hyperlink provided, or, in cases where the contact information is provided, contacting the publisher or author directly.

The National Institutes of Health

The NIH gateway to patients is located at **http://health.nih.gov/**. From this site, you can search across various sources and institutes, a number of which are summarized below.

Topic Pages: MEDLINEplus

The National Library of Medicine has created a vast and patient-oriented healthcare information portal called MEDLINEplus. Within this Internet-based system are "health topic pages" which list links to available materials relevant to epilepsy. To access this system, log on to **http://www.nlm.nih.gov/medlineplus/healthtopics.html**. From there you can either search using the alphabetical index or browse by broad topic areas. Recently, MEDLINEplus listed the following when searched for "epilepsy":

- Guides on epilepsy

  Epilepsy
  http://www.nlm.nih.gov/medlineplus/epilepsy.html

- Other guides

  Head and Brain Malformations
  http://www.nlm.nih.gov/medlineplus/headandbrainmalformations.html

  Hormones
  http://www.nlm.nih.gov/medlineplus/hormones.html

  Neurologic Diseases
  http://www.nlm.nih.gov/medlineplus/neurologicdiseases.html

  Seizures and Epilepsy
  http://www.nlm.nih.gov/medlineplus/tutorials/seizuresandepilepsyloader.html

  Tuberous Sclerosis
  http://www.nlm.nih.gov/medlineplus/tuberoussclerosis.html

Within the health topic page dedicated to epilepsy, the following was listed:

- General/Overview

  Epilepsy
  Source: National Information Center for Children and Youth with Disabilities
  http://www.nichcy.org/pubs/factshe/fs6txt.htm

  Epilepsy: An Introduction
  Source: Epilepsy Foundation
  http://www.epilepsyfoundation.org/answerplace/About-Epilepsy.cfm

  Most Frequently Asked Questions about Epilepsy
  Source: Epilepsy Foundation
  http://www.epilepsyfoundation.org/answerplace/faq.cfm

  Seizures and Epilepsy
  http://www.nlm.nih.gov/medlineplus/tutorials/seizuresandepilepsyloader.html

- Diagnosis/Symptoms

  Brain Imaging
  Source: Epilepsy Foundation
  http://www.epilepsyfoundation.org/answerplace/quickstart/newlydiagnosed/qstreatment/qstrimaging.cfm

  Computed Tomography (CT)-Head
  Source: American College of Radiology, Radiological Society of North America
  http://www.radiologyinfo.org/content/ct_of_the_head.htm

  Electrophysiology
  Source: We Move
  http://www.mdvu.org/library/pediatric/diagnostics/dia_exa_electro.html

Functional MR Imaging (fMRI) - Brain
Source: American College of Radiology, Radiological Society of North America
http://www.radiologyinfo.org/content/functional_mr.htm

Importance of EEG Tests
Source: Epilepsy Foundation
http://www.epilepsyfoundation.org/answerplace/quickstart/newlydiagnosed/qstreatment/qstreeg.cfm

Nonepileptic Seizures
Source: Epilepsy Foundation
http://www.epilepsyfoundation.org/answerplace/Medical/seizures/types/nonepileptic/weinonepilepsy.cfm

- Treatment

Frequently Asked Questions about Medicines
Source: Epilepsy Foundation
http://www.epilepsyfoundation.org/answerplace/Medical/treatment/medications/medfaqs.cfm

General Information about First Aid
Source: Epilepsy Foundation
http://www.epilepsyfoundation.org/answerplace/Medical/firstaid/

General Information about Surgery
Source: Epilepsy Foundation
http://www.epilepsyfoundation.org/answerplace/Medical/treatment/surgery/

General Information about Vagus Nerve Stimulation
Source: Epilepsy Foundation
http://www.epilepsyfoundation.org/answerplace/Medical/treatment/vns/

Special Concerns about Seizure Medications
Source: Epilepsy Foundation
http://www.epilepsyfoundation.org/answerplace/Life/adults/women/weimeds.cfm

Successful Treatment Tips
Source: Epilepsy Foundation
http://www.epilepsyfoundation.org/answerplace/Medical/treatment/medications/medscontrol.cfm

Surgery Types: Benefits and Risks
Source: Epilepsy Foundation
http://www.epilepsyfoundation.org/answerplace/Medical/treatment/surgery/benefitsrisks.cfm

Types of Medicines for Epilepsy
Source: Epilepsy Foundation
http://www.epilepsyfoundation.org/answerplace/Medical/treatment/medications/typesmedicine/

- Alternative Therapy

  Complementary Treatment
  Source: Epilepsy Foundation
  http://www.epilepsyfoundation.org/answerplace/Medical/treatment/alternative/

- Nutrition

  General Information about Ketogenic Diet
  Source: Epilepsy Foundation
  http://www.epilepsyfoundation.org/answerplace/Medical/treatment/diet/

- Coping

  Social Aspects of Epilepsy
  Source: Epilepsy Foundation
  http://www.epilepsyfoundation.org/answerplace/Social/

- Specific Conditions/Aspects

  Epilepsy and Sexual Relations
  Source: Epilepsy Foundation
  http://www.epilepsyfoundation.org/answerplace/Life/adults/weisex.cfm

  Epilepsy Syndromes
  Source: Epilepsy Foundation
  http://www.epilepsyfoundation.org/answerplace/Medical/seizures/syndromes/

  Finding Emergency Medication Assistance
  Source: Epilepsy Foundation
  http://www.epilepsyfoundation.org/answerplace/Legal/financialassistance/emmedical.cfm

  Frontal Lobe Epilepsy
  Source: Mayo Foundation for Medical Education and Research
  http://www.mayoclinic.com/invoke.cfm?id=AN00231

  Hormones and Epilepsy
  Source: Epilepsy Foundation
  http://www.epilepsyfoundation.org/answerplace/Life/adults/women/weihormones.cfm

  Lennox-Gastaut Syndrome
  Source: National Institute of Neurological Disorders and Stroke
  http://www.ninds.nih.gov/health_and_medical/disorders/lennoxgastautsyndrome_doc.htm

- Children

  Children and Medicine
  Source: Epilepsy Foundation
  http://www.epilepsyfoundation.org/answerplace/Medical/treatment/medications/medschildren.cfm

Epilepsy Education
Source: Nemours Foundation
http://kidshealth.org/kid/health_problems/brain/epilepsy.html

Epilepsy Foundation Kid's Club
Source: Epilepsy Foundation
http://www.epilepsyfoundation.org/kidsclub/nonflash/home/index.html

Epilepsy in Children
Source: Epilepsy Foundation
http://www.epilepsyfoundation.org/answerplace/Life/children/

- From the National Institutes of Health

Epilepsy
Source: National Institute of Neurological Disorders and Stroke
http://www.ninds.nih.gov/health_and_medical/disorders/epilepsy.htm

Seizures and Epilepsy: Hope through Research
Source: National Institute of Neurological Disorders and Stroke
http://www.ninds.nih.gov/health_and_medical/pubs/seizures_and_epilepsy_htr.htm

- Latest News

National Epilepsy Month November 2003
Source: 11/05/2003, Center for Mental Health Services
http://www.mentalhealth.org/highlights/november2003/epilepsy/

Promising Gene Therapy Tool May Suppress Epileptic Seizures
Source: 11/14/2003, National Institute of Neurological Disorders and Stroke
http://www.ninds.nih.gov/news_and_events/news_article_epilepsy_gene_therapy.htm

- Law and Policy

Driver Licensing
Source: Epilepsy Foundation
http://www.epilepsyfoundation.org/advocacy/govaff/pp5.cfm

Epilepsy as a Disability
Source: Epilepsy Foundation
http://www.epilepsyfoundation.org/answerplace/Legal/epasdisability.cfm

Legal Aspects of Epilepsy
Source: Epilepsy Foundation
http://www.epilepsyfoundation.org/answerplace/Legal/

- Organizations

Epilepsy Foundation
http://www.epilepsyfoundation.org/

National Institute of Neurological Disorders and Stroke
http://www.ninds.nih.gov/

- Research

  Promising Gene Therapy Tool May Suppress Epileptic Seizures
  Source: National Institute of Neurological Disorders and Stroke
  http://www.ninds.nih.gov/news_and_events/news_article_epilepsy_gene_therapy.htm

- Statistics

  FASTATS: Epilepsy
  Source: National Center for Health Statistics
  http://www.cdc.gov/nchs/fastats/epilepsy.htm

- Teenagers

  Epilepsy
  Source: Nemours Foundation
  http://kidshealth.org/teen/diseases_conditions/brain_nervous/epilepsy.html

  Special Concerns for Teenage Girls
  Source: Epilepsy Foundation
  http://www.epilepsyfoundation.org/answerplace/Life/adolescents/weigirls.cfm

- Women

  Birth Control for Women with Epilepsy
  Source: Epilepsy Foundation
  http://www.epilepsyfoundation.org/answerplace/Life/adults/women/weibirthcontrol.cfm

  Menopause and Epilepsy
  Source: Epilepsy Foundation
  http://www.epilepsyfoundation.org/answerplace/Life/adults/women/weimenopause.cfm

  Pregnancy Issues and Epilepsy
  Source: Epilepsy Foundation
  http://www.epilepsyfoundation.org/answerplace/Life/adults/women/weipregnancy.cfm

  Women and Epilepsy
  Source: Epilepsy Foundation
  http://www.epilepsyfoundation.org/answerplace/Life/adults/women/

You may also choose to use the search utility provided by MEDLINEplus at the following Web address: **http://www.nlm.nih.gov/medlineplus/**. Simply type a keyword into the search box and click "Search." This utility is similar to the NIH search utility, with the exception that it only includes materials that are linked within the MEDLINEplus system (mostly patient-oriented information). It also has the disadvantage of generating unstructured results. We recommend, therefore, that you use this method only if you have a very targeted search.

The Combined Health Information Database (CHID)

CHID Online is a reference tool that maintains a database directory of thousands of journal articles and patient education guidelines on epilepsy. CHID offers summaries that describe the guidelines available, including contact information and pricing. CHID's general Web site is **http://chid.nih.gov/**. To search this database, go to **http://chid.nih.gov/detail/detail.html**. In particular, you can use the advanced search options to look up pamphlets, reports, brochures, and information kits. The following was recently posted in this archive:

- **Epilepsy-Seizure Disorders**

  Source: Kansas City, MO: University of Missouri, School of Dentistry. 1990. 1 p.

  Contact: Available from University of Missouri, Kansas City. School of Dentistry, 650 East 25th Street, Kansas City, MO 64108. (816) 235-2111; http://www.umkc.edu/dentistry. PRICE: Single copy free.

  Summary: The dental problems associated with epilepsy or seizure disorders are related to the trauma received during a seizure. This fact sheet, part of a series on oral health and various disabling conditions, discusses epilepsy and other seizure disorders. Topics covered include oral facial trauma resulting from seizures; common dental problems associated with gingival overgrowth; and preventive management, including daily oral hygiene, the use of fluorides to reduce plaque and gingival diseases, and trauma management.

- **National Epilepsy Library: A Service for Physicians and Other Professionals**

  Source: Landover, MD: Epilepsy Foundation of America. 199x. 4 p.

  Contact: Available from Epilepsy Foundation of America. National Epilepsy Library, 4351 Garden City Drive, Landover, MD 20785. (800) EFA-4050; (301) 459-3700; FAX: (301) 577-2684. PRICE: Single copy free.

  Summary: The Epilepsy Foundation of America (EFA) National Epilepsy Library serves physicians and other health professionals, providing a wide array of information about epilepsy. This brochure describes the services available through the Library. All services are provided free of charge. These services include: custom searches of the in-house database; access to the National Epilepsy Library collection; document delivery; a quarterly update; and toll-free telephone service. The database contains citations to more than 5,000 journal articles, book chapters, monographs, government reports, and symposia proceedings.

The National Guideline Clearinghouse™

The National Guideline Clearinghouse™ offers hundreds of evidence-based clinical practice guidelines published in the United States and other countries. You can search this site located at **http://www.guideline.gov/** by using the keyword "epilepsy" (or synonyms). The following was recently posted:

- **ACR Appropriateness Criteria for epilepsy**

  Source: American College of Radiology - Medical Specialty Society; 1996 (revised 1999); 12 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=2439&nbr=1665&string=epilepsy

- **Practice advisory: the use of felbamate in the treatment of patients with intractable epilepsy. Report of the Quality Standards Subcommittee of the American Academy of Neurology and the American Epilepsy Society**

  Source: American Academy of Neurology - Medical Specialty Society; 1999 May; 6 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=2821&nbr=2047&string=epilepsy

- **Practice parameter: Evaluating a first nonfebrile seizure in children. Report of the Quality Standards Subcommittee of the American Academy of Neurology, the Child Neurology Society, and the American Epilepsy Society**

  Source: American Academy of Neurology - Medical Specialty Society; 2000 September; 8 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=2829&nbr=2055&string=epilepsy

- **Practice parameter: management issues for women with epilepsy. Report of the Quality Standards Subcommittee of the American Academy of Neurology**

  Source: American Academy of Neurology - Medical Specialty Society; 1998 October; 5 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=2827&nbr=2053&string=epilepsy

Healthfinder™

Healthfinder™ is sponsored by the U.S. Department of Health and Human Services and offers links to hundreds of other sites that contain healthcare information. This Web site is located at **http://www.healthfinder.gov**. Again, keyword searches can be used to find guidelines. The following was recently found in this database:

- **An Epilepsy Education**

  Summary: A general overview about epilepsy seizures written fro children.

  Source: Nemours Foundation

  http://www.healthfinder.gov/scripts/recordpass.asp?RecordType=0&RecordID=5532

- **Diseases & Conditions: Internet Resources for Alternative Medicine**

  Summary: Follow these links for information online related to alternative treatment options for this select group of diseases and disorders -- HIV/AIDS, asthma, cancer, epilepsy, headache, herpes, insomnia,

  Source: Educational Institution--Follow the Resource URL for More Information

  http://www.healthfinder.gov/scripts/recordpass.asp?RecordType=0&RecordID=3983

- **Epilepsy and Seizures**

  Summary: A general overview of epilepsy and seizures that includes a description of the disorder, and treatment, prognosis and research information.

  Source: National Institute of Neurological Disorders and Stroke, National Institutes of Health

  http://www.healthfinder.gov/scripts/recordpass.asp?RecordType=0&RecordID=746

- **Epilepsy Fact Sheet**

  Source: National Information Center for Children and Youth with Disabilities, U.S. Department of Education

  http://www.healthfinder.gov/scripts/recordpass.asp?RecordType=0&RecordID=3410

- **Ketogenic Diet**

  Summary: Links to information for parents, health care providers and the general public about the use of the Ketogenic diet in treating epilepsy seizure disorders.

  Source: Educational Institution--Follow the Resource URL for More Information

  http://www.healthfinder.gov/scripts/recordpass.asp?RecordType=0&RecordID=4881

The NIH Search Utility

The NIH search utility allows you to search for documents on over 100 selected Web sites that comprise the NIH-WEB-SPACE. Each of these servers is "crawled" and indexed on an ongoing basis. Your search will produce a list of various documents, all of which will relate in some way to epilepsy. The drawbacks of this approach are that the information is not organized by theme and that the references are often a mix of information for professionals and patients. Nevertheless, a large number of the listed Web sites provide useful background information. We can only recommend this route, therefore, for relatively rare or specific disorders, or when using highly targeted searches. To use the NIH search utility, visit the following Web page: **http://search.nih.gov/index.html**.

NORD (The National Organization of Rare Disorders, Inc.)

NORD provides an invaluable service to the public by publishing short yet comprehensive guidelines on over 1,000 diseases. NORD primarily focuses on rare diseases that might not be covered by the previously listed sources. NORD's Web address is **http://www.rarediseases.org/**. A complete guide on epilepsy can be purchased from NORD for a nominal fee.

Additional Web Sources

A number of Web sites are available to the public that often link to government sites. These can also point you in the direction of essential information. The following is a representative sample:

- AOL: **http://search.aol.com/cat.adp?id=168&layer=&from=subcats**

- Family Village: **http://www.familyvillage.wisc.edu/specific.htm**
- Google: **http://directory.google.com/Top/Health/Conditions_and_Diseases/**
- Med Help International: **http://www.medhelp.org/HealthTopics/A.html**
- Open Directory Project: **http://dmoz.org/Health/Conditions_and_Diseases/**
- Yahoo.com: **http://dir.yahoo.com/Health/Diseases_and_Conditions/**
- WebMD®Health: **http://my.webmd.com/health_topics**

Associations and Epilepsy

The following is a list of associations that provide information on and resources relating to epilepsy:

- **Epilepsy Canada**

  Telephone: (514) 845-7855 Toll-free: (877) 734-0873

  Fax: (514) 845-7866

  Email: epilepsy@epilepsy.ca

  Web Site: http://www.epilepsy.ca

  Background: Epilepsy Canada (EC), established in 1966, is a not-for-profit organization dedicated to enhancing the quality of life for persons affected by **epilepsy** through promotion and support of research and facilitation of education and awareness initiatives that build understanding and acceptance of **epilepsy.** Consisting of 34 members, the organization produces educational materials including a newsletter entitled 'Lumina,' a pamphlet entitled 'Your Medication for Epilepsy', and brochures entitled 'Epilepsy: Answers to Your Questions', 'Seizures and First Aid', 'Seizures and Seniors,' 'Epilepsy and Children: What Parents Need To Know' and 'Teens and Epilepsy'(new).

  Relevant area(s) of interest: Epilepsy, Seizure Disorders

- **Epilepsy Foundation**

  Telephone: (301) 459-3700 Toll-free: (800) 332-1000

  Fax: (301) 577-2684

  Email: postmaster@efa.0rg

  Web Site: http://www.epilepsyfoundation.org

  Background: The **Epilepsy** Foundation (formerly the **Epilepsy** Foundation of America) is a nonprofit organization with the goal of ensuring that people with seizures are able to participate in all life experiences; and works to prevent, control and cur **epilepsy** through research, education, advocacy and services. Established in 1968, the Foundation has national offices in metropolitan Washington, D.C., and a network of local affiliated **Epilepsy** Foundations with offices in about 100 communities. National programs include a toll-free information service, information-rich website, research grants and fellowships, legal and legislative advocacy programs, **Epilepsy** Gene Discover Project, women's health initiative, and career choice and employment assistance. Local programs include outreach to schools and the community, support groups, camps, employment services, counseling, and information and referral. The Foundation

provides informational nmaterials to the public and health care professionals. The National **Epilepsy** Library (800) 332-4050 provides information to professionals and the public by means of computer access to major medical collections.

Relevant area(s) of interest: Epilepsy, Seizure Disorders

- **Epilepsy Foundation of Victoria**

  Telephone: (03) 9813 2866 Toll-free: 1800 134 087

  Fax: (03) 9882 7159

  Email: epinet@epinet.org.au

  Web Site: http://www.epinet.org.au

  Background: The **Epilepsy** Foundation of Victoria is a voluntary organization in Australia dedicated to enhancing the quality of the lives of people living with **epilepsy,** a group of neurologic disorders characterized by sudden, recurrent episodes of uncontrolled electrochemical activity in the brain (seizures). The **Epilepsy** Foundation of Victoria was founded in 1964 and currently consists of six chapters. Its mission is to provide a comprehensive and responsive range of services and programs to meet the personal, interpersonal, socio-economic, and cultural needs of individuals affected by **epilepsy.** Such programs and services include public education programs, advocacy, referral services, employment programs, recreational support, and individual and group counseling. The Foundation also promotes and supports medical and psychosocial research, conducts parent education workshops and support groups, and offers group forums that enable affected individuals and family members to exchange information and support. In addition, the **Epilepsy** Foundation of Victoria produces comprehensive brochures, manuals, and educational videos on **epilepsy;** publishes a quarterly newsletter entitled 'Epiletter'; has a lending library containing a collection of books, journals, and videos concerning **epilepsy;** and maintains a web site on the Internet.

Finding Associations

There are several Internet directories that provide lists of medical associations with information on or resources relating to epilepsy. By consulting all of associations listed in this chapter, you will have nearly exhausted all sources for patient associations concerned with epilepsy.

The National Health Information Center (NHIC)

The National Health Information Center (NHIC) offers a free referral service to help people find organizations that provide information about epilepsy. For more information, see the NHIC's Web site at **http://www.health.gov/NHIC/** or contact an information specialist by calling 1-800-336-4797.

Directory of Health Organizations

The Directory of Health Organizations, provided by the National Library of Medicine Specialized Information Services, is a comprehensive source of information on associations.

The Directory of Health Organizations database can be accessed via the Internet at **http://www.sis.nlm.nih.gov/Dir/DirMain.html**. It is composed of two parts: DIRLINE and Health Hotlines.

The DIRLINE database comprises some 10,000 records of organizations, research centers, and government institutes and associations that primarily focus on health and biomedicine. To access DIRLINE directly, go to the following Web site: **http://dirline.nlm.nih.gov/**. Simply type in "epilepsy" (or a synonym), and you will receive information on all relevant organizations listed in the database.

Health Hotlines directs you to toll-free numbers to over 300 organizations. You can access this database directly at **http://www.sis.nlm.nih.gov/hotlines/**. On this page, you are given the option to search by keyword or by browsing the subject list. When you have received your search results, click on the name of the organization for its description and contact information.

The Combined Health Information Database

Another comprehensive source of information on healthcare associations is the Combined Health Information Database. Using the "Detailed Search" option, you will need to limit your search to "Organizations" and "epilepsy". Type the following hyperlink into your Web browser: **http://chid.nih.gov/detail/detail.html**. To find associations, use the drop boxes at the bottom of the search page where "You may refine your search by." For publication date, select "All Years." Then, select your preferred language and the format option "Organization Resource Sheet." Type "epilepsy" (or synonyms) into the "For these words:" box. You should check back periodically with this database since it is updated every three months.

The National Organization for Rare Disorders, Inc.

The National Organization for Rare Disorders, Inc. has prepared a Web site that provides, at no charge, lists of associations organized by health topic. You can access this database at the following Web site: **http://www.rarediseases.org/search/orgsearch.html**. Type "epilepsy" (or a synonym) into the search box, and click "Submit Query."

APPENDIX C. FINDING MEDICAL LIBRARIES

Overview

In this Appendix, we show you how to quickly find a medical library in your area.

Preparation

Your local public library and medical libraries have interlibrary loan programs with the National Library of Medicine (NLM), one of the largest medical collections in the world. According to the NLM, most of the literature in the general and historical collections of the National Library of Medicine is available on interlibrary loan to any library. If you would like to access NLM medical literature, then visit a library in your area that can request the publications for you.[27]

Finding a Local Medical Library

The quickest method to locate medical libraries is to use the Internet-based directory published by the National Network of Libraries of Medicine (NN/LM). This network includes 4626 members and affiliates that provide many services to librarians, health professionals, and the public. To find a library in your area, simply visit **http://nnlm.gov/members/adv.html** or call 1-800-338-7657.

Medical Libraries in the U.S. and Canada

In addition to the NN/LM, the National Library of Medicine (NLM) lists a number of libraries with reference facilities that are open to the public. The following is the NLM's list and includes hyperlinks to each library's Web site. These Web pages can provide information on hours of operation and other restrictions. The list below is a small sample of

[27] Adapted from the NLM: **http://www.nlm.nih.gov/psd/cas/interlibrary.html**.

libraries recommended by the National Library of Medicine (sorted alphabetically by name of the U.S. state or Canadian province where the library is located)[28]:

- **Alabama:** Health InfoNet of Jefferson County (Jefferson County Library Cooperative, Lister Hill Library of the Health Sciences), **http://www.uab.edu/infonet/**
- **Alabama:** Richard M. Scrushy Library (American Sports Medicine Institute)
- **Arizona:** Samaritan Regional Medical Center: The Learning Center (Samaritan Health System, Phoenix, Arizona), **http://www.samaritan.edu/library/bannerlibs.htm**
- **California:** Kris Kelly Health Information Center (St. Joseph Health System, Humboldt), **http://www.humboldt1.com/~kkhic/index.html**
- **California:** Community Health Library of Los Gatos, **http://www.healthlib.org/orgresources.html**
- **California:** Consumer Health Program and Services (CHIPS) (County of Los Angeles Public Library, Los Angeles County Harbor-UCLA Medical Center Library) - Carson, CA, **http://www.colapublib.org/services/chips.html**
- **California:** Gateway Health Library (Sutter Gould Medical Foundation)
- **California:** Health Library (Stanford University Medical Center), **http://www-med.stanford.edu/healthlibrary/**
- **California:** Patient Education Resource Center - Health Information and Resources (University of California, San Francisco), **http://sfghdean.ucsf.edu/barnett/PERC/default.asp**
- **California:** Redwood Health Library (Petaluma Health Care District), **http://www.phcd.org/rdwdlib.html**
- **California:** Los Gatos PlaneTree Health Library, **http://planetreesanjose.org/**
- **California:** Sutter Resource Library (Sutter Hospitals Foundation, Sacramento), **http://suttermedicalcenter.org/library/**
- **California:** Health Sciences Libraries (University of California, Davis), **http://www.lib.ucdavis.edu/healthsci/**
- **California:** ValleyCare Health Library & Ryan Comer Cancer Resource Center (ValleyCare Health System, Pleasanton), **http://gaelnet.stmarys-ca.edu/other.libs/gbal/east/vchl.html**
- **California:** Washington Community Health Resource Library (Fremont), **http://www.healthlibrary.org/**
- **Colorado:** William V. Gervasini Memorial Library (Exempla Healthcare), **http://www.saintjosephdenver.org/yourhealth/libraries/**
- **Connecticut:** Hartford Hospital Health Science Libraries (Hartford Hospital), **http://www.harthosp.org/library/**
- **Connecticut:** Healthnet: Connecticut Consumer Health Information Center (University of Connecticut Health Center, Lyman Maynard Stowe Library), **http://library.uchc.edu/departm/hnet/**

[28] Abstracted from **http://www.nlm.nih.gov/medlineplus/libraries.html**.

- **Connecticut:** Waterbury Hospital Health Center Library (Waterbury Hospital, Waterbury), **http://www.waterburyhospital.com/library/consumer.shtml**
- **Delaware:** Consumer Health Library (Christiana Care Health System, Eugene du Pont Preventive Medicine & Rehabilitation Institute, Wilmington), **http://www.christianacare.org/health_guide/health_guide_pmri_health_info.cfm**
- **Delaware:** Lewis B. Flinn Library (Delaware Academy of Medicine, Wilmington), **http://www.delamed.org/chls.html**
- **Georgia:** Family Resource Library (Medical College of Georgia, Augusta), **http://cmc.mcg.edu/kids_families/fam_resources/fam_res_lib/frl.htm**
- **Georgia:** Health Resource Center (Medical Center of Central Georgia, Macon), **http://www.mccg.org/hrc/hrchome.asp**
- **Hawaii:** Hawaii Medical Library: Consumer Health Information Service (Hawaii Medical Library, Honolulu), **http://hml.org/CHIS/**
- **Idaho:** DeArmond Consumer Health Library (Kootenai Medical Center, Coeur d'Alene), **http://www.nicon.org/DeArmond/index.htm**
- **Illinois:** Health Learning Center of Northwestern Memorial Hospital (Chicago), **http://www.nmh.org/health_info/hlc.html**
- **Illinois:** Medical Library (OSF Saint Francis Medical Center, Peoria), **http://www.osfsaintfrancis.org/general/library/**
- **Kentucky:** Medical Library - Services for Patients, Families, Students & the Public (Central Baptist Hospital, Lexington), **http://www.centralbap.com/education/community/library.cfm**
- **Kentucky:** University of Kentucky - Health Information Library (Chandler Medical Center, Lexington), **http://www.mc.uky.edu/PatientEd/**
- **Louisiana:** Alton Ochsner Medical Foundation Library (Alton Ochsner Medical Foundation, New Orleans), **http://www.ochsner.org/library/**
- **Louisiana:** Louisiana State University Health Sciences Center Medical Library-Shreveport, **http://lib-sh.lsuhsc.edu/**
- **Maine:** Franklin Memorial Hospital Medical Library (Franklin Memorial Hospital, Farmington), **http://www.fchn.org/fmh/lib.htm**
- **Maine:** Gerrish-True Health Sciences Library (Central Maine Medical Center, Lewiston), **http://www.cmmc.org/library/library.html**
- **Maine:** Hadley Parrot Health Science Library (Eastern Maine Healthcare, Bangor), **http://www.emh.org/hll/hpl/guide.htm**
- **Maine:** Maine Medical Center Library (Maine Medical Center, Portland), **http://www.mmc.org/library/**
- **Maine:** Parkview Hospital (Brunswick), **http://www.parkviewhospital.org/**
- **Maine:** Southern Maine Medical Center Health Sciences Library (Southern Maine Medical Center, Biddeford), **http://www.smmc.org/services/service.php3?choice=10**
- **Maine:** Stephens Memorial Hospital's Health Information Library (Western Maine Health, Norway), **http://www.wmhcc.org/Library/**

- **Manitoba, Canada:** Consumer & Patient Health Information Service (University of Manitoba Libraries), **http://www.umanitoba.ca/libraries/units/health/reference/chis.html**
- **Manitoba, Canada:** J.W. Crane Memorial Library (Deer Lodge Centre, Winnipeg), **http://www.deerlodge.mb.ca/crane_library/about.asp**
- **Maryland:** Health Information Center at the Wheaton Regional Library (Montgomery County, Dept. of Public Libraries, Wheaton Regional Library), **http://www.mont.lib.md.us/healthinfo/hic.asp**
- **Massachusetts:** Baystate Medical Center Library (Baystate Health System), **http://www.baystatehealth.com/1024/**
- **Massachusetts:** Boston University Medical Center Alumni Medical Library (Boston University Medical Center), **http://med-libwww.bu.edu/library/lib.html**
- **Massachusetts:** Lowell General Hospital Health Sciences Library (Lowell General Hospital, Lowell), **http://www.lowellgeneral.org/library/HomePageLinks/WWW.htm**
- **Massachusetts:** Paul E. Woodard Health Sciences Library (New England Baptist Hospital, Boston), **http://www.nebh.org/health_lib.asp**
- **Massachusetts:** St. Luke's Hospital Health Sciences Library (St. Luke's Hospital, Southcoast Health System, New Bedford), **http://www.southcoast.org/library/**
- **Massachusetts:** Treadwell Library Consumer Health Reference Center (Massachusetts General Hospital), **http://www.mgh.harvard.edu/library/chrcindex.html**
- **Massachusetts:** UMass HealthNet (University of Massachusetts Medical School, Worchester), **http://healthnet.umassmed.edu/**
- **Michigan:** Botsford General Hospital Library - Consumer Health (Botsford General Hospital, Library & Internet Services), **http://www.botsfordlibrary.org/consumer.htm**
- **Michigan:** Helen DeRoy Medical Library (Providence Hospital and Medical Centers), **http://www.providence-hospital.org/library/**
- **Michigan:** Marquette General Hospital - Consumer Health Library (Marquette General Hospital, Health Information Center), **http://www.mgh.org/center.html**
- **Michigan:** Patient Education Resouce Center - University of Michigan Cancer Center (University of Michigan Comprehensive Cancer Center, Ann Arbor), **http://www.cancer.med.umich.edu/learn/leares.htm**
- **Michigan:** Sladen Library & Center for Health Information Resources - Consumer Health Information (Detroit), **http://www.henryford.com/body.cfm?id=39330**
- **Montana:** Center for Health Information (St. Patrick Hospital and Health Sciences Center, Missoula)
- **National:** Consumer Health Library Directory (Medical Library Association, Consumer and Patient Health Information Section), **http://caphis.mlanet.org/directory/index.html**
- **National:** National Network of Libraries of Medicine (National Library of Medicine) - provides library services for health professionals in the United States who do not have access to a medical library, **http://nnlm.gov/**
- **National:** NN/LM List of Libraries Serving the Public (National Network of Libraries of Medicine), **http://nnlm.gov/members/**

- **Nevada:** Health Science Library, West Charleston Library (Las Vegas-Clark County Library District, Las Vegas), **http://www.lvccld.org/special_collections/medical/index.htm**
- **New Hampshire:** Dartmouth Biomedical Libraries (Dartmouth College Library, Hanover), **http://www.dartmouth.edu/~biomed/resources.htmld/conshealth.htmld/**
- **New Jersey:** Consumer Health Library (Rahway Hospital, Rahway), **http://www.rahwayhospital.com/library.htm**
- **New Jersey:** Dr. Walter Phillips Health Sciences Library (Englewood Hospital and Medical Center, Englewood), **http://www.englewoodhospital.com/links/index.htm**
- **New Jersey:** Meland Foundation (Englewood Hospital and Medical Center, Englewood), **http://www.geocities.com/ResearchTriangle/9360/**
- **New York:** Choices in Health Information (New York Public Library) - NLM Consumer Pilot Project participant, **http://www.nypl.org/branch/health/links.html**
- **New York:** Health Information Center (Upstate Medical University, State University of New York, Syracuse), **http://www.upstate.edu/library/hic/**
- **New York:** Health Sciences Library (Long Island Jewish Medical Center, New Hyde Park), **http://www.lij.edu/library/library.html**
- **New York:** ViaHealth Medical Library (Rochester General Hospital), **http://www.nyam.org/library/**
- **Ohio:** Consumer Health Library (Akron General Medical Center, Medical & Consumer Health Library), **http://www.akrongeneral.org/hwlibrary.htm**
- **Oklahoma:** The Health Information Center at Saint Francis Hospital (Saint Francis Health System, Tulsa), **http://www.sfh-tulsa.com/services/healthinfo.asp**
- **Oregon:** Planetree Health Resource Center (Mid-Columbia Medical Center, The Dalles), **http://www.mcmc.net/phrc/**
- **Pennsylvania:** Community Health Information Library (Milton S. Hershey Medical Center, Hershey), **http://www.hmc.psu.edu/commhealth/**
- **Pennsylvania:** Community Health Resource Library (Geisinger Medical Center, Danville), **http://www.geisinger.edu/education/commlib.shtml**
- **Pennsylvania:** HealthInfo Library (Moses Taylor Hospital, Scranton), **http://www.mth.org/healthwellness.html**
- **Pennsylvania:** Hopwood Library (University of Pittsburgh, Health Sciences Library System, Pittsburgh), **http://www.hsls.pitt.edu/guides/chi/hopwood/index_html**
- **Pennsylvania:** Koop Community Health Information Center (College of Physicians of Philadelphia), **http://www.collphyphil.org/kooppg1.shtml**
- **Pennsylvania:** Learning Resources Center - Medical Library (Susquehanna Health System, Williamsport), **http://www.shscares.org/services/lrc/index.asp**
- **Pennsylvania:** Medical Library (UPMC Health System, Pittsburgh), **http://www.upmc.edu/passavant/library.htm**
- **Quebec, Canada:** Medical Library (Montreal General Hospital), **http://www.mghlib.mcgill.ca/**

- **South Dakota:** Rapid City Regional Hospital Medical Library (Rapid City Regional Hospital), **http://www.rcrh.org/Services/Library/Default.asp**
- **Texas:** Houston HealthWays (Houston Academy of Medicine-Texas Medical Center Library), **http://hhw.library.tmc.edu/**
- **Washington:** Community Health Library (Kittitas Valley Community Hospital), **http://www.kvch.com/**
- **Washington:** Southwest Washington Medical Center Library (Southwest Washington Medical Center, Vancouver), **http://www.swmedicalcenter.com/body.cfm?id=72**

ONLINE GLOSSARIES

The Internet provides access to a number of free-to-use medical dictionaries. The National Library of Medicine has compiled the following list of online dictionaries:

- ADAM Medical Encyclopedia (A.D.A.M., Inc.), comprehensive medical reference: **http://www.nlm.nih.gov/medlineplus/encyclopedia.html**
- MedicineNet.com Medical Dictionary (MedicineNet, Inc.): **http://www.medterms.com/Script/Main/hp.asp**
- Merriam-Webster Medical Dictionary (Inteli-Health, Inc.): **http://www.intelihealth.com/IH/**
- Multilingual Glossary of Technical and Popular Medical Terms in Eight European Languages (European Commission) - Danish, Dutch, English, French, German, Italian, Portuguese, and Spanish: **http://allserv.rug.ac.be/~rvdstich/eugloss/welcome.html**
- On-line Medical Dictionary (CancerWEB): **http://cancerweb.ncl.ac.uk/omd/**
- Rare Diseases Terms (Office of Rare Diseases): **http://ord.aspensys.com/asp/diseases/diseases.asp**
- Technology Glossary (National Library of Medicine) - Health Care Technology: **http://www.nlm.nih.gov/nichsr/ta101/ta10108.htm**

Beyond these, MEDLINEplus contains a very patient-friendly encyclopedia covering every aspect of medicine (licensed from A.D.A.M., Inc.). The ADAM Medical Encyclopedia can be accessed at **http://www.nlm.nih.gov/medlineplus/encyclopedia.html**. ADAM is also available on commercial Web sites such as drkoop.com (**http://www.drkoop.com/**) and Web MD (**http://my.webmd.com/adam/asset/adam_disease_articles/a_to_z/a**). The NIH suggests the following Web sites in the ADAM Medical Encyclopedia when searching for information on epilepsy:

- **Basic Guidelines for Epilepsy**

  Epilepsy
  Web site: http://www.nlm.nih.gov/medlineplus/ency/article/000694.htm

  Epilepsy - resources
  Web site: http://www.nlm.nih.gov/medlineplus/ency/article/002175.htm

- **Signs & Symptoms for Epilepsy**

  Abnormal sensations
  Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003206.htm

  Changes in consciousness
  Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003202.htm

  Changes in mental status
  Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003205.htm

Changes in mood
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003213.htm

Confusion
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003205.htm

Dizziness
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003093.htm

Drowsiness
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003208.htm

Fainting
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003092.htm

Fever
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003090.htm

Flushing
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003241.htm

Hallucinations
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003258.htm

Headache
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003024.htm

Hematomas
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003235.htm

Incontinence
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003142.htm

Loss of consciousness
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003202.htm

Loss of hair
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003246.htm

Memory loss
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003257.htm

Muscle
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003193.htm

Muscle contractions
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003193.htm

Nausea
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003117.htm

Nausea/vomiting
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003117.htm

Rash
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003220.htm

Restlessness
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003212.htm

Seizure
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003200.htm

Seizures
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003200.htm

Stress
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003211.htm

Sweating
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003218.htm

Vomit
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003117.htm

Vomiting
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003117.htm

- **Diagnostics and Tests for Epilepsy**

Blood chemistry, blood glucose
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003482.htm

Head CT
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003786.htm

ANA
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003535.htm

CBC
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003642.htm

CSF (cerebrospinal fluid) analysis
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003625.htm

CT
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003330.htm

EEG
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003931.htm

Electrolyte imbalances
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003468.htm

Head CT
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003786.htm

Kidney function tests
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003435.htm

Liver function tests
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003436.htm

Lumbar puncture
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003428.htm

MRI
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003335.htm

Spinal tap
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003428.htm

- **Background Topics for Epilepsy**

Acute
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/002215.htm

Aspiration
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/002216.htm

Brain injury
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/000028.htm

Chronic
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/002312.htm

Epilepsy - support group
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/002175.htm

Incidence
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/002387.htm

Intravenous
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/002383.htm

Kidney function tests
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003435.htm

Physical examination
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/002274.htm

Stimuli
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/002309.htm

Support group
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/002150.htm

Online Dictionary Directories

The following are additional online directories compiled by the National Library of Medicine, including a number of specialized medical dictionaries:

- Medical Dictionaries: Medical & Biological (World Health Organization): **http://www.who.int/hlt/virtuallibrary/English/diction.htm#Medical**
- MEL-Michigan Electronic Library List of Online Health and Medical Dictionaries (Michigan Electronic Library): **http://mel.lib.mi.us/health/health-dictionaries.html**
- Patient Education: Glossaries (DMOZ Open Directory Project): **http://dmoz.org/Health/Education/Patient_Education/Glossaries/**
- Web of Online Dictionaries (Bucknell University): **http://www.yourdictionary.com/diction5.html#medicine**

EPILEPSY DICTIONARY

The definitions below are derived from official public sources, including the National Institutes of Health [NIH] and the European Union [EU].

1-Propanol: A colorless liquid made by oxidation of aliphatic hydrocarbons that is used as a solvent and chemical intermediate. [NIH]

Abdomen: That portion of the body that lies between the thorax and the pelvis. [NIH]

Abdominal: Having to do with the abdomen, which is the part of the body between the chest and the hips that contains the pancreas, stomach, intestines, liver, gallbladder, and other organs. [NIH]

Abdominal Pain: Sensation of discomfort, distress, or agony in the abdominal region. [NIH]

Aberrant: Wandering or deviating from the usual or normal course. [EU]

Abscess: Accumulation of purulent material in tissues, organs, or circumscribed spaces, usually associated with signs of infection. [NIH]

Acceptor: A substance which, while normally not oxidized by oxygen or reduced by hydrogen, can be oxidized or reduced in presence of a substance which is itself undergoing oxidation or reduction. [NIH]

Accommodation: Adjustment, especially that of the eye for various distances. [EU]

Acetone: A colorless liquid used as a solvent and an antiseptic. It is one of the ketone bodies produced during ketoacidosis. [NIH]

Acetylcholine: A neurotransmitter. Acetylcholine in vertebrates is the major transmitter at neuromuscular junctions, autonomic ganglia, parasympathetic effector junctions, a subset of sympathetic effector junctions, and at many sites in the central nervous system. It is generally not used as an administered drug because it is broken down very rapidly by cholinesterases, but it is useful in some ophthalmological applications. [NIH]

Acetylcholinesterase: An enzyme that catalyzes the hydrolysis of acetylcholine to choline and acetate. In the CNS, this enzyme plays a role in the function of peripheral neuromuscular junctions. EC 3.1.1.7. [NIH]

Acidosis: A pathologic condition resulting from accumulation of acid or depletion of the alkaline reserve (bicarbonate content) in the blood and body tissues, and characterized by an increase in hydrogen ion concentration. [EU]

Acoustic: Having to do with sound or hearing. [NIH]

Actin: Essential component of the cell skeleton. [NIH]

Action Potentials: The electric response of a nerve or muscle to its stimulation. [NIH]

Adamantane: A tricyclo bridged hydrocarbon. [NIH]

Adaptability: Ability to develop some form of tolerance to conditions extremely different from those under which a living organism evolved. [NIH]

Adaptation: 1. The adjustment of an organism to its environment, or the process by which it enhances such fitness. 2. The normal ability of the eye to adjust itself to variations in the intensity of light; the adjustment to such variations. 3. The decline in the frequency of firing of a neuron, particularly of a receptor, under conditions of constant stimulation. 4. In dentistry, (a) the proper fitting of a denture, (b) the degree of proximity and interlocking of restorative material to a tooth preparation, (c) the exact adjustment of bands to teeth. 5. In

microbiology, the adjustment of bacterial physiology to a new environment. [EU]

Adenine: A purine base and a fundamental unit of adenine nucleotides. [NIH]

Adenosine: A nucleoside that is composed of adenine and d-ribose. Adenosine or adenosine derivatives play many important biological roles in addition to being components of DNA and RNA. Adenosine itself is a neurotransmitter. [NIH]

Adenosine Monophosphate: Adenylic acid. Adenine nucleotide containing one phosphate group esterified to the sugar moiety in the 2'-, 3'-, or 5'-position. [NIH]

Adenylate Cyclase: An enzyme of the lyase class that catalyzes the formation of cyclic AMP and pyrophosphate from ATP. EC 4.6.1.1. [NIH]

Adjunctive Therapy: Another treatment used together with the primary treatment. Its purpose is to assist the primary treatment. [NIH]

Adjustment: The dynamic process wherein the thoughts, feelings, behavior, and biophysiological mechanisms of the individual continually change to adjust to the environment. [NIH]

Adjuvant: A substance which aids another, such as an auxiliary remedy; in immunology, nonspecific stimulator (e.g., BCG vaccine) of the immune response. [EU]

Adolescence: The period of life beginning with the appearance of secondary sex characteristics and terminating with the cessation of somatic growth. The years usually referred to as adolescence lie between 13 and 18 years of age. [NIH]

Adrenal Cortex: The outer layer of the adrenal gland. It secretes mineralocorticoids, androgens, and glucocorticoids. [NIH]

Adrenal Medulla: The inner part of the adrenal gland; it synthesizes, stores and releases catecholamines. [NIH]

Adrenergic: Activated by, characteristic of, or secreting epinephrine or substances with similar activity; the term is applied to those nerve fibres that liberate norepinephrine at a synapse when a nerve impulse passes, i.e., the sympathetic fibres. [EU]

Adverse Effect: An unwanted side effect of treatment. [NIH]

Aerobic: In biochemistry, reactions that need oxygen to happen or happen when oxygen is present. [NIH]

Aerosol: A solution of a drug which can be atomized into a fine mist for inhalation therapy. [EU]

Afferent: Concerned with the transmission of neural impulse toward the central part of the nervous system. [NIH]

Affinity: 1. Inherent likeness or relationship. 2. A special attraction for a specific element, organ, or structure. 3. Chemical affinity; the force that binds atoms in molecules; the tendency of substances to combine by chemical reaction. 4. The strength of noncovalent chemical binding between two substances as measured by the dissociation constant of the complex. 5. In immunology, a thermodynamic expression of the strength of interaction between a single antigen-binding site and a single antigenic determinant (and thus of the stereochemical compatibility between them), most accurately applied to interactions among simple, uniform antigenic determinants such as haptens. Expressed as the association constant (K litres mole -1), which, owing to the heterogeneity of affinities in a population of antibody molecules of a given specificity, actually represents an average value (mean intrinsic association constant). 6. The reciprocal of the dissociation constant. [EU]

Agar: A complex sulfated polymer of galactose units, extracted from Gelidium cartilagineum, Gracilaria confervoides, and related red algae. It is used as a gel in the

preparation of solid culture media for microorganisms, as a bulk laxative, in making emulsions, and as a supporting medium for immunodiffusion and immunoelectrophoresis. [NIH]

Agarose: A polysaccharide complex, free of nitrogen and prepared from agar-agar which is produced by certain seaweeds (red algae). It dissolves in warm water to form a viscid solution. [NIH]

Age Distribution: The frequency of different ages or age groups in a given population. The distribution may refer to either how many or what proportion of the group. The population is usually patients with a specific disease but the concept is not restricted to humans and is not restricted to medicine. [NIH]

Age Groups: Persons classified by age from birth (infant, newborn) to octogenarians and older (aged, 80 and over). [NIH]

Aged, 80 and Over: A person 80 years of age and older. [NIH]

Agonist: In anatomy, a prime mover. In pharmacology, a drug that has affinity for and stimulates physiologic activity at cell receptors normally stimulated by naturally occurring substances. [EU]

Agoraphobia: Obsessive, persistent, intense fear of open places. [NIH]

Airway: A device for securing unobstructed passage of air into and out of the lungs during general anesthesia. [NIH]

Akathisia: 1. A condition of motor restlessness in which there is a feeling of muscular quivering, an urge to move about constantly, and an inability to sit still, a common extrapyramidal side effect of neuroleptic drugs. 2. An inability to sit down because of intense anxiety at the thought of doing so. [EU]

Albumin: 1. Any protein that is soluble in water and moderately concentrated salt solutions and is coagulable by heat. 2. Serum albumin; the major plasma protein (approximately 60 per cent of the total), which is responsible for much of the plasma colloidal osmotic pressure and serves as a transport protein carrying large organic anions, such as fatty acids, bilirubin, and many drugs, and also carrying certain hormones, such as cortisol and thyroxine, when their specific binding globulins are saturated. Albumin is synthesized in the liver. Low serum levels occur in protein malnutrition, active inflammation and serious hepatic and renal disease. [EU]

Alertness: A state of readiness to detect and respond to certain specified small changes occurring at random intervals in the environment. [NIH]

Alexia: The inability to recognize or comprehend written or printed words. [NIH]

Algorithms: A procedure consisting of a sequence of algebraic formulas and/or logical steps to calculate or determine a given task. [NIH]

Alkaline: Having the reactions of an alkali. [EU]

Alkaloid: A member of a large group of chemicals that are made by plants and have nitrogen in them. Some alkaloids have been shown to work against cancer. [NIH]

Alkylating Agents: Highly reactive chemicals that introduce alkyl radicals into biologically active molecules and thereby prevent their proper functioning. Many are used as antineoplastic agents, but most are very toxic, with carcinogenic, mutagenic, teratogenic, and immunosuppressant actions. They have also been used as components in poison gases. [NIH]

Allergen: An antigenic substance capable of producing immediate-type hypersensitivity (allergy). [EU]

Allylamine: Possesses an unusual and selective cytotoxicity for vascular smooth muscle

cells in dogs and rats. Useful for experiments dealing with arterial injury, myocardial fibrosis or cardiac decompensation. [NIH]

Alpha Particles: Positively charged particles composed of two protons and two neutrons, i.e., helium nuclei, emitted during disintegration of very heavy isotopes; a beam of alpha particles or an alpha ray has very strong ionizing power, but weak penetrability. [NIH]

Alpha-1: A protein with the property of inactivating proteolytic enzymes such as leucocyte collagenase and elastase. [NIH]

Alternative medicine: Practices not generally recognized by the medical community as standard or conventional medical approaches and used instead of standard treatments. Alternative medicine includes the taking of dietary supplements, megadose vitamins, and herbal preparations; the drinking of special teas; and practices such as massage therapy, magnet therapy, spiritual healing, and meditation. [NIH]

Aluminum: A metallic element that has the atomic number 13, atomic symbol Al, and atomic weight 26.98. [NIH]

Amenorrhea: Absence of menstruation. [NIH]

Amine: An organic compound containing nitrogen; any member of a group of chemical compounds formed from ammonia by replacement of one or more of the hydrogen atoms by organic (hydrocarbon) radicals. The amines are distinguished as primary, secondary, and tertiary, according to whether one, two, or three hydrogen atoms are replaced. The amines include allylamine, amylamine, ethylamine, methylamine, phenylamine, propylamine, and many other compounds. [EU]

Amino Acid Neurotransmitters: Amino acids released by neurons as intercellular messengers. Among the amino acid neurotransmitters are glutamate (glutamic acid) and GABA which are, respectively, the most common excitatory and inhibitory neurotransmitters in the central nervous system. [NIH]

Amino Acid Sequence: The order of amino acids as they occur in a polypeptide chain. This is referred to as the primary structure of proteins. It is of fundamental importance in determining protein conformation. [NIH]

Amino Acids: Organic compounds that generally contain an amino (-NH2) and a carboxyl (-COOH) group. Twenty alpha-amino acids are the subunits which are polymerized to form proteins. [NIH]

Amino Acids: Organic compounds that generally contain an amino (-NH2) and a carboxyl (-COOH) group. Twenty alpha-amino acids are the subunits which are polymerized to form proteins. [NIH]

Aminobutyric Acids: Aliphatic four carbon acids substituted in any position(s) with amino group(s). They are found in most living things. The best known is GABA. [NIH]

Aminoethyl: A protease inhibitor. [NIH]

Ammonia: A colorless alkaline gas. It is formed in the body during decomposition of organic materials during a large number of metabolically important reactions. [NIH]

Amnestic: Nominal aphasia; a difficulty in finding the right name for an object. [NIH]

Amniotic Fluid: Amniotic cavity fluid which is produced by the amnion and fetal lungs and kidneys. [NIH]

Amputation: Surgery to remove part or all of a limb or appendage. [NIH]

Amygdala: Almond-shaped group of basal nuclei anterior to the inferior horn of the lateral ventricle of the brain, within the temporal lobe. The amygdala is part of the limbic system. [NIH]

Anaesthesia: Loss of feeling or sensation. Although the term is used for loss of tactile sensibility, or of any of the other senses, it is applied especially to loss of the sensation of pain, as it is induced to permit performance of surgery or other painful procedures. [EU]

Anal: Having to do with the anus, which is the posterior opening of the large bowel. [NIH]

Analgesic: An agent that alleviates pain without causing loss of consciousness. [EU]

Analog: In chemistry, a substance that is similar, but not identical, to another. [NIH]

Analogous: Resembling or similar in some respects, as in function or appearance, but not in origin or development;. [EU]

Anaphylatoxins: The family of peptides C3a, C4a, C5a, and C5a des-arginine produced in the serum during complement activation. They produce smooth muscle contraction, mast cell histamine release, affect platelet aggregation, and act as mediators of the local inflammatory process. The order of anaphylatoxin activity from strongest to weakest is C5a, C3a, C4a, and C5a des-arginine. The latter is the so-called "classical" anaphylatoxin but shows no spasmogenic activity though it contains some chemotactic ability. [NIH]

Anatomical: Pertaining to anatomy, or to the structure of the organism. [EU]

Androgens: A class of sex hormones associated with the development and maintenance of the secondary male sex characteristics, sperm induction, and sexual differentiation. In addition to increasing virility and libido, they also increase nitrogen and water retention and stimulate skeletal growth. [NIH]

Anemia: A reduction in the number of circulating erythrocytes or in the quantity of hemoglobin. [NIH]

Anesthesia: A state characterized by loss of feeling or sensation. This depression of nerve function is usually the result of pharmacologic action and is induced to allow performance of surgery or other painful procedures. [NIH]

Anesthetics: Agents that are capable of inducing a total or partial loss of sensation, especially tactile sensation and pain. They may act to induce general anesthesia, in which an unconscious state is achieved, or may act locally to induce numbness or lack of sensation at a targeted site. [NIH]

Aneurysm: A sac formed by the dilatation of the wall of an artery, a vein, or the heart. [NIH]

Angina: Chest pain that originates in the heart. [NIH]

Angina, Unstable: Precordial pain at rest, which may precede a myocardial infarction. [NIH]

Angioma: A tumor composed of lymphatic or blood vessels. [NIH]

Angioplasty: Endovascular reconstruction of an artery, which may include the removal of atheromatous plaque and/or the endothelial lining as well as simple dilatation. These are procedures performed by catheterization. When reconstruction of an artery is performed surgically, it is called endarterectomy. [NIH]

Animal model: An animal with a disease either the same as or like a disease in humans. Animal models are used to study the development and progression of diseases and to test new treatments before they are given to humans. Animals with transplanted human cancers or other tissues are called xenograft models. [NIH]

Anions: Negatively charged atoms, radicals or groups of atoms which travel to the anode or positive pole during electrolysis. [NIH]

Annealing: The spontaneous alignment of two single DNA strands to form a double helix. [NIH]

Anode: Electrode held at a positive potential with respect to a cathode. [NIH]

Anomalies: Birth defects; abnormalities. [NIH]

Anorexia: Lack or loss of appetite for food. Appetite is psychologic, dependent on memory and associations. Anorexia can be brought about by unattractive food, surroundings, or company. [NIH]

Anorexia Nervosa: The chief symptoms are inability to eat, weight loss, and amenorrhea. [NIH]

Anoxia: Clinical manifestation of respiratory distress consisting of a relatively complete absence of oxygen. [NIH]

Anterior Cerebral Artery: Artery formed by the bifurcation of the internal carotid artery. Branches of the anterior cerebral artery supply the caudate nucleus, internal capsule, putamen, septal nuclei, gyrus cinguli, and surfaces of the frontal lobe and parietal lobe. [NIH]

Anthelmintics: Agents destructive to parasitic worms. They are used therapeutically in the treatment of helminthiasis in man and animal. [NIH]

Anti-Anxiety Agents: Agents that alleviate anxiety, tension, and neurotic symptoms, promote sedation, and have a calming effect without affecting clarity of consciousness or neurologic conditions. Some are also effective as anticonvulsants, muscle relaxants, or anesthesia adjuvants. Adrenergic beta-antagonists are commonly used in the symptomatic treatment of anxiety but are not included here. [NIH]

Antibacterial: A substance that destroys bacteria or suppresses their growth or reproduction. [EU]

Antibiotic: A drug used to treat infections caused by bacteria and other microorganisms. [NIH]

Antibodies: Immunoglobulin molecules having a specific amino acid sequence by virtue of which they interact only with the antigen that induced their synthesis in cells of the lymphoid series (especially plasma cells), or with an antigen closely related to it. [NIH]

Antibody: A type of protein made by certain white blood cells in response to a foreign substance (antigen). Each antibody can bind to only a specific antigen. The purpose of this binding is to help destroy the antigen. Antibodies can work in several ways, depending on the nature of the antigen. Some antibodies destroy antigens directly. Others make it easier for white blood cells to destroy the antigen. [NIH]

Anticholinergic: An agent that blocks the parasympathetic nerves. Called also parasympatholytic. [EU]

Anticoagulant: A drug that helps prevent blood clots from forming. Also called a blood thinner. [NIH]

Anticonvulsant: An agent that prevents or relieves convulsions. [EU]

Antidepressant: A drug used to treat depression. [NIH]

Antidepressive Agents: Mood-stimulating drugs used primarily in the treatment of affective disorders and related conditions. Several monoamine oxidase inhibitors are useful as antidepressants apparently as a long-term consequence of their modulation of catecholamine levels. The tricyclic compounds useful as antidepressive agents also appear to act through brain catecholamine systems. A third group (antidepressive agents, second-generation) is a diverse group of drugs including some that act specifically on serotonergic systems. [NIH]

Antidote: A remedy for counteracting a poison. [EU]

Antiemetic: An agent that prevents or alleviates nausea and vomiting. Also antinauseant. [EU]

Antiepileptic: An agent that combats epilepsy. [EU]

Antigen: Any substance which is capable, under appropriate conditions, of inducing a specific immune response and of reacting with the products of that response, that is, with specific antibody or specifically sensitized T-lymphocytes, or both. Antigens may be soluble substances, such as toxins and foreign proteins, or particulate, such as bacteria and tissue cells; however, only the portion of the protein or polysaccharide molecule known as the antigenic determinant (q.v.) combines with antibody or a specific receptor on a lymphocyte. Abbreviated Ag. [EU]

Antigen-Antibody Complex: The complex formed by the binding of antigen and antibody molecules. The deposition of large antigen-antibody complexes leading to tissue damage causes immune complex diseases. [NIH]

Anti-inflammatory: Having to do with reducing inflammation. [NIH]

Antimetabolite: A chemical that is very similar to one required in a normal biochemical reaction in cells. Antimetabolites can stop or slow down the reaction. [NIH]

Antioxidant: A substance that prevents damage caused by free radicals. Free radicals are highly reactive chemicals that often contain oxygen. They are produced when molecules are split to give products that have unpaired electrons. This process is called oxidation. [NIH]

Antipsychotic: Effective in the treatment of psychosis. Antipsychotic drugs (called also neuroleptic drugs and major tranquilizers) are a chemically diverse (including phenothiazines, thioxanthenes, butyrophenones, dibenzoxazepines, dibenzodiazepines, and diphenylbutylpiperidines) but pharmacologically similar class of drugs used to treat schizophrenic, paranoid, schizoaffective, and other psychotic disorders; acute delirium and dementia, and manic episodes (during induction of lithium therapy); to control the movement disorders associated with Huntington's chorea, Gilles de la Tourette's syndrome, and ballismus; and to treat intractable hiccups and severe nausea and vomiting. Antipsychotic agents bind to dopamine, histamine, muscarinic cholinergic, a-adrenergic, and serotonin receptors. Blockade of dopaminergic transmission in various areas is thought to be responsible for their major effects : antipsychotic action by blockade in the mesolimbic and mesocortical areas; extrapyramidal side effects (dystonia, akathisia, parkinsonism, and tardive dyskinesia) by blockade in the basal ganglia; and antiemetic effects by blockade in the chemoreceptor trigger zone of the medulla. Sedation and autonomic side effects (orthostatic hypotension, blurred vision, dry mouth, nasal congestion and constipation) are caused by blockade of histamine, cholinergic, and adrenergic receptors. [EU]

Antipsychotic Agents: Agents that control agitated psychotic behavior, alleviate acute psychotic states, reduce psychotic symptoms, and exert a quieting effect. They are used in schizophrenia, senile dementia, transient psychosis following surgery or myocardial infarction, etc. These drugs are often referred to as neuroleptics alluding to the tendency to produce neurological side effects, but not all antipsychotics are likely to produce such effects. Many of these drugs may also be effective against nausea, emesis, and pruritus. [NIH]

Antiviral: Destroying viruses or suppressing their replication. [EU]

Anxiety: Persistent feeling of dread, apprehension, and impending disaster. [NIH]

Anxiety Disorders: Disorders in which anxiety (persistent feelings of apprehension, tension, or uneasiness) is the predominant disturbance. [NIH]

Anxiolytic: An anxiolytic or antianxiety agent. [EU]

Aorta: The main trunk of the systemic arteries. [NIH]

Apathy: Lack of feeling or emotion; indifference. [EU]

Aphasia: A cognitive disorder marked by an impaired ability to comprehend or express

language in its written or spoken form. This condition is caused by diseases which affect the language areas of the dominant hemisphere. Clinical features are used to classify the various subtypes of this condition. General categories include receptive, expressive, and mixed forms of aphasia. [NIH]

Apnea: A transient absence of spontaneous respiration. [NIH]

Apoptosis: One of the two mechanisms by which cell death occurs (the other being the pathological process of necrosis). Apoptosis is the mechanism responsible for the physiological deletion of cells and appears to be intrinsically programmed. It is characterized by distinctive morphologic changes in the nucleus and cytoplasm, chromatin cleavage at regularly spaced sites, and the endonucleolytic cleavage of genomic DNA (DNA fragmentation) at internucleosomal sites. This mode of cell death serves as a balance to mitosis in regulating the size of animal tissues and in mediating pathologic processes associated with tumor growth. [NIH]

Applicability: A list of the commodities to which the candidate method can be applied as presented or with minor modifications. [NIH]

Approximate: Approximal [EU]

Aqueous: Having to do with water. [NIH]

Arrhythmia: Any variation from the normal rhythm or rate of the heart beat. [NIH]

Arterial: Pertaining to an artery or to the arteries. [EU]

Arteries: The vessels carrying blood away from the heart. [NIH]

Arterioles: The smallest divisions of the arteries located between the muscular arteries and the capillaries. [NIH]

Arteriolosclerosis: Sclerosis and thickening of the walls of the smaller arteries (arterioles). Hyaline arteriolosclerosis, in which there is homogeneous pink hyaline thickening of the arteriolar walls, is associated with benign nephrosclerosis. Hyperplastic arteriolosclerosis, in which there is a concentric thickening with progressive narrowing of the lumina may be associated with malignant hypertension, nephrosclerosis, and scleroderma. [EU]

Arteriosclerosis: Thickening and loss of elasticity of arterial walls. Atherosclerosis is the most common form of arteriosclerosis and involves lipid deposition and thickening of the intimal cell layers within arteries. Additional forms of arteriosclerosis involve calcification of the media of muscular arteries (Monkeberg medial calcific sclerosis) and thickening of the walls of small arteries or arterioles due to cell proliferation or hyaline deposition (arteriolosclerosis). [NIH]

Arteriovenous: Both arterial and venous; pertaining to or affecting an artery and a vein. [EU]

Ascites: Accumulation or retention of free fluid within the peritoneal cavity. [NIH]

Aspartate: A synthetic amino acid. [NIH]

Aspartic: The naturally occurring substance is L-aspartic acid. One of the acidic-amino-acids is obtained by the hydrolysis of proteins. [NIH]

Aspartic Acid: One of the non-essential amino acids commonly occurring in the L-form. It is found in animals and plants, especially in sugar cane and sugar beets. It may be a neurotransmitter. [NIH]

Assay: Determination of the amount of a particular constituent of a mixture, or of the biological or pharmacological potency of a drug. [EU]

Astringents: Agents, usually topical, that cause the contraction of tissues for the control of bleeding or secretions. [NIH]

Astrocytes: The largest and most numerous neuroglial cells in the brain and spinal cord.

Astrocytes (from "star" cells) are irregularly shaped with many long processes, including those with "end feet" which form the glial (limiting) membrane and directly and indirectly contribute to the blood brain barrier. They regulate the extracellular ionic and chemical environment, and "reactive astrocytes" (along with microglia) respond to injury. Astrocytes have high- affinity transmitter uptake systems, voltage-dependent and transmitter-gated ion channels, and can release transmitter, but their role in signaling (as in many other functions) is not well understood. [NIH]

Asymptomatic: Having no signs or symptoms of disease. [NIH]

Ataxia: Impairment of the ability to perform smoothly coordinated voluntary movements. This condition may affect the limbs, trunk, eyes, pharnyx, larnyx, and other structures. Ataxia may result from impaired sensory or motor function. Sensory ataxia may result from posterior column injury or peripheral nerve diseases. Motor ataxia may be associated with cerebellar diseases; cerebral cortex diseases; thalamic diseases; basal ganglia diseases; injury to the red nucleus; and other conditions. [NIH]

Atrial: Pertaining to an atrium. [EU]

Atrioventricular: Pertaining to an atrium of the heart and to a ventricle. [EU]

Atrium: A chamber; used in anatomical nomenclature to designate a chamber affording entrance to another structure or organ. Usually used alone to designate an atrium of the heart. [EU]

Atrophy: Decrease in the size of a cell, tissue, organ, or multiple organs, associated with a variety of pathological conditions such as abnormal cellular changes, ischemia, malnutrition, or hormonal changes. [NIH]

Attenuated: Strain with weakened or reduced virulence. [NIH]

Atypical: Irregular; not conformable to the type; in microbiology, applied specifically to strains of unusual type. [EU]

Auditory: Pertaining to the sense of hearing. [EU]

Aura: A subjective sensation or motor phenomenon that precedes and marks the of a paroxysmal attack, such as an epileptic attack on set. [EU]

Autoantibodies: Antibodies that react with self-antigens (autoantigens) of the organism that produced them. [NIH]

Autoantigens: Endogenous tissue constituents that have the ability to interact with autoantibodies and cause an immune response. [NIH]

Autoimmune disease: A condition in which the body recognizes its own tissues as foreign and directs an immune response against them. [NIH]

Autonomic: Self-controlling; functionally independent. [EU]

Autonomic Nervous System: The enteric, parasympathetic, and sympathetic nervous systems taken together. Generally speaking, the autonomic nervous system regulates the internal environment during both peaceful activity and physical or emotional stress. Autonomic activity is controlled and integrated by the central nervous system, especially the hypothalamus and the solitary nucleus, which receive information relayed from visceral afferents; these and related central and sensory structures are sometimes (but not here) considered to be part of the autonomic nervous system itself. [NIH]

Autopsy: Postmortem examination of the body. [NIH]

Autoradiography: A process in which radioactive material within an object produces an image when it is in close proximity to a radiation sensitive emulsion. [NIH]

Autosuggestion: Suggestion coming from the subject himself. [NIH]

Axonal: Condition associated with metabolic derangement of the entire neuron and is manifest by degeneration of the distal portion of the nerve fiber. [NIH]

Axons: Nerve fibers that are capable of rapidly conducting impulses away from the neuron cell body. [NIH]

Back Pain: Acute or chronic pain located in the posterior regions of the trunk, including the thoracic, lumbar, sacral, or adjacent regions. [NIH]

Baclofen: A GABA derivative that is a specific agonist at GABA-B receptors. It is used in the treatment of spasticity, especially that due to spinal cord damage. Its therapeutic effects result from actions at spinal and supraspinal sites, generally the reduction of excitatory transmission. [NIH]

Bacteria: Unicellular prokaryotic microorganisms which generally possess rigid cell walls, multiply by cell division, and exhibit three principal forms: round or coccal, rodlike or bacillary, and spiral or spirochetal. [NIH]

Bacterial Physiology: Physiological processes and activities of bacteria. [NIH]

Bactericidal: Substance lethal to bacteria; substance capable of killing bacteria. [NIH]

Bacteriophage: A virus whose host is a bacterial cell; A virus that exclusively infects bacteria. It generally has a protein coat surrounding the genome (DNA or RNA). One of the coliphages most extensively studied is the lambda phage, which is also one of the most important. [NIH]

Barbiturate: A drug with sedative and hypnotic effects. Barbiturates have been used as sedatives and anesthetics, and they have been used to treat the convulsions associated with epilepsy. [NIH]

Basal Ganglia: Large subcortical nuclear masses derived from the telencephalon and located in the basal regions of the cerebral hemispheres. [NIH]

Basal Ganglia Diseases: Diseases of the basal ganglia including the putamen; globus pallidus; claustrum; amygdala; and caudate nucleus. Dyskinesias (most notably involuntary movements and alterations of the rate of movement) represent the primary clinical manifestations of these disorders. Common etiologies include cerebrovascular disease; neurodegenerative diseases; and craniocerebral trauma. [NIH]

Base: In chemistry, the nonacid part of a salt; a substance that combines with acids to form salts; a substance that dissociates to give hydroxide ions in aqueous solutions; a substance whose molecule or ion can combine with a proton (hydrogen ion); a substance capable of donating a pair of electrons (to an acid) for the formation of a coordinate covalent bond. [EU]

Basement Membrane: Ubiquitous supportive tissue adjacent to epithelium and around smooth and striated muscle cells. This tissue contains intrinsic macromolecular components such as collagen, laminin, and sulfated proteoglycans. As seen by light microscopy one of its subdivisions is the basal (basement) lamina. [NIH]

Behavior Therapy: The application of modern theories of learning and conditioning in the treatment of behavior disorders. [NIH]

Behavioral Symptoms: Observable manifestions of impaired psychological functioning. [NIH]

Benign: Not cancerous; does not invade nearby tissue or spread to other parts of the body. [NIH]

Benzene: Toxic, volatile, flammable liquid hydrocarbon biproduct of coal distillation. It is used as an industrial solvent in paints, varnishes, lacquer thinners, gasoline, etc. Benzene causes central nervous system damage acutely and bone marrow damage chronically and is carcinogenic. It was formerly used as parasiticide. [NIH]

Benzodiazepines: A two-ring heterocyclic compound consisting of a benzene ring fused to a diazepine ring. Permitted is any degree of hydrogenation, any substituents and any H-isomer. [NIH]

Bewilderment: Impairment or loss of will power. [NIH]

Bezoar: A ball of food, mucus, vegetable fiber, hair, or other material that cannot be digested in the stomach. Bezoars can cause blockage, ulcers, and bleeding. [NIH]

Bifida: A defect in development of the vertebral column in which there is a central deficiency of the vertebral lamina. [NIH]

Bilateral: Affecting both the right and left side of body. [NIH]

Bile: An emulsifying agent produced in the liver and secreted into the duodenum. Its composition includes bile acids and salts, cholesterol, and electrolytes. It aids digestion of fats in the duodenum. [NIH]

Bilirubin: A bile pigment that is a degradation product of heme. [NIH]

Bioavailability: The degree to which a drug or other substance becomes available to the target tissue after administration. [EU]

Biochemical: Relating to biochemistry; characterized by, produced by, or involving chemical reactions in living organisms. [EU]

Biochemical reactions: In living cells, chemical reactions that help sustain life and allow cells to grow. [NIH]

Bioengineering: The application of engineering principles to the solution of biological problems, for example, remote-handling devices, life-support systems, controls, and displays. [NIH]

Biological Transport: The movement of materials (including biochemical substances and drugs) across cell membranes and epithelial layers, usually by passive diffusion. [NIH]

Biomedical Technology: The application of technology to the solution of medical problems. [NIH]

Biopsy: Removal and pathologic examination of specimens in the form of small pieces of tissue from the living body. [NIH]

Biosynthesis: The building up of a chemical compound in the physiologic processes of a living organism. [EU]

Biotechnology: Body of knowledge related to the use of organisms, cells or cell-derived constituents for the purpose of developing products which are technically, scientifically and clinically useful. Alteration of biologic function at the molecular level (i.e., genetic engineering) is a central focus; laboratory methods used include transfection and cloning technologies, sequence and structure analysis algorithms, computer databases, and gene and protein structure function analysis and prediction. [NIH]

Biphasic: Having two phases; having both a sporophytic and a gametophytic phase in the life cycle. [EU]

Bipolar Disorder: A major affective disorder marked by severe mood swings (manic or major depressive episodes) and a tendency to remission and recurrence. [NIH]

Bladder: The organ that stores urine. [NIH]

Blast phase: The phase of chronic myelogenous leukemia in which the number of immature, abnormal white blood cells in the bone marrow and blood is extremely high. Also called blast crisis. [NIH]

Bloating: Fullness or swelling in the abdomen that often occurs after meals. [NIH]

Blood Coagulation: The process of the interaction of blood coagulation factors that results in an insoluble fibrin clot. [NIH]

Blood Glucose: Glucose in blood. [NIH]

Blood Platelets: Non-nucleated disk-shaped cells formed in the megakaryocyte and found in the blood of all mammals. They are mainly involved in blood coagulation. [NIH]

Blood pressure: The pressure of blood against the walls of a blood vessel or heart chamber. Unless there is reference to another location, such as the pulmonary artery or one of the heart chambers, it refers to the pressure in the systemic arteries, as measured, for example, in the forearm. [NIH]

Blood vessel: A tube in the body through which blood circulates. Blood vessels include a network of arteries, arterioles, capillaries, venules, and veins. [NIH]

Blood Volume: Volume of circulating blood. It is the sum of the plasma volume and erythrocyte volume. [NIH]

Blood-Brain Barrier: Specialized non-fenestrated tightly-joined endothelial cells (tight junctions) that form a transport barrier for certain substances between the cerebral capillaries and the brain tissue. [NIH]

Blot: To transfer DNA, RNA, or proteins to an immobilizing matrix such as nitrocellulose. [NIH]

Body Fluids: Liquid components of living organisms. [NIH]

Body Mass Index: One of the anthropometric measures of body mass; it has the highest correlation with skinfold thickness or body density. [NIH]

Bone Marrow: The soft tissue filling the cavities of bones. Bone marrow exists in two types, yellow and red. Yellow marrow is found in the large cavities of large bones and consists mostly of fat cells and a few primitive blood cells. Red marrow is a hematopoietic tissue and is the site of production of erythrocytes and granular leukocytes. Bone marrow is made up of a framework of connective tissue containing branching fibers with the frame being filled with marrow cells. [NIH]

Bone scan: A technique to create images of bones on a computer screen or on film. A small amount of radioactive material is injected into a blood vessel and travels through the bloodstream; it collects in the bones and is detected by a scanner. [NIH]

Bowel: The long tube-shaped organ in the abdomen that completes the process of digestion. There is both a small and a large bowel. Also called the intestine. [NIH]

Bowel Movement: Body wastes passed through the rectum and anus. [NIH]

Brain Diseases: Pathologic conditions affecting the brain, which is composed of the intracranial components of the central nervous system. This includes (but is not limited to) the cerebral cortex; intracranial white matter; basal ganglia; thalamus; hypothalamus; brain stem; and cerebellum. [NIH]

Brain Hypoxia: Lack of oxygen leading to unconsciousness. [NIH]

Brain Infarction: The formation of an area of necrosis in the brain, including the cerebral hemispheres (cerebral infarction), thalami, basal ganglia, brain stem (brain stem infarctions), or cerebellum secondary to an insufficiency of arterial or venous blood flow. [NIH]

Brain Injuries: Acute and chronic injuries to the brain, including the cerebral hemispheres, cerebellum, and brain stem. Clinical manifestations depend on the nature of injury. Diffuse trauma to the brain is frequently associated with diffuse axonal injury or coma, post-traumatic. Localized injuries may be associated with neurobehavioral manifestations; hemiparesis, or other focal neurologic deficits. [NIH]

Brain Ischemia: Localized reduction of blood flow to brain tissue due to arterial obtruction or systemic hypoperfusion. This frequently occurs in conjuction with brain hypoxia. Prolonged ischemia is associated with brain infarction. [NIH]

Brain Neoplasms: Neoplasms of the intracranial components of the central nervous system, including the cerebral hemispheres, basal ganglia, hypothalamus, thalamus, brain stem, and cerebellum. Brain neoplasms are subdivided into primary (originating from brain tissue) and secondary (i.e., metastatic) forms. Primary neoplasms are subdivided into benign and malignant forms. In general, brain tumors may also be classified by age of onset, histologic type, or presenting location in the brain. [NIH]

Brain Stem: The part of the brain that connects the cerebral hemispheres with the spinal cord. It consists of the mesencephalon, pons, and medulla oblongata. [NIH]

Brain Stem Infarctions: Infarctions that occur in the brain stem which is comprised of the midbrain, pons, and medulla. There are several named syndromes characterized by their distinctive clinical manifestations and specific sites of ischemic injury. [NIH]

Branch: Most commonly used for branches of nerves, but applied also to other structures. [NIH]

Breakdown: A physical, metal, or nervous collapse. [NIH]

Bromine: A halogen with the atomic symbol Br, atomic number 36, and atomic weight 79.904. It is a volatile reddish-brown liquid that gives off suffocating vapors, is corrosive to the skin, and may cause severe gastroenteritis if ingested. [NIH]

Bronchi: The larger air passages of the lungs arising from the terminal bifurcation of the trachea. [NIH]

Bronchial: Pertaining to one or more bronchi. [EU]

Bronchitis: Inflammation (swelling and reddening) of the bronchi. [NIH]

Bronchoconstriction: Diminution of the caliber of a bronchus physiologically or as a result of pharmacological intervention. [NIH]

Bronchus: A large air passage that leads from the trachea (windpipe) to the lung. [NIH]

Buccal: Pertaining to or directed toward the cheek. In dental anatomy, used to refer to the buccal surface of a tooth. [EU]

Bulimia: Episodic binge eating. The episodes may be associated with the fear of not being able to stop eating, depressed mood, or self-deprecating thoughts (binge-eating disorder) and may frequently be terminated by self-induced vomiting (bulimia nervosa). [NIH]

Butyric Acid: A four carbon acid, CH3CH2CH2COOH, with an unpleasant odor that occurs in butter and animal fat as the glycerol ester. [NIH]

Cachexia: General ill health, malnutrition, and weight loss, usually associated with chronic disease. [NIH]

Calcification: Deposits of calcium in the tissues of the breast. Calcification in the breast can be seen on a mammogram, but cannot be detected by touch. There are two types of breast calcification, macrocalcification and microcalcification. Macrocalcifications are large deposits and are usually not related to cancer. Microcalcifications are specks of calcium that may be found in an area of rapidly dividing cells. Many microcalcifications clustered together may be a sign of cancer. [NIH]

Calcium: A basic element found in nearly all organized tissues. It is a member of the alkaline earth family of metals with the atomic symbol Ca, atomic number 20, and atomic weight 40. Calcium is the most abundant mineral in the body and combines with phosphorus to form calcium phosphate in the bones and teeth. It is essential for the normal

functioning of nerves and muscles and plays a role in blood coagulation (as factor IV) and in many enzymatic processes. [NIH]

Calcium Channels: Voltage-dependent cell membrane glycoproteins selectively permeable to calcium ions. They are categorized as L-, T-, N-, P-, Q-, and R-types based on the activation and inactivation kinetics, ion specificity, and sensitivity to drugs and toxins. The L- and T-types are present throughout the cardiovascular and central nervous systems and the N-, P-, Q-, & R-types are located in neuronal tissue. [NIH]

Capillary: Any one of the minute vessels that connect the arterioles and venules, forming a network in nearly all parts of the body. Their walls act as semipermeable membranes for the interchange of various substances, including fluids, between the blood and tissue fluid; called also vas capillare. [EU]

Capillary Fragility: The lack of resistance, or susceptibility, of capillaries to damage or disruption under conditions of increased stress. [NIH]

Capsules: Hard or soft soluble containers used for the oral administration of medicine. [NIH]

Carbamazepine: An anticonvulsant used to control grand mal and psychomotor or focal seizures. Its mode of action is not fully understood, but some of its actions resemble those of phenytoin; although there is little chemical resemblance between the two compounds, their three-dimensional structure is similar. [NIH]

Carbohydrate: An aldehyde or ketone derivative of a polyhydric alcohol, particularly of the pentahydric and hexahydric alcohols. They are so named because the hydrogen and oxygen are usually in the proportion to form water, (CH2O)n. The most important carbohydrates are the starches, sugars, celluloses, and gums. They are classified into mono-, di-, tri-, poly- and heterosaccharides. [EU]

Carbon Dioxide: A colorless, odorless gas that can be formed by the body and is necessary for the respiration cycle of plants and animals. [NIH]

Carboxy: Cannabinoid. [NIH]

Carcinogen: Any substance that causes cancer. [NIH]

Carcinogenic: Producing carcinoma. [EU]

Cardiac: Having to do with the heart. [NIH]

Cardiac arrest: A sudden stop of heart function. [NIH]

Cardiovascular: Having to do with the heart and blood vessels. [NIH]

Cardiovascular disease: Any abnormal condition characterized by dysfunction of the heart and blood vessels. CVD includes atherosclerosis (especially coronary heart disease, which can lead to heart attacks), cerebrovascular disease (e.g., stroke), and hypertension (high blood pressure). [NIH]

Cardiovascular System: The heart and the blood vessels by which blood is pumped and circulated through the body. [NIH]

Career Choice: Selection of a type of occupation or profession. [NIH]

Carnitine: Constituent of striated muscle and liver. It is used therapeutically to stimulate gastric and pancreatic secretions and in the treatment of hyperlipoproteinemias. [NIH]

Carotene: The general name for a group of pigments found in green, yellow, and leafy vegetables, and yellow fruits. The pigments are fat-soluble, unsaturated aliphatic hydrocarbons functioning as provitamins and are converted to vitamin A through enzymatic processes in the intestinal wall. [NIH]

Carotid Arteries: Either of the two principal arteries on both sides of the neck that supply blood to the head and neck; each divides into two branches, the internal carotid artery and

the external carotid artery. [NIH]

Case report: A detailed report of the diagnosis, treatment, and follow-up of an individual patient. Case reports also contain some demographic information about the patient (for example, age, gender, ethnic origin). [NIH]

Case series: A group or series of case reports involving patients who were given similar treatment. Reports of case series usually contain detailed information about the individual patients. This includes demographic information (for example, age, gender, ethnic origin) and information on diagnosis, treatment, response to treatment, and follow-up after treatment. [NIH]

Caspase: Enzyme released by the cell at a crucial stage in apoptosis in order to shred all cellular proteins. [NIH]

Catabolism: Any destructive metabolic process by which organisms convert substances into excreted compounds. [EU]

Catalyse: To speed up a chemical reaction. [EU]

Catecholamine: A group of chemical substances manufactured by the adrenal medulla and secreted during physiological stress. [NIH]

Cathepsins: A group of lysosomal proteinases or endopeptidases found in aqueous extracts of a variety of animal tissue. They function optimally within an acidic pH range. [NIH]

Catheterization: Use or insertion of a tubular device into a duct, blood vessel, hollow organ, or body cavity for injecting or withdrawing fluids for diagnostic or therapeutic purposes. It differs from intubation in that the tube here is used to restore or maintain patency in obstructions. [NIH]

Cathode: An electrode, usually an incandescent filament of tungsten, which emits electrons in an X-ray tube. [NIH]

Cations: Postively charged atoms, radicals or groups of atoms which travel to the cathode or negative pole during electrolysis. [NIH]

Caudal: Denoting a position more toward the cauda, or tail, than some specified point of reference; same as inferior, in human anatomy. [EU]

Causal: Pertaining to a cause; directed against a cause. [EU]

Cause of Death: Factors which produce cessation of all vital bodily functions. They can be analyzed from an epidemiologic viewpoint. [NIH]

Cell: The individual unit that makes up all of the tissues of the body. All living things are made up of one or more cells. [NIH]

Cell Adhesion: Adherence of cells to surfaces or to other cells. [NIH]

Cell Death: The termination of the cell's ability to carry out vital functions such as metabolism, growth, reproduction, responsiveness, and adaptability. [NIH]

Cell Differentiation: Progressive restriction of the developmental potential and increasing specialization of function which takes place during the development of the embryo and leads to the formation of specialized cells, tissues, and organs. [NIH]

Cell Division: The fission of a cell. [NIH]

Cell membrane: Cell membrane = plasma membrane. The structure enveloping a cell, enclosing the cytoplasm, and forming a selective permeability barrier; it consists of lipids, proteins, and some carbohydrates, the lipids thought to form a bilayer in which integral proteins are embedded to varying degrees. [EU]

Cell proliferation: An increase in the number of cells as a result of cell growth and cell

division. [NIH]

Cell Respiration: The metabolic process of all living cells (animal and plant) in which oxygen is used to provide a source of energy for the cell. [NIH]

Cellobiose: A disaccharide consisting of two glucose units in beta (1-4) glycosidic linkage. Obtained from the partial hydrolysis of cellulose. [NIH]

Cellulose: A polysaccharide with glucose units linked as in cellobiose. It is the chief constituent of plant fibers, cotton being the purest natural form of the substance. As a raw material, it forms the basis for many derivatives used in chromatography, ion exchange materials, explosives manufacturing, and pharmaceutical preparations. [NIH]

Central Nervous System: The main information-processing organs of the nervous system, consisting of the brain, spinal cord, and meninges. [NIH]

Central Nervous System Diseases: Diseases of any component of the brain (including the cerebral hemispheres, diencephalon, brain stem, and cerebellum) or the spinal cord. [NIH]

Central Nervous System Infections: Pathogenic infections of the brain, spinal cord, and meninges. DNA virus infections; RNA virus infections; bacterial infections; mycoplasma infections; Spirochaetales infections; fungal infections; protozoan infections; helminthiasis; and prion diseases may involve the central nervous system as a primary or secondary process. [NIH]

Cerebellar: Pertaining to the cerebellum. [EU]

Cerebellar Diseases: Diseases that affect the structure or function of the cerebellum. Cardinal manifestations of cerebellar dysfunction include dysmetria, gait ataxia, and muscle hypotonia. [NIH]

Cerebellum: Part of the metencephalon that lies in the posterior cranial fossa behind the brain stem. It is concerned with the coordination of movement. [NIH]

Cerebral: Of or pertaining of the cerebrum or the brain. [EU]

Cerebral hemispheres: The two halves of the cerebrum, the part of the brain that controls muscle functions of the body and also controls speech, emotions, reading, writing, and learning. The right hemisphere controls muscle movement on the left side of the body, and the left hemisphere controls muscle movement on the right side of the body. [NIH]

Cerebral Infarction: The formation of an area of necrosis in the cerebrum caused by an insufficiency of arterial or venous blood flow. Infarcts of the cerebrum are generally classified by hemisphere (i.e., left vs. right), lobe (e.g., frontal lobe infarction), arterial distribution (e.g., infarction, anterior cerebral artery), and etiology (e.g., embolic infarction). [NIH]

Cerebral Palsy: Refers to a motor disability caused by a brain dysfunction. [NIH]

Cerebrospinal: Pertaining to the brain and spinal cord. [EU]

Cerebrospinal fluid: CSF. The fluid flowing around the brain and spinal cord. Cerebrospinal fluid is produced in the ventricles in the brain. [NIH]

Cerebrovascular: Pertaining to the blood vessels of the cerebrum, or brain. [EU]

Cerebrovascular Disorders: A broad category of disorders characterized by impairment of blood flow in the arteries and veins which supply the brain. These include cerebral infarction; brain ischemia; hypoxia, brain; intracranial embolism and thrombosis; intracranial arteriovenous malformations; and vasculitis, central nervous system. In common usage, the term cerebrovascular disorders is not limited to conditions that affect the cerebrum, but refers to vascular disorders of the entire brain including the diencephalon; brain stem; and cerebellum. [NIH]

Cerebrum: The largest part of the brain. It is divided into two hemispheres, or halves, called the cerebral hemispheres. The cerebrum controls muscle functions of the body and also controls speech, emotions, reading, writing, and learning. [NIH]

Character: In current usage, approximately equivalent to personality. The sum of the relatively fixed personality traits and habitual modes of response of an individual. [NIH]

Chelating Agents: Organic chemicals that form two or more coordination bonds with a central metal ion. Heterocyclic rings are formed with the central metal atom as part of the ring. Some biological systems form metal chelates, e.g., the iron-binding porphyrin group of hemoglobin and the magnesium-binding chlorophyll of plants. (From Hawley's Condensed Chemical Dictionary, 12th ed) They are used chemically to remove ions from solutions, medicinally against microorganisms, to treat metal poisoning, and in chemotherapy protocols. [NIH]

Chemoreceptor: A receptor adapted for excitation by chemical substances, e.g., olfactory and gustatory receptors, or a sense organ, as the carotid body or the aortic (supracardial) bodies, which is sensitive to chemical changes in the blood stream, especially reduced oxygen content, and reflexly increases both respiration and blood pressure. [EU]

Chemotactic Factors: Chemical substances that attract or repel cells or organisms. The concept denotes especially those factors released as a result of tissue injury, invasion, or immunologic activity, that attract leukocytes, macrophages, or other cells to the site of infection or insult. [NIH]

Chemotherapeutics: Noun plural but singular or plural in constructions : chemotherapy. [EU]

Chemotherapy: Treatment with anticancer drugs. [NIH]

Child Welfare: Organized efforts by communities or organizations to improve the health and well-being of the child. [NIH]

Chiropractic: A system of treating bodily disorders by manipulation of the spine and other parts, based on the belief that the cause is the abnormal functioning of a nerve. [NIH]

Chlorine: A greenish-yellow, diatomic gas that is a member of the halogen family of elements. It has the atomic symbol Cl, atomic number 17, and atomic weight 70.906. It is a powerful irritant that can cause fatal pulmonary edema. Chlorine is used in manufacturing, as a reagent in synthetic chemistry, for water purification, and in the production of chlorinated lime, which is used in fabric bleaching. [NIH]

Chlorophyll: Porphyrin derivatives containing magnesium that act to convert light energy in photosynthetic organisms. [NIH]

Cholesterol: The principal sterol of all higher animals, distributed in body tissues, especially the brain and spinal cord, and in animal fats and oils. [NIH]

Choline: A basic constituent of lecithin that is found in many plants and animal organs. It is important as a precursor of acetylcholine, as a methyl donor in various metabolic processes, and in lipid metabolism. [NIH]

Cholinergic: Resembling acetylcholine in pharmacological action; stimulated by or releasing acetylcholine or a related compound. [EU]

Cholinergic Agonists: Drugs that bind to and activate cholinergic receptors. [NIH]

Cholinesterase Inhibitors: Drugs that inhibit cholinesterases. The neurotransmitter acetylcholine is rapidly hydrolyzed, and thereby inactivated, by cholinesterases. When cholinesterases are inhibited, the action of endogenously released acetylcholine at cholinergic synapses is potentiated. Cholinesterase inhibitors are widely used clinically for their potentiation of cholinergic inputs to the gastrointestinal tract and urinary bladder, the

eye, and skeletal muscles; they are also used for their effects on the heart and the central nervous system. [NIH]

Chorea: Involuntary, forcible, rapid, jerky movements that may be subtle or become confluent, markedly altering normal patterns of movement. Hypotonia and pendular reflexes are often associated. Conditions which feature recurrent or persistent episodes of chorea as a primary manifestation of disease are referred to as choreatic disorders. Chorea is also a frequent manifestation of basal ganglia diseases. [NIH]

Choreatic Disorders: Acquired and hereditary conditions which feature chorea as a primary manifestation of the disease process. [NIH]

Chromatin: The material of chromosomes. It is a complex of DNA, histones, and nonhistone proteins (chromosomal proteins, non-histone) found within the nucleus of a cell. [NIH]

Chromosomal: Pertaining to chromosomes. [EU]

Chromosome: Part of a cell that contains genetic information. Except for sperm and eggs, all human cells contain 46 chromosomes. [NIH]

Chronic: A disease or condition that persists or progresses over a long period of time. [NIH]

Chronic Disease: Disease or ailment of long duration. [NIH]

Chronic lymphocytic leukemia: A slowly progressing disease in which too many white blood cells (called lymphocytes) are found in the body. [NIH]

Chronic myelogenous leukemia: CML. A slowly progressing disease in which too many white blood cells are made in the bone marrow. Also called chronic myeloid leukemia or chronic granulocytic leukemia. [NIH]

Chronic Obstructive Pulmonary Disease: Collective term for chronic bronchitis and emphysema. [NIH]

Chronic phase: Refers to the early stages of chronic myelogenous leukemia or chronic lymphocytic leukemia. The number of mature and immature abnormal white blood cells in the bone marrow and blood is higher than normal, but lower than in the accelerated or blast phase. [NIH]

Chronic renal: Slow and progressive loss of kidney function over several years, often resulting in end-stage renal disease. People with end-stage renal disease need dialysis or transplantation to replace the work of the kidneys. [NIH]

Cimetidine: A histamine congener, it competitively inhibits histamine binding to H2 receptors. Cimetidine has a range of pharmacological actions. It inhibits gastric acid secretion, as well as pepsin and gastrin output. It also blocks the activity of cytochrome P-450. [NIH]

Circadian: Repeated more or less daily, i. e. on a 23- to 25-hour cycle. [NIH]

Circadian Rhythm: The regular recurrence, in cycles of about 24 hours, of biological processes or activities, such as sensitivity to drugs and stimuli, hormone secretion, sleeping, feeding, etc. This rhythm seems to be set by a 'biological clock' which seems to be set by recurring daylight and darkness. [NIH]

Circulatory system: The system that contains the heart and the blood vessels and moves blood throughout the body. This system helps tissues get enough oxygen and nutrients, and it helps them get rid of waste products. The lymph system, which connects with the blood system, is often considered part of the circulatory system. [NIH]

CIS: Cancer Information Service. The CIS is the National Cancer Institute's link to the public, interpreting and explaining research findings in a clear and understandable manner, and providing personalized responses to specific questions about cancer. Access the CIS by

calling 1-800-4-CANCER, or by using the Web site at http://cis.nci.nih.gov. [NIH]

Clamp: A u-shaped steel rod used with a pin or wire for skeletal traction in the treatment of certain fractures. [NIH]

Cleft Palate: Congenital fissure of the soft and/or hard palate, due to faulty fusion. [NIH]

Clinical Medicine: The study and practice of medicine by direct examination of the patient. [NIH]

Clinical series: A case series in which the patients receive treatment in a clinic or other medical facility. [NIH]

Clinical study: A research study in which patients receive treatment in a clinic or other medical facility. Reports of clinical studies can contain results for single patients (case reports) or many patients (case series or clinical trials). [NIH]

Clinical trial: A research study that tests how well new medical treatments or other interventions work in people. Each study is designed to test new methods of screening, prevention, diagnosis, or treatment of a disease. [NIH]

Clonazepam: An anticonvulsant used for several types of seizures, including myotonic or atonic seizures, photosensitive epilepsy, and absence seizures, although tolerance may develop. It is seldom effective in generalized tonic-clonic or partial seizures. The mechanism of action appears to involve the enhancement of gaba receptor responses. [NIH]

Clonic: Pertaining to or of the nature of clonus. [EU]

Cloning: The production of a number of genetically identical individuals; in genetic engineering, a process for the efficient replication of a great number of identical DNA molecules. [NIH]

Cochlear: Of or pertaining to the cochlea. [EU]

Cochlear Diseases: Diseases of the cochlea, the part of the inner ear that is concerned with hearing. [NIH]

Cofactor: A substance, microorganism or environmental factor that activates or enhances the action of another entity such as a disease-causing agent. [NIH]

Cognition: Intellectual or mental process whereby an organism becomes aware of or obtains knowledge. [NIH]

Cognitive behavior therapy: A system of psychotherapy based on the premise that distorted or dysfunctional thinking, which influences a person's mood or behavior, is common to all psychosocial problems. The focus of therapy is to identify the distorted thinking and to replace it with more rational, adaptive thoughts and beliefs. [NIH]

Cohort Studies: Studies in which subsets of a defined population are identified. These groups may or may not be exposed to factors hypothesized to influence the probability of the occurrence of a particular disease or other outcome. Cohorts are defined populations which, as a whole, are followed in an attempt to determine distinguishing subgroup characteristics. [NIH]

Colitis: Inflammation of the colon. [NIH]

Collagen: A polypeptide substance comprising about one third of the total protein in mammalian organisms. It is the main constituent of skin, connective tissue, and the organic substance of bones and teeth. Different forms of collagen are produced in the body but all consist of three alpha-polypeptide chains arranged in a triple helix. Collagen is differentiated from other fibrous proteins, such as elastin, by the content of proline, hydroxyproline, and hydroxylysine; by the absence of tryptophan; and particularly by the high content of polar groups which are responsible for its swelling properties. [NIH]

Collapse: 1. A state of extreme prostration and depression, with failure of circulation. 2. Abnormal falling in of the walls of any part of organ. [EU]

Colloidal: Of the nature of a colloid. [EU]

Colostomy: An opening into the colon from the outside of the body. A colostomy provides a new path for waste material to leave the body after part of the colon has been removed. [NIH]

Comatose: Pertaining to or affected with coma. [EU]

Communication Disorders: Disorders of verbal and nonverbal communication caused by receptive or expressive language disorders, cognitive dysfunction (e.g., mental retardation), psychiatric conditions, and hearing disorders. [NIH]

Comorbidity: The presence of co-existing or additional diseases with reference to an initial diagnosis or with reference to the index condition that is the subject of study. Comorbidity may affect the ability of affected individuals to function and also their survival; it may be used as a prognostic indicator for length of hospital stay, cost factors, and outcome or survival. [NIH]

Complement: A term originally used to refer to the heat-labile factor in serum that causes immune cytolysis, the lysis of antibody-coated cells, and now referring to the entire functionally related system comprising at least 20 distinct serum proteins that is the effector not only of immune cytolysis but also of other biologic functions. Complement activation occurs by two different sequences, the classic and alternative pathways. The proteins of the classic pathway are termed 'components of complement' and are designated by the symbols C1 through C9. C1 is a calcium-dependent complex of three distinct proteins C1q, C1r and C1s. The proteins of the alternative pathway (collectively referred to as the properdin system) and complement regulatory proteins are known by semisystematic or trivial names. Fragments resulting from proteolytic cleavage of complement proteins are designated with lower-case letter suffixes, e.g., C3a. Inactivated fragments may be designated with the suffix 'i', e.g. C3bi. Activated components or complexes with biological activity are designated by a bar over the symbol e.g. C1 or C4b,2a. The classic pathway is activated by the binding of C1 to classic pathway activators, primarily antigen-antibody complexes containing IgM, IgG1, IgG3; C1q binds to a single IgM molecule or two adjacent IgG molecules. The alternative pathway can be activated by IgA immune complexes and also by nonimmunologic materials including bacterial endotoxins, microbial polysaccharides, and cell walls. Activation of the classic pathway triggers an enzymatic cascade involving C1, C4, C2 and C3; activation of the alternative pathway triggers a cascade involving C3 and factors B, D and P. Both result in the cleavage of C5 and the formation of the membrane attack complex. Complement activation also results in the formation of many biologically active complement fragments that act as anaphylatoxins, opsonins, or chemotactic factors. [EU]

Complementary and alternative medicine: CAM. Forms of treatment that are used in addition to (complementary) or instead of (alternative) standard treatments. These practices are not considered standard medical approaches. CAM includes dietary supplements, megadose vitamins, herbal preparations, special teas, massage therapy, magnet therapy, spiritual healing, and meditation. [NIH]

Complementary medicine: Practices not generally recognized by the medical community as standard or conventional medical approaches and used to enhance or complement the standard treatments. Complementary medicine includes the taking of dietary supplements, megadose vitamins, and herbal preparations; the drinking of special teas; and practices such as massage therapy, magnet therapy, spiritual healing, and meditation. [NIH]

Complete remission: The disappearance of all signs of cancer. Also called a complete response. [NIH]

Computational Biology: A field of biology concerned with the development of techniques for the collection and manipulation of biological data, and the use of such data to make biological discoveries or predictions. This field encompasses all computational methods and theories applicable to molecular biology and areas of computer-based techniques for solving biological problems including manipulation of models and datasets. [NIH]

Computed tomography: CT scan. A series of detailed pictures of areas inside the body, taken from different angles; the pictures are created by a computer linked to an x-ray machine. Also called computerized tomography and computerized axial tomography (CAT) scan. [NIH]

Computer Simulation: Computer-based representation of physical systems and phenomena such as chemical processes. [NIH]

Computerized axial tomography: A series of detailed pictures of areas inside the body, taken from different angles; the pictures are created by a computer linked to an x-ray machine. Also called CAT scan, computed tomography (CT scan), or computerized tomography. [NIH]

Computerized tomography: A series of detailed pictures of areas inside the body, taken from different angles; the pictures are created by a computer linked to an x-ray machine. Also called computerized axial tomography (CAT) scan and computed tomography (CT scan). [NIH]

Conception: The onset of pregnancy, marked by implantation of the blastocyst; the formation of a viable zygote. [EU]

Concomitant: Accompanying; accessory; joined with another. [EU]

Conduction: The transfer of sound waves, heat, nervous impulses, or electricity. [EU]

Cones: One type of specialized light-sensitive cells (photoreceptors) in the retina that provide sharp central vision and color vision. [NIH]

Confusion: A mental state characterized by bewilderment, emotional disturbance, lack of clear thinking, and perceptual disorientation. [NIH]

Congenita: Displacement, subluxation, or malposition of the crystalline lens. [NIH]

Congestion: Excessive or abnormal accumulation of blood in a part. [EU]

Conjugated: Acting or operating as if joined; simultaneous. [EU]

Conjunctiva: The mucous membrane that lines the inner surface of the eyelids and the anterior part of the sclera. [NIH]

Connective Tissue: Tissue that supports and binds other tissues. It consists of connective tissue cells embedded in a large amount of extracellular matrix. [NIH]

Connective Tissue: Tissue that supports and binds other tissues. It consists of connective tissue cells embedded in a large amount of extracellular matrix. [NIH]

Connective Tissue Cells: A group of cells that includes fibroblasts, cartilage cells, adipocytes, smooth muscle cells, and bone cells. [NIH]

Connexins: A group of homologous proteins which form the intermembrane channels of gap junctions. The connexins are the products of an identified gene family which has both highly conserved and highly divergent regions. The variety contributes to the wide range of functional properties of gap junctions. [NIH]

Consciousness: Sense of awareness of self and of the environment. [NIH]

Consolidation: The healing process of a bone fracture. [NIH]

Constipation: Infrequent or difficult evacuation of feces. [NIH]

Constitutional: 1. Affecting the whole constitution of the body; not local. 2. Pertaining to the constitution. [EU]

Constriction: The act of constricting. [NIH]

Constriction, Pathologic: The condition of an anatomical structure's being constricted beyond normal dimensions. [NIH]

Consumption: Pulmonary tuberculosis. [NIH]

Contamination: The soiling or pollution by inferior material, as by the introduction of organisms into a wound, or sewage into a stream. [EU]

Contraindications: Any factor or sign that it is unwise to pursue a certain kind of action or treatment, e. g. giving a general anesthetic to a person with pneumonia. [NIH]

Contralateral: Having to do with the opposite side of the body. [NIH]

Control group: In a clinical trial, the group that does not receive the new treatment being studied. This group is compared to the group that receives the new treatment, to see if the new treatment works. [NIH]

Controlled clinical trial: A clinical study that includes a comparison (control) group. The comparison group receives a placebo, another treatment, or no treatment at all. [NIH]

Controlled study: An experiment or clinical trial that includes a comparison (control) group. [NIH]

Contusion: A bruise; an injury of a part without a break in the skin. [EU]

Convulsants: Substances that act in the brain stem or spinal cord to produce tonic or clonic convulsions, often by removing normal inhibitory tone. They were formerly used to stimulate respiration or as antidotes to barbiturate overdose. They are now most commonly used as experimental tools. [NIH]

Convulsion: A violent involuntary contraction or series of contractions of the voluntary muscles. [EU]

Convulsive: Relating or referring to spasm; affected with spasm; characterized by a spasm or spasms. [NIH]

Coordination: Muscular or motor regulation or the harmonious cooperation of muscles or groups of muscles, in a complex action or series of actions. [NIH]

Cor: The muscular organ that maintains the circulation of the blood. c. adiposum a heart that has undergone fatty degeneration or that has an accumulation of fat around it; called also fat or fatty, heart. c. arteriosum the left side of the heart, so called because it contains oxygenated (arterial) blood. c. biloculare a congenital anomaly characterized by failure of formation of the atrial and ventricular septums, the heart having only two chambers, a single atrium and a single ventricle, and a common atrioventricular valve. c. bovinum (L. 'ox heart') a greatly enlarged heart due to a hypertrophied left ventricle; called also c. taurinum and bucardia. c. dextrum (L. 'right heart') the right atrium and ventricle. c. hirsutum, c. villosum. c. mobile (obs.) an abnormally movable heart. c. pendulum a heart so movable that it seems to be hanging by the great blood vessels. c. pseudotriloculare biatriatum a congenital cardiac anomaly in which the heart functions as a three-chambered heart because of tricuspid atresia, the right ventricle being extremely small or rudimentary and the right atrium greatly dilated. Blood passes from the right to the left atrium and thence disease due to pulmonary hypertension secondary to disease of the lung, or its blood vessels, with hypertrophy of the right ventricle. [EU]

Coronary: Encircling in the manner of a crown; a term applied to vessels; nerves, ligaments, etc. The term usually denotes the arteries that supply the heart muscle and, by extension, a pathologic involvement of them. [EU]

Coronary Arteriosclerosis: Thickening and loss of elasticity of the coronary arteries. [NIH]

Coronary Artery Bypass: Surgical therapy of ischemic coronary artery disease achieved by grafting a section of saphenous vein, internal mammary artery, or other substitute between the aorta and the obstructed coronary artery distal to the obstructive lesion. [NIH]

Coronary heart disease: A type of heart disease caused by narrowing of the coronary arteries that feed the heart, which needs a constant supply of oxygen and nutrients carried by the blood in the coronary arteries. When the coronary arteries become narrowed or clogged by fat and cholesterol deposits and cannot supply enough blood to the heart, CHD results. [NIH]

Coronary Thrombosis: Presence of a thrombus in a coronary artery, often causing a myocardial infarction. [NIH]

Corpus: The body of the uterus. [NIH]

Corpus Callosum: Broad plate of dense myelinated fibers that reciprocally interconnect regions of the cortex in all lobes with corresponding regions of the opposite hemisphere. The corpus callosum is located deep in the longitudinal fissure. [NIH]

Corpus Luteum: The yellow glandular mass formed in the ovary by an ovarian follicle that has ruptured and discharged its ovum. [NIH]

Cortex: The outer layer of an organ or other body structure, as distinguished from the internal substance. [EU]

Cortical: Pertaining to or of the nature of a cortex or bark. [EU]

Cortical Blindness: The inability to understand or interpret what is seen due to a disturbance in the cerebral associational areas, the retina, the sensory pathways, and the striate area being intact. [NIH]

Corticosteroids: Hormones that have antitumor activity in lymphomas and lymphoid leukemias; in addition, corticosteroids (steroids) may be used for hormone replacement and for the management of some of the complications of cancer and its treatment. [NIH]

Cortisol: A steroid hormone secreted by the adrenal cortex as part of the body's response to stress. [NIH]

Cranial: Pertaining to the cranium, or to the anterior (in animals) or superior (in humans) end of the body. [EU]

Cranial Nerves: Twelve pairs of nerves that carry general afferent, visceral afferent, special afferent, somatic efferent, and autonomic efferent fibers. [NIH]

Craniocerebral Trauma: Traumatic injuries involving the cranium and intracranial structures (i.e., brain; cranial nerves; meninges; and other structures). Injuries may be classified by whether or not the skull is penetrated (i.e., penetrating vs. nonpenetrating) or whether there is an associated hemorrhage. [NIH]

Creatine: An amino acid that occurs in vertebrate tissues and in urine. In muscle tissue, creatine generally occurs as phosphocreatine. Creatine is excreted as creatinine in the urine. [NIH]

Creatinine: A compound that is excreted from the body in urine. Creatinine levels are measured to monitor kidney function. [NIH]

Cribriform: Pierced with small holes as in a sieve. Refers to the appearance of a tumor when viewed under a microscope. The tumor appears to have open spaces or small holes inside. [NIH]

Cross-Sectional Studies: Studies in which the presence or absence of disease or other health-related variables are determined in each member of the study population or in a

representative sample at one particular time. This contrasts with longitudinal studies which are followed over a period of time. [NIH]

Cues: Signals for an action; that specific portion of a perceptual field or pattern of stimuli to which a subject has learned to respond. [NIH]

Cultured cells: Animal or human cells that are grown in the laboratory. [NIH]

Curare: Plant extracts from several species, including Strychnos toxifera, S. castelnaei, S. crevauxii, and Chondodendron tomentosum, that produce paralysis of skeletal muscle and are used adjunctively with general anesthesia. These extracts are toxic and must be used with the administration of artificial respiration. [NIH]

Curative: Tending to overcome disease and promote recovery. [EU]

Cutaneous: Having to do with the skin. [NIH]

Cyanide: An extremely toxic class of compounds that can be lethal on inhaling of ingesting in minute quantities. [NIH]

Cyclic: Pertaining to or occurring in a cycle or cycles; the term is applied to chemical compounds that contain a ring of atoms in the nucleus. [EU]

Cyst: A sac or capsule filled with fluid. [NIH]

Cysteine: A thiol-containing non-essential amino acid that is oxidized to form cystine. [NIH]

Cystine: A covalently linked dimeric nonessential amino acid formed by the oxidation of cysteine. Two molecules of cysteine are joined together by a disulfide bridge to form cystine. [NIH]

Cytochrome: Any electron transfer hemoprotein having a mode of action in which the transfer of a single electron is effected by a reversible valence change of the central iron atom of the heme prosthetic group between the +2 and +3 oxidation states; classified as cytochromes a in which the heme contains a formyl side chain, cytochromes b, which contain protoheme or a closely similar heme that is not covalently bound to the protein, cytochromes c in which protoheme or other heme is covalently bound to the protein, and cytochromes d in which the iron-tetrapyrrole has fewer conjugated double bonds than the hemes have. Well-known cytochromes have been numbered consecutively within groups and are designated by subscripts (beginning with no subscript), e.g. cytochromes c, c1, C2, . New cytochromes are named according to the wavelength in nanometres of the absorption maximum of the a-band of the iron (II) form in pyridine, e.g., c-555. [EU]

Cytokines: Non-antibody proteins secreted by inflammatory leukocytes and some non-leukocytic cells, that act as intercellular mediators. They differ from classical hormones in that they are produced by a number of tissue or cell types rather than by specialized glands. They generally act locally in a paracrine or autocrine rather than endocrine manner. [NIH]

Cytoplasm: The protoplasm of a cell exclusive of that of the nucleus; it consists of a continuous aqueous solution (cytosol) and the organelles and inclusions suspended in it (phaneroplasm), and is the site of most of the chemical activities of the cell. [EU]

Cytoskeletal Proteins: Major constituent of the cytoskeleton found in the cytoplasm of eukaryotic cells. They form a flexible framework for the cell, provide attachment points for organelles and formed bodies, and make communication between parts of the cell possible. [NIH]

Cytoskeleton: The network of filaments, tubules, and interconnecting filamentous bridges which give shape, structure, and organization to the cytoplasm. [NIH]

Cytotoxic: Cell-killing. [NIH]

Data Collection: Systematic gathering of data for a particular purpose from various sources, including questionnaires, interviews, observation, existing records, and electronic devices.

The process is usually preliminary to statistical analysis of the data. [NIH]

Databases, Bibliographic: Extensive collections, reputedly complete, of references and citations to books, articles, publications, etc., generally on a single subject or specialized subject area. Databases can operate through automated files, libraries, or computer disks. The concept should be differentiated from factual databases which is used for collections of data and facts apart from bibliographic references to them. [NIH]

Deamination: The removal of an amino group (NH2) from a chemical compound. [NIH]

Decarboxylation: The removal of a carboxyl group, usually in the form of carbon dioxide, from a chemical compound. [NIH]

Decision Making: The process of making a selective intellectual judgment when presented with several complex alternatives consisting of several variables, and usually defining a course of action or an idea. [NIH]

Degenerative: Undergoing degeneration : tending to degenerate; having the character of or involving degeneration; causing or tending to cause degeneration. [EU]

Dehydroepiandrosterone: DHEA. A substance that is being studied as a cancer prevention drug. It belongs to the family of drugs called steroids. [NIH]

Deletion: A genetic rearrangement through loss of segments of DNA (chromosomes), bringing sequences, which are normally separated, into close proximity. [NIH]

Delirium: (DSM III-R) an acute, reversible organic mental disorder characterized by reduced ability to maintain attention to external stimuli and disorganized thinking as manifested by rambling, irrelevant, or incoherent speech; there are also a reduced level of consciousness, sensory misperceptions, disturbance of the sleep-wakefulness cycle and level of psychomotor activity, disorientation to time, place, or person, and memory impairment. Delirium may be caused by a large number of conditions resulting in derangement of cerebral metabolism, including systemic infection, poisoning, drug intoxication or withdrawal, seizures or head trauma, and metabolic disturbances such as hypoxia, hypoglycaemia, fluid, electrolyte, or acid-base imbalances, or hepatic or renal failure. Called also acute confusional state and acute brain syndrome. [EU]

Delusions: A false belief regarding the self or persons or objects outside the self that persists despite the facts, and is not considered tenable by one's associates. [NIH]

Dementia: An acquired organic mental disorder with loss of intellectual abilities of sufficient severity to interfere with social or occupational functioning. The dysfunction is multifaceted and involves memory, behavior, personality, judgment, attention, spatial relations, language, abstract thought, and other executive functions. The intellectual decline is usually progressive, and initially spares the level of consciousness. [NIH]

Denaturation: Rupture of the hydrogen bonds by heating a DNA solution and then cooling it rapidly causes the two complementary strands to separate. [NIH]

Dendrites: Extensions of the nerve cell body. They are short and branched and receive stimuli from other neurons. [NIH]

Dendritic: 1. Branched like a tree. 2. Pertaining to or possessing dendrites. [EU]

Density: The logarithm to the base 10 of the opacity of an exposed and processed film. [NIH]

Dental Care: The total of dental diagnostic, preventive, and restorative services provided to meet the needs of a patient (from Illustrated Dictionary of Dentistry, 1982). [NIH]

Dental Care for Children: The giving of attention to the special dental needs of children, including the prevention of tooth diseases and instruction in dental hygiene and dental health. The dental care may include the services provided by dental specialists. [NIH]

Dental Caries: Localized destruction of the tooth surface initiated by decalcification of the enamel followed by enzymatic lysis of organic structures and leading to cavity formation. If left unchecked, the cavity may penetrate the enamel and dentin and reach the pulp. The three most prominent theories used to explain the etiology of the disase are that acids produced by bacteria lead to decalcification; that micro-organisms destroy the enamel protein; or that keratolytic micro-organisms produce chelates that lead to decalcification. [NIH]

Dentate Gyrus: Gray matter situated above the gyrus hippocampi. It is composed of three layers. The molecular layer is continuous with the hippocampus in the hippocampal fissure. The granular layer consists of closely arranged spherical or oval neurons, called granule cells, whose axons pass through the polymorphic layer ending on the dendrites of pyramidal cells in the hippocampus. [NIH]

Dentists: Individuals licensed to practice dentistry. [NIH]

Deoxyglucose: 2-Deoxy-D-arabino-hexose. An antimetabolite of glucose with antiviral activity. [NIH]

Depolarization: The process or act of neutralizing polarity. In neurophysiology, the reversal of the resting potential in excitable cell membranes when stimulated, i.e., the tendency of the cell membrane potential to become positive with respect to the potential outside the cell. [EU]

Depressive Disorder: An affective disorder manifested by either a dysphoric mood or loss of interest or pleasure in usual activities. The mood disturbance is prominent and relatively persistent. [NIH]

Deprivation: Loss or absence of parts, organs, powers, or things that are needed. [EU]

Desensitization: The prevention or reduction of immediate hypersensitivity reactions by administration of graded doses of allergen; called also hyposensitization and immunotherapy. [EU]

Deuterium: Deuterium. The stable isotope of hydrogen. It has one neutron and one proton in the nucleus. [NIH]

Developing Countries: Countries in the process of change directed toward economic growth, that is, an increase in production, per capita consumption, and income. The process of economic growth involves better utilization of natural and human resources, which results in a change in the social, political, and economic structures. [NIH]

Dextroamphetamine: The d-form of amphetamine. It is a central nervous system stimulant and a sympathomimetic. It has also been used in the treatment of narcolepsy and of attention deficit disorders and hyperactivity in children. Dextroamphetamine has multiple mechanisms of action including blocking uptake of adrenergics and dopamine, stimulating release of monamines, and inhibiting monoamine oxidase. It is also a drug of abuse and a psychotomimetic. [NIH]

Dextrorotatory: Turning towards the right hand. [NIH]

Diabetes Mellitus: A heterogeneous group of disorders that share glucose intolerance in common. [NIH]

Diagnostic Imaging: Any visual display of structural or functional patterns of organs or tissues for diagnostic evaluation. It includes measuring physiologic and metabolic responses to physical and chemical stimuli, as well as ultramicroscopy. [NIH]

Diagnostic procedure: A method used to identify a disease. [NIH]

Diarrhea: Passage of excessively liquid or excessively frequent stools. [NIH]

Diarrhoea: Abnormal frequency and liquidity of faecal discharges. [EU]

Diastolic: Of or pertaining to the diastole. [EU]

Diencephalon: The paired caudal parts of the prosencephalon from which the thalamus, hypothalamus, epithalamus, and subthalamus are derived. [NIH]

Dietitian: An expert in nutrition who helps people plan what and how much food to eat. [NIH]

Diffuse Axonal Injury: A relatively common sequela of blunt head injury, characterized by a global disruption of axons throughout the brain. Associated clinical features may include neurobehavioral manifestations; persistent vegetative state; dementia; and other disorders. [NIH]

Diffusion: The tendency of a gas or solute to pass from a point of higher pressure or concentration to a point of lower pressure or concentration and to distribute itself throughout the available space; a major mechanism of biological transport. [NIH]

Digestion: The process of breakdown of food for metabolism and use by the body. [NIH]

Digestive system: The organs that take in food and turn it into products that the body can use to stay healthy. Waste products the body cannot use leave the body through bowel movements. The digestive system includes the salivary glands, mouth, esophagus, stomach, liver, pancreas, gallbladder, small and large intestines, and rectum. [NIH]

Dihydroxy: AMPA/Kainate antagonist. [NIH]

Dilatation: The act of dilating. [NIH]

Dilatation, Pathologic: The condition of an anatomical structure's being dilated beyond normal dimensions. [NIH]

Dilation: A process by which the pupil is temporarily enlarged with special eye drops (mydriatic); allows the eye care specialist to better view the inside of the eye. [NIH]

Dimethyl: A volatile metabolite of the amino acid methionine. [NIH]

Direct: 1. Straight; in a straight line. 2. Performed immediately and without the intervention of subsidiary means. [EU]

Discrimination: The act of qualitative and/or quantitative differentiation between two or more stimuli. [NIH]

Disinfectant: An agent that disinfects; applied particularly to agents used on inanimate objects. [EU]

Disorientation: The loss of proper bearings, or a state of mental confusion as to time, place, or identity. [EU]

Dissociation: 1. The act of separating or state of being separated. 2. The separation of a molecule into two or more fragments (atoms, molecules, ions, or free radicals) produced by the absorption of light or thermal energy or by solvation. 3. In psychology, a defense mechanism in which a group of mental processes are segregated from the rest of a person's mental activity in order to avoid emotional distress, as in the dissociative disorders (q.v.), or in which an idea or object is segregated from its emotional significance; in the first sense it is roughly equivalent to splitting, in the second, to isolation. 4. A defect of mental integration in which one or more groups of mental processes become separated off from normal consciousness and, thus separated, function as a unitary whole. [EU]

Distal: Remote; farther from any point of reference; opposed to proximal. In dentistry, used to designate a position on the dental arch farther from the median line of the jaw. [EU]

Diuresis: Increased excretion of urine. [EU]

Dizziness: An imprecise term which may refer to a sense of spatial disorientation, motion of the environment, or lightheadedness. [NIH]

Dominance: In genetics, the full phenotypic expression of a gene in both heterozygotes and homozygotes. [EU]

Donepezil: A drug used in the treatment of Alzheimer's disease. It belongs to the family of drugs called cholinesterase inhibitors. It is being studied as a treatment for side effects caused by radiation therapy to the brain. [NIH]

Dopamine: An endogenous catecholamine and prominent neurotransmitter in several systems of the brain. In the synthesis of catecholamines from tyrosine, it is the immediate precursor to norepinephrine and epinephrine. Dopamine is a major transmitter in the extrapyramidal system of the brain, and important in regulating movement. A family of dopaminergic receptor subtypes mediate its action. Dopamine is used pharmacologically for its direct (beta adrenergic agonist) and indirect (adrenergic releasing) sympathomimetic effects including its actions as an inotropic agent and as a renal vasodilator. [NIH]

Dorsal: 1. Pertaining to the back or to any dorsum. 2. Denoting a position more toward the back surface than some other object of reference; same as posterior in human anatomy; superior in the anatomy of quadrupeds. [EU]

Dosage Forms: Completed forms of the pharmaceutical preparation in which prescribed doses of medication are included. They are designed to resist action by gastric fluids, prevent vomiting and nausea, reduce or alleviate the undesirable taste and smells associated with oral administration, achieve a high concentration of drug at target site, or produce a delayed or long-acting drug effect. They include capsules, liniments, ointments, pharmaceutical solutions, powders, tablets, etc. [NIH]

Dose-dependent: Refers to the effects of treatment with a drug. If the effects change when the dose of the drug is changed, the effects are said to be dose dependent. [NIH]

Drug Approval: Process that is gone through in order for a drug to receive approval by a government regulatory agency. This includes any required pre-clinical or clinical testing, review, submission, and evaluation of the applications and test results, and post-marketing surveillance of the drug. [NIH]

Drug Interactions: The action of a drug that may affect the activity, metabolism, or toxicity of another drug. [NIH]

Drug Resistance: Diminished or failed response of an organism, disease or tissue to the intended effectiveness of a chemical or drug. It should be differentiated from drug tolerance which is the progressive diminution of the susceptibility of a human or animal to the effects of a drug, as a result of continued administration. [NIH]

Drug Tolerance: Progressive diminution of the susceptibility of a human or animal to the effects of a drug, resulting from its continued administration. It should be differentiated from drug resistance wherein an organism, disease, or tissue fails to respond to the intended effectiveness of a chemical or drug. It should also be differentiated from maximum tolerated dose and no-observed-adverse-effect level. [NIH]

Duodenum: The first part of the small intestine. [NIH]

Dura mater: The outermost, toughest, and most fibrous of the three membranes (meninges) covering the brain and spinal cord; called also pachymeninx. [EU]

Dynorphins: A class of opioid peptides including dynorphin A, dynorphin B, and smaller fragments of these peptides. Dynorphins prefer kappa-opioid receptors (receptors, opioid, kappa) and have been shown to play a role as central nervous system transmitters. [NIH]

Dyskinesia: Impairment of the power of voluntary movement, resulting in fragmentary or incomplete movements. [EU]

Dyslexia: Partial alexia in which letters but not words may be read, or in which words may

be read but not understood. [NIH]

Dysphagia: Difficulty in swallowing. [EU]

Dysphonia: Difficulty or pain in speaking; impairment of the voice. [NIH]

Dysphoric: A feeling of unpleasantness and discomfort. [NIH]

Dysplasia: Cells that look abnormal under a microscope but are not cancer. [NIH]

Dystonia: Disordered tonicity of muscle. [EU]

Dystrophy: Any disorder arising from defective or faulty nutrition, especially the muscular dystrophies. [EU]

Eating Disorders: A group of disorders characterized by physiological and psychological disturbances in appetite or food intake. [NIH]

Echolalia: The pathological repetition by imitation of the speech of another. [NIH]

Ectopic: Pertaining to or characterized by ectopia. [EU]

Edema: Excessive amount of watery fluid accumulated in the intercellular spaces, most commonly present in subcutaneous tissue. [NIH]

Effector: It is often an enzyme that converts an inactive precursor molecule into an active second messenger. [NIH]

Effector cell: A cell that performs a specific function in response to a stimulus; usually used to describe cells in the immune system. [NIH]

Efficacy: The extent to which a specific intervention, procedure, regimen, or service produces a beneficial result under ideal conditions. Ideally, the determination of efficacy is based on the results of a randomized control trial. [NIH]

Ejaculation: The release of semen through the penis during orgasm. [NIH]

Elasticity: Resistance and recovery from distortion of shape. [NIH]

Elective: Subject to the choice or decision of the patient or physician; applied to procedures that are advantageous to the patient but not urgent. [EU]

Electrocardiogram: Measurement of electrical activity during heartbeats. [NIH]

Electrode: Component of the pacing system which is at the distal end of the lead. It is the interface with living cardiac tissue across which the stimulus is transmitted. [NIH]

Electroencephalography: Recording of electric currents developed in the brain by means of electrodes applied to the scalp, to the surface of the brain, or placed within the substance of the brain. [NIH]

Electrolyte: A substance that dissociates into ions when fused or in solution, and thus becomes capable of conducting electricity; an ionic solute. [EU]

Electrons: Stable elementary particles having the smallest known negative charge, present in all elements; also called negatrons. Positively charged electrons are called positrons. The numbers, energies and arrangement of electrons around atomic nuclei determine the chemical identities of elements. Beams of electrons are called cathode rays or beta rays, the latter being a high-energy biproduct of nuclear decay. [NIH]

Electrophysiological: Pertaining to electrophysiology, that is a branch of physiology that is concerned with the electric phenomena associated with living bodies and involved in their functional activity. [EU]

Electroshock: Induction of a stress reaction in experimental subjects by means of an electrical shock; applies to either convulsive or non-convulsive states. [NIH]

Elementary Particles: Individual components of atoms, usually subatomic; subnuclear

particles are usually detected only when the atomic nucleus decays and then only transiently, as most of them are unstable, often yielding pure energy without substance, i.e., radiation. [NIH]

Embolism: Blocking of a blood vessel by a blood clot or foreign matter that has been transported from a distant site by the blood stream. [NIH]

Embolus: Bit of foreign matter which enters the blood stream at one point and is carried until it is lodged or impacted in an artery and obstructs it. It may be a blood clot, an air bubble, fat or other tissue, or clumps of bacteria. [NIH]

Embryo: The prenatal stage of mammalian development characterized by rapid morphological changes and the differentiation of basic structures. [NIH]

Embryology: The study of the development of an organism during the embryonic and fetal stages of life. [NIH]

Emesis: Vomiting; an act of vomiting. Also used as a word termination, as in haematemesis. [EU]

Emphysema: A pathological accumulation of air in tissues or organs. [NIH]

Empiric: Empirical; depending upon experience or observation alone, without using scientific method or theory. [EU]

Emulsion: A preparation of one liquid distributed in small globules throughout the body of a second liquid. The dispersed liquid is the discontinuous phase, and the dispersion medium is the continuous phase. When oil is the dispersed liquid and an aqueous solution is the continuous phase, it is known as an oil-in-water emulsion, whereas when water or aqueous solution is the dispersed phase and oil or oleaginous substance is the continuous phase, it is known as a water-in-oil emulsion. Pharmaceutical emulsions for which official standards have been promulgated include cod liver oil emulsion, cod liver oil emulsion with malt, liquid petrolatum emulsion, and phenolphthalein in liquid petrolatum emulsion. [EU]

Encapsulated: Confined to a specific, localized area and surrounded by a thin layer of tissue. [NIH]

Encephalitis: Inflammation of the brain due to infection, autoimmune processes, toxins, and other conditions. Viral infections (see encephalitis, viral) are a relatively frequent cause of this condition. [NIH]

Encephalitis, Viral: Inflammation of brain parenchymal tissue as a result of viral infection. Encephalitis may occur as primary or secondary manifestation of Togaviridae infections; Herpesviridae infections; Adenoviridae infections; Flaviviridae infections; Bunyaviridae infections; Picornaviridae infections; Paramyxoviridae infections; Orthomyxoviridae infections; Retroviridae infections; and Arenaviridae infections. [NIH]

Encephalocele: Cerebral tissue herniation through a congenital or acquired defect in the skull. The majority of congenital encephaloceles occur in the occipital or frontal regions. Clinical features include a protuberant mass that may be pulsatile. The quantity and location of protruding neural tissue determines the type and degree of neurologic deficit. Visual defects, psychomotor developmental delay, and persistent motor deficits frequently occur. [NIH]

Encephalopathy: A disorder of the brain that can be caused by disease, injury, drugs, or chemicals. [NIH]

Endarterectomy: Surgical excision, performed under general anesthesia, of the atheromatous tunica intima of an artery. When reconstruction of an artery is performed as an endovascular procedure through a catheter, it is called atherectomy. [NIH]

Endemic: Present or usually prevalent in a population or geographical area at all times; said

of a disease or agent. Called also endemial. [EU]

Endocrine System: The system of glands that release their secretions (hormones) directly into the circulatory system. In addition to the endocrine glands, included are the chromaffin system and the neurosecretory systems. [NIH]

Endometrium: The layer of tissue that lines the uterus. [NIH]

Endopeptidases: A subclass of peptide hydrolases. They are classified primarily by their catalytic mechanism. Specificity is used only for identification of individual enzymes. They comprise the serine endopeptidases, EC 3.4.21; cysteine endopeptidases, EC 3.4.22; aspartic endopeptidases, EC 3.4.23, metalloendopeptidases, EC 3.4.24; and a group of enzymes yet to be assigned to any of the above sub-classes, EC 3.4.99. EC 3.4.-. [NIH]

Endorphin: Opioid peptides derived from beta-lipotropin. Endorphin is the most potent naturally occurring analgesic agent. It is present in pituitary, brain, and peripheral tissues. [NIH]

Endothelial cell: The main type of cell found in the inside lining of blood vessels, lymph vessels, and the heart. [NIH]

Endotoxins: Toxins closely associated with the living cytoplasm or cell wall of certain microorganisms, which do not readily diffuse into the culture medium, but are released upon lysis of the cells. [NIH]

End-stage renal: Total chronic kidney failure. When the kidneys fail, the body retains fluid and harmful wastes build up. A person with ESRD needs treatment to replace the work of the failed kidneys. [NIH]

Enkephalins: One of the three major families of endogenous opioid peptides. The enkephalins are pentapeptides that are widespread in the central and peripheral nervous systems and in the adrenal medulla. [NIH]

Entorhinal Cortex: Cortex where the signals are combined with those from other sensory systems. [NIH]

Environmental Exposure: The exposure to potentially harmful chemical, physical, or biological agents in the environment or to environmental factors that may include ionizing radiation, pathogenic organisms, or toxic chemicals. [NIH]

Environmental Health: The science of controlling or modifying those conditions, influences, or forces surrounding man which relate to promoting, establishing, and maintaining health. [NIH]

Enzymatic: Phase where enzyme cuts the precursor protein. [NIH]

Enzyme: A protein that speeds up chemical reactions in the body. [NIH]

Epidemiologic Studies: Studies designed to examine associations, commonly, hypothesized causal relations. They are usually concerned with identifying or measuring the effects of risk factors or exposures. The common types of analytic study are case-control studies, cohort studies, and cross-sectional studies. [NIH]

Epidemiological: Relating to, or involving epidemiology. [EU]

Epilepsia: An illusional seizure consisting of a rather sudden alteration of the patient's perceptions, indicative of a lesion in the temporal lobes. [NIH]

Epilepticus: Repeated and prolonged epileptic seizures without recovery of consciousness between attacks. [NIH]

Epinephrine: The active sympathomimetic hormone from the adrenal medulla in most species. It stimulates both the alpha- and beta- adrenergic systems, causes systemic vasoconstriction and gastrointestinal relaxation, stimulates the heart, and dilates bronchi

and cerebral vessels. It is used in asthma and cardiac failure and to delay absorption of local anesthetics. [NIH]

Epithalamus: The dorsal posterior subdivision of the diencephalon. The epithalamus is generally considered to include the habenular nuclei (habenula) and associated fiber bundles, the pineal body, and the epithelial roof of the third ventricle. The anterior and posterior paraventricular nuclei of the thalamus are included with the thalamic nuclei although they develop from the same pronuclear mass as the epithalamic nuclei and are sometimes considered part of the epithalamus. [NIH]

Epithelial: Refers to the cells that line the internal and external surfaces of the body. [NIH]

Erythrocyte Volume: Volume of circulating erythrocytes. It is usually measured by radioisotope dilution technique. [NIH]

Erythrocytes: Red blood cells. Mature erythrocytes are non-nucleated, biconcave disks containing hemoglobin whose function is to transport oxygen. [NIH]

Esophagus: The muscular tube through which food passes from the throat to the stomach. [NIH]

Essential Tremor: A rhythmic, involuntary, purposeless, oscillating movement resulting from the alternate contraction and relaxation of opposing groups of muscles. [NIH]

Estradiol: The most potent mammalian estrogenic hormone. It is produced in the ovary, placenta, testis, and possibly the adrenal cortex. [NIH]

Estrogen: One of the two female sex hormones. [NIH]

Estrone: 3-Hydroxyestra-1,3,5(10)-trien-17-one. A metabolite of estradiol but possessing less biological activity. It is found in the urine of pregnant women and mares, in the human placenta, and in the urine of bulls and stallions. According to the Fourth Annual Report on Carcinogens (NTP 85-002, 1985), estrone may reasonably be anticipated to be a carcinogen (Merck, 11th ed). [NIH]

Ethanol: A clear, colorless liquid rapidly absorbed from the gastrointestinal tract and distributed throughout the body. It has bactericidal activity and is used often as a topical disinfectant. It is widely used as a solvent and preservative in pharmaceutical preparations as well as serving as the primary ingredient in alcoholic beverages. [NIH]

Ether: One of a class of organic compounds in which any two organic radicals are attached directly to a single oxygen atom. [NIH]

Ethidium: A trypanocidal agent and possible antiviral agent that is widely used in experimental cell biology and biochemistry. Ethidium has several experimentally useful properties including binding to nucleic acids, noncompetitive inhibition of nicotinic acetylcholine receptors, and fluorescence among others. It is most commonly used as the bromide. [NIH]

Ethmoid: An unpaired cranial bone which helps form the medial walls of the orbits and contains the themoidal air cells which drain into the nose. [NIH]

Ethnic Groups: A group of people with a common cultural heritage that sets them apart from others in a variety of social relationships. [NIH]

Ethosuximide: An anticonvulsant especially useful in the treatment of absence seizures unaccompanied by other types of seizures. [NIH]

Eukaryotic Cells: Cells of the higher organisms, containing a true nucleus bounded by a nuclear membrane. [NIH]

Evacuation: An emptying, as of the bowels. [EU]

Evoke: The electric response recorded from the cerebral cortex after stimulation of a

peripheral sense organ. [NIH]

Evoked Potentials: The electric response evoked in the central nervous system by stimulation of sensory receptors or some point on the sensory pathway leading from the receptor to the cortex. The evoked stimulus can be auditory, somatosensory, or visual, although other modalities have been reported. Event-related potentials is sometimes used synonymously with evoked potentials but is often associated with the execution of a motor, cognitive, or psychophysiological task, as well as with the response to a stimulus. [NIH]

Excitability: Property of a cardiac cell whereby, when the cell is depolarized to a critical level (called threshold), the membrane becomes permeable and a regenerative inward current causes an action potential. [NIH]

Excitation: An act of irritation or stimulation or of responding to a stimulus; the addition of energy, as the excitation of a molecule by absorption of photons. [EU]

Excitatory: When cortical neurons are excited, their output increases and each new input they receive while they are still excited raises their output markedly. [NIH]

Excitatory Amino Acid Agonists: Drugs that bind to and activate excitatory amino acid receptors. [NIH]

Excitatory Amino Acids: Endogenous amino acids released by neurons as excitatory neurotransmitters. Glutamic acid is the most common excitatory neurotransmitter in the brain. Aspartic acid has been regarded as an excitatory transmitter for many years, but the extent of its role as a transmitter is unclear. [NIH]

Excitotoxicity: Excessive exposure to glutamate or related compounds can kill brain neurons, presumably by overstimulating them. [NIH]

Exhaustion: The feeling of weariness of mind and body. [NIH]

Exocytosis: Cellular release of material within membrane-limited vesicles by fusion of the vesicles with the cell membrane. [NIH]

Exon: The part of the DNA that encodes the information for the actual amino acid sequence of the protein. In many eucaryotic genes, the coding sequences consist of a series of exons alternating with intron sequences. [NIH]

Expectorant: 1. Promoting the ejection, by spitting, of mucus or other fluids from the lungs and trachea. 2. An agent that promotes the ejection of mucus or exudate from the lungs, bronchi, and trachea; sometimes extended to all remedies that quiet cough (antitussives). [EU]

Extracellular: Outside a cell or cells. [EU]

Extracellular Matrix: A meshwork-like substance found within the extracellular space and in association with the basement membrane of the cell surface. It promotes cellular proliferation and provides a supporting structure to which cells or cell lysates in culture dishes adhere. [NIH]

Extracellular Space: Interstitial space between cells, occupied by fluid as well as amorphous and fibrous substances. [NIH]

Extraction: The process or act of pulling or drawing out. [EU]

Extrapyramidal: Outside of the pyramidal tracts. [EU]

Eye Movements: Voluntary or reflex-controlled movements of the eye. [NIH]

Facial: Of or pertaining to the face. [EU]

Facial Pain: Pain in the facial region including orofacial pain and craniofacial pain. Associated conditions include local inflammatory and neoplastic disorders and neuralgic syndromes involving the trigeminal, facial, and glossopharyngeal nerves. Conditions which

feature recurrent or persistent facial pain as the primary manifestation of disease are referred to as facial pain syndromes. [NIH]

Facial Paralysis: Severe or complete loss of facial muscle motor function. This condition may result from central or peripheral lesions. Damage to CNS motor pathways from the cerebral cortex to the facial nuclei in the pons leads to facial weakness that generally spares the forehead muscles. Facial nerve diseases generally results in generalized hemifacial weakness. Neuromuscular junction diseases and muscular diseases may also cause facial paralysis or paresis. [NIH]

Faecal: Pertaining to or of the nature of feces. [EU]

Family Planning: Programs or services designed to assist the family in controlling reproduction by either improving or diminishing fertility. [NIH]

Fat: Total lipids including phospholipids. [NIH]

Fatty acids: A major component of fats that are used by the body for energy and tissue development. [NIH]

Febrile: Pertaining to or characterized by fever. [EU]

Feces: The excrement discharged from the intestines, consisting of bacteria, cells exfoliated from the intestines, secretions, chiefly of the liver, and a small amount of food residue. [EU]

Fetal Development: Morphologic and physiologic growth and development of the mammalian embryo or fetus. [NIH]

Fetus: The developing offspring from 7 to 8 weeks after conception until birth. [NIH]

Fibrillation: A small, local, involuntary contraction of muscle, invisible under the skin, resulting from spontaneous activation of single muscle cells or muscle fibres. [EU]

Fibrosis: Any pathological condition where fibrous connective tissue invades any organ, usually as a consequence of inflammation or other injury. [NIH]

Fissure: Any cleft or groove, normal or otherwise; especially a deep fold in the cerebral cortex which involves the entire thickness of the brain wall. [EU]

Flumazenil: A potent benzodiazepine receptor antagonist. Since it reverses the sedative and other actions of benzodiazepines, it has been suggested as an antidote to benzodiazepine overdoses. [NIH]

Fluorescence: The property of emitting radiation while being irradiated. The radiation emitted is usually of longer wavelength than that incident or absorbed, e.g., a substance can be irradiated with invisible radiation and emit visible light. X-ray fluorescence is used in diagnosis. [NIH]

Fluorine: A nonmetallic, diatomic gas that is a trace element and member of the halogen family. It is used in dentistry as flouride to prevent dental caries. [NIH]

Folate: A B-complex vitamin that is being studied as a cancer prevention agent. Also called folic acid. [NIH]

Fold: A plication or doubling of various parts of the body. [NIH]

Folic Acid: N-(4-(((2-Amino-1,4-dihydro-4-oxo-6-pteridinyl)methyl)amino)benzoyl)-L-glutamic acid. A member of the vitamin B family that stimulates the hematopoietic system. It is present in the liver and kidney and is found in mushrooms, spinach, yeast, green leaves, and grasses. Folic acid is used in the treatment and prevention of folate deficiencies and megaloblastic anemia. [NIH]

Forearm: The part between the elbow and the wrist. [NIH]

Fornix: A bundle of nerves connected to the hippocampus. [NIH]

Fossa: A cavity, depression, or pit. [NIH]

Frontal Lobe: The anterior part of the cerebral hemisphere. [NIH]

Functional Disorders: Disorders such as irritable bowel syndrome. These conditions result from poor nerve and muscle function. Symptoms such as gas, pain, constipation, and diarrhea come back again and again, but there are no signs of disease or damage. Emotional stress can trigger symptoms. Also called motility disorders. [NIH]

GABA: The most common inhibitory neurotransmitter in the central nervous system. [NIH]

Gallbladder: The pear-shaped organ that sits below the liver. Bile is concentrated and stored in the gallbladder. [NIH]

Ganglia: Clusters of multipolar neurons surrounded by a capsule of loosely organized connective tissue located outside the central nervous system. [NIH]

Gap Junctions: Connections between cells which allow passage of small molecules and electric current. Gap junctions were first described anatomically as regions of close apposition between cells with a narrow (1-2 nm) gap between cell membranes. The variety in the properties of gap junctions is reflected in the number of connexins, the family of proteins which form the junctions. [NIH]

Gas: Air that comes from normal breakdown of food. The gases are passed out of the body through the rectum (flatus) or the mouth (burp). [NIH]

Gastric: Having to do with the stomach. [NIH]

Gastric Acid: Hydrochloric acid present in gastric juice. [NIH]

Gastrin: A hormone released after eating. Gastrin causes the stomach to produce more acid. [NIH]

Gastritis: Inflammation of the stomach. [EU]

Gastroenteritis: An acute inflammation of the lining of the stomach and intestines, characterized by anorexia, nausea, diarrhoea, abdominal pain, and weakness, which has various causes, including food poisoning due to infection with such organisms as Escherichia coli, Staphylococcus aureus, and Salmonella species; consumption of irritating food or drink; or psychological factors such as anger, stress, and fear. Called also enterogastritis. [EU]

Gastrointestinal: Refers to the stomach and intestines. [NIH]

Gastrointestinal tract: The stomach and intestines. [NIH]

Gelatin: A product formed from skin, white connective tissue, or bone collagen. It is used as a protein food adjuvant, plasma substitute, hemostatic, suspending agent in pharmaceutical preparations, and in the manufacturing of capsules and suppositories. [NIH]

Gene: The functional and physical unit of heredity passed from parent to offspring. Genes are pieces of DNA, and most genes contain the information for making a specific protein. [NIH]

Gene Expression: The phenotypic manifestation of a gene or genes by the processes of gene action. [NIH]

Generator: Any system incorporating a fixed parent radionuclide from which is produced a daughter radionuclide which is to be removed by elution or by any other method and used in a radiopharmaceutical. [NIH]

Genetic Code: The specifications for how information, stored in nucleic acid sequence (base sequence), is translated into protein sequence (amino acid sequence). The start, stop, and order of amino acids of a protein is specified by consecutive triplets of nucleotides called codons (codon). [NIH]

Genetic Engineering: Directed modification of the gene complement of a living organism by such techniques as altering the DNA, substituting genetic material by means of a virus, transplanting whole nuclei, transplanting cell hybrids, etc. [NIH]

Genetic Screening: Searching a population or individuals for persons possessing certain genotypes or karyotypes that: (1) are already associated with disease or predispose to disease; (2) may lead to disease in their descendants; or (3) produce other variations not known to be associated with disease. Genetic screening may be directed toward identifying phenotypic expression of genetic traits. It includes prenatal genetic screening. [NIH]

Genetic testing: Analyzing DNA to look for a genetic alteration that may indicate an increased risk for developing a specific disease or disorder. [NIH]

Genetics: The biological science that deals with the phenomena and mechanisms of heredity. [NIH]

Genotype: The genetic constitution of the individual; the characterization of the genes. [NIH]

Geriatric: Pertaining to the treatment of the aged. [EU]

Germ Cells: The reproductive cells in multicellular organisms. [NIH]

Gestation: The period of development of the young in viviparous animals, from the time of fertilization of the ovum until birth. [EU]

Gestational: Psychosis attributable to or occurring during pregnancy. [NIH]

Gestational Age: Age of the conceptus. In humans, this may be assessed by medical history, physical examination, early immunologic pregnancy tests, radiography, ultrasonography, and amniotic fluid analysis. [NIH]

Ginseng: An araliaceous genus of plants that contains a number of pharmacologically active agents used as stimulants, sedatives, and tonics, especially in traditional medicine. [NIH]

Gland: An organ that produces and releases one or more substances for use in the body. Some glands produce fluids that affect tissues or organs. Others produce hormones or participate in blood production. [NIH]

Glioma: A cancer of the brain that comes from glial, or supportive, cells. [NIH]

Gliosis: The production of a dense fibrous network of neuroglia; includes astrocytosis, which is a proliferation of astrocytes in the area of a degenerative lesion. [NIH]

Glomeruli: Plural of glomerulus. [NIH]

Glossopharyngeal Nerve: The 9th cranial nerve. The glossopharyngeal nerve is a mixed motor and sensory nerve; it conveys somatic and autonomic efferents as well as general, special, and visceral afferents. Among the connections are motor fibers to the stylopharyngeus muscle, parasympathetic fibers to the parotid glands, general and taste afferents from the posterior third of the tongue, the nasopharynx, and the palate, and afferents from baroreceptors and chemoreceptors of the carotid sinus. [NIH]

Glucocorticoid: A compound that belongs to the family of compounds called corticosteroids (steroids). Glucocorticoids affect metabolism and have anti-inflammatory and immunosuppressive effects. They may be naturally produced (hormones) or synthetic (drugs). [NIH]

Glucose: D-Glucose. A primary source of energy for living organisms. It is naturally occurring and is found in fruits and other parts of plants in its free state. It is used therapeutically in fluid and nutrient replacement. [NIH]

Glucose Intolerance: A pathological state in which the fasting plasma glucose level is less than 140 mg per deciliter and the 30-, 60-, or 90-minute plasma glucose concentration following a glucose tolerance test exceeds 200 mg per deciliter. This condition is seen

frequently in diabetes mellitus but also occurs with other diseases. [NIH]

Glutamate: Excitatory neurotransmitter of the brain. [NIH]

Glutamic Acid: A non-essential amino acid naturally occurring in the L-form. Glutamic acid (glutamate) is the most common excitatory neurotransmitter in the central nervous system. [NIH]

Glycerol: A trihydroxy sugar alcohol that is an intermediate in carbohydrate and lipid metabolism. It is used as a solvent, emollient, pharmaceutical agent, and sweetening agent. [NIH]

Glycine: A non-essential amino acid. It is found primarily in gelatin and silk fibroin and used therapeutically as a nutrient. It is also a fast inhibitory neurotransmitter. [NIH]

Glycoprotein: A protein that has sugar molecules attached to it. [NIH]

Gonad: A sex organ, such as an ovary or a testicle, which produces the gametes in most multicellular animals. [NIH]

Gonadal: Pertaining to a gonad. [EU]

Governing Board: The group in which legal authority is vested for the control of health-related institutions and organizations. [NIH]

Gp120: 120-kD HIV envelope glycoprotein which is involved in the binding of the virus to its membrane receptor, the CD4 molecule, found on the surface of certain cells in the body. [NIH]

Grade: The grade of a tumor depends on how abnormal the cancer cells look under a microscope and how quickly the tumor is likely to grow and spread. Grading systems are different for each type of cancer. [NIH]

Graft: Healthy skin, bone, or other tissue taken from one part of the body and used to replace diseased or injured tissue removed from another part of the body. [NIH]

Grafting: The operation of transfer of tissue from one site to another. [NIH]

Granule: A small pill made from sucrose. [EU]

Granulocytes: Leukocytes with abundant granules in the cytoplasm. They are divided into three groups: neutrophils, eosinophils, and basophils. [NIH]

Grasses: A large family, Gramineae, of narrow-leaved herbaceous monocots. Many grasses produce highly allergenic pollens and are hosts to cattle parasites and toxic fungi. [NIH]

Gravis: Eruption of watery blisters on the skin among those handling animals and animal products. [NIH]

Growth: The progressive development of a living being or part of an organism from its earliest stage to maturity. [NIH]

Gynaecological: Pertaining to gynaecology. [EU]

Gyrus Cinguli: One of the convolutions on the medial surface of the cerebral hemisphere. It surrounds the rostral part of the brain and interhemispheric commissure and forms part of the limbic system. [NIH]

Habitat: An area considered in terms of its environment, particularly as this determines the type and quality of the vegetation the area can carry. [NIH]

Haematemesis: The vomiting of blood. [EU]

Haematoma: A localized collection of blood, usually clotted, in an organ, space, or tissue, due to a break in the wall of a blood vessel. [EU]

Haemorrhage: The escape of blood from the vessels; bleeding. Small haemorrhages are classified according to size as petechiae (very small), purpura (up to 1 cm), and ecchymoses

(larger). The massive accumulation of blood within a tissue is called a haematoma. [EU]

Half-Life: The time it takes for a substance (drug, radioactive nuclide, or other) to lose half of its pharmacologic, physiologic, or radiologic activity. [NIH]

Hallucinogens: Drugs capable of inducing illusions, hallucinations, delusions, paranoid ideations, and other alterations of mood and thinking. Despite the name, the feature that distinguishes these agents from other classes of drugs is their capacity to induce states of altered perception, thought, and feeling that are not experienced otherwise. [NIH]

Hamartoma: A focal malformation resembling a neoplasm, composed of an overgrowth of mature cells and tissues that normally occur in the affected area. [NIH]

Handedness: Preference for using right or left hand. [NIH]

Haptens: Small antigenic determinants capable of eliciting an immune response only when coupled to a carrier. Haptens bind to antibodies but by themselves cannot elicit an antibody response. [NIH]

Headache: Pain in the cranial region that may occur as an isolated and benign symptom or as a manifestation of a wide variety of conditions including subarachnoid hemorrhage; craniocerebral trauma; central nervous system infections; intracranial hypertension; and other disorders. In general, recurrent headaches that are not associated with a primary disease process are referred to as headache disorders (e.g., migraine). [NIH]

Headache Disorders: Common conditions characterized by persistent or recurrent headaches. Headache syndrome classification systems may be based on etiology (e.g., vascular headache, post-traumatic headaches, etc.), temporal pattern (e.g., cluster headache, paroxysmal hemicrania, etc.), and precipitating factors (e.g., cough headache). [NIH]

Health Policy: Decisions, usually developed by government policymakers, for determining present and future objectives pertaining to the health care system. [NIH]

Health Status: The level of health of the individual, group, or population as subjectively assessed by the individual or by more objective measures. [NIH]

Hearing Disorders: Conditions that impair the transmission or perception of auditory impulses and information from the level of the ear to the temporal cortices, including the sensorineural pathways. [NIH]

Heart attack: A seizure of weak or abnormal functioning of the heart. [NIH]

Heart failure: Loss of pumping ability by the heart, often accompanied by fatigue, breathlessness, and excess fluid accumulation in body tissues. [NIH]

Heartbeat: One complete contraction of the heart. [NIH]

Helminthiasis: Infestation with parasitic worms of the helminth class. [NIH]

Helminths: Commonly known as parasitic worms, this group includes the acanthocephala, nematoda, and platyhelminths. Some authors consider certain species of leeches that can become temporarily parasitic as helminths. [NIH]

Heme: The color-furnishing portion of hemoglobin. It is found free in tissues and as the prosthetic group in many hemeproteins. [NIH]

Hemiparesis: The weakness or paralysis affecting one side of the body. [NIH]

Hemoglobin: One of the fractions of glycosylated hemoglobin A1c. Glycosylated hemoglobin is formed when linkages of glucose and related monosaccharides bind to hemoglobin A and its concentration represents the average blood glucose level over the previous several weeks. HbA1c levels are used as a measure of long-term control of plasma glucose (normal, 4 to 6 percent). In controlled diabetes mellitus, the concentration of glycosylated hemoglobin A is within the normal range, but in uncontrolled cases the level

may be 3 to 4 times the normal conentration. Generally, complications are substantially lower among patients with Hb levels of 7 percent or less than in patients with HbA1c levels of 9 percent or more. [NIH]

Hemoglobin A: Normal adult human hemoglobin. The globin moiety consists of two alpha and two beta chains. [NIH]

Hemoglobinuria: The presence of free hemoglobin in the urine. [NIH]

Hemorrhage: Bleeding or escape of blood from a vessel. [NIH]

Hemostasis: The process which spontaneously arrests the flow of blood from vessels carrying blood under pressure. It is accomplished by contraction of the vessels, adhesion and aggregation of formed blood elements, and the process of blood or plasma coagulation. [NIH]

Hepatic: Refers to the liver. [NIH]

Hepatitis: Inflammation of the liver and liver disease involving degenerative or necrotic alterations of hepatocytes. [NIH]

Hepatitis A: Hepatitis caused by hepatovirus. It can be transmitted through fecal contamination of food or water. [NIH]

Hepatocytes: The main structural component of the liver. They are specialized epithelial cells that are organized into interconnected plates called lobules. [NIH]

Hepatovirus: A genus of Picornaviridae causing infectious hepatitis naturally in humans and experimentally in other primates. It is transmitted through fecal contamination of food or water. [NIH]

Hereditary: Of, relating to, or denoting factors that can be transmitted genetically from one generation to another. [NIH]

Heredity: 1. The genetic transmission of a particular quality or trait from parent to offspring. 2. The genetic constitution of an individual. [EU]

Herpes: Any inflammatory skin disease caused by a herpesvirus and characterized by the formation of clusters of small vesicles. When used alone, the term may refer to herpes simplex or to herpes zoster. [EU]

Herpes virus: A member of the herpes family of viruses. [NIH]

Herpes Zoster: Acute vesicular inflammation. [NIH]

Heterogeneity: The property of one or more samples or populations which implies that they are not identical in respect of some or all of their parameters, e. g. heterogeneity of variance. [NIH]

Hippocampus: A curved elevation of gray matter extending the entire length of the floor of the temporal horn of the lateral ventricle (Dorland, 28th ed). The hippocampus, subiculum, and dentate gyrus constitute the hippocampal formation. Sometimes authors include the entorhinal cortex in the hippocampal formation. [NIH]

Histamine: 1H-Imidazole-4-ethanamine. A depressor amine derived by enzymatic decarboxylation of histidine. It is a powerful stimulant of gastric secretion, a constrictor of bronchial smooth muscle, a vasodilator, and also a centrally acting neurotransmitter. [NIH]

Histidine: An essential amino acid important in a number of metabolic processes. It is required for the production of histamine. [NIH]

Histiocytosis: General term for the abnormal appearance of histiocytes in the blood. Based on the pathological features of the cells involved rather than on clinical findings, the histiocytic diseases are subdivided into three groups: Langerhans cell histiocytosis, non-Langerhans cell histiocytosis, and malignant histiocytic disorders. [NIH]

Homeostasis: The processes whereby the internal environment of an organism tends to remain balanced and stable. [NIH]

Homologous: Corresponding in structure, position, origin, etc., as (a) the feathers of a bird and the scales of a fish, (b) antigen and its specific antibody, (c) allelic chromosomes. [EU]

Hormonal: Pertaining to or of the nature of a hormone. [EU]

Hormone: A substance in the body that regulates certain organs. Hormones such as gastrin help in breaking down food. Some hormones come from cells in the stomach and small intestine. [NIH]

Hormone Replacement Therapy: Therapeutic use of hormones to alleviate the effects of hormone deficiency. [NIH]

Host: Any animal that receives a transplanted graft. [NIH]

Hybrid: Cross fertilization between two varieties or, more usually, two species of vines, see also crossing. [NIH]

Hybridization: The genetic process of crossbreeding to produce a hybrid. Hybrid nucleic acids can be formed by nucleic acid hybridization of DNA and RNA molecules. Protein hybridization allows for hybrid proteins to be formed from polypeptide chains. [NIH]

Hydrocephalus: Excessive accumulation of cerebrospinal fluid within the cranium which may be associated with dilation of cerebral ventricles, intracranial hypertension; headache; lethargy; urinary incontinence; and ataxia (and in infants macrocephaly). This condition may be caused by obstruction of cerebrospinal fluid pathways due to neurologic abnormalities, intracranial hemorrhages; central nervous system infections; brain neoplasms; craniocerebral trauma; and other conditions. Impaired resorption of cerebrospinal fluid from the arachnoid villi results in a communicating form of hydrocephalus. Hydrocephalus ex-vacuo refers to ventricular dilation that occurs as a result of brain substance loss from cerebral infarction and other conditions. [NIH]

Hydrofluoric Acid: A solution of hydrogen fluoride in water. It is a colorless fuming liquid which can cause painful burns. [NIH]

Hydrogen: The first chemical element in the periodic table. It has the atomic symbol H, atomic number 1, and atomic weight 1. It exists, under normal conditions, as a colorless, odorless, tasteless, diatomic gas. Hydrogen ions are protons. Besides the common H1 isotope, hydrogen exists as the stable isotope deuterium and the unstable, radioactive isotope tritium. [NIH]

Hydrolysis: The process of cleaving a chemical compound by the addition of a molecule of water. [NIH]

Hypercholesterolemia: Abnormally high levels of cholesterol in the blood. [NIH]

Hyperglycaemia: Abnormally increased content of sugar in the blood. [EU]

Hyperlipidaemia: A general term for elevated concentrations of any or all of the lipids in the plasma, including hyperlipoproteinaemia, hypercholesterolaemia, etc. [EU]

Hyperlipidemia: An excess of lipids in the blood. [NIH]

Hyperphagia: Ingestion of a greater than optimal quantity of food. [NIH]

Hypersensitivity: Altered reactivity to an antigen, which can result in pathologic reactions upon subsequent exposure to that particular antigen. [NIH]

Hypertension: Persistently high arterial blood pressure. Currently accepted threshold levels are 140 mm Hg systolic and 90 mm Hg diastolic pressure. [NIH]

Hypertrophy: General increase in bulk of a part or organ, not due to tumor formation, nor to an increase in the number of cells. [NIH]

Hyperventilation: A pulmonary ventilation rate faster than is metabolically necessary for the exchange of gases. It is the result of an increased frequency of breathing, an increased tidal volume, or a combination of both. It causes an excess intake of oxygen and the blowing off of carbon dioxide. [NIH]

Hypoglossal Nerve: The 12th cranial nerve. The hypoglossal nerve originates in the hypoglossal nucleus of the medulla and supplies motor innervation to all of the muscles of the tongue except the palatoglossus (which is supplied by the vagus). This nerve also contains proprioceptive afferents from the tongue muscles. [NIH]

Hypoglycaemia: An abnormally diminished concentration of glucose in the blood, which may lead to tremulousness, cold sweat, piloerection, hypothermia, and headache, accompanied by irritability, confusion, hallucinations, bizarre behaviour, and ultimately, convulsions and coma. [EU]

Hypoglycemia: Abnormally low blood sugar [NIH]

Hypoglycemic: An orally active drug that produces a fall in blood glucose concentration. [NIH]

Hypokinesia: Slow or diminished movement of body musculature. It may be associated with basal ganglia diseases; mental disorders; prolonged inactivity due to illness; experimental protocols used to evaluate the physiologic effects of immobility; and other conditions. [NIH]

Hypoplasia: Incomplete development or underdevelopment of an organ or tissue. [EU]

Hypotension: Abnormally low blood pressure. [NIH]

Hypothalamic: Of or involving the hypothalamus. [EU]

Hypothalamus: Ventral part of the diencephalon extending from the region of the optic chiasm to the caudal border of the mammillary bodies and forming the inferior and lateral walls of the third ventricle. [NIH]

Hypoxia: Reduction of oxygen supply to tissue below physiological levels despite adequate perfusion of the tissue by blood. [EU]

Iatrogenic: Resulting from the activity of physicians. Originally applied to disorders induced in the patient by autosuggestion based on the physician's examination, manner, or discussion, the term is now applied to any adverse condition in a patient occurring as the result of treatment by a physician or surgeon, especially to infections acquired by the patient during the course of treatment. [EU]

Ibotenic Acid: Neurotoxic isoxazole substance found in Amanita muscaria and A. pantherina. It causes motor depression, ataxia, and changes in mood, perceptions and feelings, and is a potent excitatory amino acid agonist. [NIH]

Id: The part of the personality structure which harbors the unconscious instinctive desires and strivings of the individual. [NIH]

Idiopathic: Describes a disease of unknown cause. [NIH]

Illusion: A false interpretation of a genuine percept. [NIH]

Imaging procedures: Methods of producing pictures of areas inside the body. [NIH]

Immaturity: The state or quality of being unripe or not fully developed. [EU]

Immune response: The activity of the immune system against foreign substances (antigens). [NIH]

Immune system: The organs, cells, and molecules responsible for the recognition and disposal of foreign ("non-self") material which enters the body. [NIH]

Immunity: Nonsusceptibility to the invasive or pathogenic effects of foreign

microorganisms or to the toxic effect of antigenic substances. [NIH]

Immunodeficiency: The decreased ability of the body to fight infection and disease. [NIH]

Immunofluorescence: A technique for identifying molecules present on the surfaces of cells or in tissues using a highly fluorescent substance coupled to a specific antibody. [NIH]

Immunohistochemistry: Histochemical localization of immunoreactive substances using labeled antibodies as reagents. [NIH]

Immunologic: The ability of the antibody-forming system to recall a previous experience with an antigen and to respond to a second exposure with the prompt production of large amounts of antibody. [NIH]

Immunology: The study of the body's immune system. [NIH]

Immunosuppressive: Describes the ability to lower immune system responses. [NIH]

Immunotherapy: Manipulation of the host's immune system in treatment of disease. It includes both active and passive immunization as well as immunosuppressive therapy to prevent graft rejection. [NIH]

Immunotoxin: An antibody linked to a toxic substance. Some immmunotoxins can bind to cancer cells and kill them. [NIH]

Impairment: In the context of health experience, an impairment is any loss or abnormality of psychological, physiological, or anatomical structure or function. [NIH]

Implantation: The insertion or grafting into the body of biological, living, inert, or radioactive material. [EU]

In situ: In the natural or normal place; confined to the site of origin without invasion of neighbouring tissues. [EU]

In Situ Hybridization: A technique that localizes specific nucleic acid sequences within intact chromosomes, eukaryotic cells, or bacterial cells through the use of specific nucleic acid-labeled probes. [NIH]

In vitro: In the laboratory (outside the body). The opposite of in vivo (in the body). [NIH]

In vivo: In the body. The opposite of in vitro (outside the body or in the laboratory). [NIH]

Incision: A cut made in the body during surgery. [NIH]

Incontinence: Inability to control the flow of urine from the bladder (urinary incontinence) or the escape of stool from the rectum (fecal incontinence). [NIH]

Indicative: That indicates; that points out more or less exactly; that reveals fairly clearly. [EU]

Induction: The act or process of inducing or causing to occur, especially the production of a specific morphogenetic effect in the developing embryo through the influence of evocators or organizers, or the production of anaesthesia or unconsciousness by use of appropriate agents. [EU]

Infancy: The period of complete dependency prior to the acquisition of competence in walking, talking, and self-feeding. [NIH]

Infant, Newborn: An infant during the first month after birth. [NIH]

Infantile: Pertaining to an infant or to infancy. [EU]

Infarction: A pathological process consisting of a sudden insufficient blood supply to an area, which results in necrosis of that area. It is usually caused by a thrombus, an embolus, or a vascular torsion. [NIH]

Infection: 1. Invasion and multiplication of microorganisms in body tissues, which may be clinically unapparent or result in local cellular injury due to competitive metabolism, toxins,

intracellular replication, or antigen-antibody response. The infection may remain localized, subclinical, and temporary if the body's defensive mechanisms are effective. A local infection may persist and spread by extension to become an acute, subacute, or chronic clinical infection or disease state. A local infection may also become systemic when the microorganisms gain access to the lymphatic or vascular system. 2. An infectious disease. [EU]

Infertility: The diminished or absent ability to conceive or produce an offspring while sterility is the complete inability to conceive or produce an offspring. [NIH]

Infestation: Parasitic attack or subsistence on the skin and/or its appendages, as by insects, mites, or ticks; sometimes used to denote parasitic invasion of the organs and tissues, as by helminths. [NIH]

Inflammation: A pathological process characterized by injury or destruction of tissues caused by a variety of cytologic and chemical reactions. It is usually manifested by typical signs of pain, heat, redness, swelling, and loss of function. [NIH]

Influenza: An acute viral infection involving the respiratory tract. It is marked by inflammation of the nasal mucosa, the pharynx, and conjunctiva, and by headache and severe, often generalized, myalgia. [NIH]

Infusion: A method of putting fluids, including drugs, into the bloodstream. Also called intravenous infusion. [NIH]

Inhalation: The drawing of air or other substances into the lungs. [EU]

Initiation: Mutation induced by a chemical reactive substance causing cell changes; being a step in a carcinogenic process. [NIH]

Initiator: A chemically reactive substance which may cause cell changes if ingested, inhaled or absorbed into the body; the substance may thus initiate a carcinogenic process. [NIH]

Innervation: 1. The distribution or supply of nerves to a part. 2. The supply of nervous energy or of nerve stimulus sent to a part. [EU]

Inositol: An isomer of glucose that has traditionally been considered to be a B vitamin although it has an uncertain status as a vitamin and a deficiency syndrome has not been identified in man. (From Martindale, The Extra Pharmacopoeia, 30th ed, p1379) Inositol phospholipids are important in signal transduction. [NIH]

Inotropic: Affecting the force or energy of muscular contractions. [EU]

Inpatients: Persons admitted to health facilities which provide board and room, for the purpose of observation, care, diagnosis or treatment. [NIH]

Insight: The capacity to understand one's own motives, to be aware of one's own psychodynamics, to appreciate the meaning of symbolic behavior. [NIH]

Insomnia: Difficulty in going to sleep or getting enough sleep. [NIH]

Insulator: Material covering the metal conductor of the lead. It is usually polyurethane or silicone. [NIH]

Insulin: A protein hormone secreted by beta cells of the pancreas. Insulin plays a major role in the regulation of glucose metabolism, generally promoting the cellular utilization of glucose. It is also an important regulator of protein and lipid metabolism. Insulin is used as a drug to control insulin-dependent diabetes mellitus. [NIH]

Insulin-dependent diabetes mellitus: A disease characterized by high levels of blood glucose resulting from defects in insulin secretion, insulin action, or both. Autoimmune, genetic, and environmental factors are involved in the development of type I diabetes. [NIH]

Intensive Care: Advanced and highly specialized care provided to medical or surgical

patients whose conditions are life-threatening and require comprehensive care and constant monitoring. It is usually administered in specially equipped units of a health care facility. [NIH]

Interleukin-1: A soluble factor produced by monocytes, macrophages, and other cells which activates T-lymphocytes and potentiates their response to mitogens or antigens. IL-1 consists of two distinct forms, IL-1 alpha and IL-1 beta which perform the same functions but are distinct proteins. The biological effects of IL-1 include the ability to replace macrophage requirements for T-cell activation. The factor is distinct from interleukin-2. [NIH]

Interleukin-2: Chemical mediator produced by activated T lymphocytes and which regulates the proliferation of T cells, as well as playing a role in the regulation of NK cell activity. [NIH]

Intermittent: Occurring at separated intervals; having periods of cessation of activity. [EU]

Internal Medicine: A medical specialty concerned with the diagnosis and treatment of diseases of the internal organ systems of adults. [NIH]

Interneurons: Most generally any neurons which are not motor or sensory. Interneurons may also refer to neurons whose axons remain within a particular brain region as contrasted with projection neurons which have axons projecting to other brain regions. [NIH]

Intervention Studies: Epidemiologic investigations designed to test a hypothesized cause-effect relation by modifying the supposed causal factor(s) in the study population. [NIH]

Intervertebral: Situated between two contiguous vertebrae. [EU]

Intervertebral Disk Displacement: An intervertebral disk in which the nucleus pulposus has protruded through surrounding fibrocartilage. This occurs most frequently in the lower lumbar region. [NIH]

Intestinal: Having to do with the intestines. [NIH]

Intestine: A long, tube-shaped organ in the abdomen that completes the process of digestion. There is both a large intestine and a small intestine. Also called the bowel. [NIH]

Intoxication: Poisoning, the state of being poisoned. [EU]

Intracellular: Inside a cell. [NIH]

Intracellular Membranes: Membranes of subcellular structures. [NIH]

Intracranial Embolism: The sudden obstruction of a blood vessel by an embolus. [NIH]

Intracranial Embolism and Thrombosis: Embolism or thrombosis involving blood vessels which supply intracranial structures. Emboli may originate from extracranial or intracranial sources. Thrombosis may occur in arterial or venous structures. [NIH]

Intracranial Hemorrhages: Bleeding within the intracranial cavity, including hemorrhages in the brain and within the cranial epidural, subdural, and subarachnoid spaces. [NIH]

Intracranial Hypertension: Increased pressure within the cranial vault. This may result from several conditions, including hydrocephalus; brain edema; intracranial masses; severe systemic hypertension; pseudotumor cerebri; and other disorders. [NIH]

Intracranial Pressure: Pressure within the cranial cavity. It is influenced by brain mass, the circulatory system, CSF dynamics, and skull rigidity. [NIH]

Intravenous: IV. Into a vein. [NIH]

Intraventricular infusion: The delivery of a drug into a space within an organ. [NIH]

Intrinsic: Situated entirely within or pertaining exclusively to a part. [EU]

Invasive: 1. Having the quality of invasiveness. 2. Involving puncture or incision of the skin or insertion of an instrument or foreign material into the body; said of diagnostic techniques.

[EU]

Involuntary: Reaction occurring without intention or volition. [NIH]

Iodine: A nonmetallic element of the halogen group that is represented by the atomic symbol I, atomic number 53, and atomic weight of 126.90. It is a nutritionally essential element, especially important in thyroid hormone synthesis. In solution, it has anti-infective properties and is used topically. [NIH]

Ion Channels: Gated, ion-selective glycoproteins that traverse membranes. The stimulus for channel gating can be a membrane potential, drug, transmitter, cytoplasmic messenger, or a mechanical deformation. Ion channels which are integral parts of ionotropic neurotransmitter receptors are not included. [NIH]

Ionization: 1. Any process by which a neutral atom gains or loses electrons, thus acquiring a net charge, as the dissociation of a substance in solution into ions or ion production by the passage of radioactive particles. 2. Iontophoresis. [EU]

Ionizing: Radiation comprising charged particles, e. g. electrons, protons, alpha-particles, etc., having sufficient kinetic energy to produce ionization by collision. [NIH]

Ions: An atom or group of atoms that have a positive or negative electric charge due to a gain (negative charge) or loss (positive charge) of one or more electrons. Atoms with a positive charge are known as cations; those with a negative charge are anions. [NIH]

Ipsilateral: Having to do with the same side of the body. [NIH]

Irritable Bowel Syndrome: A disorder that comes and goes. Nerves that control the muscles in the GI tract are too active. The GI tract becomes sensitive to food, stool, gas, and stress. Causes abdominal pain, bloating, and constipation or diarrhea. Also called spastic colon or mucous colitis. [NIH]

Ischemia: Deficiency of blood in a part, due to functional constriction or actual obstruction of a blood vessel. [EU]

Ischemic stroke: A condition in which the blood supply to part of the brain is cut off. Also called "plug-type" strokes. Blocked arteries starve areas of the brain controlling sight, speech, sensation, and movement so that these functions are partially or completely lost. Ischemic stroke is the most common type of stroke, accounting for 80 percent of all strokes. Most ischemic strokes are caused by a blood clot called a thrombus, which blocks blood flow in the arteries feeding the brain, usually the carotid artery in the neck, the major vessel bringing blood to the brain. When it becomes blocked, the risk of stroke is very high. [NIH]

Islet: Cell producing insulin in pancreas. [NIH]

Isoenzyme: Different forms of an enzyme, usually occurring in different tissues. The isoenzymes of a particular enzyme catalyze the same reaction but they differ in some of their properties. [NIH]

Jealousy: An irrational reaction compounded of grief, loss of self-esteem, enmity against the rival and self criticism. [NIH]

Joint: The point of contact between elements of an animal skeleton with the parts that surround and support it. [NIH]

Kainate: Glutamate receptor. [NIH]

Kainic Acid: (2S-(2 alpha,3 beta,4 beta))-2-Carboxy-4-(1-methylethenyl)-3-pyrrolidineacetic acid. Ascaricide obtained from the red alga Digenea simplex. It is a potent excitatory amino acid agonist at some types of excitatory amino acid receptors and has been used to discriminate among receptor types. Like many excitatory amino acid agonists it can cause neurotoxicity and has been used experimentally for that purpose. [NIH]

Kb: A measure of the length of DNA fragments, 1 Kb = 1000 base pairs. The largest DNA fragments are up to 50 kilobases long. [NIH]

Keto: It consists of 8 carbon atoms and within the endotoxins, it connects poysaccharide and lipid A. [NIH]

Ketone Bodies: Chemicals that the body makes when there is not enough insulin in the blood and it must break down fat for its energy. Ketone bodies can poison and even kill body cells. When the body does not have the help of insulin, the ketones build up in the blood and then "spill" over into the urine so that the body can get rid of them. The body can also rid itself of one type of ketone, called acetone, through the lungs. This gives the breath a fruity odor. Ketones that build up in the body for a long time lead to serious illness and coma. [NIH]

Kidney Disease: Any one of several chronic conditions that are caused by damage to the cells of the kidney. People who have had diabetes for a long time may have kidney damage. Also called nephropathy. [NIH]

Kinetic: Pertaining to or producing motion. [EU]

Labile: 1. Gliding; moving from point to point over the surface; unstable; fluctuating. 2. Chemically unstable. [EU]

Laceration: 1. The act of tearing. 2. A torn, ragged, mangled wound. [EU]

Lactation: The period of the secretion of milk. [EU]

Language Development: The gradual expansion in complexity and meaning of symbols and sounds as perceived and interpreted by the individual through a maturational and learning process. Stages in development include babbling, cooing, word imitation with cognition, and use of short sentences. [NIH]

Language Development Disorders: Conditions characterized by language abilities (comprehension and expression of speech and writing) that are below the expected level for a given age, generally in the absence of an intellectual impairment. These conditions may be associated with deafness; brain diseases; mental disorders; or environmental factors. [NIH]

Language Disorders: Conditions characterized by deficiencies of comprehension or expression of written and spoken forms of language. These include acquired and developmental disorders. [NIH]

Language Therapy: Rehabilitation of persons with language disorders or training of children with language development disorders. [NIH]

Large Intestine: The part of the intestine that goes from the cecum to the rectum. The large intestine absorbs water from stool and changes it from a liquid to a solid form. The large intestine is 5 feet long and includes the appendix, cecum, colon, and rectum. Also called colon. [NIH]

Laryngectomy: Total or partial excision of the larynx. [NIH]

Larynx: An irregularly shaped, musculocartilaginous tubular structure, lined with mucous membrane, located at the top of the trachea and below the root of the tongue and the hyoid bone. It is the essential sphincter guarding the entrance into the trachea and functioning secondarily as the organ of voice. [NIH]

Latent: Phoria which occurs at one distance or another and which usually has no troublesome effect. [NIH]

Laterality: Behavioral manifestations of cerebral dominance in which there is preferential use and superior functioning of either the left or the right side, as in the preferred use of the right hand or right foot. [NIH]

Laxative: An agent that acts to promote evacuation of the bowel; a cathartic or purgative. [EU]

Lectin: A complex molecule that has both protein and sugars. Lectins are able to bind to the outside of a cell and cause biochemical changes in it. Lectins are made by both animals and plants. [NIH]

Lens: The transparent, double convex (outward curve on both sides) structure suspended between the aqueous and vitreous; helps to focus light on the retina. [NIH]

Lesion: An area of abnormal tissue change. [NIH]

Lethal: Deadly, fatal. [EU]

Lethargy: Abnormal drowsiness or stupor; a condition of indifference. [EU]

Leucocyte: All the white cells of the blood and their precursors (myeloid cell series, lymphoid cell series) but commonly used to indicate granulocytes exclusive of lymphocytes. [NIH]

Leukemia: Cancer of blood-forming tissue. [NIH]

Leukocytes: White blood cells. These include granular leukocytes (basophils, eosinophils, and neutrophils) as well as non-granular leukocytes (lymphocytes and monocytes). [NIH]

Leukoencephalopathy: A condition with spongy holes in the brain's white matter. [NIH]

Libido: The psychic drive or energy associated with sexual instinct in the broad sense (pleasure and love-object seeking). It may also connote the psychic energy associated with instincts in general that motivate behavior. [NIH]

Library Services: Services offered to the library user. They include reference and circulation. [NIH]

Lice: A general name for small, wingless, parasitic insects, previously of the order Phthiraptera. Though exact taxonomy is still controversial, they can be grouped in the orders Anoplura (sucking lice), Mallophaga (biting lice), and Rhynchophthirina (elephant lice). [NIH]

Life cycle: The successive stages through which an organism passes from fertilized ovum or spore to the fertilized ovum or spore of the next generation. [NIH]

Ligament: A band of fibrous tissue that connects bones or cartilages, serving to support and strengthen joints. [EU]

Ligands: A RNA simulation method developed by the MIT. [NIH]

Limbic: Pertaining to a limbus, or margin; forming a border around. [EU]

Limbic System: A set of forebrain structures common to all mammals that is defined functionally and anatomically. It is implicated in the higher integration of visceral, olfactory, and somatic information as well as homeostatic responses including fundamental survival behaviors (feeding, mating, emotion). For most authors, it includes the amygdala, epithalamus, gyrus cinguli, hippocampal formation (see hippocampus), hypothalamus, parahippocampal gyrus, septal nuclei, anterior nuclear group of thalamus, and portions of the basal ganglia. (Parent, Carpenter's Human Neuroanatomy, 9th ed, p744; NeuroNames, http://rprcsgi.rprc.washington.edu/neuronames/index.html (September 2, 1998)). [NIH]

Linkage: The tendency of two or more genes in the same chromosome to remain together from one generation to the next more frequently than expected according to the law of independent assortment. [NIH]

Lipid: Fat. [NIH]

Lipid Peroxidation: Peroxidase catalyzed oxidation of lipids using hydrogen peroxide as an electron acceptor. [NIH]

Lipophilic: Having an affinity for fat; pertaining to or characterized by lipophilia. [EU]

Lithium: An element in the alkali metals family. It has the atomic symbol Li, atomic number 3, and atomic weight 6.94. Salts of lithium are used in treating manic-depressive disorders. [NIH]

Liver: A large, glandular organ located in the upper abdomen. The liver cleanses the blood and aids in digestion by secreting bile. [NIH]

Liver scan: An image of the liver created on a computer screen or on film. A radioactive substance is injected into a blood vessel and travels through the bloodstream. It collects in the liver, especially in abnormal areas, and can be detected by the scanner. [NIH]

Lobe: A portion of an organ such as the liver, lung, breast, or brain. [NIH]

Lobectomy: The removal of a lobe. [NIH]

Localization: The process of determining or marking the location or site of a lesion or disease. May also refer to the process of keeping a lesion or disease in a specific location or site. [NIH]

Localized: Cancer which has not metastasized yet. [NIH]

Locomotion: Movement or the ability to move from one place or another. It can refer to humans, vertebrate or invertebrate animals, and microorganisms. [NIH]

Locomotor: Of or pertaining to locomotion; pertaining to or affecting the locomotive apparatus of the body. [EU]

Longitudinal study: Also referred to as a "cohort study" or "prospective study"; the analytic method of epidemiologic study in which subsets of a defined population can be identified who are, have been, or in the future may be exposed or not exposed, or exposed in different degrees, to a factor or factors hypothesized to influence the probability of occurrence of a given disease or other outcome. The main feature of this type of study is to observe large numbers of subjects over an extended time, with comparisons of incidence rates in groups that differ in exposure levels. [NIH]

Long-Term Care: Care over an extended period, usually for a chronic condition or disability, requiring periodic, intermittent, or continuous care. [NIH]

Long-Term Potentiation: A persistent increase in synaptic efficacy, usually induced by appropriate activation of the same synapses. The phenomenological properties of long-term potentiation suggest that it may be a cellular mechanism of learning and memory. [NIH]

Loop: A wire usually of platinum bent at one end into a small loop (usually 4 mm inside diameter) and used in transferring microorganisms. [NIH]

Low Back Pain: Acute or chronic pain in the lumbar or sacral regions, which may be associated with musculo-ligamentous sprains and strains; intervertebral disk displacement; and other conditions. [NIH]

Lumbar: Pertaining to the loins, the part of the back between the thorax and the pelvis. [EU]

Lumbar puncture: A procedure in which a needle is put into the lower part of the spinal column to collect cerebrospinal fluid or to give anticancer drugs intrathecally. Also called a spinal tap. [NIH]

Lupus: A form of cutaneous tuberculosis. It is seen predominantly in women and typically involves the nasal, buccal, and conjunctival mucosa. [NIH]

Lutein Cells: The cells of the corpus luteum which are derived from the granulosa cells and the theca cells of the Graafian follicle. [NIH]

Lymphatic: The tissues and organs, including the bone marrow, spleen, thymus, and lymph nodes, that produce and store cells that fight infection and disease. [NIH]

Lymphatic system: The tissues and organs that produce, store, and carry white blood cells that fight infection and other diseases. This system includes the bone marrow, spleen, thymus, lymph nodes and a network of thin tubes that carry lymph and white blood cells. These tubes branch, like blood vessels, into all the tissues of the body. [NIH]

Lymphocyte: A white blood cell. Lymphocytes have a number of roles in the immune system, including the production of antibodies and other substances that fight infection and diseases. [NIH]

Lymphoid: Referring to lymphocytes, a type of white blood cell. Also refers to tissue in which lymphocytes develop. [NIH]

Lymphoma: A general term for various neoplastic diseases of the lymphoid tissue. [NIH]

Macrophage: A type of white blood cell that surrounds and kills microorganisms, removes dead cells, and stimulates the action of other immune system cells. [NIH]

Magnetic Resonance Imaging: Non-invasive method of demonstrating internal anatomy based on the principle that atomic nuclei in a strong magnetic field absorb pulses of radiofrequency energy and emit them as radiowaves which can be reconstructed into computerized images. The concept includes proton spin tomographic techniques. [NIH]

Magnetic Resonance Spectroscopy: Spectroscopic method of measuring the magnetic moment of elementary particles such as atomic nuclei, protons or electrons. It is employed in clinical applications such as NMR Tomography (magnetic resonance imaging). [NIH]

Magnetoencephalography: The measurement of magnetic fields over the head generated by electric currents in the brain. As in any electrical conductor, electric fields in the brain are accompanied by orthogonal magnetic fields. The measurement of these fields provides information about the localization of brain activity which is complementary to that provided by electroencephalography. Magnetoencephalography may be used alone or together with electroencephalography, for measurement of spontaneous or evoked activity, and for research or clinical purposes. [NIH]

Malabsorption: Impaired intestinal absorption of nutrients. [EU]

Malaria: A protozoan disease caused in humans by four species of the genus Plasmodium (P. falciparum (malaria, falciparum), P. vivax (malaria, vivax), P. ovale, and P. malariae) and transmitted by the bite of an infected female mosquito of the genus Anopheles. Malaria is endemic in parts of Asia, Africa, Central and South America, Oceania, and certain Caribbean islands. It is characterized by extreme exhaustion associated with paroxysms of high fever, sweating, shaking chills, and anemia. Malaria in animals is caused by other species of plasmodia. [NIH]

Malaria, Falciparum: Malaria caused by Plasmodium falciparum. This is the severest form of malaria and is associated with the highest levels of parasites in the blood. This disease is characterized by irregularly recurring febrile paroxysms that in extreme cases occur with acute cerebral, renal, or gastrointestinal manifestations. [NIH]

Malaria, Vivax: Malaria caused by Plasmodium vivax. This form of malaria is less severe than malaria, falciparum, but there is a higher probability for relapses to occur. Febrile paroxysms often occur every other day. [NIH]

Malformation: A morphologic defect resulting from an intrinsically abnormal developmental process. [EU]

Malignant: Cancerous; a growth with a tendency to invade and destroy nearby tissue and spread to other parts of the body. [NIH]

Malnutrition: A condition caused by not eating enough food or not eating a balanced diet. [NIH]

Mammary: Pertaining to the mamma, or breast. [EU]

Mania: Excitement of psychotic proportions manifested by mental and physical hyperactivity, disorganization of behaviour, and elevation of mood. [EU]

Manic: Affected with mania. [EU]

Manic-depressive psychosis: One of a group of psychotic reactions, fundamentally marked by severe mood swings and a tendency to remission and recurrence. [NIH]

Manifest: Being the part or aspect of a phenomenon that is directly observable : concretely expressed in behaviour. [EU]

Mastication: The act and process of chewing and grinding food in the mouth. [NIH]

Meatus: A canal running from the internal auditory foramen through the petrous portion of the temporal bone. It gives passage to the facial and auditory nerves together with the auditory branch of the basilar artery and the internal auditory veins. [NIH]

Medial: Lying near the midsaggital plane of the body; opposed to lateral. [NIH]

Mediate: Indirect; accomplished by the aid of an intervening medium. [EU]

Mediator: An object or substance by which something is mediated, such as (1) a structure of the nervous system that transmits impulses eliciting a specific response; (2) a chemical substance (transmitter substance) that induces activity in an excitable tissue, such as nerve or muscle; or (3) a substance released from cells as the result of the interaction of antigen with antibody or by the action of antigen with a sensitized lymphocyte. [EU]

Medical Records: Recording of pertinent information concerning patient's illness or illnesses. [NIH]

Medicament: A medicinal substance or agent. [EU]

MEDLINE: An online database of MEDLARS, the computerized bibliographic Medical Literature Analysis and Retrieval System of the National Library of Medicine. [NIH]

Megaloblastic: A large abnormal red blood cell appearing in the blood in pernicious anaemia. [EU]

Meiosis: A special method of cell division, occurring in maturation of the germ cells, by means of which each daughter nucleus receives half the number of chromosomes characteristic of the somatic cells of the species. [NIH]

Melanin: The substance that gives the skin its color. [NIH]

Melanocytes: Epidermal dendritic pigment cells which control long-term morphological color changes by alteration in their number or in the amount of pigment they produce and store in the pigment containing organelles called melanosomes. Melanophores are larger cells which do not exist in mammals. [NIH]

Melanoma: A form of skin cancer that arises in melanocytes, the cells that produce pigment. Melanoma usually begins in a mole. [NIH]

Memantine: Amantadine derivative that has some dopaminergic effects. It has been proposed as an antiparkinson agent. [NIH]

Membrane: A very thin layer of tissue that covers a surface. [NIH]

Membrane Glycoproteins: Glycoproteins found on the membrane or surface of cells. [NIH]

Membrane Proteins: Proteins which are found in membranes including cellular and intracellular membranes. They consist of two types, peripheral and integral proteins. They include most membrane-associated enzymes, antigenic proteins, transport proteins, and drug, hormone, and lectin receptors. [NIH]

Memory: Complex mental function having four distinct phases: (1) memorizing or learning,

(2) retention, (3) recall, and (4) recognition. Clinically, it is usually subdivided into immediate, recent, and remote memory. [NIH]

Memory Disorders: Disturbances in registering an impression, in the retention of an acquired impression, or in the recall of an impression. Memory impairments are associated with dementia; craniocerebraltrauma; encephalitis; alcoholism (see also alcohol amnestic disorder); schizophrenia; and other conditions. [NIH]

Menarche: The establishment or beginning of the menstrual function. [EU]

Meninges: The three membranes that cover and protect the brain and spinal cord. [NIH]

Meningitis: Inflammation of the meninges. When it affects the dura mater, the disease is termed pachymeningitis; when the arachnoid and pia mater are involved, it is called leptomeningitis, or meningitis proper. [EU]

Menstrual Cycle: The period of the regularly recurring physiologic changes in the endometrium occurring during the reproductive period in human females and some primates and culminating in partial sloughing of the endometrium (menstruation). [NIH]

Menstruation: The normal physiologic discharge through the vagina of blood and mucosal tissues from the nonpregnant uterus. [NIH]

Mental Disorders: Psychiatric illness or diseases manifested by breakdowns in the adaptational process expressed primarily as abnormalities of thought, feeling, and behavior producing either distress or impairment of function. [NIH]

Mental Health: The state wherein the person is well adjusted. [NIH]

Mental Retardation: Refers to sub-average general intellectual functioning which originated during the developmental period and is associated with impairment in adaptive behavior. [NIH]

Mentors: Senior professionals who provide guidance, direction and support to those persons desirous of improvement in academic positions, administrative positions or other career development situations. [NIH]

Mercury: A silver metallic element that exists as a liquid at room temperature. It has the atomic symbol Hg (from hydrargyrum, liquid silver), atomic number 80, and atomic weight 200.59. Mercury is used in many industrial applications and its salts have been employed therapeutically as purgatives, antisyphilitics, disinfectants, and astringents. It can be absorbed through the skin and mucous membranes which leads to mercury poisoning. Because of its toxicity, the clinical use of mercury and mercurials is diminishing. [NIH]

Mesolimbic: Inner brain region governing emotion and drives. [NIH]

Metabolic disorder: A condition in which normal metabolic processes are disrupted, usually because of a missing enzyme. [NIH]

Metabolite: Any substance produced by metabolism or by a metabolic process. [EU]

Metabotropic: A glutamate receptor which triggers an increase in production of 2 intracellular messengers: diacylglycerol and inositol 1, 4, 5-triphosphate. [NIH]

Metastasis: The spread of cancer from one part of the body to another. Tumors formed from cells that have spread are called "secondary tumors" and contain cells that are like those in the original (primary) tumor. The plural is metastases. [NIH]

Metastatic: Having to do with metastasis, which is the spread of cancer from one part of the body to another. [NIH]

Methionine: A sulfur containing essential amino acid that is important in many body functions. It is a chelating agent for heavy metals. [NIH]

Methylcellulose: Methylester of cellulose. Methylcellulose is used as an emulsifying and

suspending agent in cosmetics, pharmaceutics and the chemical industry. It is used therapeutically as a bulk laxative. [NIH]

Methylphenidate: A central nervous system stimulant used most commonly in the treatment of attention-deficit disorders in children and for narcolepsy. Its mechanisms appear to be similar to those of dextroamphetamine. [NIH]

MI: Myocardial infarction. Gross necrosis of the myocardium as a result of interruption of the blood supply to the area; it is almost always caused by atherosclerosis of the coronary arteries, upon which coronary thrombosis is usually superimposed. [NIH]

Mice Minute Virus: The type species of parvovirus prevalent in mouse colonies and found as a contaminant of many transplanted tumors or leukemias. [NIH]

Microbe: An organism which cannot be observed with the naked eye; e. g. unicellular animals, lower algae, lower fungi, bacteria. [NIH]

Microbiology: The study of microorganisms such as fungi, bacteria, algae, archaea, and viruses. [NIH]

Microdialysis: A technique for measuring extracellular concentrations of substances in tissues, usually in vivo, by means of a small probe equipped with a semipermeable membrane. Substances may also be introduced into the extracellular space through the membrane. [NIH]

Microorganism: An organism that can be seen only through a microscope. Microorganisms include bacteria, protozoa, algae, and fungi. Although viruses are not considered living organisms, they are sometimes classified as microorganisms. [NIH]

Microscopy: The application of microscope magnification to the study of materials that cannot be properly seen by the unaided eye. [NIH]

Migration: The systematic movement of genes between populations of the same species, geographic race, or variety. [NIH]

Mineralocorticoids: A group of corticosteroids primarily associated with the regulation of water and electrolyte balance. This is accomplished through the effect on ion transport in renal tubules, resulting in retention of sodium and loss of potassium. Mineralocorticoid secretion is itself regulated by plasma volume, serum potassium, and angiotensin II. [NIH]

Miotic: 1. Pertaining to, characterized by, or producing miosis : contraction of the pupil. 2. An agent that causes the pupil to contract. 3. Meiotic: characterized by cell division. [EU]

Mitochondria: Parts of a cell where aerobic production (also known as cell respiration) takes place. [NIH]

Mitochondrial Swelling: Increase in volume of mitochondria due to an influx of fluid; it occurs in hypotonic solutions due to osmotic pressure and in isotonic solutions as a result of altered permeability of the membranes of respiring mitochondria. [NIH]

Mitosis: A method of indirect cell division by means of which the two daughter nuclei normally receive identical complements of the number of chromosomes of the somatic cells of the species. [NIH]

Modeling: A treatment procedure whereby the therapist presents the target behavior which the learner is to imitate and make part of his repertoire. [NIH]

Modification: A change in an organism, or in a process in an organism, that is acquired from its own activity or environment. [NIH]

Modulator: A specific inductor that brings out characteristics peculiar to a definite region. [EU]

Molecular: Of, pertaining to, or composed of molecules : a very small mass of matter. [EU]

Molecular Structure: The location of the atoms, groups or ions relative to one another in a molecule, as well as the number, type and location of covalent bonds. [NIH]

Molecule: A chemical made up of two or more atoms. The atoms in a molecule can be the same (an oxygen molecule has two oxygen atoms) or different (a water molecule has two hydrogen atoms and one oxygen atom). Biological molecules, such as proteins and DNA, can be made up of many thousands of atoms. [NIH]

Monitor: An apparatus which automatically records such physiological signs as respiration, pulse, and blood pressure in an anesthetized patient or one undergoing surgical or other procedures. [NIH]

Monoamine: Enzyme that breaks down dopamine in the astrocytes and microglia. [NIH]

Monoamine Oxidase: An enzyme that catalyzes the oxidative deamination of naturally occurring monoamines. It is a flavin-containing enzyme that is localized in mitochondrial membranes, whether in nerve terminals, the liver, or other organs. Monoamine oxidase is important in regulating the metabolic degradation of catecholamines and serotonin in neural or target tissues. Hepatic monoamine oxidase has a crucial defensive role in inactivating circulating monoamines or those, such as tyramine, that originate in the gut and are absorbed into the portal circulation. (From Goodman and Gilman's, The Pharmacological Basis of Therapeutics, 8th ed, p415) EC 1.4.3.4. [NIH]

Monocytes: Large, phagocytic mononuclear leukocytes produced in the vertebrate bone marrow and released into the blood; contain a large, oval or somewhat indented nucleus surrounded by voluminous cytoplasm and numerous organelles. [NIH]

Monogenic: A human disease caused by a mutation in a single gene. [NIH]

Monotherapy: A therapy which uses only one drug. [EU]

Mood Disorders: Those disorders that have a disturbance in mood as their predominant feature. [NIH]

Morphine: The principal alkaloid in opium and the prototype opiate analgesic and narcotic. Morphine has widespread effects in the central nervous system and on smooth muscle. [NIH]

Morphine Derivatives: Analogs or derivatives of morphine. [NIH]

Morphological: Relating to the configuration or the structure of live organs. [NIH]

Morphology: The science of the form and structure of organisms (plants, animals, and other forms of life). [NIH]

Mosaicism: The occurrence in an individual of two or more cell populations of different chromosomal constitutions, derived from a single zygote, as opposed to chimerism in which the different cell populations are derived from more than one zygote. [NIH]

Motility: The ability to move spontaneously. [EU]

Motion Sickness: Sickness caused by motion, as sea sickness, train sickness, car sickness, and air sickness. [NIH]

Motor Activity: The physical activity of an organism as a behavioral phenomenon. [NIH]

Motor Cortex: Area of the frontal lobe concerned with primary motor control. It lies anterior to the central sulcus. [NIH]

Motor nerve: An efferent nerve conveying an impulse that excites muscular contraction. [NIH]

Movement Disorders: Syndromes which feature dyskinesias as a cardinal manifestation of the disease process. Included in this category are degenerative, hereditary, post-infectious, medication-induced, post-inflammatory, and post-traumatic conditions. [NIH]

Mucosa: A mucous membrane, or tunica mucosa. [EU]

Mucus: The viscous secretion of mucous membranes. It contains mucin, white blood cells, water, inorganic salts, and exfoliated cells. [NIH]

Multicenter study: A clinical trial that is carried out at more than one medical institution. [NIH]

Multiple sclerosis: A disorder of the central nervous system marked by weakness, numbness, a loss of muscle coordination, and problems with vision, speech, and bladder control. Multiple sclerosis is thought to be an autoimmune disease in which the body's immune system destroys myelin. Myelin is a substance that contains both protein and fat (lipid) and serves as a nerve insulator and helps in the transmission of nerve signals. [NIH]

Muscimol: Neurotoxic isoxazole isolated from Amanita muscaria and A. phalloides and also obtained by decarboxylation of ibotenic acid. It is a potent agonist at GABA-A receptors and is used mainly as an experimental tool in animal and tissue studies. [NIH]

Muscle Contraction: A process leading to shortening and/or development of tension in muscle tissue. Muscle contraction occurs by a sliding filament mechanism whereby actin filaments slide inward among the myosin filaments. [NIH]

Muscle Fibers: Large single cells, either cylindrical or prismatic in shape, that form the basic unit of muscle tissue. They consist of a soft contractile substance enclosed in a tubular sheath. [NIH]

Muscle relaxant: An agent that specifically aids in reducing muscle tension, as those acting at the polysynaptic neurons of motor nerves (e.g. meprobamate) or at the myoneural junction (curare and related compounds). [EU]

Muscle Relaxation: That phase of a muscle twitch during which a muscle returns to a resting position. [NIH]

Muscle Spasticity: Strongly marked hypertonicity of muscles. [NIH]

Muscle tension: A force in a material tending to produce extension; the state of being stretched. [NIH]

Muscular Atrophy: Derangement in size and number of muscle fibers occurring with aging, reduction in blood supply, or following immobilization, prolonged weightlessness, malnutrition, and particularly in denervation. [NIH]

Muscular Diseases: Acquired, familial, and congenital disorders of skeletal muscle and smooth muscle. [NIH]

Muscular Dystrophies: A general term for a group of inherited disorders which are characterized by progressive degeneration of skeletal muscles. [NIH]

Musculature: The muscular apparatus of the body, or of any part of it. [EU]

Mutilation: Injuries to the body. [NIH]

Myalgia: Pain in a muscle or muscles. [EU]

Myasthenia: Muscular debility; any constitutional anomaly of muscle. [EU]

Mydriatic: 1. Dilating the pupil. 2. Any drug that dilates the pupil. [EU]

Myelin: The fatty substance that covers and protects nerves. [NIH]

Myocardial infarction: Gross necrosis of the myocardium as a result of interruption of the blood supply to the area; it is almost always caused by atherosclerosis of the coronary arteries, upon which coronary thrombosis is usually superimposed. [NIH]

Myocardial Ischemia: A disorder of cardiac function caused by insufficient blood flow to the muscle tissue of the heart. The decreased blood flow may be due to narrowing of the

coronary arteries (coronary arteriosclerosis), to obstruction by a thrombus (coronary thrombosis), or less commonly, to diffuse narrowing of arterioles and other small vessels within the heart. Severe interruption of the blood supply to the myocardial tissue may result in necrosis of cardiac muscle (myocardial infarction). [NIH]

Myocardial Reperfusion: Generally, restoration of blood supply to heart tissue which is ischemic due to decrease in normal blood supply. The decrease may result from any source including atherosclerotic obstruction, narrowing of the artery, or surgical clamping. Reperfusion can be induced to treat ischemia. Methods include chemical dissolution of an occluding thrombus, administration of vasodilator drugs, angioplasty, catheterization, and artery bypass graft surgery. However, it is thought that reperfusion can itself further damage the ischemic tissue, causing myocardial reperfusion injury. [NIH]

Myocardial Reperfusion Injury: Functional, metabolic, or structural changes in ischemic heart muscle thought to result from reperfusion to the ischemic areas. Changes can be fatal to muscle cells and may include edema with explosive cell swelling and disintegration, sarcolemma disruption, fragmentation of mitochondria, contraction band necrosis, enzyme washout, and calcium overload. Other damage may include hemorrhage and ventricular arrhythmias. One possible mechanism of damage is thought to be oxygen free radicals. Treatment currently includes the introduction of scavengers of oxygen free radicals, and injury is thought to be prevented by warm blood cardioplegic infusion prior to reperfusion. [NIH]

Myocardium: The muscle tissue of the heart composed of striated, involuntary muscle known as cardiac muscle. [NIH]

Myoclonus: Involuntary shock-like contractions, irregular in rhythm and amplitude, followed by relaxation, of a muscle or a group of muscles. This condition may be a feature of some central nervous systems diseases (e.g., epilepsy, myoclonic). Nocturnal myoclonus may represent a normal physiologic event or occur as the principal feature of the nocturnal myoclonus syndrome. (From Adams et al., Principles of Neurology, 6th ed, pp102-3). [NIH]

Myopathy: Any disease of a muscle. [EU]

Myosin: Chief protein in muscle and the main constituent of the thick filaments of muscle fibers. In conjunction with actin, it is responsible for the contraction and relaxation of muscles. [NIH]

Myotonia: Prolonged failure of muscle relaxation after contraction. This may occur after voluntary contractions, muscle percussion, or electrical stimulation of the muscle. Myotonia is a characteristic feature of myotonic disorders. [NIH]

Myotonic Dystrophy: A condition presenting muscle weakness and wasting which may be progressive. [NIH]

Narcolepsy: A condition of unknown cause characterized by a periodic uncontrollable tendency to fall asleep. [NIH]

Narcotic: 1. Pertaining to or producing narcosis. 2. An agent that produces insensibility or stupor, applied especially to the opioids, i.e. to any natural or synthetic drug that has morphine-like actions. [EU]

Nasal Mucosa: The mucous membrane lining the nasal cavity. [NIH]

Nausea: An unpleasant sensation in the stomach usually accompanied by the urge to vomit. Common causes are early pregnancy, sea and motion sickness, emotional stress, intense pain, food poisoning, and various enteroviruses. [NIH]

NCI: National Cancer Institute. NCI, part of the National Institutes of Health of the United States Department of Health and Human Services, is the federal government's principal agency for cancer research. NCI conducts, coordinates, and funds cancer research, training,

health information dissemination, and other programs with respect to the cause, diagnosis, prevention, and treatment of cancer. Access the NCI Web site at http://cancer.gov. [NIH]

Necrosis: A pathological process caused by the progressive degradative action of enzymes that is generally associated with severe cellular trauma. It is characterized by mitochondrial swelling, nuclear flocculation, uncontrolled cell lysis, and ultimately cell death. [NIH]

Need: A state of tension or dissatisfaction felt by an individual that impels him to action toward a goal he believes will satisfy the impulse. [NIH]

Neocortex: The largest portion of the cerebral cortex. It is composed of neurons arranged in six layers. [NIH]

Neonatal: Pertaining to the first four weeks after birth. [EU]

Neonatal period: The first 4 weeks after birth. [NIH]

Neoplasia: Abnormal and uncontrolled cell growth. [NIH]

Neoplasm: A new growth of benign or malignant tissue. [NIH]

Neoplastic: Pertaining to or like a neoplasm (= any new and abnormal growth); pertaining to neoplasia (= the formation of a neoplasm). [EU]

Nephropathy: Disease of the kidneys. [EU]

Nerve: A cordlike structure of nervous tissue that connects parts of the nervous system with other tissues of the body and conveys nervous impulses to, or away from, these tissues. [NIH]

Nerve Growth Factor: Nerve growth factor is the first of a series of neurotrophic factors that were found to influence the growth and differentiation of sympathetic and sensory neurons. It is comprised of alpha, beta, and gamma subunits. The beta subunit is responsible for its growth stimulating activity. [NIH]

Nerve Regeneration: Renewal or physiological repair of damaged nerve tissue. [NIH]

Nervous System: The entire nerve apparatus composed of the brain, spinal cord, nerves and ganglia. [NIH]

Networks: Pertaining to a nerve or to the nerves, a meshlike structure of interlocking fibers or strands. [NIH]

Neural: 1. Pertaining to a nerve or to the nerves. 2. Situated in the region of the spinal axis, as the neutral arch. [EU]

Neural tube defects: These defects include problems stemming from fetal development of the spinal cord, spine, brain, and skull, and include birth defects such as spina bifida, anencephaly, and encephalocele. Neural tube defects occur early in pregnancy at about 4 to 6 weeks, usually before a woman knows she is pregnant. Many babies with neural tube defects have difficulty walking and with bladder and bowel control. [NIH]

Neuralgia: Intense or aching pain that occurs along the course or distribution of a peripheral or cranial nerve. [NIH]

Neurobehavioral Manifestations: Signs and symptoms of higher cortical dysfunction caused by organic conditions. These include certain behavioral alterations and impairments of skills involved in the acquisition, processing, and utilization of knowledge or information. [NIH]

Neurodegenerative Diseases: Hereditary and sporadic conditions which are characterized by progressive nervous system dysfunction. These disorders are often associated with atrophy of the affected central or peripheral nervous system structures. [NIH]

Neuroendocrine: Having to do with the interactions between the nervous system and the endocrine system. Describes certain cells that release hormones into the blood in response to

stimulation of the nervous system. [NIH]

Neurofibrils: The delicate interlacing threads, formed by aggregations of neurofilaments and neurotubules, coursing through the cytoplasm of the body of a neuron and extending from one dendrite into another or into the axon. [NIH]

Neurofilaments: Bundle of neuronal fibers. [NIH]

Neurogenic: Loss of bladder control caused by damage to the nerves controlling the bladder. [NIH]

Neuroglia: The non-neuronal cells of the nervous system. They are divided into macroglia (astrocytes, oligodendroglia, and schwann cells) and microglia. They not only provide physical support, but also respond to injury, regulate the ionic and chemical composition of the extracellular milieu, participate in the blood-brain and blood-retina barriers, form the myelin insulation of nervous pathways, guide neuronal migration during development, and exchange metabolites with neurons. Neuroglia have high-affinity transmitter uptake systems, voltage-dependent and transmitter-gated ion channels, and can release transmitters, but their role in signaling (as in many other functions) is unclear. [NIH]

Neuroleptic: A term coined to refer to the effects on cognition and behaviour of antipsychotic drugs, which produce a state of apathy, lack of initiative, and limited range of emotion and in psychotic patients cause a reduction in confusion and agitation and normalization of psychomotor activity. [EU]

Neurologic: Having to do with nerves or the nervous system. [NIH]

Neurologist: A doctor who specializes in the diagnosis and treatment of disorders of the nervous system. [NIH]

Neurology: A medical specialty concerned with the study of the structures, functions, and diseases of the nervous system. [NIH]

Neuroma: A tumor that arises in nerve cells. [NIH]

Neuromuscular: Pertaining to muscles and nerves. [EU]

Neuromuscular Junction: The synapse between a neuron and a muscle. [NIH]

Neuromuscular Junction Diseases: Conditions characterized by impaired transmission of impulses at the neuromuscular junction. This may result from disorders that affect receptor function, pre- or postsynaptic membrane function, or acetylcholinesteraseactivity. The majority of diseases in this category are associated with autoimmune, toxic, or inherited conditions. [NIH]

Neuronal: Pertaining to a neuron or neurons (= conducting cells of the nervous system). [EU]

Neuronal Plasticity: The capacity of the nervous system to change its reactivity as the result of successive activations. [NIH]

Neurons: The basic cellular units of nervous tissue. Each neuron consists of a body, an axon, and dendrites. Their purpose is to receive, conduct, and transmit impulses in the nervous system. [NIH]

Neuropathy: A problem in any part of the nervous system except the brain and spinal cord. Neuropathies can be caused by infection, toxic substances, or disease. [NIH]

Neuropeptide: A member of a class of protein-like molecules made in the brain. Neuropeptides consist of short chains of amino acids, with some functioning as neurotransmitters and some functioning as hormones. [NIH]

Neuropharmacology: The branch of pharmacology dealing especially with the action of drugs upon various parts of the nervous system. [NIH]

Neurophysiology: The scientific discipline concerned with the physiology of the nervous

system. [NIH]

Neuroprotective Agents: Drugs intended to prevent damage to the brain or spinal cord from ischemia, stroke, convulsions, or trauma. Some must be administered before the event, but others may be effective for some time after. They act by a variety of mechanisms, but often directly or indirectly minimize the damage produced by endogenous excitatory amino acids. [NIH]

Neuropsychological Tests: Tests designed to assess neurological function associated with certain behaviors. They are used in diagnosing brain dysfunction or damage and central nervous system disorders or injury. [NIH]

Neuropsychology: A branch of psychology which investigates the correlation between experience or behavior and the basic neurophysiological processes. The term neuropsychology stresses the dominant role of the nervous system. It is a more narrowly defined field than physiological psychology or psychophysiology. [NIH]

Neurosciences: The scientific disciplines concerned with the embryology, anatomy, physiology, biochemistry, pharmacology, etc., of the nervous sytem. [NIH]

Neurosis: Functional derangement due to disorders of the nervous system which does not affect the psychic personality of the patient. [NIH]

Neurosurgeon: A doctor who specializes in surgery on the brain, spine, and other parts of the nervous system. [NIH]

Neurosurgery: A surgical specialty concerned with the treatment of diseases and disorders of the brain, spinal cord, and peripheral and sympathetic nervous system. [NIH]

Neurotoxic: Poisonous or destructive to nerve tissue. [EU]

Neurotoxicity: The tendency of some treatments to cause damage to the nervous system. [NIH]

Neurotoxin: A substance that is poisonous to nerve tissue. [NIH]

Neurotransmitters: Endogenous signaling molecules that alter the behavior of neurons or effector cells. Neurotransmitter is used here in its most general sense, including not only messengers that act directly to regulate ion channels, but also those that act through second messenger systems, and those that act at a distance from their site of release. Included are neuromodulators, neuroregulators, neuromediators, and neurohumors, whether or not acting at synapses. [NIH]

Neurotrophins: A nerve growth factor. [NIH]

Neutrons: Electrically neutral elementary particles found in all atomic nuclei except light hydrogen; the mass is equal to that of the proton and electron combined and they are unstable when isolated from the nucleus, undergoing beta decay. Slow, thermal, epithermal, and fast neutrons refer to the energy levels with which the neutrons are ejected from heavier nuclei during their decay. [NIH]

Nevus: A benign growth on the skin, such as a mole. A mole is a cluster of melanocytes and surrounding supportive tissue that usually appears as a tan, brown, or flesh-colored spot on the skin. The plural of nevus is nevi (NEE-vye). [NIH]

Niacin: Water-soluble vitamin of the B complex occurring in various animal and plant tissues. Required by the body for the formation of coenzymes NAD and NADP. Has pellagra-curative, vasodilating, and antilipemic properties. [NIH]

Niche: The ultimate unit of the habitat, i. e. the specific spot occupied by an individual organism; by extension, the more or less specialized relationships existing between an organism, individual or synusia(e), and its environment. [NIH]

Nicotine: Nicotine is highly toxic alkaloid. It is the prototypical agonist at nicotinic cholinergic receptors where it dramatically stimulates neurons and ultimately blocks synaptic transmission. Nicotine is also important medically because of its presence in tobacco smoke. [NIH]

Nitrogen: An element with the atomic symbol N, atomic number 7, and atomic weight 14. Nitrogen exists as a diatomic gas and makes up about 78% of the earth's atmosphere by volume. It is a constituent of proteins and nucleic acids and found in all living cells. [NIH]

Nonverbal Communication: Transmission of emotions, ideas, and attitudes between individuals in ways other than the spoken language. [NIH]

Norepinephrine: Precursor of epinephrine that is secreted by the adrenal medulla and is a widespread central and autonomic neurotransmitter. Norepinephrine is the principal transmitter of most postganglionic sympathetic fibers and of the diffuse projection system in the brain arising from the locus ceruleus. It is also found in plants and is used pharmacologically as a sympathomimetic. [NIH]

Nuclear: A test of the structure, blood flow, and function of the kidneys. The doctor injects a mildly radioactive solution into an arm vein and uses x-rays to monitor its progress through the kidneys. [NIH]

Nuclei: A body of specialized protoplasm found in nearly all cells and containing the chromosomes. [NIH]

Nucleic acid: Either of two types of macromolecule (DNA or RNA) formed by polymerization of nucleotides. Nucleic acids are found in all living cells and contain the information (genetic code) for the transfer of genetic information from one generation to the next. [NIH]

Nucleic Acid Hybridization: The process whereby two single-stranded polynucleotides form a double-stranded molecule, with hydrogen bonding between the complementary bases in the two strains. [NIH]

Nucleus: A body of specialized protoplasm found in nearly all cells and containing the chromosomes. [NIH]

Occipital Lobe: Posterior part of the cerebral hemisphere. [NIH]

Ocular: 1. Of, pertaining to, or affecting the eye. 2. Eyepiece. [EU]

Odds Ratio: The ratio of two odds. The exposure-odds ratio for case control data is the ratio of the odds in favor of exposure among cases to the odds in favor of exposure among noncases. The disease-odds ratio for a cohort or cross section is the ratio of the odds in favor of disease among the exposed to the odds in favor of disease among the unexposed. The prevalence-odds ratio refers to an odds ratio derived cross-sectionally from studies of prevalent cases. [NIH]

Oedema: The presence of abnormally large amounts of fluid in the intercellular tissue spaces of the body; usually applied to demonstrable accumulation of excessive fluid in the subcutaneous tissues. Edema may be localized, due to venous or lymphatic obstruction or to increased vascular permeability, or it may be systemic due to heart failure or renal disease. Collections of edema fluid are designated according to the site, e.g. ascites (peritoneal cavity), hydrothorax (pleural cavity), and hydropericardium (pericardial sac). Massive generalized edema is called anasarca. [EU]

Ointments: Semisolid preparations used topically for protective emollient effects or as a vehicle for local administration of medications. Ointment bases are various mixtures of fats, waxes, animal and plant oils and solid and liquid hydrocarbons. [NIH]

Olfactory Bulb: Ovoid body resting on the cribriform plate of the ethmoid bone where the

olfactory nerve terminates. The olfactory bulb contains several types of nerve cells including the mitral cells, on whose dendrites the olfactory nerve synapses, forming the olfactory glomeruli. The accessory olfactory bulb, which receives the projection from the vomeronasal organ via the vomeronasal nerve, is also included here. [NIH]

Omega-3 fatty acid: A type of fat obtained in the diet and involved in immunity. [NIH]

Oncogene: A gene that normally directs cell growth. If altered, an oncogene can promote or allow the uncontrolled growth of cancer. Alterations can be inherited or caused by an environmental exposure to carcinogens. [NIH]

Oocytes: Female germ cells in stages between the prophase of the first maturation division and the completion of the second maturation division. [NIH]

Opacity: Degree of density (area most dense taken for reading). [NIH]

Opioid Peptides: The endogenous peptides with opiate-like activity. The three major classes currently recognized are the enkephalins, the dynorphins, and the endorphins. Each of these families derives from different precursors, proenkephalin, prodynorphin, and pro-opiomelanocortin, respectively. There are also at least three classes of opioid receptors, but the peptide families do not map to the receptors in a simple way. [NIH]

Opium: The air-dried exudate from the unripe seed capsule of the opium poppy, Papaver somniferum, or its variant, P. album. It contains a number of alkaloids, but only a few - morphine, codeine, and papaverine - have clinical significance. Opium has been used as an analgesic, antitussive, antidiarrheal, and antispasmodic. [NIH]

Opsin: A protein formed, together with retinene, by the chemical breakdown of meta-rhodopsin. [NIH]

Optic Chiasm: The X-shaped structure formed by the meeting of the two optic nerves. At the optic chiasm the fibers from the medial part of each retina cross to project to the other side of the brain while the lateral retinal fibers continue on the same side. As a result each half of the brain receives information about the contralateral visual field from both eyes. [NIH]

Oral Health: The optimal state of the mouth and normal functioning of the organs of the mouth without evidence of disease. [NIH]

Oral Hygiene: The practice of personal hygiene of the mouth. It includes the maintenance of oral cleanliness, tissue tone, and general preservation of oral health. [NIH]

Organ Culture: The growth in aseptic culture of plant organs such as roots or shoots, beginning with organ primordia or segments and maintaining the characteristics of the organ. [NIH]

Organelles: Specific particles of membrane-bound organized living substances present in eukaryotic cells, such as the mitochondria; the golgi apparatus; endoplasmic reticulum; lysomomes; plastids; and vacuoles. [NIH]

Orofacial: Of or relating to the mouth and face. [EU]

Orthostatic: Pertaining to or caused by standing erect. [EU]

Osmotic: Pertaining to or of the nature of osmosis (= the passage of pure solvent from a solution of lesser to one of greater solute concentration when the two solutions are separated by a membrane which selectively prevents the passage of solute molecules, but is permeable to the solvent). [EU]

Outpatient: A patient who is not an inmate of a hospital but receives diagnosis or treatment in a clinic or dispensary connected with the hospital. [NIH]

Ovaries: The pair of female reproductive glands in which the ova, or eggs, are formed. The

ovaries are located in the pelvis, one on each side of the uterus. [NIH]

Ovary: Either of the paired glands in the female that produce the female germ cells and secrete some of the female sex hormones. [NIH]

Overdose: An accidental or deliberate dose of a medication or street drug that is in excess of what is normally used. [NIH]

Overweight: An excess of body weight but not necessarily body fat; a body mass index of 25 to 29.9 kg/m2. [NIH]

Ovum: A female germ cell extruded from the ovary at ovulation. [NIH]

Oxidation: The act of oxidizing or state of being oxidized. Chemically it consists in the increase of positive charges on an atom or the loss of negative charges. Most biological oxidations are accomplished by the removal of a pair of hydrogen atoms (dehydrogenation) from a molecule. Such oxidations must be accompanied by reduction of an acceptor molecule. Univalent o. indicates loss of one electron; divalent o., the loss of two electrons. [EU]

Oxidative Stress: A disturbance in the prooxidant-antioxidant balance in favor of the former, leading to potential damage. Indicators of oxidative stress include damaged DNA bases, protein oxidation products, and lipid peroxidation products (Sies, Oxidative Stress, 1991, pxv-xvi). [NIH]

Pacemaker: An object or substance that influences the rate at which a certain phenomenon occurs; often used alone to indicate the natural cardiac pacemaker or an artificial cardiac pacemaker. In biochemistry, a substance whose rate of reaction sets the pace for a series of interrelated reactions. [EU]

Pachymeningitis: Inflammation of the dura mater of the brain, the spinal cord or the optic nerve. [NIH]

Palate: The structure that forms the roof of the mouth. It consists of the anterior hard palate and the posterior soft palate. [NIH]

Palliative: 1. Affording relief, but not cure. 2. An alleviating medicine. [EU]

Palsies: Disease of the peripheral nervous system occurring usually after many years of increased lead absorption. [NIH]

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Pancreas: A mixed exocrine and endocrine gland situated transversely across the posterior abdominal wall in the epigastric and hypochondriac regions. The endocrine portion is comprised of the Islets of Langerhans, while the exocrine portion is a compound acinar gland that secretes digestive enzymes. [NIH]

Pancreatic: Having to do with the pancreas. [NIH]

Pancreatic cancer: Cancer of the pancreas, a salivary gland of the abdomen. [NIH]

Panic: A state of extreme acute, intense anxiety and unreasoning fear accompanied by disorganization of personality function. [NIH]

Paralysis: Loss of ability to move all or part of the body. [NIH]

Paranoia: A psychotic disorder marked by persistent delusions of persecution or delusional jealousy and behaviour like that of the paranoid personality, such as suspiciousness, mistrust, and combativeness. It differs from paranoid schizophrenia, in which hallucinations or formal thought disorder are present, in that the delusions are logically consistent and that there are no other psychotic features. The designation in DSM III-R is delusional (paranoid) disorders, with five types : persecutory, jealous, erotomanic, somatic, and grandiose. [EU]

Paraplegia: Severe or complete loss of motor function in the lower extremities and lower portions of the trunk. This condition is most often associated with spinal cord diseases, although brain diseases; peripheral nervous system diseases; neuromuscular diseases; and muscular diseases may also cause bilateral leg weakness. [NIH]

Parasite: An animal or a plant that lives on or in an organism of another species and gets at least some of its nutrition from that other organism. [NIH]

Parasitic: Having to do with or being a parasite. A parasite is an animal or a plant that lives on or in an organism of another species and gets at least some of its nutrients from it. [NIH]

Paresis: A general term referring to a mild to moderate degree of muscular weakness, occasionally used as a synonym for paralysis (severe or complete loss of motor function). In the older literature, paresis often referred specifically to paretic neurosyphilis. "General paresis" and "general paralysis" may still carry that connotation. Bilateral lower extremity paresis is referred to as paraparesis. [NIH]

Parietal: 1. Of or pertaining to the walls of a cavity. 2. Pertaining to or located near the parietal bone, as the parietal lobe. [EU]

Parietal Lobe: Upper central part of the cerebral hemisphere. [NIH]

Parkinsonism: A group of neurological disorders characterized by hypokinesia, tremor, and muscular rigidity. [EU]

Paroxysmal: Recurring in paroxysms (= spasms or seizures). [EU]

Partial remission: The shrinking, but not complete disappearance, of a tumor in response to therapy. Also called partial response. [NIH]

Particle: A tiny mass of material. [EU]

Partnership Practice: A voluntary contract between two or more doctors who may or may not share responsibility for the care of patients, with proportional sharing of profits and losses. [NIH]

Parturition: The act or process of given birth to a child. [EU]

Parvovirus: A genus of the family Parvoviridae, subfamily Parvovirinae, infecting a variety of vertebrates including humans. Parvoviruses are responsible for a number of important diseases but also can be non-pathogenic in certain hosts. The type species is mice minute virus. [NIH]

Patch: A piece of material used to cover or protect a wound, an injured part, etc.: a patch over the eye. [NIH]

Pathogen: Any disease-producing microorganism. [EU]

Pathogenesis: The cellular events and reactions that occur in the development of disease. [NIH]

Pathologic: 1. Indicative of or caused by a morbid condition. 2. Pertaining to pathology (= branch of medicine that treats the essential nature of the disease, especially the structural and functional changes in tissues and organs of the body caused by the disease). [EU]

Pathologic Processes: The abnormal mechanisms and forms involved in the dysfunctions of tissues and organs. [NIH]

Pathologies: The study of abnormality, especially the study of diseases. [NIH]

Pathophysiology: Altered functions in an individual or an organ due to disease. [NIH]

Patient Compliance: Voluntary cooperation of the patient in following a prescribed regimen. [NIH]

Patient Education: The teaching or training of patients concerning their own health needs.

[NIH]

Pelvic: Pertaining to the pelvis. [EU]

Pepsin: An enzyme made in the stomach that breaks down proteins. [NIH]

Pepsin A: Formed from pig pepsinogen by cleavage of one peptide bond. The enzyme is a single polypeptide chain and is inhibited by methyl 2-diaazoacetamidohexanoate. It cleaves peptides preferentially at the carbonyl linkages of phenylalanine or leucine and acts as the principal digestive enzyme of gastric juice. [NIH]

Peptide: Any compound consisting of two or more amino acids, the building blocks of proteins. Peptides are combined to make proteins. [NIH]

Perception: The ability quickly and accurately to recognize similarities and differences among presented objects, whether these be pairs of words, pairs of number series, or multiple sets of these or other symbols such as geometric figures. [NIH]

Percutaneous: Performed through the skin, as injection of radiopacque material in radiological examination, or the removal of tissue for biopsy accomplished by a needle. [EU]

Perfusion: Bathing an organ or tissue with a fluid. In regional perfusion, a specific area of the body (usually an arm or a leg) receives high doses of anticancer drugs through a blood vessel. Such a procedure is performed to treat cancer that has not spread. [NIH]

Perinatal: Pertaining to or occurring in the period shortly before and after birth; variously defined as beginning with completion of the twentieth to twenty-eighth week of gestation and ending 7 to 28 days after birth. [EU]

Periodicity: The tendency of a phenomenon to recur at regular intervals; in biological systems, the recurrence of certain activities (including hormonal, cellular, neural) may be annual, seasonal, monthly, daily, or more frequently (ultradian). [NIH]

Peripheral Nerves: The nerves outside of the brain and spinal cord, including the autonomic, cranial, and spinal nerves. Peripheral nerves contain non-neuronal cells and connective tissue as well as axons. The connective tissue layers include, from the outside to the inside, the epineurium, the perineurium, and the endoneurium. [NIH]

Peripheral Nervous System: The nervous system outside of the brain and spinal cord. The peripheral nervous system has autonomic and somatic divisions. The autonomic nervous system includes the enteric, parasympathetic, and sympathetic subdivisions. The somatic nervous system includes the cranial and spinal nerves and their ganglia and the peripheral sensory receptors. [NIH]

Peripheral Nervous System Diseases: Diseases of the peripheral nerves external to the brain and spinal cord, which includes diseases of the nerve roots, ganglia, plexi, autonomic nerves, sensory nerves, and motor nerves. [NIH]

Peripheral Neuropathy: Nerve damage, usually affecting the feet and legs; causing pain, numbness, or a tingling feeling. Also called "somatic neuropathy" or "distal sensory polyneuropathy." [NIH]

Peripheral vision: Side vision; ability to see objects and movement outside of the direct line of vision. [NIH]

Peritoneal: Having to do with the peritoneum (the tissue that lines the abdominal wall and covers most of the organs in the abdomen). [NIH]

Peritoneal Cavity: The space enclosed by the peritoneum. It is divided into two portions, the greater sac and the lesser sac or omental bursa, which lies behind the stomach. The two sacs are connected by the foramen of Winslow, or epiploic foramen. [NIH]

Petechiae: Pinpoint, unraised, round red spots under the skin caused by bleeding. [NIH]

PH: The symbol relating the hydrogen ion (H+) concentration or activity of a solution to that of a given standard solution. Numerically the pH is approximately equal to the negative logarithm of H+ concentration expressed in molarity. pH 7 is neutral; above it alkalinity increases and below it acidity increases. [EU]

Phagocytosis: The engulfing of microorganisms, other cells, and foreign particles by phagocytic cells. [NIH]

Pharmaceutical Preparations: Drugs intended for human or veterinary use, presented in their finished dosage form. Included here are materials used in the preparation and/or formulation of the finished dosage form. [NIH]

Pharmaceutical Solutions: Homogeneous liquid preparations that contain one or more chemical substances dissolved, i.e., molecularly dispersed, in a suitable solvent or mixture of mutually miscible solvents. For reasons of their ingredients, method of preparation, or use, they do not fall into another group of products. [NIH]

Pharmacodynamic: Is concerned with the response of living tissues to chemical stimuli, that is, the action of drugs on the living organism in the absence of disease. [NIH]

Pharmacokinetic: The mathematical analysis of the time courses of absorption, distribution, and elimination of drugs. [NIH]

Pharmacologic: Pertaining to pharmacology or to the properties and reactions of drugs. [EU]

Pharmacotherapy: A regimen of using appetite suppressant medications to manage obesity by decreasing appetite or increasing the feeling of satiety. These medications decrease appetite by increasing serotonin or catecholamine—two brain chemicals that affect mood and appetite. [NIH]

Pharynx: The hollow tube about 5 inches long that starts behind the nose and ends at the top of the trachea (windpipe) and esophagus (the tube that goes to the stomach). [NIH]

Phenobarbital: A barbituric acid derivative that acts as a nonselective central nervous system depressant. It promotes binding to inhibitory GABA subtype receptors, and modulates chloride currents through receptor channels. It also inhibits glutamate induced depolarizations. [NIH]

Phenotype: The outward appearance of the individual. It is the product of interactions between genes and between the genotype and the environment. This includes the killer phenotype, characteristic of yeasts. [NIH]

Phenyl: Ingredient used in cold and flu remedies. [NIH]

Phenylalanine: An aromatic amino acid that is essential in the animal diet. It is a precursor of melanin, dopamine, noradrenalin, and thyroxine. [NIH]

Phobia: A persistent, irrational, intense fear of a specific object, activity, or situation (the phobic stimulus), fear that is recognized as being excessive or unreasonable by the individual himself. When a phobia is a significant source of distress or interferes with social functioning, it is considered a mental disorder; phobic disorder (or neurosis). In DSM III phobic disorders are subclassified as agoraphobia, social phobias, and simple phobias. Used as a word termination denoting irrational fear of or aversion to the subject indicated by the stem to which it is affixed. [EU]

Phobic Disorders: Anxiety disorders in which the essential feature is persistent and irrational fear of a specific object, activity, or situation that the individual feels compelled to avoid. The individual recognizes the fear as excessive or unreasonable. [NIH]

Phospholipases: A class of enzymes that catalyze the hydrolysis of phosphoglycerides or glycerophosphatidates. EC 3.1.-. [NIH]

Phospholipids: Lipids containing one or more phosphate groups, particularly those derived from either glycerol (phosphoglycerides; glycerophospholipids) or sphingosine (sphingolipids). They are polar lipids that are of great importance for the structure and function of cell membranes and are the most abundant of membrane lipids, although not stored in large amounts in the system. [NIH]

Phosphorus: A non-metallic element that is found in the blood, muscles, nevers, bones, and teeth, and is a component of adenosine triphosphate (ATP; the primary energy source for the body's cells.) [NIH]

Phosphorylates: Attached to a phosphate group. [NIH]

Phosphorylation: The introduction of a phosphoryl group into a compound through the formation of an ester bond between the compound and a phosphorus moiety. [NIH]

Photodynamic therapy: Treatment with drugs that become active when exposed to light. These drugs kill cancer cells. [NIH]

Photosensitivity: An abnormal cutaneous response involving the interaction between photosensitizing substances and sunlight or filtered or artificial light at wavelengths of 280-400 mm. There are two main types : photoallergy and photoxicity. [EU]

Phrenic Nerve: The motor nerve of the diaphragm. The phrenic nerve fibers originate in the cervical spinal column (mostly C4) and travel through the cervical plexus to the diaphragm. [NIH]

Physical Examination: Systematic and thorough inspection of the patient for physical signs of disease or abnormality. [NIH]

Physical Therapy: The restoration of function and the prevention of disability following disease or injury with the use of light, heat, cold, water, electricity, ultrasound, and exercise. [NIH]

Physiologic: Having to do with the functions of the body. When used in the phrase "physiologic age," it refers to an age assigned by general health, as opposed to calendar age. [NIH]

Physiology: The science that deals with the life processes and functions of organismus, their cells, tissues, and organs. [NIH]

Physostigmine: A cholinesterase inhibitor that is rapidly absorbed through membranes. It can be applied topically to the conjunctiva. It also can cross the blood-brain barrier and is used when central nervous system effects are desired, as in the treatment of severe anticholinergic toxicity. [NIH]

Picrotoxin: A noncompetitive antagonist at GABA-A receptors and thus a convulsant. Picrotoxin blocks the GABA-activated chloride ionophore. Although it is most often used as a research tool, it has been used as a CNS stimulant and an antidote in poisoning by CNS depressants, especially the barbiturates. [NIH]

Pigment: A substance that gives color to tissue. Pigments are responsible for the color of skin, eyes, and hair. [NIH]

Pilocarpine: A slowly hydrolyzed muscarinic agonist with no nicotinic effects. Pilocarpine is used as a miotic and in the treatment of glaucoma. [NIH]

Pilot study: The initial study examining a new method or treatment. [NIH]

Pituitary Gland: A small, unpaired gland situated in the sella turcica tissue. It is connected to the hypothalamus by a short stalk. [NIH]

Placenta: A highly vascular fetal organ through which the fetus absorbs oxygen and other nutrients and excretes carbon dioxide and other wastes. It begins to form about the eighth day of gestation when the blastocyst adheres to the decidua. [NIH]

Plants: Multicellular, eukaryotic life forms of the kingdom Plantae. They are characterized by a mainly photosynthetic mode of nutrition; essentially unlimited growth at localized regions of cell divisions (meristems); cellulose within cells providing rigidity; the absence of organs of locomotion; absense of nervous and sensory systems; and an alteration of haploid and diploid generations. [NIH]

Plaque: A clear zone in a bacterial culture grown on an agar plate caused by localized destruction of bacterial cells by a bacteriophage. The concentration of infective virus in a fluid can be estimated by applying the fluid to a culture and counting the number of. [NIH]

Plasma: The clear, yellowish, fluid part of the blood that carries the blood cells. The proteins that form blood clots are in plasma. [NIH]

Plasma cells: A type of white blood cell that produces antibodies. [NIH]

Plasma protein: One of the hundreds of different proteins present in blood plasma, including carrier proteins (such albumin, transferrin, and haptoglobin), fibrinogen and other coagulation factors, complement components, immunoglobulins, enzyme inhibitors, precursors of substances such as angiotension and bradykinin, and many other types of proteins. [EU]

Plasma Volume: Volume of plasma in the circulation. It is usually measured by indicator dilution techniques. [NIH]

Plasticity: In an individual or a population, the capacity for adaptation: a) through gene changes (genetic plasticity) or b) through internal physiological modifications in response to changes of environment (physiological plasticity). [NIH]

Platelet Activation: A series of progressive, overlapping events triggered by exposure of the platelets to subendothelial tissue. These events include shape change, adhesiveness, aggregation, and release reactions. When carried through to completion, these events lead to the formation of a stable hemostatic plug. [NIH]

Platelet Aggregation: The attachment of platelets to one another. This clumping together can be induced by a number of agents (e.g., thrombin, collagen) and is part of the mechanism leading to the formation of a thrombus. [NIH]

Platelets: A type of blood cell that helps prevent bleeding by causing blood clots to form. Also called thrombocytes. [NIH]

Platinum: Platinum. A heavy, soft, whitish metal, resembling tin, atomic number 78, atomic weight 195.09, symbol Pt. (From Dorland, 28th ed) It is used in manufacturing equipment for laboratory and industrial use. It occurs as a black powder (platinum black) and as a spongy substance (spongy platinum) and may have been known in Pliny's time as "alutiae". [NIH]

Pleural: A circumscribed area of hyaline whorled fibrous tissue which appears on the surface of the parietal pleura, on the fibrous part of the diaphragm or on the pleura in the interlobar fissures. [NIH]

Pleural cavity: A space enclosed by the pleura (thin tissue covering the lungs and lining the interior wall of the chest cavity). It is bound by thin membranes. [NIH]

Point Mutation: A mutation caused by the substitution of one nucleotide for another. This results in the DNA molecule having a change in a single base pair. [NIH]

Poisoning: A condition or physical state produced by the ingestion, injection or inhalation of, or exposure to a deleterious agent. [NIH]

Polycystic: An inherited disorder characterized by many grape-like clusters of fluid-filled cysts that make both kidneys larger over time. These cysts take over and destroy working kidney tissue. PKD may cause chronic renal failure and end-stage renal disease. [NIH]

Polymerase: An enzyme which catalyses the synthesis of DNA using a single DNA strand as a template. The polymerase copies the template in the 5'-3'direction provided that sufficient quantities of free nucleotides, dATP and dTTP are present. [NIH]

Polymerase Chain Reaction: In vitro method for producing large amounts of specific DNA or RNA fragments of defined length and sequence from small amounts of short oligonucleotide flanking sequences (primers). The essential steps include thermal denaturation of the double-stranded target molecules, annealing of the primers to their complementary sequences, and extension of the annealed primers by enzymatic synthesis with DNA polymerase. The reaction is efficient, specific, and extremely sensitive. Uses for the reaction include disease diagnosis, detection of difficult-to-isolate pathogens, mutation analysis, genetic testing, DNA sequencing, and analyzing evolutionary relationships. [NIH]

Polymorphic: Occurring in several or many forms; appearing in different forms at different stages of development. [EU]

Polymorphism: The occurrence together of two or more distinct forms in the same population. [NIH]

Polypeptide: A peptide which on hydrolysis yields more than two amino acids; called tripeptides, tetrapeptides, etc. according to the number of amino acids contained. [EU]

Polysaccharide: A type of carbohydrate. It contains sugar molecules that are linked together chemically. [NIH]

Pons: The part of the central nervous system lying between the medulla oblongata and the mesencephalon, ventral to the cerebellum, and consisting of a pars dorsalis and a pars ventralis. [NIH]

Posterior: Situated in back of, or in the back part of, or affecting the back or dorsal surface of the body. In lower animals, it refers to the caudal end of the body. [EU]

Postoperative: After surgery. [NIH]

Postsynaptic: Nerve potential generated by an inhibitory hyperpolarizing stimulation. [NIH]

Post-traumatic: Occurring as a result of or after injury. [EU]

Post-traumatic stress disorder: A psychological disorder that develops in some individuals after a major traumatic experience such as war, rape, domestic violence, or accident. [NIH]

Potassium: An element that is in the alkali group of metals. It has an atomic symbol K, atomic number 19, and atomic weight 39.10. It is the chief cation in the intracellular fluid of muscle and other cells. Potassium ion is a strong electrolyte and it plays a significant role in the regulation of fluid volume and maintenance of the water-electrolyte balance. [NIH]

Potassium Channels: Cell membrane glycoproteins selective for potassium ions. [NIH]

Potentiate: A degree of synergism which causes the exposure of the organism to a harmful substance to worsen a disease already contracted. [NIH]

Potentiation: An overall effect of two drugs taken together which is greater than the sum of the effects of each drug taken alone. [NIH]

Practice Guidelines: Directions or principles presenting current or future rules of policy for the health care practitioner to assist him in patient care decisions regarding diagnosis, therapy, or related clinical circumstances. The guidelines may be developed by government agencies at any level, institutions, professional societies, governing boards, or by the convening of expert panels. The guidelines form a basis for the evaluation of all aspects of health care and delivery. [NIH]

Precipitating Factors: Factors associated with the definitive onset of a disease, illness, accident, behavioral response, or course of action. Usually one factor is more important or

more obviously recognizable than others, if several are involved, and one may often be regarded as "necessary". Examples include exposure to specific disease; amount or level of an infectious organism, drug, or noxious agent, etc. [NIH]

Preclinical: Before a disease becomes clinically recognizable. [EU]

Precursor: Something that precedes. In biological processes, a substance from which another, usually more active or mature substance is formed. In clinical medicine, a sign or symptom that heralds another. [EU]

Predictive factor: A situation or condition that may increase a person's risk of developing a certain disease or disorder. [NIH]

Predisposition: A latent susceptibility to disease which may be activated under certain conditions, as by stress. [EU]

Pregnancy Tests: Tests to determine whether or not an individual is pregnant. [NIH]

Pregnenolone: Steroid hormone. [NIH]

Prenatal: Existing or occurring before birth, with reference to the fetus. [EU]

Presynaptic: Situated proximal to a synapse, or occurring before the synapse is crossed. [EU]

Prevalence: The total number of cases of a given disease in a specified population at a designated time. It is differentiated from incidence, which refers to the number of new cases in the population at a given time. [NIH]

Private Practice: Practice of a health profession by an individual, offering services on a person-to-person basis, as opposed to group or partnership practice. [NIH]

Probe: An instrument used in exploring cavities, or in the detection and dilatation of strictures, or in demonstrating the potency of channels; an elongated instrument for exploring or sounding body cavities. [NIH]

Prodrug: A substance that gives rise to a pharmacologically active metabolite, although not itself active (i. e. an inactive precursor). [NIH]

Progesterone: Pregn-4-ene-3,20-dione. The principal progestational hormone of the body, secreted by the corpus luteum, adrenal cortex, and placenta. Its chief function is to prepare the uterus for the reception and development of the fertilized ovum. It acts as an antiovulatory agent when administered on days 5-25 of the menstrual cycle. [NIH]

Prognostic factor: A situation or condition, or a characteristic of a patient, that can be used to estimate the chance of recovery from a disease, or the chance of the disease recurring (coming back). [NIH]

Progression: Increase in the size of a tumor or spread of cancer in the body. [NIH]

Progressive: Advancing; going forward; going from bad to worse; increasing in scope or severity. [EU]

Projection: A defense mechanism, operating unconsciously, whereby that which is emotionally unacceptable in the self is rejected and attributed (projected) to others. [NIH]

Prolactin: Pituitary lactogenic hormone. A polypeptide hormone with a molecular weight of about 23,000. It is essential in the induction of lactation in mammals at parturition and is synergistic with estrogen. The hormone also brings about the release of progesterone from lutein cells, which renders the uterine mucosa suited for the embedding of the ovum should fertilization occur. [NIH]

Promoter: A chemical substance that increases the activity of a carcinogenic process. [NIH]

Prone: Having the front portion of the body downwards. [NIH]

Pro-Opiomelanocortin: A precursor protein, MW 30,000, synthesized mainly in the anterior

pituitary gland but also found in the hypothalamus, brain, and several peripheral tissues. It incorporates the amino acid sequences of ACTH and beta-lipotropin. These two hormones, in turn, contain the biologically active peptides MSH, corticotropin-like intermediate lobe peptide, alpha-lipotropin, endorphins, and methionine enkephalin. [NIH]

Prophase: The first phase of cell division, in which the chromosomes become visible, the nucleus starts to lose its identity, the spindle appears, and the centrioles migrate toward opposite poles. [NIH]

Prophylaxis: An attempt to prevent disease. [NIH]

Proportional: Being in proportion : corresponding in size, degree, or intensity, having the same or a constant ratio; of, relating to, or used in determining proportions. [EU]

Prospective Studies: Observation of a population for a sufficient number of persons over a sufficient number of years to generate incidence or mortality rates subsequent to the selection of the study group. [NIH]

Prospective study: An epidemiologic study in which a group of individuals (a cohort), all free of a particular disease and varying in their exposure to a possible risk factor, is followed over a specific amount of time to determine the incidence rates of the disease in the exposed and unexposed groups. [NIH]

Prostate: A gland in males that surrounds the neck of the bladder and the urethra. It secretes a substance that liquifies coagulated semen. It is situated in the pelvic cavity behind the lower part of the pubic symphysis, above the deep layer of the triangular ligament, and rests upon the rectum. [NIH]

Protease: Proteinase (= any enzyme that catalyses the splitting of interior peptide bonds in a protein). [EU]

Protease Inhibitors: Compounds which inhibit or antagonize biosynthesis or actions of proteases (endopeptidases). [NIH]

Protein C: A vitamin-K dependent zymogen present in the blood, which, upon activation by thrombin and thrombomodulin exerts anticoagulant properties by inactivating factors Va and VIIIa at the rate-limiting steps of thrombin formation. [NIH]

Protein Conformation: The characteristic 3-dimensional shape of a protein, including the secondary, supersecondary (motifs), tertiary (domains) and quaternary structure of the peptide chain. Quaternary protein structure describes the conformation assumed by multimeric proteins (aggregates of more than one polypeptide chain). [NIH]

Protein S: The vitamin K-dependent cofactor of activated protein C. Together with protein C, it inhibits the action of factors VIIIa and Va. A deficiency in protein S can lead to recurrent venous and arterial thrombosis. [NIH]

Protein Subunits: Single chains of amino acids that are the units of a multimeric protein. They can be identical or non-identical subunits. [NIH]

Proteins: Polymers of amino acids linked by peptide bonds. The specific sequence of amino acids determines the shape and function of the protein. [NIH]

Proteolytic: 1. Pertaining to, characterized by, or promoting proteolysis. 2. An enzyme that promotes proteolysis (= the splitting of proteins by hydrolysis of the peptide bonds with formation of smaller polypeptides). [EU]

Protocol: The detailed plan for a clinical trial that states the trial's rationale, purpose, drug or vaccine dosages, length of study, routes of administration, who may participate, and other aspects of trial design. [NIH]

Protons: Stable elementary particles having the smallest known positive charge, found in the

nuclei of all elements. The proton mass is less than that of a neutron. A proton is the nucleus of the light hydrogen atom, i.e., the hydrogen ion. [NIH]

Proximal: Nearest; closer to any point of reference; opposed to distal. [EU]

Proxy: A person authorized to decide or act for another person, for example, a person having durable power of attorney. [NIH]

Pruritus: An intense itching sensation that produces the urge to rub or scratch the skin to obtain relief. [NIH]

Pseudotumor Cerebri: A condition marked by raised intracranial pressure and characterized clinically by headaches; nausea; papilledema, peripheral constriction of the visual fields, transient visual obscurations, and pulsatile tinnitus. Obesity is frequently associated with this condition, which primarily affects women between 20 and 44 years of age. Chronic papilledema may lead to optic nerve injury (optic nerve diseases) and visual loss (blindness). [NIH]

Psychiatric: Pertaining to or within the purview of psychiatry. [EU]

Psychiatry: The medical science that deals with the origin, diagnosis, prevention, and treatment of mental disorders. [NIH]

Psychic: Pertaining to the psyche or to the mind; mental. [EU]

Psychogenic: Produced or caused by psychic or mental factors rather than organic factors. [EU]

Psychology: The science dealing with the study of mental processes and behavior in man and animals. [NIH]

Psychomotor: Pertaining to motor effects of cerebral or psychic activity. [EU]

Psychopathology: The study of significant causes and processes in the development of mental illness. [NIH]

Psychophysiology: The study of the physiological basis of human and animal behavior. [NIH]

Psychosis: A mental disorder characterized by gross impairment in reality testing as evidenced by delusions, hallucinations, markedly incoherent speech, or disorganized and agitated behaviour without apparent awareness on the part of the patient of the incomprehensibility of his behaviour; the term is also used in a more general sense to refer to mental disorders in which mental functioning is sufficiently impaired as to interfere grossly with the patient's capacity to meet the ordinary demands of life. Historically, the term has been applied to many conditions, e.g. manic-depressive psychosis, that were first described in psychotic patients, although many patients with the disorder are not judged psychotic. [EU]

Psychotherapy: A generic term for the treatment of mental illness or emotional disturbances primarily by verbal or nonverbal communication. [NIH]

Psychotropic: Exerting an effect upon the mind; capable of modifying mental activity; usually applied to drugs that effect the mental state. [EU]

Psychotropic Drugs: A loosely defined grouping of drugs that have effects on psychological function. Here the psychotropic agents include the antidepressive agents, hallucinogens, and tranquilizing agents (including the antipsychotics and anti-anxiety agents). [NIH]

Puberty: The period during which the secondary sex characteristics begin to develop and the capability of sexual reproduction is attained. [EU]

Public Health: Branch of medicine concerned with the prevention and control of disease and disability, and the promotion of physical and mental health of the population on the

international, national, state, or municipal level. [NIH]

Public Policy: A course or method of action selected, usually by a government, from among alternatives to guide and determine present and future decisions. [NIH]

Publishing: "The business or profession of the commercial production and issuance of literature" (Webster's 3d). It includes the publisher, publication processes, editing and editors. Production may be by conventional printing methods or by electronic publishing. [NIH]

Pulmonary: Relating to the lungs. [NIH]

Pulmonary Artery: The short wide vessel arising from the conus arteriosus of the right ventricle and conveying unaerated blood to the lungs. [NIH]

Pulmonary Edema: An accumulation of an excessive amount of watery fluid in the lungs, may be caused by acute exposure to dangerous concentrations of irritant gasses. [NIH]

Pulmonary hypertension: Abnormally high blood pressure in the arteries of the lungs. [NIH]

Pulmonary Ventilation: The total volume of gas per minute inspired or expired measured in liters per minute. [NIH]

Pulse: The rhythmical expansion and contraction of an artery produced by waves of pressure caused by the ejection of blood from the left ventricle of the heart as it contracts. [NIH]

Pupil: The aperture in the iris through which light passes. [NIH]

Purines: A series of heterocyclic compounds that are variously substituted in nature and are known also as purine bases. They include adenine and guanine, constituents of nucleic acids, as well as many alkaloids such as caffeine and theophylline. Uric acid is the metabolic end product of purine metabolism. [NIH]

Purpura: Purplish or brownish red discoloration, easily visible through the epidermis, caused by hemorrhage into the tissues. [NIH]

Purulent: Consisting of or containing pus; associated with the formation of or caused by pus. [EU]

Pyramidal Cells: Projection neurons in the cerebral cortex and the hippocampus. Pyramidal cells have a pyramid-shaped soma with the apex and an apical dendrite pointed toward the pial surface and other dendrites and an axon emerging from the base. The axons may have local collaterals but also project outside their cortical region. [NIH]

Pyridoxal: 3-Hydroxy-5-(hydroxymethyl)-2-methyl-4- pyridinecarboxaldehyde. [NIH]

Quality of Life: A generic concept reflecting concern with the modification and enhancement of life attributes, e.g., physical, political, moral and social environment. [NIH]

Quinolinic: It is produced by immune cells and slowly infiltrates the brain tissues after an injury. [NIH]

Quinolinic Acid: 2,3-Pyridinedicarboxylic acid. A metabolite of tryptophan with a possible role in neurodegenerative disorders. Elevated CSF levels of quinolinic acid are significantly correlated with the severity of neuropsychological deficits in patients who have AIDS. [NIH]

Race: A population within a species which exhibits general similarities within itself, but is both discontinuous and distinct from other populations of that species, though not sufficiently so as to achieve the status of a taxon. [NIH]

Radiation: Emission or propagation of electromagnetic energy (waves/rays), or the waves/rays themselves; a stream of electromagnetic particles (electrons, neutrons, protons, alpha particles) or a mixture of these. The most common source is the sun. [NIH]

Radiation therapy: The use of high-energy radiation from x-rays, gamma rays, neutrons,

and other sources to kill cancer cells and shrink tumors. Radiation may come from a machine outside the body (external-beam radiation therapy), or it may come from radioactive material placed in the body in the area near cancer cells (internal radiation therapy, implant radiation, or brachytherapy). Systemic radiation therapy uses a radioactive substance, such as a radiolabeled monoclonal antibody, that circulates throughout the body. Also called radiotherapy. [NIH]

Radioactive: Giving off radiation. [NIH]

Radiography: Examination of any part of the body for diagnostic purposes by means of roentgen rays, recording the image on a sensitized surface (such as photographic film). [NIH]

Radioisotope: An unstable element that releases radiation as it breaks down. Radioisotopes can be used in imaging tests or as a treatment for cancer. [NIH]

Radiological: Pertaining to radiodiagnostic and radiotherapeutic procedures, and interventional radiology or other planning and guiding medical radiology. [NIH]

Radiopharmaceutical: Any medicinal product which, when ready for use, contains one or more radionuclides (radioactive isotopes) included for a medicinal purpose. [NIH]

Randomized: Describes an experiment or clinical trial in which animal or human subjects are assigned by chance to separate groups that compare different treatments. [NIH]

Rape: Unlawful sexual intercourse without consent of the victim. [NIH]

Reactive Oxygen Species: Reactive intermediate oxygen species including both radicals and non-radicals. These substances are constantly formed in the human body and have been shown to kill bacteria and inactivate proteins, and have been implicated in a number of diseases. Scientific data exist that link the reactive oxygen species produced by inflammatory phagocytes to cancer development. [NIH]

Reagent: A substance employed to produce a chemical reaction so as to detect, measure, produce, etc., other substances. [EU]

Reality Testing: The individual's objective evaluation of the external world and the ability to differentiate adequately between it and the internal world; considered to be a primary ego function. [NIH]

Receptor: A molecule inside or on the surface of a cell that binds to a specific substance and causes a specific physiologic effect in the cell. [NIH]

Receptors, Serotonin: Cell-surface proteins that bind serotonin and trigger intracellular changes which influence the behavior of cells. Several types of serotonin receptors have been recognized which differ in their pharmacology, molecular biology, and mode of action. [NIH]

Recombinant: A cell or an individual with a new combination of genes not found together in either parent; usually applied to linked genes. [EU]

Rectum: The last 8 to 10 inches of the large intestine. [NIH]

Recur: To occur again. Recurrence is the return of cancer, at the same site as the original (primary) tumor or in another location, after the tumor had disappeared. [NIH]

Recurrence: The return of a sign, symptom, or disease after a remission. [NIH]

Red Nucleus: A pinkish-yellow portion of the midbrain situated in the rostral mesencephalic tegmentum. It receives a large projection from the contralateral half of the cerebellum via the superior cerebellar peduncle and a projection from the ipsilateral motor cortex. [NIH]

Refer: To send or direct for treatment, aid, information, de decision. [NIH]

Reflex: An involuntary movement or exercise of function in a part, excited in response to a stimulus applied to the periphery and transmitted to the brain or spinal cord. [NIH]

Refraction: A test to determine the best eyeglasses or contact lenses to correct a refractive error (myopia, hyperopia, or astigmatism). [NIH]

Refractory: Not readily yielding to treatment. [EU]

Regeneration: The natural renewal of a structure, as of a lost tissue or part. [EU]

Regimen: A treatment plan that specifies the dosage, the schedule, and the duration of treatment. [NIH]

Registries: The systems and processes involved in the establishment, support, management, and operation of registers, e.g., disease registers. [NIH]

Relapse: The return of signs and symptoms of cancer after a period of improvement. [NIH]

Relative risk: The ratio of the incidence rate of a disease among individuals exposed to a specific risk factor to the incidence rate among unexposed individuals; synonymous with risk ratio. Alternatively, the ratio of the cumulative incidence rate in the exposed to the cumulative incidence rate in the unexposed (cumulative incidence ratio). The term relative risk has also been used synonymously with odds ratio. This is because the odds ratio and relative risk approach each other if the disease is rare (5 percent of population) and the number of subjects is large. [NIH]

Relaxant: 1. Lessening or reducing tension. 2. An agent that lessens tension. [EU]

Reliability: Used technically, in a statistical sense, of consistency of a test with itself, i. e. the extent to which we can assume that it will yield the same result if repeated a second time. [NIH]

Remission: A decrease in or disappearance of signs and symptoms of cancer. In partial remission, some, but not all, signs and symptoms of cancer have disappeared. In complete remission, all signs and symptoms of cancer have disappeared, although there still may be cancer in the body. [NIH]

Renal failure: Progressive renal insufficiency and uremia, due to irreversible and progressive renal glomerular tubular or interstitial disease. [NIH]

Reperfusion: Restoration of blood supply to tissue which is ischemic due to decrease in normal blood supply. The decrease may result from any source including atherosclerotic obstruction, narrowing of the artery, or surgical clamping. It is primarily a procedure for treating infarction or other ischemia, by enabling viable ischemic tissue to recover, thus limiting further necrosis. However, it is thought that reperfusion can itself further damage the ischemic tissue, causing reperfusion injury. [NIH]

Reperfusion Injury: Functional, metabolic, or structural changes, including necrosis, in ischemic tissues thought to result from reperfusion to ischemic areas of the tissue. The most common instance is myocardial reperfusion injury. [NIH]

Research Design: A plan for collecting and utilizing data so that desired information can be obtained with sufficient precision or so that an hypothesis can be tested properly. [NIH]

Resected: Surgical removal of part of an organ. [NIH]

Resection: Removal of tissue or part or all of an organ by surgery. [NIH]

Resorption: The loss of substance through physiologic or pathologic means, such as loss of dentin and cementum of a tooth, or of the alveolar process of the mandible or maxilla. [EU]

Respiration: The act of breathing with the lungs, consisting of inspiration, or the taking into the lungs of the ambient air, and of expiration, or the expelling of the modified air which contains more carbon dioxide than the air taken in (Blakiston's Gould Medical Dictionary, 4th ed.). This does not include tissue respiration (= oxygen consumption) or cell respiration (= cell respiration). [NIH]

Respiratory Paralysis: Complete or severe weakness of the muscles of respiration. This condition may be associated with motor neuron diseases; peripheral nerve disorders; neuromuscular junction diseases; spinal cord diseases; injury to the phrenic nerve; and other disorders. [NIH]

Response rate: The percentage of patients whose cancer shrinks or disappears after treatment. [NIH]

Restless legs: Legs characterized by or showing inability to remain at rest. [EU]

Restoration: Broad term applied to any inlay, crown, bridge or complete denture which restores or replaces loss of teeth or oral tissues. [NIH]

Retina: The ten-layered nervous tissue membrane of the eye. It is continuous with the optic nerve and receives images of external objects and transmits visual impulses to the brain. Its outer surface is in contact with the choroid and the inner surface with the vitreous body. The outer-most layer is pigmented, whereas the inner nine layers are transparent. [NIH]

Retinal: 1. Pertaining to the retina. 2. The aldehyde of retinol, derived by the oxidative enzymatic splitting of absorbed dietary carotene, and having vitamin A activity. In the retina, retinal combines with opsins to form visual pigments. One isomer, 11-cis retinal combines with opsin in the rods (scotopsin) to form rhodopsin, or visual purple. Another, all-trans retinal (trans-r.); visual yellow; xanthopsin) results from the bleaching of rhodopsin by light, in which the 11-cis form is converted to the all-trans form. Retinal also combines with opsins in the cones (photopsins) to form the three pigments responsible for colour vision. Called also retinal, and retinene1. [EU]

Retinoblastoma: An eye cancer that most often occurs in children younger than 5 years. It occurs in hereditary and nonhereditary (sporadic) forms. [NIH]

Retinol: Vitamin A. It is essential for proper vision and healthy skin and mucous membranes. Retinol is being studied for cancer prevention; it belongs to the family of drugs called retinoids. [NIH]

Retinopathy: 1. Retinitis (= inflammation of the retina). 2. Retinosis (= degenerative, noninflammatory condition of the retina). [EU]

Retrospective: Looking back at events that have already taken place. [NIH]

Rheumatism: A group of disorders marked by inflammation or pain in the connective tissue structures of the body. These structures include bone, cartilage, and fat. [NIH]

Rheumatoid: Resembling rheumatism. [EU]

Rheumatoid arthritis: A form of arthritis, the cause of which is unknown, although infection, hypersensitivity, hormone imbalance and psychologic stress have been suggested as possible causes. [NIH]

Rhythmicity: Regular periodicity. [NIH]

Ribose: A pentose active in biological systems usually in its D-form. [NIH]

Ribosome: A granule of protein and RNA, synthesized in the nucleolus and found in the cytoplasm of cells. Ribosomes are the main sites of protein synthesis. Messenger RNA attaches to them and there receives molecules of transfer RNA bearing amino acids. [NIH]

Rigidity: Stiffness or inflexibility, chiefly that which is abnormal or morbid; rigor. [EU]

Risk factor: A habit, trait, condition, or genetic alteration that increases a person's chance of developing a disease. [NIH]

Risk patient: Patient who is at risk, because of his/her behaviour or because of the type of person he/she is. [EU]

Rod: A reception for vision, located in the retina. [NIH]

Rolandic Epilepsy: Epilepsy induced by specific external stimuli. [NIH]

Rutin: 3-((6-O-(6-Deoxy-alpha-L-mannopyranosyl)-beta-D-glucopyranosyl)oxy)-2-(3,4-dihydroxyphenyl)-5,7-dihydroxy-4H-1-benzopyran-4-one. Found in many plants, including buckwheat, tobacco, forsythia, hydrangea, pansies, etc. It has been used therapeutically to decrease capillary fragility. [NIH]

Salicylic: A tuberculosis drug. [NIH]

Saline: A solution of salt and water. [NIH]

Salivary: The duct that convey saliva to the mouth. [NIH]

Salivary glands: Glands in the mouth that produce saliva. [NIH]

Saphenous: Applied to certain structures in the leg, e. g. nerve vein. [NIH]

Saphenous Vein: The vein which drains the foot and leg. [NIH]

Saponins: Sapogenin glycosides. A type of glycoside widely distributed in plants. Each consists of a sapogenin as the aglycon moiety, and a sugar. The sapogenin may be a steroid or a triterpene and the sugar may be glucose, galactose, a pentose, or a methylpentose. Sapogenins are poisonous towards the lower forms of life and are powerful hemolytics when injected into the blood stream able to dissolve red blood cells at even extreme dilutions. [NIH]

Sarcoid: A cutaneus lesion occurring as a manifestation of sarcoidosis. [NIH]

Sarcoidosis: An idiopathic systemic inflammatory granulomatous disorder comprised of epithelioid and multinucleated giant cells with little necrosis. It usually invades the lungs with fibrosis and may also involve lymph nodes, skin, liver, spleen, eyes, phalangeal bones, and parotid glands. [NIH]

Scans: Pictures of structures inside the body. Scans often used in diagnosing, staging, and monitoring disease include liver scans, bone scans, and computed tomography (CT) or computerized axial tomography (CAT) scans and magnetic resonance imaging (MRI) scans. In liver scanning and bone scanning, radioactive substances that are injected into the bloodstream collect in these organs. A scanner that detects the radiation is used to create pictures. In CT scanning, an x-ray machine linked to a computer is used to produce detailed pictures of organs inside the body. MRI scans use a large magnet connected to a computer to create pictures of areas inside the body. [NIH]

Schematic: Representative or schematic eye computed from the average of a large number of human eye measurements by Allvar Gullstrand. [NIH]

Schizoid: Having qualities resembling those found in greater degree in schizophrenics; a person of schizoid personality. [NIH]

Schizophrenia: A mental disorder characterized by a special type of disintegration of the personality. [NIH]

Schizotypal Personality Disorder: A personality disorder in which there are oddities of thought (magical thinking, paranoid ideation, suspiciousness), perception (illusions, depersonalization), speech (digressive, vague, overelaborate), and behavior (inappropriate affect in social interactions, frequently social isolation) that are not severe enough to characterize schizophrenia. [NIH]

Sclera: The tough white outer coat of the eyeball, covering approximately the posterior five-sixths of its surface, and continuous anteriorly with the cornea and posteriorly with the external sheath of the optic nerve. [EU]

Sclerosis: A pathological process consisting of hardening or fibrosis of an anatomical structure, often a vessel or a nerve. [NIH]

Sclerotic: Pertaining to the outer coat of the eye; the sclera; hard, indurated or sclerosed. [NIH]

Screening: Checking for disease when there are no symptoms. [NIH]

Sebaceous: Gland that secretes sebum. [NIH]

Sebum: The oily substance secreted by sebaceous glands. It is composed of keratin, fat, and cellular debris. [NIH]

Second Messenger Systems: Systems in which an intracellular signal is generated in response to an intercellular primary messenger such as a hormone or neurotransmitter. They are intermediate signals in cellular processes such as metabolism, secretion, contraction, phototransduction, and cell growth. Examples of second messenger systems are the adenyl cyclase-cyclic AMP system, the phosphatidylinositol diphosphate-inositol triphosphate system, and the cyclic GMP system. [NIH]

Secretion: 1. The process of elaborating a specific product as a result of the activity of a gland; this activity may range from separating a specific substance of the blood to the elaboration of a new chemical substance. 2. Any substance produced by secretion. [EU]

Secretory: Secreting; relating to or influencing secretion or the secretions. [NIH]

Sedative: 1. Allaying activity and excitement. 2. An agent that allays excitement. [EU]

Sedatives, Barbiturate: Those derivatives of barbituric or thiobarbituric acid that are used as hypnotics or sedatives. The structural class of all such derivatives, regardless of use, is barbiturates. [NIH]

Seizures: Clinical or subclinical disturbances of cortical function due to a sudden, abnormal, excessive, and disorganized discharge of brain cells. Clinical manifestations include abnormal motor, sensory and psychic phenomena. Recurrent seizures are usually referred to as epilepsy or "seizure disorder." [NIH]

Sella: A deep depression in the shape of a Turkish saddle in the upper surface of the body of the sphenoid bone in the deepest part of which is lodged the hypophysis cerebri. [NIH]

Semen: The thick, yellowish-white, viscid fluid secretion of male reproductive organs discharged upon ejaculation. In addition to reproductive organ secretions, it contains spermatozoa and their nutrient plasma. [NIH]

Senile: Relating or belonging to old age; characteristic of old age; resulting from infirmity of old age. [NIH]

Sensor: A device designed to respond to physical stimuli such as temperature, light, magnetism or movement and transmit resulting impulses for interpretation, recording, movement, or operating control. [NIH]

Sensory loss: A disease of the nerves whereby the myelin or insulating sheath of myelin on the nerves does not stay intact and the messages from the brain to the muscles through the nerves are not carried properly. [NIH]

Septal: An abscess occurring at the root of the tooth on the proximal surface. [NIH]

Septal Nuclei: Neural nuclei situated in the septal region. They have afferent and cholinergic efferent connections with a variety of forebrain and brainstem areas including the hippocampus, the lateral hypothalamus, the tegmentum, and the amygdala. Included are the dorsal, lateral, medial, and triangular septal nuclei, septofimbrial nucleus, nucleus of diagonal band, nucleus of anterior commissure, and the nucleus of stria terminalis. [NIH]

Sequela: Any lesion or affection following or caused by an attack of disease. [EU]

Sequencing: The determination of the order of nucleotides in a DNA or RNA chain. [NIH]

Sequester: A portion of dead bone which has become detached from the healthy bone

tissue, as occurs in necrosis. [NIH]

Serine: A non-essential amino acid occurring in natural form as the L-isomer. It is synthesized from glycine or threonine. It is involved in the biosynthesis of purines, pyrimidines, and other amino acids. [NIH]

Serotonin: A biochemical messenger and regulator, synthesized from the essential amino acid L-tryptophan. In humans it is found primarily in the central nervous system, gastrointestinal tract, and blood platelets. Serotonin mediates several important physiological functions including neurotransmission, gastrointestinal motility, hemostasis, and cardiovascular integrity. Multiple receptor families (receptors, serotonin) explain the broad physiological actions and distribution of this biochemical mediator. [NIH]

Sertraline: A selective serotonin uptake inhibitor that is used in the treatment of depression. [NIH]

Serum: The clear liquid part of the blood that remains after blood cells and clotting proteins have been removed. [NIH]

Sex Characteristics: Those characteristics that distinguish one sex from the other. The primary sex characteristics are the ovaries and testes and their related hormones. Secondary sex characteristics are those which are masculine or feminine but not directly related to reproduction. [NIH]

Sex Determination: The biological characteristics which distinguish human beings as female or male. [NIH]

Shock: The general bodily disturbance following a severe injury; an emotional or moral upset occasioned by some disturbing or unexpected experience; disruption of the circulation, which can upset all body functions: sometimes referred to as circulatory shock. [NIH]

Side effect: A consequence other than the one(s) for which an agent or measure is used, as the adverse effects produced by a drug, especially on a tissue or organ system other than the one sought to be benefited by its administration. [EU]

Signal Transduction: The intercellular or intracellular transfer of information (biological activation/inhibition) through a signal pathway. In each signal transduction system, an activation/inhibition signal from a biologically active molecule (hormone, neurotransmitter) is mediated via the coupling of a receptor/enzyme to a second messenger system or to an ion channel. Signal transduction plays an important role in activating cellular functions, cell differentiation, and cell proliferation. Examples of signal transduction systems are the GABA-postsynaptic receptor-calcium ion channel system, the receptor-mediated T-cell activation pathway, and the receptor-mediated activation of phospholipases. Those coupled to membrane depolarization or intracellular release of calcium include the receptor-mediated activation of cytotoxic functions in granulocytes and the synaptic potentiation of protein kinase activation. Some signal transduction pathways may be part of larger signal transduction pathways; for example, protein kinase activation is part of the platelet activation signal pathway. [NIH]

Signs and Symptoms: Clinical manifestations that can be either objective when observed by a physician, or subjective when perceived by the patient. [NIH]

Silicon: A trace element that constitutes about 27.6% of the earth's crust in the form of silicon dioxide. It does not occur free in nature. Silicon has the atomic symbol Si, atomic number 14, and atomic weight 28.09. [NIH]

Silicon Dioxide: Silica. Transparent, tasteless crystals found in nature as agate, amethyst, chalcedony, cristobalite, flint, sand, quartz, and tridymite. The compound is insoluble in water or acids except hydrofluoric acid. [NIH]

Skeletal: Having to do with the skeleton (boney part of the body). [NIH]

Skeleton: The framework that supports the soft tissues of vertebrate animals and protects many of their internal organs. The skeletons of vertebrates are made of bone and/or cartilage. [NIH]

Skull: The skeleton of the head including the bones of the face and the bones enclosing the brain. [NIH]

Sleep apnea: A serious, potentially life-threatening breathing disorder characterized by repeated cessation of breathing due to either collapse of the upper airway during sleep or absence of respiratory effort. [NIH]

Sleep Deprivation: The state of being deprived of sleep under experimental conditions, due to life events, or from a wide variety of pathophysiologic causes such as medication effect, chronic illness, psychiatric illness, or sleep disorder. [NIH]

Small intestine: The part of the digestive tract that is located between the stomach and the large intestine. [NIH]

Smooth muscle: Muscle that performs automatic tasks, such as constricting blood vessels. [NIH]

Social Behavior: Any behavior caused by or affecting another individual, usually of the same species. [NIH]

Social Environment: The aggregate of social and cultural institutions, forms, patterns, and processes that influence the life of an individual or community. [NIH]

Sodium: An element that is a member of the alkali group of metals. It has the atomic symbol Na, atomic number 11, and atomic weight 23. With a valence of 1, it has a strong affinity for oxygen and other nonmetallic elements. Sodium provides the chief cation of the extracellular body fluids. Its salts are the most widely used in medicine. (From Dorland, 27th ed) Physiologically the sodium ion plays a major role in blood pressure regulation, maintenance of fluid volume, and electrolyte balance. [NIH]

Sodium Channels: Cell membrane glycoproteins selective for sodium ions. Fast sodium current is associated with the action potential in neural membranes. [NIH]

Sodium Iodide: Sodium iodide (NaI). A compound forming white, odorless deliquescent crystals and used as iodine supplement, expectorant or in its radioactive (I-131) form as an diagnostic aid, particularly for thyroid function determinants. [NIH]

Solid tumor: Cancer of body tissues other than blood, bone marrow, or the lymphatic system. [NIH]

Solium: Tapeworm of the genus Taenia. The adult form is found in the small intestine of humans and some apes and the metacestode (Cysticercus cellulosae) in the skeletal and cardiac muscle of pigs and in the brain of humans. [NIH]

Solvent: 1. Dissolving; effecting a solution. 2. A liquid that dissolves or that is capable of dissolving; the component of a solution that is present in greater amount. [EU]

Soma: The body as distinct from the mind; all the body tissue except the germ cells; all the axial body. [NIH]

Somatic: 1. Pertaining to or characteristic of the soma or body. 2. Pertaining to the body wall in contrast to the viscera. [EU]

Somatosensory Cortex: Area of the parietal lobe concerned with receiving general sensations. It lies posterior to the central sulcus. [NIH]

Somatostatin: A polypeptide hormone produced in the hypothalamus, and other tissues and organs. It inhibits the release of human growth hormone, and also modulates important

physiological functions of the kidney, pancreas, and gastrointestinal tract. Somatostatin receptors are widely expressed throughout the body. Somatostatin also acts as a neurotransmitter in the central and peripheral nervous systems. [NIH]

Sound wave: An alteration of properties of an elastic medium, such as pressure, particle displacement, or density, that propagates through the medium, or a superposition of such alterations. [NIH]

Spasm: An involuntary contraction of a muscle or group of muscles. Spasms may involve skeletal muscle or smooth muscle. [NIH]

Spasmodic: Of the nature of a spasm. [EU]

Spastic: 1. Of the nature of or characterized by spasms. 2. Hypertonic, so that the muscles are stiff and the movements awkward. 3. A person exhibiting spasticity, such as occurs in spastic paralysis or in cerebral palsy. [EU]

Spasticity: A state of hypertonicity, or increase over the normal tone of a muscle, with heightened deep tendon reflexes. [EU]

Spatial disorientation: Loss of orientation in space where person does not know which way is up. [NIH]

Specialist: In medicine, one who concentrates on 1 special branch of medical science. [NIH]

Species: A taxonomic category subordinate to a genus (or subgenus) and superior to a subspecies or variety, composed of individuals possessing common characters distinguishing them from other categories of individuals of the same taxonomic level. In taxonomic nomenclature, species are designated by the genus name followed by a Latin or Latinized adjective or noun. [EU]

Specificity: Degree of selectivity shown by an antibody with respect to the number and types of antigens with which the antibody combines, as well as with respect to the rates and the extents of these reactions. [NIH]

Spectrum: A charted band of wavelengths of electromagnetic vibrations obtained by refraction and diffraction. By extension, a measurable range of activity, such as the range of bacteria affected by an antibiotic (antibacterial s.) or the complete range of manifestations of a disease. [EU]

Sperm: The fecundating fluid of the male. [NIH]

Spermatozoa: Mature male germ cells that develop in the seminiferous tubules of the testes. Each consists of a head, a body, and a tail that provides propulsion. The head consists mainly of chromatin. [NIH]

Sphenoid: An unpaired cranial bone with a body containing the sphenoid sinus and forming the posterior part of the medial walls of the orbits. [NIH]

Sphenoidal: Relating or belonging to the sphenoid bone. [NIH]

Spike: The activation of synapses causes changes in the permeability of the dendritic membrane leading to changes in the membrane potential. This difference of the potential travels along the axon of the neuron and is called spike. [NIH]

Spina bifida: A defect in development of the vertebral column in which there is a central deficiency of the vertebral lamina. [NIH]

Spinal cord: The main trunk or bundle of nerves running down the spine through holes in the spinal bone (the vertebrae) from the brain to the level of the lower back. [NIH]

Spinal Cord Diseases: Pathologic conditions which feature spinal cord damage or dysfunction, including disorders involving the meninges and perimeningeal spaces surrounding the spinal cord. Traumatic injuries, vascular diseases, infections, and

inflammatory/autoimmune processes may affect the spinal cord. [NIH]

Spinal Cord Injuries: Penetrating and non-penetrating injuries to the spinal cord resulting from traumatic external forces (e.g., wounds, gunshot; whiplash injuries; etc.). [NIH]

Spinal Nerves: The 31 paired peripheral nerves formed by the union of the dorsal and ventral spinal roots from each spinal cord segment. The spinal nerve plexuses and the spinal roots are also included. [NIH]

Spinal tap: A procedure in which a needle is put into the lower part of the spinal column to collect cerebrospinal fluid or to give anticancer drugs intrathecally. Also called a lumbar puncture. [NIH]

Spiro Compounds: A group of compounds consisting in part of two rings sharing one carbon atom in common. [NIH]

Spirochete: Lyme disease. [NIH]

Sporadic: Neither endemic nor epidemic; occurring occasionally in a random or isolated manner. [EU]

Sprains and Strains: A collective term for muscle and ligament injuries without dislocation or fracture. A sprain is a joint injury in which some of the fibers of a supporting ligament are ruptured but the continuity of the ligament remains intact. A strain is an overstretching or overexertion of some part of the musculature. [NIH]

Staging: Performing exams and tests to learn the extent of the cancer within the body, especially whether the disease has spread from the original site to other parts of the body. [NIH]

Standard therapy: A currently accepted and widely used treatment for a certain type of cancer, based on the results of past research. [NIH]

Status Epilepticus: Repeated and prolonged epileptic seizures without recovery of consciousness between attacks. [NIH]

Steady state: Dynamic equilibrium. [EU]

Steel: A tough, malleable, iron-based alloy containing up to, but no more than, two percent carbon and often other metals. It is used in medicine and dentistry in implants and instrumentation. [NIH]

Stereotactic: Radiotherapy that treats brain tumors by using a special frame affixed directly to the patient's cranium. By aiming the X-ray source with respect to the rigid frame, technicians can position the beam extremely precisely during each treatment. [NIH]

Stereotactic radiosurgery: A radiation therapy technique involving a rigid head frame that is attached to the skull; high-dose radiation is administered through openings in the head frame to the tumor while decreasing the amount of radiation given to normal brain tissue. This procedure does not involve surgery. Also called stereotaxic radiosurgery and stereotactic radiation therapy. [NIH]

Sterility: 1. The inability to produce offspring, i.e., the inability to conceive (female s.) or to induce conception (male s.). 2. The state of being aseptic, or free from microorganisms. [EU]

Steroid: A group name for lipids that contain a hydrogenated cyclopentanoperhydrophenanthrene ring system. Some of the substances included in this group are progesterone, adrenocortical hormones, the gonadal hormones, cardiac aglycones, bile acids, sterols (such as cholesterol), toad poisons, saponins, and some of the carcinogenic hydrocarbons. [EU]

Stimulant: 1. Producing stimulation; especially producing stimulation by causing tension on muscle fibre through the nervous tissue. 2. An agent or remedy that produces stimulation. [EU]

Stimulus: That which can elicit or evoke action (response) in a muscle, nerve, gland or other excitable issue, or cause an augmenting action upon any function or metabolic process. [NIH]

Stomach: An organ of digestion situated in the left upper quadrant of the abdomen between the termination of the esophagus and the beginning of the duodenum. [NIH]

Stomatitis: Inflammation of the oral mucosa, due to local or systemic factors which may involve the buccal and labial mucosa, palate, tongue, floor of the mouth, and the gingivae. [EU]

Stool: The waste matter discharged in a bowel movement; feces. [NIH]

Strand: DNA normally exists in the bacterial nucleus in a helix, in which two strands are coiled together. [NIH]

Stress: Forcibly exerted influence; pressure. Any condition or situation that causes strain or tension. Stress may be either physical or psychologic, or both. [NIH]

Striate: Recurrent branch of the anterior cerebral artery which supplies the anterior limb of the internal capsule. [NIH]

Striatum: A higher brain's domain thus called because of its stripes. [NIH]

Stroke: Sudden loss of function of part of the brain because of loss of blood flow. Stroke may be caused by a clot (thrombosis) or rupture (hemorrhage) of a blood vessel to the brain. [NIH]

Subacute: Somewhat acute; between acute and chronic. [EU]

Subarachnoid: Situated or occurring between the arachnoid and the pia mater. [EU]

Subclinical: Without clinical manifestations; said of the early stage(s) of an infection or other disease or abnormality before symptoms and signs become apparent or detectable by clinical examination or laboratory tests, or of a very mild form of an infection or other disease or abnormality. [EU]

Subcutaneous: Beneath the skin. [NIH]

Subiculum: A region of the hippocampus that projects to other areas of the brain. [NIH]

Subspecies: A category intermediate in rank between species and variety, based on a smaller number of correlated characters than are used to differentiate species and generally conditioned by geographical and/or ecological occurrence. [NIH]

Substance P: An eleven-amino acid neurotransmitter that appears in both the central and peripheral nervous systems. It is involved in transmission of pain, causes rapid contractions of the gastrointestinal smooth muscle, and modulates inflammatory and immune responses. [NIH]

Substrate: A substance upon which an enzyme acts. [EU]

Sudden death: Cardiac arrest caused by an irregular heartbeat. The term "death" is somewhat misleading, because some patients survive. [NIH]

Supine: Having the front portion of the body upwards. [NIH]

Supplementation: Adding nutrients to the diet. [NIH]

Support group: A group of people with similar disease who meet to discuss how better to cope with their cancer and treatment. [NIH]

Suppositories: A small cone-shaped medicament having cocoa butter or gelatin at its basis and usually intended for the treatment of local conditions in the rectum. [NIH]

Suppression: A conscious exclusion of disapproved desire contrary with repression, in which the process of exclusion is not conscious. [NIH]

Supraspinal: Above the spinal column or any spine. [NIH]

Survival Analysis: A class of statistical procedures for estimating the survival function (function of time, starting with a population 100% well at a given time and providing the percentage of the population still well at later times). The survival analysis is then used for making inferences about the effects of treatments, prognostic factors, exposures, and other covariates on the function. [NIH]

Sympathetic Nervous System: The thoracolumbar division of the autonomic nervous system. Sympathetic preganglionic fibers originate in neurons of the intermediolateral column of the spinal cord and project to the paravertebral and prevertebral ganglia, which in turn project to target organs. The sympathetic nervous system mediates the body's response to stressful situations, i.e., the fight or flight reactions. It often acts reciprocally to the parasympathetic system. [NIH]

Sympathomimetic: 1. Mimicking the effects of impulses conveyed by adrenergic postganglionic fibres of the sympathetic nervous system. 2. An agent that produces effects similar to those of impulses conveyed by adrenergic postganglionic fibres of the sympathetic nervous system. Called also adrenergic. [EU]

Symphysis: A secondary cartilaginous joint. [NIH]

Symptomatic: Having to do with symptoms, which are signs of a condition or disease. [NIH]

Synapses: Specialized junctions at which a neuron communicates with a target cell. At classical synapses, a neuron's presynaptic terminal releases a chemical transmitter stored in synaptic vesicles which diffuses across a narrow synaptic cleft and activates receptors on the postsynaptic membrane of the target cell. The target may be a dendrite, cell body, or axon of another neuron, or a specialized region of a muscle or secretory cell. Neurons may also communicate through direct electrical connections which are sometimes called electrical synapses; these are not included here but rather in gap junctions. [NIH]

Synapsis: The pairing between homologous chromosomes of maternal and paternal origin during the prophase of meiosis, leading to the formation of gametes. [NIH]

Synaptic: Pertaining to or affecting a synapse (= site of functional apposition between neurons, at which an impulse is transmitted from one neuron to another by electrical or chemical means); pertaining to synapsis (= pairing off in point-for-point association of homologous chromosomes from the male and female pronuclei during the early prophase of meiosis). [EU]

Synaptic Transmission: The communication from a neuron to a target (neuron, muscle, or secretory cell) across a synapse. In chemical synaptic transmission, the presynaptic neuron releases a neurotransmitter that diffuses across the synaptic cleft and binds to specific synaptic receptors. These activated receptors modulate ion channels and/or second-messenger systems to influence the postsynaptic cell. Electrical transmission is less common in the nervous system, and, as in other tissues, is mediated by gap junctions. [NIH]

Synaptic Vesicles: Membrane-bound compartments which contain transmitter molecules. Synaptic vesicles are concentrated at presynaptic terminals. They actively sequester transmitter molecules from the cytoplasm. In at least some synapses, transmitter release occurs by fusion of these vesicles with the presynaptic membrane, followed by exocytosis of their contents. [NIH]

Syncope: A temporary suspension of consciousness due to generalized cerebral schemia, a faint or swoon. [EU]

Synergistic: Acting together; enhancing the effect of another force or agent. [EU]

Syphilis: A contagious venereal disease caused by the spirochete Treponema pallidum. [NIH]

Syringomyelia: The presence in the spinal cord of elongated central fluid containing cavities

surrounded by gliosis. [NIH]

Systemic: Affecting the entire body. [NIH]

Systolic: Indicating the maximum arterial pressure during contraction of the left ventricle of the heart. [EU]

Tachycardia: Excessive rapidity in the action of the heart, usually with a heart rate above 100 beats per minute. [NIH]

Tardive: Marked by lateness, late; said of a disease in which the characteristic lesion is late in appearing. [EU]

Technetium: The first artificially produced element and a radioactive fission product of uranium. The stablest isotope has a mass number 99 and is used diagnostically as a radioactive imaging agent. Technetium has the atomic symbol Tc, atomic number 43, and atomic weight 98.91. [NIH]

Telangiectasia: The permanent enlargement of blood vessels, causing redness in the skin or mucous membranes. [NIH]

Temporal: One of the two irregular bones forming part of the lateral surfaces and base of the skull, and containing the organs of hearing. [NIH]

Temporal Lobe: Lower lateral part of the cerebral hemisphere. [NIH]

Testis: Either of the paired male reproductive glands that produce the male germ cells and the male hormones. [NIH]

Tetrahydrocannabinol: A psychoactive compound extracted from the resin of Cannabis sativa (marihuana, hashish). The isomer delta-9-tetrahydrocannabinol (THC) is considered the most active form, producing characteristic mood and perceptual changes associated with this compound. Dronabinol is a synthetic form of delta-9-THC. [NIH]

Thalamic: Cell that reaches the lateral nucleus of amygdala. [NIH]

Thalamic Diseases: Disorders of the centrally located thalamus, which integrates a wide range of cortical and subcortical information. Manifestations include sensory loss, movement disorders; ataxia, pain syndromes, visual disorders, a variety of neuropsychological conditions, and coma. Relatively common etiologies include cerebrovascular disorders; craniocerebral trauma; brain neoplasms; brain hypoxia; intracranial hemorrhages; and infectious processes. [NIH]

Thalamus: Paired bodies containing mostly gray substance and forming part of the lateral wall of the third ventricle of the brain. The thalamus represents the major portion of the diencephalon and is commonly divided into cellular aggregates known as nuclear groups. [NIH]

Therapeutics: The branch of medicine which is concerned with the treatment of diseases, palliative or curative. [NIH]

Thermal: Pertaining to or characterized by heat. [EU]

Third Ventricle: A narrow cleft inferior to the corpus callosum, within the diencephalon, between the paired thalami. Its floor is formed by the hypothalamus, its anterior wall by the lamina terminalis, and its roof by ependyma. It communicates with the fourth ventricle by the cerebral aqueduct, and with the lateral ventricles by the interventricular foramina. [NIH]

Thoracic: Having to do with the chest. [NIH]

Thorax: A part of the trunk between the neck and the abdomen; the chest. [NIH]

Threonine: An essential amino acid occurring naturally in the L-form, which is the active form. It is found in eggs, milk, gelatin, and other proteins. [NIH]

Threshold: For a specified sensory modality (e. g. light, sound, vibration), the lowest level (absolute threshold) or smallest difference (difference threshold, difference limen) or intensity of the stimulus discernible in prescribed conditions of stimulation. [NIH]

Thrombin: An enzyme formed from prothrombin that converts fibrinogen to fibrin. (Dorland, 27th ed) EC 3.4.21.5. [NIH]

Thrombomodulin: A cell surface glycoprotein of endothelial cells that binds thrombin and serves as a cofactor in the activation of protein C and its regulation of blood coagulation. [NIH]

Thrombosis: The formation or presence of a blood clot inside a blood vessel. [NIH]

Thrombus: An aggregation of blood factors, primarily platelets and fibrin with entrapment of cellular elements, frequently causing vascular obstruction at the point of its formation. Some authorities thus differentiate thrombus formation from simple coagulation or clot formation. [EU]

Thyroid: A gland located near the windpipe (trachea) that produces thyroid hormone, which helps regulate growth and metabolism. [NIH]

Thyroxine: An amino acid of the thyroid gland which exerts a stimulating effect on thyroid metabolism. [NIH]

Ticks: Blood-sucking arachnids of the order Acarina. [NIH]

Tidal Volume: The volume of air inspired or expired during each normal, quiet respiratory cycle. Common abbreviations are TV or V with subscript T. [NIH]

Tin: A trace element that is required in bone formation. It has the atomic symbol Sn, atomic number 50, and atomic weight 118.71. [NIH]

Tinnitus: Sounds that are perceived in the absence of any external noise source which may take the form of buzzing, ringing, clicking, pulsations, and other noises. Objective tinnitus refers to noises generated from within the ear or adjacent structures that can be heard by other individuals. The term subjective tinnitus is used when the sound is audible only to the affected individual. Tinnitus may occur as a manifestation of cochlear diseases; vestibulocochlear nerve diseases; intracranial hypertension; craniocerebral trauma; and other conditions. [NIH]

Tissue: A group or layer of cells that are alike in type and work together to perform a specific function. [NIH]

Tissue Culture: Maintaining or growing of tissue, organ primordia, or the whole or part of an organ in vitro so as to preserve its architecture and/or function (Dorland, 28th ed). Tissue culture includes both organ culture and cell culture. [NIH]

Tolerance: 1. The ability to endure unusually large doses of a drug or toxin. 2. Acquired drug tolerance; a decreasing response to repeated constant doses of a drug or the need for increasing doses to maintain a constant response. [EU]

Tomography: Imaging methods that result in sharp images of objects located on a chosen plane and blurred images located above or below the plane. [NIH]

Tonic: 1. Producing and restoring the normal tone. 2. Characterized by continuous tension. 3. A term formerly used for a class of medicinal preparations believed to have the power of restoring normal tone to tissue. [EU]

Tonicity: The normal state of muscular tension. [NIH]

Tooth Preparation: Procedures carried out with regard to the teeth or tooth structures preparatory to specified dental therapeutic and surgical measures. [NIH]

Topical: On the surface of the body. [NIH]

Torsion: A twisting or rotation of a bodily part or member on its axis. [NIH]

Torture: The intentional infliction of physical or mental suffering upon an individual or individuals, including the torture of animals. [NIH]

Toxic: Having to do with poison or something harmful to the body. Toxic substances usually cause unwanted side effects. [NIH]

Toxicity: The quality of being poisonous, especially the degree of virulence of a toxic microbe or of a poison. [EU]

Toxicology: The science concerned with the detection, chemical composition, and pharmacologic action of toxic substances or poisons and the treatment and prevention of toxic manifestations. [NIH]

Toxins: Specific, characterizable, poisonous chemicals, often proteins, with specific biological properties, including immunogenicity, produced by microbes, higher plants, or animals. [NIH]

Trace element: Substance or element essential to plant or animal life, but present in extremely small amounts. [NIH]

Tracer: A substance (such as a radioisotope) used in imaging procedures. [NIH]

Traction: The act of pulling. [NIH]

Tranquilizing Agents: A traditional grouping of drugs said to have a soothing or calming effect on mood, thought, or behavior. Included here are the anti-anxiety agents (minor tranquilizers), antimanic agents, and the antipsychotic agents (major tranquilizers). These drugs act by different mechanisms and are used for different therapeutic purposes. [NIH]

Transaminase: Aminotransferase (= a subclass of enzymes of the transferase class that catalyse the transfer of an amino group from a donor (generally an amino acid) to an acceptor (generally 2-keto acid). Most of these enzymes are pyridoxal-phosphate-proteins. [EU]

Transcription Factors: Endogenous substances, usually proteins, which are effective in the initiation, stimulation, or termination of the genetic transcription process. [NIH]

Transduction: The transfer of genes from one cell to another by means of a viral (in the case of bacteria, a bacteriophage) vector or a vector which is similar to a virus particle (pseudovirion). [NIH]

Transfection: The uptake of naked or purified DNA into cells, usually eukaryotic. It is analogous to bacterial transformation. [NIH]

Transient Ischemic Attacks: Focal neurologic abnormalities of sudden onset and brief duration that reflect dysfunction in the distribution of the internal carotid-middle cerebral or the vertebrobasilar arterial system. [NIH]

Translation: The process whereby the genetic information present in the linear sequence of ribonucleotides in mRNA is converted into a corresponding sequence of amino acids in a protein. It occurs on the ribosome and is unidirectional. [NIH]

Translational: The cleavage of signal sequence that directs the passage of the protein through a cell or organelle membrane. [NIH]

Transmitter: A chemical substance which effects the passage of nerve impulses from one cell to the other at the synapse. [NIH]

Transplantation: Transference of a tissue or organ, alive or dead, within an individual, between individuals of the same species, or between individuals of different species. [NIH]

Trauma: Any injury, wound, or shock, must frequently physical or structural shock, producing a disturbance. [NIH]

Tremor: Cyclical movement of a body part that can represent either a physiologic process or a manifestation of disease. Intention or action tremor, a common manifestation of cerebellar diseases, is aggravated by movement. In contrast, resting tremor is maximal when there is no attempt at voluntary movement, and occurs as a relatively frequent manifestation of Parkinson disease. [NIH]

Tricuspid Atresia: Absence of the orifice between the right atrium and ventricle, with the presence of an atrial defect through which all the systemic venous return reaches the left heart. As a result, there is left ventricular hypertrophy because the right ventricle is absent or not functional. [NIH]

Tricyclic: Containing three fused rings or closed chains in the molecular structure. [EU]

Trigeminal: Cranial nerve V. It is sensory for the eyeball, the conjunctiva, the eyebrow, the skin of face and scalp, the teeth, the mucous membranes in the mouth and nose, and is motor to the muscles of mastication. [NIH]

Trigger zone: Dolorogenic zone (= producing or causing pain). [EU]

Trophic: Of or pertaining to nutrition. [EU]

Tropism: Directed movements and orientations found in plants, such as the turning of the sunflower to face the sun. [NIH]

Tryptophan: An essential amino acid that is necessary for normal growth in infants and for nitrogen balance in adults. It is a precursor serotonin and niacin. [NIH]

Tuberculosis: Any of the infectious diseases of man and other animals caused by species of Mycobacterium. [NIH]

Tuberous Sclerosis: A rare congenital disease in which the essential pathology is the appearance of multiple tumors in the cerebrum and in other organs, such as the heart or kidneys. [NIH]

Tungsten: A metallic element with the atomic symbol W, atomic number 74, and atomic weight 183.85. It is used in many manufacturing applications, including increasing the hardness, toughness, and tensile strength of steel; manufacture of filaments for incandescent light bulbs; and in contact points for automotive and electrical apparatus. [NIH]

Tyramine: An indirect sympathomimetic. Tyramine does not directly activate adrenergic receptors, but it can serve as a substrate for adrenergic uptake systems and monoamine oxidase so it prolongs the actions of adrenergic transmitters. It also provokes transmitter release from adrenergic terminals. Tyramine may be a neurotransmitter in some invertebrate nervous systems. [NIH]

Tyrosine: A non-essential amino acid. In animals it is synthesized from phenylalanine. It is also the precursor of epinephrine, thyroid hormones, and melanin. [NIH]

Ultrasonography: The visualization of deep structures of the body by recording the reflections of echoes of pulses of ultrasonic waves directed into the tissues. Use of ultrasound for imaging or diagnostic purposes employs frequencies ranging from 1.6 to 10 megahertz. [NIH]

Unconscious: Experience which was once conscious, but was subsequently rejected, as the "personal unconscious". [NIH]

Uracil: An anticancer drug that belongs to the family of drugs called alkylating agents. [NIH]

Uranium: A radioactive element of the actinide series of metals. It has an atomic symbol U, atomic number 92, and atomic weight 238.03. U-235 is used as the fissionable fuel in nuclear weapons and as fuel in nuclear power reactors. [NIH]

Urban Population: The inhabitants of a city or town, including metropolitan areas and

suburban areas. [NIH]

Urethra: The tube through which urine leaves the body. It empties urine from the bladder. [NIH]

Urinary: Having to do with urine or the organs of the body that produce and get rid of urine. [NIH]

Urine: Fluid containing water and waste products. Urine is made by the kidneys, stored in the bladder, and leaves the body through the urethra. [NIH]

Uterus: The small, hollow, pear-shaped organ in a woman's pelvis. This is the organ in which a fetus develops. Also called the womb. [NIH]

Vaccine: A substance or group of substances meant to cause the immune system to respond to a tumor or to microorganisms, such as bacteria or viruses. [NIH]

Vagal: Pertaining to the vagus nerve. [EU]

Vagus Nerve: The 10th cranial nerve. The vagus is a mixed nerve which contains somatic afferents (from skin in back of the ear and the external auditory meatus), visceral afferents (from the pharynx, larynx, thorax, and abdomen), parasympathetic efferents (to the thorax and abdomen), and efferents to striated muscle (of the larynx and pharynx). [NIH]

Valproic Acid: A fatty acid with anticonvulsant properties used in the treatment of epilepsy. The mechanisms of its therapeutic actions are not well understood. It may act by increasing GABA levels in the brain or by altering the properties of voltage dependent sodium channels. [NIH]

Vascular: Pertaining to blood vessels or indicative of a copious blood supply. [EU]

Vasculitis: Inflammation of a blood vessel. [NIH]

Vasoconstriction: Narrowing of the blood vessels without anatomic change, for which constriction, pathologic is used. [NIH]

Vasodilation: Physiological dilation of the blood vessels without anatomic change. For dilation with anatomic change, dilatation, pathologic or aneurysm (or specific aneurysm) is used. [NIH]

Vasodilator: An agent that widens blood vessels. [NIH]

Vegetative: 1. Concerned with growth and with nutrition. 2. Functioning involuntarily or unconsciously, as the vegetative nervous system. 3. Resting; denoting the portion of a cell cycle during which the cell is not involved in replication. 4. Of, pertaining to, or characteristic of plants. [EU]

Vein: Vessel-carrying blood from various parts of the body to the heart. [NIH]

Venereal: Pertaining or related to or transmitted by sexual contact. [EU]

Venous: Of or pertaining to the veins. [EU]

Venous blood: Blood that has given up its oxygen to the tissues and carries carbon dioxide back for gas exchange. [NIH]

Ventral: 1. Pertaining to the belly or to any venter. 2. Denoting a position more toward the belly surface than some other object of reference; same as anterior in human anatomy. [EU]

Ventricle: One of the two pumping chambers of the heart. The right ventricle receives oxygen-poor blood from the right atrium and pumps it to the lungs through the pulmonary artery. The left ventricle receives oxygen-rich blood from the left atrium and pumps it to the body through the aorta. [NIH]

Ventricular: Pertaining to a ventricle. [EU]

Ventricular fibrillation: Rapid, irregular quivering of the heart's ventricles, with no

effective heartbeat. [NIH]

Venules: The minute vessels that collect blood from the capillary plexuses and join together to form veins. [NIH]

Vertebrae: A bony unit of the segmented spinal column. [NIH]

Vertebral: Of or pertaining to a vertebra. [EU]

Vertigo: An illusion of movement; a sensation as if the external world were revolving around the patient (objective vertigo) or as if he himself were revolving in space (subjective vertigo). The term is sometimes erroneously used to mean any form of dizziness. [EU]

Vesicular: 1. Composed of or relating to small, saclike bodies. 2. Pertaining to or made up of vesicles on the skin. [EU]

Vestibular: Pertaining to or toward a vestibule. In dental anatomy, used to refer to the tooth surface directed toward the vestibule of the mouth. [EU]

Vestibule: A small, oval, bony chamber of the labyrinth. The vestibule contains the utricle and saccule, organs which are part of the balancing apparatus of the ear. [NIH]

Vestibulocochlear Nerve: The 8th cranial nerve. The vestibulocochlear nerve has a cochlear part (cochlear nerve) which is concerned with hearing and a vestibular part (vestibular nerve) which mediates the sense of balance and head position. The fibers of the cochlear nerve originate from neurons of the spiral ganglion and project to the cochlear nuclei (cochlear nucleus). The fibers of the vestibular nerve arise from neurons of Scarpa's ganglion and project to the vestibular nuclei. [NIH]

Vestibulocochlear Nerve Diseases: Diseases of the vestibular and/or cochlear (acoustic) nerves, which join to form the vestibulocochlear nerve. Vestibular neuritis, cochlear neuritis, and acoustic neuromas are relatively common conditions that affect these nerves. Clinical manifestations vary with which nerve is primarily affected, and include hearing loss, vertigo, and tinnitus. [NIH]

Veterinary Medicine: The medical science concerned with the prevention, diagnosis, and treatment of diseases in animals. [NIH]

Villi: The tiny, fingerlike projections on the surface of the small intestine. Villi help absorb nutrients. [NIH]

Viral: Pertaining to, caused by, or of the nature of virus. [EU]

Virulence: The degree of pathogenicity within a group or species of microorganisms or viruses as indicated by case fatality rates and/or the ability of the organism to invade the tissues of the host. [NIH]

Virus: Submicroscopic organism that causes infectious disease. In cancer therapy, some viruses may be made into vaccines that help the body build an immune response to, and kill, tumor cells. [NIH]

Viscera: Any of the large interior organs in any one of the three great cavities of the body, especially in the abdomen. [NIH]

Visceral: , from viscus a viscus) pertaining to a viscus. [EU]

Visceral Afferents: The sensory fibers innervating the viscera. [NIH]

Visual field: The entire area that can be seen when the eye is forward, including peripheral vision. [NIH]

Visual Perception: The selecting and organizing of visual stimuli based on the individual's past experience. [NIH]

Vitro: Descriptive of an event or enzyme reaction under experimental investigation

occurring outside a living organism. Parts of an organism or microorganism are used together with artificial substrates and/or conditions. [NIH]

Vivo: Outside of or removed from the body of a living organism. [NIH]

Voltage-gated: It is opened by the altered charge distribution across the cell membrane. [NIH]

Vomeronasal Organ: A specialized part of the olfactory system located anteriorly in the nasal cavity within the nasal septum. Chemosensitive cells of the vomeronasal organ project via the vomeronasal nerve to the accessory olfactory bulb. The primary function of this organ appears to be in sensing pheromones which regulate reproductive and other social behaviors. While the structure has been thought absent in higher primate adults, data now suggests it may be present in adult humans. [NIH]

Wakefulness: A state in which there is an enhanced potential for sensitivity and an efficient responsiveness to external stimuli. [NIH]

War: Hostile conflict between organized groups of people. [NIH]

Weight Gain: Increase in body weight over existing weight. [NIH]

White blood cell: A type of cell in the immune system that helps the body fight infection and disease. White blood cells include lymphocytes, granulocytes, macrophages, and others. [NIH]

Withdrawal: 1. A pathological retreat from interpersonal contact and social involvement, as may occur in schizophrenia, depression, or schizoid avoidant and schizotypal personality disorders. 2. (DSM III-R) A substance-specific organic brain syndrome that follows the cessation of use or reduction in intake of a psychoactive substance that had been regularly used to induce a state of intoxication. [EU]

Wounds, Gunshot: Disruption of structural continuity of the body as a result of the discharge of firearms. [NIH]

Xenograft: The cells of one species transplanted to another species. [NIH]

X-ray: High-energy radiation used in low doses to diagnose diseases and in high doses to treat cancer. [NIH]

Yeasts: A general term for single-celled rounded fungi that reproduce by budding. Brewers' and bakers' yeasts are Saccharomyces cerevisiae; therapeutic dried yeast is dried yeast. [NIH]

Zygote: The fertilized ovum. [NIH]

Zymogen: Inactive form of an enzyme which can then be converted to the active form, usually by excision of a polypeptide, e. g. trypsinogen is the zymogen of trypsin. [NIH]

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