European Manual of Medicine

A. Herold · P.-A. Lehur
K. E. Matzel · P. R. O'Connell *Editors*

Coloproctology

W. Arnold · U. Ganzer *Series Editors*

U.E.M.S.

Springer

European Manual of Medicine

Coloproctology

A. Herold, P.-A. Lehur, K. E. Matzel, P. R. O'Connell
Editors

W. Arnold
U. Ganzer
Series Editors

A. Herold
P.-A. Lehur
K. E. Matzel
P. R. O'Connell
Editors

Coloproctology

With 90 Figures and 35 Tables

Springer

Series Editors

Professor Dr. Wolfgang Arnold
Department of Otorhinolaryngology,
Head & Neck Surgery
Technical University of Munich
Klinikum rechts der Isar
81675 München
Germany
Email: w.arnold@lrz.tum.de

Professor Dr. Uwe Ganzer
Department of Otorhinolaryngology,
Head & Neck Surgery
University of Düsseldorf
40225 Düsseldorf
Germany
Email: uwe.ganzer@arcor.de

Volume Editors

Professor Dr. Alexander Herold
Enddarm-Zentrum Mannheim
Bismarckplatz 1
68165 Mannheim
Germany
Email: a.herold@enddarm-zentrum.de

Professor Paul-Antoine Lehur, MD
Clinique Chirurgicale, Hôtel-Dieu
Institut des Maladies de l'Appareil Digestif
Place Ricordeau
44093 Nantes Cedex
France
Email: paulantoine.lehur@chu-nantes.fr

Professor Dr. Klaus E. Matzel
Chirurgische Klinik
Universitätsklinikum Erlangen-Nürnberg
Krankenhausstraße 12
91054 Erlangen
Germany
Email: klaus.matzel@uk-erlangen.de

Professor P. Ronan O'Connell, MD, FRCSI, FRCS (Glasg)
University College Dublin
St. Vincent's University Hospital
Elm Park
Dublin 4
Ireland
Email: ronan.oconnell@ucd.ie

ISBN 978-3-540-71216-9

e-ISBN 978-3-540-71217-6

DOI 10.1007/978-3-540-71217-6

Library of Congress Control Number: 2007939779

Cover design: Frido Steinen-Broo, eStudio, Calamar, Spain
Typesetting and Production: le-tex publishing services oHG, Leipzig, Germany

Printed on acid-free paper

9 8 7 6 5 4 3 2 1

springer.com

Foreword of the Series Editors

The European Manual of Medicine was founded on the idea of offering residents as well as specialized clinicians the latest European up-to-date information on diagnosis and treatment in medicine. In contrast to existing national textbooks, the European Manual of Medicine aims to find a consensus on the demands of a standardized European medicine based on the "logbooks" recommended by the Union of European Medical Societies (UEMS).

To fulfil these demands, we made it as a principle of our concept to recruit European editors who are well established and recognized in their specialities. At least three editors from different European countries usually are invited to be responsible for the most actual high clinical and scientific standards of their discipline.

Wherever possible the editors are asked to follow a standardized structure for each chapter so as to guarantee the reader easy and quick access to the subject-matter.

High quality illustrations and figures provide additional useful information. For the interested reader, actual and selected references allow him or her to further investigate areas of individual interest.

The Series Editors are deeply grateful to Springer Verlag, especially to Mrs. Gabriele Schröder, Mrs. Waltraud Leuchtenberger and Mrs. Stephanie Benko, for their support and assistance in the realization of this fascinating project from the early beginning.

The second volume of the European Manual of Medicine Series is devoted to "Coloproctology". The editors (Prof. Alexander Herold, Mannheim, Prof. Paul-Antoine Lehur, Nantes, Prof. Klaus. E. Matzel, Nürnberg and Prof. P. Ronan O`Connell, Dublin), are leading European experts in the field, and recruited 37 contributors from 14 European countries to compile a textbook that fulfils our original concept for the European Manual of Medicine.

Wolfgang Arnold
Uwe Ganzer
München/Düsseldorf
Fall 2008

Preface

This book forms the latest addition to the European Manual of Medicine series published by Springer. The aim is to provide surgical trainees preparing for the European Board of Surgery Qualification (EBSQ) examination with a comprehensive yet condensed guide to the core knowledge required in the subspecialty of Coloproctology. The editors have brought together a group of authors each of whom has both an international reputation within Coloproctology or an allied specialty and a desire to see ever-improving standards in Coloproctology across Europe.

The EBSQ Diploma in Coloproctology is now well established and has become the accepted qualification in Coloproctology across Europe. As the science, technologies and treatments that underlie Coloproctology develop, so too will this manual need continual revision and improvement. The manual will also be of assistance to the many practising Coloproctologists across Europe and beyond who undertake continued professional development.

Bringing together a diverse group of authors, few of whom have English as their first language, has been a rewarding challenge. The result is a book that provides great breadth of knowledge and diversity of clinical practice. The editors trust that the reader will find in it a concise view of current European Coloproctology that will be of value both in preparation for EBSQ examination and for those engaged in continued professional development.

Alexander Herold
Paul-Antoine Lehur
Klaus E. Matzel
P. Ronan O'Connell
Fall 2008

Contents

History of the Division of Coloproctology

Anatomy

Physiology

Anal Disorders

Dermatology

Functional Disorders

Inflammatory Bowel Disease

Benign Tumours

Malignant Tumours

Stomas and Stomatherapy

Endoscopy

Emergencies

Pain Syndromes

List of Contributors

Altomare, Donato F., MD, Associate Professor
University of Bari, Policlinico
General Surgery and Liver Transplantation Unit
Piazza G. Cesare 11
70124 Bari
Italy
Email: altomare@clichiru.uniba.it

Andersson, Peter, MD, PhD, Assistent Professor
University Hospital Linköping
Department of Surgery
58185 Linköping
Sweden
Email: Peter.Andersson@lio.se

Barisic, Goran I., Dr.
Institute for Digestive Diseases
Clinical Center of Serbia
First Surgical Unit
Koste Todorovica 6
11000 Belgrade
Serbia and Montenegro

Bennis, Malika, Dr.
Hôpital Saint-Antoine, AP-HP,
Université Pierre et Marie Curie
Department of Surgery
184 rue du Faubourg Saint-Antoine
75012 Paris
France
Email: Mxbennis@aol.com

Buchmann, Peter, Professor Dr.
Chirurgische Klinik
Stadtspital Waid
Tièchestrasse 99
8037 Zürich
Switzerland
Email: peter.buchmann@waid.stzh.ch

Chafai, Najim, MD
Hôpital St. Antoine
Service de Chirurgie Générale et Digestive
184 rue du Faubourg Saint-Antoine
75012 Paris
France
Email: najim.chafai@sat.aphp.fr

Conaghan, Philip, MD
University of Oxford
John Radcliffe Hospital
Department of Colorectal Surgery
Headington
Oxford, OX3 9DU
UK
Email: conaghan@doctors.org.uk

D'Hoore, André, MD
University Clinics Gasthuisberg
Department of Abdominal Surgery
Herestraat 49
3000 Leuven
Belgium
Email: andre.dhoore@uz.kuleuven.ac.be

Dziki, Adam, MD, Professor
University Hospital No. 5
Department of Colorectal Surgery
Plac Hallera 1
90-648 Lodz
Poland
Email: adziki@wp.pl

Gerjy, Roger, MD
University Hospital
Colorectal Surgery, Department of Surgery
581 85 Linköping
Sweden
Email: roger.gerjy@lio.se

Hartschuh, Wolfgang, Professor Dr.
Universitäts-Hautklinik
Voßstraße 2
69115 Heidelberg
Germany
Email: Wolfgang_Hartschuh@med.uni-heidelberg.de

Hermanek, Paul, MD, MD h.c., Professor
Chirurgische Klinik mit Poliklinik der Universität Erlangen
Krankenhausstraße 12
91052 Erlangen
Germany
Email: susanne.merkel@uk-erlangen.de

Herold, Alexander, Professor Dr.
Enddarm-Zentrum Mannheim
Bismarckplatz 1
68165 Mannheim
Germany
Email: a.herold@enddarm-zentrum.de

Krammer, Heiner, Professor Dr.
Gastroenterologie & Ernährungsmedizin
Am Enddarmzentrum Mannheim
Bismarckplatz 1
68165 Mannheim
Germany
Email: krammer@magendarm-zentrum.de

Krivokapic, Zoran, MD, FRCS, Professor
Clinical Center of Serbia
First Surgical Unit
Institute for Digestive Disease
Koste Todorovica 6
11000 Belgrade
Serbia and Montenegro
Email: kriviz@scpy.org.yu; scpy@beotel.yu

Krogh, Klaus, MD, PhD, DMSc, Professor
Aarhus University Hospital
Department of Hepatology and Gastroenterology V
Tage Hansensgade 2
8000 Aarhus C
Denmark
Email: krogh@as.aaa.dk

Labat, Jean-Jacques, Dr.
Service d´Urologie, Hôtel-Dieu
Place Alexis Ricordeau
44093 Nantes Cedex
France
Email: jjlabat@club-internet.fr

Laurberg, Soeren, MD, DMSc
Aarhus University Hospital
Department of Surgery
Tage Hansensgade 2
8000 Aarhus C
Denmark
Email: Soeren.Laurberg@as.aaa.dk

Lehur, Paul-Antoine, MD, Professor
Clinique Chirurgicale, Hôtel-Dieu
Institut des Maladies de l'Appareil Digestif
Place Ricordeau
44093 Nantes Cedex
France
Email: paulantoine.lehur@chu-nantes.fr

Mattana, Claudio, Dr.
Department of Surgery
Catholic University
Policlinico Gemelli
00191 Rome
Italy
Email: claudio.mattana@rm.unicatt.it

Matzel, Klaus E., Professor Dr.
Chirurgische Klinik
Universitätsklinikum Erlangen-Nürnberg
Krankenhausstraße 12
91054 Erlangen
Germany
Email: klaus.matzel@uk-erlangen.de

Meisner, Søren, MD
H:S Bispebjerg Hospital
Endoscopy Unit
Bakke 23
2400 Copenhagen
Denmark
Email: soeren@meisner.biz; sm01@bbh.hosp.dk

Meurette, Guillaume, MD
Clinique Chirurgicale, Hôtel-Dieu
Institut des Maladies de l'Appareil Digestif
Place Ricordeau
44093 Nantes Cedex
France
Email: guillaume.meurette@chu-nantes.fr

Mortensen, Neil, MD, FRCS, Professor
University of Oxford
John Radcliffe Hospital
Department of Colorectal Surgery
Headington
Oxford, OX3 9DU
UK
Email: neil.mortensen@nds.ox.ac.uk

Neumer, Franka, Dr., Dipl. oec. troph.
Gastroenterologie & Ernährungsmedizin
Am Enddarmzentrum Mannheim
Bismarckplatz 1
68165 Mannheim
Germany
Email: neumer@magendarm-zentrum.de

Nicholls, John, MD, MA, MChir, FRCS, Professor
St. Mark's Hospital
Watford Road
Harrow, HAI 3UJ
UK
Email: j.nicholls@thelondonclinic.co.uk; Nichollsjohn-stells@btinternet.co

Nyström, Per-Olof, MD, PhD, Professor
Department for Medical and Surgical Gastroenterology
Karolinska University Hospital - Huddinge
141 86 Stockholm
Sweden
Email: per-olof.nystrom@karolinska.se

O'Connell, P. Ronan, MD, FRCSI, FRCS (Glasg), Professor
University College Dublin
St. Vincent's University Hospital
Elm Park
Dublin 4
Ireland
Email: ronan.oconnell@ucd.ie

Ortiz, Hector, MD, PhD, Professor
Public University of Navarra
Virgen del Camino Hospital
c/Trinidad Fernandez Arenas 1,4
31002 Pamplona
Spain
Email: hortizhu@cfnavarra.es; hhortiz@telefonica.net

Påhlman, Lars, MD, PhD, FRCS, FRCS (Glasg), Professor
University Hospital Uppsala
Department of Surgery
751 85 Uppsala
Sweden
Email: lars.pahlman@surgsci.uu.se

Parc, Rolland, MD, Professor
Hopital St. Antoine
Service de chirurgie générale et digestive
184 rue du Faubourg Saint-Antoine
75012 Paris
France
Email: rolland.parc@sat.ap-hop-paris.fr

Pescatori, Mario, MD, FRCS, EBSQ, Professor
Coloproctology Unit
Villa Flaminia Hospital
Via Bodio 58
00191 Rome
Italy
Email: ucpclub@virgilio.it

Pimentel, Joao M., MD, PhD, Professor
University Hospital of Coimbra
Faculty of Medicine
Dept. of Surgery I
3000-075 Coimbra
Portugal
Email: j_m_pimentel@iol.pt; Joaopimentel@huc.min-saude.pt

Proske, Sylvia, Dr.
Universitäts-Hautklinik Heidelberg
Voßstraße 2
69115 Heidelberg
Germany
Email: proske@derma.de

Rosen, Harald R., MD, Professor
St. Vincent Hospital
Department of Surgery
Stumpergasse 5
Vienna 1060
Austria
Email: rosensurg@csi.com; Harald.Rosen@onemail.at

Schiedeck, Thomas H. K., Professor Dr.
Klinikum Ludwigsburg
Abt. für Allgemein- und Viszeralchirurgie
Posilipoststraße 4
71640 Ludwigsburg
Germany
Email: Thomas.Schiedeck@kliniken-lb.de

Schouten, W. R., Dr.
Department of Surgery, H1043
University Hospital Rotterdam
Dr. Molewaterplein 40
3015 GD Rotterdam
The Netherlands
Email: w.r.schouten@erasmusmc.nl

Sjödahl, Rune, MD, PhD, FRCS (Engl), Professor
University Hospital Linköping
Department of Surgery
581 85 Linköping
Sweden
Email: rune.sjodahl@lio.se

Tiret, Emmanuel, MD, Professor
Hôpital St. Antoine
Service de chirurgie générale et digestive
184 rue du Faubourg Saint-Antoine
75 012 Paris
France
Email: emmanuel.tiret@sat.aphp.fr

Wedel, Thilo, Professor Dr.
Anatomisches Institut
Universität Kiel
Otto-Hahn-Platz 8
24118 Kiel
Germany
Email: t.wedel@anatuni-kiel.de

Zhang, Wei, Dr.
Chirurgische Klinik
Universitätsklinikum Erlangen-Nürnberg
Krankenhausstraße 12
91054 Erlangen
Germany
Email: Wei.Zhang@uk-erlangen.de

History of the Division of Coloproctology

1.1 History of the Division of Coloproctology

JOHN NICHOLLS

1.1.1 Section of Surgery UEMS, Including the EBSQ (Coloproctology) Diploma

The Division of Coloproctology was founded in 1997 within the Section of Surgery of the Union des Médecins Spécialistes (UEMS). The UEMS is the official body in the European Union concerned with specialist medical practice and was founded in 1958 to further the interests of specialists in all medical disciplines. It has representation from the European Union (EU) member states and others, including Norway and Switzerland. Turkey is an associate member.

In 1962 the UEMS identified sections representing the principal specialities. These included the Section of Surgery representing General Surgery. Over the years the Section developed two main strategies. The first was the creation of accreditation and certification in General Surgery. This resulted in the formation of the European Board of Surgery (EBS) which went on to develop an accreditation and certification diploma in General Surgery given the title of European Board of Surgery Qualification (EBSQ Gen). Freedom of movement throughout the EU requires that the Certificate of Completion of Surgical Training (CCST) of every EU member state is recognised by the others. The CCST, however, has varying standards around the EU and the EBSQ Diploma aimed to represent a standard European surgical qualification.

The second part of the strategy of the Section of Surgery was the differentiation of General Surgery into specialities within. There are now several of these each becoming a Division within the Section. The first to be formed was in Vascular Surgery, which established the EBSQ (Vascular) Diploma in 1996 holding its first examination in Venice in that year. The second Division was in Coloproctology. EBSQ specialities within general surgery now include extended general surgery, vascular surgery, coloproctology, oncology, transplantation, trauma and hepatopancreatico-biliary. Of these, the first three now hold examinations leading to the EBSQ Diploma.

1.1.2 Division of Coloproctology

The first President of the Division of Coloproctology was Professor John Christiansen (Denmark) and Professor John Nicholls became Secretary. It held its first certification examination of six successful candidates in Malmo in 1998. The EBSQ (Coloproctology) Diploma was granted by the EBSQ and this remains the only recognised certification in the speciality of coloproctology outside the USA and Canada. Thus it parallels North American Board Certification in Colorectal Surgery. In 2004, Professor Lars Pahlman (Sweden) became President and Professor Klaus Matzel (Germany) became Secretary.

The constitution of the Division includes the appointment of two members from each country. These are nominated and appointed by the relevant body in their own country. Each appointment is of 4 years duration, renewable for 4 years. The current membership includes the member states of the European Union, Norway and Switzerland. It is the intention of the Division to expand to all other European countries, particularly since the entry of the Central European states into the EU.

In 2002, the Division has created two subcommittees. The first is the EBSQ Examination Subcommittee, with Professor Cor Baeten (Netherlands) as chairman and Professors Hector Ortiz (Spain), Soren Laurberg (Denmark) and John Nicholls (UK) as members, and the second is the Training Unit Recognition Subcommittee, with Mr. Joseph Deasy (Ireland), Professor Thorolf Hager (Germany) and Dr. Mario Pescatori (Italy) as members. This second group will continue the process of recognition of units suitable for training in Coloproctology.

To date there are over seventy holders of the diploma.

1.1.3 The EBSQ (Coloproctology) Diploma

Candidates wishing to obtain the EBSQ (Coloproctology) Diploma need to satisfy two criteria: Parts I and II.

Part I requires proof of identity and the presentation of a CCST or equivalent. The Division of Coloproctology has recommended that common trunk training should

take place over 5 years. Specialist training in Coloproctology should take two further years.

Candidates must have either a CCST or be within 3 months of obtaining a CCST. Thus accredited specialists in general surgery and those still in training but who will shortly have CCST are eligible. In the latter circumstance, candidates who satisfy the criteria set out below may take the Part II examination but will only be awarded the EBSQ (Coloproctology) Diploma when they have obtained the CCST. Applications are made to the EBSQ Administration Office in accordance with the requirements given below. This will be reviewed by the Member of the European Board of Coloproctology relevant to the country of the applicant. If satisfactory, the candidate is then eligible to proceed to Part II.

Part II takes the form of a written and a viva voce examination divided into three parts, each of half an hour's duration. Candidates are examined on the diagnosis and management of colorectal disorders, the interpretation of special investigations and a discussion of papers selected from the literature.

1.1.3.1 Part I: Eligibility

Eligibility for the EBSQ (Coloproctology) Diploma is assessed centrally within the Division of Coloproctology. The following are required:

- Copy of the EU CCST, including the date of certification—without this, the candidate is not eligible.
- Logbook of procedures countersigned by the principal trainer.

The declaration will include the following information:

a) Details of index operations performed. Candidates must have acquired a minimum operative experience of four indicator procedures to achieve 295 credit points as follows:

Index procedure	A	B	C	Total
Anterior resection	20	10	10	
Rectal prolapse procedure or total colectomy	10	5	5	
Haemorrhoidectomy	10	10	10	
Fistula in ano	10	10	10	
Points per procedure	1	4	3	
Total per category	50	140	105	
Maximum total points for index procedures				295

A = First assistant = 1 credit

B = Principal surgeon assisted by trainer = 4 credits

C = Principal surgeon not assisted by trainer = 3 credits

b) Length of training. This will be subdivided into common trunk years of training of 5 years. In addition, two further years of training in coloproctology are required. The years of training should be "in hospitals recognised by the National Authorities as appropriate for training".

c) Quality of training. Working parties and speciality boards where they exist must advise how the variety and quality of training should be assessed both in common trunk and the speciality.

d) Emergency experience. This is required for both common trunk and the speciality.

e) Proof of diagnostic skills. For example, this would include skills with sigmoidoscopy, colonoscopy, anorectal physiology and ultrasound. Colonoscopy experience is not essential for Part I eligibility.

f) Research. A year of research is optional, but must be in addition to the seven clinical years required (5 common trunk, 2 coloproctology).

g) Relationship with National Certification Body. In all UEMS countries there is a CCST in surgery. The EBSQ eligibility is more a question of a "hurdle" for the country rather than the candidate. It is conceivable that with national cooperation Part I could become virtually automatic. It is not intended to erect another "hurdle" for the trainee.

1.1.3.2 Part II: Examination

Once Part I is satisfied the candidate sits the Part II examination. This includes a written clinical examination followed by a viva voce of 30 min to discuss the written paper. This is followed by an oral discussion of 30 min of a selected paper from the literature to assess the candidate's ability to evaluate and analyse data. There is a final 30 min oral examination on general topics in coloproctology.

1.1.4 Aims of the Division of Coloproctology

The Division aims to establish quality in training in coloproctology in Europe. The EBSQ Diploma is the first part of its policy which will need continual revision and improvement. The second is the assessment of units capable of offering training in coloproctology. The third is to establish a system of continued professional development. These are all major policies that will require an administrative infrastructure to be realised.

Anatomy

2.1 Colon, Rectum, Anus, Pelvic Floor

THILO WEDEL

2.1.1 Introduction

The large intestine is the last segment of the gastrointestinal tract subdivided into the colon and the rectum (colorectum). While the mechanical and enzymatic digestion as well as the absorption of nutrients mainly take place in the upper gastrointestinal tract and small intestine, the large intestine is responsible for the following alimentary functions:

- Resorption of water and electrolytes (body fluid homeostasis)
- Utilisation of nutrients resistant to digestive enzymes (intraluminal bacterial fermentation)
- Further segmental propulsion of ingesta (peristalsis)
- Storage and controlled evacuation of faeces (continence and defaecation)

The last two functions are maintained by a complex interaction of the autonomically innervated rectal wall (endodermal origin) and the somatically innervated pelvic floor and external sphincter muscles (ectodermal origin).

2.1.2 Colon

Anatomical characteristics of the colon that are distinct from the small intestine are:

- Three bands of thickened longitudinal muscle layer (taeniae coli)
- Saccular pouches (haustra)
- Fixed transverse mucosal folds extending over approximately two thirds of the inner circumference (semilunar folds)
- Fatty tags within the tela subserosa (epiploic appendices)

2.1.2.1 Structure of the Colonic Wall

Mucosa

The epithelial lining and the underlying laminae propria mucosae and muscularis mucosae constitute the mucosal layer. The single-layered epithelium forms densely distributed crypts containing columnar absorptive enterocytes, abundant goblet cells and enteroendocrine cells. Between the epithelial crypts extends the lamina propria mucosae composed of fibroblasts, immunocompetent cells, nerve fibres and lymphatic and capillary networks embedded in loosely arranged connective tissue fibres. Solitary lymphatic follicles contact the epithelial lining and frequently protrude into the submucosa. The mucosa is delimited from the submucosa by a thin muscular sheet, the lamina muscularis mucosae, composed of up to six layers of smooth muscle cells running parallel and perpendicular to the bowel axis.

Submucosa

The submucosa makes up half of the total wall thickness and mainly consists of connective tissue and disseminated fatty nodules providing both tensile strength and a sliding plane between the mucosa and tunica muscularis. The submucosal layer contains fibroblasts and immunocompetent cells (e.g. lymphocytes, macrophages) and is richly supplied with blood vessel networks (submucosal vascular plexus) and ganglionated nerve fibre meshes (submucosal nerve plexus).

Tunica Muscularis

The tunica muscularis is composed of two distinct layers of smooth muscle cells separated by an intermuscular connective tissue space containing the myenteric nerve plexus. While the inner circular muscle layer is of uniform thickness, the outer longitudinal muscle layers is, overall, much thinner and clustered in three major bands, the taeniae coli (taenia omentalis, taenia libera, taenia mesenterialis).

Serosa

The serosa constitutes a mesothelial lining of flattened epithelial cells and resembles the visceral peritoneal surface. It is absent at retroperitoneally located parts of the colon (caecum, ascending and descending colon). Subserosal connective tissue underlies the serosal lining containing blood vessels, nerve fibres and disseminated fatty nodules, the epiploic appendices.

2.1.2.2 Colonic Segments

The colon is usually 1.4–1.6 m long and forms a frame-like arch extending throughout the entire abdominal cavity. According to its course the colon comprises the following segments:

Caecum and Appendix Vermiformis

The caecum is a blind saccular pouch with a luminal diameter ranging between 6 and 9 cm located in the right iliac fossa. Normally most of the caecum lies retroperitoneally fixed by ileocaecal plicae. However, its position may vary considerably, when its own mesentery remained after incomplete secondary retroperitonealisation of the ascending colon (caecum mobile).

Ileocaecal Junction

The ileum enters the caecum at its medial border forming a sphincter-like opening, the ileocaecal valve (Bauhin's valve). Intraluminally the orifice is composed of a superior and an inferior mucosal lip which protrude into the caecal cavity. The valvular function is established by a thickening of the circular muscle layer and musculoelastic fibres bridging the ileal and caecal muscle layers.

Appendix Vermiformis

The worm-like appendix is a blind tube of usually 7–12 cm length with an outer diameter of 3–8 mm. The base of the appendix is located below the ileocaecal valve at the medial side of the caecum where the taeniae coli fuse. The appendix is attached to the ileocaecal segment by a mesoappendix containing the appendicular artery, a branch from the ileocolic artery. Its flexible position varies, mostly in retrocaecal (two thirds) or intrapelvic (one third) locations. Other variations, e.g. subcaecal, preileal and postileal location, are only rarely encountered. In the appendix, in contrast to the colonic wall, the two muscle layers are of equal thickness, intermingle with each other and do not allow relevant dilatation of the organ. Both the mucosa and submucosa are densely packed with lymphatic follicles extending throughout the entire circumference of the appendix.

Ascending Colon

The ascending colon, as in the other colonic segments, has a smaller diameter than the caecum ranging between 4 and 7 cm. It extends retroperitoneally from the right lower abdomen up to the right colonic flexure located underneath the right liver lobe (hepatic flexure) and ventral to the right kidney. The right colonic flexure is fixed by peritoneal folds emerging from neighbouring organs: the right renocolic, hepatocolic and right phrenicocolic ligaments.

Transverse Colon

The transverse colon lies intraperitoneally and is loosely suspended by the transverse mesocolon and the gastrocolic ligament allowing highly varying positions and length. On its course from the right to the left colonic flexure it relates with the liver, gallbladder, duodenum and pancreas, the stomach, greater omentum and small intestinal loops. Blood and lymphatic vessels supply the transverse colon via the transverse mesocolon. The topographical position of the left colonic flexure is higher than the right one and relates to the spleen (splenic flexure) and the left kidney. The left colonic flexure is fixed by the splenocolic, left renocolic and left phrenicocolic ligaments.

Descending Colon

The descending colon extends from the left colonic flexure along the left side of the dorsal abdominal wall. Its diameter ranges between 3 and 4 cm. Similar to the ascending colon, the descending colon is retroperitoneally fixed and attached to the ventral sheath of the renal fascia (Gerota's fascia) and, thus, is less mobile than the transverse colon.

Sigmoid Colon

The intraperitoneally located sigmoid colon continues the descending colon and extends from the left iliac fossa into the pelvic cavity to the upper rectum. Its course is S-shaped, but may vary greatly depending on its length which ranges between 12 and 60 cm. Due to the flexible mesosigma the sigmoid colon is very mobile and can easily change its position. Thus, during defaecation it may be pushed down and compress the anterior rectal wall eventually causing incomplete rectal evacuation (sigmoidocele/outlet obstruction). The mesosigmoid radix starts from the inner border of the greater psoas muscle, crosses the left ureter, left genital blood vessels and the aortic bifurcation and reaches caudally the level of the 3rd sacral vertebra. It contains the blood and lymphatic vessels supplying the sigmoid colon.

2.1.2.3 Blood Vessel Supply of the Colon

The colon being derived from both the midgut and hindgut is supplied by branches from the superior and inferior mesenteric arteries (Fig. 2.1.1).

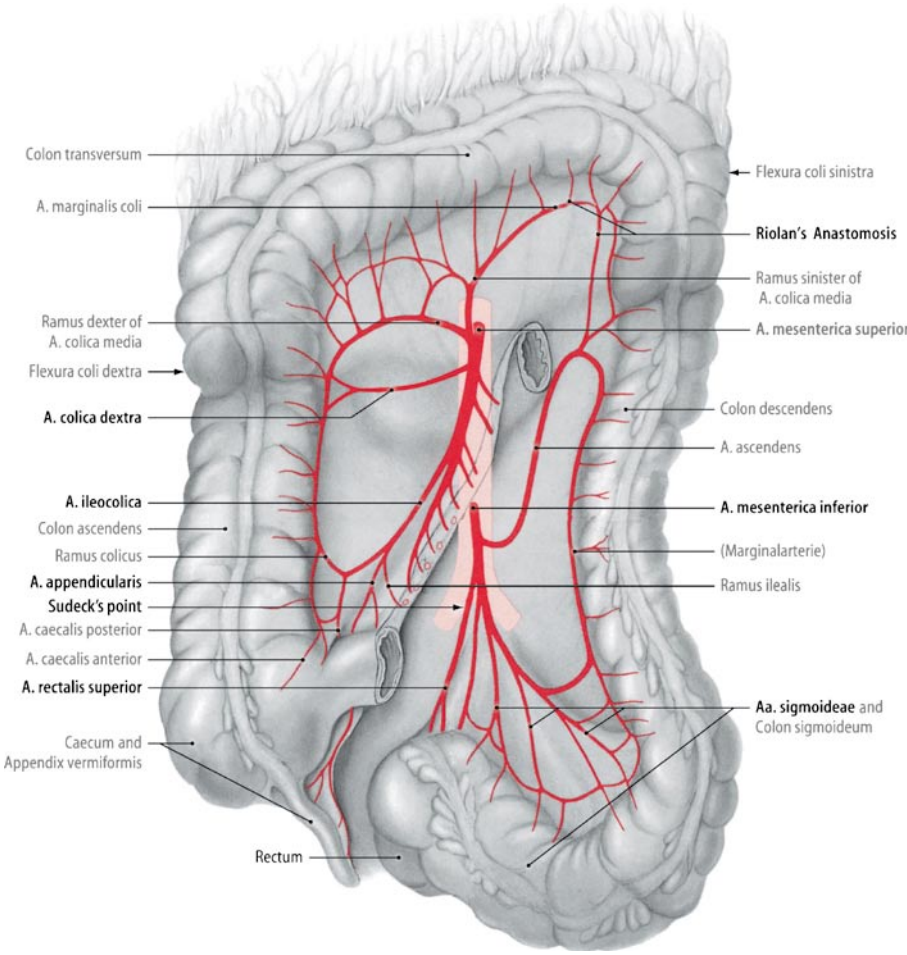


Fig. 2.1.1 Blood vessel supply of the colon

Superior Mesenteric Artery

The superior mesenteric artery supplies the caecum, appendix, ascending colon and two thirds of the transverse colon.

Ileocolic Artery

The ileocolic artery continues the superior mesenteric artery after the outlet of the ileal arteries. It usually divides into a superior branch for the ascending colon and an inferior branch for the caecum (colic branch) and the appendix (appendicular artery).

Right Colic Artery

The right colic artery (diameter 2.9 ± 0.6 mm) has an inconstant origin arising either directly from the superior mesenteric artery, the ileocolic artery or the middle colic artery. It supplies the ascending colon and the right colonic flexure. However, in 70% a clearly identifiable right colic artery is not present, so that the right colon receives its blood supply via the colic branch of the ileocolic artery and the right branch of the middle colic artery.

Middle Colic Artery

The middle colic artery (diameter 3.3 ± 0.8 mm) is a constantly present vessel that arises from the initial infrapancreatic segment of the superior mesenteric artery and passes within the transverse mesocolon right to the midline. Before reaching the transverse colon, the arterial trunk divides up in 50% into a left and right branch to reach the transverse colon and the colonic flexures.

Inferior Mesenteric Artery

The inferior mesenteric artery (diameter 4.4 ± 0.5 mm) supplies the left third of the transverse colon, the descending and sigmoid colon and most of the rectum (see *Blood Vessel Supply of the Rectum and Anus*).

Left Colic Artery

The left colic artery (diameter 3.1 ± 1.0 mm) arises from the left side of the inferior mesenteric artery, crosses the left kidney and divides up into an ascending branch passing to the left colic flexure and a descending branch passing to the descending and sigmoid colon. In 16% these branches directly originate from the inferior mesenteric artery (absence of left colic artery).

Sigmoid Arteries

The sigmoid arteries (diameter 3.0 ± 0.5 mm) are between two and five in number, branch from the inferior mesenteric artery, cross the left ureter and gonadal vessels passing within the mesosigma to reach the sigmoid colon. Branches anastomose to the left colic artery and the superior rectal artery via primary or secondary arcades (marginal artery of the colon). The latter anastomosis is also termed Sudeck's point.

Marginal Artery of the Colon

The marginal artery of the colon (Drummond's artery) is formed by the dividing arcades of the ileocolic, right, middle and left colic and sigmoid arteries. The artery runs parallel and adjacent to the colon within the mesentery and gives rise to the vasa recta and brevia which directly enter the colonic wall. In addition to the anastomosis between the middle and left colic artery via the marginal artery, a large branch may be present directly connecting the superior and inferior mesenteric artery, also termed the arch of Riolan (Griffith's point).

2.1.2.4 Lymphatic Drainage of the Colon

Colonic lymph nodes can be subdivided into four groups:

1. Epiploic lymph nodes on the serosal surface and within the epiploic appendices
2. Paracolic lymph nodes adjacent to the colonic wall
3. Intermediate lymph nodes along the colic blood vessels
4. Preterminal lymph nodes along the main trunks of the superior and inferior mesenteric artery

Preterminal lymph nodes drain into para-aortic lymph nodes located at the origin of these visceral arteries and are referred to as the highest lymph node station of the colon.

2.1.2.5 Nerve Supply of the Colon

Sympathetic Nerves

The caecum, ascending colon and two thirds of the transverse colon are supplied by sympathetic nerves originating from the 5th to the 12th thoracic segments. Preganglionic nerve fibres pass via the greater and lesser splanchnic nerves to the coeliac and superior mesenteric plexus, where they are switched over to final neurons. Nerve fibres (postganglionic) of these neurons reach the colonic wall via periarterial plexus along the superior mesenteric artery.

The left one third of the transverse colon and the descending and sigmoid colon are supplied by sympathetic nerves from the lumbar and upper sacral spinal segments. Preganglionic nerve fibres travel via lumbar splanchnic nerves to the inferior mesenteric plexus and via sacral splanchnic nerves to the superior and inferior hypogastric plexus. Postganglionic nerve fibres enter the colonic wall via periarterial plexus along the inferior mesenteric artery.

The sympathetic input mediates relaxation of the colonic wall and contraction of both the ileocaecal valve and vascular musculature. Afferent nerve fibres are primarily responsible for the sensation of visceral pain.

Parasympathetic Nerves

The caecum, ascending colon and two thirds of the transverse colon are supplied by parasympathetic nerve fibres derived from the vagus nerve. The vagal nerve fibres travel via the coeliac and superior mesenteric plexus into the colonic wall where they are switched to intramural ganglion cells.

The left one third of the transverse colon and the descending and sigmoid colon are supplied by parasympathetic nerves originating from the 2nd to the 4th sacral segment (sacral parasympathetic input). Via pelvic splanchnic nerves the parasympathetic nerve fibres pass through the inferior and superior hypogastric plexus and reach the colonic wall following the branches of the inferior mesenteric artery.

The parasympathetic input mediates contraction of the colonic wall musculature, relaxation of the internal anal sphincter and secretomotor functions. Sensations of distension and pain are carried by afferent parasympathetic nerve fibres (Fig. 2.1.2).

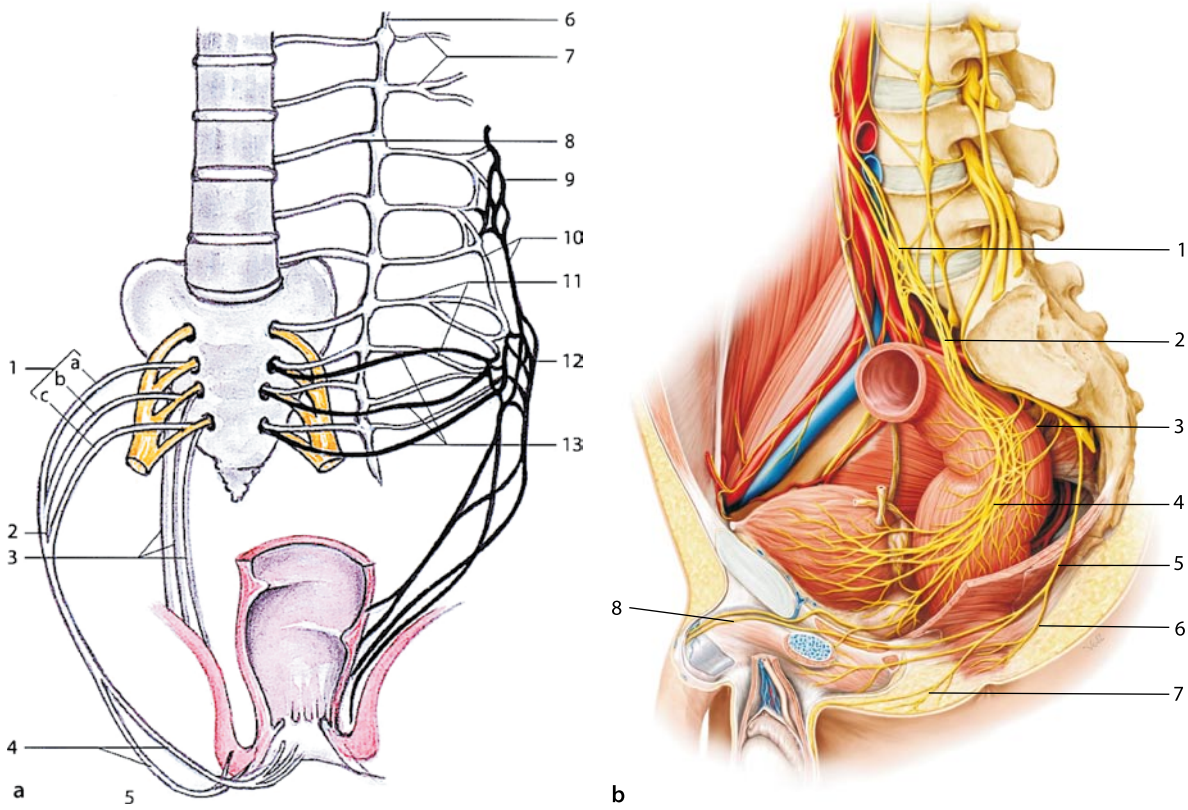


Fig. 2.1.2 Nerve supply of the anorectum and pelvic floor. **a** Somatic and autonomic innervation of the anorectum and pelvic floor. *1* sacral nerves (*a* S_2, *b* S_3, *c* S_4), *2* pudendal nerve, *3* levatory nerves, *4* inferior rectal nerves, *5* somatic innervation of the pelvic floor and external anal sphincter, *6* sympathetic trunk, *7* lumbar splanchnic nerves, *8* grey communicans nerve, *9* superior hypogastric plexus, *10* hypogastric nerves, *11* sacral splanchnic nerves, *12* inferior hypogastric plexus, *13* pelvic splanchnic nerves. **b** Somatic and autonomic innervation of the anorectum and pelvic floor in men. *1* superior hypogastric plexus, *2* hypogastric nerves, *3* sacral splanchnic nerves, *4* inferior hypogastric plexus, *5* pudendal nerve, *6* inferior rectal nerves, *7* posterior scrotal nerves, *8* dorsal nerve of the penis

Enteric Nervous System

While the connections between the central nervous system and the intestine are established by extrinsic sympathetic and parasympathetic nerves to modulate gut activities, the enteric nervous system resides within the bowel wall and is responsible for coordinating the major intestinal functions such as motility and secretion. In addition to sympathetic and parasympathetic mediators a broad spectrum of non-adrenergic, non-cholinergic neurotransmitters is released by intrinsic intramural nerve cells to establish local reflex circuits that provide control of intestinal motor functions virtually independent from higher nervous inputs.

The enteric nervous system is made up of approximately 150 million neurons ("little brain of the gut") and is organised in different nervous networks (plexus) composed of clusters of nerve cells (enteric ganglia) and interconnecting nerve fibre strands. The major plexus are located in the intermuscular space between the longitudinal and circular muscle layer (myenteric plexus), within the submucosa (external and internal submucosal plexus) and within the mucosa (mucosal plexus) (Fig. 2.1.3). The density of both ganglia and nerve cells declines continuously along the colon and is lowest within the distal rectal wall at the level of the internal anal sphincter (physiological hypoganglionosis).

In addition to nerve plexus both the circular and longitudinal muscle layer and the intermuscular space contain a network of interstitial cells of Cajal (ICC). These interdigitating cells are intercalated between nerve fibres and smooth muscle cells and generate the slow-wave activity of the colonic musculature, also referred to as intestinal

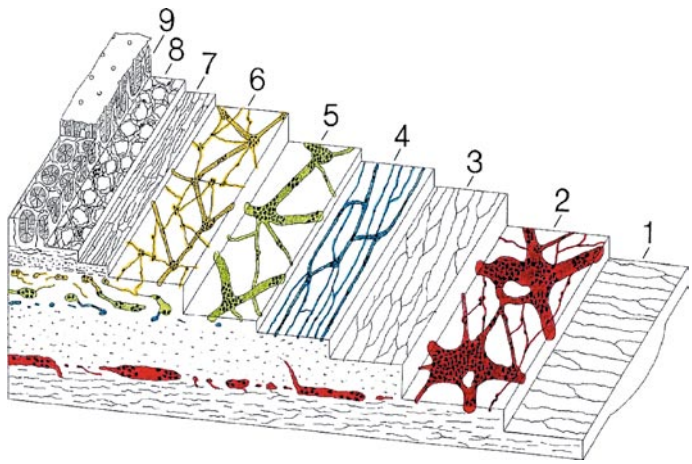


Fig. 2.1.3 Topographical organisation of the enteric nervous system in the human colon. *1* plexus of the longitudinal muscle layer, *2* myenteric plexus, *3* plexus of the circular muscle layer, *4* external submucosal plexus, *5* intermediate submucosal plexus, *6* internal submucosal plexus, *7* plexus of the lamina muscularis mucosae, *8* mucosal plexus (subglandular portion), *9* mucosal plexus (periglandular portion). Ganglionated plexus appear in color, *dark dots* represent enteric nerve cells

pacemaker cells. Moreover, they are actively involved in the intestinal neurotransmission by mediating neuronal inputs to smooth muscle cells.

2.1.3 Rectum and Anus

The rectum is the final segment of the large intestine and has a twofold function:

- Storage/retention of faeces and closure of the gastrointestinal tract (continence)
- Controlled evacuation of faeces (defaecation)

The rectum is 15–19 cm long and extends from the 3rd sacral vertebra to the perineum. It is the most dorsally located intrapelvic organ descending along the sacrococcygeal concavity (anteroposterior sacral flexure) and passing through the pelvic floor at the anorectal junction (perineal flexure, anorectal angulation).

The rectum is divided into two segments:

- Rectal ampulla
- Anal canal

In contrast to the colon the rectum is characterised by the following anatomical peculiarities:

- Confluence of taeniae coli to a continuous longitudinal smooth muscle layer
- Absence of epiploic appendices
- Presence of permanent semilunar transverse folds, the most constant middle fold (Kohlrausch's fold) and a superior and inferior fold (Houston's fold)
- Extraperitoneal position of the lower and dorsal part of the organ lacking a mesentery

2.1.3.1 Rectal Ampulla

The rectal ampulla is the widest part of the rectum with a varying perimeter of 8–16 cm. Its ventral wall is covered by visceral peritoneum reflecting onto the bladder and seminal vesicles in men (rectovesical pouch/excavatio) and onto the uterus and upper posterior vaginal wall in women (rectouterine pouch/excavatio, Douglas' pouch). The rectal musculature is arranged in a folding grille-like pattern enabling the wall to adequately adjust to the highly varying filling state.

2.1.3.2 Anal Canal and Anus

The anal canal (pars analis recti) is 2.5–4 cm long with a perimeter of 5–9 cm forming an angle of 90°–100° with the rectum (anorectal angle) caused by the constant traction of the puborectal sling (see *Pelvic Floor*). The inner lining of the anal canal varies along its course to the anus (Fig. 2.1.4).

Inner Surface of the Anal Canal

The upper part of the anal canal, delimited from the rectal ampulla by the anorectal junction, is covered with a pink-coloured intestinal mucosa (colorectal zone). At the transitional zone the wet columnar epithelium gives way to the dry squamous epithelium displaying a histological mosaic of cylindrical, cubic and flat epithelial cells. Macroscopically the transitional zone is characterised by 8–12 vertical anal columns (Morgagni's) of which each contains a terminal branch from the superior rectal artery. The anal columns are separated by anal sinuses which form pocket-like mucosal folds at their lower ends, the

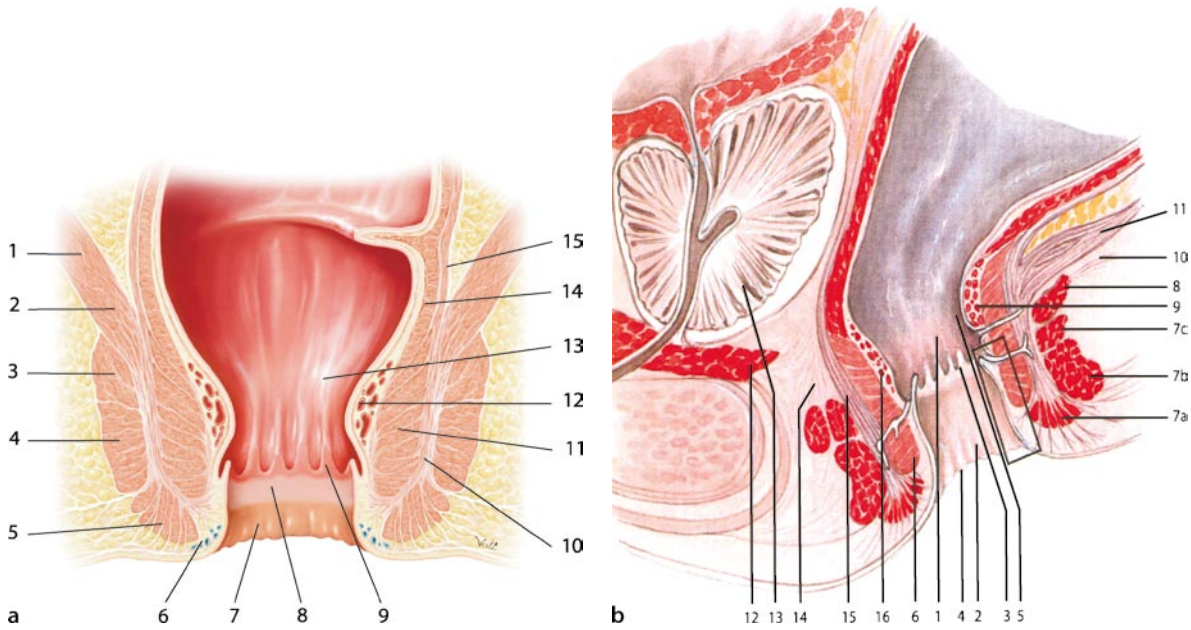


Fig. 2.1.4 Rectum and anal canal. **a** Frontal section of the anorectum. *1* levator ani muscle (iliococcygeal muscle), *2* levator ani muscle (puborectal muscle), *3–5* external anal sphincter (deep, superficial, subcutaneous part), *6* perianal veins, *7* perianal skin, *8* anoderm, *9* anal columns and crypts, *10* conjoined longitudinal muscle (corrugator ani muscle), *11* internal anal sphincter, *12* corpus cavernosum recti, *13* anorectal junction, *14* circular rectal muscle layer, *15* longitudinal rectal muscle layer. **b** Sagittal section of the anorectum in men. *1* rectum, *2* anal canal, *3* anal crypts, *4* anocutaneous line, *5* anorectal junction, *6* internal anal sphincter, *7* external anal sphincter (*a* subcutaneous part, *b* superficial part, *c* deep part), *8* puborectal muscle, *9* corpus cavernosum recti, *10* anococcygeal ligament, *11* levator ani muscle, *12* deep transverse perineal muscle, *13* prostate, *14* prerectal muscle fibres, *15* corrugator ani muscle, *16* anal canal muscle

anal valves or crypts. The row of alternating anal columns and sinuses corresponds to the dentate line (pectinate line, crypt line) considered to be the junction between the endodermal (cloacal) and ectodermal (proctodeal) parts of the anal canal. Between the dentate line and the anocutaneous line extends the pale and delicate anoderm (squamous zone) for ca. 1.5 cm to the anal verge ("anatomical" anal canal). The anoderm is lined by a non-keratinised stratified squamous epithelium devoid of glands and hairs but richly equipped with sensory nerve endings highly sensitive to touch, pain and temperature. At the lower end of the anal canal a white bluish line (linea/zona alba, Hilton's line) is occasionally visible corresponding to the underlying bulge of the internal anal sphincter.

Anus

Below the anocutaneous line, the anal canal gives way to the anus. The hairless perianal skin is of a dull brown colour and radially folded due to the contraction of the corrugator ani muscle. The skin contains sweat, sebaceous and apocrine glands and is supplied by perianal blood vessels originating from the inferior rectal artery.

Internal Anal Sphincter

The internal anal sphincter is composed of elliptical bundles of smooth muscle and corresponds to the thickened tube-like end of the circular muscle layer of the rectum (Fig. 2.1.4). The muscle is 5–8 mm thick and 2–3 cm long. In relation to the anal canal, the internal anal sphincter extends from the anorectal line down to the anocutaneous line with the most prominent part projecting onto the white line (linea alba, Hilton's line). Normally the lower border is overlaid by the subcutaneous part of the external anal sphincter. Due to its permanent involuntary contraction the internal anal sphincter is readily palpable as a rigid cylinder, in particular when the striated external anal sphincter is completely relaxed (e.g. under anaesthesia).

Conjoined Longitudinal Muscle (Corrugator Ani Muscle)

The longitudinal muscle layer of the rectum also changes its morphology approaching the anal canal (Fig. 2.1.4). Diverging bundles of smooth muscle fibres extend between the internal and external anal sphincter towards the perianal region and are joined by striated muscle fibres from the puborectalis ("conjoined" longitudinal muscle). Distally, the muscular fibres become increasingly fibroelastic and insert with small tendons in the perianal skin producing radial wrinkles ("corrugator" ani muscle). The most peripheral muscular septa radiate outwards and pass between the subcutaneous and superficial parts of the external anal sphincter into the ischioanal fossa. By inserting in the superficial perineal fascia, these fibres contribute to the separation of the ischioanal space from the subcutaneous perianal space.

Corpus Cavernosum Recti

The submucosa of the upper part of the anal canal contains a specific arrangement of arteriovenous anastomoses best described as the corpus cavernosum recti (anulus haemorrhoidalis, glomera venosa haemorrhoidalia) (Fig. 2.1.4). Branches from the superior rectal artery reach the corpus cavernosum recti from the right (7 and 11 o'clock, lithotomy position) and left side (3 o'clock) and release their arterial oxygenated blood into the cavernous tangles bare of capillaries. The position of the arterial branches supplying the corpus cavernosum recti corresponds to the typical topographical distribution pattern of haemorrhoids originating from the corpus cavernosum recti. The blood is drained by veins, which penetrate through the internal anal sphincter and are collected in the external rectal venous plexus. The subfascially located plexus drains into the inferior, medial and superior rectal vein.

Due to the transsphincteric blood drainage the blood filling of the corpus cavernosum recti is determined by the degree of contraction of the internal anal sphincter. Its constant tonus smoothly compresses the draining veins resulting in a physiological cushion-like swelling of the corpus cavernosum recti. Normally, the corpus cavernosum recti extends from the anorectal line down to the dentate line and is fixed by the anal canal muscle. However, if the vessels become dilated, the corpus cavernosum recti increases in size and may prolapse below the dentate line causing haemorrhoidal disease (see Chap. 4.1).

Proctodeal Glands

The proctodeal glands are of ectodermal origin and have formed at the junction between the cloacal and proctodeal parts of the anal canal. They mostly originate in the intermuscular space between the internal and external anal sphincter and open into the anal crypts (Fig. 2.1.4b). However, they may also bridge the intermuscular space and reach into the external anal sphincter. Along their slightly caudal oblique way towards the anal crypts they penetrate through the internal anal sphincter. The tubular excretory ducts are lined with cubic epithelium, the alveolar secretory parts are branched and covered with columnar epithelium of a primarily eccrine secretion type. Occasionally the termination of a duct is not canalised and may then form a cyst. The glands are surrounded by lymphatic tissue arranged in periglandular follicles. The number of proctodeal glands ranges between 5 and 15. Most of the glands are encountered along the dorsal anal commissure, while they are less frequently found at the lateral anal region and only occasionally present at the ventral anal commissure. This topographical distribution resembles the preferential location of perianal fistula and abscesses considered to develop from infected proctodeal glands. As rudimentary anal skin appendages proctodeal glands are not consistently present; in about one third of individuals only small subepithelial crypts end blindly within the submucosa.

2.1.3.3 Pelvic and Rectal Fasciae

While the inner pelvic wall, in particular the internal obturator, levator ani and coccygeal muscles, are covered by the parietal pelvic fascia, the pelvic organs including the rectum are ensheathed by the visceral pelvic fascia (endopelvic fascia) (Fig. 2.1.5). Both fascia are connected by condensed connective tissue structures traditionally described as ligaments (e.g. lateral rectal ligaments, rectal stalks, paraproctium). Originally they were considered to function as support components for the pelvic viscera. However, from both anatomical and embryological points of view, these ligaments do not provide substantial mechanical fixation of the pelvic organs, but primarily serve as access routes for their vascular and nervous supply.

Rectal Fascia

The part of the visceral pelvic fascia which ensheathes the rectal wall is called the rectal fascia. The rectal fascia is composed of dense connective tissue bare of blood vessel and nerves and constitutes a morphological barrier, thereby preventing an early penetration of rectal neoplasia into adjacent organs. The rectal fascia is most developed at the ventral and dorsal side of the rectum where it is also termed the ventral and dorsal "Grenzlamelle" (delimiting plate) (Fig. 2.1.5).

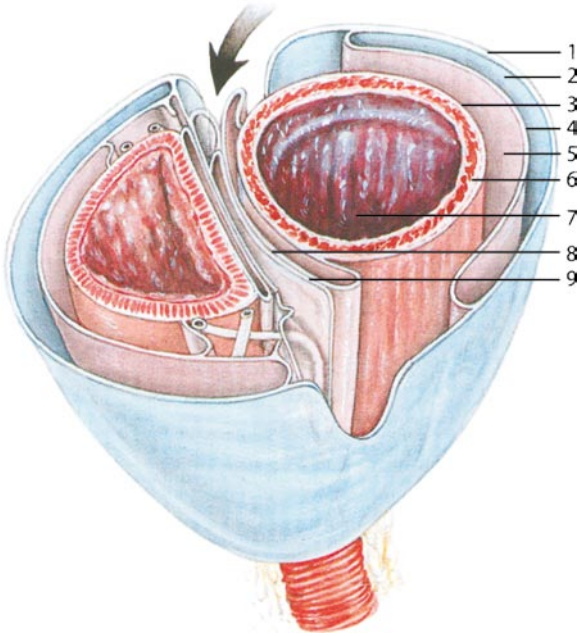


Fig. 2.1.5 Pelvic fascias. Schematic drawing of pelvic fascias in men. *1* parietal pelvic fascia, *2* retrorectal space, *3* rectal adventitia, *4* rectal fascia (dorsal "Grenzlamelle"), *5* perirectal space ("mesorectum"), *6* rectal tunica muscularis, *7* rectal mucosa, *8* rectal fascia (ventral "Grenzlamelle", Denonvillier's fascia), *9* peritoneum

Mesorectum

Dorsally the rectal fascia encloses the perirectal tissue containing the major routes of blood vessel supply and lymphatic drainage of the rectal wall. This dorsal part of the rectal fascia has also been clinically termed "mesorectum". However, this term is anatomically incorrect, as a "meso" is defined as a doubling of peritoneal layers connecting an intraperitoneal organ to the abdominal wall: this does not hold true for the rectal fascia. Between the mesorectum and the parietal pelvic fascia (Waldeyer's fascia) passing along the inner surface of the sacrum opens the retrorectal space. This avascular and nerve-free slit-like space corresponds to the access way for the dorsal mobilisation of the rectum during the total mesorectal excision (TME) manoeuvre. The retrorectal space extends down to the pelvic floor where the rectal fascia fuses with the parietal pelvic fascia. Between the parietal pelvic fascia and the sacrum opens another space, the presacral space, containing the medial and lateral sacral arteries and the origin of parasympathetic pelvic splanchnic nerves.

Rectoprostatic/Rectovaginal Septum

The ventral part of the rectal fascia comes into close contact with the dorsal urogenital fascia to form the rectoprostatic or rectovaginal septum (Fig. 2.1.5). During embryological development the deep peritoneal pouch between the rectal and urogenital pelvic compartments has fused and has been replaced by mesenchymal and smooth muscle tissue. In men the rectoprostatic septum (Denonvillier's fascia) covers the prostate, seminal vesicles and ductus deferentes separating them from the anterior rectal wall. The mesenchymal layer of the rectoprostatic septum contains nerve branches of the inferior hypogastric plexus and in particular the urogenital neurovascular bundles (Walsh's bundles) approaching the prostate and seminal vesicles dorsolaterally, which are at risk during surgical mobilisation of the anterior rectal wall.

Paraproctium

Laterally the rectal fascia reflects towards the pelvic wall to give access for blood and lymphatic vessels and, in particular, for autonomic nerves diverging from the inferior hypogastric plexus into the rectal wall. This loosely arranged connective tissue between the pelvic wall and the rectum ("T-junction") corresponds to the paraproctium, often referred to as lateral rectal ligaments or rectal stalks, approaching the rectal wall from dorsolateral.

2.1.3.4 Blood Vessel Supply of the Rectum and Anus

As a hindgut derivate the rectum is mainly supplied by the terminal branch from the inferior mesenteric artery, the superior rectal artery (diameter 3.0 ± 1.1 mm), contributing more than 80% to the rectal blood supply (Fig. 2.1.6). Passing within the mesorectum the artery divides into two or three large branches surrounding the posterolateral rectal wall. The branches ramify between the muscle layers, enter the submucosa and descend to the anal columns to open into the corpus cavernosum recti. In contrast, the medial rectal arteries originating from the internal iliac arteries are inconstant and bilaterally present in only 10%. Their contribution is rather small and their anastomoses with the superior and inferior rectal arteries are poorly developed. The lower anal canal and the internal anal sphincter are supplied by anal arteries from the inferior rectal arteries. They approach the anal region from the pudendal arteries located within the Alcock canal via the ischioanal fossa and divide into ventral and dorsal branches. Functional anastomoses are established between the inferior and superior rectal arteries within the anal canal. The posterior wall of the anal

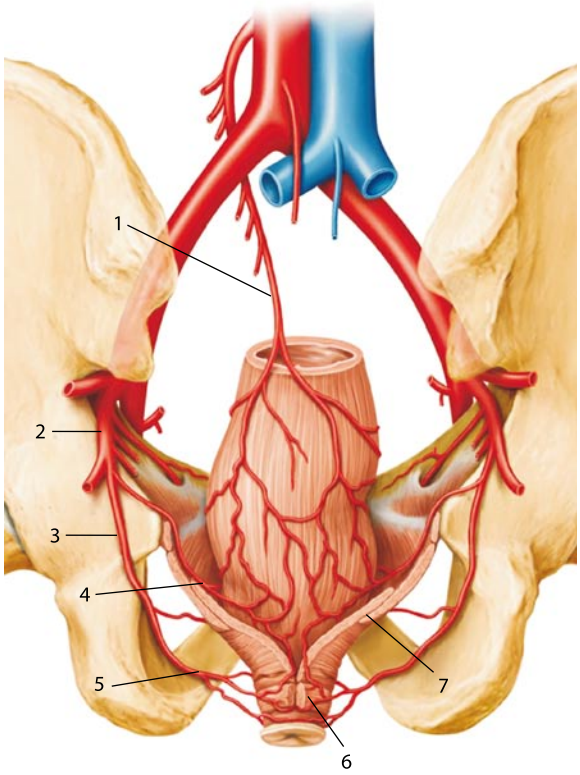


Fig. 2.1.6 Blood supply of the rectum and anal canal: rectal arteries. *1* superior rectal artery (from inferior mesenteric artery), *2* internal iliac artery, *3* pudendal artery, *4* medial rectal artery, *5* inferior rectal artery, *6* external anal sphincter, *7* levator ani muscle

canal and the internal anal sphincter are additionally supplied by the median sacral artery.

2.1.3.5 Lymphatic Drainage of the Rectum and Anus

Similar to the blood supply the main lymphatic drainage of the rectum is achieved by intramural lymphatic vessels passing to inferior mesenteric lymph nodes via the mesorectum. Only if the rectal fascia is penetrated in advanced tumour stages does the lymphatic drainage take place along the paraproctium into the internal iliac lymph nodes. Lymphatic vessels of the lower anal canal and the perianal region project to the superficial inguinal lymph nodes.

2.1.3.6 Nerve Supply of the Rectum and Anus

Whereas the rectum and upper anal canal are supplied by autonomic nerves, the lower anal canal and the anus receive a somatic input via the pudendal nerves (Fig. 2.1.2).

Autonomic Nerves

Lumbar sympathetic nerves pass along the inferior mesenteric and superior rectal artery forming considerably rigid periarterial nervous networks, the inferior mesenteric and superior hypogastric plexus. From the superior hypogastric plexus originate the left and right hypogastric nerves which enter the pelvic cavity from both sides attached to the parietal pelvic fascia (Waldeyer's fascia). They approach the rectal wall laterally and diverge into an intrapelvic nervous network, the inferior hypogastric plexus (pelvic plexus). Sacral parasympathetic nerves join the inferior hypogastric plexus via pelvic splanchnic nerves (nervi erigentes), intermingle with their sympathetic counterparts and commonly enter the rectal wall to establish connections with the intramurally located enteric nervous system.

The inferior hypogastric plexus also provides the autonomic nerve supply for the intrapelvic urogenital organs maintaining sexual and lower urinary tract functions. The autonomic nerves are at risk during rectal resection, in particular during lateral (paraproctium) and ventral (rectoprostatic/rectovaginal septum) mobilisation of the rectal wall.

Somatic Nerves

The lower anal canal is supplied by perianal branches of the pudendal nerves. In contrast to the autonomically innervated rectum, the anodermal segment is highly sensitive to touch, pressure, pain and temperature due to densely distributed somatosensory nerve endings.

2.1.4 Pelvic Floor

The pelvic floor is composed of both striated and smooth muscles covered by fasciae (rhabdo- and lissomusculofibrous systems) providing a twofold function:

- Closure of the pelvic cavity to provide support for intrapelvic organs
- Controlled opening for bladder and rectum evacuation and parturition

Due to its physiological weakness (lower muscle strength, less nervous input, wider urogenital opening) and stress-

ful strain during parturition, the female pelvic floor is generally more susceptible to insufficiency which may result in descending perineum syndrome, prolapse of pelvic organs and evacuation disorders.

2.1.4.1 Levator Ani Muscle

Most of the pelvic floor is formed by the levator ani muscle, a broad, flattened and funnel-shaped muscle attached to the pelvic wall. Ventrally the muscular sheet leaves a midline gap for the urethra and vagina (urogenital hiatus) and the anal canal (anal hiatus). The levator ani muscle is composed of the following segments (Fig. 2.1.7):

Iliococcygeal Muscles

The iliococcygeal muscles arise from the tendinous arc formed by the obturator fascia and attach to the coccyx, the last two sacral vertebrae and fuse in a midline raphe. The muscular sheet is very thin and commonly displays intramuscular, slit-like gaps particularly in women, which may give way for the propagation of ischiorectal abscesses (supralevatory spread).

Pubococcygeal Muscle

The pubococcygeal muscle extends above the iliococcygeal muscles from the pubic bone to the sacrum where it forms a tendinous plate attached to the coccygeal bone. Some fibres decussate to the periurethral musculature

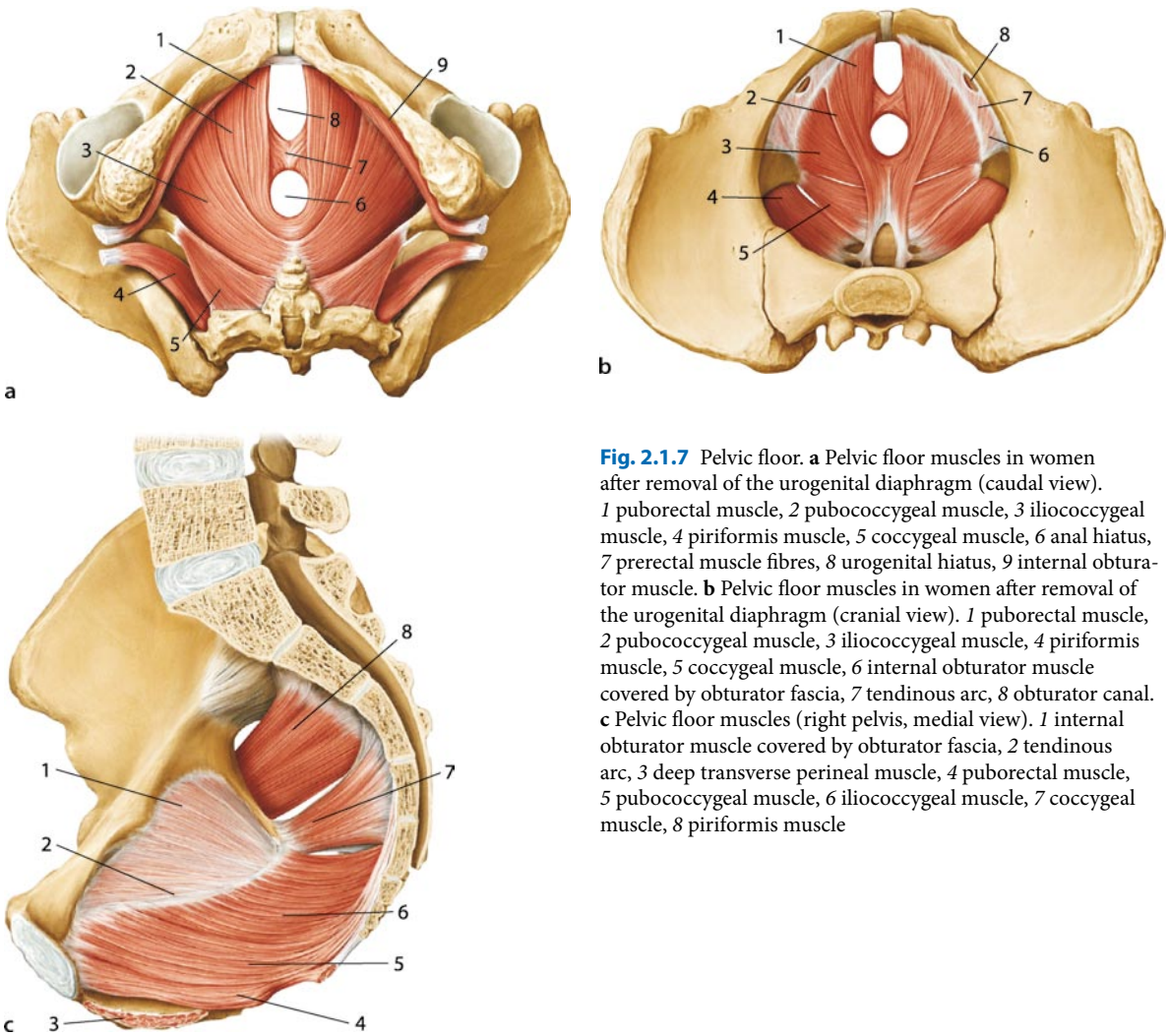


Fig. 2.1.7 Pelvic floor. **a** Pelvic floor muscles in women after removal of the urogenital diaphragm (caudal view). *1* puborectal muscle, *2* pubococcygeal muscle, *3* iliococcygeal muscle, *4* piriformis muscle, *5* coccygeal muscle, *6* anal hiatus, *7* prerectal muscle fibres, *8* urogenital hiatus, *9* internal obturator muscle. **b** Pelvic floor muscles in women after removal of the urogenital diaphragm (cranial view). *1* puborectal muscle, *2* pubococcygeal muscle, *3* iliococcygeal muscle, *4* piriformis muscle, *5* coccygeal muscle, *6* internal obturator muscle covered by obturator fascia, *7* tendinous arc, *8* obturator canal. **c** Pelvic floor muscles (right pelvis, medial view). *1* internal obturator muscle covered by obturator fascia, *2* tendinous arc, *3* deep transverse perineal muscle, *4* puborectal muscle, *5* pubococcygeal muscle, *6* iliococcygeal muscle, *7* coccygeal muscle, *8* piriformis muscle

and insert into the walls of the vagina (pubovaginal muscle) and rectum (puboanal muscle). The puboanal fibres blend with fibres of the longitudinal rectal muscle to form the conjoined longitudinal muscle.

Puborectal Muscle

The puborectal muscle is the most prominent muscle of the pelvic floor. Inseparable from the pubococcygeal muscle at its origin, the muscle bends at the anorectal junction to form a sling behind the rectum. Contraction results in a compression of the anal canal by pulling the anorectal junction towards its punctum fixum (pubic bone) thereby reducing the anorectal angle. The puborectal sling is intimately fused with the deep part of the external anal sphincter. From the caudal part of the muscle prerectal fibres decussate to insert into the perineal tendinous centre.

Coccygeal Muscles

The coccygeal muscles lie dorsocranially to the levator ani muscle and extend from the ischial spine to the lateral margins of the coccyx along the sacrospinal ligaments. Lying in the same plane as the levator ani muscle they complete the muscular pelvic diaphragm at its posterior end.

2.1.4.2 External Anal Sphincter

Below the levator ani muscle the anal canal is surrounded by the external anal sphincter (Fig. 2.1.4). The muscle forms an elliptical cylinder of about 15 mm thickness and is divided by septa into three parts. Although the external anal sphincter is a striated skeletal muscle, its fibres are mainly composed of slow-twitch type I fibres mediating a prolonged contraction suitable for maintaining an adequate basal tonus.

Subcutaneous Part

The subcutaneous part circumscribes the anal orifice deep to the skin below the lower border of the internal anal sphincter. Some fibres are anteriorly attached to the perineal tendinous centre and posteriorly to the anococcygeal ligament.

Superficial Part

The superficial part lies above and lateral to the subcutaneous part. Due to its firm attachment to both the perineal tendinous centre and the anococcygeal ligament, this part is elliptically shaped. The dorsal region frequently displays a crypt-like recess, thereby favouring the development of anal fissures at the coccygeal midline position.

Deep Part

The deep part is the thickest and most cranially located segment surrounding the internal anal sphincter. Its fibres blend inseparably with the puborectal muscle and are not attached posteriorly to the coccyx. Whereas in men all three parts of the external anal sphincter are equally present along the entire circumference, in women, in particular due to the less developed deep part, the external anal sphincter muscle is anteriorly reduced to one third of its posterior thickness.

2.1.4.3 Smooth Pelvic Muscles

In addition to striated muscles mainly composed of slow-twitch type I fibres (rhabdomusculofibrous system) the pelvic floor is also equipped with several smooth muscle elements (lissomusculofibrous system) predominantly located along the medial border of the levator sling. Smooth muscle fibres also extend from the rectal wall to the vagina (rectovaginal muscle), to the membranous part of the urethra (rectourethral muscle, Roux's muscle) and to the coccyx along the anococcygeal ligament (rectococcygeal muscle, retractor recti muscle, Treitz's muscle).

2.1.4.4 Nerve Supply of the Pelvic Floor

All striated muscles of the pelvic floor are innervated from sacral spinal segments ($S_{2–4}$) (Fig. 2.1.2). The somatomotor supply of the levator ani muscle and the external anal sphincter is provided by inferior rectal branches of the pudendal nerve and by direct branches from the sacral plexus. The smooth musculature is supplied by autonomic nerve fibres originating from the inferior hypogastric plexus (pelvic plexus) (Fig. 2.1.2).

2.1.4.5 Blood Vessel Supply of the Pelvic Floor

The pelvic floor is supplied by branches from the pudendal, inferior rectal and perineal arteries. Furthermore, the medial and lateral sacral arteries contribute at the dorsal side and the obturatory arteries from the lateral sides.

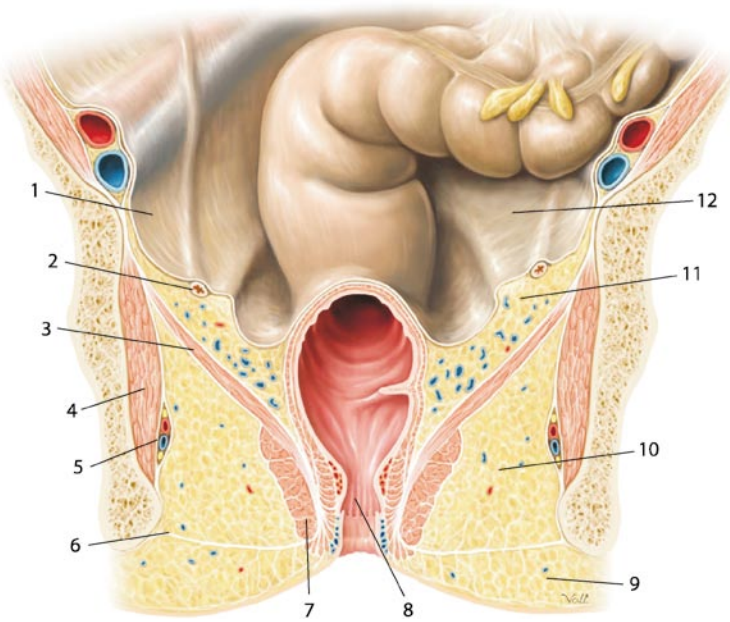


Fig. 2.1.8 Pelvic spaces. Frontal section of the pelvis (ventral view). *1* parietal peritoneum, *2* ureter, *3* levator ani muscle covered by superior and inferior pelvic diaphragmatic fascia, *4* obturator muscle covered by obturator fascia, *5* pudendal nerve and vessels ensheathed by doubling of obturator fascia (Alcock's canal), *6* superficial perineal fascia (transverse septum), *7* external anal sphincter, *8* anal canal, *9* perianal space (subcutaneous layer), *10* ischioanal space (infradiaphragmatic/infralevatory compartment), *11* subperitoneal space (supradiaphragmatic/supralevatory compartment), *12* peritoneal cavity

2.1.4.6 Anal Continence Organ

The pelvic floor muscles contribute substantially to the maintenance of anal continence. However, closure of the anal canal is a complex function achieved by synergistic interaction of different anatomical components that together resemble the anal continence "organ". Maintenance of anal continence requires both an autonomic and somatic nervous control and is mediated by the following structures:

- Puborectal sling providing a kink-like compression
- External anal sphincter providing a lace-like closure
- Internal anal sphincter providing a ring-like narrowing
- Corpus cavernosum recti providing a cushion-like closure
- Anodermal segment providing highly discriminative somatic sensation of luminal content
- Rectal ampulla providing visceral sensation of luminal content prior to defaecation

2.1.4.7 Pelvic Spaces

The musculofibrous systems of the pelvic floor divide the region between the peritoneal cavity and the perineal skin into three different compartments (Fig. 2.1.8):

Subperitoneal Space

The subperitoneal space is delimited by the pelvic peritoneum from above and ends at the pelvic diaphragm (supradiaphragmatic/supralevatory compartment). It contains loosely arranged connective tissue which condenses around the pelvic organs to form the paracystium, paraprostatium, paracolpium, parametrium and paraproctium. Towards the lateral pelvic wall the space widens to give access for the neurovascular supply of the pelvis, pelvic organs and the lower extremities. Autonomic nerve fibres (hypogastric nerves, inferior hypogastric plexus) descend from both sides passing through the subperitoneal space in a dorsoventral direction to approach the intrapelvic organs.

Ischioanal Space

Below the pelvic diaphragm extends the ischioanal fossa (infradiaphragmatic/infralevatory compartment). The space is pyramid shaped with its base towards the perineal skin and its apex at the junction of the internal obturator and levator ani muscle covered by the obturator and inferior pelvic diaphragmatic fasciae. A doubling of the obturator fascia (Alcock's canal) ensheathes the internal pudendal vessels and pudendal nerve releasing their branches into the ischioanal fossa to reach the perineal structures. The ventral part of the ischioanal fossa sur-

rounds the urethra and the vagina and is caudally closed by the urogenital diaphragm. The dorsal part surrounds the anal canal and extends towards the sacrotuberal ligaments and the gluteus maximus muscle. The ischioanal fossa is filled with loosely arranged areolar fat (corpus adiposum perinei). As the anococcygeal ligament does not completely separate both sides of the ischioanal fossa, infralevatory abscesses may easily spread from one side to the other (infralevatory "horseshoe" abscess).

Perianal Space

Towards the perianal region the ischioanal fossa is caudally delimited by a thin fascia, the superficial perineal fascia, formed by diverging tendinous endings of the conjoined longitudinal muscle. Below this connective tissue plane extends the perianal space. This space corresponds to the subcutaneous layer underlying the perianal skin and contains small-sized fat lobules separated by rigid connective tissue septa.

Suggested Reading

1. Church JM et al (1987) The surgical anatomy of the rectum: a review with particular relevance to the hazards of rectal mobilisation. Int J Colorectal Dis 2:158–166
2. Fritsch H et al (2004) Clinical anatomy of the pelvic floor. Adv Anat Embryol Cell Biol 175:1–64
3. Heald BJ, Moran BJ (1998) Embryology and anatomy of the rectum. Semin Surg Oncol 15:66–71
4. Köckerling F et al (2002) Fortschritte in der kolorektalen Chirurgie. Science Med Dr. Sperber
5. Konerding MA et al (1999) Rektumkarzinom: Optimierung durch Kenntnis der Anatomie unter besonderer Berücksichtigung des Mesorektums. Zentralbl Chir 124:413–417
6. Lange J, Mölle B, Girona J (2006) Chirurgische Proktologie. Springer, Heidelberg
7. Lienemann A et al (2003) Functional imaging of the pelvic floor. Eur J Radiol 47:117–122
8. Loeweneck H, Feifel G (2003) Lanz Wachsmuth – Praktische Anatomie, Ein Lehr- und Hilfsbuch der anatomischen Grundlagen ärztlichen Handelns, vol 2, part 6. Springer, Heidelberg
9. Michels NA et al (1965) Variant blood supply to the descending colon, rectosigmoid and rectum based on 400 dissections. Its importance in regional resections: a review of medical literature. Dis Colon Rectum 8:251–278
10. Platzer W (1989) Pernkopf-Anatomie, Atlas der topographischen und angewandten Anatomie des Menschen, vol 2. Brust, Bauch und Extremitäten, 3rd edn. Urban & Schwarzenberg, Munich
11. Schemann M, Neunlist M (2004) The human enteric nervous system. Neurogastroenterol Motil 16(suppl 1):55–59
12. Schünke M et al (2005) Prometheus, LernAtlas der Anatomie, vol 2: Hals und Innere Organe. Thieme, Stuttgart
13. Schünke M et al (2005) Prometheus, LernAtlas der Anatomie, vol 1: Allgemeine Anatomie und Bewegungssystem. Thieme, Stuttgart
14. Standring S (2004) Gray's anatomy: the anatomical basis of clinical practice, 39th edn. Churchill Livingstone, London
15. Stelzner F (1998) Chirurgie an den viszeralen Abschlußsytemen. Thieme, Stuttgart
16. Stoker J et al (2001) Pelvic floor imaging. Radiology 218:621–641
17. Tillmann B (2004) Atlas der Anatomie. Springer, Heidelberg
18. Wedel T et al (1999) Organization of the enteric nervous system in the human colon demonstrated by wholemount immunohistochemistry with special reference to the submucous plexus. Ann Anat 181:327–337

Physiology

3.1 Colon, Rectum, Anus

KLAUS KROGH, SOEREN LAURBERG

3.1.1 Functions of the Colon and Rectum

The main functions of the human colon and rectum are:
- Transport and storage of faeces
- Absorption of water and electrolytes
- Absorption of short-chain fatty acids

Most absorption of water, electrolytes and short-chain fatty acids occurs in the right colon while the main function of the left colon is storage and evacuation of faeces. Faeces are transported in the large bowel as a result of muscular contraction in the wall of the colon and rectum. A knowledge of the physiology of large-bowel motility is important in understanding the various pathological changes that may effect large-bowel function.

3.1.2 Colonic and Rectal Muscle Physiology

3.1.2.1 Resting Membrane Potential

Smooth muscle cells within the circular and longitudinal colorectal muscle layers are arranged in bundles connected by gap junctions. Bundles fuse at many points making each muscle layer function as a syncytium. The resting membrane potential of colorectal smooth muscle cells (−50 to −60 mV) is not constant, but undergoes small undulating changes called slow waves. Slow waves are generated by the interstitial cells of Cajal (the pacemaker cells).

Slow waves do not cause colorectal contractions but influence the frequency of spike potentials. Spike potentials are action potentials occurring when the resting membrane potential becomes more positive than about −40 mV. During spike potentials calcium enters the smooth muscle cells causing contraction.

Several factors influence the occurrence of spike potentials, either by depolarisation making the membrane potential more positive, and thus the cells more excitable, or by hyperpolarisation making it more negative and the cells less excitable. Depolarisation of the membrane potential is caused by stretching of the muscle cells, acetylcholine and several gastrointestinal hormones. Hyperpolarisation is caused by epinephrine and norepinephrine.

3.1.2.2 Colonic Muscle Contraction

Colorectal contractions are either phasic or tonic:
- *Phasic contractions* last a few seconds and cause elevation of intraluminal pressure. They are well defined, having a definite beginning and ending. Phasic contractions are the mechanical response of smooth muscle cells to spike potentials.
- *Tonic contractions* are less well-defined, are longer lasting, usually several minutes or more, and may or may not be associated with increased intraluminal pressure.

Transit of colonic contents is often unassociated with detectable pressure changes and may be due to changes in colonic tone. Two types of tone have been described:
- *Tetanic tone* is generated by fusion of phasic contractions and is thus dependent on phasic activity and electrical spike potentials.
- *Specific tone* is not associated with spike activity or phasic activity and is probably regulated by chemical processes.

3.1.2.3 Colonic Motility

The following patterns of phasic colonic contractions have been identified:
- Single non-propagating contractions
- Antegrade pressure waves
- Retrograde pressure waves
- Periodic colonic motor activity

Single non-propagating contractions are frequent and usually involve short segments of the colonic wall. Their main function is to mix the luminal content thereby promoting absorption.

Antegrade pressure waves (mass or high-amplitude propagating contractions) normally appear a few times each day, usually originating in the caecum or ascend-

ing colon, and span large parts of the colon propelling contents aborally. Mass contractions occur mostly during waking hours, specially on awakening or after meals. The latter constitutes the colonic component of the gastrocolic response. The main function of mass contractions is colonic transport and their frequency and amplitude is reduced in patients with slow transit constipation. Colonic mass contractions may progress into the rectum and result in defaecation.

The function of *retrograde pressuere waves* and *periodic colonic motor activity* (discrete bursts periodic contractions either propagating or localized) is unknown.

Colonic tone remains to be described in more detail in humans. However, both tetanic and specific tonic activity can be found.

3.1.2.4 Rectal Motility

Rectal motility patterns resemble colonic but there are certain differences. The following *phasic rectal contractions* have been identified:

- Isolated contractions
- Short clusters of contractions
- Powerful phasic contractions

The physiological significance of *isolated contractions* and *short clusters of contractions* (often with a low amplitude and a frequency of approximately 5–6 contractions per minute) is as yet unknown.

Powerful phasic contractions within the rectum have been termed the rectal motor complex (RMC). The RMC is usually seen every 60–120 min, it lasts several minutes and its contractions have a frequency of 3–10 per minute (Fig. 3.1.1). Accordingly, it has a strong resemblance to phase three of the migrating motor complex (MMC) within the small bowel. It is often located to a very short segment of the rectum but it can, however, propagate orally or aborally. As the RMC often is associated with contractions of the colon and the anal canal it has been proposed that its main function is to prevent defaecation.

Two types of change in *rectal tone* have been described:

- Rapid volume waves
- Slow volume waves

Rapid volume waves last less than 2 min and are associated with increased luminal pressure. They are not affected by eating. *Slow volume waves* last more than 2 min, are not associated with changes in intraluminal pressure but their frequency increases after a meal. Slow waves may increase rectal sensation to luminal contents. Increased rectal tone during defaecation may change the rectum from a capacious reservoir to a conduit.

3.1.2.5 Postprandial and Diurnal Changes

Colorectal tone and the frequency of both colonic mass contractions and haustral colonic contractions increase within a few minutes after a meal. The effect is more pronounced in the left than in the right colon and it usually lasts 30–60 min. This *gastrocolic response* is mediated by the sympathetic nerves and by the release of cholecystokinin and perhaps gastrin. The effect is to move contents over large distances of the colorectum often resulting in defaecation.

Sleep has a strong inhibitory effect on colonic mass contractions, haustral contractions and colorectal tone. However, during rapid eye movement sleep and especially on awakening colonic tonic and phasic activity increases. The RMC is more frequent during sleep and may contribute to nocturnal continence.

3.1.2.6 Neural Control of Colorectal Motility

Colorectal motility is controlled by:

- The enteric nervous system (ENS)
- The prevertebral sympathetic ganglia
- The autonomic system within the brain stem and spinal cord
- The higher cortical centres
- Circulating hormones
- The immune system

Enteric Nervous System

Enteric nerves within the intermuscular plexus (Auerbach's plexus) mainly control colorectal motility and those within the submucosal plexus (Meissner's plexus) mainly control mucosal secretion and blood flow. Neurotransmitters found in the ENS can either stimulate (acetylcholine, serotonin, histamine, cholecystokinin angiotensin, motilin and gastrin) or inhibit (dopamine, noradrenalin, glucagon, vasoactive intestinal polypeptide, enkephalin and somatostatin) motility. Receptors for histamine and serotonin have been classified into subgroups. Agonists and antagonists have been developed and may in the future have a clinical role.

The ENS generally consists of three types of neurons:

- Sensory neurons
- Interneurons
- Motor neurons

Sensory neurons, specialised for detection of mechanical stimuli, temperature or chemical properties, interact through multiple *interneurons* with *motor neurons* to either stimulate or inhibit smooth muscle contraction. Interneurons also integrate stimuli from the ENS with the extrinsic nerve system and hormones. Reflexes within the ENS can thus be activated by both local and extrinsic stimuli. Thus efferent parasympathetic fibres within the vagal and splanchnic nerves can stimulate motility over large distances of the gastrointestinal tract.

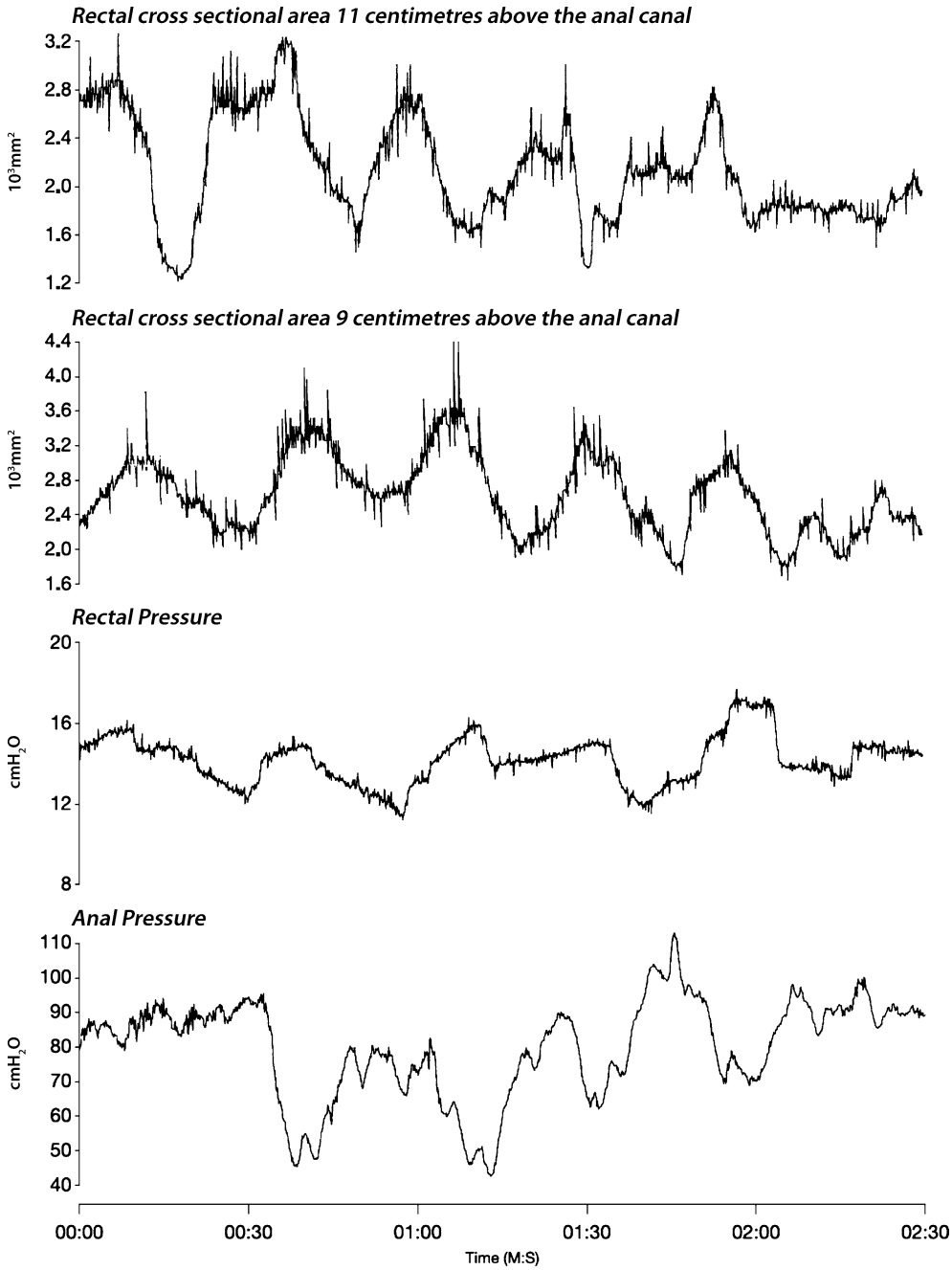


Fig. 3.1.1 Rectal motor complex

Prevertebral Sympathetic Ganglia

Sympathetic nerve fibres and *prevertebral sympathetic ganglia* are considered the most important mediators of the gastrocolic response mediating colorectal phasic and tonic activity after a meal.

Parasympathetic activity within the ENS depolarises colorectal smooth muscle cells through the release of acetylcholine and stimulates colorectal motility. If parasympathetic innervation is lost, colorectal reflex activity is reduced. A clinically important example is severe defaecation disorders due reduced left colonic and rectal reflex activity and tone after damage to the splanchnic nerves or spinal cord lesions of the conus medullaris or cauda equina.

Sympathetic activity causes hyperpolarisation of colorectal smooth muscle cells reducing colonic phasic activity and tone. The clinical effects of sympathetic denervation have not been studied in detail but observational studies indicate that it has a minor effect on colorectal transport.

Autonomic System

Non-conscious sensory information is mediated through parasympathetic afferents in the vagal nerve or through the splanchnic nerves to the sacral spinal cord. Painful stimuli are conveyed through sympathetic afferents via a three-neuron chain from the colon to the brain: The cell body of the primary afferent is located in the dorsal root ganglia of the spinal cord. This synapses with dorsal horn neurons and conveys information through the spinothalamic or spinoreticular tracts to the thalamus and reticular formation. From there, a third neuron connects to higher sensory centres such as the anterior cingulate cortex.

The colon and rectum are insensitive to most stimuli; however, they are very sensitive to stretch. The subjective experience of rectal sensation is a feeling of rectal fullness and an urge to defaecate. In contrast, colonic distension produces pain and colic. The location of rectal stretch receptors is controversial. The rectal mucosa is without any specific receptor type, probably explaining the poor discriminatory quality of rectal sensation.

Higher Brain Centres

Higher brain centres that influence colonic motility include the frontal regions of the cerebral cortex, the stria terminalis, the amygdala and the hypothalamus. The effects on colorectal motility are mainly inhibitory, thus loss of supraspinal control of the sacral reflex centre may cause increased left colonic and rectal reflex activity and tone (Fig. 3.1.2).

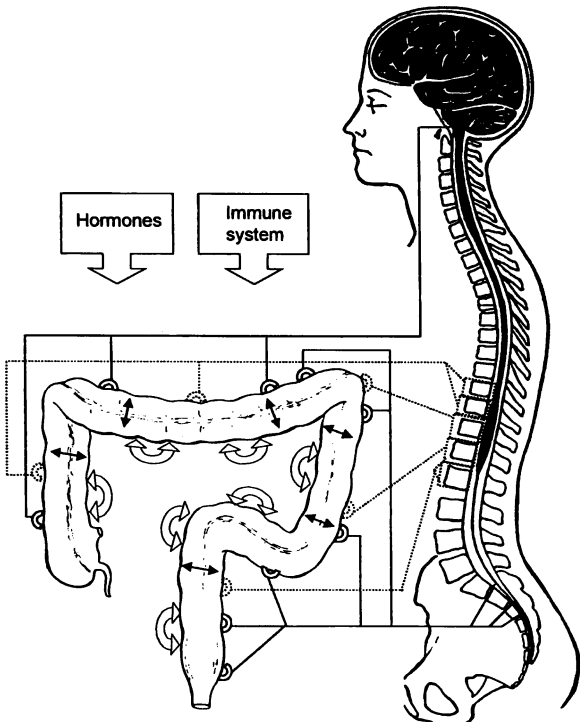


Fig. 3.1.2 Control of colorectal motility. White arrows: the enteric nervous system, solid lines: parasympathetic innervation, broken lines: sympathetic innervation

Hormonal and Immune System Control

Thyroid hormone stimulates colorectal motility and epinephrine reduces it.

The unique ability of the immune system to recognise specific antigens makes immunoneuronal integration important for bowel function. Once the immune system within the bowel wall becomes sensitised to specific antigens a second exposure to that antigen causes release of histamine and other messengers from mast cells. Histamine acts on intestinal H_2 receptors stimulating electrolyte, water and mucus secretion and promotes strong contractions called power propulsion spanning large distances of the bowel. Consequently, potentially harmful antigens are quickly cleared from the lumen.

3.1.3 Colorectal Transit Time

Total and segmental colorectal transit times show great individual variation. Healthy asymptomatic subjects may have total colorectal transit times of up to 4 days. Left co-

lonic and rectal transit time is usually longer than right colonic transit time. In healthy subjects stool frequency and consistency probably correlates better with rectosigmoid transit time than with total colonic transit time. However, stool weight per day correlates with colonic transit time.

Stool weight in healthy people living on a normal diet in Europe or North America is usually between 100 and 150 g per day. In rural Uganda it is up to 500 g per day. Dietary fibres, mainly bran, that do not undergo anaerobic bacterial fermentation retain water within stools. Accordingly, bran increases stool weight and reduces colonic transit time in most individuals. It is, however, important that extra fibre does not reduce colonic transit times in women with severe idiopathic constipation and may even further prolong transit times in patients with severely prolonged colonic transit times due to spinal cord lesions.

3.1.4 Anorectal Physiology

The main functions of the rectum and anal canal are:
- To maintain faecal continence
- To allow defaecation at an appropriate time and place

The following factors are important for the maintenance of anal continence:
- The internal anal sphincter muscle (IAS)
- The external anal sphincter muscle (EAS)
- The puborectalis muscle
- Rectal compliance
- Anorectal sensitivity
- Anorectal motility

3.1.4.1 Internal Anal Sphincter

The IAS is a continuation of the circular muscle layer of the rectum and consists of smooth muscle cells. Its main function is to contribute to the *anal resting pressure*. Anal resting pressure is extremely variable between individuals and tends to decrease with age and parity. The resting pressure undulates in a slow wave pattern of low amplitude and frequency. An ultraslow wave pattern of greater amplitude may also be present. Their physiological significance is unknown.

3.1.4.2 External Anal Sphincter

The EAS is composed of striated muscle. Its main function is to generate the anal squeeze pressure. The EAS is partly under voluntary control from Onuf's nucleus in the ventral horn of the sacral spinal cord via the pudendal nerve and the perineal branch of S4 nerve.

3.1.4.3 Puborectalis Muscle

The striated puborectalis muscle creates an angle of approximately 80° at the anal rectal junction that is considered to contribute to anal continence.

3.1.4.4 Rectal Compliance

Rectal compliance is defined as the relationship between rectal pressure and rectal volume or cross-sectional area ($\Delta V/\Delta P$ or $\Delta CSA/\Delta P$). Reduced rectal compliance is considered the most important factor causing faecal incontinence following radiotherapy.

3.1.4.5 Anorectal Sensitivity

In contrast to the rectum, the anal canal mucosa has many sensory receptors. Thus the anal canal is extremely sensitive to touch, pin-prick, temperature and movement. Even moderately reduced anal sensitivity, for instance due to diabetic neuropathy, may cause faecal incontinence.

3.1.4.6 Anorectal Motility

Coordination of motility between the rectum and anal canal is central to both continence and efficient evacuation.

Rectoanal Reflexes

The *anal sampling* and the *rectoanal inhibitory* reflexes are important to continence. The anal sampling reflex (Fig. 3.1.3) allows contents of the rectum to come into contact with the anal mucosa to determine the nature of rectal contents (i.e. solid or liquid stool or gas). After a short relaxation of the anal upper canal, anal pressure normalises forcing the contents back into the rectum.

The rectoanal inhibitory reflex mediates relaxation of the IAS during rectal distension (Fig. 3.1.4). It is conducted through intramural nerve fibres but may be enhanced by parasympathetic stimuli from the sacral spinal cord. The rectoanal inhibitory reflex is absent in Hirschsprung's disease.

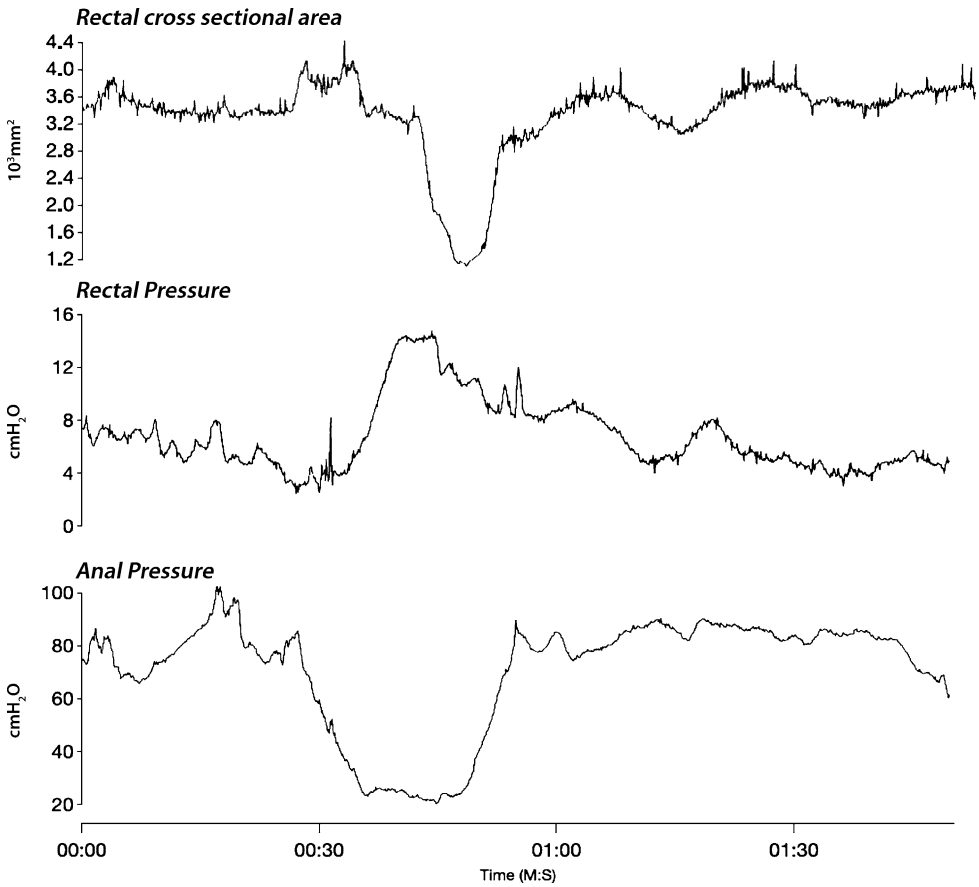


Fig. 3.1.3 Anal sampling reflex

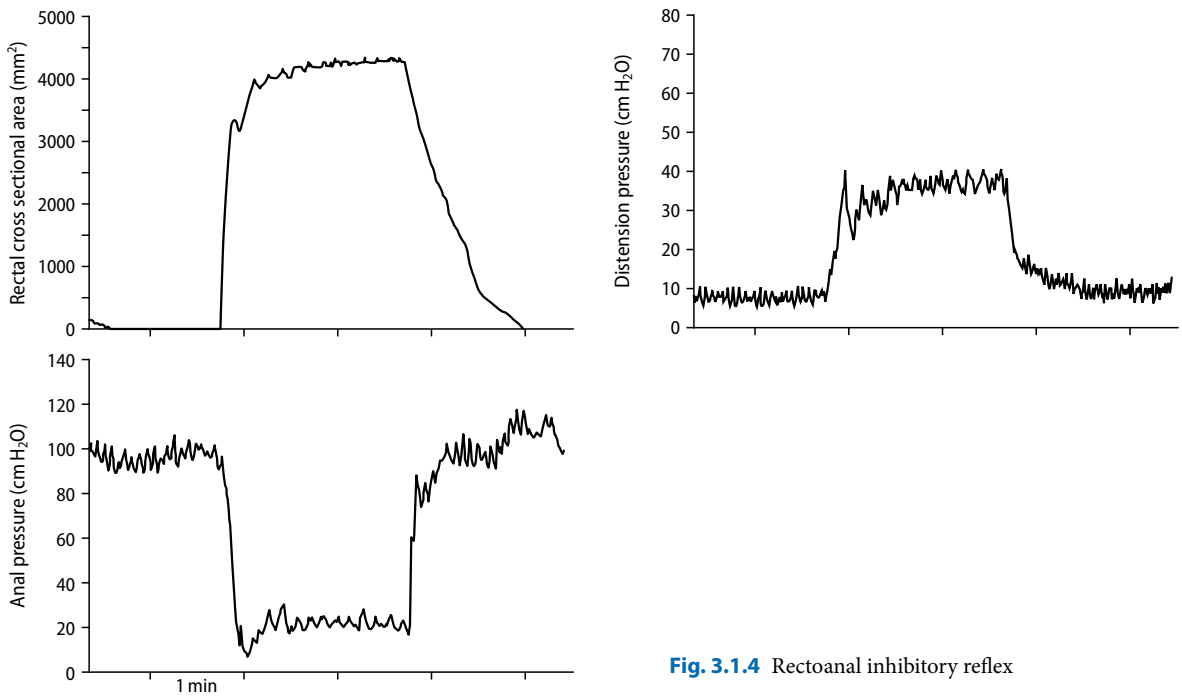


Fig. 3.1.4 Rectoanal inhibitory reflex

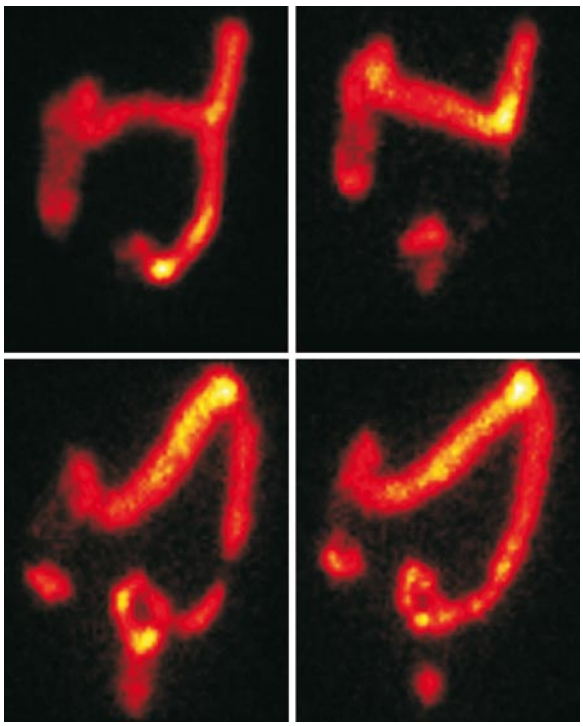


Fig. 3.1.5 Colorectal transport: scintigraphy before (left) and after (right) defaecation. Normal (*top*) and in a patient with sacral spinal cord lesion (*bottom*)

3.1.5 Defaecation

Defaecation is normally preceded by colonic mass movements that bring colonic contents to the rectum. Distension of the rectal wall may further stimulate contractions of the colon and rectum through an intrinsic reflex mediated by the ENS and by the parasympathetic *defaecation reflex* involving the sacral segments of the spinal cord. Phasic rectal contractions occur and rectal tone increases, changing the rectum from a capacious reservoir to a conduit. Filling of the rectum stimulates the rectoanal inhibitory reflex, relaxing the IAS. Relaxation of the puborectalis muscle creates an obtuse angle overcoming the anal flap valve mechanism and defaecation occurs if the EAS is relaxed. The process is enhanced by increasing the abdominal pressure through a Valsalva manoeuvre. Under normal circumstances defaecation can be postponed by voluntary contraction of the EAS. The defaecation reflex then gradually subsides and rectal compliance increases. The amount of luminal transport before and during defaecation is very variable. If the defaecation reflex is interrupted, colorectal transport at defaecation is significantly reduced (Fig. 3.1.5).

3.1.6 Physiological Assessment of the Colon and Rectum

3.1.6.1 Colonic Motility

Most studies of colorectal motility have been performed using pressure transducers connected to a luminal catheter. These are either perfused low-compliance systems or use pressure-sensitive strain gauges. Perfused catheters are especially suited for studies of sphincters as they measure contractions that obstruct their side holes. This restricts their usefulness in non-sphincteric regions. Furthermore, ambulatory studies cannot be performed and the association between changes in pressure and luminal cross-sectional area is poor. Intraluminal pressure-sensitive strain gauges are better suited for chronic measurements and ambulatory systems are available, but they are expensive and placement requires colonoscopy.

Colorectal Transit Times

Colorectal transit times can be determined by:

- Transit of radio-opaque markers
- Scintigraphy

Radio-opaque markers are either counted in stools or on plain abdominal films (Fig. 3.1.6). Markers can be taken as a single dose and followed by a single film after a fixed time interval (often 3–4 days), as a single dose followed by multiple films after fixed time intervals or as multiple doses followed by a single film (often after 7days). The first method can distinguish between constipated patients and healthy subjects but does not give any quantitative information about total or segmental colorectal transit times. If markers are followed by multiple films or if markers are taken on multiple days followed by a single film total and segmental transit times can be determined.

Scintigraphy can be used for determination of transit times throughout the gastrointestinal tract. Scintigraphy is superior for measuring gastric and small-bowel transit but less good for measuring colorectal transit. Individual variations in colonic transit times are large and many patients with subjective complaints of constipation have normal colorectal transit times.

Colorectal Emptying

Movement of colorectal contents during defaecation can be assessed by means of evacuation proctography. However, this is a highly unphysiological test and does not give any detailed quantitative measure of colorectal transport. Isotope proctography with radiolabelled material inserted into the rectum allows quantitative description of rectal emptying. It also is an unphysiological test

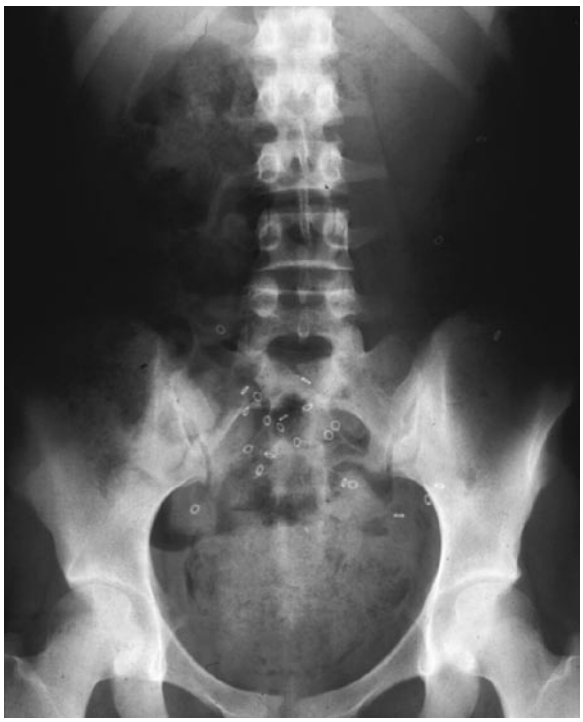


Fig. 3.1.6 Radio-opaque markers for determination of colorectal transit time

as the isotope is not mixed with the faeces and it does not give information about movement of colonic contents.

Rectal Compliance and Tone

Compliance is the parameter most often used for description of colorectal distensibility. It is usually defined as changes in volume (ΔV) or cross-sectional area (ΔCSA) divided by changes in pressure (ΔP). Rectal compliance computed from pressure-volume (P-V) curves during rectal distension is commonly used to describe rectal wall properties in research and clinical practice. Measurement of rectal cross sectional area during distension is of value principally in a research setting.

Rectal tone may be measured by use of a barostat that measures changes in intraluminal volume of a balloon at constant pressure. It is difficult to distinguish whether changes are caused by tone in the rectal wall due to muscle contraction, increased connective tissues or other factors. The method is best suited for studies of changes in rectal tone, for instance after a meal.

3.1.6.2 Anal Manometry

Anal manometry may be performed using:

- A solid-state pressure transducer
- Balloon manometry
- A perfused system

Normal parameters range greatly depending on the technique used and the population studies. Nevertheless, anal manometry is a standard part of the investigation of faecal incontinence.

3.1.7 Absorption of Water and Electrolytes

Under normal circumstances approximately 1,500–2,000 ml pass from the ileum to the colon each day. The fluid contains sodium, potassium, chloride and bicarbonate. Most water is absorbed, especially in the right colon, and only 100–150 ml is lost in the stool. Furthermore, the colon has a significant absorptive reserve capacity of approximately 5–6 l. Overall, the colon absorbs sodium and chloride while it secretes potassium and bicarbonate. Sodium absorption and bicarbonate secretion are active processes against the negative electrical potential difference between mucosa cells and lumen. Potassium secretion is mainly potential dependent but there may also be active transport.

The chemical composition of luminal contents and stretch of the wall activate receptors in the colonic wall. Through release of messengers from motor neurons to the neuroepithelial junctions, water and electrolyte transport of the epithelial cells is stimulated or inhibited. Messengers that act at the neuroepithelial junctions include acetylcholine and vasoactive intestinal peptide (VIP) (antiabsorptive) and somatostatin and neuropeptide Y (proabsorptive).

Release of norepinephrine from sympathetic nerve cells acts through alpha receptors to increase water, sodium and chloride absorption. This mechanism may be disrupted in autonomic diabetic neuropathy. Release of acetylcholine from parasympathetic fibres within the vagal or sacral nerves reduces colonic water and sodium absorption.

Mineralocorticosteroids, glucocorticoids and somatostatin stimulate colonic sodium transport while mineralocorticosteroids also stimulate potassium secretion.

3.1.8 Absorption of Short-chain Fatty Acids

Dietary fibres are complex macromolecular plant substances that are resistant to hydrolysis by human digestive enzymes. Short-chain fatty acids (SCFAs; mostly acetic, propionic and butyric acids) are produced by anaerobe bacterial fermentation of dietary fibre. Most SCFAs are produced and absorbed in the right colon. SCFAs are readily absorbed by colonic mucosa, are precursors for mucosal lipid synthesis and provide a major source of energy for the colonocytes. SCFAs stimulate colonic sodium absorption.

Suggested Reading

1. Bouchoucha M, Devroede G, Arhan P, Strom B, Weber J, Cugnenc P, Denis P, Barbier J (1992) What is the meaning of colorectal transit time measurement? Dis Colon Rectum 35:773–782
2. Krogh K, Ryhammer AM, Lundby L, Gregersen H, Laurberg S (2001) Comparison of methods used for measurement of rectal compliance. Dis Colon Rectum 44:199–206
3. Lestar B, Pennickx F, Kerremans R (1989) The composition of anal basal pressure. Int J Colorectal Dis 4:118–122
4. Whitehead WE, Delvaux M, and the Working Team (1997) Standardization of barostat procedures for testing smooth muscle tone and sensory thresholds in the gastrointestinal tract. Dig Dis Sci 2:223–241
5. Wood JD, Alpers DH, Andrews PLR (1999) Fundamentals of neurogastroenterology. Gut 45(suppl II):II6–II16

Anal Disorders

4.1 Haemorrhoids

PER-OLOF NYSTRÖM, ROGER GERJY

4.1.1 Introduction

The corpus cavernosum recti is part of the normal anatomy. If this tissue enlarges we speak of haemorrhoids; if it causes symptoms it is a haemorrhoidal disease. The circumstances under which they become symptomatic are not fully understood. Currently, diseases of the haemorrhoids are classified under the chapter of vascular diseases in the International Code of Diseases (e.g. ICD10). However, there is growing consensus that the pathological mechanism involves prolapse of redundant and detached rectal mucosa, which at defaecation slides into the anal canal together with the haemorrhoids. Its impaction in the anal canal during defaecation appears to be the circumstance that generates the symptoms. The therapeutic aim is to prevent the prolapse with one of several treatment options.

4.1.2 Anatomy

- The anoderm of keratinised squamous cell epithelium and the rectal mucosa are joined at the dentate line in the mid-anal canal.
- Above the dentate line a zone of non-keratinised intermediate cells gradually turn into the normal mucosal lining of the rectum (the transitional zone).
- Immediately above it the internal haemorrhoidal plexus (corpus cavernosum) forms three pedicles of arteriovenous spools with arterial supply from arteries running in the submucosa from above and venous return leaving through the rectal wall to drain into rectal mesenteric veins.
- Very commonly there are intermediate haemorrhoidal pedicles in the patients who come to treatment. It is assumed that the haemorrhoidal pedicles, in the resting rectum, fall together like a shutter to close the upper anal canal on top of the sphincters. This function should be important for passive continence of mucous and liquid stools.
- There is an internal haemorrhoidal plexus and an external venous plexus located at the internal and external ends of the anal canal. They are situated in submucosal and subepidermal spaces with a common fascia behind them.

4.1.3 Incidence

- It is estimated that half the adult population has suffered at least one episode of anal complaints that can be ascribed to haemorrhoids.
- Recurrent or persistent symptoms are much less frequent but it is difficult to give precise estimates because anal complaints are common and are related to disordered bowel function.
- Because haemorrhoidal tissue is a constituent of the normal anatomy it can be associated with anal symptoms without being its cause.
- Strong associations have been observed between symptomatic haemorrhoids and a number of diarrhoeal disorders, including ulcerative colitis, non-infectious gastroenteritis and functional diarrhoea. A study from the American Veterans Administration found that haemorrhoids were associated with diarrhoea, constipation, spinal cord injury and various other types of anorectal diseases.
- The yearly incidence of haemorrhoidectomy has been reported at rates of 40–50 per 100,000 population.
- Patients who attend treatment for symptomatic haemorrhoids may reach as high a rate as 4% (4,000 per 100,000 population).
- Complaints are rare before the age of 20 years and the peak is seen for the age group 45–65 years.
- Haemorrhoids are thought to affect men more often, as shown in several trials, but others have found equal gender distribution.
- Treatment for symptomatic haemorrhoids is declining in recent years. The explanation probably relates to better regulation of functional bowel disorders with dietary fibre and perhaps the much-improved availability of clean toilets in all places.

4.1.4 Symptoms

There are five cardinal symptoms of haemorrhoids:

- Anal pain
- Defaecatory bleeding
- Anal seepage or soiling
- Anal irritation and pruritus
- Mucoanal prolapse that needs manual repositioning

These symptoms appear in various frequencies and patients have periods of worse and lesser complaints. Pain is a common anal complaint but has a specific character in haemorrhoids. It is related to the prolapse and is relieved by its reduction. Bleeding is most commonly seen as stains on the toilet paper but occasionally colours the cabinet. Soiling, i.e. staining of underwear, is common in the adult population. Here it is related to the prolapse that may also occur during daily activity in between defaecations. Defaecation with prolapse that requires manual repositioning is an important feature that distinguishes patients that are likely to need an operation.

- Symptoms of anal incontinence are common in patients who are diagnosed with haemorrhoids. In particular, involuntary flatus and soiling are common features when patients are asked. Soiling will be remedied by any effective treatment for the haemorrhoids but involuntary flatus will not.
- Asking patients how often they have experienced each of the symptoms conveniently assesses the symptomatic severity. If it is documented the same questions can be repeated to assess the outcome after treatment (Fig. 4.1.1).

How often do you have pain from the haemorrhoids?	☐ Never	☐ Less than once a week	☐ 1–6 times weekly	☐ Every day (always)
How often do you have itching or discomfort of the anus?	☐ Never	☐ Less than once a week	☐ 1–6 times weekly	☐ Every day (always)
How often do you have bleeding when passing a motion?	☐ Never	☐ Less than once a week	☐ 1–6 times weekly	☐ Every day (always)
How often do you soil your underclothes (soiling from the anus)?	☐ Never	☐ Less than once a week	☐ 1–6 times weekly	☐ Every day (always)
How often do you reduce a prolapsing haemorrhoid with your hand when passing a motion?	☐ Never	☐ Less than once a week	☐ 1–6 times weekly	☐ Every day (always)

Fig. 4.1.1 Patient self-reported symptom questionnaire

4.1.5 Diagnosis

- The symptoms must be carefully evaluated in every patient before a diagnosis of symptomatic haemorrhoids is established because haemorrhoids can be associated with so many different conditions. In particular, it must be realised that anal complaints are often secondary to disordered bowel function, which must be evaluated and treated before any specific treatment for the haemorrhoids is instituted. The most common confounder is irritable bowel syndrome (IBS) of the type that is associated with rectal urgency and repeat visits to the toilet.
- Patients who report a prolapse that needs manual repositioning at defaecation singles out a group that are almost certain to have symptomatic haemorrhoids. These patients, however, represent a minority. In the majority the diagnosis can only be established by exclusion of other underlying diagnoses and a proctoscopy to inspect the haemorrhoids.
- A rigid rectoscopy visualising at least 15 cm of rectum is a minimal requirement before any treatment under the diagnosis of haemorrhoids. A full colonoscopy or barium enema is required whenever the history suggests anything more than anal symptoms.
- The presence of prolapse is evaluated at rectoscopy. The rectum is deflated and the patient is asked to push out the rectoscope through the anus. A prolapse of rectal mucosa together with one or more of the haemorrhoids into the anal canal or outside the anal verge can be seen. In most instances the prolapse is reduced spontaneously when the rectoscope is removed and the push is relaxed.
- Any external component of anodermal folds and polyps is recorded. These are a consequence of the sliding down of the anal canal lining resulting in anoderm displaced externally. Secondary enlargement and fibrosis of the folds is common.
- The terms internal and external haemorrhoids should be reserved for the internal haemorrhoidal plexus and external venous plexus, respectively. Internal haemorrhoids that are displaced to an external position as a consequence of prolapse remain internal haemorrhoids.
- The clinically important manifestation of the external haemorrhoidal plexus is the perianal haematoma, a locally painful thrombophlebitis that can be drained by excision under local anaesthesia.

4.1.6 Classification

The traditional anatomical classification remains useful.

- Grade 1 haemorrhoids do not prolapse at examination.
- Grade 2 haemorrhoids prolapse but are spontaneously reduced.
- Grade 3 haemorrhoids prolapse and need manual repositioning.
- Grade 4 haemorrhoids prolapse but cannot be reduced digitally into the anal canal by the patient.

Important confusion prevails about the grades, usually leading to overstatement of the anatomical derangement. The important divisor is the patient who reports manual repositioning of haemorrhoids at defaecation (grade 3) and those who deny manual repositioning (grades 1 and 2). The latter are divided according to the surgeon's assessment of prolapse at procto/rectoscopy. Grade 4 haemorrhoids are a difficult entity because it is often confused with a significant external component that cannot be reduced because it is composed of anoderm. Some classifications reserve grade 4 for acute thrombosed and prolapsed haemorrhoids, as shown in the algorithm of classification (Fig. 4.1.2).

It has been attempted to incorporate one or more of the associated symptoms of the haemorrhoids into the anatomical classification. However, it seems that the associated symptoms are rather independent of the anatomical derangement. Hence, some patients bleed with minor prolapse while patients with major prolapse do not all bleed. Patients must be independently evaluated on both dimensions of anatomy and symptoms.

4.1.7 Treatment

Haemorrhoids are treated with many modalities:

- Methods targeted at the origin of the cushion without excision:
  - Sclerosing injection
  - Rubber band ligation
  - Infrared coagulation
  - Diathermy coagulation
  - Cryocoagulation
  - Suture ligation
  - Doppler-guided haemorrhoid artery ligation (HAL)
- Radiofrequency ablation
- Methods of complete excision of the haemorrhoids:
  - Milligan-Morgan operation
  - Ferguson operation, including the use of diathermy

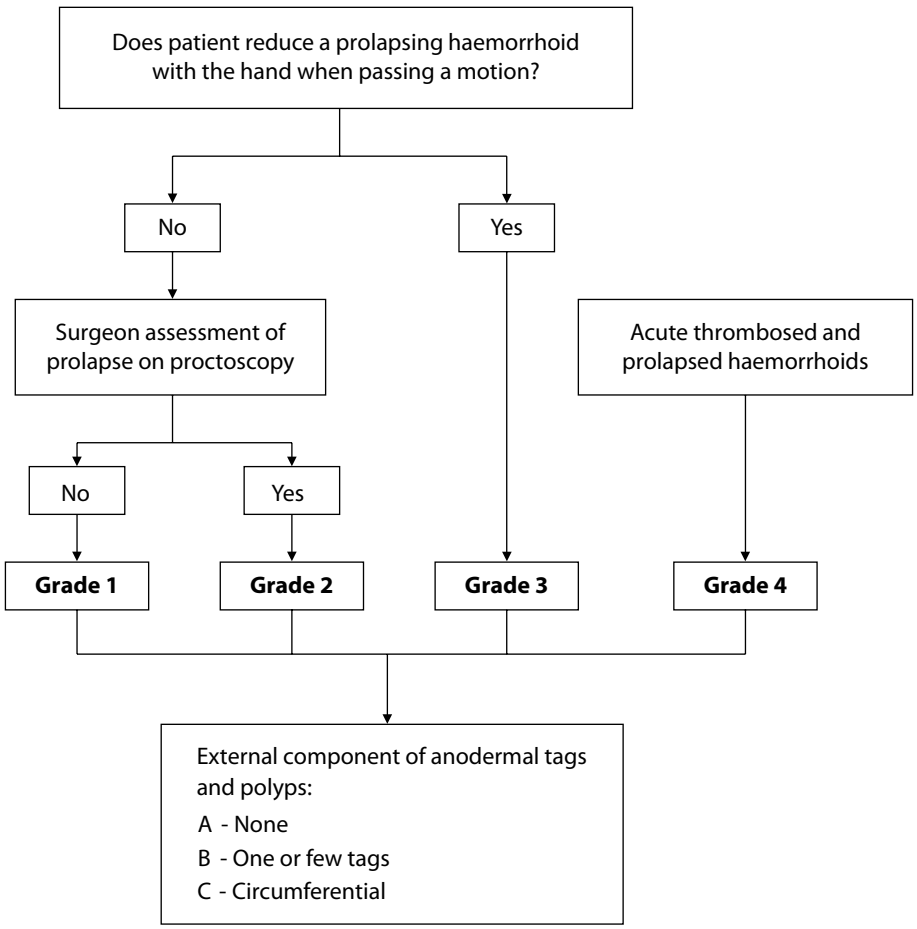


Fig. 4.1.2 Algorithm for grading haemorrhoids

  - Ultracision
  - Ligasure devices for the excision
- Methods that excise the haemorrhoid tissue with preservation and resuture of the mucosa and anoderm:
  - Whitehead operation
  - Parks operation
- Method of excision of the mucosal prolapse and "pexy" of haemorrhoids:
  - Stapled haemorrhoidopexy (anopexy)

The majority of patients belong to grades 1 and 2, usually with bleeding as the presenting symptom. They can be treated with simple measures without the need for anaesthesia. Suitable treatments are rubber band ligation and injection sclerotherapy. The divisor is the patient who has grade 3 haemorrhoids that may need an operation to correct this major prolapse. Patients with an external component cannot be treated adequately with non-operative measures. These statements will be disputed and the success with each method may depend on local expertise.

4.1.7.1 Sclerosing Injection

- This technique was introduced in Europe in the early 1900s and gained wide acceptance but is now largely replaced by rubber band ligation that has a wider therapeutic capability.
- Injections are applicable in grades 1 and 2 haemorrhoids where bleeding is the presenting symptom but prolapse is absent or minor.
- The most widely used sclerosing substance is 5% phenol in almond oil. It is a solution of high viscosity that requires a rather large-bore needle.

- Purpose-made needles with a shoulder near the tip to prevent too deep an injection should be used.
- The treatment results in fibrosis of the submucosa, possibly with obliteration of the vascular bed of the haemorrhoids, and fixation of the haemorrhoid and mucosa to the rectal wall.
- Alternatively ethoxysclerol can be used in varying concentrations.

Technique

- Each haemorrhoid is visualised in turn with the proctoscope.
- The needle is inserted into the rectal submucosa at the base of the haemorrhoid at the anorectal ring and 3–5 ml of the solution is injected.
- A bulging and bleaching of the mucosa signifies a correct application.
- The injection must be painless or aborted.
- In the majority of cases, three haemorrhoids can be treated in one session.
- Treatment sessions can be repeated at monthly intervals until bleeding has ceased.
- A mild discomfort or pain is rather common.
- The correct application will not result in ulceration.
- Short-term resolution is reached in the vast majority of patients (> 95%), but the recurrence rate is quite high (75%) within 2–3 years.

4.1.7.2 Rubber Band Ligation

- This method was introduced in the 1960s and quickly gained wide acceptance following the introduction of the Baron and McGivney instruments. These have been further improved by the addition of suction that allows the haemorrhoid to be aspirated into a cup before the application of the rubber band around its neck.
- Several modifications are available, also as single-use plastic instruments.
- It is the most common office treatment for grade 2 haemorrhoids and often used successfully for minor grade 3 haemorrhoids.
- The technique is inadequate to treat any external component.

Technique

- Each haemorrhoid is visualised in turn with the proctoscope.
- The correct application is at the base of the haemorrhoid that is grasped with the special forceps or aspirated into the cup if a suction device is used.
- The grasping of the haemorrhoid must be painless and ascertained before firing the rubber band.
- The less-experienced practitioner tends to apply the band too close to the dentate line, which causes pain.
- The tissue caught in the rubber band should be about a centimetre in size.
- From one to three applications can be made in a session.
- The sessions can be repeated at monthly intervals.
- The immediate response in the patient can be a sensation of filling or urge, occasionally associated with a temporary vasovagal reaction.
- If there is distinct pain the rubber band should be removed by cutting the band under local anaesthetic.
- In the days that follow rubber band ligation a dull pain or ache is common and is more frequent after multiple applications.
- The treatment results in a discrete tissue necrosis that is sloughed off in about 10 days without producing an ulcer. The local fibrosis will shrink the haemorrhoid and attach the mucosa to the rectal wall, which prevents further prolapse.
- Initial high success rates are followed by a recurrence rate of 25% within 3–4 years.

4.1.7.3 Thermal Coagulation

Application of energy that locally coagulates the tissue at the base of the haemorrhoid is provided as:

- Photocoagulation
- Cryocoagulation
- Electrical (diathermy) coagulation

Photocoagulation is the most widely used. These methods all work under a similar principle. The methods share a common problem of dosing the energy to avoid necrosis but induce fibrosis that attaches the mucosa to the rectal wall.

4.1.7.4 Haemorrhoid Artery Ligation

- This is a new method that is gaining recognition throughout Europe although its dissemination is currently limited to a few institutions.
- The technique originated in Japan by Morinaga and is rooted in a concept of symptomatic haemorrhoids as a vascular disease that can be controlled by interruption of the arterial supply above the haemorrhoid.
- A special proctoscope that is fitted with a window and a Doppler device is used to identify the artery 2–3 cm above the haemorrhoid.

- After identification a suture underruns the artery and is tied to interrupt the flow.
- Up to six such ligations have been applied in a single patient.
- The procedure can be performed as an office procedure but the early experience has usually to be gained in the operating room.
- Suture fixation of prolapsing haemorrhoids without Doppler identification of the artery has been suggested previously, but failed wide acceptance. It remains to be demonstrated that HAL is superior.

4.1.7.5 Radiofrequency Ablation

- This is also a new technique with limited experience.
- It is a thermal treatment, possibly with a more refined method for dosing the energy deposition to the submucosal space and haemorrhoid tissue.
- The instrument is rather expensive.

4.1.7.6 Excision of the Haemorrhoids

- Milligan-Morgan excision and Ferguson excision have somewhat different origins but are now almost identical operations that differ with respect to whether the wound is left open for secondary healing or sutured for healing by first intent.
- Several randomised studies have shown that closure of the wounds provides none or little gain, possibly because of frequent breakdown of the suture line.
- The modern excision differs from the original operations because surgeons no longer fear to leave the anal canal and lower rectum with an open wound.
- The excision was previously made with scissors but it has been universally replaced with diathermy excision, and more recently with excision by means of Ultracision or Ligasure devices for less bleeding.

Technique

- The three haemorrhoid pedicles are either retracted to a position outside the anus or the operation is performed through the anal canal using a speculum.
- The external anodermal fold is circumcised and the dissection is carried on both sides of the pedicle till about 2 cm above the dentate line, well into the rectal mucosa.
- The pedicle is suture ligated or transected with diathermy.
- The subdermal fascia of the skin fold continues as a submucosal fascia that covers the internal sphincter. Both the internal and external haemorrhoids are located superficial to this fascia that should be carefully dissected. If it can be preserved intact scarring after the excision is minimal with quicker healing and less pain.

Surgeons differ with respect to how aggressively they pursue the excision of all visible haemorrhoids, sometimes to the extent that skin bridges are opened and resutured after cleaning out residual plexus. This difference might reflect whether surgeons regard haemorrhoids as a vascular disease or a disease of mucoanal prolapse. It is conceivable that the more extensive operation leads to worse pain and longer recovery. In most studies high initial success rates (> 95%) were reported. The overall complication rate is 5–10% with a recurrence rate ranging from 2% to 25% in long-term follow-up.

4.1.7.7 Submucosal Haemorrhoidectomy

- Parks improved the original Whitehead operation.

Technique

- The anoderm and mucosa covering the haemorrhoid is incised.
- Flaps are developed to enable dissection and removal of the haemorrhoid-bearing tissue.
- The mucosa is then closed.
- The manoeuvre is repeated for the remaining haemorrhoids.

It is a demanding operation for the specialist who deals with extensive circumferential mucoanal prolapse.

4.1.7.8 Stapled Anopexy (Stapled Haemorrhoidopexy)

- This operation was devised by Longo and presented to a wider audience in 1998.
- It is based on a concept of symptomatic haemorrhoids as a disease of mucoanal prolapse.

Technique

- The redundant and loosened mucosa of the lower rectum is excised by means of the circular stapler in a prolapsectomy immediately above the haemorrhoids.
- The circumferential staple line is targeted at 2 cm above the dentate line.
- The haemorrhoids are not excised but fixed to the staple line and prevented from further prolapse in a pexy operation.
- There are no wounds of the anal canal.

The validity of this concept has been studied in a large number of randomised trials that show similar results compared with diathermy excision but less pain and shorter recovery. The operation is suitable for grade 3 haemorrhoids but in case of an external component this needs complimentary excision at the same time. If the skin tags are excised only in their extension outside the anal verge the pain advantage is retained. Grade 4 haemorrhoids with a large external component are more demanding to treat with the stapled procedure and may require a hybrid operation combining it with diathermy excision.

4.1.8 Position of the Patient

- Lithotomy
- Prone
- Left lateral

The lithotomy position is most widely used and is advantageous for the anaesthetist. The prone position provides better working conditions for the surgical team but is generally disliked by the anaesthetic team. Axonal block (spinal or epidural) allows prone position but delays discharge in ambulatory surgery. The combination of prone position and local anal block with or without mild conscious sedation is quick and acceptable to all.

4.1.9 Operation Under Local Anaesthesia

Haemorrhoidectomy can be performed under a local block. Several methods have been described but are not widely used. Marti described a block of the posterior ischiorectal fossa combined with infiltration of the perineum. Others have described a perianal block with infiltration immediately outside the sphincters up to the levators. These methods are acceptable to patients and can be used without conscious sedation in many patients. Infiltration of the anal canal and intersphincteric space with local anaesthetic is painful and cannot be applied without conscious sedation.

Infiltration of the anoderm and submucosa with local anaesthetic and adrenalin to ease dissection and diminish bleeding belongs to the time when scissors were used. Modern precise diathermy excision is made more difficult from wet tissues and does not need the haemostatic effect.

4.1.10 Pre- and Postoperative Care

This varies widely according to local traditions.

- A small enema is sufficient on the morning of surgery.
- Prophylactic antibiotics are unnecessary.
- Anal tamponade is unnecessary.
- The wounds need no special attention or dressing.
- Daily showers, sitz baths or cleaning with water after defaecation are advisable.
- A mild laxative should be provided to patients with an excision to prevent faecal impaction from the postoperative pain. Patients with stapled anopexy do not need it because they have less pain and some defaecatory urgency.
- The need for early return visits depends on the extent of the operation.
- The final evaluation of the result should wait at least 3 months.

In many hospitals haemorrhoidectomy can only be provided as an ambulatory operation in which case postoperative pain control becomes essential. The incentive to improve the operation is guided by the patients' response. In some European countries more than 90% of the operations can be performed in the ambulatory setting with adequate pain control on oral medication and less than 10% return for unacceptable pain, bleeding or urinary retention.

4.1.11 Complications

Seen at a frequency of 2–10%:

- Excessive pain despite adequate oral pain medication
- Bleeding
- Urinary retention
- Disturbed defaecation
- Delayed wound healing

Seen at a frequency of 1–2%:

- Anal fissure
- Anal abscess or fistula
- Thrombosed residual haemorrhoid
- Anal or rectal stricture
- Unacceptable scarring
- Anal incontinence

Rare complications:

- Separation of the staple line after anopexy
- Retroperitoneal gas or infection
- Fournier's gangrene

When patients are asked about the early postoperative course they will report that pain together with disturbed micturition and defaecation are the predominant complaints lasting for about a week. Only a few return because the symptoms are unbearable. The overall complication rate is usually reported in the range of 10–20% depending on what is recorded as such. Bleeding, infection, fissure, stricture and incontinence are the most feared complications among surgeons because these can be life-threatening or severely impact on long-term outcome.

4.1.12 Incontinence

- Patients with symptomatic haemorrhoids that require treatment represent a group with increased rate of disordered bowel function and disturbed anal continence. In particular, patients will report involuntary flatus and soiling at heightened rates.
- A few patients have mucoanal prolapse associated with weak sphincters and failed pelvic floor syndrome.
- A special case in this respect is the patient with a spinal cord injury with a short everted anal canal and significant prolapse of haemorrhoids and mucosa.
- Most studies find an association between haemorrhoids and increased sphincter pressure with a return to normal pressure after haemorrhoidectomy. This finding is difficult to reconcile with the epidemiological studies that show an association between haemorrhoids and conditions of diarrhoea. A reasonable explanation is that the increased sphincter pressure is a response to pain from the haemorrhoids, which is relieved after treatment.
- Some patients, especially those with IBS associated with urgency and repeat visits for defaecation, may rather have a persistent sphincter relaxation reflex which also increases the risk of incontinence.
- The anal continence is improved after treatment, especially with regard to soiling and leakage of loose stool.
- Involuntary passage of gas is improved only to a minor degree.

4.1.13 Recurrence of Haemorrhoids

The precise cure rate depends on:

- The stage of the mucoanal prolapse
- The symptom profile
- The elected treatment modality
- The expertise in its exertion

Recurrence after treatment reflects both incomplete resolution of the prolapse and symptoms by the treatment in case, as well as the appearance of new symptoms after a period of cure. The long-term cure rate is much less than generally appreciated and new symptoms are more common in the long run. Two late follow-up studies after Milligan-Morgan excision showed that about one third complained of anal symptoms after 8–17 years or had had repeat treatment.

- Recurrent symptoms after injection or banding, and similar non-resection methods, are expected and amenable to repeat treatment.
- The haemorrhoidectomy, by whichever method, provides a much better chance of lasting cure.
- Patients should be evaluated after treatment according to the same principles as they were selected for treatment.
- The ideal post-treatment patient has no prolapse (grade 1), no external component and no associated symptoms. Far from all patients will achieve such a result 1 year after treatment.

Suggested Reading

1. Corman ML, Gravie JF, Hager T, Loudon MA, Mascagni D, Nyström PO, Seow-Choen F, Abcarian H, Marcello P, Weiss E, Longo A (2003) Stapled haemorrhoidopexy: a consensus position paper by an international working party: indications, contra-indications and technique. Colorectal Dis 5:304–310
2. Gabrielli F, Cioffi U, Chiarelli M, Guttadauro A, De Simone M (2000) Hemorrhoidectomy with posterior perineal block: experience with 400 cases. Dis Colon Rectum 43:809–812
3. Ho YH, Cheong WK, Tsang C, Ho J, Eu KW, Tang CL, Seow-Choen F (2000) Stapled hemorrhoidectomy: cost and effectiveness. Randomized, controlled trial including incontinence scoring, anorectal manometry, and endoanal ultrasound assessments at up to three months. Dis Colon Rectum 43:1666–1675
4. Kanellos I, Goulimaris I, Christoforidis E, Kelpis T, Betsis D (2003) A comparison of the simultaneous application of sclerotherapy and rubber band ligation, with sclerotherapy and rubber band ligation applied separately, for the treatment of haemorrhoids: a prospective randomized trial. Colorectal Dis 5:133–138
5. Konsten J, Baeten CG (2000) Hemorrhoidectomy vs. Lord's method: 17-year follow-up of a prospective randomized trial. Dis Colon Rectum 43:503–506
6. Longo A (2002) Stapled anopexy and stapled hemorrhoidectomy: two opposite concepts and procedures. Dis Colon Rectum 45:571–572

7. Lunniss PJ, Mann CV (2004) Classification of internal haemorrhoids: a discussion paper. Colorectal Dis 6:226–232
8. MacRae HM, McLeod RS (1995) Comparison of hemorrhoidal treatment modalities. A meta-analysis. Dis Colon Rectum 38:687–694
9. Morgado PJ, Suarez JA, Gomez LG, Morgado PJ Jr (1988) Histoclinical basis for a new classification of hemorrhoidal disease. Dis Colon Rectum 31:474–480
10. Nisar PJ, Acheson AG, Neal KR, Scholefield JH (2004) Stapled hemorrhoidopexy compared with conventional hemorrhoidectomy: systematic review of randomized, controlled trials. Dis Colon Rectum 47:1837–1845
11. Nyström PO, Derwinger K, Gerjy R (2004) Local perianal block for anal surgery. Tech Coloproctol 8:23–26
12. Thompson W (1975) The nature of haemorrhoids. Br J Surg 62:542–552

4.2 Fissures

MARIO PESCATORI, CLAUDIO MATTANA

4.2.1 Definition

- Anal fissure is a common anorectal condition, particularly in young adults, with an incidence of 11–13% similar in the two genders.
- Anal fissure is a linear ulcer in the squamous epithelium of the anus, just distal to the dentate line, usually in the posterior midline.
- Recent studies discuss Goligher's rule that almost 90% of fissures are posterior, 10% are anterior and in 1% of patients they occur simultaneously; they found anterior fissures to be more common than expected, but the fissures were still on the midline.
- A different functional motor pattern in the anal canal has been found according to the location of the fissure.
- Acute fissure is usually superficial involving only the epithelium.
- A fissure is considered chronic when it is symptomatic for more than 3 months (some studies take 6 weeks) and tends to be deeper leading to the exposition of the underlying internal sphincter and is associated with anal lesions such as tags, induration of the edge of the fissure and hypertrophied anal papilla.
- Atypical fissures may be multiple, irregular, large or off the midline.

4.2.2 Aetiology

- Anal fissure may be associated with or caused by malignancy (both local and systemic), inflammatory bowel diseases, trauma and venereal infections.
- Previous anorectal surgery (i.e. haemorrhoidectomy, anal fistula) resulting in anoderm loss of elasticity may predispose to fissure formation.
- Anal fissure/ulceration, causing pain and bleeding, is one of the most common indications for reintervention after stapled haemorrhoidopexy.
- The aetiology of the typical benign lesion is not completely clear and understood. For many years it was thought that the passage of firm stools through the anal canal forced the internal sphincter and disrupted the anoderm leading to muscle spasm; the spastic internal sphincter fail to relax during the next dilatations and this lead to further tearing and deepening of the fissure, instituting a self-perpetuating cycle, followed by difficult healing of the skin and persistence of the symptoms. However, such a sequence was found in 25% of cases and fissures are associated with diarrhoea only in 4–7%; as a result, the stools' passage through the anoderm seems to be a cofactor of this pathology.
- The evacuation of hard stools with infrequent bowel movement has been reported only in a minority of patients (18%) suffering from anal fissure.
- A recent theory assumed that anal fissure is due to a chronic ischaemia of the posterior anal commissure exacerbated by internal sphincter spasticity.
- Laser Doppler studies have demonstrated poor blood flow in the posterior midline, improved by sphincterotomy; this seems to be the cause of the delayed healing of the scar and the presence of the anal spasm. The onset and persistence of symptoms are attributed to the same physiopathological mechanism.

4.2.3 Function of the Internal Sphincter

There are three factors which influence the tone and the function of the internal anal sphincter and may have a relevance in the pathogenesis of anal fissure:

- The myogenic system, due to the oscillation of the membrane potentials across the membrane of the smooth muscle cells;
- The intrinsic nervous system, which is mediated through the submucosal and myenteric plexuses;
- The extrinsic nervous system, mediated through the sympathetic and parasympathetic autonomic nerves.

There is a relative dominance of the sympathetic over parasympathetic neural input leading to a tonic state of the internal sphincter which provides the closure of the anal canal and prevents soiling.

4.2.4 Symptoms and Diagnosis

- With an acute and also a chronic fissure, the most important symptom is severe pain during defaecation.
- Usually, the pain continues after defaecation, subsiding after some hours.
- Bleeding and pruritus are very often associated with fissures.
- During examination, tenderness at the site of the fissure and anal spasm, which may make digital insertion for a rectal examination difficult, are always present in the acute situation.
- A gentle inspection can be achieved in the chronic form.
- A secure diagnoses of fissure can be obtained based on symptoms and gently dilating the anal verge, without anoscopy. The patient should then be advised that the lesion will be touched, at that time the symptoms will be reproduced, confirming the diagnosis.
- As above mentioned, a differential diagnosis with lesions associated with malignancy, Crohn's disease or immunodeficiency states should be carefully considered.
- Analysing internal sphincter pressure and activity by means of anal manometry may be useful to better select the type of surgery and to predict the outcome of both surgical and medical treatments.
- Anal hypertonia is likely to be associated with anal fissure, but 19% of men and 42% of women have a normal or a reduced anal resting tone.

4.2.5 Therapy

Although the precise aetiology of the fissure remains elusive, relief of the anal spasm has been associated with relief of symptoms and healing of the tear. The gold standard of therapy is to achieve anal sphincter relaxation using either conservative or surgical procedures.

4.2.5.1 Conservative Treatment

Diet Therapy

- Diet therapy was the first proposed therapy for the care of fissures.
- It is still in use and should be proposed and continued in all the patients presenting with a fissure associated with a severe and also mild constipation.
- The diet consists of a high residue of fibre and increased fluid ingestion in order to obtain easier spontaneous defaecation and to avoid evacuation of hard stools.
- The use of stool softeners (e.g. psyllium, lactulose, docusate sodium or calcium) could be useful in conservative treatment.
- With diet therapy the overall recovery rate is 87% in acute fissure, but almost 30% of the patients experienced recurrent fissures.

Local Anaesthetic Ointments

- Local anaesthetic ointments (e.g. 2% lidocaine) with or without steroid and bulk laxative used for a month can achieve complete healing of the fissure in 42–54% of patients.
- Healing is maintained in less than half of the patients during the following period.
- Anaesthetic ointments do not show better results than the diet regimen alone.

Anal Dilatation

- Anal dilatation has been proposed to resolve anal spasm and to reduce anal pain.
- This can be achieved under anaesthesia or with progressive and gradual manoeuvres in outpatients. The second method is the most valid alternative because of the minor complication rate (i.e. incontinence).
- A lubricated dilator of progressively increasing diameter is introduced daily through the anal verge by the patients themselves.
- The recovery rate ranges from 36% to 44%, but long-term follow-up does not show better results than other conservative treatments.
- Compliance of the patients with home anal dilatations is not very high, as the manoeuvre may be considered uncomfortable.
- The presence of hypertrophied anal papillae and fibrous polyps seems to affect negatively the outcome of all these conservative treatments.

Chemical Sphincterotomy

- Under the term chemical sphincterotomy, we include all the medical procedures which determine a relaxing effect on the internal smooth muscle sphincter.
- The internal sphincter tone is maintained by sympathetic α-adrenergic stimulation and sphincter relaxation is mediated by parasympathetic stimulation, sympathetic β-adrenergic receptors and direct inhibition of calcium entry into the muscle cells. All medical drugs counteracting the first action or supporting the second could potentially be helpful in achieving anal relaxation, in order to obtain anal fissure healing, without permanent damage to the sphincter.

- Nitric oxide donor (NOD) agents, like glyceryl trinitrate (GTN) or isosorbide dinitrate (ISDN) act as inhibitory neurotransmitters on the internal anal sphincter. They are available as ointments for local application and are favoured for fissure healing by reducing anal spasm and improving smooth muscle blood flow.
- GTN (0.2% cream, two applications a day for 6 weeks) achieves a healing rate ranging from 40% to 80% and an anal tone pressure reduction of 44%. Resumption of the symptoms after GNT treatment has been noted in 17–45% of the healed fissures within 36 weeks; however, the therapy can be repeated.
- ISDN results are similar to those for GTN.
- The most important and limiting complication of NOD agents is headache, because of cerebral induced vasodilatation. Patients refer to this problem in 20–100% of cases and almost 10% of them have to abandon the therapy because of the severe headache. Moreover, other side effects, such as hypotensive episodes, palpitations, dizziness and anal irritation, have been reported, overall accounting for a complication rate of 37%, significantly higher than the 18% reported after lateral internal sphincterotomy. However, several controlled trials have failed to confirm the brilliant results of previous studies.

Botulinum Toxin

- The use of botulinum toxin (BT) has been recently proposed to produce a chemical sphincterotomy.
- *Clostridium botulinum* produces different kinds of endotoxins: type A is used in different fields of medical therapy.
- The toxin produces a rapid muscular paralysis because of its selective tie with presynaptic cholinergic nerves: this binding prevents the exciting impulse reaching the muscular fibres.
- The toxin has to be injected into the anal sphincters by mean of an insulin syringe with a 27-gauge needle.
- In 1993, Jost proposed to inject the external sphincter, while in 1994 Gui et al. suggested a smooth muscle infiltration. Both the methods showed a recovery of the symptoms and a transient decrease of both resting and squeeze pressure.
- Up to the present day, controversies still exist on the site of injections, the number of units injected, and the number of treatments that have to be repeated.
- The dose injected varies from 5 to 40 IU.
- A complete healing of the fissure occurs in 50–83% of cases.
- A temporary incontinence was noted in 12% of patients; it was more evident in those with external sphincter infiltration and was dose dependent.
- The resumption of symptoms has been noted in 25% of patients after 1 year. A new cycle of toxin injections can be suggested.
- BT may be effective in the management of secondary fissures, i.e. fissures following haemorrhoidectomy or associated with ulcerative colitis.
- The use of BT is not widely adopted because of the cost of the drug and the aversion of the patients to repeat the treatment.
- Recently, a case of long-term faecal incontinence has been reported following the injection of BT, possibly due to the injection of an excessive dose both in the internal and in the external anal sphincter.

Calcium Channel Antagonists

- By inhibiting the migration into the muscle cells of calcium ions, calcium channel antagonists (CA) reduce muscular contraction. This effect has been used by some authors to obtain internal anal sphincter relaxation (up to 30% less than the normal resting pressure) in order to cure anal fissures.
- Calcium antagonist ointments seem to produce better results in healing of fissures when compared with anaesthetic or steroid salves. No randomised trials against placebo are present in the literature to check the efficacy of this therapy.
- No adverse effect has been noted.

Summary of Conservative Treatment

- In conclusion, conservative and medical care of acute or chronic anal fissures can be offered to the patient as the first step in the care of this pathological condition, even though a randomised prospective study showed the superiority of lateral internal sphincterotomy over GTN in managing chronic fissure.
- Chemical agents may well be especially advised for elderly patients, those who have a previous history of incontinence or anal surgery and to women who have had a previous difficult vaginal delivery.
- Successful non-surgical treatment of chronic anal fissure leads to a symptomatic improvement and beneficially affects health-related quality of life.
- For second-line conservative therapy, Lindsey et al. report seven trials describing a further course of GNT after primary use of GNT in a total of 60 relapsing patients, with short-term healing in 77%, and two case series where nifedipine was successful in 48% of patients after GNT failure; one trial of BT for GNT-resistant fissures had modest results.

4.2.5.2 Surgical Treatment

For many authors surgical therapy remains the best option for the care of anal fissure. It can be offered to the patient as the first choice, without being an overtreatment. The rationale of surgical therapy is to bring about rapid internal anal sphincter relaxation through a sphincterotomy; this manoeuvre permits healing of the fissure and recovery from the symptoms. In this chapter, manual anal dilatation under anaesthesia is not considered: this operation should be abandoned, as postoperative incontinence affects up to 28% of patients after dilatation. As mentioned above, gradual balloon dilatation can be offered to the patient with good results.

Posterior Anal Sphincterotomy

- Posterior anal sphincterotomy (PS) consists of incision of the internal anal sphincter posteriorly, dividing the muscle at the level of the fissure. This technique gained popularity in the early 1950s, and was reintroduced by Eisenhammer.
- Ninety-five per cent of the fissures heal with this approach, but healing time is longer than 6 weeks and incontinence ranges from 5% to 28%, probably due to an anal key-hole deformity, as in the posterior commissure there is a weak point represented by an intersphincteric groove, i.e. a triangle between the internal and the external sphincter, which, once the sphincterotomy is performed, may facilitate either mucus or faecal soiling.
- Recurrences may occur in up to 13% of patients. For these reasons today the technique is to be avoided, unless there are particular situations, as shown in Fig. 4.2.1.
- PS is inevitable when a fissure is associated with intersphincteric fistulae or abscess.

Fissurectomy

- Fissurectomy shows results similar to PS, but has been recently reported to be effective with the adjunct of BT in cases of anal hypertonia and of anoplasty in cases of anal normo- or hypotonia.

Lateral Internal Sphincterotomy

- Lateral internal sphincterotomy (LS) has been the gold standard procedure for the treatment of chronic anal fissures since the late 1980s.
- LS can be performed either by an open or a closed technique, dividing the internal sphincter at 3 or 9 o'clock, far from the fissure.
- In the open technique, a 1-cm radial incision of the anoderm is carried out, and an internal sphincter section is performed under direct vision. The skin can be closed or not after the procedure; no differences were noted in the results, even if a longer time of healing is reported leaving the skin open.
- Closed sphincterotomy is performed using a short stab incision and blind division of the internal anal muscle is guided by the surgeon's finger.
- Both open and closed methods do not show differences in the outcome, either in healing or in recurrence.
- A low complication rate of 8.7% has been reported after LS, the most frequent complication being delayed healing at the sphincterotomy site.
- The recurrence rate following LS is very low: 0–7.5%.
- LS is usually carried out up to the dentate line, but may be alternatively carried out by:
  - Dividing the whole sphincter
  - Dividing the lower part of the sphincter up to the cranial end of the fissure, the so-called tailored sphincterotomy
  - Performing a conservative (short) sphincterotomy
  - Performing the sphincter division on the basis of the anal hypertonia measured at preoperative manometry, the so-called spasm-related sphincterotomy which may decrease postoperative soiling when compared with the standard sphincterotomy at the dentate line in a randomised prospective study
- Others suggest to grade the extent of LS on the basis of the degree of anal stenosis or of both anal pressure and fissure length.
- These manoeuvres are aimed at reducing the risk of postoperative incontinence, frequently following LS, even in multiparous women undergoing conservative sphincter division. The wide variations of both recurrence and incontinence rate may be due to several factors:
  - Different extent of muscle division
  - Specialisation of the surgeon
  - Preoperative work-up, whether only clinical or also based on anal manometry and ultrasound
  - Proportion of elderly patients and of multiparous females
  - Number of patients with preoperative soiling
  - Length of follow-up
  - Type of study, whether prospective or retrospective
  - Last, but not least, the accuracy and the type of the follow-up, whether based on a telephone interview or a written questionnaire or on an outpatient visit, with or without endoscopy, manometry, ultrasound and quality of life evaluation

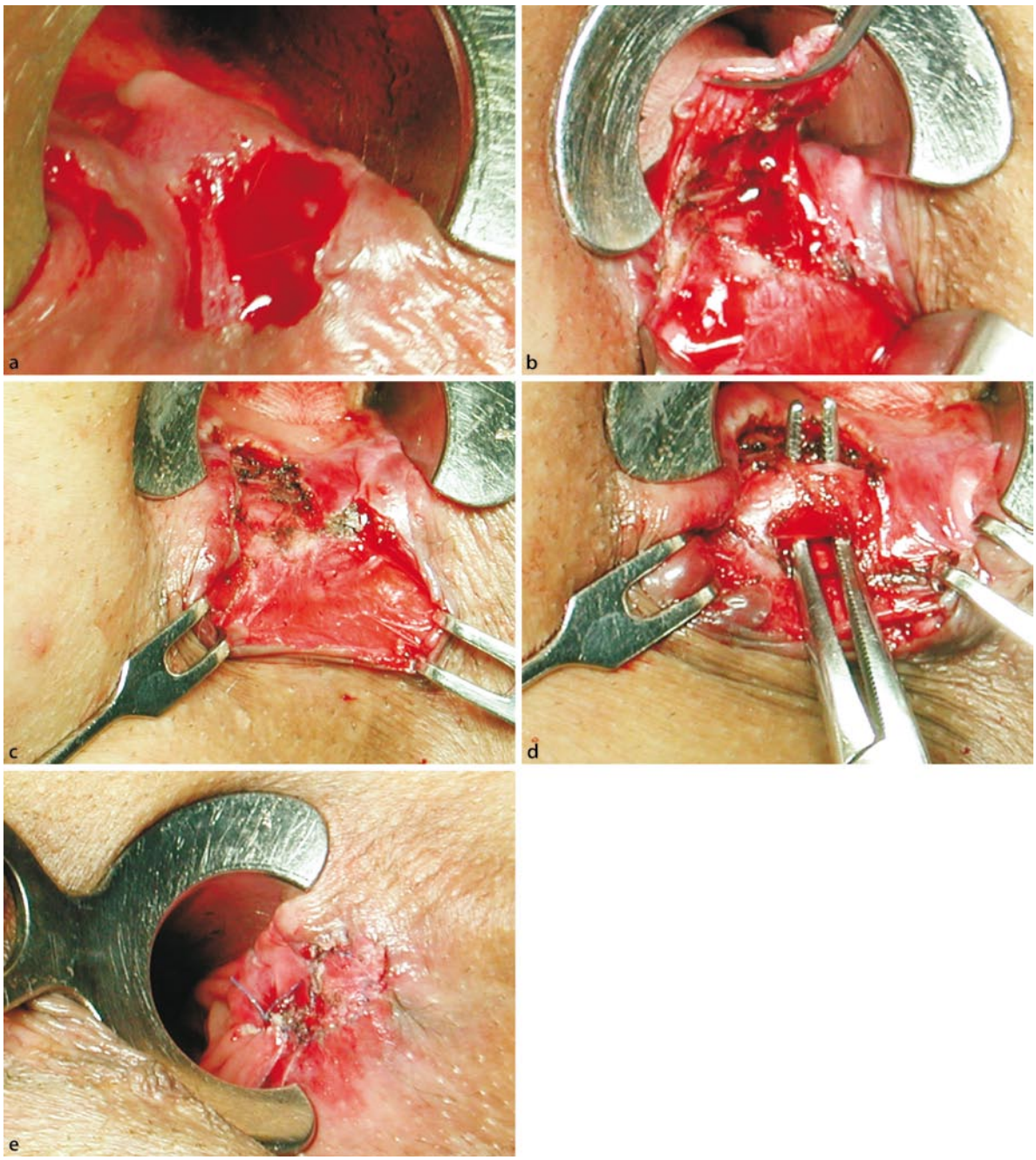


Fig. 4.2.1 **a** Bleeding recurrent chronic fissure with hypertrophied papilla and anal hypertonia. **b** Fissurectomy and papillectomy. The rectal advancement flap is raised. **c** Postfissurectomy wound. **d** Posterior internal sphincterotomy, carried out posteriorly to avoid another surgical wound on the lateral aspect. **e** Mucocutaneous anoplasty aimed at covering the surgical defect and preventing postoperative soiling due to posterior anal deformity

Anal Manometry

- Benefit from routine anal manometry was not demonstrable in a manometric study conducted before and after operation in 177 patients with chronic fissure.
- It has been shown in a prospective study that there are basic differences in rectoanal inhibition and pressure profile between those patients who remain continent following sphincterotomy and those who complain of postoperative incontinence even when the length of the sphincterotomy on coronal imaging does not differ between the two groups.

Outcome After Closed and Open LS

- The last randomised prospective study comparing the outcome after closed and open LS did not show any difference to far as recurrence and incontinence.
- Not surprisingly, the functional results with a complete division of the internal sphincter are worse than those after conservative, i.e. short LS, or from those in which the muscle division was tailored on the basis of fissure length, even if no recurrence of anal fissure was observed.

Postoperative Incontinence

- The results of a prospective study of postoperative incontinence reveal that this problem only rarely diminishes quality of life.
- Out of 111 patients who experienced gross faecal incontinence after LS at the Mayo Clinic, only one complained of severe faecal incontinence after 1 month.
- The overall parameters of quality of life scores were in the normal range whereas the faecal incontinence Wexner scores were 13.4 ± 13.7 in a group of 90 patients with soiling (31% of those who had surgery) followed up for at least 5 years after LS at the Cleveland Clinic Ohio.
- Those who had LS under local anaesthesia on a day surgery basis were more likely to have postoperative soiling.
- Minor incontinence ranges from 1% to 37%, while severe incontinence ranges from 1% to 8%.
- According to an anal ultrasound study, patients with incontinence following LS may have had an undesired division of external sphincter.
- In contrast to LS in men, division of the internal anal sphincter in most women tends to be more extended than intended. This is probably related to their shorter anal canal.
- In some women, LS may compromise sphincter function and precipitate anal incontinence, particularly in the presence of other sphincter defects.
- Recently, Patel et al. did not find any correlation between the occurrence of postoperative incontinence and previous vaginal delivery in a group of female patients who underwent LS for anal fissure, but reported an early postoperative disordered continence in 3.6% of the patients, which increased to 24.5% in the long term. Eight per cent of the patients ended with gross incontinence to solid stool.

Prevention of Incontinence

Different parameters have been investigated in order to prevent soiling:

- Longer sphincterotomies are more often associated with soiling, however some authors present very good results with entire sphincter division.
- There is no difference according to the side of LS.
- Magnetic resonance imaging is useful to detect sphincter alternations related to LS.
- LS has to be more limited in female patients because they have, anatomically, a shorter anal canal. Recurrence rate of LS is lower than 6%; two authors report relapsing in 11% in longer follow-up.
- Sphincterotomy up to the dentate line provided a faster and definitive healing within the time limits of this study, but it was associated with a significant alteration in anal continence.
- In turn, sphincterotomy up to the fissure apex was free of significant disturbances of incontinence, but its healing effect was slower and it was prone to an insignificantly higher rate of treatment failure.
- Various alternative types of lateral sphincterotomy have been proposed aimed at minimising the risk of postoperative incontinence.

Management of Concomitant Anal Lesions

Concerning the management of concomitant anal lesions, such as fibrous polyps and hypertrophied anal papillae, a recent prospective randomised study reported a better outcome in those patients whose anal lesions were excised at the time of LS.

Management of Recurrent Anal Fissure

Several options exist for the management of recurrent anal fissure after LS:

- Conservative measures alone may be successful.
- In women, 0.2% nifedipine cream or BT injections may provide healing.
- In refractory cases a contralateral sphincterotomy or mucosal advancement flap or anoplasty may be indicated.
- LS for anal fissure combined with other anorectal procedures does not increase the rate of postoperative complications and, in particular, incontinence.

Y-V Anal Advancement Flap

- Y-V anal advancement flap (AF) has been proposed for recurrent chronic anal fissure previously treated with LS.
- AF can be used for very symptomatic fissures in multiparous and postdelivery women with low anal resting pressure.
- The median healing time is 4 months, without decrease in anal pressure.
- AF may be offered to those patients whose anal canal pressures are not increased and, therefore, do not need a sphincterotomy which might well cause postoperative incontinence.

Summary of Surgical Treatment

Surgical management is still a correct way to approach chronic anal fissure. According to the literature we may propose:

- Manual anal dilatation, or anal stretch, should be to abandoned because of the high rate of incontinence.
- Posterior sphincterotomy has to be reserved for those patients in whom fissure is associated with posterior intersphincteric abscess or fistula.
- Lateral sphincterotomy is the gold standard operation, and it can be offered as the first choice to patients with chronic anal fissure, provided that they have anal spasm.
- The length of the division of the internal anal sphincter may be "tailored" on the basis of preoperative anal manometry and fissure size, in order to prevent postoperative incontinence, particularly in women, the elderly and patients with previous anal surgery.
- The anal advancement flap could be an alternative procedure in recurrent fissure for those patients who underwent a previous sphincterotomy or for those patients with a primary fissure who do not present with anal spasm.

Acknowledgements. The authors wish to thank C. De Bono, M. Fiorino, C. Miliacca and M. Spyrou for their contribution to the preparation of the manuscript.

Suggested Reading

1. Abcarian H (1980) Surgical correction of chronic anal fissure: results of lateral internal sphincterotomy versus fissurectomy-midline sphincterotomy. Dis Colon Rectum 23:31–36
2. Bove A, Balzano A, Perrotti P, Antropoli C, Lombardi G, Pucciani F (2004) Different anal pressure profiles in patients with anal fissure. Tech Coloproctol 8:151–157
3. Eisenhammer S (1951) The surgical correction of chronic anal (sphincteric) contracture. S Afr Med J 25:486–489
4. Evans J, Luck A, Hewett P (2001) Glyceryl trinitrate vs. lateral sphincterotomy for chronic anal fissure: prospective randomized trial. Dis Colon Rectum 44:93–97
5. Goligher JC (1975) Surgery of the anus, rectum and colon, 3rd edn. Bailliere and Tindall, London
6. Gupta PJ, Kalaskar S (2003) Removal of hypertrophied anal papillae and fibrous anal polyps increases patient satisfaction after anal fissure surgery. Tech Coloproctol 7:155–158
7. Jensen SL (1987) Maintenance therapy with unprocessed bran in the prevention of acute anal fissure recurrence. J R Soc Med 80:296–298
8. Jost WH (1997) One hundred cases of anal fissure treated with botulinum toxin. Early and long-term results. Dis Colon Rectum 40:1029–1032
9. Klosterhalfen B, Vogel P, Rixen H, Mittermayer C (1989) Topography of the inferior rectal artery: a possible cause of chronic, primary anal fissure. Dis Colon Rectum 32:43–52
10. Lindsey I, Jones OM, Cunningham C, Mortensen NJ (2004) Chronic anal fissure. Br J Surg 91:270–279
11. Lund JN, Scholefield JH (1997) A randomized, prospective, double-blind, placebo-controlled trial of glyceryl trinitrate ointment in the treatment of anal fissure. Lancet 349:11–14
12. McDonald, Driscoll AM, Nicholls RJ (1983) The anal dilator in the conservative management of acute anal fissures. Br J Surg 70:25–26
13. Nelson RL (1999) Meta-analysis of operative techniques for fissure-in-ano. Dis Colon Rectum 42:1424–1431
14. Nelson R (2004) Operative procedure for fissure-in-ano. Cochrane Colorectal Cancer Group. Cochrane Database of Systematic Reviews, January 2004
15. Nelson R (2004) A systematic review of medical therapy for anal fissure. Dis Colon Rectum 47:422–431
16. Orsay C, Rakinic J, Perry WB et al (2004) Practice parameters for the management of anal fissure (revised). Dis Colon Rectum 47:2003–2007
17. Renzi A, Brusciano L, Pescatori M et al (2005) Pneumatic balloon dilatation for chronic anal fissure: a prospective, clinical, endosonographic, and manometric study. Dis Colon Rectum 48:121–126
18. Schouten WR, Auwerda JJA (1994) Relationship between anal pressure and anoderm blood flow. The vascular pathogenesis of anal fissure. Dis Colon Rectum 37:664–669
19. Zbar AP, Aslam M, Allgar V (2000) Faecal incontinence after internal sphincterotomy for anal fissure. Tech Coloproctol 4:25–28
20. Zbar AP, Pescatori M (2004) Functional outcome following lateral internal anal sphincterotomy for chronic anal fissure. Colorect Dis 6:210–211
21. Zutshi M, Hull TL, Casillas-Romero S, Trzoinski R, Bast JF (2004) Incontinence after a lateral internal sphincterotomy: are we underestimating it? Dis Colon Rectum 47:599

4.3 Abscess, Fistula

W.R. SCHOUTEN

4.3.1 Introduction

- A perianal abscess, not related to Crohn's disease, originates in one of the anal glands. These glands are located in the subepithelial layer of the anal canal at the level of the dentate line. The duct of each gland ends in one of Morgagni's crypts. Obstruction of a duct, caused by faecal material, foreign bodies or trauma, may result in stasis and infection.
- Since the internal anal sphincter is a competent barrier against bacterial contamination, chronic infection of an anal gland can only result in a perianal abscess when this gland extends beyond the internal anal sphincter into the intersphincteric plane. It has been shown that 50% of the anal glands penetrate into this plane.
- Usually an intersphincteric abscess will follow one of two avenues of extension. It can either pursue a course downwards in the intersphincteric plane or it overcomes the barrier of the external anal sphincter, thereby penetrating the ischiorectal fossa. Consequently, a perianal abscess located at the anal verge has tracked downwards in the intersphincteric plane, whereas an abscess located at a further distance from the anus has pursued a transsphincteric course.
- Perianal abscesses must be adequately drained. The sooner this is performed, the better. In most cases a small incision with or without contra incision is insufficient. Removing an ellipse of skin above the abscess or a cruciate incision are more appropriate.
- There is little, if any, use for antibiotics. Only in patients with rheumatic or acquired valvular heart disease and in those who are immunosuppressed is adjunctive antibiotic therapy indicated.
- In about half of all cases anal suppuration will recur after adequate drainage either as a recurrent abscess or as a perianal fistula.

4.3.2 Classification

Parks et al. identified four types of perianal fistulas: intersphincteric, transsphincteric, suprasphincteric and extrasphincteric. These different types of fistulas are depicted in Figs. 4.3.1 and 4.3.2.

- An intersphincteric fistula runs downwards between the internal and external anal sphincter. The external opening of an intersphinteric fistula is located near the anal verge.
- A transsphincteric fistula extends from the intersphincteric plane through the external anal sphincter into the ischiorectal fossa. The external opening of a transsphincteric fistula is almost always located at a distance of several centimetres from the anal verge.
- A suprasphincteric fistula extends upwards between the two sphincters and bends around the puborectalis muscle. Then the fistulous track pursues a downward course through the pelvic floor and the ischiorectal fossa.
- An extrasphincteric fistula penetrates the external anal sphincter and branches into two tracks: one extending cephalad (passing through the pelvic floor and finally ending in the rectum) and one extending caudad through the ischiorectal fossa.

Although this classification does not take circumferential extensions into account, it is widely used. One reason is the relative simplicity. Another reason is that this classification relates the course of the fistulous track to the anal sphincters, which is relevant for the choice of surgical treatment.

4.3.3 Epidemiology

- Most patients presenting with a perianal fistula are 30–50 years old. Perianal fistulas are rare among patients younger than 20 or older than 60 years.

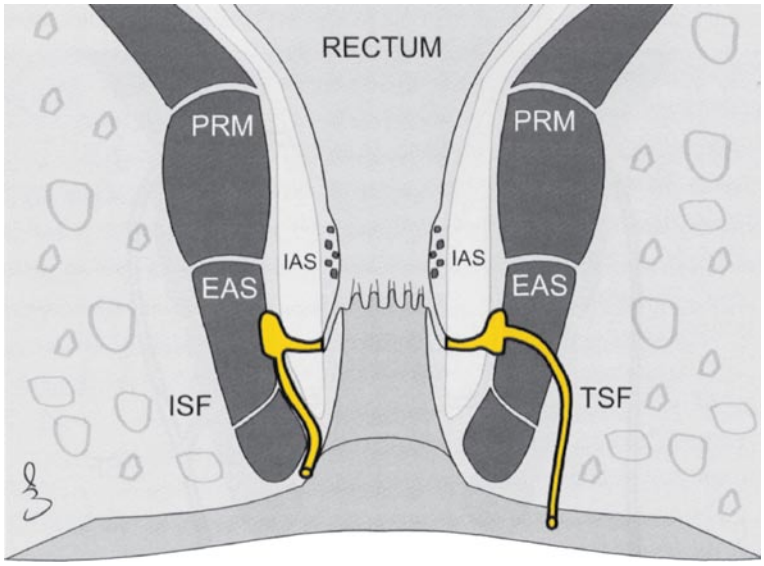


Fig. 4.3.1 Schematic drawing of the course of an intersphincteric (*ISF*) and a transsphincteric (*TSF*) fistula. *EAS* external anal sphincter, *IAS* internal anal sphincter, *PRM* puborectal muscle

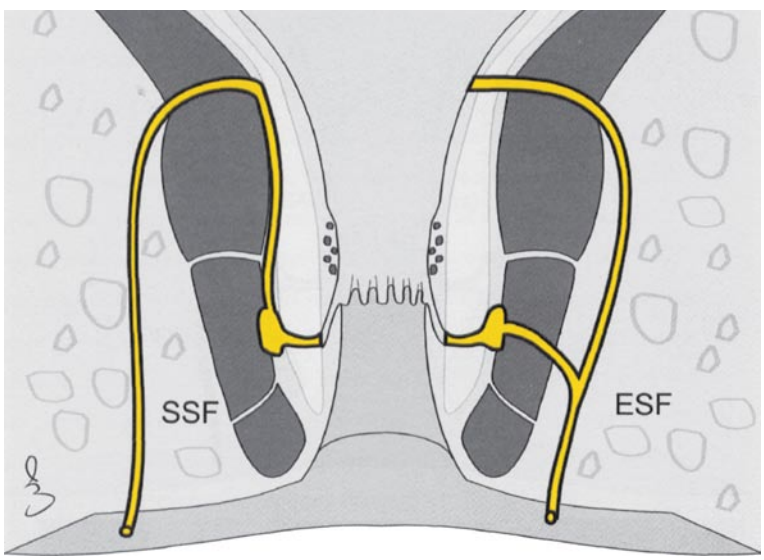


Fig. 4.3.2 Schematic drawing of the course of an extrasphincteric (*ESF*) and a suprasphincteric (*SSF*) fistula

- Men are five times more likely to develop a perianal fistula than women. This is probably due to a higher number of anal glands in men.
- Sainio reported that the incidence of perianal fistulas is about 12.3% per 100,000 men and 5.6% per 100,000 women.

4.3.4 Assessment

Localisation of the external opening in most cases enables the classification of perianal fistulas. The external opening of an intersphincteric fistula is almost always located near the anal verge, whereas the distance between the external opening of a transsphincteric fistula and the anal verge is several centimetres or more. In the past Goodsall and Miles described several aspects regarding the relation between the external and the internal opening of perianal fistulas. For many years Goodsall's rule has been used in predicting the course of fistulous tracts. Recently the accuracy of this rule has been questioned. Cirocco and Reilly conducted a prospective study in a consecutive series of 216 patients with a perianal fistula. Goodsall's rule was found to be accurate in only 50% of these patients.

4.3.4.1 Digital Examination

- Although advocated by some authors, it is questionable whether the internal opening of a perianal fistula can be localised accurately by digital examination. This method of examination is still important, however, since a tender palpable mass in the pelvis may reveal a supralevator abscess. It also provides some information regarding the quality of the anal sphincters by assessing sphincter tone.
- In some cases the course of a fistulous tract can be assessed by introducing a probe into the external opening. Probing, however, is not advocated on an outpatient basis, since probing can be painful. Furthermore there is a considerable risk of creating a false passage into the anal canal or into the rectum.
- It has been suggested that injection of a diluted solution of methylene blue into the external opening enables the identification of the internal opening of a perianal fistula. A major drawback of this technique is staining of the surrounding tissues. An alternative is hydrogen peroxide, which does not stain the operative field.

4.3.4.2 Fistulography

For many years fistulography was the only imaging technique for the preoperative assessment of perianal fistulas, including the localisation of their internal opening. However, data regarding its accuracy are scarce. In a retrospective study Kuijpers and Schulpen observed that fistulography identified the location of the internal opening in only 29% of their patients. The outcome of fistulography was false-negative and false-positive in 64% and 8% of the cases, respectively. Ahlbäck and co-workers utilised a specially designed balloon catheter to demarcate the upper and lower boundary of the anal canal during fistulography. With the help of this balloon catheter, they were able to localise the internal opening correctly in 72% of their patients. The outcome was false-negative and false-positive in 10% and 18% of the cases, respectively. Based on these limited and rather conflicting data it is impossible to assess the exact role of fistulography in the preoperative imaging of perianal fistulas.

4.3.4.3 Endosonography and Magnetic Resonance Imaging

- Nowadays fistulography has been surpassed by endosonography and magnetic resonance imaging (MRI). Advantages of both techniques over fistulography are the direct visualisation of the fistulous track and the imaging of the anal sphincters.
- Endosonography is performed with a 10-MHz mechanically rotated transducer to give a 360° axial image. Installation of hydrogen peroxide improves the accuracy of the technique.
- Initially, MRI was performed with a body coil. Nowadays, intraluminal coils and standard external phased array coils are used in order to increase the accuracy. In addition, fat suppression sequences are advocated to enhance fistula identification.
- Although it has been reported that endoanal ultrasound (EAUS) is very accurate for the detection of the primary fistulous track, most reports show an accuracy rate varying between 50% and 70%.
- In 1993 Cheong and co-workers found that installation of hydrogen peroxide through the external opening of the fistula enhances the identification of the primary track. This finding has been confirmed by others. In patients in whom the external opening is closed temporarily, is enhancement of EAUS with hydrogen peroxide not possible.

MRI is a useful tool for the identification of primary fistulous tracks. In the early 1990s MRI was performed with a body coil or external surface coil. After the introduction of endoanal and external coils with high spatial resolution, it was debated which modality yields the best imaging results. Based on a recent study using phased array MRI, Beets-Tan and co-workers reported that the sensitivity and specificity for detecting primary fistulous tracks is 100% and 86%, respectively. According to Beckingham and colleagues, MRI can be enhanced by intravenous administration of gadolinium. With this contrast-enhanced technique they obtained a sensitivity and specificity for the correct prediction of a primary track of 97% and 100%, respectively. These data indicate that the accuracy of the modern external coils is comparable to that of endoanal coils. Examples of MRI of fistulous tracks are shown in Figs. 4.3.3–4.3.5.

The question is whether preoperative decision making and last but not least the surgical procedure itself, are optimised by these high accuracy rates. It is quite clear that MRI has no clinical benefit when it depicts only lesions that are easily found by the surgeon during the operative treatment. In most studies regarding this issue, surgical exploration is considered to be the gold standard. According to some authors, however, surgical exploration is actually less accurate than MRI. Barker and colleagues, for example, reported that in 9% of their patients the fistula did not heal because tracks that were identified by endoanal MRI were not recognised during surgery. In two other studies, such an additional value of MRI could not be demonstrated. Recently, Beets-Tan and co-workers reported that MRI provides important additional information in one out of five patients with a perianal fistula, especially in patients with Crohn's disease and in those

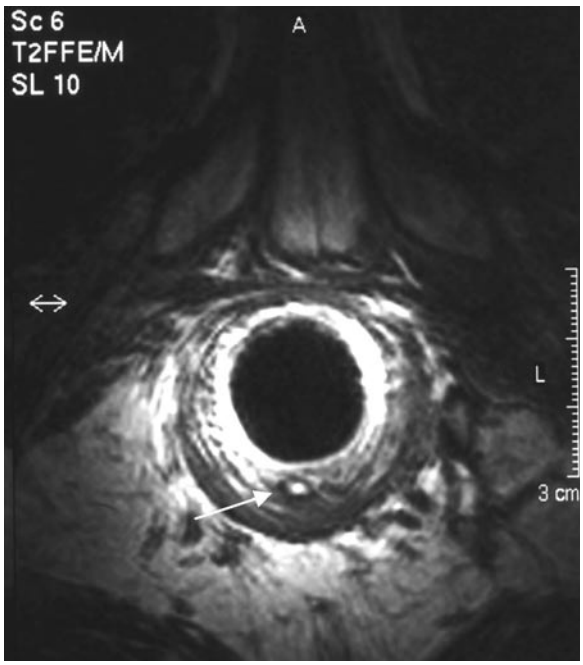


Fig. 4.3.3 Axial T2-weighted turbo spin-echo with endoanal coil reveals an intersphincteric track in the posterior midline (*arrows*)

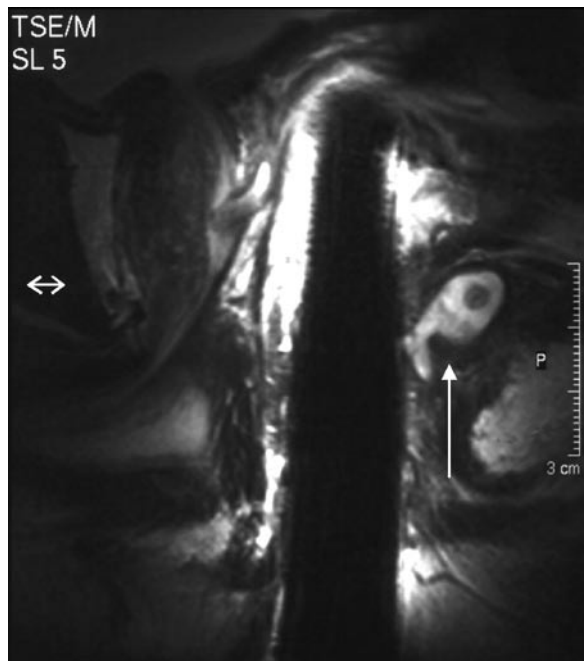
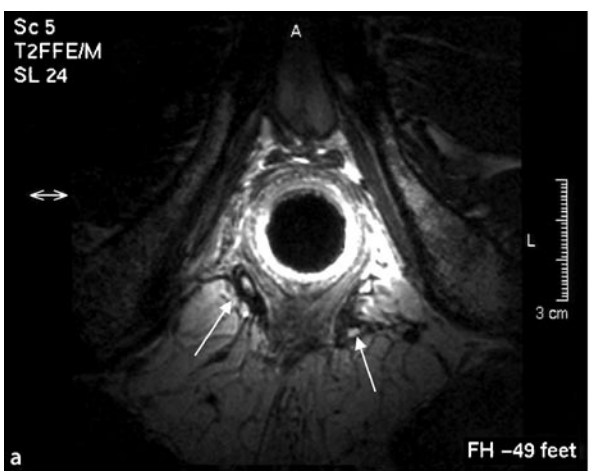


Fig. 4.3.5 Sagittal T2-weighted turbo spin-echo with endoanal coil reveals an abscess at the level of the puborectal sling in the posterior midline (*arrows*)



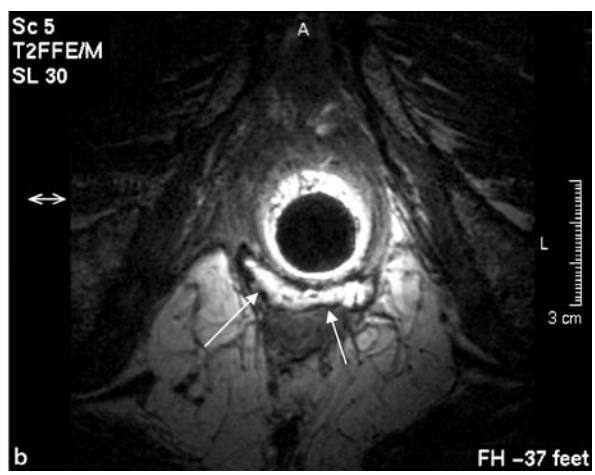


Fig. 4.3.4 **a** Axial T2-weighted turbo spin-echo with endoanal coil shows two tracks outside the external anal sphincter (*arrows*). **b** At a more proximal level these two tracks pass through the external anal sphincter. At this level both tracks connect in a horseshoe-like fashion in the intersphincteric plane (*arrows*)

with a recurrent fistula. It has been shown that tracks detected by MRI are present at re-evaluation or follow-up surgery, if they cannot be identified during the primary surgical exploration.

Despite its excellent accuracy, MRI of perianal fistulas has several drawbacks:

- It is rather expensive and time consuming.
- It cannot be performed in patients who have a metal implant or a pacemaker.
- It cannot be used in patients with claustrophobia.

Imaging with EAUS is advantageous, since it is not associated with these drawbacks. However, the disadvantages of conventional EAUS (without hydrogen peroxide) are that:

- It is less accurate than MRI.
- It is rather difficult to differentiate between a fistulous track and scar tissue. This can be a major problem, especially in patients who have undergone prior attempts at repair.
- It is less suitable for the detection of secondary tracks and for the identification of the external anal sphincter, which is necessary for correct classification of the fistula.

Until now, four studies have been conducted, comparing the accuracy of conventional EAUS to that obtained with MRI. Three of these studies clearly demonstrate that MRI provides a more sensitive tool for the preoperative classification of perianal fistulas than conventional EAUS. In contrast with this finding, Orsoni and co-workers reported EAUS to be more sensitive than MRI. This observation, however, is disputed by others, considering Orsoni's MRI technique as suboptimal.

Until now no studies have been conducted comparing MRI and hydrogen peroxide-enhanced EAUS. According to some authors conventional EAUS without hydrogen peroxide enables correct localisation of the internal opening of a fistula in more than 50% of the cases. Other investigators have found conventional EAUS to be less accurate. According to Cho et al. this poor accuracy of conventional EAUS can be enhanced by utilising a combination of several endosonographic criteria for the internal opening. Doing so, he found a sensitivity of 94% and a specificity of 87%. In our opinion, these results reflect the experience of one highly skilled endosonographer, as others have not been able to reproduce this. There is growing evidence that installation of hydrogen peroxide has an additional value for the localisation of the internal opening. Poen and co-workers were able to predict the location of the internal opening accurately in only 5% of their patients when using conventional EAUS and in 48% of their patients when using hydrogen peroxide-enhanced EAUS. MRI seems to be more accurate in depicting the internal opening of a fistula. The use of an endoluminal coil is especially advantageous because of the high spatial resolution near the coil.

4.3.5 Therapy

The ideal treatment of a perianal fistula should fulfil the following criteria: healing of the fistula in the shortest period of time with the lowest possible recurrence rate and without alteration in faecal continence. The principal objective (healing of the fistula) can be achieved either by fistulotomy (laying open of the fistula) or by fistulectomy (complete excision of the fistulous tract). In the past considerable debate existed as to whether the lay open technique or excision of the fistulous tract was the most appropriate treatment of perianal fistulas. Nowadays fistulotomy is recommended for several reasons:

- Complete excision of the fistulous tract with removal of adjacent scar tissue results in a larger wound and a wider separation of both ends of the sphincter muscles.
- The healing time is longer with fistulectomy.
- The risk of impaired continence is greater with fistulectomy.

4.3.5.1 Fistulotomy of an Intersphincteric Fistula

- During fistulotomy of an intersphincteric fistula, only the distal part of the internal anal sphincter is divided.
- Subsequent incontinence for solid stool is rare, since the external anal sphincter remains intact. However, the permanent defect in the internal anal sphincter might result in soiling, incontinence for gas or liquid stool.
- The reported incidence of these "minor" continence disturbances varies between 8% and 50%.

4.3.5.2 Fistulotomy of a Transsphincteric Fistula

- In the past it was stated that the risk of incontinence after fistulotomy of a transsphincteric fistula was kept to a minimum as long as the puborectalis muscle remained intact. However, over time, it has become clear that division of a substantial part of the external anal sphincter affects continence considerably. The reported incidence of impaired continence varies between 30% and 50%.

- Nowadays, most surgeons hesitate to perform a fistulotomy in patients with a transsphincteric fistula, except for those with a fistula passing through the lower third of the external anal sphincter.
- The management of high transsphincteric fistulas, crossing the middle or upper third of the external anal sphincter remains a surgical challenge.

4.3.5.3 Staged Cutting Seton Technique for High Transsphincteric Fistula

The staged cutting seton technique has been recommended as an alternative in the treatment of these high transsphincteric fistulas.

Technique

- After initial loose placement, the seton is tightened at 2- to 4-week intervals.
- Gradual pressure necrosis will result in slow, yet controlled division of the enclosed anal sphincters.
- As the muscle is transected, local fibrosis ensures that separation of the muscle ends is not as wide as the separation after one-stage fistulotomy. Until now, this theoretical advantage has not been confirmed by endosonographic studies.

Prognosis/Complications

The reported incidence of continence disturbances after staged cutting seton treatment varies enormously between 0% and 67%. Despite this wide variation, most reports indicate that impairment of continence occurs more frequently than expected. Based on these findings the role of the staged cutting seton technique as a valuable alternative in the treatment of high transsphincteric fistulas is doubted.

Use of a Seton as a Drain

- A seton can also be used as a drain prior to fistulotomy at a second stage.
- The seton prevents abscess formation and promotes local fibrosis. It has been suggested that this fibrosis prevents wide separation of the muscle ends at the time of the fistulotomy.
- Studies regarding the impact of this technique on faecal continence are scarce. Based on the data reported by van Tets et al. and those reported by García-Aguilar and colleagues, it seems unlikely that the staged seton fistulotomy has any advantage over the cutting seton technique in preventing impairment of faecal continence.

4.3.5.4 Fibrin Glue for High Transsphincteric Fistula

Recently the use of fibrin glue has gained some popularity in the treatment of high transsphincteric fistulas. According to those who advocate the use of fibrin glue, this treatment modality has several advantages. Fibrin glue enables the obliteration of the fistulous tract without sphincter damage and without subsequent impairment of faecal continence. Studies regarding the use of fibrin glue are scarce and the data, reported so far, are rather conflicting. Further studies are warranted to elucidate the exact role of fibrin glue in the treatment of high transsphincteric fistulas.

4.3.5.5 Transanal Mucosal Advancement Flap Repair for High Transsphincteric Fistula

In 1902 Noble was the first to describe transanal mucosal advancement flap repair of rectovaginal fistulas. Ten years later Elting applied this technique in patients with a transsphincteric fistula. In 1948 Laird described a modification by adding fibres of the internal anal sphincter to the flap of mucosa and submucosa. Since the early 1980s this type of flap repair has gained more popularity in the treatment of high transsphincteric fistulas. Those who propose the use of this repair argue that this procedure ensures obliteration of the internal opening and thereby healing of the fistula with preservation of the entire external anal sphincter.

Technique

- A transanal mucosal advancement flap repair is performed with the patient in the prone jack-knife position.
- The fistulous track is excised from the external opening to the external anal sphincter.
- Using an anal retractor, a flap consisting of mucosa, submucosa and some fibres of the internal anal sphincter is raised from the level of the dentate line and mobilised over a distance of 4–6 cm proximally.
- Care is taken to design the flap in such a way that the base of the flap is about twice the width of its apex.
- The crypt-bearing tissue around the internal opening, as well as the overlying anoderm, is then excised.
- The remaining fistulous tract is cored out of the sphincters.
- The defect in the internal anal sphincter is closed with absorbable sutures.
- After excision of its apex, the flap is advanced and sutured to the neodentate line with absorbable sutures.

Prognosis/Complications

Initially, the reported healing rates varied between 84% and 100%. Recently, however, less favourable results have been reported. It is still unclear which factors affect the outcome after transanal advancement flap repair. In two studies higher recurrence rates were noted among patients who had undergone previous attempts at repair. Another study revealed that smoking also affects the outcome of this type of repair. In this study the observed healing rate among patients who smoked was 59%, whereas a healing rate of 79% was found in patients who did not smoke. Based on the studies conducted so far, it is still unclear whether the transanal advancement flap repair affects continence or not. Aguilar and co-workers observed impairment of continence in 10% of their patients, whereas Wedell and associates reported that none of their patients experienced deterioration of faecal continence. Schouten et al. observed continence disturbances in 35% of their patients after the flap procedure. According to these authors this rather high incidence might be due to overstretching of the sphincters by the Parks' retractor. This retractor was utilised in all their patients for 15–20 min, in order to gain exposure. They suggest that the use of a ring retractor with multiple skin hooks on elastic bands minimises the risk of sphincter damage and subsequent impairment of continence.

4.3.5.6 Anocutaneous Advancement Flap Repair for High Transsphincteric Fistula

In 1996 Del Pino and co-workers described the anocutaneous advancement flap repair of high transsphincteric fistulas. They reported a small number of patients with promising results. According to these authors, this procedure does not result in anatomical alteration of the anal canal, so all other operative choices are still feasible.

Technique

- The anocutaneous advancement flap repair is performed with the patient in the prone jack-knife position.
- The internal opening of the fistula is exposed using an anal retractor.
- The crypt-bearing tissue around the internal opening, as well as the overlying anoderm, is excised.
- The fistulous tract is excised from the external opening to the external anal sphincter.
- The tract running through the sphincters is curetted.
- The defect in the internal anal sphincter is closed with absorbable sutures.
- An (inverted) U-shaped flap including perianal skin and fat is created, taking care not to undermine the flap in order to prevent ischaemia.
- The base of the flap should be approximately twice the width of its apex.
- The flap is advanced into the anal canal and sutured to the mucosa and underlying internal anal sphincter in a single layer, proximal to the closed internal opening, using interrupted, absorbable sutures.
- The perianal wound is left open.

Prognosis/Complications

This type of flap repair can be performed without deep intra-anal dissection. According to some authors, this is a major advantage, resulting in less sphincter damage. The healing rates, reported so far, seem to be comparable with those observed after transanal mucosal advancement flap repair. In a recent study, however, Zimmerman and colleagues observed a healing rate of only 49%. In patients who had undergone no, or only one previous attempt at repair, the healing rate after the anocutaneous advancement flap repair was similar to that reported by others. In addition, these authors reported deterioration of faecal continence in 30% of their patients.

Suggested Reading

1. Aguilar PS, Plasencia G, Hardy TG, Hartman RF, Stewart WRC (1985) Mucosal advancement in the treatment of anal fistula. Dis Colon Rectum 28:496–498
2. Ahlbäck S, Holmström B, Syk B (1974) Anal fistulography. Acta Radiol 15:282–287
3. Barker PG, Lunniss PJ, Armstrong P, et al (1994) Magnetic resonance imaging of fistula-in-ano: technique, interpretation and accuracy. Clin Radiol 49:7–13
4. Beckingham IJ, Spencer JA, Ward J, Dyke GW, Adams C, Ambrose NS (1996) Prospective evaluation of dynamic contrast enhanced magnetic resonance imaging in the evaluation of fistula in ano. Br J Surg 83:1396–1398
5. Beets-Tan RG, Beets GL, van der Hoop AG, et al (2001) Preoperative MR imaging of anal fistulas: does it really help the surgeon? Radiology 218:75–84
6. Belliveau P, Thomson JP, Parks AG (1983) Fistula in ano: a manometric study. Dis Colon Rectum 26:152–154
7. Cataldo PA, Senagore A, Luchtefeld MA (1993) Intrarectal ultrasound in the evaluation of perirectal abscesses. Dis Colon Rectum 36:554–558
8. Cheong DM, Nogueras JJ, Wexner SD, Jagelman DG (1993) Anal endosonography for recurrent anal fistulas: image enhancement with hydrogen peroxide. Dis Colon Rectum 36:1158–1160

9. Cho DY (1999) Endosonographic criteria for an internal opening of fistula-in-ano. Dis Colon Rectum 42:515–518
10. Choen S, Burnett S, Bartram CI, et al (1991) Comparison between anal endosonography and digital examination in the evaluation of anal fistulae. Br J Surg 78:445–447
11. Cirocco WC, Reilly JC (1992) Challenging the predictive accuracy of Goodsall's rule for anal fistulas. Dis Colon Rectum 35:537–542
12. Deen KI, Williams JG, Hutchinson R, Keighley M, Kumar D (1994) Fistulas in ano: endoanal ultrasonographic assessment assists decision making for surgery. Gut 35:391–394
13. Del Pino A, Nelson RL, Pearl RK, Abcarian H (1996) Island flap anoplasty for treatment of transsphincteric fistula-in-ano. Dis Colon Rectum 39:224–226
14. deSouza NM, Gilderdale DJ, Coutts GA, Puni R, Steiner RE (1998) MRI of fistulo-in-ano: a comparison of endoanal coil with external phased array coil techniques. J Comput Assist Tomogr 22:357–363
15. Elting AW (1912) The treatment of fistula in ano with special reference to the Whitehead operation. Ann Surg 56:744–752
16. García-Aguilar J, Belmonte C, Wong WD, Goldberg SM, Madoff RD (1996) Anal fistula surgery: factors associated with recurrence and incontinence. Dis Colon Rectum 39:723–729
17. García-Aguilar J, Belmonte C, Wong D, Goldberg SM, Madoff RD (1998) Cutting seton versus two-stage seton fistulotomy in the surgical management of high anal fistula. Br J Surg 85:243–245
18. Goodsall DH, Miles WE (1900) Diseases of the anus and rectum, part I. Longmans, Green and Co, London, p 121
19. Graf D, Aeberhard P (1995) Imaging of perianal and perirectal abscesses and fistulae using intraluminal ultrasound diagnosis. Swiss Surg 6:294–297
20. Halligan S (1998) Review: imaging fistula-in ano. Clin Radiol 53:85–95
21. Hussain SM, Stoker J, Schouten WR, Hop WCJ, Laméris JS (1996) Fistulo-in-ano: endoanal sonography vs endoanal MR imaging in classification. Radiology 200:475–481
22. Joo JS, Son KS, Lee HS, Lee SK (1998) Preoperative evaluation of anal fistula by endorectal ultrasonography. Dis Colon Rectum 41:A46–A47
23. Jun SH, Choi GS (1999) Anocutaneous advancement flap closure of high anal fistulas. Br J Surg 86:490–492
24. Kodner IJ, Mazor A, Shemesh EI, Fry RD, Fleshman JW, Birnbaum EH (1993) Endorectal advancement flap repair of rectovaginal and other complicated anorectal fistulas. Surgery 114:682–690
25. Kohler A, Athanasiadis S (1996) Anodermal advancement flap-plasty as alternative treatment method to endorectal closure techniques in therapy of high anal fistulas. A prospective study of 31 patients (in German). Chirurg 67:1244–1250
26. Kuijpers HC, Schulpen T (1985) Fistulography for fistula-in-ano: is it useful? Dis Colon Rectum 28:103–104
27. Laird DR (1948) Procedures used in the treatment of complicated fistulas. Am J Surg 76:701–708
28. Law PJ, Talbot RW, Bartram CI, Northover J (1989) Anal endosonography in the evaluation of perianal sepsis and fistula in ano. Br J Surg 76:752–755
29. Lindsey I, Humphreys M, George D, Mortensen NJMC (2002) The role of ultrasound in the management of anal fistulas. Colorectal Dis 4:118–122
30. Lunniss PJ, Barker PG, Sultan AH, Armstrong P, Reznek RH, Bartram CI, Cottam KS, Phillips RK (1994) Magnetic resonance imaging of fistulo-in ano. Dis Colon Rectum 37:708–718
31. Lunniss PJ, Kamm MA, Phillips RKS (1994) Factors affecting continence after surgery for anal fistula. Br J Surg 81:1382–1385
32. Maier AG, Funovics MA, Kreuzer SH et al (2001) Evaluation of perianal sepsis: comparison of anal endosonography and magnetic resonance imaging. J Magn Reson Imaging 14:254–260
33. Navarro A, Rius J, Collera P, Garcia MI, Marco C (1998) Anal fistulas: results of ultrasonographic studies. Dis Colon Rectum 41:A57
34. Nelson RL, Cintron J, Abcarian H (2000) Dermal island flap anoplasty for transsphincteric fistula in ano. Dis Colon Rectum 43:681–684
35. Noble GH (1909) A new operation for complete laceration of the perineum designed for the purpose of eliminating danger of infection from the rectum. Trans Am Gynecol Soc 27:357–363
36. Oh C (1983) Management of high recurrent anal fistula. Surgery 93:330–332
37. Orsoni P, Barthet M, Portier F, Panuel M, Desjeux A, Grimaud JC (1999) Prospective comparison of endosonography, magnetic resonance imaging and surgical findings in anorectal fistula and abscess complicating Crohn's disease. Br J Surg 86:360–364
38. Ozuner G, Hull TL, Cartmill J, Fazio VW (1996) Long-term analysis of the use of transanal rectal advancement flaps for complicated anorectal/vaginal fistulas. Dis Colon Rectum 39:10–14
39. Parks AG, Gordon PH, Hardcastle JD (1976) A classification of fistula in ano. Br J Surg 63:1–12
40. Pearl RK, Andrews JR, Orsay CP, Weisman RI, Prasad ML, Nelson RL, Cintron JR, Abcarian H (1993) Role of seton in the management of anorectal fistulas. Dis Colon Rectum 36:573–577
41. Poen AC, Felt-Bersma RJF, Eijsbouts QAJ, Cuesta MA, Meuwissen SGM (1998) Hydrogen peroxide enhanced transanal ultrasound in the assessment of fistula-in-ano. Dis Colon Rectum 41:1147–1152

42. Ratto C, Gentile E, Merico M et al (2000) How can the assessment of fistula-in ano be improved? Dis Colon Rectum 43:1375–1382
43. Robertson WG, Mangione JS (1998) Cutaneous advancement flap closure: alternative method for treatment of complicated anal fistulas. Dis Colon Rectum 41:884–886
44. Sainio P (1984) Fistula in ano in a defined population. Incidence and epidemiologic aspects. Ann Chir Gynaecol 73:219–224
45. Scholefield JH, Berry DP, Armitage NC, Wastie ML (1997) Magnetic resonance imaging in the management of fistula in ano. Int J Colorectal Dis 12:276–279
46. Schouten WR, van Vroonhoven TJ (1991) Treatment of anorectal abscess with or without primary fistulectomy. Results of a prospective randomized trial. Dis Colon Rectum 34:60–63
47. Schouten WR, Zimmerman DDE, Briel JW (1999) Transanal advancement flap repair of transsphincteric fistulas. Dis Colon Rectum 42:1419–1422
48. Spencer JA, Chapple K, Wilson D, Ward J, Windsor ACJ, Ambrose NS (1998) Outcome after surgery for perianal fistula: predictive value of MR imaging. AJR 171:403–406
49. Stoker J, Hussain SM, van Kempen D, Elevelt AJ, Laméris JS (1996) Endoanal coil in MR imaging of anal fistulas. AJR 166:360–362
50. Van Tets WF, Kuijpers HC (1994) Continence disorders after fistulotomy. Dis Colon Rectum 37:1194–1197
51. Van Tets WF, Kuijpers JH (1995) Seton treatment of perianal fistula with high anal or rectal opening. Br J Surg 82:895–897
52. Wedell J, Meier zu Eissen P, Banzhaf G, Kleine L (1987) Sliding flap advancement for the treatment of high level fistulae. Br J Surg 74:390–391
53. Zbar AP, deSouza NM (1999) Prospective comparison of endosonography, magnetic resonance imaging and surgical findings in anorectal fistula and abscess complicating Crohn's disease. Br J Surg 86:1093–1094
54. Zimmerman DDE, Briel JW, Gosselink MP, Schouten WR (2001) Anocutaneous advancement flap repair of transsphincteric fistulas. Dis Colon Rectum 44:1474–1480
55. Zimmerman DDE, Delemarre JBVM, Gosselink MP, Hop WCJ, Briel JW, Schouten WR (2003) Smoking affects the outcome of transanal advancement flap repair of transsphincteric fistulas. Br J Surg 90:351–354

Dermatology

5.1 Pruritus Ani

SYLVIA PROSKE, WOLFGANG HARTSCHUH

5.1.1 Aetiology

- Pruritus ani is not a single disease by itself but an accompanying symptom of a number of dermatological, proctological and microbiological disorders. Therefore, it has been divided into acute and chronic pruritus as well as into the two subtypes: secondary and idiopathic.
- Secondary pruritus is diagnosed when an underlying cause can be identified.
- In idiopathic pruritus the aetiology remains unclear. In these cases a psychological aetiology is often inferred.
- Comparable to chronic pain, chronic pruritus may lead to physical and psychological exhaustion.
- The main diagnosis is anal eczema which must be differentiated into atopic, irritant and allergic contact dermatitis. A history of atopy may be relevant since 25% of anal eczemas are atopic and many patients with atopic dermatitis can experience disproportionate pruritus to all causes. In these patients even small amounts of faecal contamination or mucus discharge secondary to haemorrhoids may be responsible for anal itching.
- Obese patients and patients with a funnel anus are at increased risk for irritant contact dermatitis with sweat and moisture as other contributing factors. Heat and sitting probably exacerbate the problem.
- A local reaction to contact with faeces, especially loose faeces, has been implicated. There is, however, no evidence that the microbial content of soft faeces is different. In most cases fungal or yeast organisms are not the primary cause of pruritus ani except in patients with extensive intestinal candidiasis .
- Coffee, wine, beer and certain foods, citrus fruits or spices, may aggravate pruritus by making the stool more acidic or due to capsaicin contained in peppers.
- Pruritus may occur as a severe and therapy-refractory symptom of various underlying dermatological and systemic diseases.
- Malignancy must be ruled out (see Table 5.1.1).
- Chronic, severe pruritus induces chronic rubbing, scratching, or pinching which leads to secondary skin lesions such as erosions, excoriations, hyperpigmentation or hypopigmentation, and lichenification.
- Itching results from the irritation of free nerve endings of cutaneous sensory C-nerve fibres at the epidermal-dermal junction, identified as slow-conducting unmyelinated C-polymodal neurons. Recent studies have shown that there is a distinct neuronal pathway for itch, with its own mediators, spinal neurons and cortical areas.
- Albeit being distinct, there are complex interactions between pain and itch: The inhibition of itch by pain can explain the antipruritic effect of scratching. The inhibition of pain processing can generate itch. Chemical itch mediators such as histamine, serotonin, prostaglandins, acetylcholine, neuropeptides (substance P) or bradykinin act pruritogenically on C-fibres.

5.1.2 Incidence

Anal itching often is the main symptom that leads the patient to a proctologist. It occurs in approximately 1–3% of the population with a male-to-female ratio from 2:1 to 4:1 in different studies and an average age of around 40–50 years.

5.1.3 Differential Diagnosis

In Table 5.1.1 common causes of acute and chronic anogenital pruritus are listed.

5.1.4 Diagnostic Procedures

- History (onset of the pruritus, intermittent or persistent, history of defaecation with bowel movements, stool consistency, frequency, blood, pain, atopic diathesis, etc.), use of haemorrhoid creams or ointments, different medications.

Table 5.1.1 Common causes of acute and chronic anogenital pruritus

Inflammatory dermatoses
Atopic anal eczema
Perianal irritant contact dermatitis
Perianal allergic contact dermatitis
Seborrhoeic dermatitis
Psoriasis
Lichen sclerosus
Lichen ruber planus
Porokeratosis of the natal clefts
Bacterial diseases
Erythrasma
Perianal streptococcal dermatitis
Fungal diseases
Candidiasis
Tinea perianalis
Infestation
Scabies
Pinworms
Hereditary acantholytic diseases
Darier's disease, Hailey-Hailey disease
Viral diseases
Herpes simplex infection
Human papillomavirus infections
Malignancies
Extramammary Paget's disease
Bowen's disease
Squamous cell carcinoma of the anal margin
Basal cell carcinoma
Langerhans cell histiocytosis
Hodgkin's disease
Pruritus caused by internal diseases
Uraemia
Cholestasis
Diabetes mellitus
Idiopathic pruritus

- Inspection of the anal region (erythema, erosions, excoriations, lichenification, fissuring, large anal tags, fistula or anal fissures).
- Complete proctological examination including rectal-digital examination, proctoscopy, sigmoidoscopy and, when indicated, colonoscopy.
- Examination of the skin and mucous membranes searching for an underlying mucocutaneous disorder. Generalised dermatoses such as seborrhoeic dermatitis, psoriasis and atopic dermatitis may present with perianal features.
- Skin biopsies in altered skin, resistant to treatment.
- Patch testing to rule out perianal allergic contact dermatitis.
- Wood light examination to rule out erythrasma.
- Tape test to demonstrate pinworms.
- Differential blood count, checking for eosinophilia.
- Bacteriological and fungal cultures (not in routine diagnostics!)

5.1.5 Therapy

5.1.5.1 Conservative Treatment

The first priority is the identification and correction of any underlying dermatosis or irritation. Once these have been excluded, both general and specific measures must be initiated.

General measures for relieving symptoms of pruritus are aimed at limiting exacerbating factors such as sweat, occlusion and improper cleansing habits:

- Limiting constipation and diarrhoea appropriately with either a high-fibre diet or stool softeners
- Reduction of excessive cleaning and use of toilet paper; washing with clear water
- Avoidance of tight-fitting pants (improved air circulation)
- During menses, tampons as better alternative to pads
- Choice of underwear: comfortable absorptive cotton underwear preferred to synthetic materials

Topical treatment with an antipruritic effect can include:

- Cooling agents: 3% menthol in basic lotion
- 3% Urea in basic lotion
- 2% Polidocanol in basic lotion
- Topical steroids (hydrocortisone 0.1% for short-term treatment)
- Calcineurin inhibitors (pimecrolimus, tacrolimus)
- Camphor gel
- UVA or UVA radiation
- Capsaicin cream 0.025% (natural alkaloid derived from plants of the Solanaceae)
- Cannabinoid agonists

Systemic treatment may include:

- Antihistamines
- Internal steroids
- Oral opioid receptor antagonist naltrexone
- In addition, bedtime sedation in order to provide a reprieve from scratching

5.1.5.2 Surgical Treatment

Surgery to "tidy up" the anus (anal tags) is not helpful. Attempts to treat intractable idiopathic pruritus ani may include:

- Perianal injection of anaesthetic agents
- Surgical disruption of the sensory nerve supply to the perianal area
- Cryotherapy
- Intradermal methylene blue injection (to destroy sensory nerve endings)

5.1.6 Special Considerations

Prognostic considerations of anal itch depend very much on the underlying disease. Management of acute anogenital pruritus depends upon the clinician identifying the aetiology of the symptoms. However, when the aetiology is clarified, appropriate therapy should lead to prompt resolution of symptoms. Chronic pruritus ani can be very recalcitrant. In cases of severe pruritus ani sine materia therapy by a psychiatrist can be necessary.

Suggested Reading

1. Botterill ID, Sagar PM (2002) Intra-dermal methylene blue, hydrocortisone and lignocaine for chronic, intractable pruritus ani. Colorectal Dis 4:144–146
2. Harrington CI, Lewis FM, McDonagh AJ, Gawkrodger DJ (1992) Dermatological causes of pruritus ani. BMJ 305:955
3. Heard S (2004) Pruritus ani. Aust Fam Physician 33:511–513
4. Laurent A, Boucharlat J, Bosson JL, Derry A, Imbert R (1997) Psychological assessment of patients with idiopathic pruritus ani. Psychother Psychosom 66:163–166
5. Staender S, Steinhoff, M, Schmelz M, Weisshaar E Metze D, Luger T (2003) Neurophysiology of pruritus: cutaneous elicitation of itch. Arch Dermatol 139:1463–1470
6. Weichert GE (2004) An approach to the treatment of anogenital pruritus. Derm Therapy 17:129–133

5.2 Hidradenitis Suppurativa (Acne Inversa)

WOLFGANG HARTSCHUH

5.2.1 Aetiology

- Hidradenitis suppurativa (HS) is a chronic relapsing cutaneous inflammation mainly of intertriginous areas rich in terminal hair follicles and apocrine sweat glands. But it occurs also on the scalp devoid of any apocrine glands.
- HS is primarily a disorder of the follicular epithelium, with hyperkeratosis of the follicular infundibulum, occlusion and follicular rupture resulting in inflammation, secondary infection and cellulitis. Apocrine glands are only secondarily involved in the inflammatory process.
- Follicular occlusion encompasses a wide clinical spectrum, HS, acne conglobata, pilonidal sinus and dissecting cellulitis of the scalp. All these entities share a follicular occlusion as the initial event, followed by a cellulitis with draining sinuses. Therefore, HS is a misnomer and the term acne inversa (AI), as an all-inclusive term for this group of related disorders is the more appropriate designation.
- Rupture of the hair follicle, spilling foreign-body material such as keratinocytes, bacteria, sebum products and hairs into the dermis induces a severe acute inflammation with abscesses dissecting through the dermis.
- Free hair shafts are responsible for a persistent granulomatous, fibrosing tissue reaction and the formation of sinuses.
- The sinuses are generated from epithelial strands originating from ruptured hair follicles.
- Subsequent bacterial infection leads to permanent malodorous purulent secretion. The contribution of bacteria in this process is not fully clarified. The endogenous flora may represent an immunogenic factor different from that of a simple bacterial infection. Often coagulase-negative staphylococci, but also anaerobic bacteria and later on also *Staphylococcus aureus* are present.
- Obesity, while not playing a role in the primary pathogenesis, aggravates AI together with tight fitting underwear by creating an optimal environment via occlusion and maceration in sweat gland-rich intertriginous areas.
- In women shaving in the genital region may provoke a first episode of AI mostly localised at the outside of the labia majora.
- The use of tobacco products is significantly more common in patients with AI than in healthy controls. In perianal AI 70% are smokers. The aetiological basis is unknown, but an altered chemotaxis of polymorphic neutrophils altered by smoking may be one possible mechanism.
- The influence of hormones in AI is uncertain but flair-ups premenstrually, postpartum and in association with contraceptive pills are well documented. The mechanism is explained by an extragenital end-organ hypersensitivity to androgens. However, no supporting evidence for hyperandrogenism has been found in woman with AI compared with age-, weight- and hirsute-matched controls.
- AI may be aggravated by increased psychological stress.
- An occasional association or co-occurrence of AI with Crohn's disease, spondyloarthropathy and pyoderma gangrenosum suggests an inflammatory pathogenesis. However, an underlying immune abnormality has not been established in AI, although dysfunctional neutrophils have been implicated.

5.2.2 Incidence

Acne inversa has an estimated prevalence of approximately 2% in the general population. A family history is reported in 26% with an autosomal dominant mode of inheritance by single gene transmission. A variable degree of gene penetrance and possibly hormonal influences on gene expression may explain the reduced risk to first-degree relatives. A novel connexin 26 gene mutation associated with follicular occlusion triad has been reported recently. However, the identification of an exact genetic locus in AI remains to be found.

5.2.3 Epidemiology

- For unknown reasons women are more affected than men. The female-to-male ratio is 2:1 up to 5:1.
- Genitoinguinal lesions are more common in woman but axillary involvement shows no gender predilection.
- The age of onset may vary from childhood to middle age, with an average of 23 years.
- Severe prepubertal cases in obese girls, some of whom show a complex hormonal dysfunction, are rare but well documented.
- There seems to be no racial predilection.

5.2.4 Diagnostic Procedures

The important features of AI are:

- Mostly adults are affected, not juveniles as in acne vulgaris
- Polyporous secondary comedones
- Abscesses with communicating epithelium-lined channels
- Draining sinuses, foul-smelling discharge
- Hypertrophic scars and contractures, particularly in the axillae and groin
- Psychosomatic problems, conflicts with partners and at work, social isolation

The clinical picture in advanced stages of AI is characteristic. However, initial AI with tunnelled abscesses is often misdiagnosed as furunculosis, but the abscesses are deep and round without pointing or central necrosis, unlike staphylococcal abscesses.

Routine laboratory checks are recommended in chronic disease:

- Full blood count
- Sedimentation rate
- Serum iron
- Blood sugar serum electrophoresis
- Bacteriology is recommended in chronic purulent disease

5.2.5 Therapy

5.2.5.1 Conservative Treatment

- Initial management consists of weight reduction, avoidance of humidity enforced by tight-fitting synthetic clothing, and washing with antiseptic soaps to reduce the bacterial load.
- Acne inversa is a multifocal disease often involving several lesions in different regions. Therefore, systemic treatment measures should be introduced but results are disappointing.
- Medical treatment with antibiotics can be helpful in early and mild stages of the disease and for improving disease control before curative surgery in more advanced stages. The role of antibiotics in AI is unclear. A regular bacteriostatic effect is conceivable as is also an influence on the inflammatory response. Antistaphylococcal agents in axillary disease, and a more broad-spectrum coverage for perianal disease are recommended. Topical treatment with clindamycin or 2% triclosan ointment seems to be equally effective as systemically applied antibiotics.
- Non-steroidal anti-inflammatory drugs may alleviate pain and inflammation and also may be seen as an intermediate therapy aimed at preparing the patient for subsequent radical surgery.
- Systemic and intralesional corticosteroids still represent an important clinically proven management tool for AI but only for short-term treatment in acute and early inflammatory stages.
- Unlike in acne vulgaris, systemic retinoids are disappointing in the treatment of AI. Infliximab or etanercept by destroying (infliximab) or decoying (etanercept) the proinflammatory cytokine TNF-alpha recently have been found to be effective in recalcitrant cases of AI, but severe side effects of this therapy must be considered. Randomised controlled studies have found that cyproterone acetate and ethinyl oestradiol may be useful.

Treatment measures are summarised in Table 5.2.1.

All patients suffering from this disabling dermatosis should be offered reassurance and psychological support.

5.2.5.2 Surgical Treatment

Fluctuant abscesses are best unroofed to provide optimal drainage and pain relief.

Isolated Lesions (Sinus Tracts)

Excision and primary closure may be indicated in isolated chronic, non-inflammatory lesions. Secondary healing is the preferred method when lesions are purulent. Laying open of sinus tracts is an alternative, but recurrences are high.

Table 5.2.1 Treatment of acne inversa

Disease severity	Characteristics	Treatment
Mild	Solitary nodules (boil-like) No abscesses Minimal pain	Avoidance of humidity, tight clothing, shaving if irritation occurs Reduction of body weight Topical antiseptics and soaps Stress management Restriction of smoking **Caution: No incision in non-fluctuant abscesses** Non-steroidal anti-inflammatory drugs Botulinum toxin A to reduce sweating[a]
Moderate	Multiple, recurrent painful abscesses with purulent discharge from sinus tracts	Retinoids in patients with concomitant acne conglobata Antibiotics (topical, systemic or both) Dapsone[a] Oral contraceptive agents with high oestrogen-to-progesterone ratio and low androgenicity of progesterone in selected women Corticosteroids (short term)[a] Laser therapy[a] ALA-PDT[a] Blue light therapy[a] Cryotherapy[a] **Consider:** Referral to an experienced surgeon for patients who do not respond to therapy
Severe	Dissecting cellulitis with draining sinuses, malodorous discharge, induration and contraction of soft tissues	Radical surgery! In recalcitrant cases, not healed by surgery: Cyclosporine A Anti-TNF-alpha Methotrexate Radiotherapy

[a]Only limited clinical experience available

Late Extended Stages of AI

The best results are achieved by radical wide excision with the intention to remove all apocrine-bearing skin in the affected area to obtain a hair-free, dry skin area. Wounds can heal by secondary intention or be covered by immediate or delayed skin grafting. Negative pressure dressings may accelerate the healing process. Primary skin cover by flaps may compromise the excision margin. Recurrences occur mostly from either inadequate excision or a wide, ill-defined distribution of apocrine glands as in the case of the submammary region. In addition the recurrence rates depend on the body region. Low recurrence rates are reported in perianal disease, 3% in axillary disease and 37% in inguinoperineal disease. Obesity and chronic skin infection favour the incidence of recurrence.

5.2.6 Complications

- Dermal contraction, restricted limb mobility from scarring
- Local or systemic infection
- Erysipelas, rarely occurring in the anogenital region
- Rectal or urethral fistulas (often iatrogenic)
- Lymphoedema
- Symmetrical polyarthritis secondary to inflammatory injury; association between AI disease activity and arthropathy activity
- Nephrotic syndrome
- Osteomyelitis
- Systemic amyloidosis → renal failure
- Bacterial meningitis, bronchitis, pneumonia
- Anaemia from chronic infection
- Marasmus
- Squamous cell carcinoma (Marjolin ulcer)

Suggested Reading

1. Barth JH, Layton AM, Cunliffe W (1996) Endocrine factors in pre- and postmenopausal women with hidradenitis suppurativa. Br J Dermatol 134:1057–1059
2. Hurley HJ (1996) Axillary hyperhidrosis, apocrine bromhidrosis, hidradenitis suppurativa and familial benign pemphigus. Surgical approach. In: Roenigk RK, Roenigk HH Jr (eds) Dermatologic surgery. Principles and practice, 2nd edn. Dekker, New York, pp 623–645
3. Jemec GBE (2004) Medical treatment of hidradenitis suppurativa. Expert Opin Pharmacother 5:1767–1770
4. Plewig G, Steger M (1989) Acne inversa (alias acne triad, acne tetrad or hidradenitis suppurativa). In: Marks R, Plewig G (eds) Acne and related disorders. Dunitz, London, pp 345–357
5. Sartorius K, Lapins J, Emterstam L, Jemec GBE (2003) Suggestions for uniform outcome variables when reporting treatment effects in hidradenitis suppurativa. Br J Dermatol 149:211–213
6. Slade DEM, Powell BW, Mortimer PS (2003) Hidradenitis suppurativa: pathogenesis and management. Br Assoc Plast Surg 56:451–461

5.3 Condylomata Acuminata

SYLVIA PROSKE, WOLFGANG HARTSCHUH

5.3.1 Aetiology

- Condylomata acuminata are epidermal tumours that result from the proliferation of keratinocytes infected with human papilloma virus (HPV), low risk genotypes 6 and 11 being found in > 90% of patients. However, it is common to have infection with multiple HPV types.
- Manifestations range from clinically overt lesions to subclinical and latent infection. Three different types are distinguished:
  - Condylomata acuminata
  - Condylomata plana
  - Giant condylomata (Buschke-Loewenstein tumour)
- Cervix, vulva, urethra and anus are predominantly affected. Genotypes 6 and 11 are also reported to infect other mucous membranes, including conjunctivae, respiratory tract and oropharynx.
- Anal warts are seldom found proximal of the dentate line.
- Intra-anal condylomata are present primarily in patients who have practised receptive anal intercourse, although perianal warts can occur in men or women who have no history of such practice.
- The HPV high-risk types 16, 18, 31, 33, 35, 39 and 41–45 found in genitoanal warts are associated with squamous intraepithelial neoplasia; types 16 and 18 are associated most strongly with malignant potential.
- Persistent infections with high-risk HPV types are associated with the development of intraepithelial neoplasia, called cervical intraepithelial neoplasia (CIN), vulvar intraepithelial neoplasia (VIN) or penile intraepithelial neoplasia (PIN) in the genital area, and anal intraepithelial neoplasia (AIN) in the anal region.
- The intraepithelial neoplasias may progress to invasive anogenital cancer. Bowen's disease, erythroplasia of Queyrat and bowenoid papulosis are clinically different, but all exhibit an identical histopathology, i.e. intraepithelial neoplasia. They are most commonly associated with HPV 16.

5.3.2 Incidence

According to PCR investigations, roughly 10% of the general population have been latently infected with HPV in their life. Up to 60% of the population have antibodies against HPV. The incidence of visible warts is up to 1% of sexually active persons between the ages of 15 and 45 years.

5.3.3 Epidemiology

- Condylomata acuminata are one of the most common sexually transmitted diseases caused by HPV. The main age is 20–24 years.
- Risk factors for the presence of HPV are:
  - A high number of sexual partners
  - Early cohabitarche
  - Young age at first delivery
  - Suppression and alteration of immune status
  - Young age
  - Hormonal influences
  - Tobacco use
- During the past few decades an explosive increase in the incidence of cases in adults and young children have been reported.
- Although non-venereal transmission of anogenital warts, such as autoinoculation from extragenital sites to genitalia may occur in children, each child requires particularly careful examination to exclude sexual abuse.
- Non-venereal sources can be considered in children with the onset of lesions at less than 3 years of age, when warts are present in close contacts, particularly genital warts in mothers (vertical transmission).
- Possible routes of transmission also include other skin warts (HPV 1–4) from the child's own hands or those of other children or adults who have hand warts simulating condylomata acuminata in the genital area.

5.3.4 Diagnostic Procedures

- Typical clinical findings in the genital and anal region.
- Digital examination and proctoscopy of anus and rectum.
- Topical application of 3–5% acetic acid (aceto-whitening) as an essential adjunct to inspection.
- A representative biopsy for histology is generally indicated.
- Anal cytology alone is not accurate for detecting high-risk lesions.
- Viral typing is not routinely required, however, in children and their contact persons it may provide evidence for venereal or non-venereal transmission of HPV.
- Condylomata lata (syphilis) should be ruled out by examination by syphilis serology.
- Investigations for other sexually transmitted diseases including HIV, gonorrhoea and chlamydia.
- Examination of the sexual partner is recommended.

5.3.5 Therapy

Although HPV anogenital infection represents an epidemiological problem, there is still no gold standard therapy as all treatment options show high recurrence rates (8–65%). Treatments of anogenital warts are aimed at eradicating the lesions or stimulating the immune system to generate clearance and prevent recurrence. The first goal is the clearance of visible warts. Some evidence suggests that treatment may reduce the persistence of HPV DNA in the tissue and therefore may reduce infectivity. However, there is currently no evidence that treatment has a favourable impact on the incidence of cervical, genital and anal cancer, and there have been no controlled studies on the effects of treatment of condylomata and HPV transmission rates.

The choice of therapy is based on the number, size, site and morphology of lesions, as well as patient preferences. Treatment costs, adverse effects and clinician experience are also decisive. In general, chemical treatments are more effective on moist, soft, non-keratinised warts. Keratinised lesions, extensive perianal or intra-anal condylomata respond better to physical ablative procedures.

Routine follow-up at least at 2–3 months is advised to monitor response to therapy and evaluate for recurrence.

5.3.5.1 Conservative Treatment

Patient-Applied Treatments

- Podophyllotoxin (0.15% cream or 0.5% solution)
  - Purified, major biologically active component of podophyllin resin; cytotoxic, antimitotic
  - Application twice daily for 3 days, followed by 4 rest days
  - Repetition for 4 cycles
- Imiquimod (5% cream)
  - Cell-mediated immune response modifier, induction of interferon production and recruitment of immune cells including $CD4^+$ T cells
  - Application at bedtime for 3 days, followed by 4 rest days; alternatively, application every other day for three applications
  - Repetition of weekly cycles up to 16 weeks
- Imiquimod 5% by suppositories (anal tampons) for intra-anal warts; off-label use

Physician-Applied Treatments

- Trichloroacetic acid (TCA) 30% to 60% solutions
  - Application of a small amount to visible condylomata
  - Repetition weekly, if necessary
- Porphyrin-based photodynamic therapy (PDT), induced by 5-aminolaevulinic acid (ALA)
  - One treatment first
  - Repetition after several weeks, if necessary

Therapies Not Generally Recommended

The following treatment modalities are not recommended for use in the primary care setting because of low efficacy and toxicity problems:

- Interferons alpha and beta
- 5-Fluorouracil cream
- Podophyllin 20–25%

Podophyllin is a crude plant extract with low efficacy, high toxicity, and a serious mutagenicity profile which does not comply with the WHO guidelines for plant-derived treatments and should be removed from clinical treatment protocols. The UK and the USA national guidelines for the management of anogenital warts continue to recommend the use of podophyllin; however, applied in larger volumes it is associated with bone marrow suppression, CNS and cardiovascular side effects.

5.3.5.2 Surgical Treatment

There are no clear directions for the surgical method of choice, as this is a matter of wart distribution and the clinical skills and experience of the physician.

Excision by Scissors

- Only superficial because condylomata acuminata are intraepidermally growing tumours; useful when only a few exophytic lesions are present.
- Wide excisions are contraindicated.

Electrosurgical Removal, "Wet-Field" Technique

- The operation field is cooled by water to minimise thermal damage.
- Electrocautery is performed with the use of surgical masks by the treatment team.
- A smoke evacuator is required.

Laser Vaporisation (CO_2 or Nd:YAG laser)

- Performed with the use of surgical masks by the treatment team.
- A smoke evacuator is required.

Cryotherapy

- Application with a cryoprobe, liquid nitrogen spray or a cotton-tipped applicator.

5.3.6 Differential Diagnosis

Differential diagnostic considerations vary depending on the extent and location of the lesions, but include the following disorders:

- Verrucae vulgares
- Fibromata pendulantia
- Dermal nevus
- Micropapillomatosis labialis vulvae
- Papillae coronae glandis
- Seborrhoeic keratoses
- Lichen planus
- Bowenoid papulosis
- Condylomata lata (secondary syphilis)
- Mollusca contagiosa
- Pemphigus vegetans
- Verrucous carcinoma

5.3.7 Special Considerations

- The treatment of condylomata acuminata is not complicated, but both conservative and surgical approaches are fraught with a high recurrence rate (up to 70%), especially within 3–6 months after treatment.
- Long-standing condylomata acuminata can progress to the giant, destructive variant (Buschke-Loewenstein).
- Human papilloma virus has been implicated as the primary aetiological agent of cervical and anal cancer. Potential vaccines against high-risk HPV types are in clinical trials and might be a promising therapeutic option also in condylomata acuminata.
- Recently a vaccine has been developed against certain strains of HPV. This holds promise in reducing the incidence of cervical cancer in women. Its role in protecting against HPV infection in the general population remains to be seen.

Suggested Reading

1. Gross G (2001) Condylomata acuminata und andere HPV-assoziierte Krankheitsbilder des Genitale und der Harnröhre. Leitlinie der Deutschen STD-Gesellschaft (DSTDG). Hautarzt 52:405–410
2. Kodner CM, Nasraty S (2004) Management of genital warts. Am Fam Physician 70:2335–2342
3. Papaconstantinou HT, Lee AJ, Simmang CL, Ashfaq R, Gokaslan ST, Sokol S, Huber PJ, Gregorcyk SG (2005) Screening methods for highgrade dysplasia in patients with anal condyloma. J Surg Res 127:8–13
4. Von Krogh G, Lacey CJ, Gross G, Barrasso R, Schneider A (2001) European Course on HPV Associated Pathology (ECHPV), European Branch of the International Union against Sexually Transmitted Infection and the European Office of the World Health Organization (2001): European guideline for the management of anogenital warts. Int J STD AIDS 12(suppl 3):40–47
5. Wienert V, Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften (2002) Feigwarzen. Leitlinie der Deutschen Dermatologischen Gesellschaft und der Deutschen Gesellschaft für Koloproktologie. AWMF online Nr. 013/008

5.4 Pilonidal Sinus

WOLFGANG HARTSCHUH

5.4.1 Aetiology

- The aetiology of pilonidal sinus disease (PSD) is unclear although it is probably an acquired disease.
- The following have been identified as risk factors for the development of symptomatic PSD:
  - A deep intergluteal groove
  - Hirsute, young individuals
  - Obesity
  - Long-standing pressure or friction
  - Inadequate personal hygiene
  - These features together with moisture make the skin especially in this area susceptible to penetration of shed hair shafts
- On the other hand, the midline pits, characteristic for early stages of PSD, have been shown to be a result of marked hyperkeratosis of the enlarged hair follicle ostium.
- Not uncommonly, PSD occurs in patients together with acne conglobata or acne inversa, sharing the same pathological process, i.e. an occluding follicular hyperkeratosis followed by a dissecting cellulitis and the formation of draining sinuses.
- Additionally, friction between the buttocks may be responsible for sucking or sticking hairs into the pits. The stiffness of the body hairs and the hair scales functioning as microbarbs facilitate penetration of hair shafts deeper and deeper into the skin.
- Hair acts as a potent foreign body causing a prolonged inflammatory reaction and the development of sinus tracts filled with granulation tissue and, quite often, with masses of hair shafts. By this time these tracts are always lined by epithelium, at least partially.

5.4.2 Incidence

Pilonidal sinus disease mostly occurs in the second and third decades, and is twice as frequent in men. The incidence is highest among Caucasians. A recent American study estimated that 1.1% of young male students and 0.11% of female students suffered from PSD.

5.4.3 Epidemiology

- A positive family history is common and in more than 20% a coincidence with acne inversa (hidradenitis suppurativa) suggesting a similar pathogenetic mechanism in both conditions.
- The prevalence of PSD in men reflects the importance of anatomical differences as promoting factors between both sexes, e.g. the configuration of the intergluteal groove and the hair status.

5.4.4 Diagnostic Procedures

- Pilonidal sinus (Latin: "nest of hairs") is characterised by visible single or a series of midline pits in the natal cleft which have the microscopic appearance of enlarged hair openings. Often these pits are minute, whereas others may contain a tuft of hairs.
- The clinical picture in a developing acute abscess may be inconspicuous showing only a slight bulging of the skin in the anal cleft.
- Recurrent painful indurations in this area with purulent secretion followed by silent periods are a characteristic medical history of PSD.
- Chronic PSD may reveal a paramedian opening in the upper parts of the buttocks filled with granulation tissue resembling pyogenic granuloma. Examination with a probe easily demonstrates the connection with the sinus tract.
- In selected cases computed tomography or magnetic resonance imaging may be indicated.

5.4.5 Therapy

5.4.5.1 Conservative Treatment

- Asymptomatic PSD may be treated conservatively by meticulous hair control, shaving the natal cleft and improved hygiene (mechanical removal of shed hairs).

- There is no reasonable conservative therapy of symptomatic PSD and the mainstay of treatment is surgical.
- Antibiotics may be indicated in purulent stages of PSD prior surgery or in rare cases of systemic infection.
- Prophylactic use of antibiotics in the surgical treatment of PSD is still controversial.

5.4.5.2 Surgical Treatment

There are several techniques described. Recurrence rates are variable with any procedure and may reach 20% and more. Postoperative professional wound care and hair control is of crucial importance for optimal wound healing and is likely to play an important role in the avoidance of complications and recurrences.

The main therapeutic goals are:
- Flattening of the natal grove
- Low rate of complications and recurrences
- Minimal discomfort for the patient
- Short healing and off-work time
- Good cosmetic results
- Suitable for a day case operation

Minimally Invasive

Pilonidal abscess should be drained or, better, unroofed to provide optimal drainage. This rapidly alleviates symptoms and can control PSD in the outpatient setting. General anaesthesia allows curettage of the sinus in the same session and together with removal of the pits occasionally may heal PSD, but recurrences are high.

Open Surgery

Wide excision of all involved skin with shallow resection margins and open granulation is still the preferred surgical treatment in the majority of patients. However, a short stay hospitalisation (approximately 2 days) often is unavoidable. Leaving the wound open results in longer healing periods and requires repeated visits by a community nurse with associated costs of time and dressing. However, the longer healing time is not an obstacle to an early return to work and social activities in patients. A shorter healing time can be achieved by the lay-open technique, modified with marsupialisation. The use of vacuum-assisted closure therapy may facilitate healing by secondary intention. Delayed skin grafting in this location is not a good alternative because a second operation with a high risk of graft failure prolongs limitations in work and social activities of the patients.

Wound Closure Procedures

Wound closure methods offer significant advantages: Shorter hospital stay, or even day case operation, earlier healing and shorter time off work. The disadvantages are a higher rate of complications and recurrences, and inferior cosmetic results when wound closure is achieved by flaps.

The following methods of wound closure are mostly used:
- Simple excision of the sinus complex with primary closure in the midline. This procedure is frequently complicated by wound breakdown caused by haematoma formation.
- Better results are reported for oblique and asymmetric excisions and closure techniques to minimise or to avoid the midline suture. The latter procedure can be combined with an advancement flap to facilitate wound closure and to create a flattened anal cleft.
- A tension-free wound closure is achieved by plastic flaps (rotational-, rhomboid flaps and Z-plasty), but the goal to attenuate the natal groove is fulfilled only in the upper part; the lower part of the cleft remains deep, sometimes bulging under the flap and recurrences are programmed. Flap techniques have a higher complication rate and the cosmetic results are often poor compared with the other techniques. Therefore, plastic flaps can be regarded as overtreatment and may be indicated mainly in some complicated cases, e.g. in malignant transformation of PSD.

5.4.6 Complications

- Early bridging is not an uncommon complication in secondary healing and is a result of inadequate wound stretching.
- Occasionally chronic failure to heal may occur for unknown reasons even under optimal wound care conditions.
- Many recurrences in our view are created by unprofessional wound management.

5.4.7 Special Considerations

It is difficult to finally estimate the pros and cons of each method in the surgical treatment of PSD due to the great divergence of the published results and in the understanding of the pathogenesis of PSD. Thus, the personal experience of the operator seems to be of importance for the outcome of any procedure. Prospective randomised

studies are warranted to evaluate the most effective method for each patient. The pathogenetic relationship with acne inversa so far has not been adequately estimated in the literature of PSD. Standardisation of each method, done only by well-trained operators will further optimise the results. Therefore, it appears to be too early to consider primary asymmetric closure procedures as simple day-case standard procedures for the vast majority of uncomplicated PSD.

Suggested Reading

1. Arda I S, Güney L H, Sevmis S and Hicsönmez A (2005) High body mass index as a possible risk factor for pilonidal sinus disease in adolescents. World J Surg 29:469–471
2. Bascom J (1983) Pilonidal disease: long-term results of follicle removal. Dis Colon Rectum 26:800–807
3. Gencosmanoglu R, Incoglu R (2005) Modified lay-open (incision, curettage, partial lateral wall excision and marsupialization) versus total excision with primary closure in the treatment of chronic sacrococcygeal pilonidal sinus. A prospective, randomized clinical trial with a complete two-year follow-up. Int J Colorectal Dis 20:415–422
4. Karydakis GE (1992) Easy and successful treatment of pilonidal sinus after explanation of its causative process. Aust N Z J Surg 62:285–289
5. Petersen S, Koch R, Stelzner S, Wendlandt TP, Ludwig K (2002) Primary closure techniques in chronic pilonidal sinus: a survey of the results of different surgical approaches. Dis Colon Rectum 45:1458–1467
6. Senepati A, Cripps NP, Tompson MR (2000): Bascom's operation in the day-surgical management of symptomatic pilonidal sinus. Br J Surg 87:1067–1070

Functional Disorders

6.1 Incontinence

ALEXANDER HEROLD

6.1.1 Aetiology

Continence is defined as the voluntary control of bowel content and the ability of its voluntary emptying. Incontinence is the loss of this ability. Incontinence must also be considered a symptom. Its causes are manifold. Incontinence can be directly related to the anorectal continence organ itself, or be a secondary symptom to various pathological conditions (Table 6.1.1). Traditionally incontinence was described as being sensory, muscular, neurogenic, mixed, psychoorganic and idiopathic. These categories carry limitations as they do not take factors determining continence into consideration, such as:

- Stool frequency
- Stool consistency
- Sphincter strength
- Anorectal sensitivity
- Capacity and compliance of the rectum

Especially with regard to a required therapy, a treatment-oriented structuring makes sense (Table 6.1.1). Incontinence is mostly multifactorial. If incontinence occurs secondary to another underlying disease or disorder, treatment should be directed to the primary. The following is focused on incontinence due to disorders of the anorectal continence organs.

6.1.2 Incidence

- The true incidence of faecal incontinence is unknown.
- The incidence is reported between 0.3% and 1.5% in larger population-based studies; even up to 5% is quoted.
- The incidence increases with age and reaches up to 30% in nursing homes.
- Faecal incontinence is associated with physical inabilities and cognitive function.
- As incontinence appears to be underreported, one may estimate. Presupposing an incidence of anal incontinence in Central Europe between 3% and 5% and taking into consideration that only 10–20% of all per-

Table 6.1.1 Therapy-orientated classification of the aetiology of anal incontinence

1.	**Altered stool consistency:**
	Irritable bowel syndrome
	Inflammatory bowel disease
	Diarrhoea
	Radiation enteritis
	Malabsorption
2.	**Disturbed reservoir function capacity and compliance:**
	Altered rectal reservoir (postoperative, ileal pouch)
	Inflammatory bowel disease
	Collagenosis
	Rectal tumours
	External rectal compression
3.	**Pelvic floor disorders:**
	Pelvic floor denervation (descending pelvic floor, pudendal neuropathy)
	Congenital lesions (anal atresia, spina bifida, myelomeningocele)
	Others (rectal prolapse, dyscoordination, chronic constipation)
4.	**Disorders of the sphincter:**
	Sphincter defect (obstetric trauma, anorectal surgery, trauma)
	Sphincter degeneration (internal sphincter sclerosis, hypotrophia)
	Tumour (benign, malignant)
	Inflammation (irritable bowel disease)
5.	**Disturbed sensitivity:**
	Neurological causes (dementia, neuropathy, trauma, tumour)
	Overflow incontinence (constipation, encopresis, drug medication)
6.	**Combinations of 1–5**

sons concerned report this to their physician, we can estimate that 300,000 to 1 million patients in Germany need treatment.
- Older people are especially affected and their general and mental state of health often excludes major surgical interventions and renders conservative measures almost impossible. The majority are therefore treated almost exclusively by nursing.

6.1.3 Classification

Continence is defined as the ability to control bowel content, to discriminate faeces from gases and to empty the bowel at will. Incontinence can range from occasional staining of underwear to the complete inability to control solid stool. Both may result in an impairment of social life. The simplest, pragmatic classification states:
- Incontinence 1°: disability to hold back wind
- Incontinence 2°: disability to hold back liquid stool
- Incontinence 3°: disability to hold back solid stool

Various classifications have been introduced in the past aiming to quantify the extent and severity of incontinence.

6.1.4 Diagnostic Procedures

The diagnostic modalities have improved considerably since the 1990s. Various diagnostic methods are available and can be applied depending on the findings of history and physical examination alone: To address the various aspects of history and the various morphological structures and their functions it is necessary to examine these in a systematic way and to take individual specifics into consideration.

- As incontinence occurs in different extents and grades of severity and its impact on quality of life does not correlated with its extent, a standardised classification is necessary for a comparative evaluation, aiming to achieve objective information. Continence scores aim to retrieve a further differentiation in causes, characteristics and severity of the dysfunction through patient interviews taking a detailed patient's history. The one achieving broadest acceptance is the Cleveland Clinic incontinence score (Table 6.1.2). None of the scores used today is validated.
- Recently also instruments to measure quality of life in patients suffering from incontinence are increasingly being used, both disease-unspecific and disease-specific quality of life scores, e.g. the Rockwood Quality of Life score.
- Inspection, palpation, proctoscopy and rectoscopy (rigid sigmoidoscopy) are mandatory in the basic diagnostic work-up of a patient. Based on these findings further diagnostics can be considered.

6.1.4.1 Inspection and Palpation

- Simple inspection shows distinct alterations such as deformities, muscular defects, scars and mutations of the skin.
- Inspection of the pelvic floor while asking the patient to contract the anal sphincter and the pelvic floor and while straining can provide signs of a perineal descend, less obviously located muscle defects, perineocele and also urological or gynaecological combined disorders.
- The skin prick test (touching/scratching of the anal skin) and subsequent reflex contraction of the anal sphincter (anocutaneous reflex) can serve as a basic neurological investigation testing cutaneous sensitivity, motor function and the afferent and efferent innervation.

Table 6.1.2 Patient form of the Cleveland Clinic incontinence score

How often do you lose solid stool?	Never	< 1/month	> 1/month	> 1/week	Every day
How often do you lose fluid stool?	Never	< 1/month	> 1/month	> 1/week	Every day
How often do you lose gases?	Never	< 1/month	> 1/month	> 1/week	Every day
How often do you wear a pad?	Never	< 1/month	> 1/month	> 1/week	Every day
How often do you have to change your life style?	Never	< 1/month	> 1/month	> 1/week	Every day

Evaluation: 1st column 0 points, 2nd column 1 point, 3rd column 2 points, 4th column 3 points, 5th column 4 points, 0: continent, 20: completely incontinent

- The digital examination of the pelvic floor and of the sphincters at rest, during active contraction and during the Valsalva manoeuvre provide the first impression of resting pressure, squeeze pressure, sphincter defects, length of the anal canal, rectocele, intussusception and scars following surgery.
- In some cases inspection and palpation by an experienced examiner can provide sufficient, qualitative information to imply a certain therapy without further special diagnostics, e.g. incontinence post partum caused by an obvious clearly visible defect following sphincter laceration may be treated by surgery without the need of further diagnostics.

6.1.4.2 Proctoscopy and Rigid Sigmoidoscopy (Rectoscopy)

- The visual evaluation of the internal aspects of the anal canal and the rectum by means of proctoscopy and rigid sigmoidoscopy serves to identify causes of primary incontinence and to exclude potential causes of secondary incontinence (such as inflammatory diseases, tumours, intussusception, internal mucosal prolapses, scarred warpings of the rectal ampulla after surgery).

6.1.4.3 Endoanal Ultrasound

- Regarding faecal incontinence endoanal ultrasound is the ideal examination technique for the imaging and the morphological evaluation of the rectal mucosa, rectal wall, internal anal sphincter, external anal sphincter, puborectalis muscle and adjacent anatomical structures, such as prostate, vagina and bladder.
- These structures can be demonstrated in longitudinal and horizontal planes.
- Also potential causes of secondary incontinence disorders, e.g. fistula tracts, and concomitant disorders, e.g. small abscesses, can be detected.
- Comparative examinations have proven an excellent correlation of the endoanal ultrasound with intraoperative findings (Fig. 6.1.1).

6.1.4.4 Anorectal Manometry

- Anorectal manometry can evaluate the function of various anatomical structures contributing to the maintenance of faecal continence.
- Evaluation of both voluntary and reflex motor function and rectal sensory function are essential for establishing the individual therapy.
- The different parameters in routine use in a qualified pelvic floor laboratory are listed in Table 6.1.3.
- As a variety of systems and techniques (water perfused catheters, solid state catheters, stationary pull through, mechanical pull through) are used, interpretation of the findings depends in general on the normal values of the anorectal physiology laboratory.

6.1.4.5 Neurological Examination

- Neurophysiological diagnostics have to differentiate neurogenic from muscular lesions.

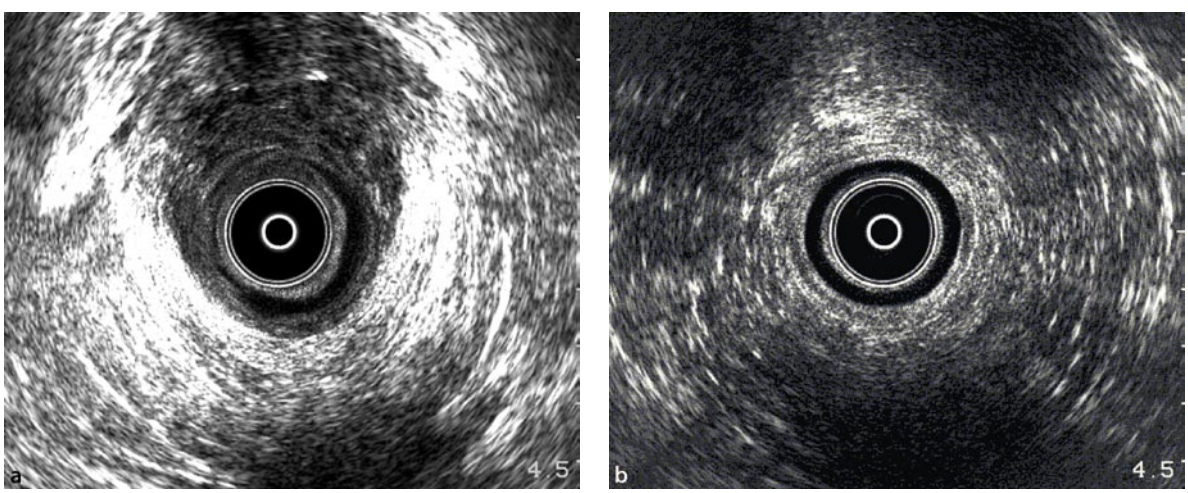


Fig. 6.1.1 **a** Endoanal ultrasound: female, 34 years, birth trauma, defect of the internal anal sphincter from 9 to 2 o'clock and defect of the external anal sphincter from 10 to 2 o'clock. **b** Physiologically "normal" sphincter on endoanal ultrasound

Table 6.1.3 Measurement parameters in anorectal manometry

Resting pressure
Squeeze pressure
Stress pressure
Straining pressure
Rectal compliance
Rectal capacity
Inhibitory reflex
Anocutaneous reflex
Anorectal sensitivity
First perception level
Urge level
Pain level
Maximal tolerable volume
Anal canal length
Vector volume measurement

- As well as a routine clinical-neurological examination, electromyography (EMG) of the pelvic floor and the pudendal nerve terminal motor latency (PNTML) are being used.
- Electromyography of the external anal sphincter and the puborectalis muscle serves as the basic procedure for measuring electrical activity and as such the display of denervation.
- Pudendal nerve terminal motor latency consists of the recording of different latencies between stimulation place and the muscle in relation to the passed length. Examinations are made at both pudendal nerves because traumatic lesions can affect asymmetrically only one side of the pelvic floor.
- Available are the conventional PNTML electrode (St. Mark's electrode), the determination of latency of the reflex and the determination of evoked potentials. The last two can evaluate the nerve's electrical stream in both directions, that is, afferent and efferent.
- The clinical value of these measurements is demonstrated most explicitly in a descending perineum. Compared to the normal nerve velocity we find a more than twice the normal value in pathological extension.
- With the help of the mentioned electrophysiological examinations it is possible to distinguish between muscular and neurogenic, central and peripheral, and acute and chronic lesions. This sometimes renders a prognosis of the disease or its therapy.

6.1.4.6 Sensitivity Tests

- Anorectal sensitivity is an elementary part of continence. Its disturbance—as the single cause alone—can result in incontinence.
- A clinical examination of the sensitive anoderm using needle and brush are part of the basic clinical examination.
- Special examination techniques such as electrosensitivity and temperature sensitivity can complement the investigation of anal sensitivity.
- Testing of rectal sensitivity with balloon distension of the rectum during anorectal manometry can already point towards a deficit.
- In cases of neurogenic continence disorder, anorectal sensitivity is almost always disturbed.
- Temperature perception is recorded with a water-perfused temperature probe.
- Incontinent patients are significantly less sensitive in these tests.

6.1.4.7 Defaecography

- Defaecography, both video technique or magnetic resonance imaging, allows a radiological presentation of the dynamic process of defaecation.
- In the context of incontinence its only value is to exclude potential disorders, such as intussusception, enterocele and rectocele, that may lead to secondary incontinence.

6.1.4.8 Continence Tests

- In recent years general global continence tests have been widely displaced by the above-mentioned, very differentiated examinations. They are, however, a good resource to globally judge the continence function when it is in doubt, e.g. the instillation of porridge or mashed potato and requesting the patient to hold this for 15 min while walking around and then have a normal defaecation.

6.1.4.9 Special Considerations

- In 25–40% of patients faecal incontinence is associated with pelvic floor prolapse.
- Gynaecological and urological investigations are indicated if, during history and clinical investigation, signs of concomitant gynaecological or urological disorders are found.
- Special emphasis should be given to address the issues of concomitant dysfunction with the patient as faecal

incontinence is in 30–40% of patients associated with urinary incontinence.

6.1.5 Therapy

As the potential causes of incontinence are multiple, its severity varies and its impact on quality of life is different among individuals, the therapy should be adapted to the needs of each individual. Conservative treatment options and surgical options are available. The decision should be based on thorough diagnostics and the aim is to pinpoint the underlying cause and direct the decision making. Only if all potential causes of secondary incontinence are excluded should incontinence, as such, be addressed.

6.1.5.1 Conservative Treatment

- Various conservative treatment options are used. They evolved empirically and, thus, no validated data to prove their efficacy are available.
- Conservative treatment aims to affect stool consistency, colonic transit, bowel emptying, sphincter function, perception of sphincteric function and rectal filling.
- Conservative therapy is considered first-line treatment, unless it becomes evident during diagnostics that conservative treatment is questionable because of the cause, extent and severity of the disease.

Local Measures

- Skin care (correct anal hygiene, skin care lotions or ointments, soft napkins, diapers).
- Anal plugs: in general poorly accepted by the patient. Only 10–20% of patients that once tested those continence plugs regularly.

Regulation of Bowel Emptying

- Laxative suppositories
- Retrograde lavage
- Regular use of enemas to create time intervals without bowel emptying

Regulation of Stool Consistency

- High-fibre diet
- Non-bloating meals
- Constipating medication (e.g. psyllium, *Plantago ovata*, loperamide, codeine)

Individual testing is always necessary because paradoxical reactions may occur. In general, the aim should be a change in attitude accompanied by a regular daily routine and regular defaecation.

Sphincter Exercise

- Indicated in patients with reduced voluntary sphincter action.
- Should be taught under the guidance of a physiotherapist.

Biofeedback

- Its principle is based on the concept of operant conditioning (Fig. 6.1.2). The patient learns to coordinate the activity of the pelvic floor muscles by using optic and/or acoustic signals via analogue or digital signal transfer.
- The therapeutic effect is considered to be based on a increase of the contractive strength, the duration of contraction, an improvement of coordination, an improvement of the sensitive perception and the oppression of internal relaxation.
- Training should follow a strict protocol: After instruction training the patient has to conduct training at home for some months.
- Data regarding the therapeutic effect of biofeedback are inconsistent and inconclusive. Success rates between 56% and 92% were reported in single-centre studies for very heterogeneous as well as for highly selected patient groups. Recent randomised trials failed to demonstrate superiority of biofeedback compared to general conservative measures.

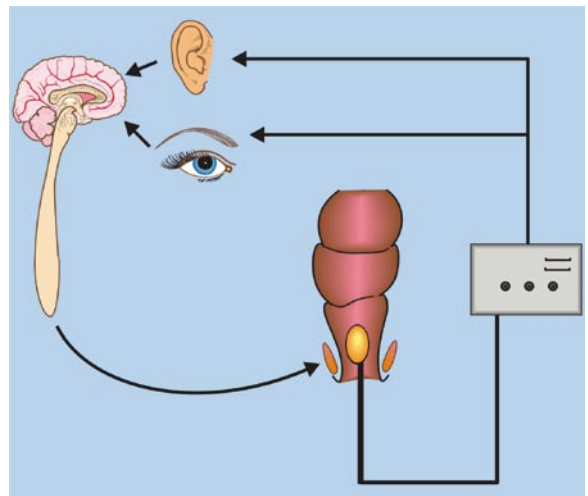


Fig. 6.1.2 Biofeedback

Anal Electrostimulation

- Periodocal application of anal electrostimulation to passively strengthen the sphincter muscles.
- Very few, mostly anecdotal, experiences report an improvement in 16–60% of patients in heterogeneous groups. Neither actual nor randomised results from trials are available.

6.1.5.2 Surgical Treatment

Sphincter Repair

- In the case of a sphincter defect—post partum, postoperatively and post trauma—a direct repair of the ruptured sphincter is still considered the gold standard.
  - The dehiscent muscles are identified, freed up and adapted.
  - Suturing can either be overlapping or by direct adaptation (Fig. 6.1.3).
- Reported short and midterm success rates range between 43% and 89%.
- Long-term follow-up indicated a substantial loss of the initial therapeutic effect.
- While the age of the patient and the duration of the sustained trauma have no influence, coexisting neurogenic damage has repeatedly be discussed as a predictor of lower success rates. However, these findings remain controversial and they do not influence the decision making, but should be taken into consideration when counselling the patient.
- Especially after obstetric trauma, the procedure of reconstruction can be combined with an approximation of the levator muscles (levatoroplasty). Additional separate identification and repair of the internal anal sphincter is technically challenging and of unproven therapeutic effect.
- Repeated sphincter repair is a valid option, if initial repair fails.

Preanal Repair, Postanal Repair, Total Pelvic Floor Repair

In patients presenting with incontinence due to a generalised weakness of the pelvic floor and the external anal sphincter without signs of sphincteric disruption, operative reefing of the sphincter complex can be considered: postanal repair (Fig. 6.1.4), preanal repair and total pelvic floor repair.

Postanal repair was the treatment of choice during the 1970s and 1980s. Since the first results reported success rates up to 90% and the complication rate was very low, the method became broadly accepted and uncritically ap-

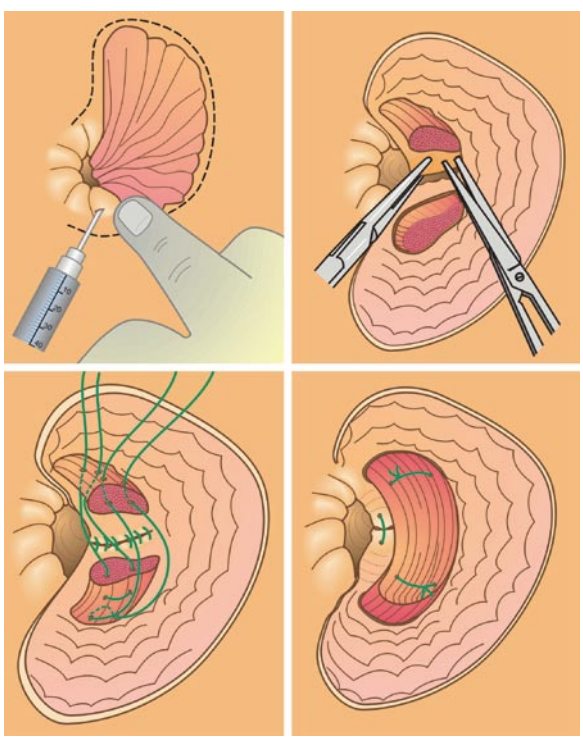


Fig. 6.1.3 Overlapping sphincter repair

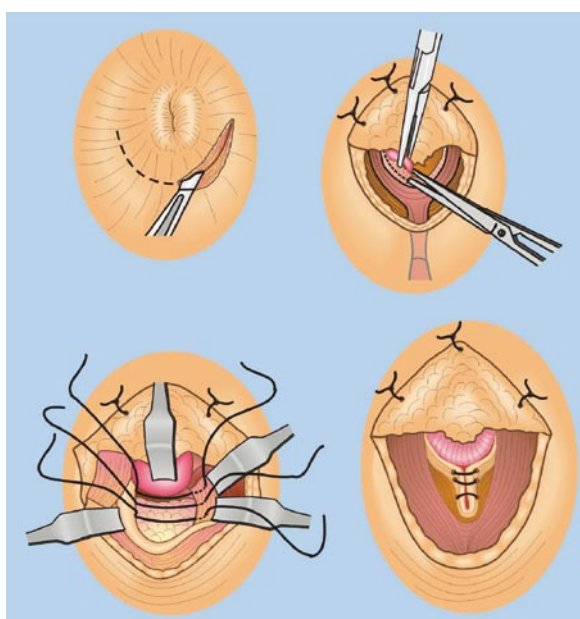


Fig. 6.1.4 Postanal sphincter repair

plied. Only during the last 10–15 years (1990 onwards) have long-term results been published. The initial success rates of 60–80% decreased within 5 years to 22–27%. Subsequently these methods have been used only very selectively, if a time-limited therapeutic benefit is acceptable.

The concept of these procedures is:

- To narrow and lengthen the high pressure zone of the anal canal
- To lift the pelvic floor
- To increase the anorectal angle

Sphincter Replacement

Various sphincter replacement procedures have been initiated since the late 1980s. Either topographically appropriate muscles (e.g. gluteoplasty, graciloplasty) were harvested and applied as neosphincters, or foreign material was used as sphincter substitutes. Dynamic graciloplasty and the artificial bowel sphincter were performed in larger series. All of these methods are technically elaborate, demanding for the patients and expensive. They are, therefore, only indicated when the earlier mentioned therapies fail in cases of severe incontinence.

Dynamic Graciloplasty

- The transposition of the gracilis muscle around the anus failed to achieve a long-term effect due to fibrosis of the muscle and inability of proper activation and durable contraction.
- With the introduction of continuous low-frequency electrical stimulation of the supplying nerve the phenotype of the transposed muscle was transformed to a fatigue-resistant one (fast twitch type 2 muscle fibres into slow twitch type 1 fibres) capable of sustained contraction and mimicking the physiological characteristics of the external anal sphincter.
- Chronic low frequency stimulation is applied by means of a fully implantable neurostimulator device consisting of an impulse generator and electrodes (Fig. 6.1.5). The implanted system is controlled by a remote device by the patients themselves. Longevity of the battery is limited, thus after several years minor reoperations for impulse generator replacement are required.
- Depending on the underlying aetiology the success rates of dynamic graciloplasty range from 55% to 83%. The therapeutic benefit can be maintained long term.
- The procedure is associated with high comorbidity that may require repeated surgical interventions.
- The most common severe complication prompting removal of the device is infection. Complication rates as high as 50% have been described.
- Evacuation disorders may occur due to hypercontinence requiring the regular use of enemas. Thus for patient selection and preoperative counselling it is important to address any underlying history of constipation.

Artificial Bowel Sphincter

- The artificial bowel sphincter is composed of:
  - A fluid-filled cuff, to be placed around the anal canal
  - A pressure balloon, to be positioned intra-abdominally
  - A connection device with a pump allowing the patient to deflate the cuff to open the anal canal.
- The deflation of the cuff is limited to several minutes; refilling allows a pressure gradient between the pressure balloon and the cuff (Fig. 6.1.6).
- Reported success rates range from 50% to 75%.
- Continence for liquid and solid can be achieved.
- The complication rate is high. Infection and technical failure most often lead to a removal of the device; removal in 30–50% of patients has been reported.
- The system can be reimplanted with success rates comparable to the first implantation.

Despite their high complication rates dynamic graciloplasty and the artificial bowel sphincter remain alternatives to the creation of a stoma in end-stage faecal incontinence. The spectrum of indications is comparable, even though certain conditions would lead to a preference for one of the techniques, such as poor trophic conditions of the soft tissue to cover the artificial sphincter or neurological deficits of the gracilis muscle.

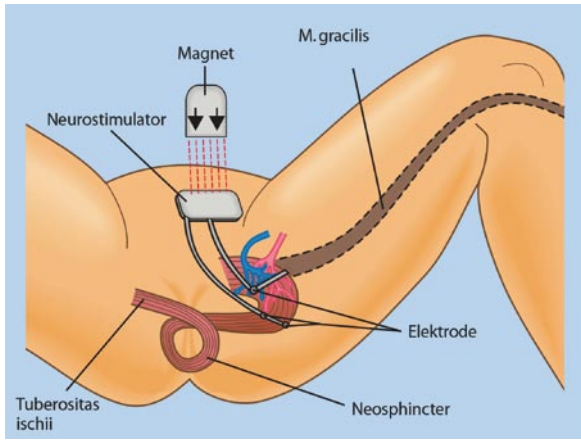


Fig. 6.1.5 Dynamic graciloplasty

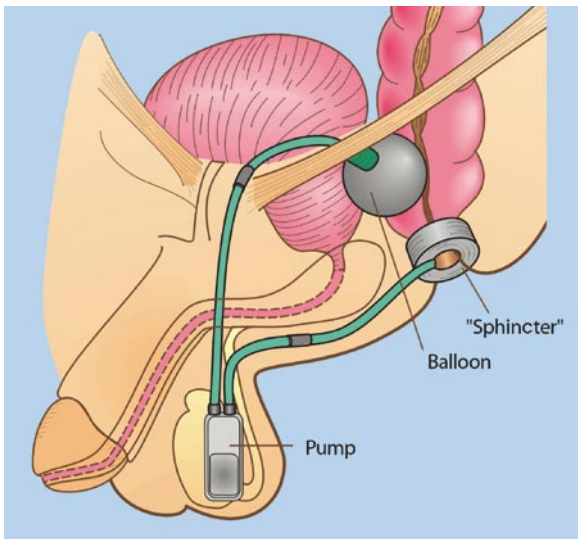


Fig. 6.1.6 Artificial bowel sphincter

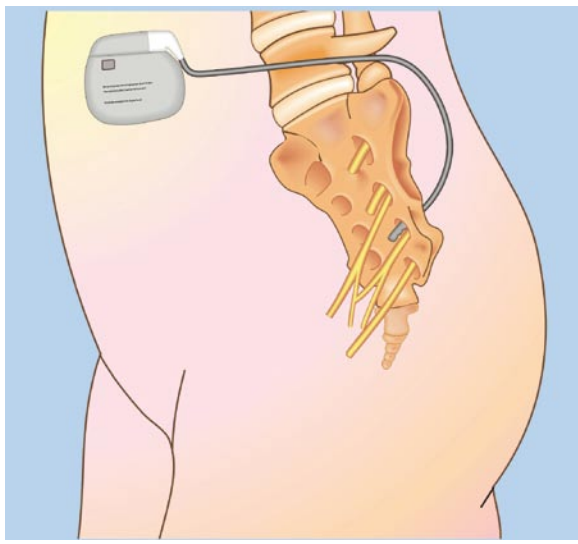


Fig. 6.1.7 Sacral nerve stimulation

Sacral Nerve Stimulation

- Sacral nerve stimulation (SNS) aims to recruit residual function of the anorectal continence organ.
- The system consists of a fully implantable electrode to be placed close to a target nerve at the level of the sacral spinal nerves, most likely S3 or S4, connected to an impulse generator that can be programmed and activated via telemetry (Fig. 6.1.7).
- Patients are selected with the help of a time-limited period of test stimulation with an external impulse generator. Based on the extent of clinical improvement during test stimulation, chronic stimulation with a permanent neurostimulation device is considered.
- The initial spectrum of indications for SNS is currently being expanded. Prerequisites for success are residual sphincter function and an existing neuromuscular connection to the sphincter. Thus SNS can be offered to patients with idiopathic and neurogenic incontinence.
- The mechanism of action seems multifold: somatomotor and somatosensory, as well as peripheral and cortical systems are affected by peripheral nerve stimulation at the level of the sacral spinal nerve.
- Based on patient selection by test stimulation a success rate of 85–90% is achieved.

Anterograde Irrigation

- The concept of regular cleaning of the large bowel via a small opening in the caecum is the creation of time intervals without discharge of bowel content through the functionally insufficient continence organ.
- Various procedures are currently applied: appendicostomy (Malone's procedure), endoscopic or open transcutaneous caecal catheter placement.
- Good results can be achieved, but psychological distress persists and the treatment is dependent on the patient's cooperation.

Stoma

- Diverting stoma creation remains an option of treatment for faecal incontinence, if other treatment modalities are not applicable or not acceptable for the patient or have failed.
- The creation of a stoma per se and the stoma also have a risk of comorbidity.

Bulking Agents

- The most recent treatment evolution is based on the idea to augment the sphincter complex by injection of bulking agents.
- Several new alternatives are proposed. Subanodermal or intersphincteric injection of collagen, silicon, microballoons, dextranomer microspheres or carbon-coated spheres are proposed especially in lesions of the internal sphincter.
- Experience is limited to small-centre studies.
- Patient selection and several technical issues, such as location of application and dosage, are not yet clarified.
- Midterm results are pending.

Radiofrequency

- "Radiofrequency energy delivery" (SECCA) to the cranial part of the internal sphincter creates local degeneration and collagen modification.
- As with bulking agents experience is limited and data are preliminary.

6.1.5.3 Recommendations for Therapy

- Surgical treatment should only be considered if conservative treatment fails or is inappropriate and not feasible.
- In all cases conservative treatment with general measures is indicated.
- Additionally biofeedback is recommended in less severe forms of incontinence, mainly incontinence 1° and 2°.
- The majority of patients can be treated with one or a combination of conservative measures (Fig. 6.1.8).
- Surgical intervention should be based on the findings of clinical and physiological evaluation (Fig. 6.1.9) and be aimed at either reconstructing the anatomy and by this restoring function or recruiting residual function of the continence organ.
- The first-choice therapy for sphincter defects is a sphincter reconstruction. In case of a clearly defined "small" defect no more than one third of the circumference (< 120°) the improvement reaches up to 90%. When lesions are larger than this, direct repair might be technically problematic and an additional or primary sphincter augmentation becomes necessary. At present the dynamic graciloplasty and the artificial anal sphincter compete with each other. Success rates of 70–80% face still relatively high complication rates.

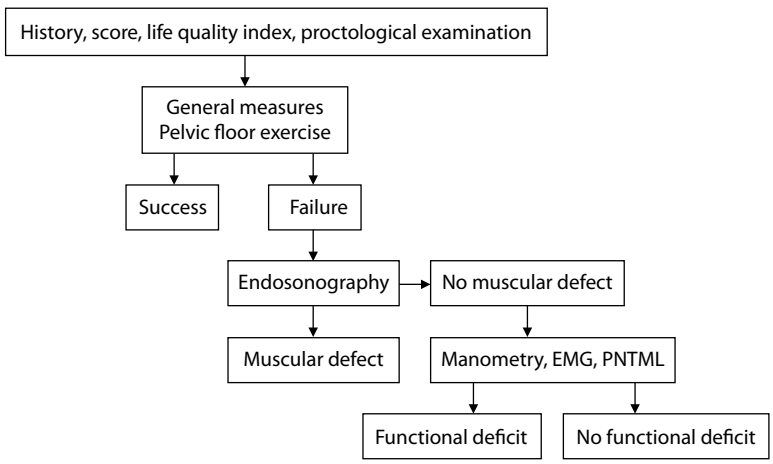


Fig. 6.1.8 Algorithm for diagnostics and conservative treatment

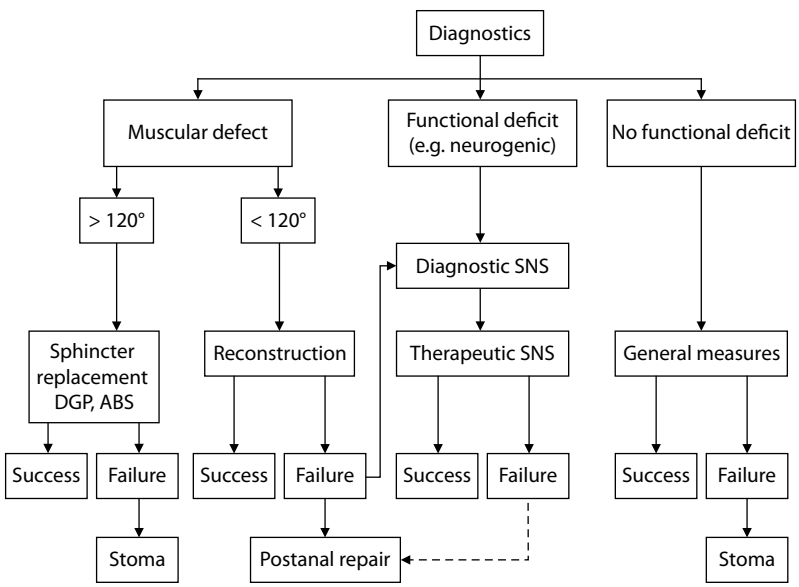


Fig. 6.1.9 Algorithm for surgical treatment

- For patients suffering from neurogenic incontinence, which is being diagnosed in increasing numbers, all traditional procedures show only low success rates despite modern technology. Conservative measures are mostly without any effect and postanal repair, which had been looked upon as a good option for a long time, only achieves satisfactory results in 20–25% of patients in long-term follow-up. Therefore here sacral nerve stimulation is already the first-choice treatment.

Suggested Reading

1. Baeten CG, Konsten J, Spaans F et al (1991) Dynamic graciloplasty for treatment of faecal incontinence. Lancet 338:1163–1165
2. Bannister JJ (1987) Effect of aging on anorectal function. Gut 28:353–357
3. Felt-Bersma RJF, Cuesta MA (1994) Faecal incontinence 1994: which test and which treatment. Neth J Med 44:182–188
4. Halverson AL, Hull TL (2002) Long-term outcome of overlapping anal sphincter repair. Dis Colon Rectum 45:345–348
5. Herold A (2002) Anale Inkontinenz. In: Brühl, Herold, Wienert (eds) Aktuelle Proktologie. UNI-MED Science 2002, Bremen
6. Jorge JMN, Wexner SD (1993) Etiology and management of fecal incontinence. Dis Colon Rectum 36:77–97
7. Jost WH, Raulf F, Mielke U, Schimirgk K (1992) Rationelle neurologische Diagnostik bei Stuhlinkontinenz. Z Ges Inn Med 47:154–158
8. Karulf RE, Coller JA, Bartolo DCC (1991) Anorectal physiology testing. A survey of availability and use. Dis Colon Rectum 34:464–468
9. Madoff RD (2004) Surgical treatment options for fecal incontinence. Gastroenterology 126:S48–S54
10. Madoff RD, Parker SC, Varma MC, Lowry AC (2004) Faecal incontinence in adults. Lancet 364:621–632
11. Matzel KE, Besendörfer M (2006) Surgery for fecal incontinence. In: Cardozo L, Staskin D (eds) Textbook for female urology and urogynecology, 2nd edn. Taylor and Francis, London, pp 1119–1138
12. Matzel KE, Stadelmaier U, Hohenfellner M, Gall FP (1995) Electrical stimulation of sacral spinal nerves for treatment of faecal incontinence. Lancet 346:1124–1127
13. Niriella DA, Deen KI (2000) Neosphincters in the management of faecal incontinence. Br J Surg 87:1617–1628
14. Orrom WJ, Miller R, Comes H, Duthie G, Mortensen NJMcC, Bartolo DCC (1991) Comparison of anterior sphincteroplasty and post anal repair in the treatment of idiopathic fecal incontinence. Dis Colon Rectum 34:305–310
15. Rockwood TH, Church JM, Flesahman JW et al (1999) Patient and surgeon ranking of severity of symptoms associated with fecal incontinence: the fecal incontinence severity index. Dis Colon Rectum 42:1525–1532
16. Rockwood TH, Church JM, Fleshman JW et al (2000) Fecal incontinence quality of life scale: quality of life instrument for patients with fecal incontinence. Dis Colon Rectum 43:9–17
17. Rudolph W, Galandiuk S (2002) A practical guide to the diagnosis and management of fecal incontinence. Mayo Clin Proc 77:271–275
18. Tjandra, J, Kim L, Matzel KE (2004) Sacral nerve stimulation: an emerging treatment for fecal incontinence. ANZ J Surg 74:1098–1106
19. Vaizey CJ, Norton C, Thornton MJ, Nicholls RJ, Kamm MA (2004) Long-term results of repeat anterior anal sphincter repair. Dis Colon Rectum 47:858–863
20. Wong WD, Jensen LL, Bartolo DCC et al (1996) Artificial anal sphincter. Dis Colon Rectum 39:1345–1351
21. Zorcolo L, Covotta L, Bartolo DCC (2005) Outcome of anterior sphincter repair for obstetric injury: comparison of early and late results. Dis Colon Rectum 48:524–531

6.2 Constipation

PETER BUCHMANN

6.2.1 Aetiology

The term constipation covers several forms and causes of impaired defaecation. The differentiation between acute and chronic constipation is important (Fig. 6.2.1).

- An *acute constipation* is the sudden inability to empty the bowel. The most common reasons are colonic obstructions (carcinoma, inflammation) or painful anal lesions that lead to sphincter spasm or the inability to relax (e.g. fissure-in-ano, intersphincteric abscess). In particular diverticulitis and colonic carcinoma can lead to a mechanical colonic ileus (obstruction).
- In *chronic constipation* defaecation is irregular with a frequency of two or less evacuations per week. Another definition is "straining at stool for more than 25% of the time". Chronic constipation itself can divided into:
  - Colonic slow-transit constipation
  - Outlet obstruction (Chap. 6.3)

In this chapter, we will concentrate on slow-transit constipation.

6.2.1.1 Colonic Constipation

Colonic constipation is classified into:
- Extracolonic causes
- Intracolonic causes

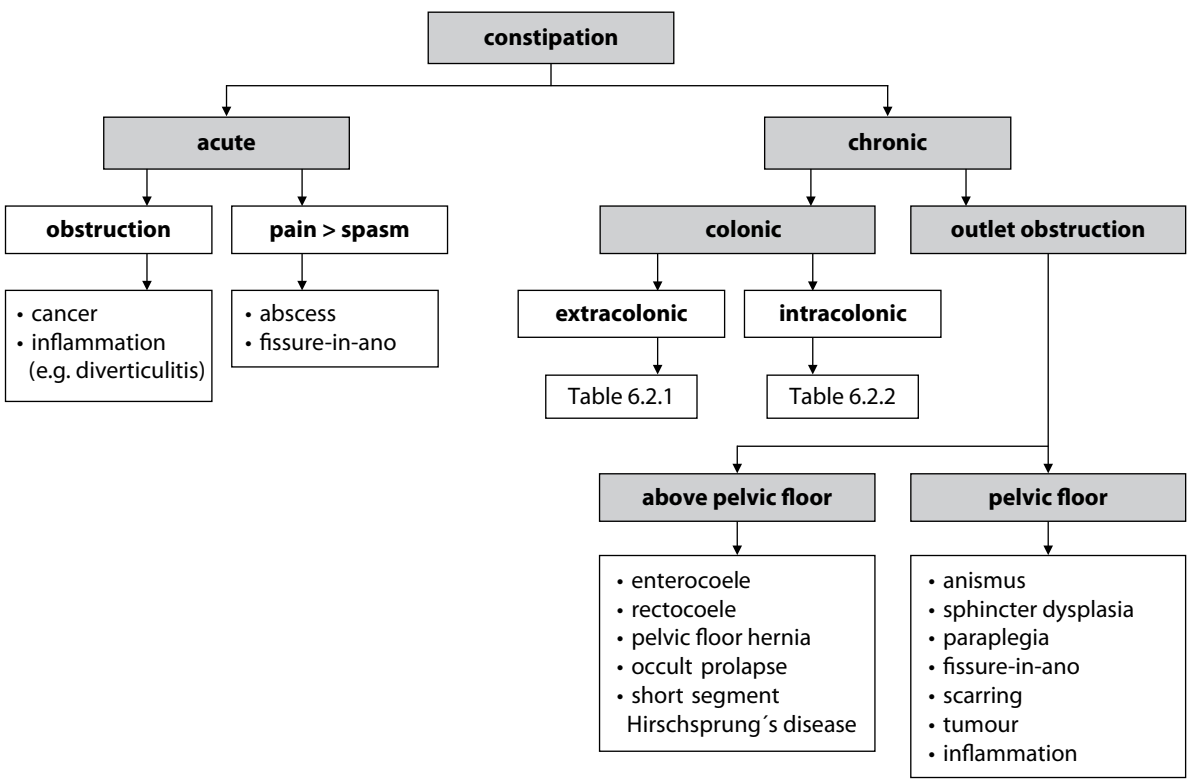


Fig. 6.2.1 Constipation, forms and causes

Table 6.2.1 Extracolonic causes of chronic constipation (from Pemberton 1992)

Faulty diet and habits	**Psychiatric factors**
Inadequate bulk (fibre)	Depression
Lack of physical exercise	Psychoses
Ignoring the call to stool (life style, poor life conditions)	Anorexia nervosa
Pharmacological factors	**Neurological factors**
Analgesics	Iatrogenic
Antacids	Resection of nervi erigentes
Anticholinergics	Bed rest
Anticonvulsants	Spinal
Antidepressants	Neoplasm
Antiparkinson agents	Lumbosacral cord trauma
Diuretics	Spinal cord trauma
Ganglionic blockers	Paraplegia
Hypotensives (monoamine oxidase inhibitors)	Multiple sclerosis
Iron	Tabes dorsalis
Laxative abuse	Shy-Drager syndrome
Metallic intoxication (arsenic, lead, mercury, phosphorus)	Meningocele
Opiates (especially codeine)	Cerebral
Psychotropics (especially phenothiazines)	Neoplasm
Metabolic and endocrine factors	Stroke
Amyloidosis	Parkinson's disease
Diabetes mellitus	Peripheral
Hypopituitarism	Autonomic neuropathy
Hypothyroidism	Ganglioneuromatosis (von Recklinghausen's disease)
Hypercalcaemia	
Hypokalaemia	
Hyperparathyroidism	
Pheochromocytoma	
Pregnancy	
Porphyria	

The different aetiologies of extracolonic causes are summarised in Table 6.2.1. The intracolonic causes of chronic constipation (Table 6.2.2) refer to the current knowledge of colonic wall morphology (see Chap. 2.1). But tabular listing of causes can be limited as seen in chronic intestinal pseudo-obstruction (CIPO). CIPO can originate from a visceral neuropathy but also from a visceral myopathy. Degenerative causes (enteric ganglionitis) as well as inflammatory causes (enteric leiomyositis) are other potential causes. We accordingly refer to CIPO in different sections.

6.2.1.2 Functional Constipation

Functional constipation is defined according to the Rome II diagnostic criteria for functional bowel disorders (Table 6.2.3). In relation to these criteria a functional constipation can result from different causes of both colonic constipation and outlet obstruction. Irritable bowel syndrome needs to be considered as a differential diagnosis, as intermittent constipation can be a symptom of this syndrome. IBS is explained in a separate chapter (see Chap. 6.5).

Table 6.2.2 Intracolonic causes of chronic constipation

Enteric nervous system
Aganglionosis (e.g. Hirschsprung's disease, megacolon/megarectum)
Hypoganglionosis (e.g. slow-transit constipation)
Intestinal neuronal dysplasia
Enteric ganglionitis (e.g. chronic intestinal pseudo-obstruction)
Smooth muscle
Generalised visceral myopathy (e.g. chronic intestinal pseudo-obstruction)
Fibrotic transformation (e.g. chronic intestinal pseudo-obstruction)
Enteric leiomyositis (e.g. chronic intestinal pseudo-obstruction, megacolon)
Systemic disorders
Amyloidosis
Scleroderma

Table 6.2.3 Diagnostic criteria for functional constipation according to Rome II. For at least 12 weeks, which need not be consecutive, in the preceding 12 months two or more of the criteria should be present

1.	Straining in more than one of four defaecations
2.	Lumpy or hard stools in more than one of four defaecations
3.	Sensation of incomplete evacuation in more than one of four defaecations
4.	Sensation of anorectal obstruction/blockage in more than one of four defaecations
5.	Manual manoeuvres to facilitate more than one of four defaecations (e.g. digital evacuation, support of the pelvic floor)
6.	Less than three defaecations/week
7.	Loose stools are not present and there are insufficient criteria for irritable bowel syndrome (IBS)

6.2.2 Incidence/Epidemiology

- The incidence of constipation is unknown. Studies on the frequency of constipation are difficult due to the variety of forms and causes of constipation (Fig. 6.2.1).
- There is consensus about the rising constipation rate with increasing age in various studies; nevertheless even this finding is debatable.
- Data about the rate of chronic constipation depend on the diagnostic criteria. In 99% of a healthy population bowel movements occurs 3 times per week to 3 times per day. If this is defined as normal, the constipation rate is about 1%. However, rates up to 20% have been described. Self-reported constipation includes hard faeces, heavy straining and also rare evacuation leading to rates ranging from 2% to 28%.
- Women are more affected than men (21% women versus 8% men).
- The socioeconomic relevance is shown in a survey with more than 10,000 persons. The prevalence of constipation in this study is 28%, i.e. 55 million people in the USA.
- It remains questionable whether functional constipation correlates with the civilisation standard, standard of living, alimentary habits or even genetic factors. Burkitt reported that Africans who live in rural areas as herdsmen, living on vegetable nutrition, have regular defaecations. By migrating into South African urban areas and adapting to low-fibre, industrialised diets they develop constipation problems.

6.2.3 Classification

One classification of chronic constipation is given in Fig. 6.2.1. Another is as follows:

1. Chronic constipation
   a. Functional constipation
   b. Slow-transit constipation
   c. Hirschsprung's disease
   d. Idiopathic megacolon/megarectum
2. Impaired defaecation reflex
   a. Neural disorder (paraplegia, iatrogenic damage of the hypogastric plexus [rectal akinesia])
   b. Motor disorder
   c. Anismus (spastic pelvic floor syndrome)
3. Impaired defaecation stimulation
   a. Intussusception
   b. Rectocele

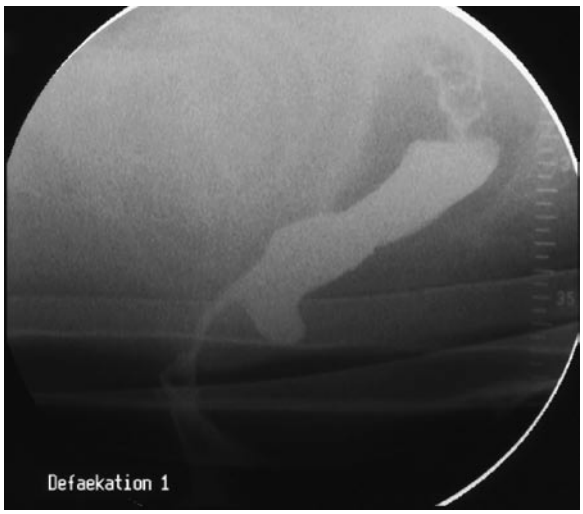


Fig. 6.2.2 Pelvic floor hernia

4. Impaired distal passage
   a. Enterocele
   b. Intussusception
   c. Pelvic floor hernia (Fig. 6.2.2)
   d. Sphincter dysplasia (Fig. 6.2.3)
   e. Short segment Hirschsprung's disease

The variety of classifications and the difficulty to precisely separate causes and effects of intestinal motion and defaecation reflect the complexity of colorectal and anal functions. For therapeutic decision making identifying a cause in a particular case is more important than the classification (Tables 6.2.1, 6.2.2).

6.2.4 Diagnostics

The diagnostic algorithm is summarised in Fig. 6.2.4.

6.2.4.1 Patient's History

A first impression of the extent/severity of constipation is obtained by addressing the following issues:

- Frequency of bowel movements
- Stool consistency
- Necessity to strain
- Amount of stool
- Incompleteness of emptying
- Defaecation stimulus without emptying
- Gas along with faeces

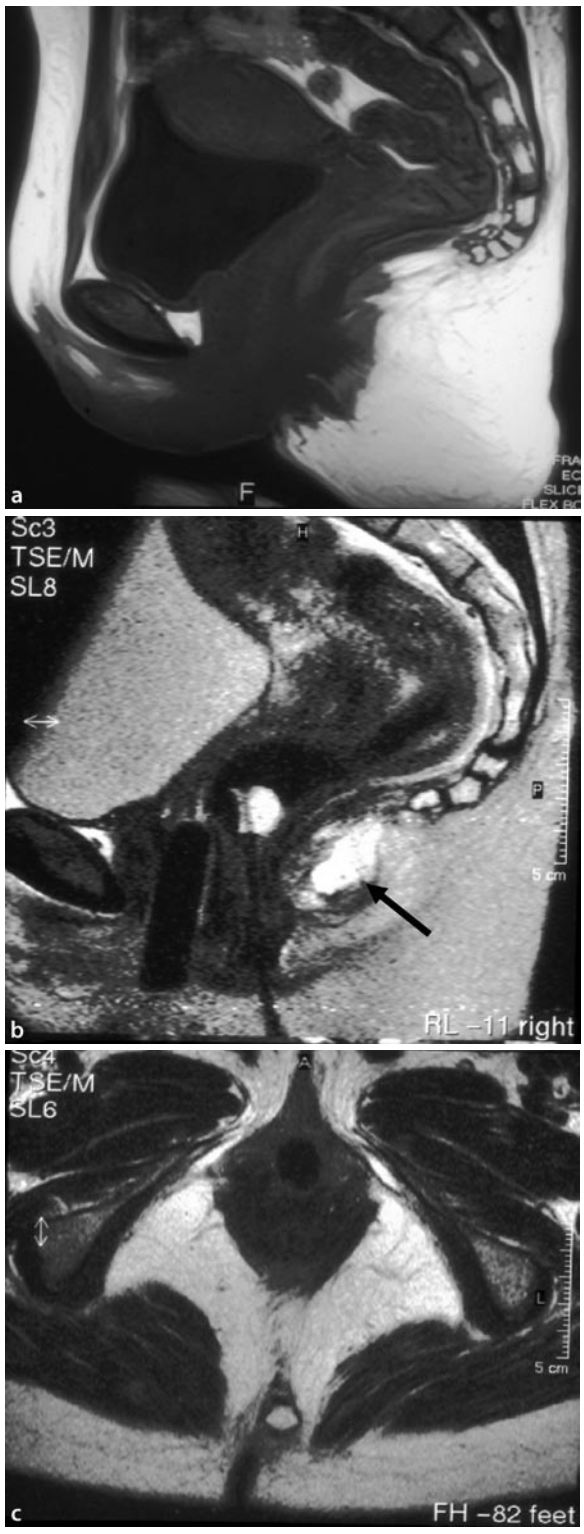


Fig. 6.2.3 Sphincter dysplasia (MRI). **a** Normal, with corpus anococcygeum. **b**, **c** Corpus anococcygeum inserts in subcutis *(arrow)*

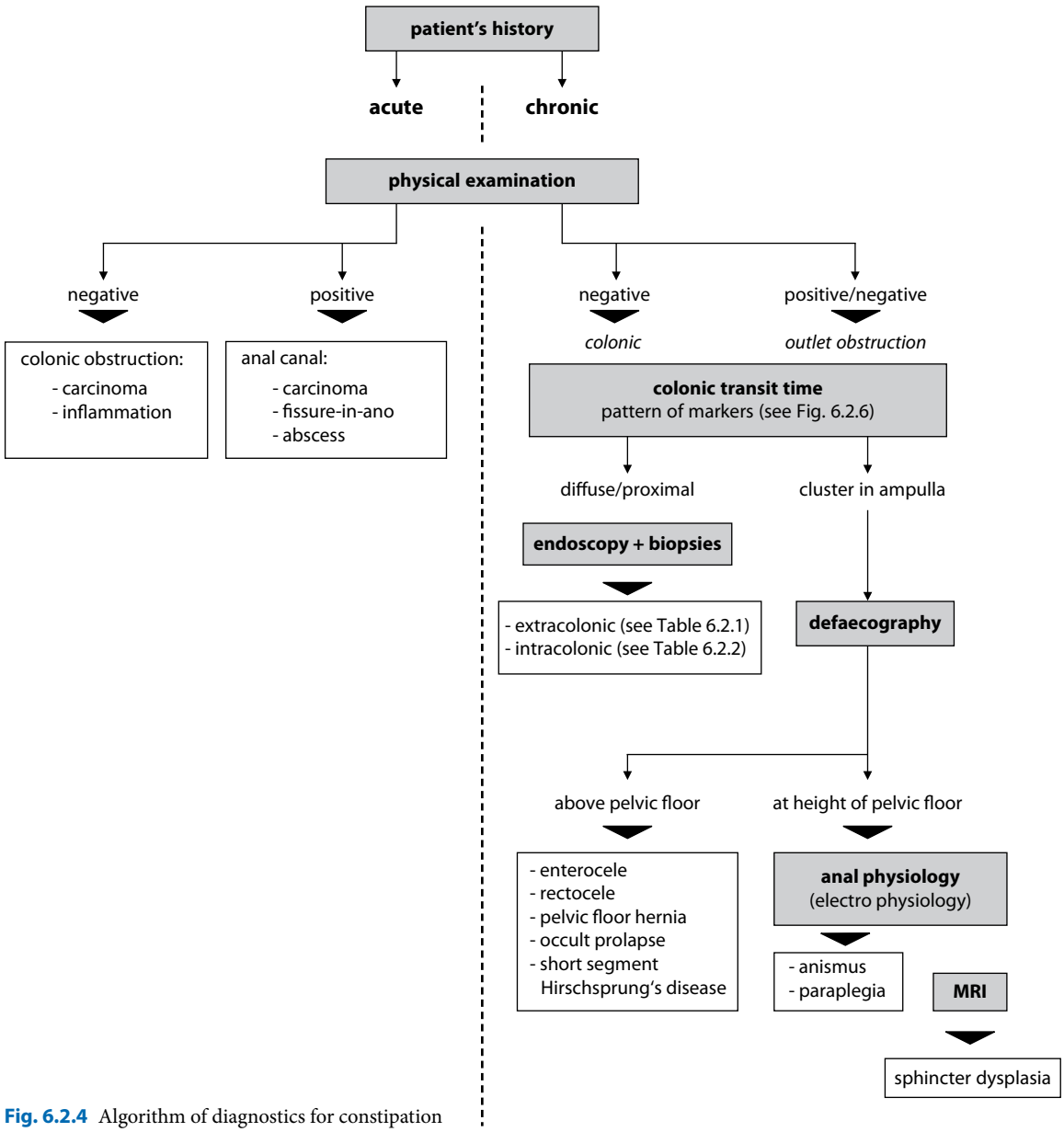


Fig. 6.2.4 Algorithm of diagnostics for constipation

The next step is to exclude extracolonic causes (Table 6.2.1). Standard questions are itemised to help in getting detailed information on defaecation behaviour (Table 6.2.4). To objectify the complaints a stool protocol is recommended that has to be completed over several weeks and contains information about frequency of bowel movements and stool consistency (Fig. 6.2.5). This protocol is helpful in differentiating slow-transit constipation from outlet obstruction.

6.2.4.2 Physical Examination

By means of abdominal examination any distended as well as palpable stool-filled colon sections are searched. The proctological examination consists of:

- *Inspection*: descensus perinei, perianal dermal changes, position of the anus within the perianal pigmentation zone (anteriorly displaced anus)

Table 6.2.4 Specific questions to assess constipation (adapted from Pfeifer et al. 1996)

Frequency of bowel movements	Once or twice every 1–2 days
	Twice per week
	Less than once per week
	Less than once per month
Consistency of bowel content, meteorism, flatulence	See Fig. 6.2.5
Difficulty, painful evacuation effort	Always
	Usually
	Sometimes
	Rarely
	Never
Pain, abdominal pain during defaecation	Always
	Usually
	Sometimes
	Rarely
	Never
Time (min) spent on the lavatory per attempt	Less than 5
	5–10
	10–20
	20–30
	More than 30
Induction of defaecation	Same time every day
	After breakfast, cigarette, coffee
	Compulsion
Position on the lavatory (toilet seat)	
Assistance, use of help	Digital help or enema
	Stimulative laxatives
	Without assistance
	Straining
Failure, unsuccessful attempts of evacuation per 24 h	Never
	Once to three times
	Three to six times
	Six to nine times
	More than nine times
History, constipation duration (years)	0
	1–5
	5–10
	10–20
	More than 20

day												
	time											
	consistency											
	time											
	consistency											
	time											
	consistency											
	time											
	consistency											
	time											
	consistency											
	time											
	consistency											

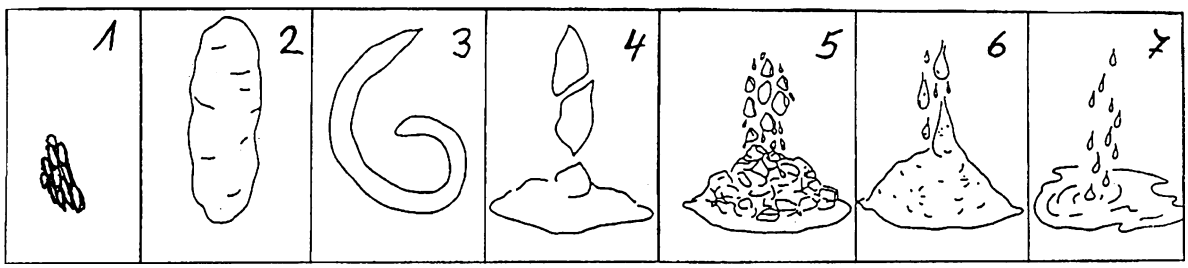


Fig. 6.2.5 Protocol of bowel habits

- *Functional examonation*: during active increase of intra-abdominal pressure/press act: haemorrhoidal/anal prolapse, rectal prolapse, vaginal prolapse
- *Brief neurological examination*: comparison of perianal sensation of the dermatomes S5 to S3 and sensation of the upper limb, cutanoanal reflex (pin prick)
- *Digital rectal examination*: tonus of the sphincter muscle, anterior rectocele, intussusception or enterocele when pressing (also bimanual rectal vaginal examination), solitary rectal ulcer
- *Proctoscopy*: withdrawal of the instrument while the patient is pressing: haemorrhoidal or rectal prolapse, prolapse of the anterior rectal wall as in the rectocele

6.2.4.3 Colonic Transit Time

- Determination of colonic transit time means to investigate the duration of the passage of a stool sample from the caecum to final emptying.
- Usually radio-opaque markers or scintigraphic investigation with technetium-99m or indium-111 are applied. One common technique is to apply on 6 successive days one capsule of ten markers and to take an x-ray of the abdomen on the 8th day (after 168 h) (Fig. 6.2.6). Transit time is calculated by the formula: colonic transit time in hours = total of visible markers × 2.4. The standard time for women is 70 h, and for men is 60 h. Other techniques following the same principle are used.
- Transit time studies are helpful to distinguish between slow-transit constipation (colonic inertia) and outlet obstruction.
- Delays in passage, in certain sections of the colon, can be recognised by accumulation of ingested markers. However, this investigation does not give any information about the aetiology of the constipation.

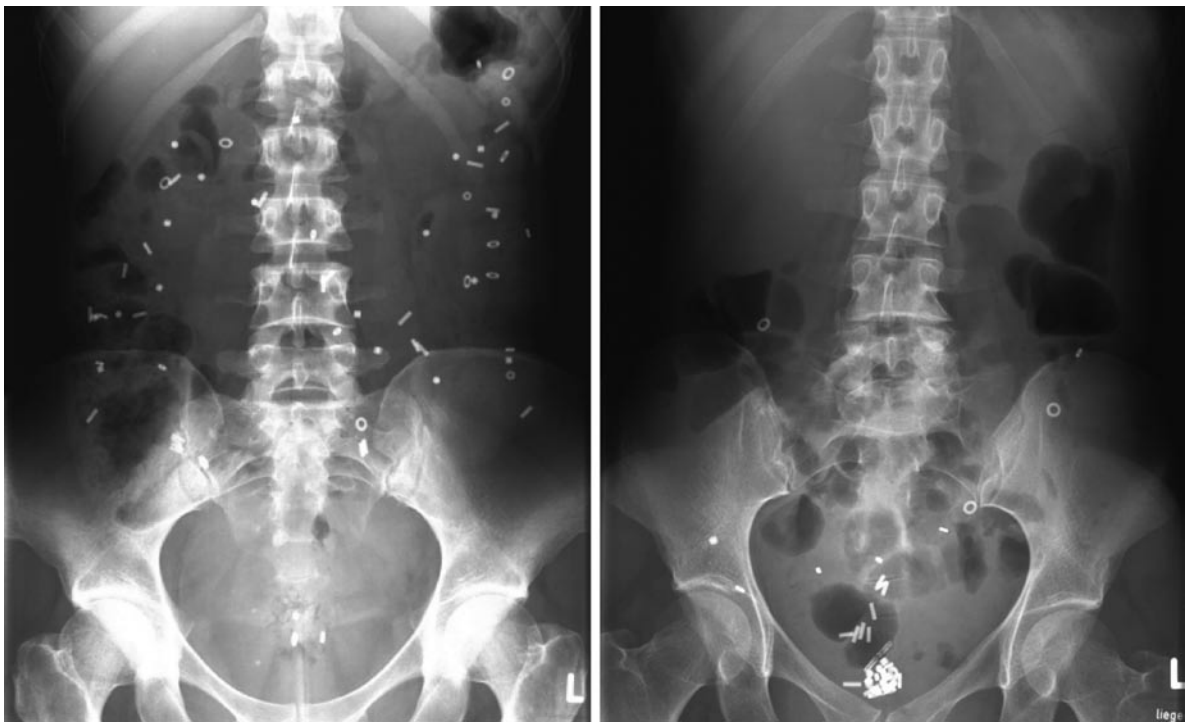


Fig. 6.2.6 Colonic transit time. *Left* Inertia coli. *Right* Outlet obstruction

Table 6.2.5 Indications for defaecography (from Buchmann and Brühlmann 1992)

Symptoms	
Feeling of incomplete evacuation	+
Blocked evacuation	+
Heaviness, "perineal mass"	+
Heavy straining during defaecation	+
Need for digital assistance	+
Chronic constipation	(+)
Faecal incontinence	–
Objective findings	
Mucosal lesion of anterior rectal wall	+
Rectocele of more than 2 cm on palpation	+
Slow transit through distal part of colon	+
Intussusception as seen by rectoscopy	(+)
Suspicion of:	
Occult intussusception	+
Occult prolapse	+
Enterocele	+

6.2.4.4 Defaecography

- The dynamic examination of defaecation can be performed by conventional x-ray or by magnetic resonance imaging (MRI). The major advantage of MRI examination is the absence of radiation. On the other hand the radiation can be minimised in conventional x-rays by working with well-defined combinations of short video sequences and freeze images.
- In a consensus of experienced radiologists, colorectal surgeons and gastroenterologists a list of indications for defaecography was compiled (Table 6.2.5) which includes:
  - Rectocele
  - Intussusception
  - Rectal prolapse
  - Enterocele
  - Cul de sac with defaecation block or in combination with rectal prolapse or vaginal prolapse
  - Hernias of the pelvic floor
- To capture all the pathological changes, x-rays from the side and ap should be performed. Concomitant contrast filling of the bladder and the small bowel are advisable.

6.2.4.5 Anorectal Manometry

The following parameters can be determined in an anorectal laboratory with anorectal manometry:

- Resting, squeeze and straining pressure
- Rectal perception (threshold, constant feeling, need to defaecate)
- Rectal compliance
- Rectoanal inhibitory reflex
- Balloon expulsion

6.2.4.6 Electrophysiological Examinations

- Electromyography is needed to evaluate the coordination of the muscles during the defaecation act, e.g. in anismus an active contraction of the external anal sphincter is assessed during the straining sequence.
- In mapping for sphincter lesions the electromyogram has lost its diagnostic relevance since the morphology of the sphincter can be assessed more precisely by ultrasound.
- The pudendal nerve terminal motor latency in the context of a constipation examination is irrelevant.

6.2.4.7 Endoscopy and Biopsy

- Prior to an operation because of constipation a colonoscopy is mandatory to exclude additional pathologies.
- In cases of suspected intracolonic constipation biopsies are gained through colonoscopy. According to the clinical signs the extent/level of the biopsy has to be chosen. In general multilevel biopsies are needed, for example the extension of an aganglionosis in Hirschsprung's disease can thus be specified.

6.2.4.8 Magnetic Resonance Imaging

- Magnetic resonance imaging, as mentioned above, is performed as a dynamic investigation of defaecation.
- The considerations pointed out in the section on defaecography on an examination in the lying position have to be taken into account.
- Static MRI is appropriate to depict the specific underlying anatomy of the pelvic floor in outlet obstruction.
- In particular in anal sphincter dysplasia the anococcygeal body is best demonstrated in the sagittal plane, the missing fixation at the coccygeal bone becoming obvious (Fig. 6.2.3).

6.2.4.9 Psychosocial Evaluation

- The influence of psychological and social factors on defaecation is undoubted but difficult to define.
- Without a doubt formative experiences in life (sexual harassment, torture, lack of privacy) can lead to impaired defaecation.
- Depending on the history and patient's presentation, psychological and/or psychiatric evaluation is advisable, especially before engaging in surgery.
- A patient who agrees to psychological or psychiatric analysis immensely supports the finding of the optimal therapy. Therefore, a close cooperation between surgeon, gastroenterologist and psychological therapist is most helpful.

6.2.5 Therapy

- The treatment of constipation has to be adapted according to aetiology and by practical means has to be designed as a step-by-step approach.
- First the faulty habits and several other extracolonic causes (Table 6.2.1) should be discussed.
- Above all, pharmaceuticals should be eliminated as far as possible, though this is not always possible (e.g. Parkinson's disease).
- Correction of alimentation and of the diet are also basic factors in the treatment of constipation.
- In addition to sufficient fibre intake in the daily nutrition plan, an adequate hydration during the meals is important, so that the fibres can soak and do not congest.
- Various dietary fibres and swelling agents are merchandised. Frequently this treatment causes initial flatulence that keeps the patients from continuation of the therapy. However, this disorder is dose-related and often is temporary.
- Physical activity is considered to be even more effective. In a series of 3,327 women with relevant constipation, daily activity reduced the risk of constipation by two thirds compared to only one third with a high fibre diet.

6.2.5.1 Medical Treatment

- Various laxatives are merchandised for constipation. In particular long-term treatment is questionable although the impairing effect on the enteric nervous system as reported in the past is questioned again

today. However, in outlet obstruction the use of oral laxatives is not recommended.
- Suppositories have their indication as lubricants and initiators of defaecation. Carbon dioxide suppositories induce a defaecation stimulus by gas production in the ampulla recti and support thereby an impaired rectal perception.
- Sphincter pressure reducing ointments should be tested in pelvic floor spasticity as they are used in the treatment of anal fissures (e.g. calcium antagonists, botulins).
- Biofeedback training aiming for sphincter relaxation has always been recommended in the treatment of outlet obstruction. A prerequisite is the diagnosis of anismus or spastic pelvic floor syndrome.
- In therapy-refractory constipation a regular application of enemas is helpful. The range is from miniclysma to daily retrograde irrigation with special apparatus, used for stoma retrograde irrigation.

6.2.5.2 Surgical Treatment

Intracolonic Causes

- The only adequate operation in constipation with slow transit time due to intracolonic causes (Table 6.2.2) is a colectomy with an ileorectal anastomosis. The operation can be performed open or laparoscopically.
- Caecostomy as well as ileosigmoidostomy has been abandoned and rectal anastomosis should not be less than 7–10 cm from the anal verge because of the risk of frequency and incontinence.
- The indication for colectomy with ileorectal anastomosis is given after exclusion of an outlet obstruction or pseudo-obstruction, and after consequent conservative treatment applying the various modalities and psychological evaluation have failed. Ultimately only a small minority of patients presenting with constipation are appropriate candidates for resective surgery.
- However, large studies (n=74) showed an increased quality of life in 90% of patients after surgery with an average follow up of 6 years. Twelve per cent of the patients suffered from a postoperative prolonged ileus and 9% developed a long-term intestinal obstruction. In a small trial of 17 women follow-up investigation after an average of 6 years (± 27 months) using the SF-36 health survey showed that quality of life had increased but was significantly lower than that of the general population ($p < 0.005$). Mean complaints were bloating (61%), abdominal pain (41%) and occasional incontinence to gas or liquid stool (47%).
- In children antegrade continence enema through an appendicostomy are advocated. In adults a similar procedure is proposed using a modified Marsh and Kiff ileostomy.
- Preliminary data with sacral nerve stimulation demonstrates promising results not only in incontinence but also in slow-transit constipation. Therefore, a test with sacrally placed electrodes and external stimulation seems to be indicated before any type of invasive, especially resective surgery.

Long-Segment Morbus Hirschsprung, Megacolon, Megarectum

- The general principles of operations in Hirschsprung's disease are either the bypassing of the aganglionic segment or its removal. In a bypass operation the proximal colon has to come close to the anal sphincter. Generally this surgery is performed in infants. The alternative is to resect the pathological segment. This, in the most extensive cases, can result in proctocolectomy with a J-pouch anal anastomosis. This procedure is also appropriate to treat patients who are still symptomatic after failed bypass operation.
- Removal of the pathologically altered segment is also the main goal in megacolon or megarectum. In megarectum a coloanal anastomosis, in megacolon an ileorectal anastomosis and in those patients with dilatation of the colon and rectum a restorative proctocolectomy is most suitable. One of the major problems is to determined the extent of resection as the histological alteration of the colonic wall can only be confirmed on the specimen, not by endoscopic means.
- In megarectum, alternatively, ventral reduction rectoplasty offers a short-term success rate of 83%.
- The colo- or ileostomy should be the ultimate solution in cases of untreatable disorders.

Suggested Reading

1. Altomare DF, Rinaldi M, Rubini D et al (2007) Long-term functional assessment of antegrade colonic enema for combined incontinence and constipation using a modified Marsh and Kiff technique. Dis Colon Rectum 50:–1023–1031
2. Buchmann P, Brühlmann W (1992) Anorectal investigation of functional disorders with special respect to defecography. Springer, Heidelberg
3. Buchmann P, Bruhin R, Sartoretti C, De Lorenzi D (1997) Sphincteropexy: a new operation to cure outlet obstruction in adults. Dig Surg 14:413–418
4. Burkitt DP, Walker ARP, Painter NS (1972) Effect of dietary fibre on stool and transit-times, and its role in the causation of disease. Lancet 2:1408–1411

5. Dinning PG, Fuentealba SE, Kennedy ML et al (2007) Sacral nerve stimulation induces pan-colonic propagating pressure waves and increases defecation frequency in patients with slow-transit constipation. Colorectal Dis 9:123–132
6. Dukas L, Willett WC, Giovannucci EL (2003) Association between physical activity, fiber intake, and other lifestyle variables and constipation in a study of women. Am J Gastroenterol 98:1790–1796
7. Gladman MA, Scott SM, Lunniss PJ, Williams NS (2005) Systematic review of surgical options for idiopathic megarectum and megacolon. Ann Surg 241:562–574
8. Kamm MA, Lennard-Jones JE (1992) Pathophysiology of constipation. In: Henry MM, Swash M (eds) Coloproctology and the pelvic floor. Butterworths, London
9. Locke GR, Pemberton JH, Phillips SF (2000) AGA technical review on constipation. Gastroenterology 119:1766–1778
10. Nyam DC, Pemberton JH, Ilstrup DM, Rath MD (1997) Long-term results of surgery for chronic constipation. Dis Colon Rectum 40:273–279
11. Pemberton JH (1992) Management of constipation. In: Henry MM, Swash M (eds) Coloproctology and the pelvic floor. Butterworths, London
12. Pfeifer J, Agachan F, Wexner SC (1996) Surgery for constipation. Dis Colon Rectum 39:444–460
13. Rao SS, Tuteja AK, Vellema T et al (2004) Dyssynergic defecation: demographics, symptoms, stool pattern, and quality of life. J Clin Gastroenterol 38:680–685
14. Sewart WF, Liberman JN, Sandler RS et al (1999) Epidemiology of constipation (EPOC) study in the United States: relationship of clinical subtypes to socioeconomic features. Am J Gastoenterol 94:3530–3540
15. Thompson WG, Longstreth GF, Drossman DA et al (1999) Functional bowel disorders and functional abdominal pain. Gut 45(suppl 2:II):43–47

6.3 Defaecation Disorders

PAUL-ANTOINE LEHUR, GUILLAUME MEURETTE

6.3.1 Introduction

- Defaecation disorders refer to the inability to efficiently and rapidly empty the rectum of its contents on demand.
- Defaecation disorders are a source of discomfort and impair significantly the quality of life of affected patients.
- Management requires a thorough clinical and functional assessment for identification of a cause.
- Medical treatment and pelvic floor retraining are first-line treatments.
- Various types of surgical approaches currently designed to correct anatomical abnormalities and improve function can be carried out in selected patients.

6.3.2 Definition

6.3.2.1 Normal Defaecation

The process by which the rectum normally empties is complex. It requires a series of coordinated actions of the colon, rectum, pelvic floor and the anal sphincter muscles. Physiological steps of a successful evacuation of the bowel are as follows:

- Mass movement in the sigmoid colon moves a faecal bolus to the rectum and may initiate the call to defaecate. The sensation of rectal filling plays a key role in normal defaecation.
- Distension of the rectum results in relaxation of the internal anal sphincter (so-called rectoanal inhibitory reflex) and secondary reflex contraction of the external sphincter to prevent incontinence.
- Discrimination between solid or liquid stool and gas is allowed by exposure of the sensory receptor-rich anal transitional zone to the rectal contents. The rectoanal inhibitory reflex is therefore known as the "sampling reflex" and is of paramount importance in social behaviour.
- If socially convenient, defaecation can be attempted by adopting a sitting position. Flexion of the hips relaxes the pelvic floor and facilitates the passage of stools by opening the anorectal angle.
- Straining is obtained by contraction of the diaphragm and abdominal wall (Valsalva manoeuvre). It raises intra-abdominal and intrarectal pressure. Contraction of the rectal wall also participates in the pressure rise. Meanwhile, the anal sphincters and the puborectalis muscle relax. Tightening of the iliococcygeal muscles stabilises the levator plate to counterbalance the intra-abdominal push. Inversion of the pressure gradient between rectum and the anal canal allows stool evacuation.

6.3.2.2 Impaired Defaecation

- Impaired defaecation is a commonly reported symptom.
- It is covered by the general term of constipation that refers to "infrequent or qualitatively inadequate defaecation" when compared to the normal scheme.
- Defaecation disorders, also termed "outlet obstruction/delay" or "dyschesia", are integrated into the "Rome II" definition of chronic constipation (Table 6.3.1).
- The two categories of constipation, slow-transit constipation and outlet obstruction, frequently overlap, but it is important to differentiate between them for appropriate clinical management.

Table 6.3.1 'Rome II" definition of chronic constipation. Two or more of the following complaints for at least 12 months when not taking laxatives define a chronically constipated patient

1.	Straining during > 25% of bowel movements[a]
2.	Sensation of incomplete evacuation on > 25% of bowel movements[a]
3.	Hard or pellet-type stools on > 25% of bowel movements
4.	Less than three stools passed per week

[a]Symptoms 1 and 2 refer clearly to a defaecation disorder

6.3.3 Epidemiology

Even though the exact prevalence of outlet delay constipation type is unknown, it is recognised as a quite frequent health problem. In several community population surveys, the prevalence of symptoms compatible with outlet obstruction has been as high as 10%. It is accepted that about 30% of patients who present to their physician complaining of constipation demonstrate evidence of outlet obstruction. Studies from referral centres also show a higher incidence of outlet delay than slow-transit constipation (60% versus 30% with a combination of the two types of constipation in 5% of cases).

Defaecation disorders are significantly more frequent in women than in men. With advancing age prevalence increases in both sexes. The elderly population, especially women, are highly affected. The reasons for the female predisposition to evacuation problems include:

- Pelvic floor alteration related to childbirth with vaginal delivery
- Long-lasting excessive straining at stool
- Postmenopausal hormonal oestrogen deprivation
- Frequency of previous hysterectomy
- Association with urogenital prolapse and urinary incontinence
- Genetic predisposition to pelvic organ prolapse has also been evoked

6.3.4 Aetiology/Pathophysiology

Impaired defaecation may result from various functional and/or anatomical disorders combined in a complex syndrome still incompletely understood.

6.3.4.1 Functional Anal Obstacle

- Inappropriate contraction of the pelvic floor or ineffective relaxation of pelvic floor striated muscles on attempted defaecation impedes the passage of stool. Anal dyssynergia or anismus refers to this situation.
- Neurological disorders such as spine lesions and multiple sclerosis may also be responsible for functional obstacle.
- In some rare instances, functional obstacle is due to an ineffective inhibition of the internal anal sphincter: it is observed in Hirschsprung's disease, Chagas' disease and hereditary myopathy of the internal anal sphincter.

6.3.4.2 Rectal Inertia, Rectal Hyposensitivity, Megarectum

- The failure to raise intra-abdominal/intrarectal pressure to a sufficient level to allow defaecation is frequently found in elderly or debilitated patients and generates an accumulation of stools in the rectum forming faecaloma.
- In some conditions defined as "rectal inertia" or "megarectum" found in young patients, the rectum and often the distal sigmoid colon become very dilated and cannot be evacuated.
- Sensitive defects in rectal filling defining "rectal hyposensitivity" (blunted rectum) may be causative. Its causes include diabetes mellitus, multiple sclerosis, cerebrospinal disease or direct injury to the pelvic nerves during hysterectomy or following disc (L5–S1) surgery.

6.3.4.3 Excessive Perineal Descent

- Often associated with the preceding disorder in the elderly, perineal descent exceeding 4 cm is a factor in evacuation difficulties. It is due to weakness of the pelvic floor support.
- The severe stress to the nerves, ligaments and muscles of the pelvis during childbirth is considered to be causative.
- Perineal descent may be associated with sacral nerve damage, secondary muscular atrophy and eventually faecal incontinence leading to the so-called descending perineum syndrome.

6.3.4.4 Anatomical Defects and Deformity of the Rectal Reservoir

Besides functional disorders, anatomical abnormalities may lead to impaired rectal evacuation. Any prolapsing organ pressing on mechanoreceptors adjacent to the rectum may give the patient the perception of impending defaecation and disturb the normal evacuation process:

- Rectocele is defined as a herniation of the anterior rectal wall into the vagina
- Enterocele is the insinuation of a viscus (small bowel or sigmoid colon) between the posterior vaginal wall and rectum into a herniated Douglas pouch
- Rectal intussusception (also known as "internal procidentia" or "occult rectal prolapse") is defined as an incomplete, non-exteriorised rectal prolapse. Infolding of the rectal wall is a common finding in normal individuals, but high-grade intussusception reaching the anal canal may contribute to defaecation disorders

6.3.5 Diagnostics

6.3.5.1 Symptoms

History taking plays a key role in defining what gives the patient the most problems. Questions must assess:

- Presence of a call to defaecate (patients with colonic inertia will rarely have a need but patients with defaecation disorders will have the urge to defaecate daily)
- Bowel frequency, stool consistency and size
- Use of laxatives, suppositories and enemas
- Duration of the problem, circumstances in which it occurred
- Manoeuvres that the patient does to help him/herself (vaginal digitation suggests a rectocele, forward leaning on the toilet seat suggests an enterocele, massaging lateral to the anus suggests poor rectal contractility, enemas and/or suppositories may suggest megarectum, supporting the perineum is found in perineal descent)

Typical symptoms of obstructed defaecation, with variation according to the type of disorder, include:

- Inability to empty the rectum (sometimes even for soft or liquid stool)
- Excessive and prolonged straining efforts and time spent in toilets
- Feeling of incomplete and/or fragmented, unsatisfactory evacuation
- Pain and perineal discomfort in standing position and/or at defaecation
- Need for (intra-anal, perineal or vaginal) stimulation and manual evacuation
- Rectal bleeding and mucous discharge
- Use of laxatives, suppositories and enemas

These symptoms are best assessed on standardised questionnaires specifically designed for this purpose. A diary of gastrointestinal complaints and defaecation habits can be helpful. Faecal incontinence is also searched and scored if present. Abdominal pain and bloating may be present as constipation-predominant irritable bowel syndrome is frequently associated with defaecation disorders.

Associated urogynaecological symptoms including urinary incontinence, dyspareunia and manifestations of urogenital prolapse are identified. Proctological, obstetrical, gynaecological and urological past history is carefully traced. In selected cases, psychological or psychiatric advice is relevant, particularly if surgery is to be contemplated. Underlying personal problems are frequent and it is known that this patient population more often claim to be sexually abused in childhood and to be more depressed.

6.3.5.2 Examination/Clinical Findings

After abdominal examination, the patient is placed in the lithotomy position for a complete perineal and anorectal examination. The following must be clinically assessed:

- Descent/elevation of the perineum on command, at inspection. The inability to coordinate pelvic floor relaxation with failure of the perineum to descend more than 1 cm on straining (frozen perineum) is strongly in favour of anismus.
- Anal resting tone and squeeze pressure on digital examination—integrity of the sphincteric ring. Anismus is evoked in case of hypertonia. Faecal incontinence and soiling may result from low anal tone.
- Presence of anal stenosis.
- Presence of associated haemorrhoidal disease, mucosal or full-thickness prolapse. Insertion of a proctoscope allows visualisation of an anterior wall prolapse, internal prolapse or the beginning of an external prolapse at strain.
- Rectovaginal wall and anterior rectal wall to identify a rectocele or an enterocele, not always easy to distinguish on simple clinical grounds (vaginal and rectal examination, bidigital examination, speculum, standing position). Vaginal bulging is graded as I (intravaginal), II (reaching the introitus) or III (exteriorised). Rectoceles are also classified according to their position relative to the vagina: low (with thinning of the perineal body and sometimes anal sphincter disruption), middle and high (commonly associated with enterocele).
- Entire pelvic floor and relationship of the rectum to the remainder of the pelvic organs to document anterior compartment prolapse (uterine, cystocele or vaginal vault), urinary incontinence and poor vaginal trophicity.

6.3.5.3 Work-up

Most patients clinically identified as suffering from defaecation disorders require a series of tests assessing anorectal and colonic function for further management (Table 6.3.2). These methods used for evaluation of constipated patients give objective measurements of the colorectal function. However, their limitations must be kept in mind and results will be analysed in the light of symptoms and clinical findings.

The presence of an organic cause of constipation (e.g. cancer, stricture from any cause, etc.) will be eliminated by appropriate means (colonoscopy, barium enema). Information on standard gynaecological work-up (mammography, pelvic ultrasound, cervicovaginal stains) is obtained accordingly.

Table 6.3.2 List of tests eventually required when assessing disordered defaecation

- Dynamic defaecography
- Anorectal physiology tests
- Colonic transit time
- Endoanal ultrasound
- Electromyographic studies
- Urological work-up

6.3.5.4 Dynamic Defaecography

Different methods evaluate rectal emptying. Dynamic changes of the anatomical structures of the pelvis are studied during a simulated defaecation.

Standard Dynamic Defaecography

- Technique: A semi-solid artificial barium stool is injected into the rectum and concomitant filling of the small bowel (eventually vagina and bladder also) is obtained. The patient is placed on a specially designed commode. Lateral videoradiographs are taken before, during and after defaecation.
- Defaecographic parameters include: position of the pelvic floor, anorectal angle at rest, straining and evacuation, opening of the anal canal, time and completeness of emptying. Rectocele will be defined by its size, barium trapping in the rectocele and poor rectal evacuation (Fig. 6.3.1). Rectal intussusception is graded according to its distance from the anal canal. Enterocele can be identified. Non-relaxing puborectal muscle may evoke anismus.
- Results must be interpreted with caution and related to the symptoms and physical findings as small rectoceles and minor rectal intussusceptions occur in up to 50% of normal subjects and their clinical significance is unclear.

Dynamic Magnetic Resonance Imaging

- Its place is so far unproven.
- If available, this investigation may replace barium defaecography, as fast image acquisition yields data similar to standard defaecography without the need for radiation.
- It also helps to characterise associated pelvic organ prolapse (Fig. 6.3.2).

Defaecation Scintigraphy

- Efficiency of defaecation is measured by calculating the percentage of artificial radiolabelled stool evacuated from the rectum.
- Normal individuals evacuate 60% of stool in 10 s. Due to the limited availability of gamma cameras, use in clinical practice is not easy.

6.3.5.5 Anorectal Physiology Tests

Anorectal physiology tests include standard manometry, rectal sensation/rectal wall properties assessment and the balloon expulsion test.

- High resting anal pressures suggest the presence of anismus. Absence of the rectoanal inhibitory reflex raises the possibility of adult Hirschsprung's disease. Patients with defaecation disorders have inappropriate contraction of the pelvic floor and anal sphincter while straining.
- Rectal sensation and rectal wall properties can be tested by controlled balloon distension of the rectum. Recorded measures are the volume first experienced, the volume that elicits a desire to defaecate and the maximum tolerated volume.
- The balloon expulsion test is a cheap, easy-to-perform and quite reproducible method to assess the ability to empty the rectum. Failure to expel the balloon is often seen in patients with dysfunction of the pelvic floor and anismus.

6.3.5.6 Colonic Transit Time

- Colonic transit may be studied by several methods.
- The simplest and most popular involves the ingestion of radio-opaque markers. The markers are followed along the large bowel with abdominal radiographs.
- Patients with transit times greater than 72 h are classified as having slow-transit constipation. Scintigraphic methods to determine panintestinal transit are also available.

6.3.5.7 Endoanal Ultrasound

Endoanal ultrasound is required in case of faecal incontinence to document anal sphincter tears. It may impact the surgical approach.

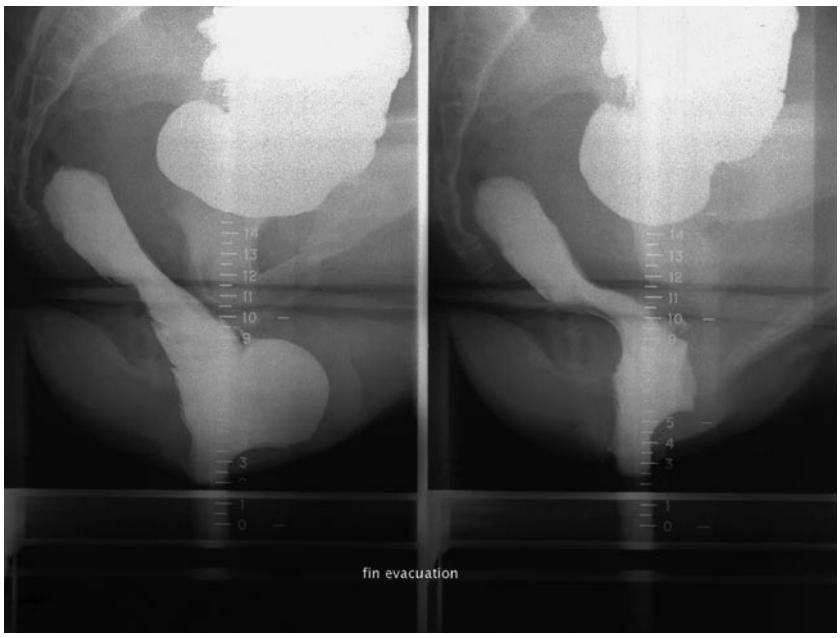


Fig. 6.3.1 Standard dynamic defaecography with small bowel barium filling. Evacuation series: rectocele and low-grade rectal intussusception, no enterocele, perineal descent. On the *right*, patient digitates to empty the rectocele

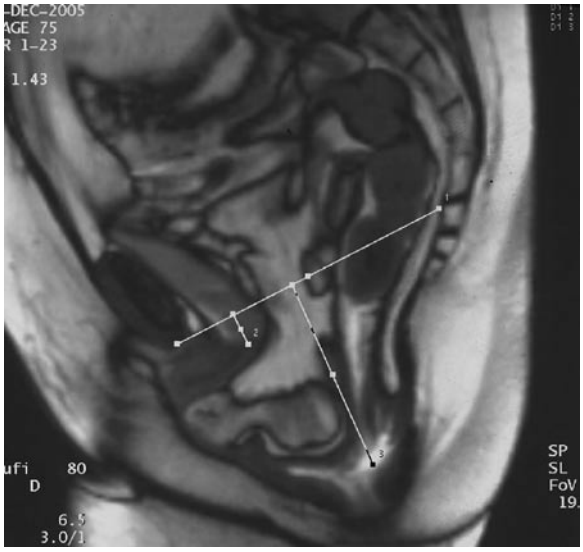


Fig. 6.3.2 Dynamic MRI. Large enterocele associated with a sigmoidocele. Normal aspect of the anterior compartment

6.3.5.8 Electromyographic Studies

Electromyographic (EMG) activity of the external anal and puborectalis muscles can be recorded either by needle or surface electrode to detect the absence of relaxation or inappropriate contraction of the sphincters during attempted expulsion. It is indicative of anismus, the EMG signal being then used during biofeedback therapy.

6.3.5.9 Urological Work-up

Voiding studies are needed in case of urinary incontinence or symptoms.

6.3.6 Therapy

6.3.6.1 Medical Treatment

- Dietary and hygienic measures are recommended as first-line treatment and cause an improvement of symptoms in about 30% of patients.
- Simple measures include increase in fibre (20–25 g/day) and in non-caffeinated, non-alcoholic fluids.
- Illustrated explanations of the defaecatory process and advice on the position on toilet seat, use of suppositories, small enemas and manual support of the perineum are simple and helpful primary care measures to reassure the patient.
- In case of rectal hyposensitivity and megarectum, treatment is usually the use of prokinetic suppositories or drugs and enemas.

6.3.6.2 Biofeedback Therapy/ Pelvic Floor Retraining

- Behavioural relaxation techniques may re-establish normal rectal expulsion. Patients with constipation secondary to pelvic floor dysfunction are guided through a retraining program to relax pelvic floor muscles during straining.
- It is a well-established (but still controversial) treatment modality.
- Several techniques are available: ambulatory or inpatient approach, microballoon system, surface EMG recording or anal EMG probe. Overall, two thirds of patients with anismus achieve success with pelvic floor retraining.

6.3.6.3 Surgical Treatment

- Surgical treatment of defaecation disorders concerns anatomical abnormalities with the intent that their correction will improve function. Therefore, surgically concerned disorders include, nearly exclusively:
  - Rectocele
  - Intussusception
  - Enterocele
- Approach can be from three directions:
  - From the rectum through the anal canal
  - From the vagina or perineum
  - From the abdomen either by Pfannenstiel laparotomy or laparoscopically

Transanal Approach

Transanal repair addresses the anorectal component of rectoceles. The patient is placed in the jack-knife or lithotomy position. The anal canal is dilated to expose the lower rectum.

- Option 1. Anterior (longitudinal or transversal) plicature of the rectal wall and resection of the excess mucosa allow correction of rectocele (Sullivan-Khubchandani).
- Option 2. Recently a stapled transanal rectal resection (STARR) procedure using two sets of PPH 01 stapler has been proposed. It allows an easy-to-perform resection of the anterior and posterior rectal wall correcting both rectocele and intussusception and restoring a normal shape to the rectal ampulla. The procedure is currently under investigation.

The internal Delorme operation has also been proposed to treat high-grade internal prolapse.

Transperineal/Vaginal Approach

- In contrast, the transvaginal/perineal approach to correct a rectocele uses a transverse perineal and/or a vertical vaginal incision.
- After exposing the whole of the rectovaginal septum, the anterior rectal wall is plicated from outside, vaginal sacroligamentopexy (Richter) can be done and the levator ani are plicated (levatoroplasty), taking great care not to reduce the vaginal introitus.
- In large or recurrent defects, some authors proposed to insert various types of mesh to add support. This approach allows also for sphincter repair in addition to rectocele repair.
- Resection of the Douglas pouch can also be done through this approach.

Transabdominal Approach

- Through an open or laparoscopic approach, mesh inserted in the rectovaginal septum suspended without tension to the promontory (vaginorectopexy) allows correction of deep enterocele, sigmoidocele and rectocele, gives support to associated rectal intussusception and elevates a deep Douglas pouch.
- This technique differs from standard rectopexy as it avoids dorsolateral mobilisation of the rectum and does not endanger the pelvic autonomic innervation.
- Some authors support a combined abdominal and perineal approach to achieve a complete rectovaginal suspension (Zaccharin). Rectovaginal mesh suspension is easily combined on demand with bladder and anterior vaginal wall suspension for urogenital prolapse.

Results/Outcome

- The level of evidence in the literature is poor regarding the surgical approach for defaecation disorders. A wide spectrum of results has been reported, for instance, for rectocele repair, combined with variable criteria for surgery, and no difference has been clearly shown when comparing the transrectal and transvaginal/perineal approaches. Controlled studies are strongly requested to better define recommended attitudes in this field.
- The outcome of surgery is often hard to predict. The patient must be informed and understand that whatever technique is tried, there is the risk of failure.
- Patients should be given realistic expectations and must be warned that symptoms may persist following surgery. Incomplete or absence of resolution of the problem as well as occurrence of new symptoms of variable severity may define failure of the surgical approach.
- Complications following transanal repair, including onset of faecal incontinence and a decrease in sphincter pressures, have been reported.
- Dyspareunia may complicate transvaginal repair.
- Increased constipation frequently occurs following abdominal mesh suspension and rectopexy, especially when treating rectal intussusception, making patients sometimes worse than before surgery.

Indications for Surgery/Special Conditions

In defaecation disorders, surgery can be discussed for patients who are unresponsive to dietary measures and rehabilitative therapy.

- *Non-relaxing puborectalis or anismus*. Surgical treatment for this condition (uni- or bilateral division of sphincter muscle or puborectalis) has been abandoned. Some benefit can be obtained with botulinum toxin injection.
- *Perineal descent*. It is not a surgical condition. Pelvic floor retraining can be offered with limited success. Prevention is recommended (atraumatic childbirth, limited straining at stool, pelvic floor exercises).
- *Rectocele*. Frequently asymptomatic, rectocele can be an incidental finding on examination and on defaecography that does not require surgery. Selection of patients for surgical intervention on symptomatic rectocele remains an area of debate. Currently accepted criteria of patient selection for surgery are the need of rectal/vaginal digitation in order to facilitate rectal evacuation, rectal and/or vaginal symptoms for longer than 12 months not solved by an increase of fibre in diet, rectocele greater than 3 or 4 cm in diameter on defaecography, and none or partial emptying of rectocele on defaecography.
- *Enterocele*. Abdominal approach and mesh suspension is recommended in younger patients. In older or fragile patients, perineal repair gives satisfactory results at lesser risk and is, therefore, the preferred option.
- *Rectal intussusception*. The role of surgery is controversial. Abdominal rectopexy gives poor results and should be avoided. Some success has been reported with the perineal approach (internal Delorme). Stapled transanal rectal resection is a new investigational procedure that is presently suggested in this condition.
- *Megarectum, slow-transit constipation*. Vertical reduction rectoplasty and concomitant sigmoidectomy has been recently proposed for the treatment of idiopathic megarectum. In the most severe cases, and when defaecation disorders are associated with slow-transit constipation, there may be an indication for antegrade colonic enemas using a Malone-type caecostomy for easier bowel management. Refractory cases may end up with an ileo- or colostomy.
- *Adult Hirschsprung's disease*. This very rare phenomenon can be diagnosed on anorectal manometry. Absence of the rectoanal inhibitory reflex raises the possibility of adult Hirschsprung's disease. The patient should then undergo a full-thickness rectal biopsy to confirm the absence of ganglion cells. For ultrashort aganglionosis, lateral internal sphincterotomy or anorectal myectomy are recommended.

6.3.7 Conclusion

Defaecation disorders represent a complex field where thorough assessment of the terminal bowel anatomy and function is needed (Fig. 6.3.3). A multidisciplinary approach as developed in "pelvic floor clinics" is a use-

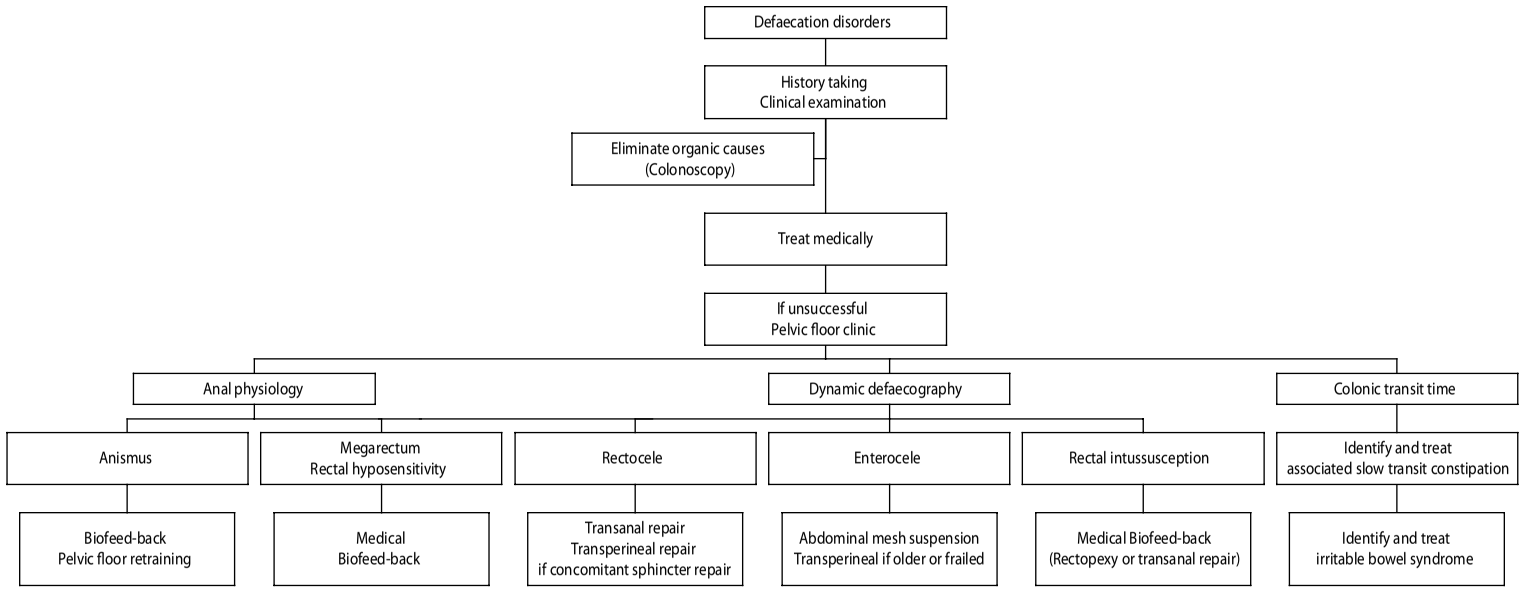


Fig. 6.3.3 How to manage a defaecation disorder

ful adjunct to the traditional colorectal approach. In this difficult area of functional disorder, information to the patient and his/her relatives is essential, especially when surgery is considered.

Suggested Reading

1. Boccasanta P, Carriero A, Stuto A, Caviglia A (2004) Stapled rectal resection for obstructed defecation. A prospective multicenter trial. Dis Colon Rectum 47:1285–1297
2. Chaussade S, Khyari A, Roche H et al (1989) Determination of total and segmental colonic transit time in constipated patients. Dig Dis Sci 34:1168–1172
3. DeLancey JOL (1999) Structural anatomy of the posterior pelvic compartment as it relates to rectocele. Am J Obstet Gynecol 180:815–823
4. Gladman MA, Scott SM, Williams NS, Lunniss PJ (2003) Clinical and physiological findings, and possible aetological factors of rectal hyposensitivity. Br J Surg 90:860–866
5. Heriot AG, Skull A, Kumar D (2004) Functional and physiological outcome following transanal repair of rectocele. Br J Surg 91:1340–1344
6. Heymen S, Jones, KR Scarlett Y, Whitehead WE (2003) Biofeedback treatment of constipation: a critical review. Dis Colon Rectum 46:1208–1217
7. Jean F, Tanneau Y, Le Blanc-Louvy AA, Leroi M, Denis P, Michot F (2002) Treatment of enterocele by abdominal colporectosacropexy: efficacy on pelvic pressure. Colorectal Dis 4:321–336
8. Kahn MA, Stanton SI (1997) Posterior colporrhaphy: its effects on bowel and sexual function. Br J Obstet Gynaecol 104:882–886
9. Knowles CH, Eccersley AJ, Scott SM, Walker SM, Reeves B, Lunniss PJ (2000) Linear discriminant analysis of symptoms in patients with chronic constipation: validation of a new scoring system (KESS). Dis Colon Rectum 43:1419–1426
10. Lehur PA, Hamy A (2000) Cure chirurgicale des rectocèles par voie périnéo-vaginale: plicature rectale, sacro-spinofixation vaginale et périnéorraphie postérieure. J Chir 137:165–169
11. Mellgren A, Bremmer S, Johansson C et al (1994) Defecography: results of investigations of 2816 patients. Dis Colon Rectum 37:1133–1141
12. Mellgren A, Anzen B, Nilsson BY, Johansson C et al (1995) Results of rectocele repair. A prospective study. Dis Colon Rectum 38:7–13
13. Mellgren A, Lopez A, Schultz I, Anzen B (1998) Rectocele is associated with paradoxical anal sphincter reaction. Int J Colorectal Dis 13:13–16
14. Mimura T, Roy AJ, Storrie JB, Kamm MA (2000) Treatment of impaired defecation associated with rectocele by behavioral retraining. Dis Colon Rectum 43:1267–1272
15. Richardson AC (1993) The rectovaginal septum revisited: its relationship to rectocele and its importance in rectocele repair. Clin Obstet Gynecol 36:976–983
16. Silvis R, Gooszen HG, van Essen A, de Kruif ATCM, Janssen LWM (1999) Abdominal rectovaginopexy: modified technique to treat constipation. Dis Colon Rectum 1999;42:82–88
17. Siproudhis L, Dautreme S, Ropert A, Bretagne JF et al (1993) Dyschezia and rectocele: a marriage of convenience? Physiologic evaluation of the rectocele in a group of 52 women complaining of difficulty in evacuation. Dis Colon Rectum 36:1030–1036
18. Stojkovic SG, Balfour L, Burke D, Finan PJ, Sagar PM (2003) Does the need to self digitate or the presence of a large or non emptying rectocele on proctography influence the outcome of transanal rectocele repair? Colorectal Dis 5:169–172
19. Sullivan ES, Leaverton GH, Hardwick CE (1968) Transrectal perineal repair, an adjunct to improved function after anorectal surgery. Dis Colon Rectum 11:106–114
20. Van Dam JH, Schouten WR, Ginai AZ. Huisman WM, Hop WC (1996) The impact of anismus on the clinical outcome of rectocele repair. Int J Colorectal Dis 11:238–242
21. Van Dam JH, Ginai AZ, Gosselink MJ, Huisman WM, Bonjer HJ, Hop WC, Schouten WR (1997) Role of defecography in predicting clinical outcome of rectocele repair. Dis Colon Rectum 40:201–207
22. Van Dam JH, Hop WCJ, Schouten WR (2000) Analysis of patients with poor outcome of rectocele repair. Dis Colon Rectum 43:1544–1550
23. Yeh CY, Pikarsky A, Wexner SD et al (2003) Electromyographic findings of paradoxical puborectalis contraction correlate poorly with cinedefecography. Tech Coloproctol 7:77–81

6.4 Rectal Prolapse, Intussusception, Solitary Rectal Ulcer

ANDRÉ D'HOORE

6.4.1 Introduction

- Rectal prolapse is an uncommon but disabling condition that requires surgical correction to treat symptoms and prevent progressive anal sphincter damage. The majority of patients complain of perineal pressure and a feeling of "something coming down". This is commonly associated with mucus discharge or frank faecal soiling. Many patients will describe a protrusion through the anal opening, that may reduce spontaneously, but frequently, with time, manual reduction is required. There is considerable controversy regarding the indications for surgical intervention and the most appropriate surgical technique to be used.
- Rectal intussusception is a common finding at defaecography and may be present in normal subjects; internal rectal prolapse is a term used in patients with obstructed defaecation and in whom this proctographic finding is identified.
- Solitary rectal ulcer is a term used to describe ulceration, usually on the anterior rectal wall, at the level of the puborectalis sling. Local trauma due to repeated straining with intussusception and obstructed defaecation is thought to be responsible.
- In terms of treatment, intussusception and internal prolapse, with or without ulceration, are generally treated conservatively.

6.4.2 Classification

- Full-thickness prolapse of the rectum extending beyond the anal verge is called an external rectal prolapse (procidentia).
- Prolapse of the rectum retained above the anal verge is referred to as intussusception or internal prolapse.
- Three grades of rectal intussusception are defined at cinedefaecography:
  - Grade I prolapse remains above the level of the puborectalis muscle
  - Grade II prolapse at the level of the puborectalis muscle
  - Grade III prolapse into the anal canal but not beyond the anal verge
- Isolated erythema or ulceration of the rectal wall in patients with obstructed defaecation is referred to as a rectal ulcer. It occurs in 10–30% of patients with an external or internal rectal prolapse.

6.4.3 Aetiology

- The aetiology of rectal prolapse is unknown, however the condition is more common in women than men, parous women than nulliparous, and patients with a history of constipation and straining.
- Full-thickness rectal prolapse in children is thought to be due to constipation and excessive straining.
- Common anatomical findings in patients with prolapse include:
  - A redundant sigmoid colon
  - A deep pouch of Douglas
  - A patulous anal sphincter
  - Diastasis of the levator ani
  - Laxity of the normal fascial supports of the rectum
- In the young patient a congenital or acquired deficiency in suspension of the rectum can lead to prolapse.
- A prolonged history of obstructed defaecation and straining disorder or constipation seems to precede prolapse in a significant number of patients.
- In elderly female patients, generally, it is part of a more complex pelvic prolapse due to a weakened sphincter and pelvic floor. Frequently there is an antecedent history of hysterectomy for genital prolapse.
- Patients with a rectal ulcer are a heterogeneous group: ischaemia at the site of intussusception or direct trauma due to digitation are plausible explanations.

6.4.4 Epidemiology

- External rectal prolapse is an uncommon feature.
- Female patients outnumber male patients by about ten to one.

- Multiparous women have an increased risk. Also a hysterectomy seems to increase the risk.
- In tropical countries where there is a preponderance of male patients; it is associated with schistosomiasis or amoebic dysentery.
- Rectal ulcer predominantly affects young people with an average age of 30 years. There is no sex preponderance.
- Ninety per cent of rectal ulcers involve the anterior rectal wall, however 25% are circumferential.

6.4.5 Clinical Features

- Prolapse during defaecation with mucous or bloody discharge is the most common feature. The prolapse may reduce spontaneously or need manual reduction.
  - *Faecal incontinence* is present in up to 70% of patients. The prolapse may dilate the anal sphincter. Pudendal neuropathy is a common finding. A typical patulous anus can be found at clinical examination. In contrast, most male patients have a normal continence.
  - *Constipation*, especially obstructed defaecation and incomplete evacuation is present in 60% of patients. Slow colonic transit constipation is rare.
- Obstructed defaecation with a sense of incomplete evacuation, a persisting desire to defaecate and prolonged straining are the leading symptoms in patients with rectal intussusception with or without a rectal ulcer.

6.4.6 Differential Diagnosis

- Rectal mucosal prolapse (anterior, circular)
- Prolapsing internal haemorrhoids
- Prolapsing adenoma/carcinoma of the rectum
- Proctitis

6.4.7 Diagnosis

- External rectal prolapse is a clinical diagnosis. Sigmoidoscopy or colonoscopy should be performed to exclude coexisting or precipitating colorectal pathology. Anorectal physiology testing can be useful to document anal sphincter injury and compromise to the sphincter mechanism if faecal incontinence is present.
- If there is a history of chronic constipation, a colonic transit time study is indicated.
- Internal rectal prolapse is a radiological diagnosis. Video colpo-cystodefaecography with opacification of the small bowel should be performed to document the disequilibrium between the pelvic compartments that can result in descent of the middle compartment, and present as an enterocele, a high rectocele or vaginal prolapse. The value of dynamic MRI is still investigational.
- The histology of a "rectal ulcer" is diagnostic with fibrous obliteration of the lamina propria and distortion of the muscularis mucosae with muscle fibres protruding into the lamina propria. Misdiagnosis may lead to protracted medical treatment for proctitis and inappropriate surgery in up to one quarter of patients.
- Colitis cystica profunda, a distinctive histological entity, is commonly observed as a late stage of rectal ulcer. Pathological examination reveals cystic dilated glands and mature colonic epithelium extending into the submucosa and deeper parts of the intestinal wall.

6.4.8 Therapy

The treatment of full-thickness rectal prolapse is generally surgical to anatomically correct the prolapse, alleviate symptoms of incontinence and/or obstructed defaecation and to prevent functional sequelae (Fig. 6.4.1). A recent Cochrane review concluded that the small sample size of included trials, together with methodological weakness, severely limits the usefulness of the review for guiding clinical practice. Long-term follow-up is missing in many of the published series, often reflecting the elderly population so affected.

Surgical procedures for rectal prolapse can be broadly classified according the surgical approach:

- Perineal approach
  - Anal encirclement (Thiersch)
  - Delorme mucosectomy
  - Altemeier rectosigmoidectomy
- Abdominal approach
  - Suture rectopexy
  - Mesh rectopexy
    - Posterior (Wells, Ivalon sponge)
    - Anterior (Ripstein)
    - Lateral (Orr-Loygue)
    - Ventral
  - Anterior resection (Muir, Mayo Clinic)
  - Resection rectopexy (Frykman-Goldberg)

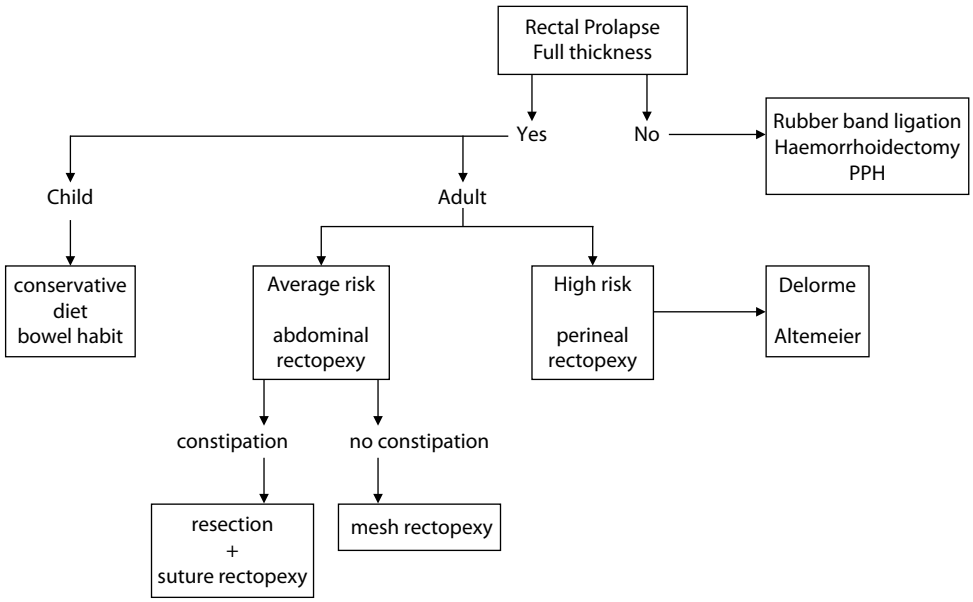


Fig. 6.4.1 Decision making in the treatment of full-thickness rectal prolapse

6.4.8.1 Perineal Procedures

Anal Encirclement (Thiersch)

- The purpose is to narrow the anal canal sufficiently to maintain reduction of the prolapse without causing obstruction.
- A circumferential suture of stainless steel or monofilament non-absorbable suture is placed at the level of the puborectalis muscle.
- Infection, suture breakage or erosion and outlet obstruction are common complications.
- The procedure is obsolete and is rarely if ever indicated.

Delorme Mucosectomy

- The purpose is to excise the mucosa of the prolapsing rectum and to plicate the remaining rectal muscle vertically to reduce the prolapse.
- The mucosectomy commences at the anorectal junction and continues in a circumferential manner to the upper margin of the prolapse.
- Dissection is facilitated by submucosal injection of a dilute adrenaline solution and the mucosal tube dissected from the prolapsed bowel.
- Plicating sutures, usually 8 to 12 monofilament absorbable, are inserted in the muscular wall and tightened to reduce the prolapse above the sphincter.
- Mucosal continuity is restored by interrupted suture of the rectal mucosa to the mucosa of the upper anal canal.

Altemeier Rectosigmoidectomy

- The purpose is to perform a full-thickness resection of the prolapsing rectum and to restore continuity by coloanal anastomosis.
- A full-thickness incision is performed above the dentate line and the prolapsing rectum is mobilised by perirectal dissection of the mesorectum.
- Dissection continues into the peritoneal cavity anteriorly, facilitating delivery of the upper rectum or distal sigmoid colon.
- The prolapsing segment is resected and a straight coloanal anastomosis performed.
- The technique allows reconstruction of the pelvic floor by anterior and/or posterior levatoroplasty.

Summary

Perineal procedures:

- Are well tolerated by elderly and infirm patients
- May be performed under local or regional anaesthesia
- Have recurrence rates varying from 5% to 35% higher than following abdominal rectopexy

- Have low anastomotic leak rates after resection
- Have infrequent postoperative problems with defaecation
- Reduce rectal capacity and compliance and this can exacerbate faecal urgency and incontinence

6.4.8.2 Abdominal Procedures

- Abdominal rectopexy procedures are based on the principles of complete rectal mobilisation and fixation of the rectum.
- The mobilised mesorectum can be allowed to adhere to the sacrum following anterior resection (Muir) or be fixed to the presacral fascia using non-absorbable sutures or a non-absorbable mesh (Ripstein's procedure) or Ivalon sponge (Well's procedure). The latter has been associated with increased postoperative presacral sepsis and is performed infrequently.
- An alternative approach is to resuspend the pelvic floor using lateral strips of mesh sutured to the lateral aspect of the mobilised rectum and the sacral promontory (the Orr-Loygue procedure).
- Patients in whom chronic constipation is a preoperative feature may have a better outcome if resection of a redundant sigmoid colon is combined with suture rectopexy (Frykman-Goldberg procedure). However, resection and anastomosis increases the risk of postoperative complications.
- Abdominal procedures:
  - Are major abdominal procedures that require general anaesthesia
  - Are generally not suitable for elderly and infirm patients
  - Have low recurrence rates (0–16%)
  - Are most likely to improve continence
  - Have postoperative constipation as the most common functional side effect (up to 50% of patients)
- Full mobilisation of the rectum may cause autonomic nerve damage and result in disturbed rectosigmoid motility. In this regard rectal mobilisation without transection of the so-called lateral ligaments results in less postoperative constipation.
- The risk of postoperative constipation is less following techniques that limit rectal dissection and mobilisation. In ventral rectopexy dissection is limited to the anterior aspect of the rectum (within the rectovaginal septum). A mesh is sutured to the anterior aspect of the rectum and fixed to the sacral promontory.
- Conventional abdominal rectopexy is performed though a lower midline abdominal or Pfannenstiel incision.
- There are increasing data to show that a laparoscopic technique is associated with similar functional outcomes with less postoperative pain, reduced ileus, earlier recovery and shorter hospital stay.
- Of special concern in male patients is the potential risk for autonomic nerve damage and sexual dysfunction. Some favour a perineal approach in male patients.

6.4.8.3 Choice of Procedure

- High-risk patient
  - Small prolapse: Delorme
  - Large prolapse: Altemeier + levatoroplasty
- Average patient
  - Without constipation: (laparoscopic) rectopexy (limited rectal mobilisation)
  - With obstructed defaecation: (laparoscopic) rectopexy
  - With slow-transit constipation: (laparoscopic) suture rectopexy + total colectomy, only if sphincter function is normal

6.4.8.4 Rectal Intussusception

- The treatment of rectal intussusception and solitary rectal ulcer is difficult as intussusception of some degree is a common finding and correlation with symptoms is problematic.
- Most patients will benefit from additional fibre intake and bowel retraining or biofeedback.
- Surgical intervention is reserved for unresponsive patients with significant symptoms.
- Rectopexy will improve symptoms in 50–70% of patients but is associated with the morbidity of a major abdominal procedure. Furthermore, constipation may be worsened postoperatively.
- In patients with predominant symptoms of irritable bowel syndrome the results are less favourable.
- The presence of a solitary rectal ulcer is associated with better outcome, as the associated bleeding and mucus discharge are likely to respond.
- In refractory cases, restorative rectal resection with coloanal anastomosis has been tried but the outcome is disappointing.
- Recently, Longo has proposed a transanal double-stapled technique for obstructed defaecation associated with intussusception (STARR procedure). The results in selected patients are promising but prospective randomised data are awaited.

Suggested Reading

1. Brazzelli M, Bachoo P, Grant A (2004) Surgery for complete rectal prolapse in adults (Cochrane Review). From The Cochrane Library, Issue 2. Chichester, UK. www.cochrane.org/cochrane/revabstr/AB001758.htm (2004) Accessed 20 April 2004
2. D'Hoore A, Cadoni R, Penninckx F (2004) Long-term outcome of laparoscopic ventral rectopexy for total rectal prolapse. Br J Surg 91:1500–1505
3. Dolk A, Broden G, Holstrom B, Johansson C, Nilsson BY (1990) Slow transit of the colon associated with severe constipation after the Ripstein procedure. A clinical and physiologic study. Dis Colon Rectum 33:786–790
4. Eu KW, Seow-Choen F (1997) Functional problems in adult rectal prolapse and controversies in surgical treatment. Br J Surg 84:904–911
5. Madiba TE, Baig MK, Wexner SD (2005) Surgical management of rectal prolapse. Arch Surg 140:63–73
6. Speakman CTM, Madden MV, Nicholls RJ, Kamm MA (1991) Lateral ligament division during rectopexy causes constipation but prevents recurrence: results of a prospective randomized study. Br J Surg 78:1431–1433

6.5 Irritable Bowel Syndrome

HEINER KRAMMER, FRANKA NEUMER

6.5.1 Definition

- Irritable bowel syndrome (IBS) (synonym: spastic colon) is characterised by abdominal discomfort or pain, associated with altered bowel function (diarrhoea and/or constipation) and disordered defaecation.
- There are no diagnostic biochemical, physiological or structural abnormalities in IBS.

Over the years groups of experts have developed clinical measures based on positive symptom analysis. Manning and colleagues were the first to propose key symptoms ("Manning criteria") to help the diagnosis of IBS. The Rome I, II and III criteria are the results of multinational consensus workshops. Table 6.5.1 lists the symptom-based criteria which are so far established for the diagnosis of IBS. The Rome classification system characterises IBS in terms of multiple physiological determinants contributing to a common set of symptoms rather than a single disease entity. The current Rome III criteria subtype IBS according to the stool form by using the Bristol Stool Form Scale.

The IBS-related symptoms overlap with those of other diseases. Experienced clinicians often diagnose these disorders on symptoms alone, but, as functional disorders are so much more common than organic diseases, any diagnostic strategy is likely to have a deceptively high positive predictive value.

6.5.2 Epidemiology

Irritable bowel syndrome is one of the most common disorders in gastrointestinal clinical practice. The overall prevalence rate is similar (10–20%) in most industrialised countries. These findings reflect the tremendous impact of IBS on social costs due to healthcare use, drug consumption and absenteeism from work. The exact prevalence of IBS is poorly defined, probably because of the different definitions and clinical criteria used to define the syndrome. Similarly, the incidence of IBS is unknown, but it has been estimated at almost 1% per year. This certainly underestimates the real incidence of IBS as only one in three patients seek doctors. Those who do consult a doctor report more severe symptoms and an increased level of psychological disturbance (anxiety, depression, as well as sleep disturbance).

IBS is commonly believed to be a female disease. IBS symptoms are at least twice as common in women as men. The reasons why women appear to be more prone than men to IBS are unknown, although health-seeking behaviour and other factors may play a role in this gender predominance.

The first presentation of patients to a physician is often between the ages of 30 and 50 years, and there is a decrease in reporting frequency among older people.

6.5.3 Aetiology/Pathophysiology

Since the mid 1990s significant advances have been made in the understanding of the pathophysiology of IBS. For many patients the most consistent, and probably interrelated, characteristics are:

- Altered intestinal motility
- Visceral hypersensitivity
- Postinfection bowel dysfunction
- Dietary factors
- Stress as well as psychological morbidity

6.5.3.1 Altered Motility

Abnormal small intestinal and colonic motility has been demonstrated in IBS patients and in some patients it has been shown to correlate with symptoms. Abnormalities of intestinal motility may lead not only to the onset of pain but also to bloating and, if the abdominal motility results in changes in intestinal transit, constipation and diarrhoea.

6.5.3.2 Visceral Hypersensitivity

Patients with functional bowel diseases exhibit decreased pain thresholds to balloon distension of the gut. This was

Table 6.5.1 Symptom-based criteria so far established for the diagnosis of IBS

Manning
• Pain relieved by defaecation
• More frequent stools at the onset of pain
• Looser stools at the onset of pain
• Visible abdominal distension
• Passage of mucus
• Feeling of incomplete evacuation
Rome I
Abdominal pain or discomfort for at least 3 months with at least one of the following symptoms:
• Relieved with defaecation
• Associated with a change in frequency of stools
Associated with a change in form of stools and two more of the following symptoms:
• Altered stool frequency and/or form, altered stool passage
• Passage of mucus
• Bloating or abdominal distension
Rome II
At least 12 weeks, which need not be consecutive, in the preceding 12 months of abdominal discomfort or pain that has two of three features:
• Relieved with defaecation; and/or
• Onset associated with a change in frequency of stool; and/or
• Onset associated with a change in form (appearance) of stool
Symptoms that cumulatively support the diagnosis of IBS:
• Abnormal stool frequency (less than or more than three bowel movements per week)
• Abnormal stool passage (straining, urgency or feeling of incomplete evacuation)
• Passage of mucus
• Bloating or feeling of abdominal distension
Rome III
Diagnostic criteria[a] for IBS. Recurrent abdominal pain or discomfort[b] at least 3 days per month in the last 3 months associated with two or more of the following:
1. Improvement with defaecation
2. Onset associated with a change in frequency of stool
3. Onset associated with a change in form (appearance) of stool
Subtyping IBS by predominant stool pattern
1. IBS with constipation (IBS-C): hard or lumpy stools ≥ 25% and loose (mushy) or watery stools < 25% of bowel movements
2. IBS with diarrhoea (IBS-D): loose (mushy) or watery stools ≥ 25% and hard or lumpy stool < 25% of bowel movements
3. Mixed IBS (IBS-M): hard or lumpy stools ≥ 25% and loose (mushy) or watery stools ≥ 25% of bowel movements
4. Unsubtyped IBS: insufficient abnormality of stool consistency to meet criteria for IBS-C, D or M

[a]Criteria fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis

[b]Discomfort means an uncomfortable sensation not described as pain. In pathophysiology research and clinical trials, a pain/discomfort frequency of at least 2 days a week during screening evaluation for subject eligibility

first described in the rectum of patients with IBS almost 30 years ago and subsequently confirmed by others. In addition, it is often noted with air insufflation during colonoscopy. This phenomenon is referred to as visceral hyperalgesia. Explanations for this include an alteration of the sensitivity of sensory receptors through the recruitment of nociceptors in response to infection, intraluminal factors, ischaemia, distension or psychiatric factors There may be increased excitability of the neurons in the dorsal horn of spinal cord, and centrally there may be differences in the way the brain modulates afferent signals from the dorsal horn neurons through ascending pathways.

6.5.3.3 Gastrointestinal Infection

There is an increased risk of patients developing IBS symptoms following an episode of gastrointestinal infection. It was shown that around one third of patients hospitalised for infectious diarrhoea had developed new IBS. In most cases, persistent bowel dysfunction was noted in patients following documented *Campylobacter*, *Shigella* and *Salmonella* gastroenteritis. Factors predisposing to persisting symptoms are severity and duration of diarrhoea, anxiety, depression and somatisation, as do adverse life events. Mechanisms underlying postinfection IBS are unclear, but immunological abnormalities at the intestinal level have been demonstrated in these patients, as has increased mucosal T lymphocytes and serotonin-producing enteroendocrine cells. Also, response to the pathogen is undoubtedly influenced by genetic factors that influence immune response.

6.5.3.4 Dietary Factors

Many patients with IBS believe that their symptoms are food related and some have considerably restricted their diet by the time they consult. The gut has an extensive immune system but current understanding of processing of food antigens in health and disease is limited. At present no clinically useful marker is available to test for food hypersensitivity in IBS. Researchers have employed both skin tests and serum immunoglobulins (IgG and IgE) as markers of food hypersensitivity in various disorders including IBS, but published data are equivocal. Moreover, many unscrupulous practitioners are benefiting from the confusion, leading patients to more and more restricted and illogical diets.

The role of sugar malabsorption in the pathogenesis of IBS is still a debated problem. Demographic data show that the prevalence of IBS patients with sugar malabsorption is similar to that found in controls. Symptoms, such as diarrhoea and bloating, can typically be reproduced by lactose intake and reduced following lactose exclusion from the diet. Lactose malabsorption may coexist with IBS. Nevertheless, a lactose-free diet is effective in improving symptoms only in about 10% of patients with IBS.

True food allergy is much less common. It is usually not difficult to recognise if food ingestion is associated with urticaria, asthma, eczema, angiooedema and rhinorrhoea with a high incidence of positive skin prick or high RAST scores. Such patients see an immunologist rather than a gastroenterologist and are not usually thought to have IBS.

6.5.3.5 Stress and Psychological Morbidity

Psychological observations have shown that psychological symptoms of anxiety and depression are more common in IBS patients than either healthy volunteers or patients with organic gastrointestinal disease. More than 50% linked the onset of their symptoms to a stressful event such as employment difficulties, family death, a surgical procedure or marital stress. Clinicians agree that stress can cause symptoms of IBS, but it cannot be seen as the only cause. The magnitude of psychological stress also correlates with symptomatic outcome. Important in regard to psychological stress is the recently demonstrated association of sexual, emotional or verbal abuse with IBS. Sexual abuse, often combined with physical abuse, has been reported in 20–30% of patients with IBS. These findings are significantly more common than in the general population or in patients with organic disease.

6.5.4 Symptoms

- Irritable bowel syndrome patients suffer from various gastroenterological symptoms. These include recurrent abdominal pain, altered bowel function, bloating, abdominal distension, the sensation of incomplete evacuation and the increased passage of mucus (Table 6.5.1).
- In addition, several *non-gastroenterological symptoms* are more frequent in IBS patients such as lethargy, poor sleep, fibromyalgia, backache, urinary frequency and dyspareunia.
- Anxiety, depression and somatisation are frequent but do not reliably discriminate between IBS and other gastrointestinal diseases.
- Functional diseases such as IBS usually interfere with the patients' comfort and their daily activities.
- On the other hand, IBS is a benign disorder and there are no long-term organic complications such as cancer or colitis.

6.5.5 Diagnosis

- The diagnosis of IBS is based on the identification of symptoms consistent with the syndrome (Table 6.5.1).
- The first step is a careful assessment of the patient's symptoms. Patients should be carefully interviewed. Ideally, no time limitation should exist as patients need to think about the diagnosis.
- Second, IBS is diagnosed after excluding structural or biochemical abnormalities that could indicate organic or other functional disorders.

6.5.5.1 Physical Examination

- A physical examination should be performed on the first visit and subsequent visits as needed to exclude findings not consistent with IBS and to meet patients' expectations of a thorough evaluation.
- A pelvic examination is often indicated for lower abdominal/pelvic symptoms and/or if there is a change in menstrual pattern.
- A rectal examination, particularly for patients reporting symptoms of incontinence and constipation, can help to identify a lax sphincter or paradoxical pelvic floor muscle contraction.

6.5.5.2 Investigation

- These tests include:
  - Complete blood cell count and sedimentation rate
  - Serum chemistry
  - Thyroid-stimulating hormone (TSH)
  - Stool haemoculture
- Additional tests are performed depending on the age of the patient and the predominant clinical picture.
- Abdominal ultrasound contributes little in the evaluation of patients with suspected IBS.
- Colonoscopy is recommended for patients over age 50 years due to higher pretest probability of colon cancer. In younger patients, performing a colonoscopy or sigmoidoscopy is determined by clinical features suggestive of disease and may not be indicated.

Pain-predominant Symptoms

- The persistence of pain often requires plain abdominal radiography during an acute episode to exclude bowel obstruction and/or other abdominal pathology.
- Additional imaging studies (e.g. small-bowel radiography, CT scan) may be necessary if there are other symptoms present (e.g. vomiting, weight loss).

Constipation-predominant Symptoms

- In patients with infrequent bowel movements, measurement of the whole gut transit time is indicated to discriminate between IBS and slow-transit constipation or outlet obstruction.
- When symptoms of dyschesia or incomplete evacuation are prominent, suggesting obstruction to defaecation, further anorectal tests are required including anorectal motility testing and defaecography.

Diarrhoea-predominant Symptoms

- If diarrhoea is persistent a stool sample should be examined for pathological bacteria, ova and parasites.
- Exocrine pancreas insufficiency should be excluded.
- Small-bowel biopsy and aspirate should be obtained for *Giardia lamblia* or sprue.
- A colonoscopy (possibly with ileoscopy) and multiple biopsies are necessary to exclude inflammatory bowel disease.
- Colonic biopsies can be considered to evaluate for collagenous or microscopic colitis.
- Especially, when postprandial symptoms of bloating accompany the diarrhoea, a breath hydrogen test to exclude bacterial overgrowth is helpful.
- Lactose intolerance and other carbohydrate malabsorption (e.g. fructose, sorbitol) are common causes of diarrhoea.
- Rare cases of diarrhoea include metabolic disorders such as diabetes (due to autonomic neuropathy and motility disorders), hormonal abnormalities (e.g. hyperthyroidism), other causes of malabsorption (e.g. chronic pancreatitis) and endocrine tumours secreting serotonin, vasoactive intestinal polypeptide or gastrin.

6.5.6 Management and Therapy

Making a definitive diagnosis helps both doctor and patient by reassuring them that it is unlikely that another alternative diagnosis will emerge over the ensuing years. Doctors should avoid comments such as "it is untreatable" or "you will learn to live with it" as this quite obviously results in despondency. However, patients often appreciate a short tutorial on the anatomy and physiology of the gut as well as being informed about the current theories on pathophysiology, such as motility and visceral sensitivity. Some information on the role of stress and psychological factors, if put in simple terms, is also recommended, e.g. "stress can make symptoms worse but does not cause IBS".

Table 6.5.2 Symptom-directed therapy for IBS

Pain-predominant	Antispasmodics (e.g. mebeverine, butylscopolamine)
	Herbal remedies (menthol, *Iberis amara*)
	Antidepressants (amitriptyline, *cave*: constipation)
	Selective serotonin reuptake inhibitors (fluoxetine)
Meteorism-predominant	Polydimethylsiloxane (dimethicone)
	Probiotics
	Herbal remedies (*Iberis amara*)
Diarrhoea-predominant	Ispaghula husk, Psyllium
	Loperamide
Constipation-predominant	Ispaghula husk, Psyllium
	Probiotics
	Herbal remedies (*Iberis amara*)
	Osmotic laxatives (polyethylene glycol)
	Stimulating laxatives (Bisocodyl, Natriumpicosulfat)
	CO_2 laxatives (suppositories) to support evacuation

6.5.6.1 Lifestyle Advice

Lifestyle advice means a carefully dietary and lifestyle history to identify food fads or deficiencies, e.g. excess or lack of dietary fibre. Other common factors are lack of exercise as well as not allowing adequate and suitable time for regular defaecation, which are particularly relevant to constipated IBS sufferers. Patients should be instructed to keep a two-week diary of symptoms, stresses and dietary intake to identify any trigger factors.

6.5.6.2 Dietary Factors

Food products have variously been reported as perpetuating or treating IBS. For instance, especially patients who suffer from diarrhoea and bloating may have excessively large intakes of indigestible carbohydrate, fruits or caffeine. They may also benefit from a diet low in lactose and/or fructose. Constipated patients with low fibre intake should be given a trial of a high fibre diet. However, there is growing evidence that bran can upset the symptoms of IBS whereas soluble forms of fibre (e.g. Ispaghula) tend to be more effective and have less adverse effects such as bloating. Exclusion diets may be useful in controlling symptoms in some patients.

6.5.6.3 Psychotherapy

Patients with anxiety but without psychiatric disease who do not respond satisfactorily to the above may benefit from relaxation therapy. On the other hand, patients with prominent psychiatric morbidity may respond to psychotherapy or cognitive behavioural therapy or require conventional psychiatric treatment.

6.5.6.4 Conservative Medical Treatment

Recommended European Standard

One of the commonest problems facing clinicians treating patients with IBS is the lack of uniformity of symptoms. In the majority of cases, current pharmacological treatments have limited value. However, for those patients who require therapy for specific symptoms, the following treatments have proved effective (summarised in Table 6.5.2).

Abdominal Pain and Bloating

- For pain and bloating, antispasmodic medication should be considered. These drugs have differing modes of action, some exhibiting anti-smooth muscle activity (e.g. herbel remedies mebeverine) and others anticholinergic activity (e.g. butylscopolamine).
- Antidepressants can be used for treating IBS as they not only treat underlying depression but also modify

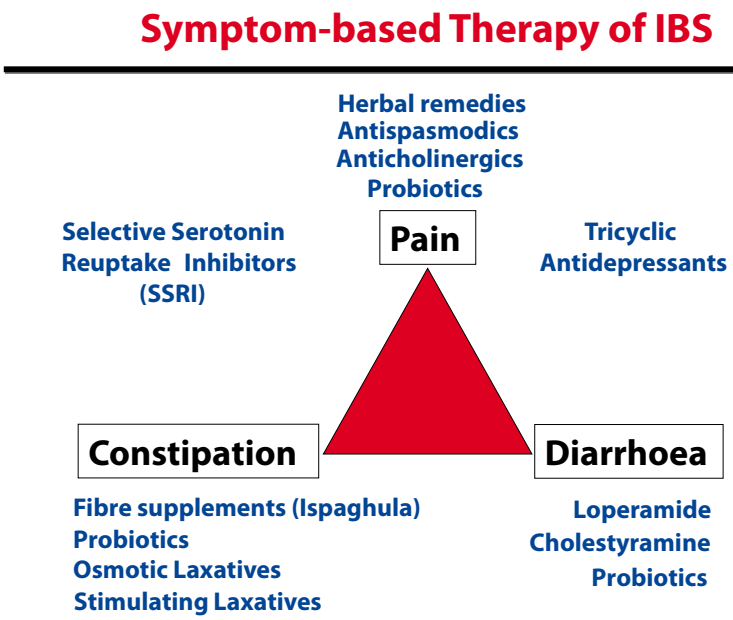


Fig. 6.5.1 Practical guide to the therapy of IBS

gut motility and alter visceral nerve responses. However, tricyclic antidepressants can intensify constipation. That is why pain-predominant patients who also suffer from constipation should be given selective serotonin reuptake inhibitors. The most advanced area of research in the field of IBS is that of drugs that modify 5-HT in the gut (5-HT antagonists and 5-HT agonists). The major receptor targets that have been explored are the 5-HT_3 and 5-HT_4 receptors.

- There have been a number of trials of probiotics in IBS though patient numbers as well as treatment periods are rather small.

Diarrhoea

- Loperamide slows small and large intestinal transit and reduces stool frequency and urgency in patients with diarrhoea-predominant IBS.
- Cholestyramine may also be considered as about 10% of diarrhoea-predominant IBS patients show evidence of bile salt malabsorption.
- Fibre supplements such as Ispaghula husk and psyllium may be helpful to increase stool consistency.

Constipation

- Patients with IBS and constipation should be given a trial of increased intake of dietary fibre to increase stool weight and accelerate gut transit. In particular, Ispaghula husk is a useful alternative to wheat bran as it does not lead to meteorism and flatulence.
- Probiotics such as *E. coli* strain Nissle 1917 (EcN), *L. casei Shirota* (LcS), Bifidobacterium animalis have been shown to increase stool frequency and soften stool consistency.
- Osmotic laxatives such as polyethylene glycol may be used.
- Stimulating laxavites such as Bisocodyl or Natriumpicosulfat.

The symptom-based therapy of IBS is summarised in Fig. 6.5.1.

6.5.7 Prognosis

Irritable bowel syndrome is generally regarded as a chronic relapsing condition. There is no cure for IBS, but symptoms can be managed with dietary changes, stress reduction and, if necessary, medication. Therefore, the prognosis is likely to be individualised based on patient's anticipation and a successful management.

Previous abdominal surgery has a poor prognostic implication in IBS. Patients undergoing surgery are likely to be more symptomatic in the postoperative year than are non-IBS patients. Underlying reasons involve a questionable indication for the surgery and possible alterations in gut physiology following the procedure.

Suggested Reading

1. Bonaz BL, Papillon E, Baciu M, Segebarth C, Bost R, LeBas J, Fournet J (2000) Central processing of rectal pain in IBS patients: an MRI study. Gastroenterology 118(suppl):A615
2. Camilleri M, Heading RC, Thompson WG (2002) Clinical perspectives, mechanisms, diagnosis and management of irritable bowel syndrome. Aliment Pharmacol Ther 16:1407–1430
3. Corney RH, Stanton R (1990) Physical symptom severity, psychological and social dysfunction in a series of outpatients with irritable bowel syndrome. J Psychosom Res 34:483–491
4. Dapoigny M (1999) Functional intestinal disorders. Diagnosis and treatment. Rev Prat 49:1559–1564
5. De Giorgio R, Barbara G, Stanghellini V, Cremon C, Salvidi B, De Ponti F, Corinaldesi R (2004) Diagnosis and therapy of irritable bowel syndrom. Aliment Pharmacol Ther 20 Suppl 2:10–22
6. Farthing MJ (2004) Treatment options in irritable bowel syndrome. Best Pract Res Clin Gastroenterol 18:773–786
7. Jones R (2000) IBS: prime problem in primary care. Gut 46:7–8
8. Longstreth GF, Drossman DA (2002) New developments in the diagnosis and treatment of irritable bowel syndrome. Curr Gastroenterol Rep 4:427–434
9. Longstreth GF, Thompson WG, Chey WD, Houghton LA, Mearin F, Spiller RC (2006) Functional bowel disorders. Gastroenterology 130:1480–1491
10. Manning AP, Thompson WG, Heaton KW, Morris AF (1978) Towards positive diagnosis of the irritable bowel. BMJ 2:653–654
11. Small PK, Loudon MA, Han CM, Noor N, Campbell FC (1997) Large scale ambulatory study of post prandial jejunal motility in irritable bowel syndrome. Scand J Gastroenterol 32:39–47
12. Spiller RC (2003) Postinfectious irritable bowel syndrome. Gastroenterology 124:1662–1671
13. Thompson WG, Longstreth GF, Rossman DA, Heaton KW, Irvine EJ, Muller-Lissner SA (1999) Functional bowel disorders and functional abdominal pain. Gut 45(suppl 2):II43–II47
14. Zimmerman J (2003) Extraintestinal symptoms in irritable bowel syndrome and inflammatory bowel diseases: nature, severity, and relationship to gastrointestinal symptoms. Dig Dis Sci 48:743–749

Inflammatory Bowel Disease

7.1 Ulcerative Colitis

PHILIP CONAGHAN, NEIL MORTENSEN

7.1.1 Definition

Chronic relapsing idiopathic inflammation of the rectum and variable length of the adjoining colon.

7.1.2 Epidemiology

7.1.2.1 Incidence

The incidence is relatively constant in the USA and northern Europe at about 12 cases per 100,000. It is rising, however, in areas where it was previously low, such as southern Europe and East Asia. This may be partly due to an increasing awareness of the condition and improved means of detection but some of this increase is likely a real phenomenon. It has been attributed to a "westernisation" of the lifestyle in these countries but an accurate cause is not known. It should be noted that rates for isolated ulcerative proctitis are often excluded from these statistics.

7.1.2.2 Prevalence

This obviously reflects the incidence although the rates quoted vary widely in the literature. Rates for northern Europe are in the region of 100–250 per 100,000 but are as low as 20 per 100,000 in central/southern Europe.

This geographical variation also influences migrants where the rate of ulcerative colitis (UC) tends towards that of the host population. This supports the view that environmental factors must play a major role in the development of UC. There is also a higher rate in urban compared with rural populations.

The onset of UC is commonly between 25 and 35 years of age but has a bimodal distribution with a second smaller peak later in life above 60 years of age. Men and women are affected equally.

Many risk factors have been proposed for the development and exacerbation of UC. However the literature is often contradictory.

- Cigarette smoking is the most strongly linked risk to UC. Smoking is protective against the development of UC reducing the risk to 40% of that of non-smokers. However, ex-smokers have the highest risk, 1.5–2 times greater than that of non-smokers.
- Many studies have suggested that appendicectomy exerts a protective effect on the development of UC, reducing the risk to about 30% of those who still have their appendix. However, the reducing rate of appendicectomies has not seen an equal rise in the incidence of UC so the effect is likely to be minor.
- Non-steroidal anti-inflammatory drugs (NSAIDs), oral contraceptive pills, perinatal infections, social class and various dietary substances have all been implicated but the literature is not conclusive on these.

7.1.3 Aetiology

The cause of UC is unknown but it is likely to involve an inappropriate and exaggerated immune response in the colonic mucosa to antigens in the normal colonic microflora brought about by environmental triggers in people who are genetically susceptible. In other words an interaction of a number of genes with environmental factors is likely and the trigger for inflammation may involve the normal colonic flora. These genetic, immunological and microbiological factors are all interrelated.

7.1.3.1 Genetic Factors

The concordance rate of UC in monozygotic twins is 18%, compared with 5% for dizygotic twins. This confirms a genetic influence in the development of UC although its contribution is not as substantial as that seen in Crohn's disease. There are some genes which contribute towards the susceptibility to a broader inflammatory bowel disease leading to the incidence of UC being greater amongst relatives of those with either UC or Crohn's disease and vice versa. There have been three major loci of interest termed IBD2, IBD3 and IBD7 and these are found on chromosomes 12q, 6p and 1p, respectively. The

most important of these is the 6p locus where evidence for linkage is strongest in the region of the MHC genes. Consistent with this, UC has associations with particular HLA genotypes. HLA-DR2 has a positive association with UC, which interestingly also has a positive association with the development of primary sclerosing cholangitis (PSC) and a negative association with the development of Crohn's disease. These genetic factors may also influence the clinical phenotype of the condition especially in relation to the extraintestinal manifestations such as arthritis and PSC.

7.1.3.2 Immunological Factors

These are obviously closely linked with the genetic factors and in particular the HLA genotype of the individual. The immunological status quo of the colonic mucosa is maintained by appropriate levels of stimulatory and regulatory T cells and their respective cytokines. The mucosal epithelium also plays a role in controlling immune functions. These epithelial cells can recognise conserved products unique to microorganisms (e.g. lipopolysaccharide that coats some gram-negative bacteria) via toll-like receptors (TLRs) and through these receptors can release cytokines, chemokines and other pro- or anti-inflammatory substances. The cytokine response in UC is believed to be a dysregulated TH_2 response predominantly, as opposed to the predominant TH_1 response in Crohn's disease.

7.1.3.3 Microbiological Factors

The inappropriate immune response may be in response to normal colonic flora and there has been a suggestion that patients with UC have failed to develop oral tolerance to gut luminal antigens. No specific bacteria have been identified as a causative agent; it is possible that people with different HLA genotypes will interact abnormally with different bacteria, but resulting in the same immune dysregulation to produce UC.

7.1.4 Symptoms and Signs

- Ulcerative colitis usually presents with passing bloody stool with an associated increase in frequency. The consistency of stool often depends on the extent of the disease with more extensive involvement often leading to an increased looseness of stool. In fact severe proctitis can present with constipation although the patient often passes blood and mucus independent of stool in these situations. Abdominal pain is more common in more extensive and severe disease, as are systemic symptoms such as fever, anorexia and weight loss.
- Some patients have extraintestinal manifestations of the disease such as PSC and pyoderma gangrenosum, which are unrelated to the disease activity of the colitis, and others such as arthritis and erythema nodosum which follow the clinical course of the gastrointestinal (GI) disease.
- The main symptoms are summarised in Table 7.1.1.
- Abdominal examination is often unremarkable apart from mild tenderness. Significant tympanitic distension or any evidence of peritonism are of great concern and need urgent attention. During acute attacks

Table 7.1.1 Presenting symptoms of UC

Gastrointestinal	Diarrhoea usually mixed with blood ± mucus
	Frequency
	Constipation in some cases of severe proctitis
	Urgency
	Tenesmus
	Incontinence
	Abdominal pain
Systemic	Tiredness
	Weight loss
	Fever
	Anorexia
Extraintestinal	*Related to disease activity:*
	Arthritis
	Uveitis/iritis
	Deep vein thrombosis (DVT)
	Erythema nodosum
	Unrelated to disease activity:
	Primary sclerosing cholangitis (PSC)
	Ankylosing spondylitis
	Pyoderma gangrenosum
Complications	Colorectal cancer
	Acute lower GI haemorrhage
	Colonic perforation

the patient may become dehydrated, hypokalaemic (from diarrhoea) and anaemic (from GI blood loss).
- A relapsing and remitting course is the usual pattern of illness with about 50% of patients with UC having a relapse in any one year.
- Symptoms and signs can be formally scored using validated disease activity scores for UC (e.g. Lichtiger; see Table 7.1.2).

Table 7.1.2 Activity score for UC: Lichtiger et al. (1994)

Factor	Score
Diarrhoea	0 = 1–2/day 1 = 3–4/day 2 = 5–6/day 3 = 6–9/day 4 = > 10/day
Nocturnal bowel movement	0 = No 1 = Yes
Bloody stools	0 = None 1 = < 50% 2 = 50% or more of time 3 = Every time
Incontinence / soiling	0 = No 1 = Yes
Abdominal pain	0 = None 1 = Mild; minimal interference with daily activity 2 = Moderate; interferes with daily activity 3 = Severe; incapacitating
Wellbeing	0 (excellent) up to 5 (terrible)
Antidiarrhoeal or opioid drugs	0 = No
Abdominal tenderness	1 = Yes 0 = None 1 = Mild to moderate but localised 2 = Mild to moderate but diffuse 3 = Severe or evidence of peritonism

7.1.5 Complications

7.1.5.1 Colorectal Cancer

This is the commonest neoplastic complication of UC. It is more likely to be multiple, higher grade and non-polypoid than sporadic non-colitic cancers. Particular risk factors in the cohort of people with UC are:
- Pancolitis
- Diagnosis of PSC
- History of colitis of more than 8 years
- Severity of colitis and particularly of the first attack
- Early age of onset of colitis
- Family history of colorectal cancer

Considering all patients with UC, the risk of cancer increases with duration of disease:
- 2% at 10 years
- 10% at 20 years
- 20% at 25 years

The risk in the subgroup of those with pancolitis is significantly greater:
- 5% at 10 years
- 20% at 20 years
- 40% at 25 years

Dysplasia in UC can be difficult to detect and can be one of three different morphological forms:
- Sporadic adenomas (as in non-colitic patients)
  - Treated by polypectomy as in non-colitic patients
- Dysplasia-associated lesion or mass (DALMs)
  - Plaque-like lesions of mucosa, colectomy is advised
- Flat dysplasia
  - May be invisible to naked eye but seen histologically, often over a wide area of the colonic surface, hence the importance of multiple biopsies even from normal-looking areas of the colon

A colectomy should be recommended to all patients with:
- Cancer
- DALM
- High-grade dysplasia in any mucosal lesion
- Low-grade dysplasia at multiple sites

As a result screening for colorectal cancer in patients with UC is important. Screening guidelines are as follows:
- Performed when patient is in remission.

- First surveillance colonoscopy after 8–10 years from onset of symptoms that also accurately documents disease extent.
- Regular surveillance should begin at 8–10 years for pancolitis, and after 15–20 years for left-sided disease.
- The interval between colonoscopies should decrease with time. For pancolitis:
  - Every 3 years in the second decade following symptom onset
  - Every 2 years in the third decade
  - Annually in the fourth decade
- Two to four random biopsies every 10 cm from the entire colon and rectum. Additional biopsies should be taken of suspicious areas.
- Patients diagnosed with PSC should have annual colonoscopies irrespective of the state of their liver disease and the activity of the UC.
- In patients with low-grade dysplasia at one site, colonoscopy should be carried out every 6 months until two successive colonoscopies are negative.

7.1.5.2 Cholangiocarcinoma

- Increased in patients with UC on account of the relationship between UC and PSC.
- About 4% of UC patients develop PSC during their lifetime and in this population the lifetime risk of cholangiocarcinoma is about 10%.
- The risk of cholangiocarcinoma, like PSC, is not influenced by the disease activity UC.

7.1.5.3 Toxic Megacolon

This is a non-obstructive dilatation of colon > 6 cm in conjunction with pancolitis (rarely just left-sided disease) and systemic disturbance. The incidence is falling and currently occurs in less than 4% of UC patients. Patients are at greatest risk early after diagnosis, especially during the first attack. It often follows a prolonged attack of drug-resistant acute colitis and precipitants are believed to include hypokalaemia, opioid analgesics, constipating drugs, anticholinergics and possibly superadded infections such as *Clostridium difficile* and cytomegalovirus. Examination reveals mild tympanitic distension but any evidence of localised or generalised peritonism should be an indication for emergency surgery.

Medical management of their UC is permissible in the first instance (see later) but any deterioration or failure to improve should again lead to emergency surgery.

The criteria for diagnosis are as follows:

- Diagnosis of colitis
- Radiographic evidence of colonic distension > 6 cm
- Fever > 38°C
- Heart rate > 120 bpm
- Neutrophilia > 10×10^9
- One of the following:
  - Anaemia
  - Dehydration
  - Electrolyte disturbance
  - Hypotension
  - Reduced Glasgow Coma Scale

The dilatation is accompanied by and possibly due to inflammation of the bowel wall extending beyond the mucosa into the muscle. This leaves the bowel prone to perforation which is why the condition is so dangerous. Perforation of a toxic megacolon carries a mortality of 40%.

7.1.5.4 Acute Gastrointestinal Haemorrhage

- Severe bleeds occurs in less than 5% of all UC patients but accounts for about 10% of the emergency colectomies performed for UC.
- The risk of significant haemorrhage obviously increases with the extent of the disease.

7.1.5.5 Benign Strictures

- These occur in about 4% of all UC patients, predominantly in the left colon.
- Treatment depends on the degree of symptoms and the extent of disease elsewhere in the colon.
- Total colectomy is the usual surgical option.

7.1.6 Diagnosis

The diagnosis of UC is made by a suggestive history and examination leading to a combination of endoscopic, histological and microbiological investigations.

7.1.6.1 Endoscopy

The gold standard for diagnosing colitis is flexible sigmoidoscopy/colonoscopy. This shows acute inflammation starting in the rectum and extending proximally and allows biopsies to be taken for histology. Care is required, however, as the risk of perforation is high in acute disease and colonoscopy should be reserved for assessing the ex-

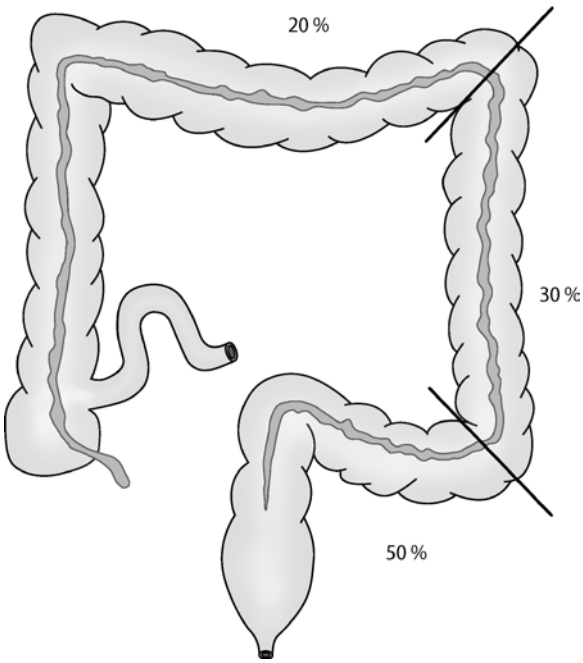


Fig. 7.1.1 Proportion of people with varying extent of disease at presentation

tent of disease after the acute attack has been treated. At presentation 20% of patients have disease throughout the colon, i.e. pancolitis (Fig. 7.1.1).

In active disease the mucosa is erythematous, granular, friable and demonstrates contact bleeding. Pseudopolyps, which are islands of mucosa within an area of extensive ulceration, may be present in severe disease. In quiescent chronic disease the mucosa usually shows the signs of chronic injury with loss of the normal vascular pattern and may look featureless. Inflammatory polyps may be present.

Biopsies should be taken from multiple sites along the colon (including normal-looking areas) and always including the rectum. The contiguous nature of the disease is one of the major features that distinguishes UC from Crohn's, although this is not always apparent macroscopically. However, even when there is variation in the severity of the colitis between different segments of the bowel, which can falsely give the impression of skip lesions, biopsies from the apparent "skip" area usually show features of chronic inflammation typical of UC, highlighting the importance of multiple biopsies. Another area of confusion is near the ileocaecal valve where the "caecal patch" can give the impression that it is a focus of inflammation distant from a more distal area of colitis and therefore a "skip lesion". This can be seen even in normal asymptomatic individuals. In patients who have had topical therapy the rectum can look relatively normal giving the false impression of rectal sparing. Again biopsy is crucial in the diagnosis.

Once colitis is established as a cause of the patient's symptoms, histology and microbiology will help confirm the diagnosis of UC.

7.1.6.2 Microbiology

All patients with colitis should have stool sent for microbiological assessment to exclude an infectious cause of their colitis. This should include virology, parasitology and *C. difficile* toxin.

7.1.6.3 Histology

Ulcerative colitis is confined to the large bowel although up to 30 cm of terminal ileum can be involved with "backwash ileitis".

Biopsies taken at the time of flexible sigmoidoscopy should describe whether the tissue shows the features of UC, to distinguish it from other common causes of colitis such as Crohn's, pseudomembranous and diverticular. They should also comment on any dysplasia seen within the specimen.

The severity of the inflammatory reaction seen correlates well with the clinical course of the disease. Most of the cardinal features of UC include:

- Inflammation limited to the mucosa and superficial submucosa although deeper layers can be involved in fulminant colitis.
- Diffuse and severe distortion of crypt architecture, although this can take 6/52 to develop.
- Diffuse and severe reduction in crypt density.
- Heavy infiltration of inflammatory cells in the lamina propria. In active disease neutrophils are prevalent and these can form crypt abscesses which are a reliable indicator of disease severity.
- Severe mucin depletion.
- Superficial ulceration in active disease.

7.1.6.4 Additional Useful Diagnostic Procedures

Blood Tests

Often show a chronic or acute-on-chronic inflammatory response. Look for:

- Raised C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), white cell count.
- Low haemoglobin (Hb), albumin.
- Renal function in all patients presenting with severe acute colitis.
- Liver function tests to assess progressive PSC.
- Perinuclear anticytoplasmic antibodies (pANCA) serology is commonly positive in UC whilst Crohn's disease is often negative for pANCA but positive for anti-*Saccharomyces cerevisiae* mannan antibodies (ASCA). Patients who are pANCA positive and ASCA negative are far more likely to have UC than Crohn's.

Imaging

- Plain abdominal radiograph is vital in cases of severe acute colitis to exclude any toxic dilatation of the colon. If there is any suspicion of toxic megacolon clinically or radiologically this should be repeated on a daily basis until the clinical condition improves. Oedema of the bowel wall can be seen as "thumbprinting".
- Barium enema may show a "drain pipe" colon in chronic cases with loss of haustrations and normal mucosal features. Pseudopolyps are a sign of severe mucosal disease, not necessarily acute. Barium enema is inferior to endoscopy and as such should be reserved for cases where endoscopy has failed.
- An erect chest radiograph is also useful in cases of suspected perforation.
- Computed tomography (CT) has become useful in assessing the extent of inflammation in UC although this is non-specific and does not help in separating the various possible aetiologies of the inflammation.

7.1.7 Therapy

Ulcerative colitis should be managed jointly by physicians and surgeons.

7.1.7.1 Conservative Treatment

No evidence that elemental diets or any other treatment outside pharmacological or surgical treatment is of benefit either in the induction or maintenance of remission in UC. Medical treatment is divided into treatment for acute disease, chronic active disease and maintenance of remission. Following ileal pouch formation (see later) patients can develop pouchitis. This is also discussed.

Acute Colitis

Patients with mild/moderate disease can be managed as outpatients whereas those with severe disease require inpatient care. Severe attacks are characterised by:

- Stool frequency > 6 per day
- Plus any one from:
  - Temperature > 37.8°C
  - Pulse > 90 bpm
  - Hb < 10.5 g/dl
  - ESR > 30 mm/h

Severe Attacks

- Frequent clinical evaluation including stool charts.
- Daily blood (full blood count (FBC), CRP, electrolytes, albumin) assessment.
- Daily abdominal radiograph if any suspicion of colonic dilatation.
- High-dose intravenous (e.g. hydrocortisone 100 mg q.d.s.) and topical steroids administered rectally (e.g. prednisolone enemas b.d.).
- Intravenous cyclosporin if no significant improvement after 3 days followed by oral cyclosporin when in remission (2 mg/kg i.v. and 4–9 mg/kg orally) or oral azathioprine (1.5–2.5 mg/kg/day). This has been shown to reduce the colectomy rate in patients not responding to steroids although there is a high relapse rate once the cyclosporin is stopped.
- Intravenous electrolyte-rich fluid ± blood as required.
- Anticoagulation is essential in UC given the increased risk of deep vein thrombosis (DVT) in these patients (e.g. subcutaneous low-dose heparin 5,000 U once daily).
- Avoid antidiarrhoeal drugs (e.g. loperamide, codeine), opioids, anticholinergics and, if possible, NSAIDs all of which increase the risk of perforation. Remember that significant pain may indicate perforation.
- Oral 5-aminosalicylic acid (5-ASA) compounds provide no advantage in acute colitis.
- Broad-spectrum antibiotics can be used in those showing signs of septic complications.
- After 3 days treatment, patients with stool frequency > 8/day or a CRP > 45 are unlikely to improve without a colectomy.
- Failure to improve within 5 days of treatment or deterioration within that period indicates that surgery is required.
- Once the clinical condition has improved patients should convert to oral treatment as for mild-moderate acute attacks.

Mild-moderate Acute Colitis

- These can be treated by oral steroids with a reducing oral dose starting at 40 mg prednisolone daily and reducing over 8 weeks until treatment is stopped.
- This should be combined with rectal steroids or 5-ASA compounds (e.g. mesalazine enemas 1 g daily). These should be reduced slowly as the symptoms improve.
- If symptoms deteriorate during the reducing regimen then the steroids should be increased again until symptoms settle. 5-ASA enemas may be superior to local steroids for left-sided disease.
- Oral mesalazine 2–4 g daily which should be continued after remission is established, initially, and then at half this dose after 2 months (see below).

Chronic Active Disease

- Oral steroids and 5-ASA, such as mesalazine 4 g daily initially, form the basis of treatment. These are used in conjunction with 5-ASA enemas (e.g. mesalazine 1 g daily) as above.
- Failure to wean completely from steroids should lead to consideration of azathioprine as a steroid-sparing agent (aim for a maintenance dose of 1.5–2.5 mg/kg/day).
- Cyclosporin may also be useful in reducing the dose of steroid required.
- For distal disease (proctosigmoiditis) topical and oral mesalazine should be considered, with oral and rectal steroids reserved for those who fail to respond.

Maintenance of Remission in Quiescent Disease

- Lifelong treatment if tolerated.
- 5-ASA compounds are the mainstay of treatment (e.g. mesalazine 1–2 g/day).
- For distal disease treatment with topical 5-ASA therapy alone is acceptable if tolerated (e.g. mesalazine 500 mg daily).
- For those with frequent relapses despite or intolerant to 5-ASA compounds, consider azathioprine 1.5–2.5 mg/kg/day.

Pouchitis

- Antibiotic therapy is the first-line treatment, commonly with metronidazole (400 mg t.d.s.) or ciprofloxacin (500 mg b.d.s.) for 2 weeks.
- There is some evidence that combined ciprofloxacin and metronidazole for 4 weeks is superior in reducing remission.
- Low-dose long-term antibiotics can be used for those with frequent relapses.
- Topical mesalazine or steroids are used when antibiotics fail to improve the pouchitis.
- Concentrated preparations of probiotic bacteria (e.g. lactobacilli, bifidobacteria combinations) have been used with some success in maintaining remission in chronic pouchitis.

7.1.7.2 Surgical Treatment

Up to 30% of patients with UC will ultimately require a colectomy. Indications for surgery are:

- Development of complications (e.g. perforation, haemorrhage, cancer)
- Failure of medical treatment
  - Intractable symptoms
  - Frequent relapses or steroid resistance
  - Drug side effects including steroid dependence

In both situations there are those who require emergency surgery (e.g. severe acute colitis not responding to medical treatment (Fig. 7.1.2), colonic perforation) and those who can have their surgery planned electively.

Emergency

Emergency surgery involves total colectomy and end ileostomy as a life-saving procedure. Patients presenting with severe acute colitis for their first attack are the most likely to require colectomy (up to 25%).

Following recovery from a total colectomy, thought must be given to the fate of the remaining rectum as it can continue to cause bloody anal discharge if the inflammation fails to subside and it remains a site of potential cancer, although the risk is about 5% over 20 years. There are four options for the residual rectum:

1. Progression to restorative proctocolectomy if suitable (see *Exemplary Surgical Procedures*).
2. Completion proctectomy (see *Additional Useful Surgical Procedures*).
3. Rectal mucosectomy: Elderly patients with significant rectal disease in whom the rectum has been divided at the level of the levators during emergency surgery, knowing that a pouch or ileorectal anastomosis would never be considered. Rarely used.
4. Surveillance only: Elderly patient without significant disease.

Elective

In the elective situation there are three surgical options:

1. Panproctocolectomy and end ileostomy
2. Total colectomy and ileorectal anastomosis

Fig. 7.1.2 Severe acute colitis

3. Panproctocolectomy and ileal pouch–anal anastomosis

The choice of operation depends on patient fitness, sphincter function and choice. All three elective procedures can now be carried out with laparoscopic assistance.

Preoperative Preparation

This is most important in the emergency situation.

- Patients must be adequately hydrated with a good urine output.
- A haemoglobin concentration > 9 g/dl is usually acceptable in an otherwise fit patient without prior transfusion.
- Renal and hepatic function should be checked and significant electrolyte or clotting abnormalities corrected.

In the elective situation more attention is directed at choosing the best time for surgery when nutritional status is optimised and the steroid dose is as low as possible.

Additional Useful Surgical Procedures

Completion Proctectomy

If the rectum has been divided in the lower third during a previous operation, the anus and residual rectum can be removed via an intersphincteric circumanal incision, much in the same way as for a panproctocolectomy and end ileostomy (see later). The defect in the perineum is closed in layers. Otherwise a combined abdominal and perineal approach is required to remove the rectum.

Closure of Loop Ileostomy

This is usually a third-stage procedure after restorative proctocolectomy. After checking with a pouchogram and pouchoscopy that the pouch has healed and that there is no stenosis of the pouch–anal anastomosis the loop ileostomy is mobilised around its site in the right iliac fossa (RIF), reanastomosed and the abdomen closed. There is rarely a need to open the midline abdominal wound.

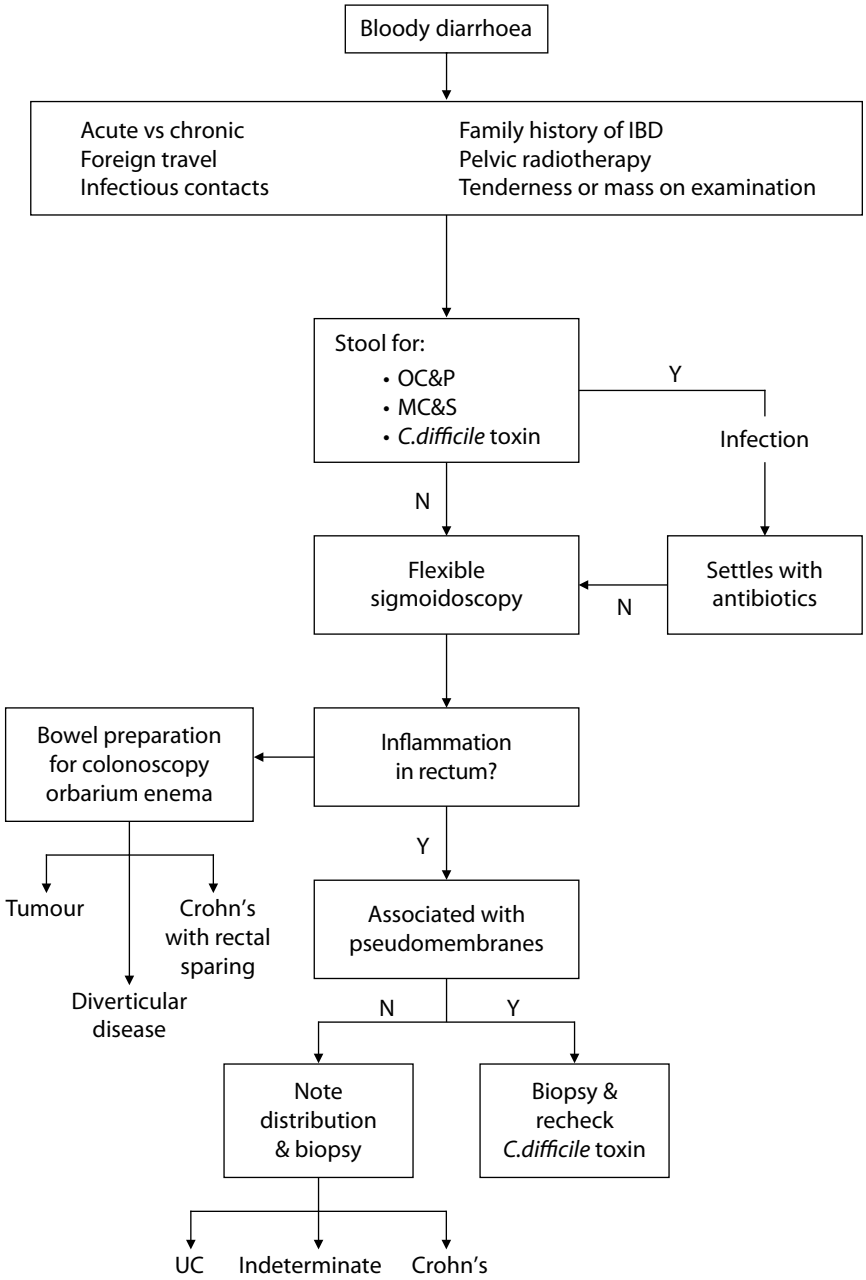


Fig. 7.1.3 Basic algorithm for investigation of bloody diarrhoea. *IBD* irritable bowel disease, *MC&S* , *OC&P* , *N* no, *Y* yes

Table 7.1.3 Differences between UC and Crohn's disease

	Ulcerative colitis	Crohn's disease
Clinical:		
Distribution	Continuous	Skip/focality
Small-bowel disease	Not involved	Common
Rectal involvement	Always	Often spared
Anal disease	Rare	Common
Fistulae	Rare	Common
Strictures	Rare	Common
Histological:		
Depth of inflammation	Mucosa/submucosa	Full thickness
Mucin depletion	Common	Uncommon
Crypt abscesses	Frequent	Occasional
Granulomata	Rare	Common
Serological:		
ASCA	15%	65%
pANCA	70%	20%

7.1.8 Differential Diagnosis

Figure 7.1.3 shows the algorithm for investigation of bloody diarrhoea. Other causes of colitis need to be excluded:

- Crohn's – this is the closest differential to UC. The differences are highlighted in Table 7.1.3. Occasionally biopsies are not diagnostic of any specific inflammatory bowel disease and these are given the title of indeterminate colitis
- Infective
  - Recent contact with infectious patient
  - Recent antibiotic use for *C. difficile* infection
- Diverticular
  - Rectum looks normal in these patients
  - Bleeding diverticulae seen on endoscopy or diverticular disease noted on CT scan
- Radiation
- Ischaemic
  - Onset in older person with features of vascular disease elsewhere or recent surgery for an abdominal aneurysm.
  - Often associated with significant abdominal pain
- Beçhet's enterocolitis
  - Associated past history of genital ulceration, arthropathy, uveitis

These other causes can normally be excluded by a combination of:

- Clinical history and examination
- Sigmoidoscopy and biopsy
- Histology
- Microbiology

7.1.9 Prognosis

- Surgery is curative in UC and the morbidity and mortality associated with the disease has improved as a result of better timing of surgery and improved surgical and anaesthetic techniques.
- Surgery is not reserved for complications of UC; if quality of life is poor as a result of uncontrolled disease or the side effects of medication, surgery is a sensible option.
- About 30% of patients will eventually have a colectomy.
- When surgery is necessary, the availability of restorative proctocolectomy as an alternative to an end ileostomy has also improved the quality of life in those for whom a permanent ileostomy seems unbearable.
- The majority of patients live an unrestricted life and have a normal life expectancy.

Table 7.1.4 Comparison of the three common elective operations for UC

	Proctocolectomy/ end ileostomy	Colectomy and ileorectal anastomosis	Restorative proctocolectomy
Advantages:	Curative	One operation	Curative
	One operation	No risk to sphincter	Avoids permanent ileostomy
		No risk to pelvic nerves	
Disadvantages:	Permanent ileostomy	Not curative: may require continuing treatment	Failure rate 10%
		Requires surveillance	Frequency of evacuation
			Two operations required
Complications:	Stoma revision 10–20%	Small-bowel obstruction 10–20%	Pouchitis 40%
	Perineal wound problems 20%	Anastomotic leak 5%	Fistulae to pouch
	Small-bowel obstruction 10–20%		Small-bowel obstruction 10–20%
	Minimal bladder or sexual dysfunction		Anastomotic leak 5%
			Sexual dysfunction 5%
Contraindications:	Aversion to stomas	Weak anal sphincters	Low rectal cancer or dysplasia
		Severe proctitis	Weak anal sphincters
		Rectal dysplasia or cancer	

7.1.10 Exemplary Surgical Procedures

We will discuss four operations:

1. Emergency colectomy, end ileostomy and preservation of the rectal stump
2. Colectomy and ileorectal anastomosis
3. Proctocolectomy and end ileostomy
4. Restorative proctocolectomy (with diverting ileostomy)

A comparison of all the elective techniques (2–4) is given in Table 7.1.4.

All four operations share these common factors:

- All operations involving stomas should be seen by a stomatherapy nurse and sited on the ward if possible
- General anaesthesia (combined with epidural in the elective setting)
- Lloyd Davis position
- Urinary catheter
- Midline incision

7.1.10.1 Emergency Colectomy and End Ileostomy

This is the operation of choice for the emergency situation. It can occasionally be used in the elective situation where a patient is undecided about long-term options and gives them invaluable experience of managing a stoma and the quality of life that could be expected with a permanent stoma. Indications are given above.

Technique

- If the colon is dilated, insert a rigid sigmoidoscope to deflate prior to incision and leave a rectal catheter postoperatively.
- Mobilisation of the right colon and ileocaecal junction to avoid tension on the ileocolic and right colic vessels when the left colon is mobilised.
- Division of ileum just proximal to the ileocaecal junction.
- Left colon mobilised and divided at the level of the distal sigmoid to retain enough length for a mucous fistula (Fig. 7.1.4). However, it may be necessary to divide the bowel more distally in cases where there is severe bleeding rectal ulceration. Division below the area of bleeding is obviously necessary in these cases.

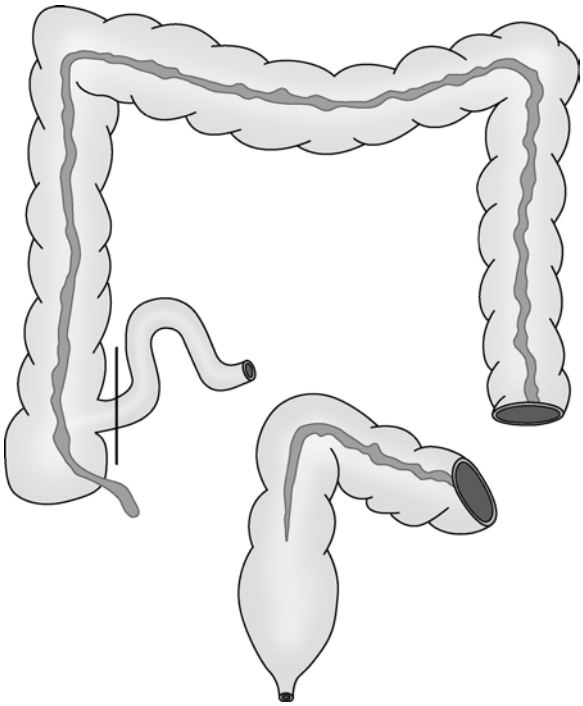


Fig. 7.1.4 Division of the distal colon in emergency colectomy leaving a long distal stump to form a mucous fistula

- The ileum is brought out through a trephine in the RIF, premarked on the ward if the clinical condition allows.
- The distal sigmoid is brought out as a mucous fistula, or closed and attached to the anterior abdominal wall.

Possible Complications

- The stump leak rate is about 2% although this is prevented by forming a mucous fistula and perhaps leaving a rectal catheter.
- Complications specific to the stoma include high-output stomas, parastomal hernias, stomal prolapse, stricture, retraction and ischaemia of the stoma. About 25% will need revision at 5 years (see Table 7.1.4).

7.1.10.2 Colectomy and Ileorectal Anastomosis

Indicated only in young patients with minimal rectal inflammation, no sphincter dysfunction and good rectal compliance. There must be no evidence of dysplasia anywhere in the large bowel.

Technique

- The colonic mobilisation occurs as for a total colectomy (above).
- Only the upper rectum is mobilised.
- The bowel is divided at the upper rectum and a hand-sewn end-end ileorectal anastomosis can be carried out with ease at this level.
- It is possible to perform an end-end stapled anastomosis with a peranal circular stapling device or by hand sutures. However, this would have to be negotiated along the entire length of the rectum, avoiding injury to the diseased mucosa. It offers no advantage to a sutured anastomosis.

Possible Complications

- The risk of cancer in the rectum is low but still requires annual surveillance with flexible sigmoidoscopy and biopsy.
- Anastomotic leak and the risk of small-bowel obstruction are equivalent to those for restorative proctocolectomy (see Table 7.1.4).

7.1.10.3 Proctocolectomy and End Ileostomy

Indicated in:

- Weak sphincters
- Low rectal cancers
- Patients who find potential complications of restorative proctocolectomy unacceptable
- Patients who are keen for permanent ileostomy

Technique

- Purse-string suture to close the anus.
- Some advocate making trephine for ileostomy before midline incision to avoid the distortion later created in the abdominal wall by the laparotomy incision.
- In non-neoplastic cases the colonic mobilisation is as described for total colectomy (above).
- In operations for dysplasia or carcinoma, a cancer technique should be employed with high ligation and wide clearance.
- The rectum should be mobilised by a technique designed to minimise the risk to the pelvic nerves: either a close perimuscular dissection or a mixed dissection utilising the mesorectal plane in areas where the risk to the autonomic nerves is not high and a perimuscular technique in areas of greatest risk. In neoplastic cases, however, the mesorectal plane should be used as in other cancer operations.
- Perineal dissection of the lower rectum should take place in the intersphincteric plane to minimise

perineal complications. Again for neoplastic complications, the extrasphincteric plane should be used as for abdominoperineal resections for cancer.
- The empty pelvis is drained with drains via the lower abdominal wall.
- The distal ileum is brought out as an end ileostomy and everted to form a spout of about 2.5 cm from the anterior abdominal wall.

Possible Complications
- Obstruction and pelvic sepsis are the commonest postoperative complications.
- Perineal wound problems are common.
- Ileostomy complications as mentioned above (see Table 7.1.4).

7.1.10.4 Restorative Proctocolectomy

Before surgery, consideration needs to be given to the following:
- Age: caution at both extremes. In the elderly thought needs to be given to sphincter function and the added morbidity of the elderly patient undergoing major abdominal surgery. In the paediatric patient, smaller anatomy especially with respect to the pelvic nerves, and the implications of teenage years with a pouch need consideration.
- Sphincter assessment: endoanal ultrasound and physiology to ensure good sphincter function.
- Fertility: all men who would consider having children in the future should have a semen specimen taken for storage. All women considering having children should be advised that fecundity is reduced following this operation and if possible to wait until their family is completed before having pouch surgery.
- Pregnancy: most women should be advised to have a caesarean section for future pregnancies.
- Histology: the slides should be reviewed by an experienced pathologist with a specialist interest in colorectal pathology. The pouch failure rates in indeterminate colitis and Crohn's disease is 30–50%.
- Patients with PSC have a higher incidence of pouchitis and pouch failure and need to be counselled accordingly.

Technique
- Abdominal mobilisation of the colon and rectum is as for proctocolectomy and end ileostomy. There is no perineal dissection and the rectum is mobilised to the anorectal junction from above.
- A clamp is placed on the mid-rectum and the rectum is washed out per anum.
- Care to avoid the vagina anteriorly in women.
- A transverse right-angled stapler is applied to the anorectal junction and the bowel divided leaving a cuff of rectum as short as possible. The surgeon can check the length by introducing a finger per rectum and closing the stapler just above the finger tip. There is no advantage in doing a hand-sutured anastomosis with mucosectomy and in addition the mucosectomy may cause functional problems. The cancer risk of a remnant mucosa is limited.
- Ileum transected just proximal to the ileocaecal valve.
- Small-bowel mesentery mobilised completely to the junction of third and fourth parts of the duodenum.
- Selected mesenteric vessels can be divided to provide extra length if required.
- J-pouch formed from the terminal 30–40 cm of ileum by folding it into two 15- to 20-cm limbs and using a linear stapler to form a common lumen with a side-side anastomosis (Fig. 7.1.5). It will require two firings of the 100-mm stapler to complete the pouch.
- Purse-string suture placed around the enterotomy used for the linear stapler and this secures the anvil of the stapler.
- Circular per anal stapler advanced to staple line and spike advanced through the staples and then removed. United with the anvil and the stapler fired (Fig. 7.1.6).
- Donuts inspected and anastomosis tested.
- Loop ileostomy through RIF trephine.

Possible Complications

Overall pouch failure occurs in about 10% of cases. Common causes of failure (see Table 7.1.4) include:
- *Pelvic sepsis including fistulae:* About one third of pouches complicated by pelvic sepsis will fail. Common reasons include anastomotic leaks or infected haematomas. Later, fistulae from the pouch, particularly to vagina or perineum, occur in 7–8% of patients and usually require defunctioning followed by further surgery.
- *Poor function:* Good pouch function is considered to be anything up to 6/day. Frequency, especially associated with urgency and poor gas-liquid discrimination, significantly impacts on a patient's quality of life. There are a number of possible causes given in Table 7.1.5.
- *Pouchitis:* Inflammation can develop in the ileal pouch which can lead to symptoms of frequency of stool, urgency and occasional per rectum bleeding and pelvic pain. It is diagnosed by positive criteria in all of:
  - Clinical history
  - Endoscopic findings
  - Histological findings

It is a significant problem affecting 30–40% of people following ileal pouch surgery but only 10% will have recurrent attacks. In 1–2% of cases it is so severe as to require pouch excision or rediversion with a loop ileostomy. Treatment is detailed above.

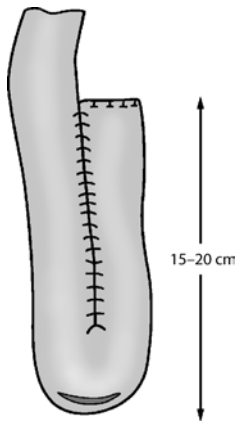


Fig. 7.1.5 Ileal J-pouch construct

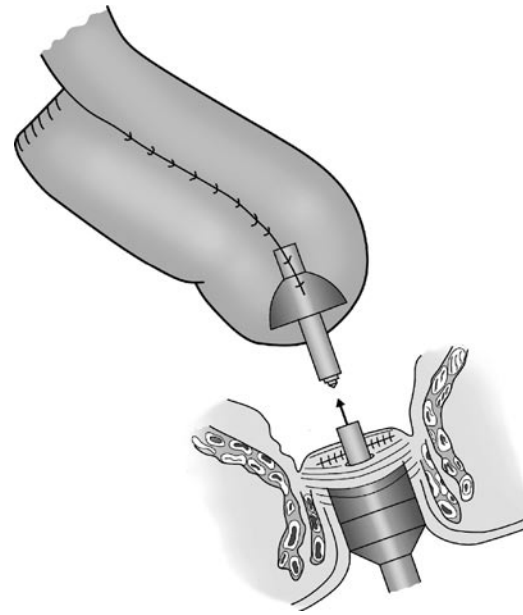


Fig. 7.1.6 Formation of the stapled ileal pouch–anal anastomosis

Table 7.1.5 Causes of poor pouch function

Small bowel	Incomplete bowel obstruction
	Bacterial overgrowth
	Irritable bowel
	Dietary sensitivities, e.g. lactose intolerance
Outlet problems	Anastomotic stricture
	Weak sphincters
Inflammatory	Pouchitis
	Cuffitis
	Crohn's disease
Septic	Chronic pelvic abscess
Pouch structure	Small volume pouch

7.2 Crohn's Disease

PETER ANDERSSON, RUNE SJÖDAHL

7.2.1 Introduction

- Crohn's disease is a chronic inflammation which initially was believed to be located to the terminal ileum. However, it is now well known that it may involve any part of the gastrointestinal tract from mouth to anus.
- Characteristic is its segmental distribution, often with rectal sparing but frequently with anorectal disease.
- The onset is common in young people and the burden to the healthcare system as well as the community is substantial.
- Until now there is no cure for Crohn's disease and both the medical and surgical treatment aims at reducing the symptom load.
- Many patients can live a fairly normal life but 20–30% have more or less severe restrictions of their working ability.
- The cumulative mortality has been increased, approximately twofold.
- Sepsis, liver failure and thromboembolism are the main causes of death in patients with severe chronic disease.

7.2.2 Distribution of Crohn's Disease

- Terminal ileitis and ileocaecal involvement 45%
- Colitis (segmental or general) 25%
- Ileocolitis 20%
- Extensive small bowel 5%
- Other 5%
  (anorectal, jejunal, gastroduodenal, oral only)

The rectum is involved in about 10% of patients with Crohn's disease. Anorectal manifestations are seen in about 25% of patients.

7.2.3 Epidemiology

Crohn's disease is more common in western countries than in Africa, Asia or South America. The incidence in western Europe is 5–10/10^5/year and there is a major peak at 20–40 years of age. The prevalence is 50–150/10^5 population.

7.2.4 Aetiology

The aetiology is unknown but there is consensus that the chronic inflammation in Crohn's disease is associated with an immunological dysfunction that may be related both to a genetic predisposition and to environmental factors.

There is no single mendelian pattern of inheritance, but the evidence is increasing for a heterogeneous polygenic disorder. There seems to be an association between NOD2 gene mutations on chromosome 16 and increased susceptibility to Crohn's disease. NOD2 is an intracellular protein expressed in monocytes/macrophages where it might be a receptor for bacterial products transducing signals that lead to activation of NFκB and transcription of proinflammatory genes. Thus mutations of the NOD2 gene may lead to an altered inflammatory response.

There is substantial clinical and experimental evidence showing the importance of the faecal stream for initiating and/or maintaining the inflammatory process. In animal models the presence of gut flora is essential for creating chronic intestinal inflammation. Patients with active disease show reduced immunological tolerance to intestinal microflora. Antibiotics have a therapeutic role particularly in colonic and anorectal Crohn's disease but the role of probiotics is still not known. Specific infections such as *Mycobacterium paratuberculosis*, measles virus and *Listeria monocytogenes* have been studied for a long time but still the data are controversial. Smoking is harmful in Crohn's disease and increases the risk of relapse and surgery.

7.2.5 Pathogenesis

Increased mucosal permeability and altered immune regulation are associated with the prolonged inflammatory reaction. The up-regulation of nuclear transcription factors such as NFκB leads to local release of cytokines, growth factors, reactive oxygen metabolites, nitric oxide, eicosanoids and other mediators. T cells and regulatory cytokines have a central role and mediate a Th1-induced cell-mediated response. The Th1 response comprises IL-2, interferon, IL-12, IL-1 and IL-6. TNFα is a highly proinflammatory molecule released by activated T cells, mast cells and macrophages. High concentrations are found both in normal and inflamed mucosa in patients with Crohn's disease suggesting that TNFα has an early role in the cytokine cascade of the inflammatory process. Animal models that overexpress TNFα genes develop terminal ileitis and blockade of TNFα induces healing of a Crohn-like enteritis.

7.2.6 Pathology

- Typically the inflammation is segmental. Sometimes the segment is very short involving only 1–3 cm (skip lesions).
- The first histological lesion is lymphoid follicular enlargement. It leads to an aphthoid ulcer which progresses to deep fissuring ulcers which can further develop into cobble-stoning, fibrosis, stenosis and fistulae.
- The fibrosis can result in intestinal strictures or local perforation with abscess formation.
- The inflammation is characterised by transmural chronic inflammatory cell infiltration (lymphocytes) and histiocytic cell proliferation with ulcers and microabscesses.
- Non-caseating epithelioid granulomas sometimes with giant cells are found in about 25% of patients when colonoscopic biopsies are investigated and in about 60% when resected bowel specimens are examined. Granulomas can be detected in about 10% of macroscopically normal mucosa in Crohn's disease patients.

7.2.7 Symptoms

The symptoms and signs depend on the site of the Crohn's disease inflammation and the dominating pathological process.

- *Active ileocaecal and terminal ileal disease:*
  - Pain (dominating)
  - Weight loss
  - Frequent bowel movements
  - Tender mass in the right iliac fossa

The pain is constant when it is caused by inflammation or abscess while it is intermittent and sometimes associated with vomiting when there are episodes of intestinal obstruction caused by a stenosis. The diarrhoea can be due to mucosal inflammation, bile salt malabsorption or bacterial overgrowth proximal to a stenosis.

- *Active colitis:*
  - Frequent diarrhoea (bleeding not common, diarrhoea more prominent than pain)
  - Peridefaecatory abdominal pain
  - Fever
  - Malaise
  - Anorexia
  - Weight loss
- *Extensive small bowel disease:*
  - Symptoms as above
  - Malabsorption, e.g. steatorrhoea
  - Anaemia
  - Weight loss
- *Proctitis:*
  - Tenesmus
  - Abscess/fistula in 40–80%
  - Anal ulcerations and stenosis
- *Anorectal disease (fistula, fissure, abscess):*
  - Pain
  - Discharge
- *Gastroduodenal disease:*
  - Upper abdominal pain
  - Dyspepsia
  - Anorexia
  - Nausea/vomiting
  - Weight loss
- *Oral disease:*
  - Chronic ulceration
  - Induration

7.2.8 Extraintestinal Manifestations

Most occur in colitis:

- Arthropathy (enteropathic arthritis)
- Ankylosing spondylitis
- Erythema nodosum
- Pyoderma gangrenosum
- Episcleritis
- Uveitis

When the arthropathy is associated with active disease it usually involves one large joint, for example the knee. Small joints may also be affected but they are usually chronic and not related to the activity of Crohn's disease.

Ankylosing spondylitis occurs in about 5% of patients with Crohn's disease with colitis, usually HLA B27 positive. Sacroilitis is a common manifestation. Typical symptoms are back pain and stiffness. The ankylosing spondylitis is independent of the disease activity and may appear years before Crohn's disease is diagnosed.

Erythema nodosum occurs in about 8% of Crohn's disease with colitis. It is related to active disease. Typically red and tender nodules appear on the anterior surface of the lower legs and on the posterior surface of the lower arms. They gradually subside and leave a brownish spot.

Pyoderma gangrenosum is seen in about 2% of patients. It presents initially as a pustule with a surrounding erythema which develops into an indolent undermined ulcer. The lesions are usually multiple and can be seen on the legs, around a stoma or in operation scars.

Episcleritis and uveitis are usually associated with active disease but occur in less than 5% of patients.

7.2.9 Disease Activity

The heterogeneous and fluctuating picture of Crohn's disease makes it important to assess the disease activity in order to choose the optimal treatment. The activity can be measured by scores based on clinical and laboratory parameters. Crohn's disease activity index (CDAI) was developed from a number of clinical and common laboratory measurements best predicting the physician's global assessment of the clinical status. Remission is defined as CDAI < 150, mild disease 150–250, moderate disease 251–400, severe disease > 400. However, the original CDAI is rather complicated and has mostly been used in clinical trials. Best et al. simplified their original CDAI from 1976 to a modified version in 1981 where the laboratory tests are omitted (see Table 7.2.1). A problem with some of the activity indices is that the disease activity is biased by stool frequency which may also be high in inactive disease after surgery.

From a practical point of view the working definitions of the American College of Gastroenterology may be preferred in daily work:

- Remission (asymptomatic patients)
- Mild to moderate (oral nutrition, symptoms but no dehydration, no fever, no abdominal tenderness or mass, no obstruction)
- Moderate to severe (no treatment effect, symptoms such as fever, weight loss more than 10% of the body weight, abdominal pain or tenderness, anaemia, intermittent nausea or vomiting)
- Severe to fulminant (persistent symptoms despite oral steroids, or high fever, persistent vomiting, intestinal obstruction, rebound tenderness, cachexia or abscess)

Some blood tests are used to assess the disease activity. High activity is associated with high values of C-reactive protein (CRP), erythrocyte sedimentation rate (ESR) and platelet count while albumin is low.

7.2.10 Diagnosis

The diagnosis is suspected by segmental thickening of the bowel wall, by fistulae and by an intra-abdominal abscess. In addition, strictures, cobblestone mucosa, linear ulcerations, skip lesions and anorectal disease may suggest the diagnosis.

In patients under 50 years of age the main differential diagnoses are infection (Yersinia, *Clostridium difficile*, Campylobacter, Salmonella, Shigella), irritable bowel syndrome and ulcerative colitis. Diarrhoea may be caused by coeliac disease but it is usually excluded by a negative test for endomysial antibodies. In elderly people common differential diagnoses are small-bowel lymphoma, cancer, diverticular disease and ischaemic colitis.

For the clinician, the goals are as follows:

- To make a correct diagnosis of Crohn's disease
- To determine its location, its extent and its disease activity
- To identify any complications

Patients may have abdominal pain, diarrhoea, anaemia, raised platelet count, raised ESR but that is not diagnostic of Crohn's disease. In extensive small-bowel disease the patients may have low serum B_{12}. Low folate may indicate active chronic inflammation, reduced intake or malabsorption. Iron deficiency is common. Raised CRP and low serum albumin are associated with active disease.

Abdominal pain and a mass in the right iliac fossa may have several causes except Crohn's disease:

- Appendix mass
- Caecal carcinoma
- Lymphoma
- Carcinoid
- Ovarian cyst
- Endometriosis

7.2.10.1 Endoscopy

Although rectal inflammation or ulcerations can be seen, rectal sparing is common. In spite of this, perianal manifestations are, however, sometimes noticed. In a minority of patients with Crohn's disease with macroscopically normal rectal mucosa the biopsies reveal epithelioid granulomata. Endoscopy of the terminal ileum is important for the macroscopic and microscopic diagnosis. In early disease the red-ring sign (prominent lymphoid follicles) and

Table 7.2.1 Assessment of symptoms and illness in Crohn's disease

A. Modified Crohn's disease activity index (CDAI):
Assessed the day before the visit.
X1 = Number of soft or liquid stools per day
X2 = Abdominal pain rating
0 = well, 1 = mild, 2 = moderate, 3 = severe
X3 = Rating of feeling of well-being
0 = well, 1 = slightly below par, 2 = poor, 3 = very poor, 4 = terrible
X4 = Number of extraintestinal findings
X5 = Abdominal mass
0 = none, 2 = questionable, 5 = present
Modified CDAI: (X1+(X2+X3+X4+X5)2)20

aphthoid ulcerations are seen. In later stages deep ulcers separated by normal mucosa or a cobble-stone picture can be demonstrated. In the colon the inflammation is often segmentally distributed. Panendoscopic assessment of the small bowel via ingested capsule plays an increasing role in evaluation of patients with Crohn's disease. (see Fig. 7.2.1)

7.2.10.2 Radiography

A plain film can help diagnose an intestinal obstruction, a mass in the right iliac fossa and estimate the extent and severity of Crohn's colitis. Contrast examination of the small bowel showing stenoses, ulcerations and sometimes fistulae is crucial for the diagnosis of Crohn's disease proximal to the distal ileum. In active disease abdominal ultrasound and computed tomography (CT) can be very useful for the diagnosis of an abscess or a fluid collection but like magnetic resonance imaging (MRI) they can also be used to demonstrate inflammatory changes of the intestinal wall. (see Fig. 7.2.2 and Fig. 7.2.3)

Radiolabelled leukocyte scanning can be used to identify inflammation of deeper layers of the intestinal wall and to detect abscesses.

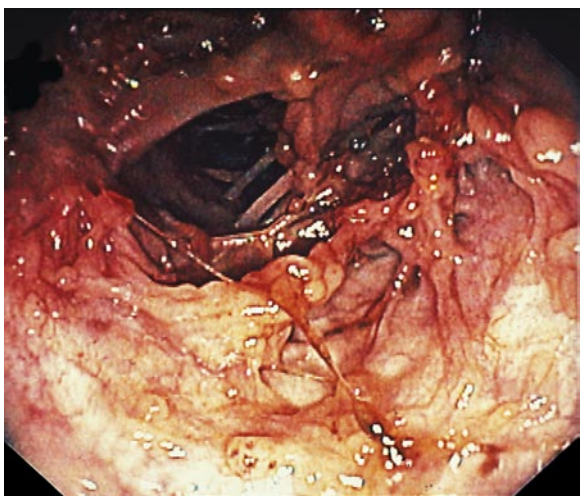


Fig. 7.2.1 Endoscopic appearance of Crohn's colitis

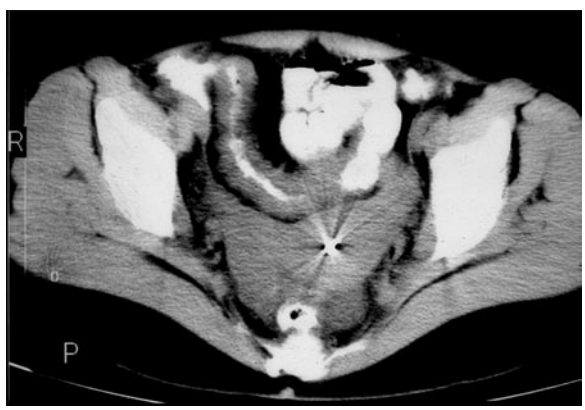


Fig. 7.2.2 CT-scan: Terminal ileitis

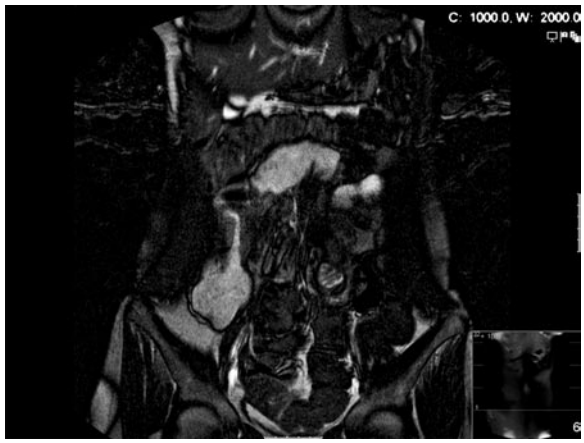


Fig. 7.2.3 MRI: Preanastomotic stricture

7.2.10.3 Clinical Findings, Histology and Serology

Clinical, histological and serological differences between ulcerative colitis and Crohn's disease are shown in Table 7.1.3.

7.2.11 Complications

Acute complications include:

- Complete intestinal obstruction. It is often caused by obturation and strangulation is extremely uncommon. Bowel rest and parenteral nutrition is recommended as first-line treatment. Emergency surgery is seldom necessary.
- Abscess of the abdominal cavity or wall. Percutaneous drainage is the treatment of choice.
- Free perforation to the abdominal cavity. Extremely rare condition but needs emergency surgery.
- Bleeding. It is uncommon and can usually be managed with non-surgical methods.

Chronic complications include:

- Malnutrition. Enteral and parenteral nutrition is usually necessary. In children and adolescents there is growth delay.
- Systemic inflammatory response syndrome (SIRS) with elevated CRP.
- Enterocutaneous fistula. Treatment of sepsis, adequate nutrition, mapping of anatomy, protection of skin and planning of management. More complex fistula (bladder, vagina, small bowel or large bowel are common.
- Sepsis. Eradication of septic focus; antibiotic treatment when necessary.

7.2.12 Classification

The pattern of Crohn's disease shows varying appearances. The disease can be classified as:

- Fibrostenotic
- Inflammatory
- Fistulating

Another classification is:

- Non-fistulating disease
- Fistulating disease
- Extensive disease
- Aggressive disease

The transmural inflammation which is characteristic for Crohn's disease predisposes to the formation of fistulae. The inflammatory tissue may penetrate the bowel wall into adjacent organs or more seldom the skin. If the fistula terminates into other organs or other parts of the bowel they are called internal fistulae while those penetrating the skin are called external.

Extensive disease can be defined as:

- Continuous involvement of more than 60 cm of small bowel
- Multiple skip lesions involving more than 1 m of small bowel
- General colitis with or without proctitis
- Inflammation of several segments of the colon together with more than 40 cm of the small bowel or multiple skip lesions
- Relapsing ileitis after surgery extending more than 40 cm

Aggressive disease can be defined as:

- Severe symptoms (CDAI > 250–300) within the first year after bowel resection
- Recurrent ileitis of more than 20 cm within a year after ileocolic resection
- General colitis within a year after segmental resection of the colon

7.2.13 Therapy

7.2.13.1 Medical Treatment

- *Aminosalicylates* (5-ASA) act on epithelial cells by modulating the release of cytokines.
- *Corticosteroids* act through suppressing interleukin transcription, induction of IκB that stabilises NFκB, suppression of arachidonic acid metabolism and stimulation of apoptosis of lymphocytes in the intestinal wall. It causes a leukocytosis.
- *Azathioprine* and *mercaptopurine* (6-MP) are immunomodulators inducing T cell apoptosis. 6-MP is metabolised to azathioprine.
- *Methotrexate* probably inhibits the cytokine and eicosanoid synthesis.
- *Infliximab* is a chimeric anti-TNF monoclonal antibody with potent anti-inflammatory effects. It probably acts by inducing apoptosis of various inflammatory cells.

The choice of treatment depends on disease activity and location but also on the predominant underlying pathology as inflammation, obstruction, abscess, or fistulae. A multidisciplinary team is ideal to govern the management. Honest information to patients about the disease is crucial. There are four main principles in the medical treatment:

- Offering help to smokers to stop smoking
- Assessment of the nutritional status (body mass index)
- Enteral or parenteral nutrition to restore deficits
- Anti-inflammatory drugs

First-Line Treatment

- In mild ileocolonic disease mesalazine (4 g/day) may be sufficient. About 40% of patients will go into remission within 2–3 months.
- In moderate to severe disease oral corticosteroids are given (prednisolone 40–60 mg/day or budesonide 9 mg/day) and to patients who did not respond to mesalazine.
- In active disease corticosteroids provide an adequate response in 60–80% of patients. In most cases prednisolone is used and the dosage is tapered by 5 mg every week once improvement has started which often takes 3–4 weeks.
- Long-term treatment with costico steroids is not desirable.
- In selected patients elemental or polymeric diets can substitute corticosteroids.
- In active colitis sulphasalazine can be appropriate in selected patients.
- Metronidazole has a role in selected patients with colonic and anal disease.
- Topical mesalazine may be effective in left-sided colitis.

Second-Line Treatment

- Azathioprine (1.5–2.5 mg/kg/day) or 6-MP (0.75–1.5 mg/kg/day), which has a slow onset of action, is used in active disease as a steroid-sparing agent.
- Methotrexate (25 mg i.m./week) is used in patients refractory or intolerant to azathioprine/6-MP.

Third-Line Treatment

- Infliximab (5 mg/kg) is effective in about 80% of patients with moderate to severe disease refractory to 5-ASA, corticosteroids or immunomodulators. It may also be used as maintenance therapy in selected cases.

Maintenance of Remission

Smoking cessation is probably the single most important factor to maintain remission. Mesalazine is ineffective for those who have been treated with corticosteroids to induce remission. Azathioprine and 6-MP are effective. Methotrexate is effective in patients who have responded to methotrexate in their acute disease. Infliximab is effective when the infusion is given every 8 weeks in patients who have responded to that treatment in the acute phase. Sulphasalazine is not recommended due to its side effects. Corticosteroids are not effective as maintenance therapy. In steroid-refractory or steroid-dependent disease the first choice is to use azathioprine/6-MP. Patients with intolerance or insufficient response to immunosuppression can get methotrexate. Infliximab is reserved for patients who are refractory or intolerant to treatment with mesalazine, corticosteroids, methotrexate or azathioprine/6-MP. In every situation with moderate to severe disease or intolerance to an anti-inflammatory drug, surgery is considered before escalating the medical treatment.

Side Effects of Medical Treatment

- Mesalazine intolerance occurs in about 15% of patients (diarrhoea, headache, nausea, rash) but new 5-ASA agents have adverse events similar to placebo. Side effects of sulphasalazine are dose-dependent but in addition to the same adverse events as 5-ASA it may rarely cause the Stevens-Johnson syndrome, pancreatitis or agranulocytosis.

- About 50% of patients do not have any adverse events with corticosteroids, but initial high doses may cause acne, moon face, oedema, sleep and mood disturbance, dyspepsia or glucose intolerance. Prolonged use (> 12 weeks) may cause osteoporosis, osteonecrosis of the femoral neck, myopathy and susceptibility to infection. Rapid withdrawal may cause adrenal insufficiency.
- Intolerance to azathioprine/6-MP has occurred in up to 20% of patients. Characteristically myalgia, headache and diarrhoea are seen after 2–3 weeks. They cease rapidly after withdrawal. Severe leukopenia (< 3%) can develop suddenly. Pancreatitis or toxic hepatitis is uncommon (< 5%). It is unusual that side effects of azathioprine develop later than after 3 weeks.
- Treatment with methotrexate is discontinued in 10–18% of patients because of side effects. Most common are nausea, vomiting, diarrhoea and stomatitis. Rare but more severe side effects are hepatotoxicity and pneumonitis. Folic acid may reduce the side effects.
- Infusion reactions of infliximab are treated with antihistamines, paracetamol or corticosteroids. The major risk, however, is infection. Abscesses are an absolute contraindication for infliximab because of the risk for septicaemia. Reactivation of tuberculosis has been reported in patients with rheumatoid arthritis treated with infliximab. It may also exacerbate cardiac failure.

7.2.13.2 Surgical Treatment

Indications for Surgery

A prerequisite for surgical treatment of Crohn's disease is that the patient is operable and that the lesion is suitable for surgical treatment. Resectional surgery is for instance not suitable if it will result in a short-bowel syndrome.

There are two major groups of indications for surgery:

- Complications
- Symptom load not controlled by medical treatment

Surgical treatment should be considered when medical treatment is insufficient to induce a remission or when a relapse appears during maintenance treatment. Escalation of the medical treatment may cause a delay of surgery but usually it does not prevent an operation.

Acute Complications

- Complete intestinal obstruction
- Abscess
- Bleeding
- Perforation

They are seldom indications for emergency surgery. Obstruction of the small bowel is the most common emergency situation in Crohn's disease. Too early surgery in those patients may result in unnecessary resection as the obstruction is resolved without surgery in the great majority of cases. Usually the obstruction is due to a combination of a fibrotic stenosis and obturation which often is best treated by bowel rest and parenteral nutrition. A palpable mass with pus or fluid can be drained percutaneously by the guidance of ultrasound or CT scanning. Sometimes a terminal ileitis is diagnosed during the night-time by surgeons on call and the recommendation is to avoid resection except when there is a complete obstruction with proximal dilatation of the small bowel. The appendix—healthy or not—can be safely removed if the caecum is healthy.

Non-Acute Complications

These complications are common indications for elective surgery:

- Attacks of intestinal obstruction
- Intestinal fistula
- Intestinal perforation
- Abdominal abscess?

The most common indication for surgery is repeated episodes of intestinal obstruction that are associated with stenoses where the diameter of the lumen is less than 10 mm. Intestinal fistula to other visceral organs, such as the urinary bladder and other parts of the intestines, are usually symptomatic and require an operation. Enterocutaneous fistulae seldom develop spontaneously but are most often associated with previous surgery. These patients need special and time-consuming preparations before they are in optimal condition for surgery. Perforations, in most cases, develop slowly and are associated with fistulae or abscesses located either to the abdominal cavity or the abdominal wall. They are commonly drained percutaneously and not by open surgery.

Risk Factors and Timing of Surgery

Surgery for Crohn's disease is characterised by impaired healing and surgical complexity. The healing process can be affected by:

- High disease activity
- Systemic inflammation
- Malnutrition
- Low albumin
- Corticosteroids
- Immunosuppression

The surgical approach, which may vary depending on the site of the disease and the indication, is often complex because of repeat operations, fistulae, abscess and the need for difficult intraoperative decisions.

It is generally accepted that timing is crucial in surgery for Crohn's disease to reduce postoperative morbidity and mortality to a minimum. However, the knowledge is inadequate and based more on common sense and experience than evidence. The timing is dependent both on the general condition of the patient and the type of complication. Furthermore, timing means not only when to operate but also how to operate.

There is a risk to operate too early on various occasions, i.e. before the patient is in optimal condition:

- Acute obstruction
- Chronic intermittent obstruction
- Palpable mass
- Malnutrition
- Enterocutaneous fistula
- Resection for inflammation before attempting anti-inflammatory treatment

On the other hand it is too late to be optimal when the patient is severely immune compromised after prolonged medical treatment, in longstanding septic conditions, when there is liver failure or when intestinal cancer has developed. Chronic systemic inflammation is associated with elevated CRP reflecting a perforating complication or an ongoing and uncontrollable inflammation in the gut.

To obtain an optimal condition before surgery the management is focused on four different areas, particularly in high-risk patients:

- Detection and treatment of sepsis: It includes drainage of fluid or pus whenever possible and antibiotic treatment in selected cases.
- Nutrition: Enteral nutrition is preferred. Not only too low but also too high caloric intake must be avoided when total parenteral nutrition (TPN) is necessary and about 1,800 kcal per day is often adequate. Enteral nutrition can be used also as a complement to oral feeding and TPN as it has several advantageous effects. It reduces inflammation and fistula activity, prevents liver failure, allows tapering of corticosteroids and restores the nutritional state. Enteral nutrition for 6–12 weeks can be a bridge to safe surgery in high-risk patients.
- Mapping the anatomy, using various imaging techniques, such as CT scan, MRI, ultrasound and contrast studies, is crucial when planning the surgery in high-risk patients.
- When surgery is delayed because of preoperative preparation for several weeks it is important to have a clear plan for the management where the patient is fully informed and has an active role.

Enterocutaneous fistulae is a special case often requiring surgery in steps and careful preoperative preparation as those patients are often in bad condition due to longstanding sepsis and malnutrition.

When it is not possible to improve the general condition of the patient, surgery may be necessary despite the increased risk for postoperative complications. It should then be adapted to the situation and sometimes it is safest to avoid restorative surgery and perform the surgical treatment in stages. To obtain adequate timing of surgery the overall health, the radiographic mapping and the endoscopic evaluation should be assessed. Also the body weight and the CRP and albumin levels in serum should at least have a trend towards normal values.

Recently it has been reported that surgery should be considered when there is no response within 3 months to initial medical treatment for ileocaecal Crohn's disease because in spite of changes in the medical treatment still half of the patients had been operated on after 6 months. Relapse during adequate medical maintenance treatment may also be an indication for surgery without any further attempts to escalate the anti-inflammatory treatment.

There is no specific point in time after diagnosis or after an identified complication when surgery should be performed. Instead the time for surgery should be tailored to the individual patient. The imaging must be updated. The decision regarding timing of surgery should preferably be made by a multidisciplinary team.

7.2.14 Surgical Principles

At least 70% of patients with Crohn's disease will require surgery during their life-time and it has been reported that 33–82% will be reoperated on due to relapsing disease. Depending on the site of the disease and the indication for surgery, the surgical approach may vary. Important decisions must be made regarding the extent of resection, the selection of skip lesions for surgical treatment and the construction of a primary or staged anastomosis.

7.2.14.1 Primary Surgical Treatment

Surgery in Crohn's disease is not curative. The aim is to reduce the symptom load by intestinal resection of areas causing symptoms and to save as much bowel as possible. A resection margin of only 1–2 cm from the border between bowel with macroscopic disease and normal appearance is sufficient.

Laparoscopically assisted bowel resection may be of some advantage as it can reduce postoperative pain and discomfort as well as disability and long scars. The laparoscopic approach may, however, be difficult when there is a fistula between abdominal organs. Diseased bowel, may also be more difficult to assess particularly colonic disease without the ability to palpate structures. With increasing experience laparoscopically assisted surgery will probably be done frequently in the future, at least in centres treating many patients with Crohn's disease every year.

Ileocaecal Disease

Resection is done according to the principles mentioned above and an anastomosis is constructed between the ascending colon and the ileum. The construction can be end-to-end (hand sewn) or side-to-side (stapled as functional end-to-end). A wide stapled anastomosis may postpone the need for reoperation because of symptomatic relapse. (see Fig. 7.2.4 and Fig. 7.2.5)

Small-Bowel Disease

A short segment of Crohn's disease (less than 50 cm) of the jejunum or the ileum is treated with resection and anastomosis. However, most often several short segments—skip lesions—are present and they are treated surgically with strictureplasty or sometimes with a combination of intestinal resection.

Indications for strictureplasty are (see Fig. 7.2.6):

- Strictures (lumen < 12 mm) after major resections (> 1 m)
- Rapid recurrent obstructive symptoms (aggressive disease)
- Extensive inflammation of the small bowel with multiple strictures
- Non-phlegmonous fibrotic strictures

The luminal diameter of areas with a stricture can be evaluated during the operation by enteroscopy with the colonoscope introduced through inflamed bowel close to normal bowel. Strictures that cannot be passed by the colonoscope are treated either by strictureplasty or resection. Another method to test the lumen is the use of a Foley catheter introduced through a small opening of the intestinal wall.

Colitis

The large bowel can be divided into six segments: caecum, ascending colon, transverse colon, descending colon, sigmoid colon and rectum. Segmental resection means removal of 1–3 segments, and colectomy/proctocolectomy removal of 4–6 segments. During the last 10 years the major indication for surgery has changed from active inflammation to strictures that cannot be passed by the colonoscope or when malignancy cannot be excluded. Still there is some controversy over segmental resection versus colectomy and ileorectal anastomosis (IRA). It has been argued that recurrence is more frequent and rapid after segmental resections but with modern treatment using azathioprine and other immune-modulating agents the risk for re-resection is the same as after colectomy. The symptom load is lower after segmental resection than after colectomy with IRA and the anorectal function is better.

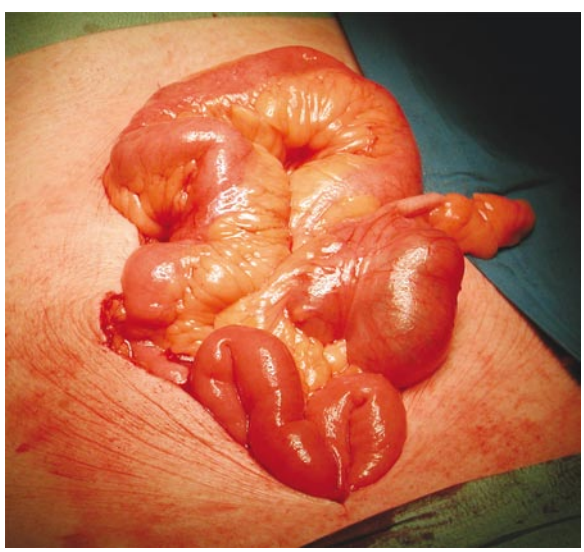


Fig. 7.2.4 Classic ileoceacal Crohn's disease

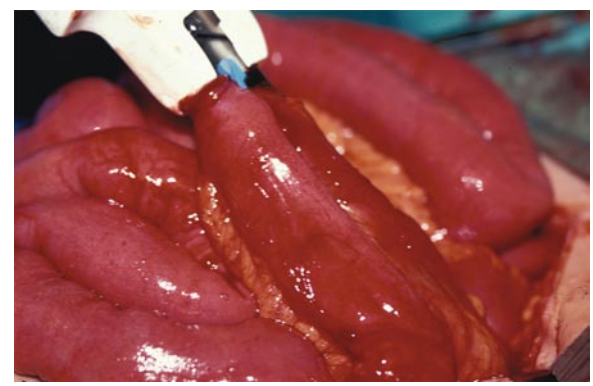


Fig. 7.2.5 Stapled ileocolic anastomosis

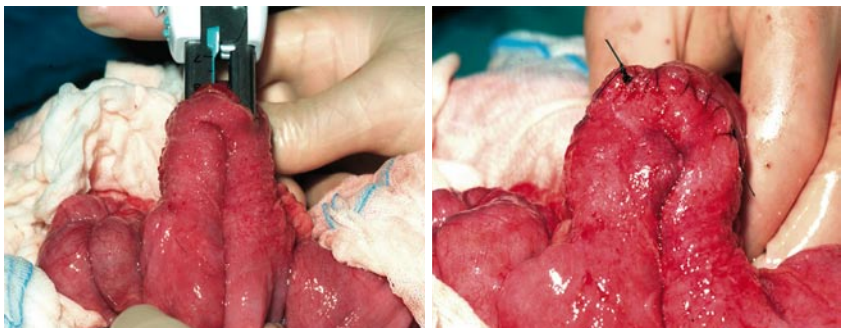


Fig. 7.2.6 Stapled strictureplasty

Extensive Disease

The aim is to avoid short-bowel syndrome by saving as much as possible of the small bowel but the colon can compensate for some of the losses of fluid and electrolytes also after major small-bowel resections. On the other hand, when the colon is resected and only the rectum is left behind it is critical to have enough length of the small bowel to avoid intestinal cripples. Resections of the small bowel should be avoided in these patients whenever possible and strictureplasties are preferred. Continuous anti-inflammatory treatment using immunosuppression or biological therapy is mandatory in those patient.

Duodenal Disease

Balloon dilatation or strictureplasty is used if possible but still gastrojejunostomy or a Roux-en-Y anastomosis can be preferred in selected cases.

Proctitis

Modern anti-inflammatory treatment has reduced the need for proctectomy in Crohn's disease. The annual risk for a permanent stoma is today only about 0.2%. The commonest indication is not inflammation but intractable anorectal fistula disease, anal stenosis or faecal incontinence.

7.2.14.2 Secondary Surgical Treatment for Recurrent Disease

In recurrent disease the exterior surface of the small bowel often shows changes due to previous surgery but sometimes also due to fistulae or abscesses. It has been shown that in those cases intraoperative enteroscopy may be of use to define the extent of the mucosal inflammation permitting precise resections. In about 50% of patients the mucosal inflammation is less extensive than the inflammation on the outer surface which can be shown by endoscopy. Accordingly this results in less extensive resections. The enteroscopy can also give information on residual inflammation of the remaining bowel.

The intestinal resections are done according to similar principles as in primary surgery (see Fig. 7.2.7).

7.2.14.3 Special Cases

In high risk groups the surgical treatment is adapted to the general condition of the patients. Sometimes it is worthwhile to do it in stages:

- Damage control
- Source control
- Restorative surgery

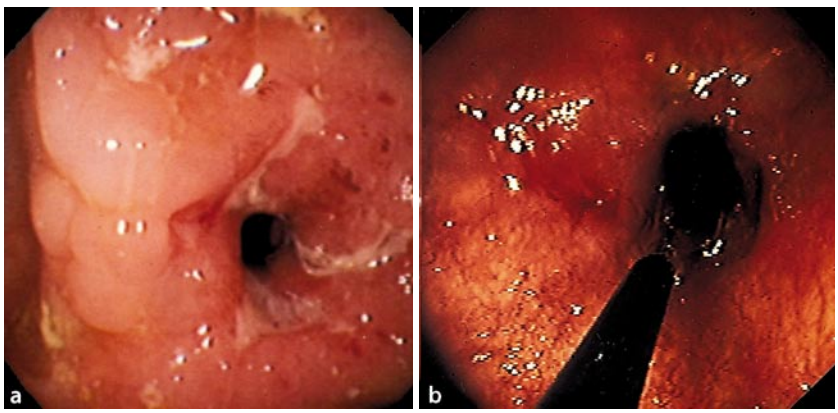


Fig. 7.2.7a,b Anastomotic stricture (**a**) treated with endoscopic dilatation (**b**)

An example of damage control is to drain an abscess percutaneously (see Fig. 7.2.8) When the general condition is improved source control may be obtained by resection of the diseased intestine with exteriorisation of the bowel ends (see Fig. 7.2.9). After 3–6 months restorative surgery is performed with the bowel ends connected. This can be done without an abdominal incision if the bowel ends were taken out in the same opening of the abdominal wall at the time of resection.

7.2.14.4 Postoperative Complications

Early Complications

- Anastomotic dehiscence resulting in peritonitis, abscess or fistula has, in collected series, been reported in 5–13% of patients.
- Infectious/septic complications (wound infection, abscess, septicaemia) occur in 10–30%.
- After staged surgery in high-risk patients the rate of anastomotic complications is about 7%.
- Complications requiring reoperations are more frequent (5–10%) after secondary surgical treatment than after primary operations.
- Other complications are small-bowel obstruction and stoma complications (retraction, prolapse, mucocutaneous separation, ischaemia and necrosis).
- Delayed healing of the perineal wound is not uncommon.

Late Complications

- Small-bowel obstruction is usually caused by obturation and is not uncommon. It is treated conservatively in the great majority of cases.
- Late stoma complications are stenosis, parastomal hernia, prolapse, retraction or peristomal skin problems such as pyoderma gangrenosum.
- Sometimes healing disturbances of a perineal wound lead to the development of a chronic perineal sinus.

7.2.14.5 Sequelae to Bowel Resection

- It has been shown that the cumulative length of previous small bowel resection is an independent factor determining the symptoms.
- Resection of the terminal ileum leads to passage of bile salts into the colon where they induce mucosal secretion of water and electrolytes leading to diarrhoea. The bile salts also increase the mucosal permeability to dietary oxalate in the colon with an increased risk for urinary stones. The loss of bile salts with faeces may increase the risk for gallstones and for steatorrhoea. There is a risk for deficiency of vitamin B_{12} after resection of the terminal ileum.
- Short-bowel syndrome is malabsorption of fluids, electrolytes and nutrients as a result of extensive bowel resections. They present soon after surgery with watery diarrhoea that improves as the intestine adapts. Steatorrhoea will appear as bile salt deficiency develops. Later complications include urinary stones and bile stones. These patients are usually managed by gastroenterologists but in rare cases small-bowel transplantation may be considered.

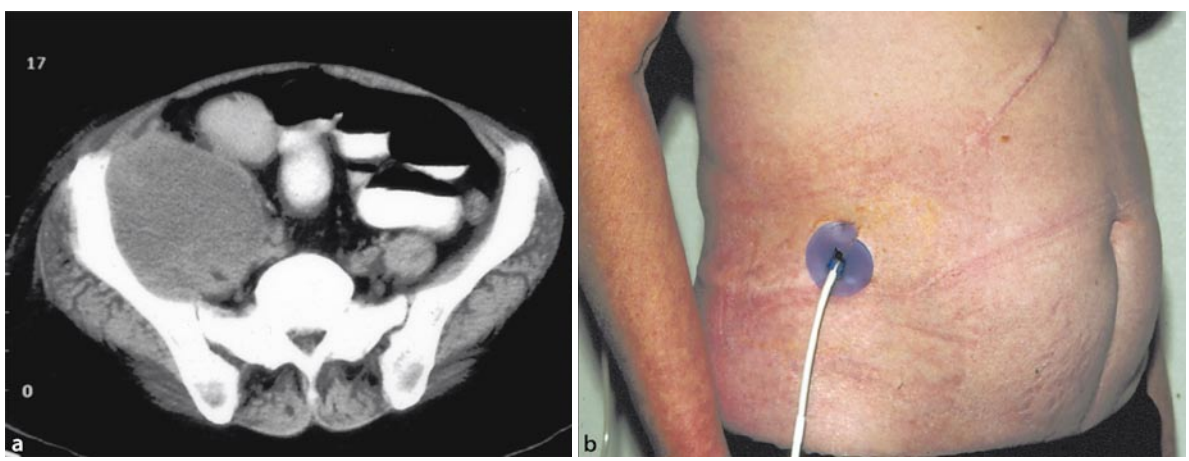


Fig. 7.2.8a,b Intraabdominal abscess (**a**) drained percutaneously (**b**)

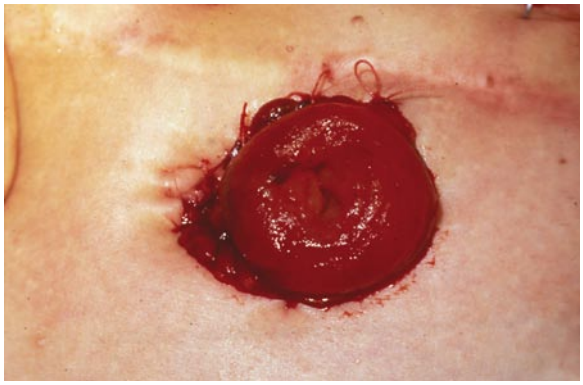


Fig. 7.2.9 Ileocolostomy after ileocolic resection

7.2.14.6 Recurrent Disease

The site of recurrence after intestinal resection is proximal to or sometimes on both sides of the anastomosis between the small and the large bowel. The length of the small-bowel recurrence proximal to the anastomosis is the same as the length of small-bowel inflammation at the primary resection. Patients with ileostomy have a lower risk of recurrence which implies that proximity to the colon is of importance and that reflux of colonic contents may be harmful to the small bowel mucosa. The rate of recurrence is determined by how long the follow-up is and the definition of recurrence based on:

- Clinical symptoms
- Endoscopy
- Radiology
- Biochemical markers
- Secondary surgical treatment

Clinical symptoms can be assessed according to the scoring systems already mentioned. The risk for symptomatic recurrence is similar after strictureplasty and bowel resection. About 70% of patients are free from clinical symptoms after 5 years and 50–60% after 10 years.

Endoscopic examination is the most sensitive method to detect recurrent inflammation and can be strictly classified. In patients without any maintenance treatment, 73–84% have endoscopic recurrence already after 3 months. After 1 and 3 years the range is 20–93% and 57–100%, respectively. The endoscopic findings 1 year after resection can be used to predict subsequent clinical symptoms and secondary surgical treatment. However, about 40% of patients with endoscopic lesions will not become symptomatic, at least not within 6 years.

Recurrence is rarely defined merely by radiological findings but it is of value when a stricture or a proximal location makes endoscopy impossible.

No blood test is useful in predicting recurrence but raised ESR, CRP and platelet count and low albumin are of some help in detecting a manifest recurrence.

Before the modern era of drug therapy secondary surgery because of recurrent ileal or ileocolic disease was done in 20%, 30% and 45% of patients after 5, 10 and 15 years, respectively. Symptomatic/radiological recurrence after the same follow-up was 35%, 50% and 60%, respectively. In a population-based cohort study including all patients with Crohn's disease, secondary surgery was done in 33% after 5 years and in 44% after 10 years. Smoking, female gender, small-bowel disease, ileocolic disease and perianal fistulae increase the risk for reoperation.

- Recurrence after surgery is almost inevitable irrespective of the type of operation done.
- Microscopic disease at the resection margin does not affect the recurrence rate and there is no difference in clinical or surgical recurrence when the macroscopic clearance is 2 cm or 12 cm.
- A wide (75–80 mm) functional end-to-end anastomosis with staples seems to postpone the need for secondary surgery compared with a sutured conventional end-to-end anastomosis.
- An ileostomy is associated with later and lower risk for recurrence compared with an ileocolic anastomosis.

7.2.15 Anorectal Manifestations

Common anorectal manifestations of Crohn's disease occurring in about 25% of patients are (see Fig. 7.2.10):

- Fistula
- Abscess
- Anal ulceration
- Stenosis
- Fissure
- Haemorrhoids
- Skin tags

Faecal incontinence is sometimes a consequence. Haemorrhoids, skin tags and fissures rarely need surgery in Crohn's disease patients and should in most cases be avoided due to the risk of impaired healing. Anorectal fistula is reported in 8–30% overall but as high as 41–92% in colitis. Fistulae can of course be a manifestation of Crohn's disease but some patients can develop fistulae as a complication to disordered anorectal function with diarrhoea as the dominating symptom. The pathological sequence is probably an initial fissure, leading to ulcer-

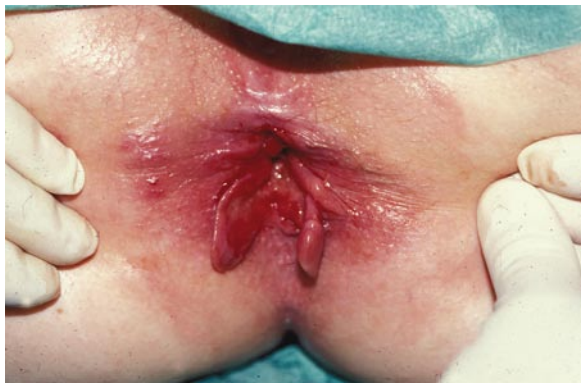


Fig. 7.2.10 Skin-tags in perianal Crohn's disease

ation and a stenosis. Subsequently a retroanal abscess and fistula may develop.

The activity can be measured by the Perianal Disease Activity Index (PDAI) scoring the following parameters:

- Discharge
- Pain/restriction of activities
- Restriction of sexual activity
- Type of perianal disease
- Degree of induration

The diagnosis is made by:

- History
- Bedside examination
- Examination in general anaesthesia
- Surgical exploration

The history will disclose how often a fistula has flared and if it has been treated previously. The Crohn's disease activity and the overall health is evaluated. It is also necessary to elicit medications, the obstetrical history and previous surgical operations.

Inspection at the bedside examination reveals the external opening, purulent discharge, erythema, scars, anal deformity and any gaping of the anus. The digital examination can demonstrate induration, inflammation or stenosis and also evaluate the anatomy and function of the sphincters. A structured form is of great help. Sometimes, severe pain and tenderness make it not possible to examine the patient without general anaesthesia.

It is crucial to answer following questions before making any decision to operate:

- Any proctitis?
- The extension of the fistulous track(s)?
- Any abscess?
- Is the striated muscle involved or not?
- How does the fistula affect the patient's lifestyle?

Such evaluation can utilise various methods:

- Endoscopy
- MRI
- Endorectal ultrasound
- Anorectal manometry
- Fistulography

In patients with Crohn's disease the fistulae are often not easy to classify according to Parks' classification or other classifications. A simple classification of anorectal fistulae in Crohn's disease is:

- Grade I: Superficial fistula (subcutaneous)
- Grade II: Involving smooth muscle (intersphincteric)
- Grade III: Involving striated muscle (trans- or suprasphincteric)

When all information is obtained, the goal of the treatment can be defined. Some patients do not need any local therapy, others are operated on with either curative or palliative intention. Like surgery for Crohn's disease in other areas, anorectal surgery cannot always be done for cure. Realistic goals are to relieve symptoms and to prevent the development of abscesses.

7.2.15.1 Medical Treatment

First-line treatment includes:

- Medical treatment of the intestinal inflammation (CDAI < 250)
- Reduction of number of stools to three or less per day
- Control of local sepsis with drainage and sometimes treatment with metronidazole or ciprofloxacin

Second-line treatment includes:

- Immunomodulation

7.2.15.2 Surgical Treatment

- *Cure* can be obtained by lay open of the fistula (fistulotomy) but when too much muscle is divided faecal incontinence will develop. Proctectomy with a permanent stoma is curative but causes a handicap. Thus it is a challenge to identify candidates for fistulotomy and for proctectomy. Superficial fistulae (grade I) are always laid open. Fistulae involving smooth muscle (grade II) are laid open to the dentate line. Grade I and grade II heal in 82–95% of patients. High fistulae involving striated muscle (grade III) are more difficult to heal. Curative intention involves excision of track(s) and suture of the internal opening which is covered by a mucosal flap. Another option is a fistula plug. Approximately 60% will heal after surgery but recurrence or new

fistulae will occur in about 20%. In patients with colitis and proctitis the results are worse.

- *Palliative surgery* means excision of track(s) and placement of a *loose seton*. This is usually done after non-healing or recurrence after attempts at curative surgery or in patients with severe rectal disease. Permanent setons are usually well tolerated but must be changed at intervals.
- An anal stenosis is initially gently dilated under general anaesthesia and *self-dilatation* is often enough to prevent a relapse.
- *Fibrin glue* may also be tried to avoid dead space after flap surgery.
- *Infliximab* can reduce the inflammatory reaction surrounding the fistula and heal the opening of the skin for some time but the fistulous track persists and there is an increased risk of abscess formation. A seton is therefore used initially until healing is observed after the second infusion. In addition, azathioprine is used as maintenance therapy.
- *Faecal diversion* is indicated when the fistula cannot be controlled or when faecal incontinence cannot be managed. The stoma can improve the quality of life substantially in such situations. However, faecal diversion is of no advantage with respect to healing.
  - A temporary defunctioning stoma may be indicated in a complex fistula/abscess with sepsis and in reoperations.
  - Proctectomy is considered when the anorectal function is severely disordered due to intolerable proctitis, severe stenosis or when there is no sphincter function.
- A *rectovaginal/anovaginal fistula* can be operated on through the anal canal, the vagina or the perineum. Irrespective of the approach it is important to introduce muscle tissue into the rectovaginal septum for nutrition and oxygenation of the fistulous area. Healing is initially obtained in about 50% of patients, but with additional procedures, including reoperations, about 70% will heal. The combination of a fairly low healing rate and sometimes a complex surgical procedure implies that surgery may be avoided in patients with minor symptoms such as occasional leakage of gas.

7.2.15.3 Recommendations for Treatment of Perianal Fistulae

- Anti-inflammatory treatment (acute and maintenance)
- Treatment of diarrhoea
- Control of perianal sepsis (loose seton)
- Dilatation of an anal stenosis
- Lay open for grade I–II fistulae
- Excision and mucosal flap, or fistula plug for grade III fistulae

7.2.16 Special Remarks

7.2.16.1 Cancer

There is a small but significant increase in mortality from tumours of the digestive tract in patients with Crohn's disease. Extensive colitis and severe chronic perianal disease may be associated with an increased risk for cancer of the colon, rectum and anus. Sclerosing cholangitis is a significant risk factor for colorectal cancer not only in ulcerative colitis but also in Crohn's disease. A remnant rectum is also considered to be a risk factor.

The carcinoma in patients with Crohn's disease is diagnosed about 20 years earlier than in sporadic colorectal cancer and is more proximally distributed than sporadic cancer and cancer associated with ulcerative colitis. This is in line with the tendency of a Crohn-associated cancer to develop in areas of macroscopic inflammation.

Longstanding infection/inflammation without any extensive dysplasia seems to be the major path in the development of cancer in Crohn's disease patients. Surveillance has not been generally accepted but it may be of value in risk patients and should aim at detecting early cancer and not dysplasia.

Awareness of the risk for digestive cancer is necessary after a duration of Crohn's disease of 15 years, particularly if new symptoms develop and the diagnosis was made before the age of 20 years. Information on digestive cancer in relatives may add to the decision to start a surveillance programme.

Risk factors for cancer in patients with Crohn's disease:

- Young age at diagnosis
- Long history of Crohn's disease
- Extensive colitis/severe proctitis
- Chronic severe anorectal disease
- Remnant rectum
- Strictures of the bowel
- Bypassed segments
- Sclerosing cholangitis
- Ieolosectal cancer in relatives

7.2.16.2 Pregnancy

Corticosteroids and mesalazine can be used safely during pregnancy and lactation. The role of azathioprine/6-MP

in pregnancy is still unclear but there are reports of uneventful pregnancies. Other immunomodulatory agents as well as metronidazole are contraindicated.

7.2.16.3 Quality of Life

Patients with Crohn's disease, at least those with colitis, who are in remission have a similar quality of life as the general population. The symptom load is the most important factor for the quality of life.

7.2.16.4 Multidisciplinary Team

Despite advances in medical therapy, surgery is still required in many patients with Crohn's disease. However, treatment is multimodal and close collaboration is necessary between gastroenterologists, surgeons, endoscopists, radiologists, anaesthesiologists, pathologists, specialised nurses of IBD and stoma nurses to obtain optimal results and to have about 90% of the patients in remission or with mild disease.

Suggested Reading

1. Andersson P, Olaison G, Hallböök O, Sjödahl R (2002) Segmental resection or subtotal colectomy in Crohn's colitis? Dis Colon Rectum 45:47–53
2. Andersson P, Olaison G, Bentsen P, Myrelid P, Sjödahl R (2003) Health-related quality of life in Crohn's proctocolitis does not differ from the general population when in remission. Colorectal Dis 5:56–62
3. Bernell O, Lapidus A, Hellers G (2000) Risk factors for surgery and postoperative recurrence in Crohn's disease. Ann Surg 231:38–45
4. Best WR (2006) Predicting the Crohn's disease activity index from the Harvey-Bradshaw Index. Inflamm Bowel Dis 12:304–310
5. Canavan C, Abrams KR, Mayberry J (2006) Meta-analysis: colorectal and small bowel cancer risk in patients with Crohn's disease. Aliment Pharmacol Ther 23:1097–1104
6. Cosnes J, Beaugerie L, Carbonnel F, Gendre JP (2001) Smoking cessation and the course of Crohn's disease: an intervention study. Gastroenterology 120:1093–1099
7. D'Haens G, Geboes K, Peeters M, Baert F, Penninckx F, Rutgeerts P (1998) Early lesions of recurrent Crohn's disease caused by infusion of gastrointestinal contents in excluded ileum. Gastroenterology 114:262–267
8. D'Haens G, Geboes K, Rutgeerts P (1999) Endoscopic and histologic healing of Crohn's (ileo-) colitis with azathioprine. Gastrointest Endosc 50:667–671
9. Galandiuk S, Kimberling J, Al-Mishlab TG, Stromberg AJ (2005) Perianal Crohn's disease: predictors of need for permanent diversion. Ann Surg 241:796–802
10. Gasche C, Scholmerich J, Brynskov J, D'Haens G, Hanauer SB, Irvine EJ, Jewell DP, Rachmilewitz D, Sachar DB, Sandborn WJ Sutherland LR (1998) A simple classification of Crohn's disease: report of the Working Party for the World Congresses of Gastroenterology, Vienna
11. Gaya DR, Russell RK, Nimmo ER, Satsangi J (2006) New genes in inflammatory bowel disease: lessons for complex diseases? Lancet 367:1271–1284
12. Munoz-Juarez M, Yamamoto T, Wolff BG, Keighley MR (2001) Wide-lumen stapled anastomosis vs. conventional end-to-end anastomosis in the treatment of Crohn's disease. Dis Colon Rectum 44:20–26
13. Rutgeerts P, Geboes K, Vantrappen G, Kerremans R, Coenegrachts JL, Coremans G (1984) Natural history of recurrent Crohn's disease at the ileocolonic anastomosis after curative surgery. Gut 25:665–672
14. Rutgeerts P, Diamond RH, Bala M, Olson A, Lichtenstein GR, Bao W, Patel K, Wolf DC, Safdi M, Colombel JF, Lashner B, Hanauer SB (2006) Scheduled maintenance treatment with infliximab is superior to episodic treatment for the healing of mucosal ulceration associated with Crohn's disease. Gastrointest Endosc 63:433–442

7.3 Indeterminate Colitis

NAJIM CHAFAI, ROLLAND PARC

7.3.1 Definition and History

The term "indeterminate colitis" was first introduced by Ashley Price, a pathologist at St. Mark's Hospital in London, UK. He used it to describe colectomy specimens where a definite diagnosis of ulcerative colitis or Crohn's disease could not be established due to overlapping features. At the time it was felt that indeterminate colitis was likely to represent a temporary state in the evolution of inflammatory bowel disease, which in due course would declare itself as either ulcerative colitis or Crohn's disease.

Up to today there is a significant amount of confusion relating to the exact definition of the term "indeterminate colitis".

- First there is confusion as to whether indeterminate colitis represents a separate entity, i.e. a "third" type of inflammatory bowel disease, or rather a provisional diagnosis.
- The second confusing issue relates to the classification of indeterminate colitis: it may either be seen as a purely histopathological diagnosis or viewed in a more ample clinical context that includes endoscopy, radiology and pathology findings.
- Third and probably most importantly there remains confusion about the natural history and evolution of indeterminate colitis and its impact on patient management.

7.3.2 Epidemiology

Taking the absence of a generally accepted definition of indeterminate colitis into account it is hardly surprising that the knowledge of its epidemiology is scarce and imprecise. A further obstacle is the well-known interobserver variability in the interpretation of the histological findings in inflammatory bowel disease. Prospective population-based data are mainly available from Scandinavia. Indeterminate colitis accounts for around 5% of all newly diagnosed cases of inflammatory bowel disease. The annual incidence varies from 0.9 to 1.6 per 100,000 adults. For children both lower and higher rates have been reported. Both sexes are affected equally.

7.3.3 Diagnosis

Traditionally, the diagnosis of indeterminate colitis relies solely on the pathologist. Over time, however, there has been a trend towards the development of broader clinicopathological diagnostic criteria that take endoscopic and radiological features into consideration. More recent studies focus on the role of serological and genetic markers.

Of crucial importance for the accuracy of the histopathological diagnosis is the material used. Price in his original description diagnosed indeterminate colitis only on excised colon specimens and this remains the gold standard. Preoperative endoscopic biopsies tend to be fraught with pitfalls for the pathologist. It has, therefore, been proposed to use the term "unclassified inflammatory bowel disease" rather than indeterminate colitis for biopsies that cannot be classified as either ulcerative colitis or Crohn's disease. Microscopically crypt architectural distortion as well as non-specific changes of acute and chronic inflammation are seen, however, the specific features of ulcerative colitis or Crohn's disease are lacking.

Several scenarios when the distinction between ulcerative colitis and Crohn's disease may be difficult and the histological picture therefore evokes indeterminate colitis have been described:

- The classical case is fulminant colitis, where histological features commonly overlap.
- The other not uncommon scenario relates to otherwise typical ulcerative colitis presenting with an atypical pattern of distribution such as discontinuous patchy right-sided inflammation (caecal patch) in otherwise left-sided colitis or as in backwash ileitis.

Colonoscopy in patients with suspected indeterminate colitis tends to show chronic pancolitis without any specific features. The same findings apply to radiological contrast studies. MRI scanning has recently been reported as a diagnostic tool in the distinction between ulcerative

colitis and Crohn's disease: whether it may have a role in the diagnosis of indeterminate colitis has as not yet been investigated.

More recently interest has focused on the value of serological markers. Anti-*Saccharomyces cerevisiae* antibody (ASCA) and atypical antineutrophil cytoplasmic antibody (pANCA) are antimicrobial antibodies that have been suggested as a method of differentiating ulcerative colitis from Crohn's disease. The limitations of their clinical usefulness are a lack of sensitivity and specificity. It has, however, been demonstrated that seronegative patients are more likely to retain a diagnosis of indeterminate colitis over time than patients with one or both antibodies. Further studies are required to elucidate the significance of the lack of inflammatory bowel disease-associated antibodies in indeterminate colitis.

7.3.4 Natural History

Patients labelled with a diagnosis of indeterminate colitis are likely to represent a heterogeneous group made up of those who will eventually be given a diagnosis of ulcerative colitis or Crohn's disease and those who will remain "indeterminate" over time. Reclassification of indeterminate colitis may occur with new clinical, imaging and endoscopy findings but also following review of previous biopsies or when new pathology material becomes available. Price reclassified about half of his patients with indeterminate colitis over time. In recent studies, at least 50% of those initially diagnosed with indeterminate colitis have been given a definitive diagnosis of ulcerative colitis or Crohn's disease over the following years.

7.3.5 Therapy

7.3.5.1 Medical Treatment

Patients with newly diagnosed inflammatory colitis require medical treatment unless immediate or urgent surgery is required. The subspecification of the inflammatory process will rely on biopsy material obtained during endoscopy. It has been suggested to use the term unclassified rather than indeterminate colitis in this setting. Indeterminate colitis should only be diagnosed following pathological examination of the excised colon.

The mainstay of medical treatment is anti-inflammatory drugs and the choice for an individual patient will depend on the location and extent of the inflammatory process. The role of immunomodulatory drugs such as azathioprine or infliximab in the treatment of indeterminate colitis is not yet fully established. On the rationale that prophylactic mesalazine has been shown to decrease postoperative recurrence of Crohn's disease, its routine use has been suggested following ileal pouch anal surgery, when the specimen shows features of indeterminate colitis.

7.3.5.2 Surgical Issues Relating to Indeterminate Colitis

Since the 1980s the gold standard in the surgical treatment of ulcerative colitis is restorative proctocolectomy. Although numerous studies have examined its outcome when carried out for indeterminate colitis there are few secure data as most studies are retrospective, the criteria for diagnosing indeterminate colitis vary and follow-up is limited. This is somewhat surprising when one considers that up to 1 in 5 patients undergoing pouch surgery has overlapping histological features making the disease unclassifiable. In large, retrospective series patients with indeterminate colitis account for 5–10% of all patients undergoing ileal pouch–anal anastomosis.

The overall incidence of significant complications following pouch surgery in patients with a diagnosis of indeterminate colitis appears to be around 20% which represents an "intermediate" figure between the complication rate for those with underlying ulcerative colitis and Crohn's disease. The incidence of pouchitis and pouch-related sepsis and fistula has been examined as well as the long-term functional outcome and ultimately the pouch failure rate.

The incidence of pouchitis is controversial and has been reported as both similar and higher in patients with an underlying diagnosis of indeterminate colitis compared to ulcerative colitis. Several reports suggest that pouch fistulas as well as pouch-related sepsis are more frequent in patients with indeterminate colitis. There appears to be a consensus that the functional outcome in indeterminate colitis does not vary from that of patients with other diagnoses, although requirements of antidiarrhoeal medication may be different. The incidence of pouch failure in indeterminate colitis varies from 3% to 30% in the literature. A recent study suggests that pouch failure and complication rates in indeterminate colitis are slightly higher than in ulcerative colitis but clearly much lower than those observed in patients with Crohn's disease.

Of relevance for both patient and clinician are indicators that may predict a change of diagnosis from indeterminate to Crohn's colitis. Skip lesions and rectal sparing may be pathological features pointing towards a future evolution into Crohn's disease. Deep ulcers extending to

the muscularis propria seem to be associated with an increased risk of complications following pouch surgery.

Currently most institutions tend to offer ileal pouch–anal anastomosis surgery to patients with indeterminate colitis following a period of careful observation in order to minimise the possibility of a diagnosis change to Crohn's disease and following appropriate counselling regarding the likelihood of a higher complication rate. Patients with unclassified disease should not be treated with a one-stage surgical approach.

Suggested Reading

1. Burakoff R (2004) Indeterminate colitis: clinical spectrum of disease. J Clin Gastroenterol 38:S41–S43
2. Gramlich T, Delaney CP, Lynch AC, Remzi FH, Fazio VW (2003) Pathological subgroups may predict complications but not late failure after ileal pouch–anal anastomosis for indeterminate colitis. Colorectal Dis 5:315–319
3. Guindi M, Riddell RH (2004) Indeterminate colitis. J Clin Pathol 57:1233–1244
4. Odze RD (2004) Pathology of indeterminate colitis. J Clin Gastroenterol 38:S36–S40
5. Price AB (1978) Overlap in the spectrum of non-specific inflammatory bowel disease: colitis indeterminate. J Clin Pathol 31:567–577

7.4 Diverticular Disease

HECTOR ORTIZ

7.4.1 Introduction

Colorectal diverticular disease and its complications are highly prevalent disorders in daily practice in Western countries. Although the surgical treatment of recurrent diverticulitis and the management of diverticular disease in young patients have changed in recent years, these issues continue to be a matter of controversy.

7.4.2 Definition

Diverticula are herniations through the colonic wall at the sites of entry of blood vessels into the colon wall. It is usual to find two rows of diverticula, one on either side of the antimesenteric taeniae. An additional row of diverticula is found between the antimesenteric taeniae in approximately half the cases. The number of diverticula may vary from a single one to hundreds, and their size varies between 5 and 10 mm. Giant diverticula can be exceptionally observed. Diverticula occur most commonly in the sigmoid colon (95% of cases), as the sole site of diverticula in about 30% of patients with diverticular disease, and together with other colonic sites in 65% of patients. The rectum is rarely involved.

7.4.3 Aetiology

Different causative factors have been studied:

- *Structure of the intestinal wall*. Increased thickness of the bowel muscular layer is one of the most prominent and constant features of diverticular disease.
- *Compliance*. The colonic segments involved in diverticular disease have shown an abnormal compliance.
- *Motility of the colon*. Baseline motility of the affected segments is increased. Propulsive activity is qualitatively and quantitatively abnormal. Moreover, there is an abnormal colonic motor response to food ingestion.
- *Intracolonic pressure*. Multiple studies have demonstrated an increase in intraluminal pressure of the colon.
- *Age*. Increasing age is associated with changes in collagen fibres of the submucosa and a decrease in connective tissue between the circular and longitudinal muscular layers. In addition, the content of elastin increases, elastic fibres modify and there is an increase in the thickness of the colonic wall, although tensile force decreases.
- *Diet*. Epidemiological studies have provided evidence for the prominent role of low-residue and highly refined flour and sugar diets in the causation of diverticular disease. The highly refined Western diet is deficient in dietary fibre or roughage. It has been proposed that such diets result in decreased faecal bulk, narrowing of the colon and an increase in intraluminal pressure in order to move the smaller faecal mass. In contrast, a diet high in dietary fibre results in increased faecal bulk and is associated with speedy stool transit, which is an important element of healthy bowel function.
- *Genetic factors*. The presence of diverticula in children and young adults with Marfan's syndrome or Ehlers-Danlos syndrome, and the strong relationship between polycystic kidney disease and diverticular perforation suggest a possible genetic relationship.
- *Race*. Right-sided diverticula are more commonly seen in Far Eastern populations.

However, it has been shown that none of these factors can explain by itself the development of colonic diverticular disease. It is likely that complex interactions between motility, structure of the colonic wall, age, diet and even other less well known factors, such as genetics, may play a role in the causation of diverticula.

7.4.4 Incidence

The exact incidence is not known. Diverticular disease is a very common disorder in industrialised countries probably because of an increase in the incidence of the disease

and ageing of the population. The incidence rises with age, from 5% in people under 40 years of age to 65–80% in subjects older than 65 years. The incidence in both genders is similar.

7.4.5 Epidemiology

- Diverticular disease of the colon is a frequent disease in Western countries, which is in contrast to the rarity of colonic diverticula in underdeveloped nations. The disease is very infrequent in Africa and Asia. In these continents, however, the incidence of diverticular disease is greater in urban areas with more industrialised habits than in rural areas. The incidence of colonic diverticular disease also increases in these populations when they migrate to Western countries.
- In Western countries, diverticular disease predominantly affects the sigmoid colon. Right-sided disease is almost exclusively found in the Asian population.

7.4.6 Uncomplicated Diverticular Disease

7.4.6.1 Symptoms

- Diverticular disease of the colon is usually an asymptomatic condition. The majority of patients never have trouble enough to require medical attention, or the diagnosis is incidentally established coinciding with work-up studies for other conditions. In some cases, the first manifestation is a symptomatic complication of the disease.
- The most common symptom is abdominal pain, usually on the lower left side, ranging from slight tenderness to more severe pain, abdominal distension, cramps and bloating, and alteration of bowel habit.
- Abdominal pain typically occurs in episodes of one to several days duration, mostly in association with an episode of constipation. Pain is aggravated by food ingestion, and is relieved by defaecation and expulsion of flatus.

7.4.6.2 Diagnosis

- Physical examination is usually unrevealing.
- A patient with suspicion of colonic diverticular disease should undergo a barium enema or colonoscopy, not only to confirm the diagnosis, but also to exclude other colonic disorders with similar clinical manifestations. In this respect, colonoscopy has the advantage of visualisation of the colonic mucosa and the possibility of biopsy sampling.

7.4.6.3 Differential Diagnosis

The differential diagnosis includes most common colonic diseases:

- Colon or rectal cancer
- Irritable bowel syndrome
- Inflammatory bowel disease
- Ischaemic colitis
- Radiation-induced colitis
- Infectious colitis

7.4.6.4 Treatment

- Most patients are asymptomatic and, therefore, treatment is not required.
- In symptomatic patients, a high-fibre diet and antispasmodic agents are recommended. However, there is no good evidence that eating a high fibre diet is particularly effective.
- In some patients, antispasmodic medication may make the symptoms worse.
- Different studies have shown that cyclic administration of rifaximin, 400 mg daily, 7 days a month, may decrease the abdominal symptoms and even the incidence of diverticulitis.

7.4.7 Diverticulitis

Diverticulitis is the most frequent complication of colonic diverticular disease, and the reported incidence varies from 10% to 25%. In uncomplicated diverticulitis, the inflammation remains localised in the colonic wall and mesocolon, whereas in complicated diverticulitis, the inflammation extends to produce pericolonic or distant abscesses, or diffuse peritonitis.

7.4.7.1 Symptoms

- Abdominal pain is the cardinal symptom. It is referred to the left lower quadrant or suprapubic region. Change in bowel habits and rectal bleeding are also common.
- Nausea, vomiting and abdominal distension are less frequent.

Table 7.4.1 Hinchey stages

Stage	Complication
I	Diverticulitis associated with pericolic abscess
II	Distant abscess (retroperitoneal or pelvis)
III	Diffuse purulent peritonitis
IV	Diffuse faecal peritonitis

- Urinary symptoms are sometimes present as a result of inflammation close to the bladder or ureter.

7.4.7.2 Diagnosis

- The diagnosis is made by physical examination and radioimaging studies.
- Physical examination reveals pain in the left lower quadrant when palpatory pressure is exerted. Right-sided pain may be seen in cases of redundant sigmoid colon (pseudo-appendicitis). Diffuse abdominal pain may even exist. The intensity of pain varies according to severity of the inflammatory process, from abdominal discomfort to deep palpation to severe pain elicited on superficial and gentle pressure. Tenderness and some rigidity may be present. Occasionally, a mass corresponding to the thickened and inflamed underlying colon can be palpated. On digital examination of the rectum, pain is felt in the pelvis; a localised mass may also be palpated. An increase in the temperature is a common finding (57–100% of cases).
- Leukocytosis is present in 69–83% of patients. This laboratory finding, however, shows a poor correlation with the severity of diverticulitis, but leukocytosis is useful for following the clinical course of the disease.
- Although the patient's history and findings on physical examination are highly suggestive of diverticulitis, the diagnosis of diverticulitis should not be based only on these data. In addition, signs and symptoms are less evident in old patients and in the immunocompromised patients, and are frequently masked by chronic treatment with anti-inflammatory drugs. For this reason, some of the following diagnostic procedures should be systematically performed to confirm the diagnosis of diverticulitis:
  - Diverticulitis is a disorder localised out of the colonic wall. Thus, abdominal ultrasound studies and computed tomography (CT) scan are the radioimaging techniques most frequently used.
  - Abdominal ultrasound examination has a high sensitivity and specificity for the diagnosis of diverticulitis and for the detection of abscesses. It is very useful in women to exclude other pelvic or gynaecological conditions. This technique, however, is operator-dependent.
  - Contrast-enhanced CT scan of the abdomen and pelvis with the administration of intravenous, oral and rectal contrast material is increasingly used as the initial radioimaging technique in patients with suggestive manifestations of acute diverticulitis, particularly in attacks of complicated diverticulitis.
  - Colonoscopy should not be performed in patients with suspected colonic diverticulitis.

7.4.7.3 Complications

The inflammation may remain localised as a simple diverticulitis or extend to produce secondary complications, such as perforation with abscess or spreading peritonitis. Severity of complicated diverticulitis is classified into four stages according to the classification of Hinchey (Table 7.4.1).

- Development of an abscess or peritonitis that was not present at the time of diagnosis should be suspected when the patient's symptoms and physical signs deteriorate despite adequate medical treatment.
- Patients in whom abscess formation is suspected should undergo abdominal ultrasound or CT scan to confirm the diagnosis as well as to assess the size, localisation and the possibility of performing a percutaneous drainage.

7.4.7.4 Treatment

- If the patient's condition requires hospitalisation, treatment consists of parenteral fluids and antibiotic therapy. After subsidence of acute symptoms, oral intake can be resumed and antibiotic treatment completed at home. Immunocompromised patients should continue to be treated at the hospital.
- The following considerations should be taken into account in the selection of antibiotic treatment:
  - Pathogens usually involved in diverticular infection are gram-negative and anaerobes, especially *Bacteroides fragilis*, which is present in 65–94% of intra-abdominal infections.
  - Treatment with a single antimicrobial drug active against aerobic and anaerobic bacteria has shown similar efficacy than a therapeutic approach based on the combination of synergistic agents.

- The association of mesalazine with an antibiotic shows a significant superiority in improving the severity of symptoms and in preventing symptomatic recurrence of diverticulitis than antibiotics alone. Probiotics also seem to be effective in preventing recurrence of the disease.
- After resolution of the acute attack, patients should be evaluated by means of colonoscopy or sigmoidoscopy associated with double-contrast barium enema in order to confirm the diagnosis or to exclude other disorders that may present similar symptoms and radiological images to those of acute diverticulitis.
- Failure of medical treatment should be considered if the patient's condition does not improve in 24–48 h. In this case, the patient should be re-evaluated by CT scanning.
- Treatment of an abscess depends on the size, localisation and condition of the patient. Ultrasound or CT-guided percutaneous drainage is the method of choice that allows postponing emergency surgical treatment.
- If an abscess cannot be drained percutaneously, the patient should be operated on urgently. Resection with primary anastomosis is the intervention of choice. There is evidence to support the safety of resection with primary anastomosis in patients with diffuse purulent peritonitis. There is increasing evidence that drainage per laparoscopic approach can be successful and allow to defer sigmoid resection to a second stage.
- Hartmann resection should only be considered in cases of septic shock, multiorgan failure, immunocompromised patients or in high-risk patients (ASA physical status IV). The Hartmann procedure is also the technique of choice in patients with faecal peritonitis

Surgical Treatment of Complicated Acute Diverticulitis: Basic Principles

- There is agreement that colostomy alone is inadequate.
- Resection with colostomy is the minimal intervention.
- Resection with primary anastomosis, associated or not with proximal diverting stoma is an appropriate option when the septic process can be controlled. In these cases, intraoperative colonic irrigation is sometimes performed.
- In the presence of faecal peritonitis, septic shock, multiorgan failure, immunosuppression, or high-risk (ASA physical status IV), the Hartmann procedure is the technique of choice.

Elective Surgical Treatment of Diverticular Disease

Elective surgical treatment of diverticular disease is usually considered in the following clinical circumstances:

- When a fistula or symptomatic stenosis has developed.
- After a first episode of complicated diverticulitis with an abscess successfully resolved by percutaneous drainage. This argument is controversial because most patients remain asymptomatic after resolution of the abscess. In these cases, there is no evidence regarding the appropriate approach, so that decisions on treatment should rely on individual considerations of each clinical case.
- Patients who have presented two episodes of uncomplicated diverticulitis should be operated on on a case-by-case basis. Elective operative intervention should only rarely be offered. These statements are based on the following data:
  - The incidence of new episodes of acute diverticulitis after two previous episodes is low.
  - Recurrent episodes of diverticulitis are no more severe nor are they associated with a higher mortality.
  - Most cases of complicated diverticulitis occur in patients without a history of diverticular disease.
  - The criteria for elective surgery after two episodes of complicated acute diverticulitis imply an unnecessary surgical operation in a high percentage of patients, with a not negligible morbidity and mortality.

Surgical Treatment of Diverticular Disease: Basic Principles

- Surgical resection should include the thickened colonic segment but not necessarily the whole colon involved with diverticula.
- The entire sigmoid colon should be resected.
- The splenic angle should be mobilised when necessary to perform an adequate resection and anastomosis.
- Anastomosis should be performed on the healthy upper rectum.
- Diverting stomas are usually not necessary, but can be indicated in cases of urgent surgery for Hinchey stage III peritonitis, for instance.
- The surgical operation may be performed through the laparotomy or laparoscopy approach.

7.4.7.5 Fistulas

- Pericolic or distant abscess may drain into adjacent organs or through the abdominal wall. The incidence of this complication varies between 5% and 33%. Fistulas

develop more frequently during recurrent episodes when the acute attack has subsided; in some cases, the acute episode may have been passed unnoticed.

- Colovesical (65%) and colovaginal (25%) fistulas are the most common types. Colovesical fistulas are more frequent in men.
- The main symptom is the passage of gases or faeces through the urethra or the vagina. Other symptoms are related to recurrent urinary infection.
- Clinical suspicion of colovesical fistulas is confirmed by CT scanning. Cystography and cystoscopy are generally not useful for diagnostic purposes. However, in some cases, the diagnosis is not confirmed until operation.
- Although diverticular disease is the first cause of fistulas, colorectal cancer accounts for the second cause, and for this reason, colonoscopy is mandatory.
- Treatment is surgical and should be carried out when the fistula is stabilised and the septic process that originated this complication has been cured. The operative procedure consists of resection of the involved colonic segment with primary anastomosis and closure of the fistulous opening in the other affected organ.

7.4.7.6 Obstruction

- Intestinal obstruction may complicate an acute episode of diverticulitis or develop in patients with recurrent inflammatory episodes.
- Obstruction that develops during an episode of diverticulitis is due to the inflammatory process and usually responds to parenteral fluids and broad-spectrum antibiotics.
- Complete colonic obstruction after recurrent episodes of the disease is rare and requires urgent operative therapy. The diagnosis is confirmed by barium enema or CT scan.
- The choice of operative procedure is total resection of the sigmoid colon with intraoperative colonic irrigation. Anastomosis should be performed on the healthy upper rectum.
- When a caecal perforation exists, total colectomy with ileorectal anastomosis is the operation of choice (see Chap. 7.1).

7.4.7.7 Bleeding

- Diverticular disease of the colon is the most frequent cause of lower gastrointestinal haemorrhage. In contrast to the remaining complications, the inflammatory process does not seem to be involved in the pathogenesis of bleeding in diverticular disease. The use of non-steroidal anti-inflammatory agents plays a role in the aetiology.
- In most cases, bleeding is self-limited, with no effect or minimal clinical relevance. However, in 3–5% of cases, massive bleeding is reported.
- In patients with lower gastrointestinal haemorrhage independent of clinical recurrence, colonoscopy is mandatory to confirm the diagnosis or to exclude other disorders. Massive bleeding should be managed according to therapeutic criteria for any lower gastrointestinal haemorrhage (see Chap. 12.3).

7.4.8 Special Considerations

7.4.8.1 Diverticulitis in Young Patients

- There is no agreement regarding the age limit to consider that a patient with a diverticular disease is young. Some studies consider the limit at the age of 40 years and others at the age of 50 years.
- Incidences of diverticular disease range between 2% and 29%; the true incidence in this population is unknown.
- Treatment of diverticular disease of the colon in young patients is controversial because the natural history of the disease is unclear. Some authors consider that the disease in young patients is different and more aggressive and, for this reason, elective surgical resection after the first episode of acute diverticulitis is recommended. However, data available indicate that the evidence on which this recommendation is based is questionable. Accordingly, it may be stated that there is little evidence for recommending elective surgery after a first episode of acute diverticulitis in young people.

7.4.8.2 Diverticulum of the Right Colon

- The incidence of diverticular disease of the right colon is 6–14%.
- Two different entities are recognised: the presence of multiple diverticula similar to those found in the left colon, and the presence of a solitary caecal diverticulum containing all layers of the bowel wall.
- Right colon diverticular disease usually develops in people younger than those with left-side diverticulitis.
- In the great majority of cases the presence of diverticula cannot be suspected.
- Symptoms and signs of acute right diverticulitis closely mimic those of acute appendicitis. Therefore, most patients undergo surgical operation.

- At operation, diverticular resection may be the procedure of choice if technically feasible and if the diagnosis of diverticular disease is unequivocal. In these cases, an associated appendectomy is usually recommended to prevent misdiagnoses in the future.
- However, in most cases, the process cannot be distinguished from colonic cancer and right hemicolectomy is the technique of choice.

7.4.8.3 Immunocompromised Patients

- In immunocompromised patients, diverticular disease of the colon may present with a paucity of typical signs and symptoms, with the subsequent delay in diagnosis and treatment.
- Medical management is effective in a lower percentage of patients and free perforation is a frequent complication. Surgical treatment should be indicated in the presence of any suspicion of perforation.

7.4.8.4 Recurrent Diverticulitis After Resection

- The rates of recurrences following operation in patients with complicated diverticular disease varied between 4% and 7%.
- In case of relapse, it is important to determine whether the initial diagnosis and the first operative procedure were adequate.
- The likelihood of recurrence after the first operation is higher when the anastomosis has been performed at the level of the sigmoid colon.

Suggested Reading

1. Ambrosetti P, Chautems R, Soravia C, Peiris-Waser N, Terrier F (2005) Long-term outcome of mesocolic and pelvic diverticular abscesses of the left colon: a prospective study of 73 cases. Dis Colon Rectum 48:787–791
2. Broderick-Villa G, Burchette RJ, Collins JC, Abbas MA, Haigh PI (2005) Hospitalization for acute diverticulitis does not mandate routine elective colectomy. Arch Surg 140:576–581
3. Chapman JR, Dozois EJ, Wolff BG, Gullerud RE, Larson DR (2006) Diverticulitis: a progressive disease? Do multiple recurrences predict less favorable outcomes? Ann Surg 243:876–880
4. Comparato G, Fanigliolo L, Cavallaro LG, Aragona G, Cabestro GM, Iori V et al (2007) Prevention of complications and symptomatic recurrences in diverticular disease with mesalazine: a 12-month follow-up. Dig Dis Sci 52:2934–2941
5. Janes S, Meagher A, Frizelle FA (2005) Elective surgery after acute diverticulitis. Br J Surg 92:133–142
6. Nelson RS, Velasco A, Mukesh DN (2006) Management of diverticulitis in younger patients. Dis Colon Rectum 49:1341–1345
7. Purkayastha S, Constantinides VA, Tekkis PP, Athanasiou T, Aziz A, Tilney H et al (2006) Laparoscopic vs. open surgery for diverticular disease: a meta-analysis of nonrandomized studies. Dis Colon Rectum 49:446–463
8. Rafferty J, Shellito P, Hyman, NH, Buie WD (2006) Practice parameters for sigmoid diverticulitis. Dis Colon Rectum 49:939–944
9. Salem TA, Molloy RG, O'Dwyer PJ (2007) Prospective, five-year follow-up study of patients with symptomatic uncomplicated diverticular disease. Dis Colon Rectum 50:1460–1464

7.5 Other Colitides

ADAM DZIKI

7.5.1 Necrotising Enterocolitis

7.5.1.1 Definition

Necrotising enterocolitis (NEC) represents a significant clinical problem. Ischaemic and necrotic alterations in the intestinal wall more frequently refer to the terminal ileum than to the caecum and ascending colon. The necrosis begins in the mucous layer and then may involve the full thickness of the bowel wall resulting in perforation.

7.5.1.2 Epidemiology/Aetiology

Necrotising enterocolitis is the most common gastrointestinal emergency occurring in neonates predominantly in preterm infants. About 8% of babies with birth weights from 750 to 1,500 g can reveal symptoms of NEC but less than 10% of neonates with the disease are full term. The symptoms occur in episodic epidemics and approximately 80% of them within the first month of life but almost never during the first days of life.

The real aetiology of the condition is still unknown and is regarded as multifactorial. Only some predisposing factors are established. Prematurity is considered as the most important risk factor, but also hyaline membrane syndrome, infection, hyperosmolar formula feeding, the lack of breast milk, ischaemia and reperfusion injury play essential roles. Non-breast-fed newborns develop NEC signs six times more frequently than naturally fed babies.

7.5.1.3 Symptoms

The clinical manifestation of NEC may be non-specific. The symptoms develop after 10 days of life in relation to the onset of artificial formula feeding. Initially they include:

- Temperature instability
- Feeding intolerance, vomiting
- Abdominal distension and tenderness
- Decreased bowel movements and ileus

In advanced stages:

- Blood-streaked stools
- Abdominal wall erythema

As NEC progresses, systemic signs may be developed with apnoea, lethargy, low peripheral perfusion with hypoxia, coagulopathy and cardiorespiratory deterioration resulting in septic shock presentation.

Non-specific laboratory test abnormalities include:

- Leukopenia or leukocytosis with a shift to the left
- Low platelet count
- Hypoglycaemia
- Prolonged prothrombin time (PT) and activated partial thromboplastin time (APTT)
- Decreased fibrinogen
- Severe metabolic acidosis

7.5.1.4 Complications

Necrotising enterocolitis can lead to death as a consequence of systemic septic shock. The survival rate is estimated at approximately 75%, whereas 50% of survivors may reveal long-term complications mainly as:

- Intestinal strictures (25–33% of incidence). The main location of strictures is the left side of the colon. Symptoms reveal 2–3 weeks after recovery from the initial disease.
- Short-bowel syndrome, which is the result of surgical resections of excessive portions of absorption-related small bowel. Short-bowel syndrome can also lead to malnutrition.

7.5.1.5 Diagnosis

Diagnosis of NEC is obviously based on clinical manifestation and laboratory test results as well as radiological findings:

- Abdominal x-ray is essential diagnostic imaging for neonates with signs of suspected NEC. An anteroposterior radiograph and left lateral decubitus image should be performed to view all available signs of the

condition. Serial radiograms performed at 8-h intervals may help assess progression of the disease.
- Pneumatosis intestinalis is a pathognomonic marker of NEC comprised of the characteristic layer of hydrogen gas corresponding with the submucosal layer of the bowel wall. Gas is generated by bacterial fermentation.
- Free intraperitoneal air is a sign of perforation of the bowel and also an obvious indication for emergency surgical intervention.

Radiography may reveal other signs of NEC such as fixed and dilated loops, ascites and portal vein gas.

Abdominal ultrasound also seems to be an effective and useful tool in assessing the progression of NEC. Ascites and portal vein gas can be easily observed in ultrasonographs.

7.5.1.6 Therapy

Conservative Treatment

If the diagnosis of NEC is well established conservative treatment should be applied initially with nasogastric tube decompression, intravenous fluids and adequate oxygenation. The administration of broad-spectrum antibiotic therapy is begun with a change to more specific antibiotics according to the results of bacteriological findings. Medical therapy is associated with about a 50% success rate after about a week of continuous treatment.

Surgery

The absolute and obvious indication for surgery is intestinal perforation in the course of NEC, with free air on plain abdominal X-ray and full thickness necrotic alterations of the bowel wall. The relative indications for surgery comprise the worsening of clinical manifestations, a falling white blood cell count and signs such as persistent fixed loops revealed on repeated abdominal radiographs. Surgical procedures are also necessary when medical management fails. The essential concern in the surgical treatment of NEC is the preservation of as much intestinal length as possible.

7.5.1.7 Surgical Procedures

Procedure I
- The resection of altered parts of intestine with creation of a stoma is essential especially in cases with the symptoms of peritonitis.
- The "second look" operation should be performed after a 24-h interval to check for possible ischaemic signs in the intestinal wall.
- Bowel resection with an anastomosis is associated with a higher risk of anastomotic leak and stricture and thus the procedure has to be limited only to stable conditions with minimal peritoneal contamination.
- Prior to procedure of elective stoma closure a radiological contrast study has to be performed because of the relatively high risk of stricture.

Procedure II
- Bedside placement of peritoneal drains under local anaesthesia is the more recently used approach and the way of surgical treatment. The procedure helps stop the progression of sepsis.

7.5.1.8 Differential Diagnosis

Many conditions may be considered in the differential diagnosis of NEC:
- Enteroviral infections
- Candidiasis
- Hirschsprung's disease
- Bacteraemia
- Gastroesophageal reflux disease
- Hospital-acquired infections
- Neonatal sepsis of another origin

Spontaneous intestinal perforation with radiographic image of perforation (SIP) also appears in premature babies but without of any of the systemic signs usually present in NEC. The prognostic rate of NEC is higher than in SIP.

7.5.1.9 Prognosis

The survival rate of all treated babies reaches about 75% but the overall mortality of surgically treated patients ranges from 0% to 50%.

7.5.2 Pseudomembranous Colitis

7.5.2.1 Synonyms

Enterocolitis pseudomembranacea, antibiotic-associated colitis, necrotising colitis, *C. difficile* colitis or *C. difficile* diarrhoea

7.5.2.2 Definition

Pseudomembranous colitis (PMC) is an acute inflammatory disease of the colon. It is a commonly occurring

complication after antibiotic exposure that may lead to serious morbidity but usually is treated easily.

7.5.2.3 Epidemiology/Aetiology

- *C. difficile* was first implicated as a causative factor in the 1970s.
- *C. difficile*, a gram-positive, spore-forming, anaerobic bacillus, is isolated in almost all of these cases.
- *C. difficile* is an unusual component of healthy bowel flora and it is found in 3–5% of healthy adults.
- The antibiotic-induced change in the balance of normal flora allows overgrowth of *C. difficile*. The bacteria release a powerful toxin that causes an inflammatory reaction and the symptoms. The most important toxins are:
  - Toxin A: enterotoxin, causes diarrhoea
  - Toxin B: cytotoxin
- The incidence is 1 in a 1,000
- Almost any antibiotic can cause PMC. Clindamycin, lincomycin, ampicillin or cephalosporins have been implicated in most of the reported cases.
- Pseudomembranous colitis complicates 10% of the cases of antibiotic-associated diarrhoea.
- The low incidence of colitis in the paediatric population is attributed to the strength of the immune system or protective antibodies from the mother.
- Risk factor are:
  - Advanced age
  - Chemotherapy
  - Antibiotic therapy
  - Recent surgery
  - Patients in intensive care units
  - Patients with cancer, uraemia or burns
  - History of previous PMC

7.5.2.4 Symptoms

- Diarrhoea
- Leukocytosis (50–60% of patients)
- Fever (30–50% of patients)
- Abdominal pain or cramping (20–33% of patients)
- Bloody, mucoid, green, foul-smelling stools
- Urge to defaecate
- Other: dehydration, electrolyte disturbances, nausea, vomiting, malaise, anorexia, hypoalbuminaemia, anasarca

In most cases symptoms begin 3–9 days after starting the antibiotics. However, symptoms may begin a few weeks after discontinuation of the antibiotic.

Rare extraintestinal manifestations:

- Bacteraemia
- Splenic abscess
- Osteomyelitis
- Reactive arthritis or tenosynovitis

7.5.2.5 Complications

- Dehydration with electrolyte imbalance and hypovolaemic shock
- Haemorrhage and sepsis
- Perforation of the colon
- Toxic megacolon
- Recurrent colitis and diarrhoea

7.5.2.6 Diagnosis

- Signs of dehydration: dry skin, dry mouth, glassy appearance of the eyes, sunken fontanelles in infants, rapid pulse, low blood pressure, confusion, excessive tiredness
- Signs of toxic megacolon: fever, vomiting, ileus
- Signs of perforation: rigid abdomen, rebound tenderness

Additional/Useful Diagnostic Procedures

Laboratory Studies

- Complete blood count (CBC): Leukocytosis with WBC varying from 10,000 to 50,000/ml.
- Blood chemistry: Hypoalbuminaemia is common.
- Faecal leukocytes: Positive tests for faecal leukocytes, 3–5 leukocytes per high-power field, excludes benign diarrhoea.
- A stool culture positive for *C. difficile* toxin: does not differentiate between non-toxigenic and toxigenic.
- Stool assay for *C. difficile* toxins (mostly toxin B): sensitivity 95%, this test requires 2 days.
- Enzyme-linked immunosorbent assay (ELISA) for toxin A: sensitivity 75–85%, is completed in 2.5 h.
- Latex agglutination test: poor sensitivity and specificity.
- Polymerase chain reaction (PCR): to detect the gene sequences for toxins A and B in the stool. It is a fast, sensitive and specific diagnostic method but expensive and still it is not available commercially.

Imaging Studies

Endoscopy

- It is the most rapid and definitive diagnostic method.
- The mucosa of the colon is often covered with loosely adherent nodular or diffuse exudates. These raised

exudative plaques are 2–5 mm in size. Coalescence of these plaques generates an endoscopic appearance of yellowish pseudomembranes lining the colonic mucosa. When the pseudomembranes are manipulated, ulcerated mucosa is uncovered.
- Rigid proctosigmoidoscopy is diagnostic in 77% of patients.
- Flexible sigmoidoscopy is diagnostic in 91% of patients.
- Colonoscopy may be required in 10% of the cases where the disease is localised in the caecum or transverse colon with rectal sparing.
- It is a hazardous procedure in patients with toxic megacolon.

Plain Abdominal X-ray
- It is useful for ruling out toxic megacolon or colonic perforation.
- Ileus pattern was described in 28% of patients.
- Small-bowel dilation or air–fluid levels may be present.
- Dilated colon > 7 cm in greatest diameter.

Computed Tomography (CT)
- It may show distension and diffuse and also focal thickening of the wall of the colon, along with pericolonic inflammation.

Histological Findings
- On microscopic examination of the biopsy sample the earliest sign is focal necrosis of the surface epithelial cells in the glandular areas, plugging of capillaries in the lamina propria and mucus hypersecretion in adjacent crypts.
- As the disease progresses, necrosis and denudation of the mucosa occurs with thrombosis. Inflammation tends to remain superficial.

7.5.2.7 Therapy

Conservative Treatment

General Measures
- The antibiotic causing the condition should be stopped.
- Rehydration with electrolyte solutions or intravenous therapy should be started to replace fluids lost with diarrhoea.
- Most patients, 75% symptomatic and 25% with colitis, will experience complete recovery within 10 days.
- In fulminant or intractable cases, hospitalisation will be necessary.
- Oral treatment with an antimicrobial agent effective against *C. difficile* is the preferred treatment:
  - Metronidazole is the first-line therapy for PMC, with a response rate of 86–92%. An oral dosage of 250 mg q.i.d. for 7–10 days is recommended. It is not recommended for children or for pregnant women.
  - Vancomycin is the most reliable treatment of the disease, response rate is 90–100%. The recommended dosage is 125 mg every 6 h for 7–14 days for adults and 500 mg/1.73m^2 every 6 h for infants.
  - Second-line agents: oral bacitracin (500–1,000 mg q.i.d. for 7–19 days), teicoplanin (100 mg b.i.d.).

When parenteral therapy is the only possible treatment the use of both vancomycin and metronidazole intravenously, supplemented by vancomycin 500 mg q.i.d. via nasogastric tube or by enema, is recommended. Recurrences should be treated with vancomycin. Multiple recurrences should be treated with a long course of oral antibiotics (4–6 weeks).

Additional/Useful Therapeutic Measures
- Avoid narcotics: postoperative narcotics may play an antiperistaltic role.
- Antidiarrhoeal agents: diphenoxylate hydrochloride, including loperamide; they may protract the disease by prolonging the mucosal exposure to the bacterial toxins.
- Anion-exchange resin agents (e.g. cholestyramine, colestipol): eliminate toxins from the colonic lumen. The recommended oral dosage is 4 g q.i.d. It should not be used with vancomycin.
- Restoration of normal flora: in patients with multiple relapses probiotics such as oral lactobacillus GG and *Saccharomyces boulardii* have been used.
- Diet: clear liquid diet until resolution of diarrhoea is achieved.

Surgical Treatment
- Surgery is required in rare cases to treat infections that worsen or do not respond to conservative treatment or when there are any complications.
- Surgical therapy should be considered only as a life-saving measure, such as in cases of perforation or toxic megacolon. Two thirds of patients with megacolon require surgical intervention.
- The overall mortality rate for patients requiring surgery is reported to be as high as 30–35%.
- Various approaches can be used including:
  - Early subtotal colectomy
  - Colectomy
  - Colostomy or ileostomy
  - Resection of diseased bowel.

- For fulminant toxic cases that do not respond after a week of intensive medical therapy surgery is required because the risk of perforation increases after 7 days of ineffective conventional treatment.

7.5.2.8 Differential Diagnosis

- Staphylococcal enterocolitis and typhlitis
- Other bacterial colitis: Salmonellosis, Shigellosis, Campylobacter, *Escherichia coli*, Yersinia infection
- Amoebiasis
- Acute exacerbation of Crohn's disease and ulcerative colitis
- Ischaemic colitis
- Chemical colitis
- Human immunodeficiency virus colitis

7.5.2.9 Prognosis

- The overall mortality rate is 2%
- The mortality rate in untreated elderly or debilitated patients is 10–20%
- The mortality rate in patients with toxic megacolon is 35%
- If there are no complications, the prognosis is generally good
- Pseudomembranous colitis recurs in up to 20% of cases

7.5.2.10 Special Remarks

- Many patients remain asymptomatic carriers for *C. difficile*, and most of them never relapse.
- Some patients may develop PMC without a clearly identified agent.
- For prevention: use antibiotics prudently, wash hands, use examination gloves routinely, clean potentially contaminated surfaces.
- In some cases (5–19%) the disease will be localised to the caecum and the proximal colon.

7.5.3 Ischaemic Colitis

7.5.3.1 Definition

- The most common ischaemic injury of the gastrointestinal tract
- One of the most common disorders of the large bowel in the elderly
- Occurring with an increasing frequency

7.5.3.2 Aetiology/Epidemiology

- Atherosclerosis
- Shock
- Congestive heart failure

The disease is also associated with aortoiliac surgery, with incidence ranging from 3% to 6%. Risk factors connected with such operations are:

- Patency of the inferior mesenteric artery
- Preoperative shock
- Intraoperative blood loss
- Previous pelvic radiation therapy

Most patients are elderly. In younger patients the condition is associated with oral contraceptive use, vasculitis and hypercoagulable states.

Some cases of ischaemic colitis have been described in connection with mild allergy, hypertension, rectal prolapse, acute pancreatitis, sickle cell crisis, colon cancer, systemic lupus erythematosus, amyloidosis, anticardiolipin antibody syndrome, Buerger's disease, Degos' disease and Kawasaki syndrome. Other case reports have associated development of ischaemic colitis with use of certain agents (progesterone, ergotamine derivatives, methamphetamine hydrochloride, non-steroidal anti-inflammatory drugs and danazol), intravenous vasopressin therapy, renal transplantation, chronic intermittent peritoneal dialysis, cocaine abuse, snake bite and marathon running.

7.5.3.3 Symptoms

Clinical presentation is usually acute:

- Cramping abdominal pain
- Abdominal distension
- Bloody diarrhoea
- Local signs of peritoneal irritation over the affected segment

Manifestations may vary widely, from severe pain with transmural infarction and early perforation to mild abdominal pain and only slight tenderness. Colonic injury may consist of:

- Reversible colonopathy (35%)
- Chronic ulcerating colitis (20%)
- Transient colitis (15%)
- Gangrene (15%)
- Colonic stricture (10%)
- Fulminant extensive colitis (< 5%)

More than two thirds of patients with ischaemic colitis respond favourably and rapidly to simple conservative treatment. The most common outcome is spontaneous

recovery within 24–48 h. Remaining patients require exploratory laparotomy without benefit of established preoperative diagnosis.

7.5.3.4 Complications

- Chronic ischaemic colitis
- Gangrene resulting in perforation and peritonitis
- Stricture, usually developed 3–4 weeks after the acute insult
- Inflammatory polyposis
- Pyocolon (pus collection within the colon)
- Toxic megacolon

Location and incidence:

- Descending colon 37%
- Splenic flexure 33%
- Sigmoid colon 24%
- Transverse colon 9%
- Ascending colon 7%
- Rectum 3%

7.5.3.5 Diagnostic Procedures

Laboratory Studies

Non-specific laboratory testing:

- CBC: very high number of leukocytes with absence of other symptoms.

Radiography

Plain radiographic studies show:

- Mild diffuse bowel dilatation
- Gasless abdomen
- Bowel wall thickening: radiographic finding of thumbprinting
- Sawtoothing: due to multiple superficial ulcerations
- Tubular narrowing

Advanced ischaemia or colonic infarction:

- Free air in the abdominal cavity
- Air within the bowel wall
- Air in the portal venous system

Contrast studies (barium must be used with caution due to the risk of perforation and subsequent severe barium peritonitis):

- Thickening of the bowel wall
- Narrowing and spasm
- Ulcerations
- Eccentric deformity
- Sacculation
- Transverse ridging

Colonoscopy

Three endoscopic stages are recognised:

- Acute: with petechiae, pale mucosa, hyperaemia and necrosis
- Subacute: ulceration and exudation
- Chronic: stricture, decreased haustration and mucosal granularity

Computed Tomography and Ultrasonography

These procedures may show irregular thickening of the submucosa or narrowing of the lumen. Colour Doppler scans have been used to differentiate the bowel wall thickening seen in ischaemic colitis from that seen in inflammatory bowel disease.

Angiography

- Is not routinely used
- Rarely shows significant vascular occlusions
- Is limited to clinical situations in which ischaemic colitis involves the ascending colon: acute thrombosis or embolism of the superior mesenteric artery

7.5.3.6 Differential Diagnosis

- Crohn's disease
- Ulcerative colitis
- Colonic injury induced by non-steroidal anti-inflammatory drugs
- Pseudomembranous colitis
- Infectious colitides
- Diverticular disease
- Carcinoma of the colon

7.5.3.7 Therapy

Ischaemic colitis accounts for only a small percentage of colonic disease seen in medical and surgical offices. Most patients with ischaemic colitis do not have peritoneal signs, which results in frequent misdiagnoses and a large underestimation of its incidence.

Conservative Treatment

Outpatient therapy is possible in patients with mild symptoms. Patients with abdominal pain and no evidence of peritonitis or systemic toxicity should be treated expectantly.

General Measures

- Conservative treatment includes intensive care and monitoring of vital signs.
- Patients must have repeated, frequent abdominal examinations.
- Intravenous hydration, bowel-rest measures and administration of wide-spectrum antibiotics that cover enteric flora are usually required.

Pharmaceutical Measures

- Use of pharmaceutical agents, other than antibiotics should be avoided, particularly vasoconstricting drugs.
- Use of vasodilators, such as glucagon and papaverine, is controversial.
- Use of anticoagulants also has not gained wide acceptance.
- Use of corticosteroids is contraindicated in patients with ischaemic colitis because it can lead to silent colonic perforation.
- Patients usually respond to conservative measures within a few days to 2 weeks.
- Follow-up colonoscopy may be necessary to find progression of the colonic injury or stricture formation.

Surgical Treatment

- Surgery is indicated in patients with peritonitis, transmural infarction or perforation of the colon, or bleeding from ulcerations.
- Surgical intervention may also be necessary in patients with chronic, segmental colitis or formation of stricture after ischaemic injury.
- Before referring patients with stricture to surgery, forceful endoscopic balloon dilation may be attempted in asymptomatic stricture patients.
- Surgical intervention usually involves resection of the ischaemic segment of the colon and exteriorisation of the remaining ends of the bowel.
- Primary anastomosis and revascularisation attempts are contraindicated.

7.5.4 Infectious Colitis

7.5.4.1 Definition

Infectious colitis is one of the most common forms of colitis, usually caused by bacterial, viral and parasitic agents. It often occurs in childhood.

7.5.4.2 Aetiology

- Bacterial: The most common bacterial agents responsible for infectious colitis are: *Escherichia coli* and species of *Shigella*, *Salmonella*, *Campylobacter* and *Yersinia*.
- Parasitic: *Entamoeba histolytica* is the most common cause of parasitic colitis in the world.
- Viral: Cytomegalovirus (CMV) infection-induced colitis occurs rarely and is mainly in immunocompromised patients.

7.5.4.3 Symptoms

- *E. coli*-mediated colitis is characterised by diarrhoea, abdominal cramps and fever. It mostly affects children. The risk of haemolytic uraemic syndrome and haemorrhagic colitis after infection with enterohaemorrhagic *E. coli* strains is estimated to be in 10–15% of children.
- Shigellae infections range from asymptomatic ones, through mild gastroenteritis to severe dysentery. The dysentery has a sudden onset with high fever (39–40°C), abdominal pains and diarrhoea. The stools are frequent, over 10 times daily, and contain blood and mucus. Symptoms of central nervous system irritation can be also observed.
- Salmonellae infections usually occur in summer and autumn, and most commonly are in children. They are characterised by sudden onset within 8–48 h after ingestion of contaminated food. The patients present with abdominal cramps, nausea and fever. The stools are watery and sometimes contain blood.
- Enteritis caused by *Campylobacter* is characterised by sudden onset, fever (sometimes over 40°C) and abdominal pain, followed by diarrhoea. The stools are watery and very frequent (2–20 times daily) and usually contain blood.
- *Yersinia enterocolitica* infection presents with an abrupt onset of watery diarrhoea containing blood. The patients complain of severe abdominal pain, joint pain and skin eruption. A febrile response occurs in older children.
- Amoebiasis is manifested commonly with bloody diarrhoea, abdominal pain and fever.

7.5.4.4 Complications

In cases of severe diarrhoea and vomiting one must take care of physical signs suggestive of dehydration (e.g. dry mucous membranes, decreased skin turgor, orthostasis) leading to dysregulation of the acid-base balance.

7.5.4.5 Diagnostic Procedures

Most of the infectious factors may be cultured from the stool by using appropriate media. Gram and methylene blue staining of the stool is recommended. The WBC counts can be elevated or normal. However, in many cases, no pathogen is identified and diagnosis is established by medical history and clinical symptoms. In typical infectious colitis, the lamina propria of the large intestine is infiltrated by polymorphonuclear leukocytes.

7.5.4.6 Therapy

Conservative Treatment

- Management of bacterial colitis depends on the clinical symptoms and the patient's general condition. It is always necessary to control acid-base balance and supplementation of fluids is obligatory.
- In shigellosis trimethoprim-sulphamethoxazole is the drug of choice; fluoroquinolones and ceftriaxone are the alternatives.
- If *Salmonella* bacteraemia is suspected, i.v. cefotaxime (200 mg/kg/day in four divided doses) or ceftriaxone (100 mg/kg/day in two divided doses) should be initiated. Alternative treatments include chloramphenicol (100 mg/kg/day in four divided doses) or, in adolescents, fluoroquinolones. Trimethoprim-sulphamethoxazole is the drug of choice when oral treatment is indicated.
- In *Yersinia enterocolitica*, antibiotic therapy of i.v. gentamicin (5–7.5 mg/kg/day in three divided doses) is indicated in patients with persistent diarrhoea or suspected sepsis. Alternative antibiotics may include chloramphenicol, colistin and kanamycin.
- *Campylobacter* enteritis is usually self-limited. Erythromycin or ciprofloxacin may be used.
- Treatment of amoebic colitis includes metronidazole and iodoquinol or paromomycin.

Surgical Treatment

Surgical intervention is indicated for patients who developed toxic megacolon with subsequent risk for perforation or existing perforation. The frequency of surgical intervention is low (0.39–3.6% of cases).

7.5.5 Collagenous Colitis

7.5.5.1 Synonyms

Microscopic colitis

7.5.5.2 Definition

Collagenous colitis (CC), which was first described by Lindstrom in 1976, is a rare inflammatory disorder of the colon. Both CC and another disease, lymphocytic colitis, are also described as microscopic colitis. The disease is a cause of prolonged watery diarrhoea, with no changes in endoscopic appearance of the colonic mucosa, but with prominent, unique changes in microscopic assessment of biopsies.

7.5.5.3 Epidemiology/Aetiology

Collagenous colitis is recognised as a rare disease, although it has been increasingly diagnosed in the last few years. Still the true incidence is not known. Surprisingly, a few epidemiological studies performed in Scandinavian countries showed a much higher incidence than was expected. In one of them the rate was even similar to that of Crohn's disease.

It usually affects people older than 40 years and it is much more frequent in women.

Different aspects of causative agents have recently been discussed, although no definite aetiology can be given for now. It is supposed to be an autoimmune disease. Infection and drugs (non-steroidal anti-inflammatory drugs, ranitidine and antidepressants) seem to be possible triggering factors for inflammation. The coincidence of CC with infections, celiac sprue and presence of increased mast cells suggests a luminal agent plays a role in aetiology.

7.5.5.4 Symptoms

As mentioned before CC is typically presented as watery, non-bloody, high volume diarrhoea. It usually begins suddenly with no prodromal symptoms. Usually the only symptom is diarrhoea. Patient may pass up to 30 stools/day and lose more than 1,500 ml of fluid/day. Some of them complain of abdominal discomfort and a feeling of distension. Symptoms persist from a few weeks even to years.

7.5.5.5 Complications

The most frequent complications are due to diarrhoea. Malabsorption, dehydration, weight loss and deficiencies are among them.

7.5.5.6 Diagnostic Procedures

The diagnosis of CC is given in cases of watery, non-bloody diarrhoea with typical microscopic changes. The diarrhoea should last at least 3 weeks. There should be no changes in endoscopic appearance. Microscopic changes consist of:

- Thickening of subepithelial collagen wall (> 10 mm)
- Infiltration of intraepithelium with lymphocytes
- Mononuclear inflammatory cell infiltration in lamina propria

One must remember that lymphocytic colitis is an entity with exactly the same symptoms. The diagnosis is based on differences in pathological assessment.

Additional Useful Diagnostic Procedures

Some procedures are helpful in diagnosing CC. They include stool examination for parasites, ova and other pathogens, and radiological assessment.

7.5.5.7 Therapy

Conservative Treatment

As CC is a fairly seldom seen disease, treatment is based on anecdotal evidence. So far no standard or guidelines have been established in this field. Antidiarrhoeal agents (loperamide, diphenoxylate hydrochloride/atropine sulphate, bismuth subsalicylate) should be given. These drugs are especially useful in mild cases of the disease. In particular cases cholestyramine (when symptoms of bile salt malabsorption appear) and hyoscyamine (when one of the main symptoms is cramping pain) may be helpful.

When the disease does not respond to antidiarrhoeal drugs, the next therapeutic step would be drugs traditionally used in inflammatory bowel diseases: topical anti-inflammatory drugs (sulphasalazine, mesalazine) and corticosteroids (prednisone, budesonide). Finally immunosuppressants (azathioprine, methotrexate) could be used.

Surgical Treatment

In most cases surgery is unnecessary. In cases with no positive response to conventional therapy or intolerance to drugs, colectomy or ileostomy is the only choice.

7.5.5.8 Differential Diagnosis

Inflammatory bowel diseases must be taken into consideration (Crohn's disease and ulcerative colitis). One should consider irritable bowel syndrome, celiac sprue, giardiasis and non-colon-specific diseases such as hyperthyroidism or laxative abuse.

7.5.5.9 Prognosis

According to anecdotal papers only 15% of patients still have major symptoms after 6 months of treatment, while half of them are totally free of symptoms after the same time.

Unfortunately there are some patients in whom symptoms might come and go over many years.

Benign Tumours

8.1 Benign Tumours

THOMAS SCHIEDECK

8.1.1 Introduction

Benign tumours of the colon and rectum (Table 8.1.1) should be separated into:

- Non-neoplastic epithelial lesions
- Neoplastic epithelial lesions
- Mesenchymal lesions
- Other lesions

Epithelial lesions are mostly polyps. The term "polyp" is defined as any projection of tissue into the lumen of the digestive tract. Non-neoplastic epithelial polyps are the result of abnormal mucosal maturation, inflammation or architecture. They have no tendency to malignant transformation.

In contrast neoplastic epithelial lesions result from proliferative dysplasia. They are categorised as adenomatous polyps or adenomas. These are premalignant lesions.

Mesenchymal lesions originate from connective tissue cells and are located in the submucosal or mural layer. Sometimes they are summarised with other non-epithelial lesions as polypoid tumours.

8.1.2 Non-neoplastic Epithelial Lesions

- The incidence of these polyps increases with age.
- Formation occurs on a sporadic basis.

8.1.2.1 Hyperplastic Polyps

Hypoplastic polyps are epithelial lesions with a diameter often less than 5 mm occurring almost always in a multiple manner. They can be found in the whole colorectum. They definitely have no malignant potency.

Symptoms

- Patients are completely asymptomatic.

Diagnosis and Treatment

- Diagnosis is performed with high diagnostic specificity by endoscopy.
- To confirm the benign nature of the lesion one of the usually multiple hyperplastic polyps should be excised endoscopically.

8.1.2.2 Hamartomas

Hamartomas are benign lesions composed of an abnormal mixture of epithelial and mesenchymal elements. They used to be considered as developmental abnormalities, but today they are categorised as benign mesenchymal neoplasms: the epithelial component is reactive.

Table 8.1.1 Benign lesions in colon and rectum

Non-neoplastic lesions	Neoplastic lesions	Mesenchymal lesions	Others
Hyperplastic Polyps	Adenomas	Lipoma	Endometriosis
Hamartomas	Tubular adenomas		
Juvenile polyps	Villous adenomas		
Peutz-Jeghers' polyps	Tubulovillous adenomas		
Inflammatory polyps		Leiomyoma	Pneumatosis cystoides intestinalis
Lymphoid polyps		Neuroma	
		Angioma	

Juvenile Polyps

Epidemiology

- Juvenile polyps, most commonly paediatric gastrointestinal polyps, have been typically characterised as either hamartomatous overgrowths or reactive inflammatory proliferations.
- Dilated cystic glands lined by mucous-secreting epithelium and prominent, inflamed and congested lamina propria are typical histological findings of juvenile or retention type (hamartomatous) lesions.
- These lesions typically occur in children of less than 10 years of age.
- The incidence in boys is higher than in girls.
- The lesions usually are larger than 1 cm.
- Juvenile polyps can be solitary or multiple.
- The presence of multiple juvenile polyps (more than five) is termed juvenile polyposis.

Diagnosis

- Diagnosis is confirmed by histology of endoscopically resected specimen.
- In any case of a juvenile polyp the complete colon should be explored to exclude a juvenile polyposis syndrome.

A juvenile polyp is neither a neoplasm nor a premalignant condition. However, these patients carry an increased risk of developing carcinomas of the pancreas, breast, lung, ovary and uterus. Gastrointestinal adenocarcinomas in this disease arise from concomitant adenomatous lesions. Their preferred sites are in the colon and rectum. The differentiation between juvenile and adenomatous polyps is crucial. Because of the increased incidence of cancers in other organs, in these patients a careful follow-up is recommended. The surveillance programme should be risk-adopted regarding the diseases that are specifically known in the family history of the patient.

Juvenile Polyposis Syndrome

Epidemiology

- Solitary juvenile polyps are considered benign. In contrast, juvenile polyposis syndrome is associated with malignancy and poor long-term outcome.
- Observations of excessive colonic and gastric carcinoma and dysplasia in juvenile polyposis have prompted reclassification of this entity as a premalignant condition.
- Juvenile polyposis syndrome is an uncommon condition with multiple polyps arising in the colon but also in the remaining intestinal tract.
- The disease can be familial. Familial juvenile polyposis has been associated with mutations in two genes: SMAD4 on chromosome 18 and PTEN on chromosome 10. It has been estimated that SMAD4 mutations account for a subset of 20% to > 50% of juvenile polyposis families.

Symptoms

- In juvenile polyposis, polyps can be found in the large intestine, the small intestine and the stomach.
- Usually the colorectal polyps are the ones causing unspecific symptoms, such as bleeding, diarrhoea, abdominal cramps, hypoproteinaemia, hypokalaemia and anaemia.
- Furthermore concomitant extracolonic congenital and acquired manifestations can occur, such as macrocephaly, alopecia, bony swellings, cleft lip, cleft palate, double renal pelvis and ureter, acute glomerulonephritis, undescended testicle and bifid uterus and vagina.

Treatment

- If symptomatic surgery is performed, there is a choice between the same operations offered to patients with familial adenomatous polyposis: colectomy and ileorectal anastomosis, proctocolectomy and pouch, or proctocolectomy and ileostomy. It depends on whether the rectum is involved or not.
- There is a significant risk of cancer in patients with juvenile polyposis, mostly due to development of adenomatous tissue in juvenile polyps. The risk of developing cancer of the colon before 60 years of age in patients with juvenile polyposis ranges from 20% up to 60%. Thus surgery should be considered when there are too many polyps to be taken care of endoscopically.

Peutz-Jeghers' Polyps

Peutz-Jeghers syndrome is a rare autosomal dominant disorder that is characterised by hamartomatous polyposis of the gastrointestinal tract and melanotic pigmented spots. The pigmented spots appear as flat cutaneous lesions located mainly in the perioral area, especially in the mucous membrane of the oral cavity and lips.

The polyps can be located anywhere in the gastrointestinal tract, except in the mouth. They are most commonly found in the small intestine (100%), especially in the jejunum, but can also occur in the stomach (25%) and occasionally in the oesophagus, duodenum and colon (30%). They are hamartomas of smooth muscle that extend into the lamina propria; they usually have a broad base and present in variable sizes. Histologically they present as a

network of connective tissue and well-developed smooth muscle extending into the polyp. The risk of polyps undergoing malignant transformation is only 2–3%.

Symptoms

- The polyps can present with some unspecific complications, most commonly chronic rather than acute bleeding and intestinal obstruction due to intussusception or intraluminal obstruction.

Diagnosis

- Diagnosis of the syndrome is based on family history, skin pigmentation and gastrointestinal symptoms.
- Contrast enema and endoscopy are used to define the extent of the disease.

Treatment

- Preoperatively, once polyps are detected endoscopically, attempts should be made to snare them by upper and lower endoscopies.
- An aggressive approach for endoscopic removal is justified because the frequency of tumours decreases with age.
- At laparotomy or laparoscopy, intussusception is usually reduced and polyps acting as leading points are excised.
- Polypectomy in the small intestine is usually performed via multiple enterotomies.
- As many polyps as possible should be removed to minimise the risk of future obstruction or bleeding that may necessitate further surgical intervention.
- Large broad-base polyps may be treated by limited small bowel resection but this should be applied restrictively.

8.1.2.3 Inflammatory Polyps

Inflammatory polyps are pseudopolyps representing regenerating inflamed mucosa surrounded by ulcerative tissue. This kind of lesion is usually seen in patients with long-lasting chronic inflammatory bowel disease such as ulcerative colitis or Crohn's disease.

8.1.2.4 Lymphoid Polyps

Lymphoid polyps are benign lesions in a focal or diffuse condition occurring typically where clusters of lymphoid follicles are present. Benign nodular lymphoid hyperplasia of the colon is a rare entity, distinct from lymphoid polyps, and must be differentiated from malignant lymphomas (Fig. 8.1.1). The polyp is composed of well-differentiated lymphoid tissue.

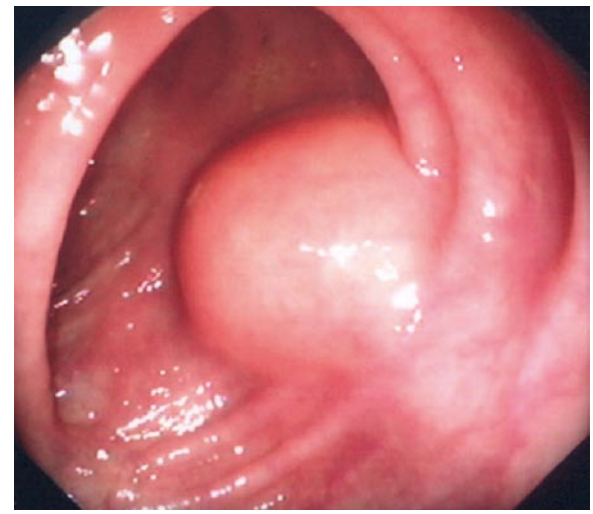


Fig. 8.1.1 Lipoma

8.1.3 Neoplastic Epithelial Lesions

8.1.3.1 Adenoma

Epidemiology

- Adenomas, or adenomatous polyps, are benign tumours representing proliferation and unrestricted cell division in a well-circumscribed area of glandular epithelium within the colonic or rectal mucosa. By definition, multiple polyps number between 5 and 100 in colon and rectum. In 25–30% of cases there is more than one lesion encountered. Polyposis coli is defined in patients with more than 100 polyps.
- It is generally accepted that a benign adenomatous polyp has been the precursor to colorectal cancer in the majority of cases. Nevertheless, it is demonstrated by Shimoda that cancers may also arise de novo in non-adenomatous mucosa. In these cases the change between flat adenoma and cancer runs with rapid progress along the adenoma-carcinoma sequence postulated by Fearon and Vogelstein.
- Macroscopically polyps are separated into three types:
  - Pedunculated
  - Sessile (flat)
  - Semisessile (raised)

All of these may have similar a histological appearance and the same histology.

- According to their architecture three types of adenomatous polyps can be distinguished:
  - Tubular adenomas
  - Tubulovillous adenomas
  - Villous adenomas
- The majority (65–80%) of all adenomatous polyps removed are tubular ones. Up to 25% are tubulovillous and only 5–10% are pure villous adenomas. Although tubular adenomas in their majority are pedunculated and villous tumours are usually sessile, the architectural arrangement is never pure. All types of histological characteristics can be found in each type of polyp.
- A clear relationship exists between the size and type of polyp. Adenomas smaller than 1 cm are 90% tubular. In contrast only 54% of those whose sizes range between 1.1 and 2 cm and just 18% of those greater than 3 cm are tubular. On the other hand only 0.8% of adenomas smaller than 1 cm but 26% of all adenomas between 2 and 3.1 cm and 40% of adenomas larger than 4 cm are villous types.
- The incidence of early invasive carcinoma in villous adenomas is reported to be between 30% and 70%.
- Tubulovillous adenomas contain a significantly mixed structure. This is defined as more than 25% of the adenoma being composed of elements differing from the dominant form. The incidence of malignancy in tubulovillous adenomas is 17% and is between that of tubular and villous types. It depends on the size, the villous elements and whether or not the tumour is sessile.
- The incidence of adenomatous polyps depends on age, sex and geography. The incidence in Europe and North America is estimated to be 7–12%.
- As predisposing factors diets poor in fibre and rich in fat are discussed. Other risk factors are a family history of either colorectal or gynaecological cancer, atherosclerosis, nulliparous women and age.
- The incidence of adenomas rises to a maximum at the ages from 60 to 70 years.

Dysplasia

As mentioned above all neoplastic polyps are characterised by cellular atypia resulting in dysplastic growth. Morson and Sobin have defined three types of dysplasia:

- Mild
- Moderate
- Severe

In this context it should be mentioned that "severe dysplasia" defines the finding of malignancy in the epithelium of a polyp that has not invaded through the muscularis mucosae of the bowel. Such lesions were previously referred to as "carcinoma in situ" but this terminology should be abandoned so as not to be confused with colorectal cancer. In these lesions the risk of metastasis is minimal. Severe dysplasia breaching the submucosal layer in contrast is defined as early invasive carcinoma. The risk of metastasis in these cases ranges from 5% to 33%.

Familial Adenomatous Polyposis

- Familial adenomatous polyposis (FAP) is an autosomal dominant syndrome defined in patients with more than 100 polyps in the colon or if a member of an FAP family has any number of adenomas in colon or rectum detected.
- The genetic defect is described on chromosome 5 (q21). The gene has been named as APC (adenomatous polyposis coli) gene.
- The common expression of the syndrome is the presence of multiple polyps in the colon and rectum associated with extraintestinal lesions (epidermoid cysts, desmoid tumours, osteomas, gliomas and medulloblastomas).
- The gene expression occurs in 100% of patients with the defect and all patients with the defective gene will develop cancer of the colon.
- The average age of a patient newly discovered to have colorectal cancer in FAP is 39 years. For that reason in each patient with FAP proctocolectomy with ileal pouch is recommended.
- Surgery should be performed before the 20th year of age. Only in patients without involvement of the rectum might a subtotal colectomy be considered.
- After subtotal colectomy with ileorectal anastomosis the risk to develop cancer in the rectal remnant after 25 years is from 13% up to 40%. Due to that in patients with ileorectal anastomosis proctorectoscopy of the rectum is recommended biannually.
- Because of the generally increased incidence of adenomas of the duodenum in FAP patients and the associated risk to develop cancer in the duodenum and/or papilla vateri an oesophago-gastroduodenoscopy is recommended on a regular basis every 3 years.

Symptoms

- The signs and symptoms of colorectal adenomas are varied and non-specific.
- The symptoms that most often prompt patients to seek a physician's advice include haemorrhage, change in bowel habit and sometimes abdominal pain.
- Whether a patient presents symptoms and what kind of symptoms depends on the location and extent of the adenoma.

- Large adenomas, i.e. mucus-secreting tumours (often villous adenomas), may cause diarrhoea.
- Patients might notice dark stools due to haemorrhage but more often in adenomas bleeding is occult.

Diagnostic Procedures

- While it is accepted that all symptomatic patients should undergo a complete diagnostic (test for occult blood, colonoscopy, proctorectoscopy) the treatment of asymptomatic patients is still under debate.
- As it is impossible to perform colonoscopy on the entire population, a high-risk group has been defined to improve cost/benefit and risk/benefit ratios in the patients. The high-risk group includes:
  - Patients aged over 50 years
  - Patients with premalignant condition (ulcerative colitis longer than 10 years, Crohn's disease with stricture, FAP, hereditary non-polyposis colorectal cancer (HNPCC) syndrome, previous history of colon polyps)
  - Patients with family history of colorectal cancer or polyps (in a patient with colorectal cancer in their family history, the first colonoscopy should be performed 10 years earlier than the cancer was diagnosed in the relative)
- Unfortunately the guidelines in several countries are not in complete accordance. However, it seems generally agreed upon that asymptomatic patients over 50 years and younger ones with positive family history should have a test for occult bleeding annually.
- In case of a positive result, colonoscopy and proctoscopy with digital examination is recommended. Sigmoidoscopy should be performed above the age of 50 years every 5 years.
- Colonoscopy together with digital examination has shown the highest sensitivity in diagnosing adenomas and colorectal cancer.
- After a negative examination it is recommended to be repeated after 10 years. After positive colonoscopy re-evaluation is indicated after 1 year.

Treatment

- Colonoscopic resection is the treatment of choice in all pedunculated tubular adenomas, tubulovillous adenomas and severely dysplastic adenomas.
- In general a polyp should not be biopsied, but completely removed and subjected to histological examination.
- If endoscopic treatment is not possible, colonic resection is indicated.
- The complications of colonoscopic polypectomy include perforation (immediate or delayed) due to a cautery burn or snare of full thickness bowel wall during removal of a sessile or semisessile polyp.
- Immediate bleeding after polypectomy is possible if the stalk vessel is not cauterised adequately. Bleeding may also occur 7–10 days later when the eschar over the vessel is sloughed.
- Surgery is indicated when cancer is found at the line of excision or within 2 mm from the excised border, in case of lymphatic or venous invasion and in poorly differentiated grade III (WHO) tumours.
- Surgery should follow the standardised protocols for colorectal cancer (see Chap. 9.2).

8.1.4 Mesenchymal Lesions

8.1.4.1 Lipoma

Epidemiology

- Lipomas are benign tumours arising from adipose connective tissue in the bowel wall.
- Despite the fact that they are often described as rare colonic tumours, it is a matter of fact that they present as the most common mesenchymal tumour found in the colon, and the second most common benign colonic polypoid lesion second to adenomatous polyps.
- According to colonoscopy studies the incidence ranges between 0.11% and 0.15%, while autopsy studies estimate prevalence between 0.2% and 4.4%.
- Colonic lipomas are more common in women (56%) than in men (44%).
- They occur in older patients (average age 60 years).
- Seventy per cent are localised in the right hemicolon. Men have a slightly increased propensity towards left-sided lesions.
- Pathologically these tumours are well differentiated. Ninety per cent are of submucosal origin. Ten per cent are located in the subserosal or intramuscular layers.

Symptoms

- Colonic lipomas are commonly small and asymptomatic.
- Symptoms depend on location.
- Unspecific abdominal pain (23%) and rectal bleeding due to ulceration of overlaying mucosa (20%) are most common.
- Other symptoms such as anaemia, weight loss, nausea, vomiting and meteorism are reported less frequently.
- Specifically the rare rectal lipomas cause abdominal pain due to obstruction or intermittent intussusception.

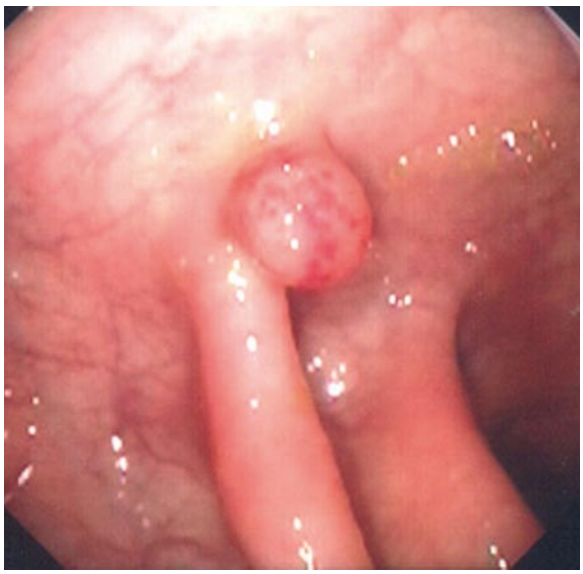


Fig. 8.1.2 Non-Hodgkin's lymphoma

Diagnostic

- The vast majority of colonic lipomas are detected incidentally.
- Preoperative diagnosis is important specifically in symptomatic patients as lipomas in these patients are presented in the same age group with similar symptoms as colorectal malignancies.
- Colonoscopy is of foremost importance. Lipomas present as yellowish tumours most often covered by intact mucosa (Fig. 8.1.2).
- Especially in cases of unspecific recurrent pain computed tomography or contrast enema is helpful in detection of intussusception or invagination.

Treatment

- Asymptomatic lipomas need not to be treated.
- Larger lesions will often need resection, either due to symptoms or uncertainty of differential diagnosis.
- Colonoscopic resection is the treatment of choice in smaller lipomas.
- If endoscopic treatment is not possible colonic resection is recommended.
- Rectal lipomas may be excised and enucleated if confined to the rectal wall.

8.1.4.2 Leiomyoma

A great majority of rectal smooth muscle and stromal tumours are gastrointestinal stromal tumours (GISTs) that are very heterogeneous, ranging from minimal indolent tumours to overt sarcomas. Intramural leiomyomas are exceptional, and true leiomyomas are rare and similar to colonic ones; they often present as intraluminal polypoid masses that appear to have a better prognosis than GISTs with similar mitotic rates.

Epidemiology

- True leiomyomas are more common in the oesophagus, and they have been noted in the colon and rectum only occasionally.
- The small number of reported cases allow no clinicopathological profiling.
- Leiomyomas are histologically typical spindle cell neoplasms.
- The most important criterion for estimating potential malignancy is the mitotic rate. Additional markers are diameter of lesion and presence or absence of ulceration.
- In cases of high mitotic rate, rapid growth, ulceration and if the lesion is larger than 2.5 cm, malignant degeneration must be suspected.

Symptoms

- The intracolonic type of leiomyoma may be pedunculated or sessile. The former tend to protrude causing pain and signs of intestinal obstruction (invagination) and meteorism (Fig. 8.1.3).
- Haematochezia and even intra-abdominal haemorrhage have been described in single cases.

Diagnosis

- Most often leiomyomas in colon or rectum are diagnosed incidentally.
- Especially in the rectum endosonography may be very helpful for differential diagnosis.
- Endorectal ultrasonography (EUS) may show typical findings of colonic leiomyoma and may be used to assess the location of the submucosal tumour.
- Definitive diagnosis regarding malignancy and differential diagnosis is provided only by immunohistopathology and is mandatory in each removed specimen.

Treatment

- Smaller leiomyomas are often found by routine examination.

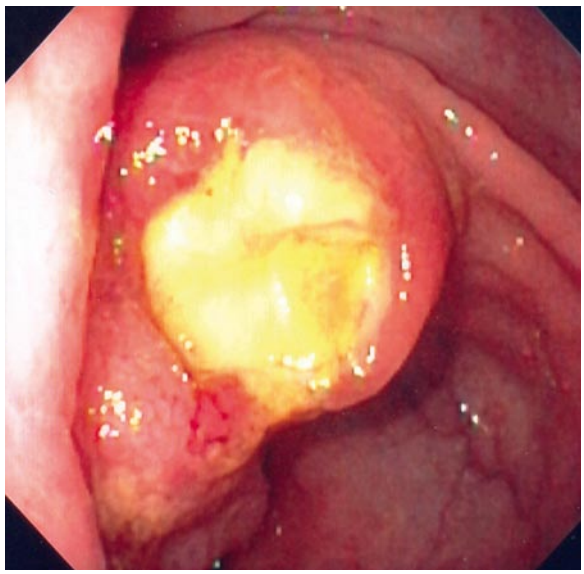


Fig. 8.1.3 Leiomyoma

- Snare polypectomy or transanal excision is adequate treatment, but the complete removal must be ensured and follow-up is necessary as a precaution for tumours with any atypia or mitotic activity.
- Recurrences are frequent, mostly due to malignant transformation.
- However, leiomyomas of muscularis mucosae are benign. They should be separated from gastrointestinal stromal tumours that have a distinct clinicopathological spectrum including frequent disease-related mortality.

8.1.5 Other Lesions

8.1.5.1 Neuroma

Neuromas as well as neurofibromas are very rare lesions in colon or rectum. Especially neurofibromas associated with the syndrome of Neurofibromatosis von Recklinghausen are very seldom. Leading symptoms are gastrointestinal bleeding or ileus due to intestinal obstruction.

Treatment

- If possible the treatment of choice should be complete local excision or resection.
- In most cases excision via endoscopic approach is sufficient.

8.1.5.2 Angioma

Haemangiomas are very rare tumours in colon and rectum. Typically they are congenital lesions. In general, capillary haemangiomas should be separated from cavernous haemangiomas:

- Capillary haemangiomas arise from the submucosal layer with closely packed vessels and often they are encapsulated. Due to this, bleeding in capillary haemangiomas is recognised only episodically and slowly.
- Cavernous haemangiomas are much larger. Not uncommonly 20 cm or more of bowel is involved. Calcification and thrombosis are frequent. The most common complication is bleeding (in more than 60%), mostly massive haemorrhage.

Diagnosis is established endoscopically showing a typical deeply red or blue aspect. Selective angiography in some cases is helpful in establishing the diagnosis of vascular malformation. The advantage of this diagnostic tool may be the option to apply angiographically placed endo-coils for control of haemorrhage.

Treatment

- The optimal treatment is complete endoscopic resection.
- Local excision is adequate.
- In every case the benign nature of the lesion should be confirmed by histological examination.

8.1.5.3 Lymphangioma

(Cystic) lymphangiomas of the colon are extremely rare lesions that present as submucosal masses in the large intestine. Most of the cases have been reported from Japan. They are felt to represent dilated lymphatic channels lined by endothelial cells, the exact cause of which remains unknown. They are usually found incidentally in asymptomatic patients during routine endoscopy or barium radiography, however unspecific symptoms, such as abdominal pain and rectal bleeding, can occur. Endoscopically these lesions appear as solitary submucosal masses with smooth overlying mucosa. The pillow sign is usually positive after applying pressure to the mass with a closed biopsy forceps. These lesions have no malignant poten-

tial, thus, if diagnosed in an asymptomatic patient, can be left. If intervention is necessary because of symptoms excision, surgically or endoscopically, should be done as aspiration of these cysts invariably leads to reaccumulation of cystic fluid.

8.1.6 Others

8.1.6.1 Endometriosis

Endometriosis, which can affect up to 20% of premenopausal women, is defined as the presence of functioning extrauterine endometrial tissue. This tissue is located most commonly in the uterosacral ligament but can in rare instances affect the rectosigmoid colon. Symptoms are dependent on the location and degree of tissue infiltration and include infertility, pelvic pain, dysmenorrhoea and dyspareunia. Gastrointestinal symptoms occur in approximately one third of patients and include rectal bleeding, which is more prominent during menses as are most of the other symptoms. Infiltration of the rectosigmoid colon by endometrial tissue, so-called enteric endometriosis, can present as a submucosal mass. Endosonographically, the differential diagnosis can be challenging, especially the separation from GISTs. The endosonographic appearance of endometriosis is hypoechoic, and the merging of the muscularis propria and the endometrial tissue simulates the endosonographic features of a GIST. Clues that may help in differentiating these from GISTs include occasional thickening of the adjacent submucosa which can occasionally be involved with functioning endometrial tissue, localisation to the anterior of lateral rectal wall which is in direct proximity to the uterus or seeing hypoechoic masses adjacent to the rectosigmoid colon representing endometrial deposits in the surrounding tissue. Management of these lesions is dependent on the patient's symptoms; those who are symptomatic usually require a segmental resection depending on the site of enteric involvement.

8.1.6.2 Pneumatosis Cystoides Intestinalis

Pneumatosis cystoides intestinalis (PCI), also known as pneumatosis coli, refers to the presence of air in the bowel wall. Many theories of its aetiology have been proposed including the mechanical theory with trauma to the mucosa allowing luminal air to dissect into the bowel wall, the bacterial theory where gas-producing bacteria translocate into the submucosa through mechanical breaches in the mucosa and the pulmonary theory where increased intrathoracic pressure in patients with chronic obstructive pulmonary disease (COPD), asthma and patients on mechanical ventilation leads to alveolar rupture with air tracking along the mediastinum, retroperitoneum to the mesentery eventually to the bowel wall via breaks in the serosa. Although none of these theories explain all cases of PCI, it is more likely that several mechanisms play a role in the pathogenesis of PCI. Most patients presenting with PCI are asymptomatic and lesions are found incidentally during endoscopic or radiological examinations for other indications. Patients who are symptomatic can present with a wide variety of symptoms from non-specific complaints of abdominal pain and distension, diarrhoea, constipation, mucus discharge and excessive flatulence to more specific symptoms of rectal bleeding, those consistent with bowel obstruction and life-threatening peritonitis requiring emergency intervention. Colorectal PCI presents as broad-based submucosal masses at endoscopy, which may have a pale appearance or may be covered by haemorrhagic mucosa. The endoscopic appearance, however, is certainly not characteristic (Fig. 8.1.4) and evaluation by EUS can lead to a definitive diagnosis by showing multiple hyperechoic lesions in the submucosa with acoustic shadowing obscuring the outer layers of the bowel wall due to the air-filled cystic spaces in the submucosa. Management depends on whether these lesions are found incidentally, in which case it follows a benign course, or whether the patient's symptoms are caused by PCI in which case medical, endoscopic or surgical therapy may be indicated.

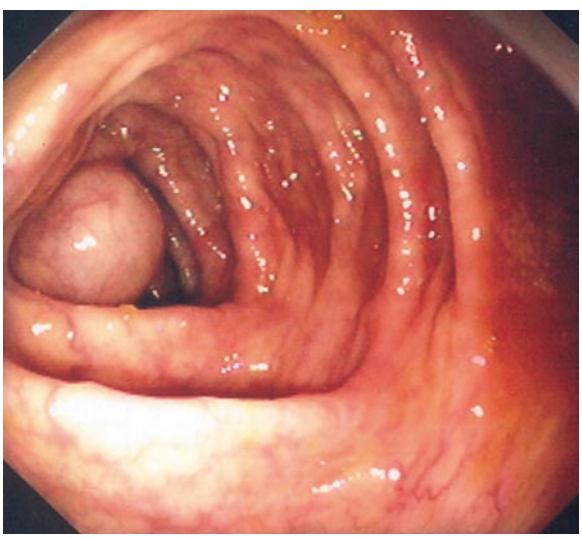


Fig. 8.1.4 Pneumatosis cystoides intestinalis

Suggested Reading

1. Agnifili A, Verzaro R, Gola P et al (1999) Juvenile polyposis: case report and assessment of the neoplastic risk in 271 patients reported in the literature. Dig Surg 16:161–166
2. Agnifili A, Schietroma M, Mattucci S et al (2000) [Clinical assessment of juvenile polyposis with particular reference to the risk of neoplastic malignancy. Analysis of 412 patients reported in the international literature]. Chir Ital 52:393–404
3. Barnard JA (2004) Gastrointestinal polyps and polyp syndromes in adolescents. Adolesc Med Clin 15:119–129
4. Chak A (2002) EUS in submucosal tumors. Gastrointest Endosc 56(4 suppl):S43–S48
5. Cho HS, Kim HY, Song YL et al (2004) [A case of pedunculated leiomyoma found during colonoscopic examination for anal bleeding]. Korean J Gastroenterol 43:129–132
6. Coburn MC, Pricolo VE, DeLuca FG, Bland KI (1995) Malignant potential in intestinal juvenile polyposis syndromes. Ann Surg Oncol 2:386–391
7. Crozier F, Portier F, Wilshire P et al (2002) [CT scan diagnosis of colo-colic intussusception due to a lipoma of the left colon]. Ann Chir 127:59–61
8. Cunningham JD, Vine AJ, Karch L, Aisenberg J (1998) The role of laparoscopy in the management of intussusception in the Peutz-Jeghers syndrome: case report and review of the literature. Surg Laparosc Endosc 8:17–20
9. Desai DC, Neale KF, Talbot IC et al (1995) Juvenile polyposis. Br J Surg 82:14–17
10. Di Roma A, Cafferati M, Ghersi T et al (1996) [Hemoperitoneum caused by leiomyoma of the colon]. Minerva Chir 51:725–727
11. Eglinton T, Bagshaw P, Bayliss S (2005) Colo-colonic intussusception secondary to a colonic lipoma diagnosed with preoperative CT scan. N Z Med J 118:U1442
12. Giardiello FM, Offerhaus JG (1995) Phenotype and cancer risk of various polyposis syndromes. Eur J Cancer 31A:1085–1087
13. Graeme-Cook F (1996) Pathology neoplastic and non-neoplastic. Surg Oncol Clin N Am 5:487–512
14. Hendi JM (2004) Case of the month. Lipoma of the sigmoid colon. Crit Rev Comput Tomogr 45:279–283
15. Hoer J, Truong S, Virnich N et al (1998) Pneumatosis cystoides intestinalis: confirmation of diagnosis by endoscopic puncture a review of pathogenesis, associated disease and therapy and a new theory of cyst formation. Endoscopy 30:793–799
16. Irisawa A, Bhutani MS (2001) Cystic lymphangioma of the colon: endosonographic diagnosis with through-the-scope catheter miniprobe and determination of further management. Report of a case. Dis Colon Rectum 44:1040–1042
17. Kuhlgatz J, Sander B, Golas MM et al (2006) Differential diagnosis of gastrointestinal leiomyoma versus gastrointestinal stromal tumor. Int J Colorectal Dis 21:84–88
18. Ladurner R, Mussack T, Hohenbleicher F et al (2003) Laparoscopic-assisted resection of giant sigmoid lipoma under colonoscopic guidance. Surg Endosc 17:160
19. Meshikhes AW, Al-Saif O, Al-Otaibi M (2000) Duodenal and ampullary obstruction by a Peutz-Jeghers polyp. Eur J Gastroenterol Hepatol 12:1239–1241
20. Meyer P (1990) Polyps. In: Marti MC, Givel JC (eds) Surgery of anorectal diseases. Springer, Berlin, pp 151–161
21. Miettinen M, Sarlomo-Rikala M, Sobin LH (2001) Mesenchymal tumors of muscularis mucosae of colon and rectum are benign leiomyomas that should be separated from gastrointestinal stromal tumors: a clinicopathologic and immunohistochemical study of eighty-eight cases. Mod Pathol 14:950–956
22. Montgomery D, Reidy J (2004) Giant submucosal colonic lipomata: report of a case and review of the literature. Scott Med J 49:71
23. Morson B, Sobin L (1976) Histological typing of intestinal tumors. World Health Organization, Geneva, pp 13–58
24. Nagaoka S, Bandoh T, Takemura T (2000) Lymphoid hyperplasia of the large intestine: a case report with immunohistochemical and gene analysis. Pathol Int 50:750–753
25. Oktenli C, Gul D, Deveci MS et al (2004) Unusual features in a patient with neurofibromatosis type 1: multiple subcutaneous lipomas, a juvenile polyp in ascending colon, congenital intrahepatic portosystemic venous shunt, and horseshoe kidney. Am J Med Genet A 127:298–301
26. Rogers SO Jr, Lee MC, Ashley SW (2002) Giant colonic lipoma as lead point for intermittent colo-colonic intussusception. Surgery 131:687–688
27. Roseau G, Dumontier I, Palazzo L et al (2000) Rectosigmoid endometriosis: endoscopic ultrasound features and clinical implications. Endoscopy 32:525–530
28. Schreibman IR, Baker M, Amos C, McGarrity TJ (2005) The hamartomatous polyposis syndromes: a clinical and molecular review. Am J Gastroenterol 100:476–490
29. Spigelman AD, Arese P, Phillips RK (1995) Polyposis: the Peutz-Jeghers syndrome. Br J Surg 82:1311–1314
30. Thomeer M, Carbone I, Bosmans H et al (2003) Stool tagging applied in thin-slice multidetector computed tomography colonography. J Comput Assist Tomogr 27:132–139
31. Tzilinis A, Fessenden JM, Ressler KM, Clarke LE (2003) Transanal resection of a colonic lipoma, mimicking rectal prolapse. Curr Surg 60:313–314
32. Watanabe T, Kato K, Sugitani M et al (2000) A case of multiple lymphangiomas of the colon suggesting colonic lymphangiomatosis. Gastrointest Endosc 52:781–784
33. Woodford-Richens KL, Rowan AJ, Poulsom R et al (2001) Comprehensive analysis of SMAD4 mutations and protein expression in juvenile polyposis: evidence for a distinct genetic pathway and polyp morphology in SMAD4 mutation carriers. Am J Pathol 159:1293–1300
34. Yatabe Y, Nakamura S, Nakamura T et al (1998) Multiple polypoid lesions of primary mucosa-associated lymphoid-tissue lymphoma of colon. Histopathology 32:116–125

Malignant Tumours

9.1 Genetics

MALIKA BENNIS, EMMANUEL TIRET

9.1.1 Basics

The two main inherited colorectal cancer syndromes, familial adenomatous polyposis (FAP) and hereditary non-polyposis colorectal cancer (HNPCC) or Lynch syndrome are characterised by a single mutation leading to a dramatically increased predisposition for colorectal cancer. FAP is an autosomal dominantly inherited condition that has been shown to be due to mutations in the adenomatous polyposis coli (APC) gene, a tumour suppressor gene active in the Wnt/Wingless signalling pathway. The much commoner HNPCC is caused by a germline mutation in one of the DNA mismatch repair genes (hMLH1, hMSH2, hMSH6). These genes correct errors of DNA replication and any defect of this repair system will lead to rapid accumulation of mutations. Both syndromes are characterised by early onset of colorectal tumours, by synchronous and metachronous tumours as well as numerous extracolonic benign and malignant manifestations.

More recently, another syndrome has been reported, the MAP syndrome, that is due to biallelic germline mutation of a DNA base excision repair (BER) gene: *hMYH*. The hereditary transmission is recessive, but this syndrome predisposes also to synchronous and metachronous colorectal neoplasm and like the two main dominantly inherited colorectal cancer syndromes requires practice parameters for treatment and surveillance.

9.1.1.1 Familial Adenomatous Polyposis

Although FAP accounts for less than 1% of all colorectal cancers, it has provided knowledge about carcinogenesis in the general population and colon cancer in particular.

Histologically, FAP is characterised by multiple adenomas, averaging less than 5 mm in diameter. The oft-cited number of 100 polyps varies according to the age of the patient. Because puberty is the general age of onset, an adolescent with less than 10 adenomas and a confirmed family history of FAP must be considered as affected.

Two phenotypes have been described: classic FAP and attenuated adenomatous polyposis. Attenuated adenomatous polyposis regroups a subset of patients whose phenotype does not quite fit with classic FAP, in that the age of onset of both adenomas and cancer is later, usually from the age of 40 years onwards; adenomas are fewer in number, often sessile, 1–2 mm in diameter, with apparent rectal sparing. However, in 1992 this variant was linked to the APC gene and so declared part of the normal spectrum of FAP. Nevertheless, with the description of the MAP syndrome, a possible eponymic debate will have to be disclosed on the basis of genetic testing.

The APC gene, which controls epithelial growth was discovered in 1991. The APC protein, when functional, inhibits the signalling Wnt pathway by degrading β-catenin. When inactivated, APC/β-catenin pairing is impossible and the β-catenin excess enters the cell nuclei, activating growth regulator genes, such as c-myc and vascular endothelial growth factor (VEGF), which then induce colorectal epithelial proliferation and polyp formation.

In sporadic cancer, somatic APC mutations are observed in 70% of cases. The two alleles are mutated, mainly, in the Mutation Cluster Region between codons 1250 and 1550. For patients with FAP, one of the two alleles is already inactivated by a germline mutation. A somatic event, such as loss of the chromosome part containing the wild APC gene copy (loss of heterozygosity), will lead to APC inactivation and so to the appearance of adenomas. Other genes like k-ras and P53 will mutate and cancer will develop in these adenomas.

9.1.1.2 Hereditary Non-Polyposis Colorectal Cancer

The observation that HNPCC tumours exhibited a distinct molecular abnormality called DNA microsatellite instability (MSI) led to the identification of DNA mismatch-repair (MMR) genes as the genetic basis for HNPCC. MMR proteins recognise and then correct base pair mismatches as well as small insertions or deletions that can occur during normal DNA replication. Multiple genes from the mutS (*hMSH2*, *hMSH3*, *hMSH6*) and mutL (*hMLH1*, *hMLH3*, *hPMS1*, *hPMS2*) families interact to repair these mismatched DNA sequences. Microsatellite DNA sequences, which are defined as short repetitive

mononucleotide or dinucleotide sequences, are particularly susceptible to errors of replication. Most microsatellite sequences are located in the non-coding regions of the genome. However, microsatellite sequences can be found within the coding regions of certain growth-regulatory genes and a loss of MMR proofreading activity results in the accumulation of frameshift somatic mutations in these genes. These target genes include receptors for growth factors (transforming growth factor-β receptor II, insulin-like growth factor II receptor), cell cycle regulators (E2F4), regulators of apoptosis (BAX), and some of the MMR genes themselves (*hMSH3* and *hMSH6*).

9.1.1.3 The MAP Syndrome

The thus far discussed high-risk colon cancer syndromes display an autosomal dominant pattern of inheritance. However, the discovery that biallelic mutations in the base excision repair gene, *MYH*, result in an increased risk of colorectal adenomas and cancers led to the first description of an autosomal recessive colon cancer syndrome.

8-Oxo-guanine is a by-product of oxidative DNA damage and it inappropriately pairs with adenines, leading to G:C→T:A mutations. The role of *MYH* is to excise the mispaired adenines. Dysfunction of *MYH* results in the accumulation of somatic G:C→T:A mutations in specific growth-regulatory genes, and *APC* appears to be a preferred target. Genetic testing is now available, and analysis is focused on exons 7 and 13 of the *MYH* gene. Two specific mutations in these exons (Y165C and G382D) account for 87% of all *MYH* mutations in the Northern European populations.

9.1.1.4 Other Syndromes

Peutz-Jeghers Syndrome

Peutz-Jeghers syndrome (PJS) is an autosomal dominant hamartomatous polyposis syndrome that carriers a 39% lifetime risk of colon cancer. There is, however, a 93% cumulative risk of developing any type of malignancy. PJS has been linked to germline mutations of *LKB1*, a serine-threonine kinase located on chromosome 19p. Among its many functions, *LKB1* regulates p53-mediated apoptosis. Recently, adenosine monophosphate-activated protein kinase has been identified as a direct phosphorylation target for *LKB1*, implicating *LKB1* in the control of cellular metabolism. However, 50–60% of patients with classic features of PJS have identifiable germline mutations of *LKB1*, suggesting there may be additional disease loci yet to be identified.

Juvenile Polyposis Syndrome

Like PJS, the juvenile polyposis syndrome (JPS) is inherited in an autosomal dominant pattern and is characterised by the development of hamartomatous intestinal polyps. JPS patients exhibit a 10–38% lifetime risk of colon cancer and the average age at diagnosis is 34 years. Clinical diagnosis of JPS is made when the all criteria are fulfilled.

Two genes, *MADH4* and *BMPR1A*, have been linked to JPS. *MADH4*, located on chromosome 18q, encodes the Smad4 protein that regulates intracellular signalling of transforming growth factor-β (TGF-β). The *BMPR1A* gene on chromosome 10q encodes a receptor for bone morphogenetic protein, a member of the TGF-β superfamily. However, a pathogenic mutation in one of these two genes is detected in only 40–50% of patients with JPS.

Hyperplastic Polyposis Syndrome

Sporadic hyperplastic polyps are encountered incidentally in the distal sigmoid and rectum and traditionally have been thought not to possess any malignant potential. However, rare individuals and families exhibit numerous hyperplastic polyps distributed throughout the colon, and approximately 25–35% of these patients were found to have associated synchronous colorectal cancers. The aetiology of this syndrome termed hyperplastic polyposis syndrome (HPS) has yet to be elucidated and its diagnosis remains purely clinical.

9.1.2 Familial Adenomatous Polyposis

9.1.2.1 Molecular Screening

Molecular testing for FAP is currently offered by direct mutation analysis and in vitro synthesised protein (IVSP) assay, which looks directly at the truncated protein product of the APC gene. The best age for genetic testing is still matter of debate. It should be preceded by counselling about psychological and social issues and the results should be communicated during a counselling session.

Mutation of the APC gene, either point mutation or genomic deletion, is found in about 85% of patients with an FAP phenotype. However, in some patients no mutation can be demonstrated. Moreover, about 20% of patients with an APC mutation explaining their FAP phenotype are de novo mutants without a family history of FAP.

9.1.2.2 Screening Guidelines

- Early detailed registry pedigrees have provided generational proof that the majority of children and siblings are diagnosed between the ages of 15 and 25 years. Consequently, screening guidelines were established from age 10 to 14 years.
- One of the major drawbacks of screening has been the lack of compliance from patients subjected to excessive screening. Colonoscopy remains the screening standard and it is advocated once the diagnosis of FAP has been established either clinically or genetically. However, flexible sigmoidoscopy may be preferred as the first screening tool because it is minimally invasive, allows biopsy and is generally acceptable to the adolescent.
- Follow-up is recommended every 2 years until the age of 35 and every 3–5 years thereafter for at-risk first-degree relatives who have not undergone predictive testing or who are uninformative subsequent to DNA analysis.
- Patients in whom an APC mutation cannot be proven but who have several affected and available relatives should be considered as mutant and monitored accordingly.
- Patients who do not have the APC mutation found in their family, are not at risk and depending on the quality of the laboratories performing the molecular diagnosis should not be considered at risk.

9.1.2.3 Colorectal Polyposis

The known adenoma-carcinoma sequence does not appear to be accelerated in FAP and, therefore, the disease is a prototype for cancer prevention through prophylactic surgery. The lifetime risk of colorectal cancer in patients with FAP approaches 100% and is related to the severity of colorectal polyposis. The cancer risk for patients with severe polyposis, i.e. > 1,000 polyps is thought to be double the risk for patients with < 1,000 polyps.

Timing for Colectomy

Although colorectal polyps often start to develop during the teenage period invasive cancer is exceedingly rare before the end of puberty and even the age of 20 years. In known FAP patients screening should commence around the age of 12 years with yearly flexible sigmoidoscopy, which if polyps are found should be supplemented by colonoscopy. In patients with mild disease surgery can be deferred until the late teenager years. In severe disease with dense polyposis surgery should be carried out as soon as possible, but preferably after the puberty.

Type of Surgery

There are three surgical options in the treatment of FAP:

- Proctocolectomy with permanent end ileostomy (PC)
- Colectomy with ileorectal anastomosis (IRA)
- Restorative proctocolectomy with ileal pouch–anal anastomosis (IPAA)

Each of these options has advantages and disadvantages:

- PC is nowadays rarely performed as a permanent stoma is usually unacceptable to young patients. It, however, still has its role in the treatment of very low rectal cancer, when sphincter preservation is not possible.
- IRA carries a low rate of morbidity and mortality with good functional results and is commonly performed without a temporary diverting stoma. The major drawback is the persistent cancer risk in the retained rectum. The overall cumulative risk of rectal cancer has been shown to be up to 30% by the age of 60 years. It, however, remains an option in individuals with a low rectal cancer risk (mild rectal polyposis, late onset, certain mutations). Following recent reports on severely reduced fecundity after IPAA, IRA should be discussed with women who have not yet completed their families.
- IPAA greatly reduces the rectal cancer risk, especially when performed with mucosectomy and hand-sewn peranal anastomosis. It is, however, a technically more demanding procedure, often requires a diverting ileostomy and is associated with a higher morbidity than IRA.

The options, including the possibility of a laparoscopically assisted procedure, need to be discussed with the patient on an individual basis.

An IPAA should be recommended to those with rectal polyposis (> 20 polyps in the distal 10 cm of the rectum) or when there is concern about the compliance with long-term surveillance of the rectum. Young women with FAP need to be counselled about the fertility implications of IPAA. It needs to be emphasised to patients that, regardless of the type of operation performed, long-term follow-up will be required for either the rectal stump after IRA or the "neorectum" after IPAA as well as for extracolonic disease manifestations.

Surveillance After Surgery

Regular follow-up is mandatory after all procedures. The standard care includes peranal digital and flexible endoscopic examination at yearly intervals.

The risk of rectal cancer after IRA is closely related to the severity of the polyposis. At surveillance endoscopy random biopsies to check for dysplasia are mandatory.

Adenomas under 5 mm may be observed and those over 5 mm are snared. Over time repeated endoscopic polypectomy can induce dense scarring which makes assessment of the rectal mucosa more difficult. Reduced rectal compliance due to scarring can eventually result in functional disturbances with rectal frequency, urgency and incontinence, and eventually lead to proctectomy. Completion proctectomy is indicated for villous adenomas > 1 cm as well as biopsy proven high-grade dysplasia or invasive cancer.

The non-steroidal anti-inflammatory drug (NSAID) sulindac has been shown to produce regression of rectal as well as pouch adenomas. Temporary regression of rectal polyps is observed in approximately two thirds of patients but with longer follow-up this effect is lost. However, new cancers have been diagnosed under sulindac treatment. Celecoxib, a selective cyclo-oxygenase-2 inhibitor also induces regression of colonic polyps in FAP but is no longer available due to its adverse cardiovascular effects.

Endoscopic pouch examination allows surveillance of pouch adenomas, which tend to occur more frequently with longer follow-up. Their significance will become clearer in due course, once large cohorts of FAP patients with IPAA reach 20–25 years of follow-up.

Chemoprevention as Primary Therapy for Colorectal Polyposis

The NSAIDs sulindac, celecoxib and exisulind have been shown to induce regression of colorectal adenomas in FAP. This effect has been demonstrated up to 4 years in patients with IRA. Of concern are case reports of the occurrence of cancers despite chemoprevention and regular surveillance. It is, therefore, clear that chemoprevention cannot be recommended as an alternative to surgery. NSAIDs are indicated to control pouch polyposis and rectal polyposis following IRA, especially when surgery is contraindicated or declined. The need for close surveillance with 6–12 monthly flexible endoscopy must be emphasised.

9.1.2.4 Duodenal Adenomas

Surveillance

Duodenal adenomas occur in the vast majority of patients with FAP (> 90%) but only 10% develop severe disease and malignant transformation occurs in just under 5%. Nevertheless, duodenal cancer is the commonest cancer-related death in FAP after proctocolectomy. Screening of the upper gastrointestinal tract usually begins around the age of 20 years and its further intervals are determined by disease severity. Endoscopic screening has been shown to result in a moderate gain of life expectancy. The aim of endoscopy is not to remove all adenomas but to stage and control disease severity.

Treatment for duodenal polyposis is difficult. Endoscopic interventions, which include snaring, electrocoagulation, laser ablation and photodynamic therapy are often technically demanding if not impossible and carry substantial potential for complications. Small adenomas should be biopsied. The Spigelman classification allows staging of the severity of duodenal polyposis according to number and size of polyps as well as histological type and degree of dysplasia (Table 9.1.1).

Surgical intervention needs to be considered for patients with stage III/IV tumours. Treatment with celecoxib has been shown to be effective in reducing duodenal polyposis, but the drug has now been taken off the market.

Surgery for Duodenal Adenomas

Both endoscopic and open surgical excision of duodenal adenomas are associated with a high risk of recurrence. The only chance of permanent cure for patients with advanced duodenal polyposis is a duodenal resection. The operation of choice is a pylorus-preserving pancreaticoduodenectomy or a pancreas-preserving duodenectomy in selected cases when there is no concern about malignancy. In specialist centres the outcome is good with low recurrence rates and an acceptable morbidity. Duodenal polyposis appears to follow the adenoma-carcinoma sequence. Therefore surgery should be discussed with patients with progressive and severe duodenal polyposis as invasive disease carries a poor prognosis, even when treated by radical surgery (Whipple's procedure).

9.1.2.5 Desmoid Tumour

Desmoids are histologically benign but locally invasive monoclonal proliferations of fibroblasts. They are only very occasionally seen in the general population but affect 10–15% of all FAP patients. Desmoids are together with duodenal polyposis/cancer the major cause of morbidity and mortality after proctocolectomy. In approximately 10% they are fatal. Desmoids arise either within the abdominal cavity, in particular within the small bowel mesentery or on the abdominal wall, occasionally also on extremities. Their natural history shows great variation with episodes of rapid and destructive growth as well as spontaneous regression. Intra-abdominal desmoids can cause small bowel and ureteric obstruction. Occasionally a desmoid tumour arising within the small bowel mesentery, and thereby shortening it, will make a restorative procedure with IPAA impossible.

Medical treatment options include NSAIDs, anti-oestrogens and chemotherapy and are used in an

Table 9.1.1 Classification of the severity of duodenal polyposis (according to Groves et al. 2002)

	Number of points		
	1	2	3
Number of polyps	1–4	5–20	>20
Polyp size (mm)	1–4	5–10	>10
Histology	Tubulous	Tubulovillous	Villous
Degree of dysplasia	Mild	Moderate	Severe

Stage 0: 0 points, Stage I: 1–4 points, Stage II: 5–6 points, Stage III: 7–8 points, Stage IV: 9–12 points

attempt to stabilise the tumour and induce regression. Several small studies have reported success for treatment with sulindac and/or tamoxifen but evidence from controlled randomised studies is lacking. Cytotoxic therapy with vinblastine and methotrexate has shown some response. A more aggressive regimen combining dacarbazine with doxorubicin appears to be effective in rapidly expanding desmoid tumours. For stable intra-abdominal desmoid tumours sulindac alone may be used. For slowly growing or symptomatic tumours tamoxifen may be added and the dose gradually increased to 80–120 mg/day. Chemotherapy is reserved for rapidly growing tumours and the rate of growth will determine the drug regimen.

Surgery is recommended as the first-line treatment for abdominal wall desmoids. Morbidity and mortality rates are low, but even with a 1-cm excision margin recurrence is common. The abdominal wall may require reconstruction with prosthetic material. Surgery for intra-abdominal desmoids is associated with a high risk of major complications (including haemorrhage, recurrence and long-term parenteral nutrition) and death and, therefore, should be avoided whenever possible. Intestinal ischaemia and perforation resulting in peritonitis may, however, require an emergency laparotomy. In the future small-bowel transplantation may become a treatment option for intra-abdominal desmoid tumours.

9.1.3 Hereditary Non-Polyposis Colorectal Cancer Syndrome

9.1.3.1 Molecular Screening

Following a careful personal and familial history of cancer some patients will fulfil the Amsterdam I or II or some of the Bethesda criteria (Table 9.1.2). However, these criteria are too stringent and most patients carrying a deleterious germline mutation of a mismatch repair gene will not be identified. At present the recommendation is to try to determine the MSI phenotype after selection with these criteria and to test patients showing an MSI phenotype on polymerase chain reaction (PCR) products for mutations. An alternative would be to test all colorectal cancers with immunohistochemical staining with anti-MLH1 and anti-MSH2 antibodies. The loss of expression of one of these proteins found by immunohistochemistry correlates with the MSI phenotype. All patients presenting with a cancer deficient for one of these proteins should, therefore, be counselled for mutation search on the gene of the deficient protein. Moreover, if several mechanisms can explain MLH1 deficiency, most patients presenting with an MSH2-deficient cancer will have germline mutation of this gene.

9.1.3.2 Screening Guidelines

- Hereditary non-polyposis colorectal cancer is more complex than FAP because more genes are involved, penetrance is less complete and expression is more varied. Furthermore, patients may be diagnosed with HNPCC clinically or biologically. These two subgroups are not identical, especially with regard to the colorectal cancer risk for their relatives. Therefore, there are no clear recommendations for surveillance.
- However, once the diagnosis of HNPCC has been established by either clinical or molecular criteria, an aggressive cancer screening programme should be initiated.
- Colonoscopy should begin between 20 and 25 years of age and then repeated every 1–2 years.
- Annual transvaginal ultrasound and endometrial aspiration biopsy are recommended due to the high risk of endometrial cancer after the age of 30 years.
- There are no standardised guidelines for screening for other extracolonic tumours, and this is usually based on the specific family history.

Table 9.1.2 Clinical guidelines for the diagnosis of hereditary non-polyposis colorectal cancer

Amsterdam I criteria	
1.	Three relatives with colorectal cancer, one a first-degree relative of the other two
2.	Cases that span at least two generations
3.	At least one colorectal cancer case diagnosed before age 50 years
Amsterdam II criteria	
1.	Three relatives with an HNPCC-associated cancer (colorectal, endometrial, small bowel, ureter or renal pelvis), one a first-degree relative of the other two
2.	Cases that span at least two generations
3.	At least one cancer case diagnosed before age 50 years
Bethesda criteria (revised 2004)	
1.	Colorectal cancer before age 50 years
2.	Synchronous or metachronous colorectal cancer or other HNPCC-related cancer (endometrial, ovarian, gastric, small bowel, urinary tract, biliary tract, pancreas, brain and sebaceous gland) regardless of the age
3.	Colorectal cancer with MSI-H morphology (characterised by the presence of tumour infiltrating lymphocytes, mucinous differentiation/signet-ring-cell carcinoma, peritumoral Crohn's-like lymphocytic reaction, medullary growth pattern) before the age of 60 years
4.	Colorectal cancer with one or more first-degree relatives with colorectal cancer or another HNPCC-related cancer, one of the cancers diagnosed before the age of 50 years
5.	Colorectal cancer with two or more relatives with colorectal cancer or another HNPCC-related cancer regardless of age

- Screening for ovarian cancer should include annual transvaginal ultrasound and pelvic examination.
- Upper gastrointestinal endoscopy should be carried out every 2 years starting from the age of 30–35 years and then every 1–2 years.
- An approach to screening for tumours of the uroepithelial tract would incorporate annual renal ultrasound, urinalysis and urine cytology.

9.1.3.3 Colon and Rectum

The theoretical options for HNPCC mutation carriers with a normal colon are surveillance or prophylactic colectomy as a cancer prevention method in very selected patients. A decision analysis model has shown large gains in life expectancy for HNPCC patients when offered some intervention. The benefit was greater for prophylactic colectomy than for colonoscopic surveillance and decreased the longer surgery was delayed. The benefit was minimal when colectomy was carried out at the time of diagnosis of colorectal cancer. Randomised controlled data comparing surveillance and prophylactic surgery are, however, not available. During the decision-making process the patient needs to be told that the optimal management strategy is not yet known and counselled regarding risks and benefits of the available options.

For HNPCC mutation carriers with an invasive colorectal cancer the choice lies between a conventional segmental colectomy or a total colectomy with IRA. Regardless of the procedure lifelong postoperative surveillance is required with yearly to 2-yearly colonoscopy or proctoscopy following IRA. It appears that the adenoma-carcinoma sequence is accelerated in HNPCC and there is evidence that cancers can develop within 2 years of a negative colonoscopy. Unless the first cancer carries a poor prognosis, prophylactic colectomy seems a reasonable option as the risk of a metachronous colorectal tumour is around 45%. The risk of rectal cancer following a total colectomy with IRA has been shown to be approximately 12% at 12 years follow-up making surveillance mandatory. Patient compliance as well as the availability of high standard colonoscopy will also influence the individual decision.

Rectal cancer is an uncommon index cancer in HNPCC. The principal options are anterior resection of the rectum or proctocolectomy with IPAA. Likely functional outcome, long-term morbidity and impact on quality of life of each procedure as well as the need for lifelong colonoscopic surveillance if the proximal colon is preserved need to be discussed in detail with the patient.

9.1.3.4 Endometrial Cancer

The cumulative risk of endometrial cancer in women with HNPPC is 42% and appears to be linked to mutation of MSH6 in particular and to a lesser degree to mutation of MSH2 and MLH1. The risk of ovarian cancer is also high and synchronous ovarian and endometrial cancers have been reported in up to 21.5% of patients. The option of prophylactic hysterectomy and bilateral salpingo-oophorectomy needs to be carefully discussed with the patient. At present the best option appears to be surveillance until the patient has completed her family. Hysterectomy and oophorectomy may then be carried out at the time of colectomy or on a separate occasion.

9.1.4 Other Syndromes

9.1.4.1 The MAP Syndrome

- Until official guidelines are established, it is reasonable to follow the recommendations for colorectal cancer screening in attenuated FAP.

9.1.4.2 The Peutz-Jeghers Syndrome

- Because of the colon cancer risk, colonoscopy is recommended every 3 years starting at age 18 years.
- In addition, upper gastrointestinal endoscopy should be performed every 3 years starting at age 25 years.
- Screening for small-bowel cancer should be undertaken with a small-bowel series or video capsule endoscopy every 2 years.
- Screening for pancreatic cancer should include endoscopic or abdominal ultrasonography starting at 30 years of age and thereafter every 1–2 years.
- Annual breast examination with mammography every 2–3 years starting at the age of 25 years should be recommended.
- Screening for endometrial and ovarian cancer should be started at the age of 20 years with annual pelvic examination, a Pap smear and a pelvic ultrasound.
- In men annual testicular examination should be commenced at 10 years of age and testicular ultrasonography should be performed if feminising features are observed.

9.1.4.3 Juvenile Polyposis Syndrome

- Patients with JPS should have their first colonoscopy around the age of 15–18 years, and this should be repeated every 1–2 years.
- Upper gastrointestinal endoscopy is recommended from the age of 25 years and then every 1–2 years.

9.1.4.4 Hyperplastic Polyposis Syndrome

- Cancer screening guidelines have not yet been established. However, a possible strategy is to repeat colonoscopy 1 year after the diagnosis is made and then every 2–3 years.
- Colectomy may be appropriate in cases where the polyp burden is unmanageable endoscopically.

Suggested Reading

1. Clark S, Neale KF, Landgrebe JC et al (1999) Desmoid tumours complicating familial adenomatous polyposis. Br J Surg 86:1185–1189
2. Giardiello FM, Offerhaus JA, Tersmette AC et al. (1996) Sulindac induced regression of colorectal adenomas in familial adenomatous polyposis: evaluation of predictive factors. Gut 38:578–581
3. Groves CJ, Saunders BP, Spigelman AD et al (2002) Duodenal cancer in patients with familial adenomatous polyposis (FAP): results of a 10 year prospective study. Gut 50:636–641
4. Middleton SB, Frayling IM, Phillips RK (2000) Desmoids in familial adenomatous polyposis are monoclonal proliferations. Br J Cancer 82:827–832
5. Olsen KO, Juul S, Buelow S et al (2003) Female fecundity before and after operation for familial adenomatous polyposis. Br J Surg 90:227–231
6. Penna C, Bataille N, Balladur P et al (1998) Surgical treatment of severe duodenal polyposis in familial adenomatous polyposis. Br J Surg 85:665–668
7. Rodriguez-Bigas MA, Vasen HFA, Pekka-Mecklin J et al (1997) Rectal cancer risk in hereditary nonpolyposis colorectal cancer after abdominal colectomy. Ann Surg 225:202–206
8. Solomon SD, McMurray JJV, Pfeffer MA et al (2005) Cardiovascular risk associated with celecoxib in a clinical trial for colorectal adenoma prevention. N Engl J Med 352:1071–1080
9. Syngal S, Weeks JC, Schrag D et al (1998) Benefits of colonoscopic surveillance and prophylactic colectomy in patients with hereditary nonpolyposis colorectal cancer mutations. Ann Intern Med 129:787–796
10. Vasen HFA, Buelow S, Myrhoj T et al (1997) Decision analysis in the management of duodenal adenomatosis in familial adenomatous polyposis. Gut 40:716–719
11. Wallace MH, Phillips RKS (1998) Upper gastrointestinal disease in patients with familial adenomatous polyposis. Br J Surg 85:742–750

9.2 Colon Cancer

KLAUS E. MATZEL, WEI ZHANG

9.2.1 Introduction

Colon cancer is common and usually presents with a history of altered bowel habit, rectal bleeding or anaemia. The onset and severity of symptoms depends on tumour location. Advanced disease at first presentation is not uncommon, as diagnosis of proximal tumours is difficult and often delayed. Outcome is most closely related to the extent of disease at presentation. Surgical resection is the primary treatment for any, also advanced stages; adjuvant chemotherapy improves outcome.

9.2.2 Anatomy

- Colonic tumours occur between the ileocaecal junction and the rectosigmoid junction (15 cm from the anal verge measured with rigid sigmoidoscopy).
- The colon is topographically divided into caecum, ascending colon, transverse colon, descending colon and sigmoid colon.
- The great majority of colon cancers are adenocarcinomas. Rare tumours, such as carcinoid tumours, leiomyosarcoma and haematopoietic and lymphoid neoplasm, are not included in this chapter (see Chap. 9.5)

9.2.3 Incidence

- Colorectal cancer is the second most common malignant tumour in developed countries with a lifetime incidence of approximately 2%.
- Colon cancer constitutes approximately two thirds of all large-bowel neoplasms.
- Within Europe the survival from colon cancer varies, being highest in western and northernmost countries.
- Colorectal cancer is the second most common cause of cancer death (after lung cancer) in the UK. In Germany in 1999, 57,000 patients developed colorectal cancer and there were 29,800 deaths.
- The risk for colorectal cancer is increased in certain groups (see below).

9.2.4 Aetiology/Epidemiology

The great majority (approximately 90%) of colon cancers are sporadic and only 5% are associated with a recognised familial pattern of inheritance. Several extrinsic factors are associated with an increased risk of developing colon cancer.

9.2.4.1 Extrinsic Factors

- The most important extrinsic factor is diet. There is evidence that a diet rich in vegetables is protective because of the presence of substances with anticarcinogenic properties, such as carotenoids, folate, phenols and flavonoids. Consumption of non-digestible fructo-oligosaccharides may selectively promote the growth and activity of potentially beneficial bacteria, such as *Bifidobacterium* and *Lactobacillus*. Diets high in starch, non-starch fibre and carotenoids possibly decrease risk.
- Physical activity, especially lifelong activity, is considered to decrease the risk of colon cancer.
- Obesity is associated with a doubled risk of colon cancer. The frequency of colonic polyps is higher with higher body mass index.
- High alcohol consumption potentially increases risk. Also, a synergistic effect of smoking and alcohol is assumed. Smoking early in life is likely to increase risk of colon cancer.
- Red meat (probably by facilitating the effect of fat on bile acid production and the formation of carcinogenic nitrosamine) and processed meat are thought to increase risk.
- The chronic use of aspirin and NSAIDs is associated with significant risk reduction in certain groups.

9.2.4.2 Genetic Factors

Familial Adenomatous Polyposis

- Familial adenomatous polyposis (FAP) is associated with mutation or loss of the FAP gene (also termed the adenomatous polyposis coli (APC) gene).
- The risk of developing colorectal cancer is nearly 100%.
- The onset of polyp disease is the second decade, and more than 100 polyps are characteristic.
- Extracolonic intestinal manifestations (approximately 75% of patients) include adenomas of the duodenum and the ampulla of Vater, both considered to be precancerous.
- Incidence of gastric adenoma is less than 10%.
- Extraintestinal manifestations include desmoid tumours, thyroid carcinoma, medulloblastoma, hepatoblastoma, osteoma, epidermoid cysts and pigment anomalies of the retina.

Attenuated Familial Adenomatous Polyposis

- Attenuated FAP (AAPC) typically presents with < 100 polyps and at an older age, often the fourth decade.
- Extracolonic manifestation can occur.
- AAPC is caused by a heterogeneous group of APC mutations and MYH mutation. Proof of microsatellite instability, APC and MYH can be helpful to differentiate from hereditary non-polyposis colorectal cancer (HNPCC).

Hereditary Non-polyposis Colorectal Cancer

- Hereditary non-polyposis colorectal cancer (HNPCC) syndrome is associated with germline mutations in six DNA mismatch repair genes (MLH1, MLH2, MSH2, MSH6, PMS1, PMS2). Almost 90% of the detected mutations are located in MSH2 and MLH1.
- Unlike FAP, clinical diagnosis is difficult because HNPCC does not present with a distinct phenotype. Thus, clinical criteria (Amsterdam/Bethesda; Tables 9.2.1–9.2.3) were defined for use as a screening tool for mutation. HNPCC is clinically diagnosed if the Amsterdam I criteria are met. The Amsterdam II criteria refer to extracolonic manifestations (endometrial, urothelial and small-bowel carcinoma).
- As many families today are small, a negative family history does not preclude HNPCC. The less-specific Bethesda criteria aim to determine the diagnosis in small families by clinical means.
- Microsatellite instability can be found in tumour tissue harvested in 80–90% of patients who fulfil the Amsterdam I/II criteria and in 30% of patients who fulfil the Bethesda criteria.
- General tumour risk in HNPCC is considered to be 80–90%, with colorectal cancer being the most common (at a median age of 44 years; very uncommon before age 25 years). The second most common cancer in HNPCC is endometrial carcinoma: lifetime risk is 40–60% at a median age of 46 years. Ovarian cancer occurs in 3–12%; gastric cancer, mostly intestinal tumour type, in 2–13%; small-bowel cancer in 1–4% (around one third in the duodenum).

Table 9.2.1 Amsterdam I criteria

1.	At least three relatives with histopathological verified colorectal cancer: one is a first-degree relative of the other two
2.	At least two successive generations affected
3.	At least one of the relatives with colorectal cancer diagnosed at less than 50 years of age
4.	Familial adenomatous polyposis has been excluded

Table 9.2.2 Amsterdam II criteria

1.	At least three relatives with an HNPCC-associated cancer (colorectal cancer, endometrial, stomach, ovary, ureter/renal pelvis, brain, small bowel, hepatobiliary tract and skin (sebaceous tumours)): one is a first-degree relative of the other two
2.	At least two successive generations affected
3.	At least one of the HNPCC-associated cancers should be diagnosed at less than 50 years of age
4.	Familial adenomatous polyposis should be excluded in any colorectal cancer cases
5.	Tumours should be verified whenever possible

Table 9.2.3 Bethesda guidelines for testing of colorectal tumours for microsatellite instability

1.	Individuals with cancer in families that meet the Amsterdam criteria
2.	Individuals with two HNPCC-related cancers, including synchronous and metachronous colorectal cancers or associated extracolonic manifestations[a]
3.	Individuals with colorectal cancer and a first-degree relative with colorectal cancer and/or HNPCC-related extracolonic cancer and/or a colorectal adenoma; one of the cancers diagnosed at age less than 45 years and the adenoma diagnosed at age less than 40 years
4.	Individuals with colorectal cancer or endometrial cancer diagnosed at age less than 45 years
5.	Individuals with right-sided colon cancer with an undifferentiated pattern (solid/cribriform) on histopathology diagnosed at age less than 45 years[b]
6.	Individuals with signet-ring-cell-type colorectal cancer diagnosed at age less than 45 years[c]
7.	Individuals with adenomas diagnosed at age less than 45 years

[a]Endometrial, ovarian, gastric, hepatobiliary or small-bowel cancer or transitional cell carcinoma of the renal pelvis or ureter

[b]Solid/cribriform defined as poorly differentiated or undifferentiated carcinoma composed of irregular, solid sheets of large eosinophilic cells and containing small gland-like spaces

[c]Composed of more than 50% signet-ring cells

Hamartomatous Polyposis Syndrome

- Peutz-Jeghers syndrome and juvenile polyposis coli (FJP) are rare hamartomatous polyposis syndromes.
- Peutz-Jeghers syndrome is an autosomal-dominant germline mutation of the STK11/LKB1 gene.
- The cumulative lifetime risk for malignant tumours reaches 90%; the risk for colorectal cancer is 39%, most commonly diagnosed at age 30–50 years.

Chronic Inflammatory Bowel Disease

- Colorectal cancer risk is increased in ulcerative colitis (UC) and is dependent on manifestation, extent and duration of the disease.
- The cumulative risk to develop cancer in pancolitis is 2% after 10 years, 9% after 20 years and 18% after 30 years.
- Crohn's disease is also associated with an increased risk for colorectal and small-bowel cancer, although it is less well defined; a 3.5- to 7-fold increase is suggested.

9.2.5 Diagnosis

Colorectal cancer is diagnosed either as a result of a screening programme or when a patient becomes symptomatic. Early colorectal cancer is often asymptomatic (especially if located in the right hemicolon) or presents with non-specific symptoms; thus, screening programmes for early detection are of major importance. Since the late 1950s a gradual shift towards right-sided or proximal colon cancers has been observed.

9.2.5.1 Screening in the Healthy Population

- For prevention of colorectal cancer, screening is proposed for the healthy population, aiming for detection and removal of precancerous lesions to address the 90% of sporadic colorectal cancers occurring above the age of 50 years. Two screening strategies are currently of clinical importance: faecal occult blood test (FOBT) and colonoscopy.
- The sensitivity of the FOBT for confirmed colorectal cancer is 50% and for polyps around 10%. The predictive value of a positive test averages 10% for cancer. The efficacy of FOBT has been shown in three major randomised trials in which colorectal cancer mortality was reduced by 15–33% (average reduction 23%). Annual testing was more advantageous than biennial testing. Patient compliance is often unsatisfactory.
- Flexible sigmoidoscopy and colonoscopy are the best methods for detecting colonic neoplasms for confirmation by biopsy. Sensitivity and specificity are highest for colonoscopy. Two case-control studies have demonstrated a reduction in colorectal cancer incidence of 66–90%. A 10-year interval is appropriate if findings on colonoscopy are negative.
- The protective effect of sigmoidoscopy for distal neoplasms seems to last 6–10 years. However, recently a

0.8% detection rate was found for distal adenomas or carcinoma 3 years after sigmoidoscopy without pathological findings.

- The Advisory Committee on Cancer Prevention in the European Union has suggested that screening programmes for colorectal cancer should use the FOBT. Colonoscopy should be used for follow-up of positive findings. Screening should be offered to men and women age 50 to approximately 74 years, with an interval of 1–2 years.
- Immunological and molecular screening methods cannot as yet be considered reliable and are not recommended. However, preliminary results are encouraging.

9.2.5.2 Screening in Populations at Increased Risk

- Persons with increased risk for colorectal cancer due to certain predispositions comprise the following three groups:
  - Increased family risk (genetic background unknown)
  - Proven or potential risk of hereditary colorectal cancer
  - Presence of chronic inflammatory bowel disease
- Family history of colorectal cancer or adenomatous polyps: Advise screening colonoscopy beginning at age 40 years or 10 years younger than the earliest diagnosis in the family; repeat at 5-year intervals. This protocol should be followed in:
  - Persons with a first-degree relative (parent, sibling or child) with colon cancer or adenomatous polyps diagnosed at age ≤ 60 years
  - Persons with two first-degree relatives diagnosed with colorectal cancer at any age

These screening recommendations must be considered provisional, however, as mortality-reduction studies are not yet available.

- Familial adenomatous polyposis (FAP): Colorectal cancer mortality is lower in patients with FAP who have been screened than in those who present with symptoms. Genetic testing should be performed at age 10 years; if a genetic mutation can be excluded, no further special screening is required. Annual colonoscopy from age 10–12 years should be advised in:
  - Persons with a genetic diagnosis of FAP
  - Persons with a risk of FAP in whom genetic testing has not been performed and/or a mutation cannot be excluded
- Attenuated FAP (AAPC): In patients with attenuated FAP, treatment should be based on age, number of polyps and histopathological findings. Colonoscopy should be performed annually throughout the patient's life if colectomy is not indicated. In persons from a family with attenuated FAP, the first colonoscopy should be at age 15 years; if without findings, the next colonoscopy is indicated in 5 years.
- Hereditary non-polyposis colorectal cancer (HNPCC): Colonoscopy can reduce of risk and mortality from colorectal cancer in families fulfilling the Amsterdam criteria. Genetic testing for HNPCC should be offered to first-degree relatives of persons with a known inherited mismatch repair (MMR) gene mutation. Yearly or biennial colonoscopy should start at age 20–25 years or 10 years earlier than the youngest age of colorectal cancer in the family in persons with a genetic or clinical diagnosis of HNPCC.
- History of adenomatous polyps (see Chap. 8.1).
- History of colorectal cancer: If synchronous neoplasm is excluded at the time of resection with curative intent, subsequent colonoscopy should be performed at 2 and 5 years after surgery and 5 yearly thereafter.
- Inflammatory bowel disease: Colonoscopy with systematic four quadrant biopsies at 10-cm intervals should be performed in patients with ulcerative colitis presenting as long-standing pancolitis (> 8 years) or left-sided inflammatory colitis (> 15 years). If intraepithelial neoplasia is detected and confirmed, colectomy is indicated. For patients with Crohn's disease, no general recommendation can be given.
- There are no randomised controlled trials of surveillance colonoscopy in patients with ulcerative colitis or Crohn's colitis. A case-control study has found better survival in ulcerative colitis patients in surveillance programmes.

9.2.5.3 Symptoms

- **The majority of patients present with alteration in bowel habit, frank rectal bleeding or anaemia due to occult bleeding.**
- Symptoms such as intermittent abdominal pain, nausea or vomiting are often secondary to partial obstruction or peritoneal dissemination.
- **Patients may occasionally notice a palpable mass**. This is more common in right-sided colon cancer.
- Intestinal obstruction is most commonly associated with cancer of the sigmoid colon. This may lead to acute colonic perforation if the ileocaecal valve is competent. If the valve is incompetent, presentation is less dramatic, with increasing constipation and abdominal distension noticed over many days.
- Perforation of colon cancer may be acute or chronic. Perforation may be at the site of the tumour or more

proximal in a distended colon. Perforation may occur into the retroperitoneum, bladder or genital tract with fistula formation.

9.2.5.4 Diagnostic Strategies

- Diagnosis is established by colonoscopy and biopsy.
- The precise location of the neoplasm must be documented and the base of any suspicious polyp tattooed at the time of snare excision.
- Careful clinical examination for regional lymphatic and distant metastatic disease should be performed.
- To exclude synchronous malignancies, the entire large bowel should be examined if the lumen is not obstructed.
- If colonoscopy is not possible or complementary information is required, x-ray with water-soluble contrast (if risk of perforation) or barium contrast filling of the colon or computed tomography (CT) colonography is mandatory.

9.2.6 Differential Diagnosis

The most common differential diagnoses are:
- Diverticular disease with stenosis or phlegmon
- Inflammatory bowel disease
- Colonic ischaemia
- Infection
- Other malignancies

9.2.7 Staging

Clinical staging aims to determine the local and distant extent of the disease according to the clinical segment of the TNM system (see Chap. 9.5). Staging requires local assessment of the tumour and screening for metastatic disease. The clinical classification, cTNM, is the basis for clinical decision-making and determines the therapeutic algorithm.

Clinical staging:
- History, including family history (see Amsterdam, Bethesda criteria).
- Physical examination.
- Colonoscopy.
- Chest radiography.
- CT scan abdomen and pelvis.
- Serum carcinoembryonic antigen (CEA): elevated CEA levels that do not normalise after surgical resection imply persistent disease and the need for further evaluation. For follow-up: a postoperative rise in CEA indicates a potential recurrence.
- Liver chemistry.
- Positron emission tomography (PET) is indicated for the following:
  - Candidates for resection of isolated colorectal cancer metastases
  - Restaging of possible recurrence or metastatic disease

9.2.8 Treatment

Primary treatment of colon cancer is surgical resection of the primary tumour and lymph nodes. Open and laparoscopic approaches appear to be equally safe in experienced hands. The term curative resection (R0) should be based on histological confirmation of complete excision without residual tumour.

9.2.8.1 Curative Intent

Operative Intervention

Operative intervention aims to achieve a curative resection. If adjacent organs are involved, en bloc resection is indicated. In colon cancer (unlike rectal cancer), the need for a radical approach has not been proved in prospective randomised trials. However, based on histopathological findings, prospective observational studies, and theoretical concepts, the resection of colon cancer should adhere to the following principles of radicality:
- A 2-cm safety margin is sufficient with regard to microscopic tumour spread, but insufficient for lymphatic spread (as regional lymph drainage exceeds this distance).
- Lymph node metastases travel along the vascular supply, primarily with the paracolic supply, up to 10 cm from the macroscopic edge of the primary tumour. Thus, at least 10 cm of the colon should be removed if vascular division is radicular.
- The extent of the resection is determined by the vascular supply and the consequently defined area of lymphatic drainage. In principle, if the tumour is located between two major vessels, both should be divided centrally (Figs. 9.2.1–9.2.5).

Special Considerations
- Multiple colon cancers: Total colectomy is not mandatory. The extent of the resection should follow the principles of radicality as described above. However,

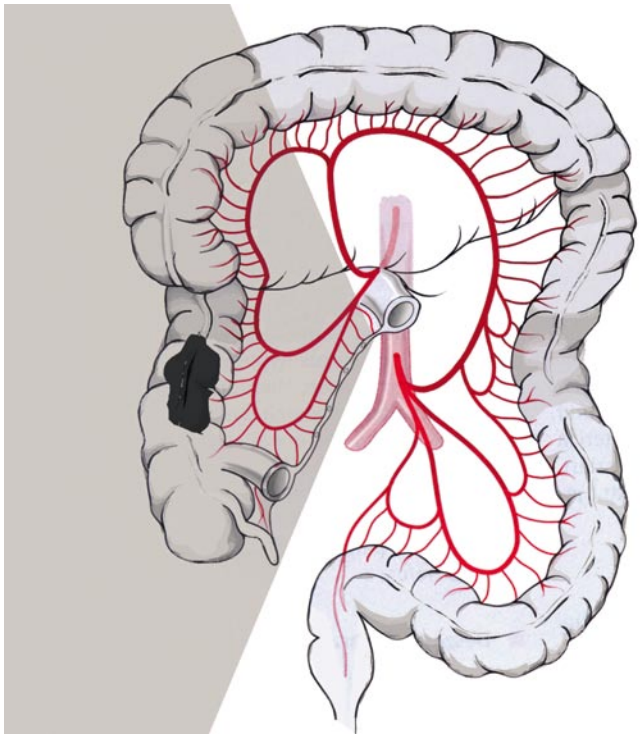


Fig. 9.2.1 Cancer: ascending colon. Right-sided hemicolectomy with central ligation of the ileocolic artery and the right colonic artery

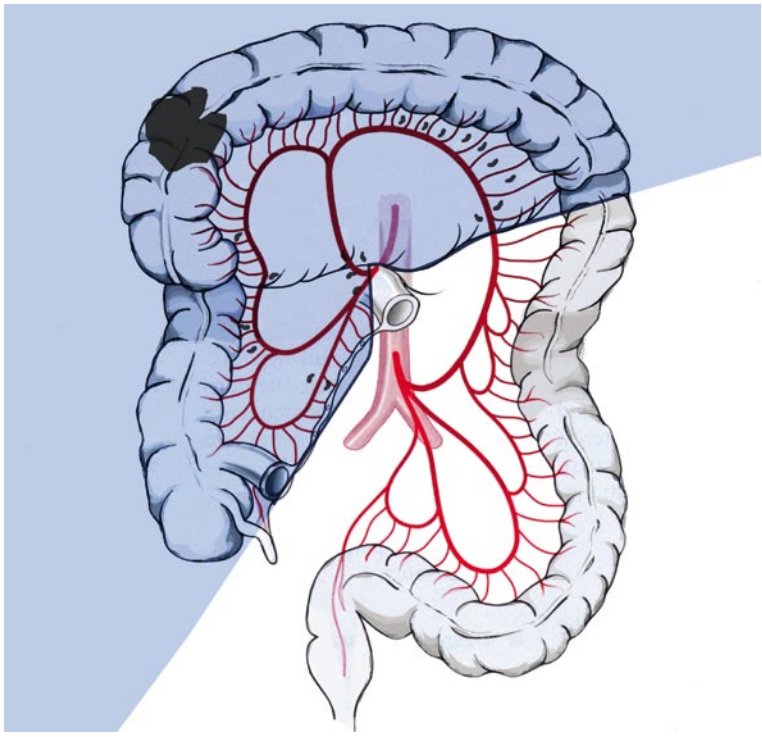


Fig. 9.2.2 Cancer: hepatic flexure. Extended right hemicolectomy with central ligation of the ileocolic, right colonic and middle colic arteries

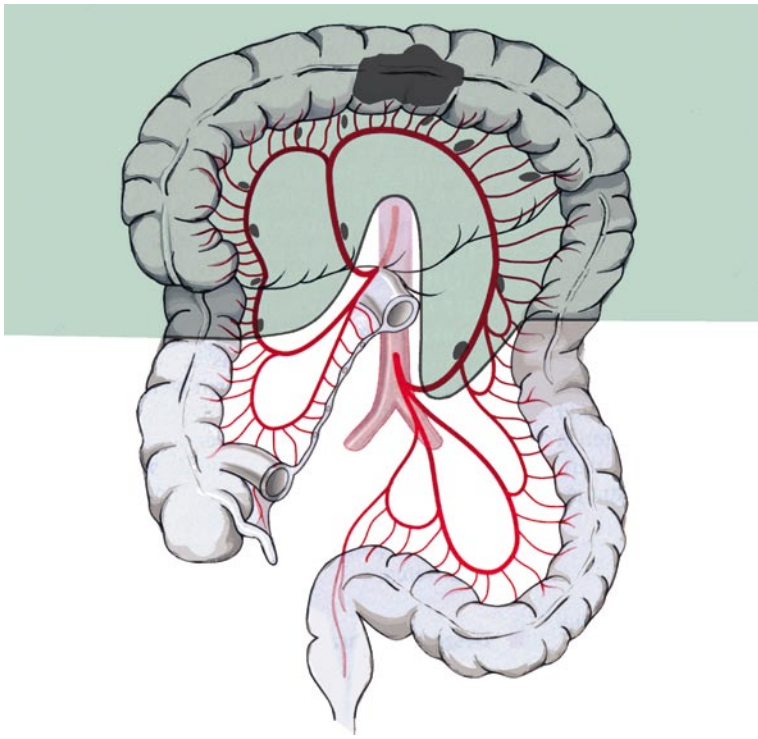


Fig. 9.2.3 Cancer: transverse colonic. Transverse colon resection with central ligation of the middle and left colonic arteries

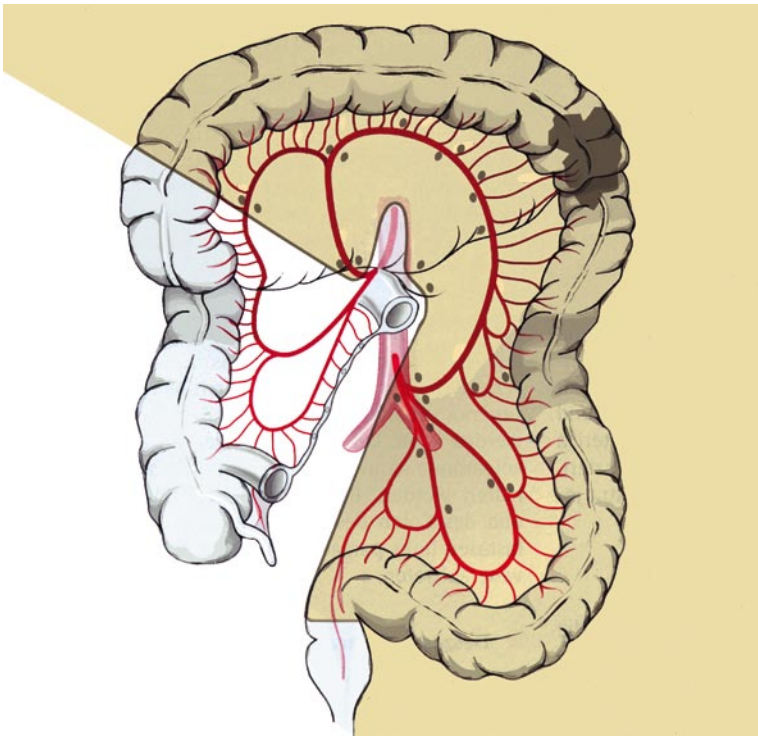


Fig. 9.2.4 Cancer: splenic flexure. Extended left hemicolectomy with central ligation of middle colic and inferior mesenteric arteries

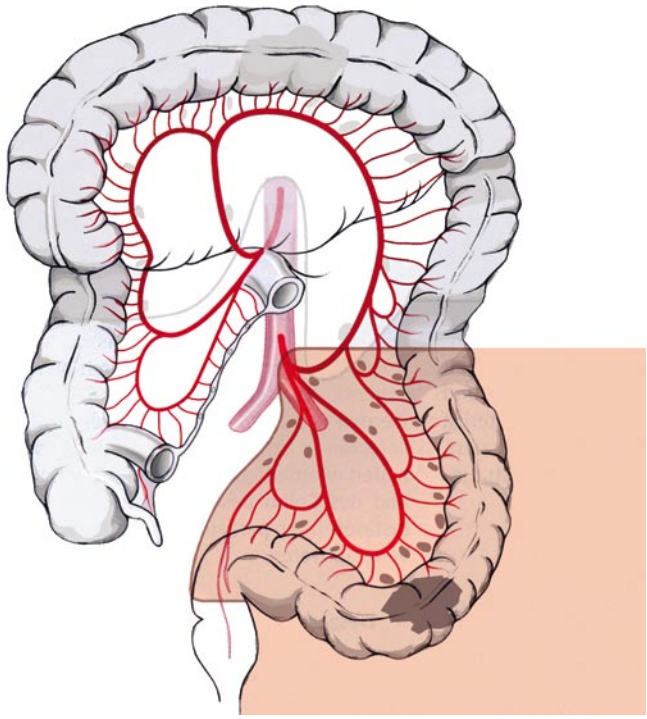


Fig. 9.2.5 Cancer: sigmoid. Sigmoid resection with central ligation of the inferior mesenteric artery

many would advocate subtotal colectomy and ileorectal anastomosis.

- Synchronous distant metastases: can be resected at the same time or later.
- Emergency operation: If possible, a radical procedure should be performed. In the case of obstruction, intraluminal stenting can be used for bridging if technically feasible. If perforation is excluded, obstruction can be considered urgent, not emergent, unless the ileocaecal valve is competent and the caecum is at risk of perforation.
- Cancer in FAP: A radical procedure should be attempted by restorative proctocolectomy. If complete resection (R0) is not achievable, limited procedures can be considered. In cases with an insufficient anal sphincter, stoma creation can be advised. Lifelong surveillance is mandatory if a subtotal colectomy with ileorectal anastomosis is feasible. The patient must be counselled accordingly.
- Cancer in attenuated FAP with limited manifestation in the rectum: Subtotal colectomy with ileorectal anastomosis is acceptable.
- Cancer in HNPCC: Oncological resection may be performed as in sporadic colonic cancer, however prophylactic subtotal colectomy may be considered in patients known to have a genetic mutation.
- Cancer in ulcerative colitis: Restorative proctocolectomy is indicated if anal sphincter function is adequate.

Local/Limited Procedures

A local procedure for colon cancer can only be considered oncologically adequate if, after full-thickness complete resection (R0), tumour stage is confined to pT1, grade is good or moderate (G1–2), no lymphatic (L0) or vascular invasion (V0) has occurred and the tumour diameter is less than 3 cm.

Postoperative Histopathological Evaluation/ Histopathological Reporting

The following histopathological findings of the specimen are necessary to ensure adequate classification of tumour stage:

- Location of the primary tumour
- Type of tumour
- Level of invasion (pT)
- Status of local lymph nodes (pN)
- Number of examined lymph nodes (≥ 12 recommended)
- Number of lymph nodes with tumour
- Grading

- Distance of resection margins
- Completeness of tumour removal (R)
- Invasion of lymphatic and vascular tract (L, V)
- Microsatellite instability (in HNPCC)

Adjuvant Therapy

The prerequisite for adjuvant therapy is complete removal of the primary (R0). The indication is based on histopathological staging, especially nodal status (pTN), determined by examination of at least 12 lymph nodes. Positive immunocytological findings of isolated tumour cells and positive cytological findings from peritoneal lavage are not considered indications.

Contraindications for adjuvant therapy in colon cancer:

- Incomplete removal of the primary (R1/2) local/distal
- UICC stage I
- UICC stage II, if possible only in randomised clinical trials
- Poor performance status
- Liver cirrhosis Child B and C
- Cardiac insufficiency (NYHA III; IV)
- Preterminal and terminal renal failure
- Reduced bone marrow function
- Inability to participate in follow-up

Neoadjuvant chemotherapy, radiotherapy and radiochemotherapy are not indicated in colon cancer.

Adjuvant Chemotherapy

For patients with stage III colon cancer (R0), adjuvant chemotherapy is advised. Several randomised clinical trials have demonstrated a significant reduction in recurrence and improved overall survival after 5-fluorouracil (5-FU) and folinic acid-based adjuvant therapy. Recent developments have shown that 5-FU/folinic acid and oxaliplatin (FOLFOX regimen) further improves disease-free survival.

For patients with stage II colon cancer (R0), adjuvant chemotherapy is not indicated. It can be considered in settings implying increased risk, such as T4 tumours, tumour perforation/incision, extramural vascular invasion and emergency cases.

The following regimens are commonly used:

- **Mayo regimen:** 20 mg/m² folinic acid (i.v.) plus 425 mg/m² 5-FU (i.v. < 5 min) at days 1–5 in weeks 1, 4 and 8; 3 additional cycles at 5-week intervals thereafter
- **NSABP regimen:** 500 mg/m² folinic acid (2-h infusion) once a week for 6 weeks followed by 500 mg/m² 5-FU (1-h infusion) every 8 weeks; a total of 4 cycles
- **LV5FU2 + Oxaliplatin** (FOLFOX) (MOSAIC TRIAL): 200 mg/m² folinic acid (2-h infusion, days 1 and 2) plus 5-FU (400 mg/m² bolus followed by 600 mg/m² (22-h infusion, days 1 and 2) plus 85 mg/m² oxaliplatin (2-h, day 1); one cycle every 2 weeks for a total of 12 cycles

9.2.8.2 Palliative Treatment

Depending on the individual situation, various modes are used for palliative treatment, e.g. surgery, endoscopic interventions, radiotherapy, chemotherapy and interventional radiology. Surgery should be attempted even with palliative intent to minimise the risk of the primary tumour and its complications, such as stenosis, bleeding and tumour infiltration of adjacent organs. If not indicated, bowel passage can be re-established by local treatment, bypass procedures or stoma creation.

If the tumour is not resectable, 5-FU/folinic acid-based chemotherapy with palliative intent is indicated: irinotecan/5-FU/folinic acid infusions, oxaliplatin/5-FU/folinic acid infusions, 5-FU/folinic acid infusion or bolus are considered standard regimens. Less toxic capecitabine and UFT/5FA can be used as an alternative to the 5-FU/folinic acid infusion in first-line treatment. Second-line treatment after 5-FU/folinic acid is monotherapy with irinotecan, after irinotecan/5-FU/folinic acid or oxaliplatin/5-FU/folinic acid. Recently vascular endothelial growth factor (VEGF)-receptor antagonist and epidermal growth factor (EGF)-receptor antagonist are under investigation for palliative treatment of colorectal cancer.

9.2.8.3 Special Considerations: Metastases and Local Recurrence

- Patients with resectable metastases of the liver or lung should undergo primary resection. PET should be considered as upstaging of disease has been shown in 30% of patients. Patients presenting with liver metastases not amenable to radical resection should be treated with systemic chemotherapy. The role of interventional procedures needs to be defined.
- Isolated bone metastases with pain should be treated with local radiation: single high-dose application seems to be equivalent to fractioned radiation.
- In local recurrence the reintervention aims for radicality. If an R0 resection is not achievable, reintervention aims for symptom relief and avoidance of complications, such as stenosis, bleeding, obstruction and ileus.

9.2.8.4 Current Treatment Recommendations

- The mainstay of therapy is surgery with curative intent: colon resection with lymphadenectomy (guided by the vascular supply).
- Histopathological evaluation should include at least 12 lymph nodes.
- Adjuvant chemotherapy is indicated in stage UICC III.

9.2.9 Follow-up

The follow-up regimen should be adapted to tumour stage. In UICC I after R0 resection, the risk of recurrence is low. Colonoscopy in years 2 and 5 serves for early detection of secondary tumours. The regimen should be modified in cases of increased risk of recurrence (e.g. G3/4, L+,V+, tumour perforation) and should include regular follow-up with CEA levels every 6 months (up to year 5), ultrasound or CT of the abdomen and pelvis every 6 months for 2 years and chest X-ray every year.

In patients with HNPCC after hemicolectomy, colonoscopy is indicated every year if adenomas were present; after subtotal colectomy, sigmoidoscopy is advised every second year. In patients after colectomy with ileal pouch–anal reconstruction, pouchoscopy is indicated yearly and duodenogastroscopy every 3 years (every year in patients with adenomas).

Suggested Reading

1. ACCP. Advisory Committee on Cancer Prevention (2000) Recommendations on cancer screening in the European union. Eur J Cancer 36:1473–1478
2. Andre T, Boni C, Mounedji-Boudiaf L et al (2004) Oxaliplatin, fluorouracil, and leucovorin as adjuvant treatment for colon cancer. N Engl J Med 350:2343–2351
3. Bingham SA, Day NE, Luben R, Ferrari P, Slimani N, Norat T et al (2003) Dietary fibre in food and protection against colorectal cancer in the European Prospective Investigation into Cancer and Nutrition (EPIC): an observational study. Lancet 361:1496–1501
4. Figueras J, Valls C, Rafecas A et al (2001) Resection rate and effect of postoperative chemotherapy on survival after surgery for colorectal liver metastases. Br J Surg 88:980–985
5. Gatta G, Capocaccia R, Berrino F, EUROPREVAL Working Group (2004) Prevalence of colon cancer and estimation of variation of care needs of colon cancer patients. Ann Oncol 15:1136–1142
6. Heiskanen I, Luostarinen T, Jarvinen HJ (2000) Impact of screening examinations on survival in familial adenomatous polyposis. Scand J Gastroenterol 35:1284–1287
7. Imperiale TF, Wagner DR, Lin CY, Larkin GN, Rogge JD, Ransohoff DF (2002) Results of screening colonoscopy among persons 40 to 49 years of age. N Engl J Med 346:1781–1785
8. Jarvinen HJ, Aarnio M, Mustonen H, Aktan-Collan K, Aaltonen LA, Peltomaki P et al (2000) Controlled 15-year trial on screening for colorectal cancer in families with hereditary nonpolyposis colorectal cancer. Gastroenterology 118:829–834
9. Mandel JS, Church TR, Ederer F, Bond JH (1999) Colorectal cancer mortality: effectiveness of biennial screening for fecal occult blood. J Natl Cancer Inst 91:434–437
10. Petersen VC, Baxter KJ, Love SB, Shepherd NA (2002) Identification of objective pathological prognostic determinants and models of prognosis in Dukes' B colon cancer. Gut 51:65–69
11. Sargent DJ, Goldberg RM, Jacobson SD et al (2001) A pooled analysis of adjuvant chemotherapy for resected colon cancer in elderly patients. N Engl J Med 345:1091–1097
12. Schoemaker D, Black R, Giles L, Toouli J (1998) Yearly colonoscopy, liver CT, and chest radiography do not influence 5-year survival of colorectal cancer patients. Gastroenterology 114:7–14
13. Thorn M, Bergstrom R, Kressner U et al (1998) Trends in colorectal cancer incidence in Sweden 1959-93 by gender, localization, time period, and birth cohort. Cancer Causes Control 9:145–152
14. Towler B, Irwig L, Glasziou P et al () A systematic review of the effects of screening for colorectal cancer using the faecal occult blood test, hemoccult. BMJ 317:559–565
15. Umar A, Boland CR, Terdiman JP et al (2004) Revised Bethesda Guidelines for hereditary nonpolyposis colorectal cancer (Lynch syndrome) and microsatellite instability. J Natl Cancer Inst 96:261–268
16. Winawer S, Fletcher R, Rex D, Bond J, Burt R, Ferrucci J et al (2003) Colorectal cancer screening and surveillance: clinical guidelines and rationale-update based on new evidence. Gastroenterology 124:544–560

9.3 Rectal Cancer

LARS PÅHLMAN

9.3.1 Introduction

Rectal cancer is a common disease that frequently presents with rectal bleeding and altered bowel function. Unfortunately, patients often seek medical advice late in the disease process in the mistaken belief that the symptoms are due to haemorrhoidal disease. Since the late 1980s surgery for rectal cancer of the middle and lower thirds has evolved to a precise surgical technique that requires accurate mesorectal dissection and total mesorectal excision (TME) for cancer. In addition, there have been considerable advances in adjuvant therapies including preoperative radiotherapy and chemoradiotherapy.

9.3.2 Anatomy

- The rectum is defined surgically as the distal 15 cm of the large bowel as measured with a rigid sigmoidoscope. Only tumours arising from adenomatous mucosa of the rectum are considered as rectal cancer.
- Radiologically, the rectum extends from the anorectal ring to the sacral promontory as measured on a lateral radiograph.

9.3.3 Incidence

- Rectal cancer is common, constituting approximately one third of all large bowel neoplasms.
- The incidence is 15–25 per 100,000 population in European countries.
- The average age of onset is in the seventh decade.
- The incidence is higher among men.

9.3.4 Classification

- The predominant tumour type is adenocarcinoma (95–98%).
- Rare tumours include squamous carcinoma, neuroendocrine tumours, sarcoma, lymphoma and malignant melanoma.

9.3.5 Aetiology/Epidemiology

- Aetiology for rectal cancer is similar to that of colon cancer.
- A diet high in polyunsaturated fats increases biliary secretion of cholesterol that in turn is converted by normal bacterial flora within the bowel to potential carcinogens.
- A high-fibre diet may be protective by reducing bowel transit time, diluting faecal matter and thus exposure of the colonic mucosa to carcinogens.
- Recent data support the hypothesis that the incidence of colorectal cancer can be reduced with aspirin, calcium and an increased intake of antioxidants.
- In common with carcinoma of the colon, most rectal cancers are thought to follow the adenoma-carcinoma sequence and slowly progress from a benign tubular or tubulovillous adenoma to villous adenoma with dysplasia eventually becoming invasive adenocarcinoma.
- Patients with familial adenomatous polyposis, hereditary non-polyposis colon cancer and inflammatory bowel disease are at increased risk of developing rectal cancer.
- Previous irradiation to the pelvis is known to increase the incidence of rectal cancer.

9.3.6 Symptoms

- The most common presenting symptoms in rectal cancer are altered bowel habit, tenesmus (a feeling of incomplete evacuation) together with mucus discharge and fresh rectal bleeding.
- Rarely complete rectal cancer may present with large bowel obstruction or profuse rectal bleeding.

9.3.7 Diagnosis

- Diagnosis is usually established with digital anorectal examination, sigmoidoscopy and biopsy.
- At diagnosis it is important to document the exact location of the tumour from the anal verge including an evaluation of the circumferential extent, tumour fixity and possible extension to surrounding organs.
- A complete examination, endoscopic or radiological, of the large bowel should be undertaken to identify synchronous significant adenomas (approximately 8%) and cancer (approximately 2%).

9.3.8 Differential Diagnosis

The differential diagnosis of rectal cancer includes almost all common proctological conditions, particularly haemorrhoids, anal fissure, solitary rectal ulcer, benign polyps, rectal prolapse and inflammatory bowel disease. In addition it is important to distinguish carcinoma of the anal canal.

9.3.9 Staging

- All patients must be evaluated with a digital examination. This may require examination under anaesthesia for reasons of patient comfort or to establish exact tumour location and/or fixity (Fig. 9.3.1).
- For mobile tumours in which local excision is considered, endorectal ultrasonographic examination should be performed.
- Larger tumours, or those staged by endorectal ultrasound as T3 or higher, require magnetic resonance imaging (MRI) of the pelvis to identify those in whom neoadjuvant radiotherapy could be considered.
- Positron emission tomography (PET) scanning has a role in defining suspected metastatic disease.

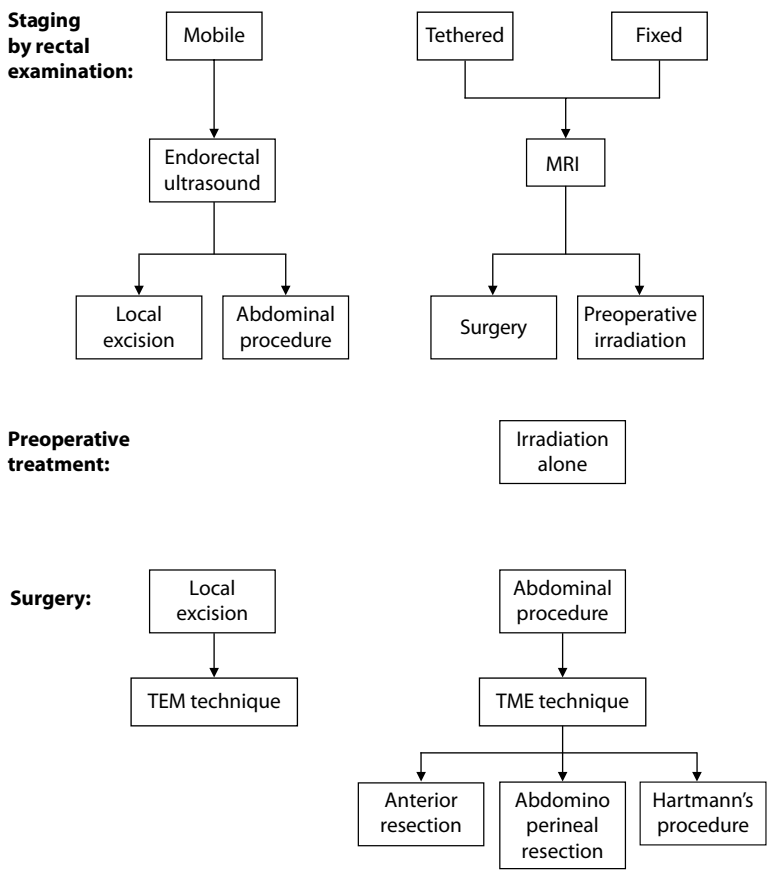


Fig. 9.3.1 Treatment algorithm for rectal cancer

9.3.10 Treatment

Before any form of treatment of a rectal cancer tumour is undertaken a multidisciplinary discussion should take place to include surgeons, medical and radiation oncologists, radiologists and pathologists. Although, surgery is the most important component of treatment, treatment must be based on the results of local staging and screening for distant metastases. Thus, treatment may include surgery alone, preoperative radiotherapy followed by surgery or preoperative chemoradiotherapy followed by surgery. Patients with metastases may require palliation only or chemotherapy. In a subset of patients chemotherapy may downstage metastatic disease and allow later surgical intervention with curative intent.

9.3.10.1 Surgery Alone, T1 Tumours

- In patients with a T1 tumour, local excision could be considered as a curative procedure.
- If the tumour is situated in the lower third of the rectum transanal excision is appropriate.
- In situations where the tumour is situated in middle or upper third of the rectum, transanal endoscopic microsurgical excision (TEM) is more appropriate.
- The advantage of local excision is the possibility of having a full thickness specimen for histopathological examination.
- Endocavity radiotherapy has also been used to treat T1 rectal cancer, however, a major disadvantage is the absence of a specimen for histopathological examination Endocavity radiotherapy is only used in a few centres in Europe.

9.3.10.2 Surgery Alone, T2–3 Tumours

- In patients with a T2–3 tumour considered not to be at risk of circumferential margin involvement, based on preoperative MRI examination and multidisciplinary review, an abdominal procedure without preoperative radiotherapy is sufficient.
- Based on the level of the tumour, either an abdominal perineal excision or an anterior resection is performed (see below).
- In patients with impaired faecal continence due to anal sphincter dysfunction, a Hartmann's procedure may be considered for tumour in the upper or middle thirds of the rectum.

9.3.10.3 Preoperative Radiotherapy and Surgery, T3 Tumours

- Patients with a T3N0–2 tumour with predicted involvement of the circumferential margin are at high risk of developing a local recurrence.
- Preoperative radiotherapy followed by surgery is the treatment of choice.
- Based on the size of the tumour and the level from the anal verge, abdominal perineal excision, anterior resection or Hartmann's procedure should be used.

9.3.10.4 Preoperative Chemoradiotherapy and Surgery, T3–4 Tumours

- In patients with a T3–4N0–2 tumour extending to the perirectal fascia or infiltrating surrounding organs or with lymph node metastases close to the circumferential margin, preoperative chemoradiotherapy followed by delayed surgery is the recommended treatment.
- Again, based on the size of the tumour, quality of anal sphincter function and the position of the tumour in the rectum, an abdominal perineal excision, anterior resection or Hartmann's procedure may be performed.
- Sometimes, if the tumour is growing anteriorly into the prostate or bladder in male patients or vagina, uterus and bladder in female patients, a pelvic exenteration could be considered provided an R0 resection can be performed and no distant metastases are present.

9.3.10.5 Radiotherapy

There is strong evidence that preoperative radiotherapy in rectal cancer is superior to postoperative radiotherapy. Short-course radiotherapy (5×5 Gy during 1 week) followed by surgery the next week has been used in many trials and shown a decreased local recurrence rate and a prolonged survival. Conventional radiotherapy (25×2 Gy during 5 weeks) with delayed surgery has also been used with similar good results. Both these treatment options can be used if radiotherapy alone is considered. The value of adding chemotherapy to radiotherapy in patients with T3 tumours is questionable and there is, so far, no strong evidence supporting this combination.

9.3.10.6 Chemoradiotherapy

There are, as yet, no randomised data regarding survival to favour chemoradiotherapy over radiotherapy alone in patients with T3 tumours. In T4 tumours, however, al-

though the evidence is not clear-cut in favour of neoadjuvant chemoradiotherapy, this option has been widely introduced on an empiric basis to achieve downsizing, thus rendering the tumour resectable.

As many as 20–25% of all patients treated with modern chemoradiation will have a complete response. The completeness of response is difficult to evaluate. An expectant approach may be adopted with a policy of salvage surgery for recurrence or, based on the pretreatment staging, submit all patients for resection following neoadjuvant therapy. No randomised data are available but institutional data support a wait-and-see policy.

9.3.10.7 Preoperative Chemoradiotherapy and Sphincter Preservation

It has been claimed that preoperative chemoradiotherapy will increase the number of patients in whom the anal sphincters can be preserved. However, based upon five randomised trials, there is no strong evidence to support the hypothesis that preoperative chemoradiotherapy increases the number of patients in whom the anal sphincter mechanism can be preserved. This remains a contentious issue as the accepted minimum "safe" distal margin for resection has reduced dramatically since the late 1980s from 5 cm to less than 1 cm.

9.3.10.8 Surgical Technique (Total Mesorectal Excision)

- There is considerable evidence, although no randomised prospective data, to support the use of the total mesorectal excision (TME) technique in surgical excision of rectal cancer. Using this technique a precise excision of the tumour-bearing rectum and mesorectum is carried out following the anatomical fascial planes that enclose the rectum and mesorectum. In tumours situated in the upper third of the rectum, it is not necessary to do a complete mesorectal excision. If it is technical feasible, a 5-cm distal margin is accepted, provided that the mesorectum is divided 5 cm below the edge of the tumour. In mid and low rectal cancers a TME is recommended following the rectal fascia and fascia of Denonvilliers down to the pelvic floor, where the rectum is divided just on the top of the anal canal and an anastomosis is created.
- Training in the TME technique has been proven to be beneficial.
- If an abdominal perineal excision is carried out, it is important to avoid a coning effect created by following the mesorectal dissection along the upper surface of the levator ani muscle to the level of the puborectalis muscle. It is, therefore, important to finish the abdominal and pelvic dissection at the level of the levator ani muscle and complete the dissection in a cylindrical excision of the rectum and puborectalis muscle performed transperineally. This is facilitated by turning the patient into a prone jack-knife position for completion of the resection.
- If a sphincter-preserving procedure is carried out with an anastomosis to the top of the anal canal, there are convincing data to support construction of a neorectal reservoir using a colonic pouch, coloplasty or side-to-end anastomosis. Doing so improves defaecatory function and quality of life.

9.3.10.9 Chemotherapy

- Chemotherapy in the treatment of rectal cancer can be used to enhance radiotherapy with a synergistic effect or cell kill. There are data from phase II trials to indicate that patients with a T4 tumour who have received chemoradiotherapy have a better outcome compared to those with who received radiotherapy alone, however, randomised data are as yet lacking. The results with modern chemotherapy (irinotecan, oxaliplatin and capecitabine) are promising, and complete tumour response up to 15% and resectability up to 70% has been reported.
- Chemotherapy may also be used with radiotherapy in patients with T2–3 tumours to achieve tumour downsizing, increase resectability and possibly anal sphincter preservation. As yet, as many as 6 trials have not confirmed the value of chemoradiotherapy in increasing the rate of anal sphincter preservation and toxicity may be increased.
- Chemotherapy may be used following surgery in patients who have received neoadjuvant chemoradiotherapy or in conjunction with postoperative radiotherapy in patients with pT3–4 or pN1–2 disease who have not had neoadjuvant therapy. This is currently widely practiced in North America. However, the recently published German multicentre randomised trial has shown clear advantages for neoadjuvant over postoperative chemoradiotherapy in terms of morbidity and local recurrence rates, with equivalent survival outcomes. There have been two trials that have shown no survival benefit for adjuvant chemotherapy in patients with rectal cancer, however, based on data for stage III colon cancer, patients with stage III rectal cancer often receive chemotherapy despite the lack of solid evidence.

9.3.10.10 Current Treatment and Recommendations

Stage I and II disease without a predicted compromised circumferential margin based on preoperative staging with MRI:

- Surgery alone is sufficient in terms of local recurrence rate and overall survival.

Stage II and III disease with a predicted threatened circumferential margin based on preoperative MRI:

- Neoadjuvant radiotherapy (short-course or conventional course) is sufficient together with optimised surgery.

Stage II and III with a predicted involved circumferential margin or T4 disease based on MRI:

- Neoadjuvant chemoradiotherapy followed by delayed surgery is advocated.

9.3.11 Follow-up

- The majority of metastatic or local recurrences following resection of rectal cancer occur within 2–3 years of surgery.
- The most common sites for recurrence are liver and lung.
- Provided that surgery has been done in an optimised way with appropriate addition of radiotherapy, the local recurrence rate should not exceed 5%, but the rate of distant metastasis is approximately 30%. Therefore, a follow-up programme based on screening for metastatic disease is appropriate.
- There are no data about how often the liver and lung should be screened but computed tomography (CT) imaging every 6–12 months for 2 years in the postoperative period is probably sufficient. However, more frequent outpatient review of bowel function and stoma care is appropriate, particularly in the first postoperative year.
- Colonoscopy to prevent metachronous colonic neoplasia should be undertaken. The optimum frequency is unknown, however full colonoscopy at 2 and 5 years postoperatively and then every 5 years is reasonable.

9.3.12 Complications

9.3.12.1 Complications of Surgery

Rectal cancer surgery is an advanced procedure associated with many complications. Data from population-based registries indicate that up to 35% of all patients will suffer some form of complication, such as an anastomotic leakage, wound dehiscence or infection (approximately 25%). Up to 10% of all patients with a low anterior resection will have an anastomotic leak requiring reoperation. Other serious morbidities include cardiac (5%) and respiratory or urinary sepsis (5%). In large series, postoperative mortality of 1–5% has been reported, related to age, comorbidity, tumour stage and whether treatment was elective or urgent.

9.3.12.2 Complications of Radiotherapy

Acute toxicity, vomiting, diarrhoea and sometimes neuropathy, is relatively common and is related to the irradiation technique employed. Most of the acute toxicity is self limiting. Late toxicity due to irradiation is a more important problem in rectal cancer treatment, but is also more difficult to evaluate. Postoperative bowel function is compromised if radiotherapy has been used, an effect seen after preoperative radiotherapy as well as postoperative radiotherapy, however preoperative treatment seems to be less problematic. Preoperative radiotherapy has also an impact on sexual function with increased rate of impotence and ejaculation disorders in men and dyspareunia in women. Again, postoperative radiotherapy seems to be worse than preoperative.

Long-term adverse effects of radiotherapy have not been well studied. The Swedish Rectal Cancer Trial has shown that there is an increased risk of a second cancer, not only within but also outside the irradiated area in the group of patients who received radiotherapy. Moreover, abdominal problems such as small-bowel obstruction, pain and radiation enteritis are more common in the irradiated group.

9.3.13 Recurrence

9.3.13.1 Local

- Local recurrence was the predominant problem in rectal cancer surgery in the late 1970s and early 1980s and was the main reason why radiotherapy was explored to reduce the local recurrence rate. It has now been conclusively shown that with optimised surgery the local recurrence rate can be kept very low and particularly if radiotherapy is added when appropriate to optimised surgery.
- After an R0 resection the local recurrence rate should not exceed 5%. Local recurrences, when they do occur, often do so in remnants of the mesorectum not excised

at the original surgery. Occasionally, local recurrences arise in the pelvic side wall, probably in lymph nodes in the internal iliac chain, or in perineural lymphatic channels associated with the hypogastric nerves. There are no convincing data to support radical pelvic sidewall dissection, however this continues to be practiced in certain centres in Japan.

9.3.13.2 Distant Metastases

- Thirty per cent of patients having had potentially curative rectal cancer surgery will suffer from distant metastases. Most common sites are the liver and lung.
- Liver resection for metastases can be curative and, if R0 surgery is possible, 30–40% 5-year survival is possible. Preoperative PET scanning is recommended to screen for occult metastases prior to resection.
- Surgery for lung metastases has a similar survival rate (30–40%) provided that surgery can be curative.

9.3.14 Summary

- Rectal cancer treatment must be based on a multidisciplinary approach.
- Optimised staging using preoperative endorectal ultrasound and MRI will guide use of neoadjuvant therapy.
- Approximately one third of patients with rectal cancer require neoadjuvant radiotherapy or chemoradiotherapy.
- Radiotherapy reduces local recurrence but has adverse effects.
- The role of chemotherapy in patients with resectable rectal cancer is still unresolved.

Suggested Reading

1. Camma C, Giunta M, Fiorica F et al (2000) Preoperative radiotherapy for resectable rectal cancer: a meta-analysis. JAMA 284:1008–1015
2. Colorectal Cancer Collaborative Group (2001) Adjuvant radiotherapy for rectal cancer: a systematic overview of 8,507 patients from 22 randomised trials. Lancet 358:1291–1304
3. Hallböök O, Påhlman L, Krog M et al (1996) Randomized comparison of straight and colonic J pouch anastomosis after low anterior resection. Ann Surg 224:58–65
4. Heald RJ, Ryall RDH (1986) Recurrence and survival after total mesorectal excision for rectal cancer. Lancet i:1479–1482
5. Kapiteijn E, Matijnen CA, Naggtegaal ID et al (2001) Preoperative radiotherapy combined with total mesorectal excision for resectable rectal cancer. N Engl J Med 345:638–646
6. Mantyh CR, Hull TL, Fazio VW (2001) Coloplasty in low colorectal anastomosis. Manometric and functional comparison with straight and colonic J-pouch anastomosis. Dis Colon Rectum 44:37–42
7. Marijnen CA, van de Velde CJ, Putter H et al (2005) Impact of short-term preoperative radiotherapy on health-related quality of life and sexual functioning in primary rectal cancer: report of a multicenter randomized trial. J Clin Oncol 20:1847–1858
8. Martling AL, Holm T, Rutquist LE et al (2000) Effect of a surgical training programme on the outcome of rectal cancer in the County of Stockholm. Lancet 356:93–96
9. Sauer R, Becker H, Hohenberger W et al (2004) Preoperative versus postoperative chemoradiotherapy for rectal cancer. New Engl J Med 351:1731–1740
10. Swedish Rectal Cancer Trial (1997) Improved survival with preoperative radiotherapy in resectable rectal cancer. N Engl J Med 336:980–987

9.4 Anal Cancer

P. RONAN O'CONNELL

9.4.1 Introduction

Anal cancer is rare and may be confused with benign proctological conditions, leading to delayed presentation and diagnosis. Treatment has changed radically since the late 1980s from primarily radical surgical excision to combined chemoradiotherapy with surgery generally reserved for persistent or recurrent disease.

9.4.2 Anatomy

- The anal canal is lined by a transitional epithelium between the rectal mucosa above and the anal margin below. This epithelium consists of an area of squamous and non-squamous non-keratinised epithelium above the dentate line and keratinised squamous mucosa below this line (the anoderm).
- The non-squamous elements represent remnants of the embryological cloaca that may persist. In the past, this has led to confusion regarding terminology used to describe tumours that arise in the anal canal.
- The terms epidermoid, transitional cell, cloacogenic, basaloid, epitheloid and mucoepidermoid carcinoma have been used to describe the various histological features that may predominate.
- There is now broad consensus that these tumours are similar in their presentation and their response to treatment and should be treated as squamous cell tumours, whether keratinising or not.

9.4.3 Incidence

- Tumours of the anal canal are relatively rare, with an incidence of approximately 1/100,000 population in western countries.
- They constitute approximately 1.5% of all large-bowel neoplasms.
- The average time of onset is the sixth decade.
- The incidence is higher among women.
- There is increasing incidence among homosexual men, particularly those with human immunodeficiency virus (HIV) infection.

9.4.4 Classification

- Malignant tumours of the anal canal are classified as squamous (75–85%), adenocarcinoma (5–10%), melanoma (5%), neuroendocrine, sarcoma or lymphoma (< 5%).
- Neoplasms above the anorectal junction are considered rectal cancers.
- Tumours below the anal margin are considered skin tumours.

9.4.5 Aetiology/Epidemiology

Anal trauma and chronic irritation are thought to be important. No association has been found with anal fissure, haemorrhoidal disease or other common proctological diagnoses. There is, however, a clear association with anogenital condylomata, particularly those due to human papilloma virus (HPV) type 16. A history of receptive anal intercourse, sexually transmitted disease and contact with more than ten sexual partners are significant associated features. HPV may lead to dysplastic changes in anal canal mucosa, termed anal intraepithelial neoplasia (AIN), that are similar to changes observed in the uterine cervix. Mild and moderate dysplasia (AIN I and AIN II, respectively) may progress to severe dysplasia (AIN III). AIN III may be found in close proximity to invasive squamous cancer. Progression to invasive cancer is more common in patients with chronic immunosuppression or HIV. In HIV, the risk is proportional to CD4 lymphocyte counts. Smoking increases the risk in susceptible individuals.

9.4.6 Symptoms

- The most common presenting symptom is outlet (fresh, bright red) rectal bleeding. Less frequently, pain in the anal canal or a perianal lump may be noticed.
- Perianal irritation, pruritus ani or incontinence of varying degree may be present. These symptoms may lead to a delay in diagnosis, the most frequent misinterpretation being haemorrhoidal disease.
- Approximately 20% of patients are asymptomatic and present with inguinal adenopathy or distant metastases.

9.4.7 Diagnosis

- Diagnosis is established by digital anorectal examination, anoscopy and biopsy.
- Any suspicious ulcer or persistent fissure should be biopsied.
- Excision biopsy is acceptable in selected patients with small tumours.
- It is important to document the precise location and circumferential extent of the tumour as subsequent treatment may make identification of the tumour site difficult.
- Careful clinical examination looking for regional lymphatic and distant metastatic disease should be performed.
- Formal examination of the large bowel should be undertaken.

9.4.8 Differential Diagnosis

The differential diagnosis includes most common proctological conditions, chronic fissures and non-healing ulcers. Sexually transmitted diseases should be considered in the diagnosis as they increase the risk of anal neoplasia.

- Haemorrhoids
- Chronic fissure
- Hypertrophied anal papilla
- Condyloma
- Lymphogranuloma
- Syphylic ulcer
- Tuberculosis

9.4.9 Staging

Staging requires local assessment of the tumour and screening for metastatic disease. Examination under anaesthetic, endoanal ultrasound and computed tomography (CT) scan of pelvis, abdomen and thorax should be performed. Magnetic resonance imaging (MRI) may be used in addition to CT and endoanal ultrasound. Staging is by the TNM classification (see Chap. 9.5).

9.4.10 Treatment

Treatment of cancer of the anal canal is multidisciplinary (Fig. 9.4.1). Chemoradiotherapy is the standard treatment for the majority of patients but treatment should be individualised on the basis of the overall condition of the patient and the biology and staging of the tumour. Patients with suspected or established anal cancer should be referred to a unit with established expertise and access to radiotherapy facilities.

9.4.10.1 Chemoradiotherapy

Chemoradiotherapy achieves survival rates similar to those of radical surgical excision without loss of continence. Several randomised clinical trials have shown that combination chemoradiotherapy based on 5-fluorouracil (5-FU) and mitomycin C is superior to radiotherapy alone.

- The United Kingdom Co-ordinating Committee for Cancer Research (UKCCCR) trial randomised 585 patients to receive radiation alone or combined with 5-FU and mitomycin C. The failure rate was higher in the radiation alone arm (59%) than in the chemoradiotherapy group (36%). Although there was no overall survival advantage (58% versus 65% at 4 years, respectively), disease-specific survival was higher in the chemoradiotherapy group.
- The European Organization for Research and Treatment of Cancer (EORTC) trial randomised 110 patients. The complete response rate was higher in the chemoradiotherapy group (80%) than in the radiation only group (54%). Although overall survival was no different (59% and 52%, respectively), the 5-year colostomy-free survival rate was 32% greater in the chemoradiotherapy group.
- The Radiation Therapy Oncology Group (RTOG) assessed the role of mitomycin C in 310 patients randomised to receive radiation plus 5-FU or radiation with 5-FU and mitomycin C. Patients who received

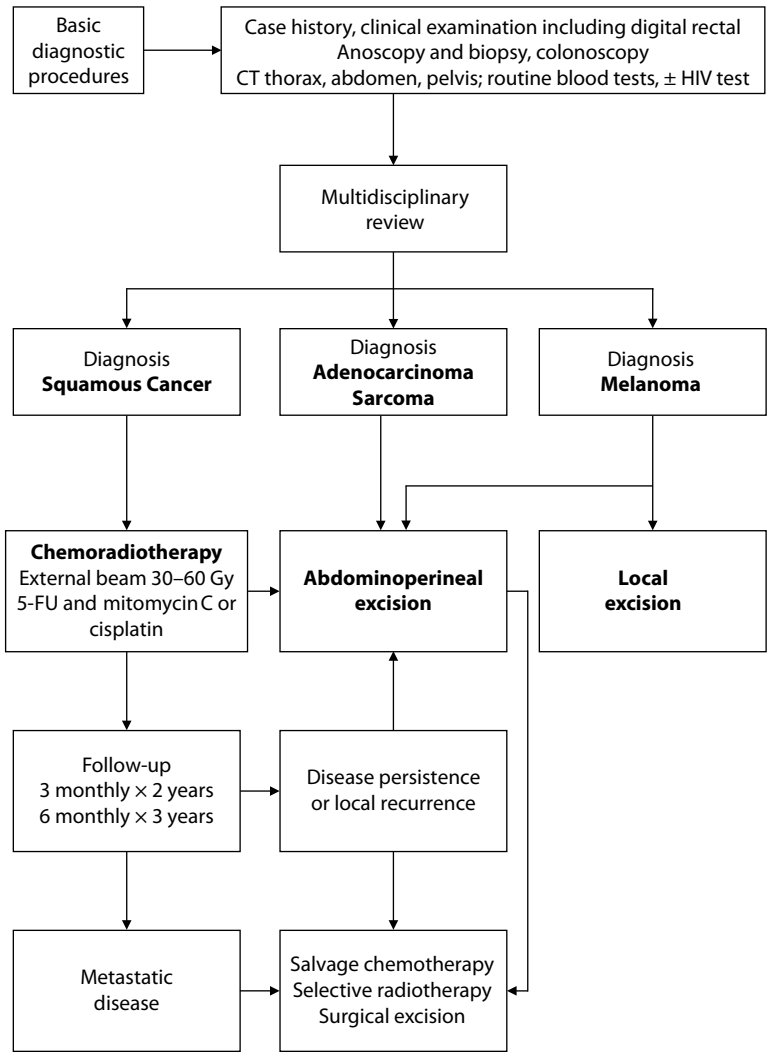


Fig. 9.4.1 Treatment algorithm for anal canal lesions

both 5-FU and mitomycin C were less likely at 5 years to have locoregional recurrence (17% versus 36%) and had higher disease-free survival (67% versus 50%) than patients who received 5-FU alone. Overall survival was no different (65% and 67%, respectively).

Recent evidence suggests that cisplatin can be used in place of mitomycin C with similar response rate and lower toxicity. This is currently the subject of a large clinical trial.

9.4.10.2 Current Treatment Recommendations

- Fractionated external beam radiotherapy of 30–60 Gy, depending on tumour burden and patient suitability
- 5-FU, 1,000 mg/m² delivered by continuous infusion given on days 1–4 and 29–32
- Mitomycin C 10 mg/m² on days 1 and 29 of treatment

Older patients and those with significant comorbidities may not tolerate this regime. In such patients radiotherapy alone may be used with lower response rates; however, in the absence of chemotherapy, the probability of cure

is reduced to approximately 50% in patients with nodal involvement or tumours greater than 5 cm in diameter.

9.4.10.3 Follow-up

- Anorectal examination should be performed 3 months after treatment has finished.
- Any residual abnormality or ulceration in the anal canal should be biopsied.
- Regular examination of the anal canal is important to detect disease persistence or recurrence at an early stage.
- Review every 3 months for 2 years and then every 6 months up to 5 years following treatment is considered reasonable.
- Regular clinical and radiological follow-up for metastatic disease may be undertaken; however, there is no proven benefit to early detection of distant metastatic disease.

9.4.10.4 Abdominoperineal Excision

- Until recent advances in chemoradiotherapy, abdominoperineal excision was the standard treatment for squamous carcinoma of the anal canal.
- Reported 5-year survival rates varied between 40% and 70%, similar to those achieved with chemoradiotherapy but at the price of a permanent colostomy.
- Currently abdominoperineal excision is reserved for persistent, unresponsive or recurrent squamous cell carcinoma of the anal canal.
- Salvage resection may achieve 40–50% 5-year survival.
- A positive resection margin is a strong negative prognostic marker.
- Reconstruction of the perineum may require use of myocutaneous flap techniques, as failure of the perineal wound to heal is a significant problem in radiated patients.
- Abdominoperineal excision continues to be used for treatment of primary adenocarcinoma of the anal canal.

9.4.10.5 Local Excision

- Local excision is acceptable treatment for carcinoma of the perianal skin (anal margin), which is treated in the same manner as skin carcinomas in other areas.
- Local excision may also be considered for T1 tumours of the anal canal with confirmed histologically free margins (> 0.5 cm). Such patients need very careful selection and follow-up.
- Local excision should not be undertaken if it is likely to compromise continence or delay chemoradiotherapy.

9.4.10.6 Brachytherapy

- Brachytherapy has generally been superseded by external beam radiation in the primary treatment of anal canal cancer.
- In high-volume or locally persistent disease, interstitial brachytherapy using iridium-192 can achieve local control and avoid radical surgery.
- Brachytherapy may also have a role in supplementing local excision of perianal skin (anal margin) cancers with excision margins close to the external anal sphincter.

9.4.10.7 Nodal Disease

- Prophylactic inguinal lymph node dissection is not recommended.
- Clinically involved lymph nodes should be sampled using fine-needle aspiration cytology.
- Therapeutic lymphadenectomy is controversial; however, inguinal lymph nodes may be included in therapeutic radiation fields.
- The role of sentinel node biopsy remains to be determined.

9.4.11 Complications

- The most common complications of chemoradiotherapy are skin reactions (erythema, desquamation) and local effects of treatment (proctitis, cystitis, enteritis) that may require treatment interruption.
- Mitomycin has a significant toxic profile and may have long-term effects on renal, pulmonary and bone marrow function. Leukaemia is a rare but often incurable late consequence.
- Faecal incontinence generally reflects pre-existing impairment in anal sphincter function, especially in parous women, coupled with the extent of tumour. Late anal stenosis may also contribute.
- Incontinence or anal stenosis may require a temporary or permanent defunctioning stoma.

9.4.12 Recurrence

9.4.12.1 Local

- Local disease persistence or recurrence occurs in 30–40% of patients treated with chemoradiotherapy.
- Salvage abdominoperineal excision after radiotherapy is associated with high incidence of perineal wound breakdown.
- Use of pedicled rectus abdominis or gracilis flaps has been shown to improve primary wound healing.
- Rectus abdominis flaps are to be preferred.
- Overall 5-year surgical salvage rates of 30–60% are reported.

9.4.12.2 Lymph Node

- Isolated locoregional lymph node metastases may be treated by chemotherapy and radiotherapy if not included in the original treatment field.
- Block dissection in a previously irradiated groin is associated with high morbidity.

9.4.12.3 Distant

- The most common sites for metastatic disease are lung, liver, bone and brain.
- Treatment usually consists of combination chemotherapy using 5-FU and cisplatin.
- Palliative radiotherapy may be used for pulmonary or bone metastases.
- Rarely, resection of isolated metastases may be considered.

9.4.13 Rare Tumours

9.4.13.1 Adenocarcinoma

Adenocarcinomas of the anal canal are rare and are thought to arise in the ducts of anal glands. Local excision has a high local recurrence rate and abdominoperineal resection is the preferred treatment.

9.4.13.2 Melanoma

Anal canal melanoma is rare and frequently is amelanotic. It is an aggressive tumour, locally invasive and has a high propensity to metastasise. Results of local and radical excision are similar in terms of survival.

9.4.13.3 Sarcoma

Sarcomas of the anorectal area are rare and are generally resistant to radiotherapy. Abdominoperineal excision is the preferred treatment.

9.4.14 Carcinoma of the Perianal Skin (Anal Margin)

Squamous and basal cell tumours may affect the perianal skin. Treatment is wide local excision with adequate margins (>5 mm). Split-thickness skin grafting or local skin flap rotation may be required to achieve skin closure. Brachytherapy may occasionally allow sphincter preservation in a more deeply invasive tumour. Late anal canal stenosis can be problematic, with contraction of extensive skin graft of the perianal skin.

9.4.15 Premalignant Conditions

9.4.15.1 Bowen's Disease

- Bowen's disease presents as an itchy plaque-like lesion of the perianal skin that may be considered premalignant.
- Punch biopsy of the perianal skin under local anaesthetic should be performed on any suspicious lesion.
- There is an association with invasive carcinoma of the rectum, which should be excluded.
- In the absence of invasive cancer, local excision and observation is sufficient.

9.4.15.2 Paget's Disease

- Paget's disease is a rare intraepithelial adenocarcinoma found in tissues containing apocrine glands.
- Patients tend to be older and present with a bleeding, painful eczematous lesion of the perianal skin.
- Wide local excision is sufficient in the absence of invasive malignancy.
- Split-thickness skin grafting with a defunctioning loop stoma is sometimes required.
- Local recurrence may prove difficult and require more radical excision.

9.4.15.3 Buschke-Lowenstein Disease

- A rare well-differentiated squamous cell cancer of the perianal skin arising in large anal condylomata.
- Wide local excision is required.

Suggested Reading

1. Bartelink H, Roelofsen F, Eschwege F et al (1997) Concomitant radiotherapy and chemotherapy is superior to radiotherapy alone in the treatment of locally advanced anal cancer: results of a phase III randomized trial of the European Organization for Research and Treatment of Cancer Radiotherapy and Gastrointestinal Cooperative Groups. J Clin Oncol 15:2040–2049
2. Esiashvili N, Landry J, Matthews RH (2002) Carcinoma of the anus: strategies in management. Oncologist 7:188–199
3. Flam M, John M, Pajak TF et al (1996) Role of mitomycin C in combination with fluorouracil and radiotherapy, and of salvage chemoradiotherapy in the definitive nonsurgical treatment of epidermoid carcinoma of the anal canal: results of a phase III randomised intergroup study. J Clin Oncol 14:2527–2539
4. Hung A, Crane C, Delclos M et al (2003) Cisplatin-based combined modality therapy for anal carcinoma: a wider therapeutic index. Cancer 97:1195–1202
5. National Institute for Clinical Excellence (2004) Guidance on cancer services. Improving outcomes in colorectal cancers. www.nice.org.uk (accessed 11 Nov 2004)
6. Ryan DP, Compton CC, Mayer RJ (2000) Carcinoma of the anal canal. N Engl J Med 342:792–800
7. UKCCCR Anal Cancer Trial Working Party (1996) Epidermoid anal cancer: results from the UKCCCR randomized trial of radiotherapy alone versus radiotherapy, 5-fluorouracil and mitomycin. Lancet 348:1049–1054

9.5 Current Tumour Classification

PAUL HERMANEK

9.5.1 General Considerations

9.5.1.1 Principles of Current Tumour Classification

The current classification of malignant tumours is based on four bases or axes (Table 9.5.1).

9.5.1.2 Objectives of Uniform Tumour Classification

A uniform classification of malignant tumours is a prerequisite for epidemiological studies and any meaningful and comparative analysis of treatment results. To enable international comparisons tumours should always be classified according to established international recommendations of the UICC and WHO. Since 1987 the UICC classification is identical with the classification of the American Joint Committee on Cancer (AJCC).

9.5.1.3 Principles of TNM Classification

- The TNM classifications specific for various tumour sites are applicable for defined histological types only, usually for carcinomas only.
- For tumour types not classified by TNM the anatomical extent is described by the following general categories:
  - In situ: Non-invasive
  - Localised: Limited to the site of origin
  - Regional: Invading adjacent structures and/or regional lymph node metastasis
  - Distant: Distant metastasis
- The anatomical extent of cancer is described by assessment of three components:
  - T: The extent of the primary tumour
  - N: The absence or presence and extent of regional lymph node metastasis
  - M: The absence or presence of distant metastasis
- For T, N and M, categories and subcategories are provided, e.g. T1, T2a, T2b, T3, etc.
- For each site, *two classifications* are described:
  - TNM (or cTNM) (prefix "c" indicating pretreatment clinical classification): Based on evidence acquired

Table 9.5.1 Current classification of malignant tumours

Axes	Classification system	Coding	References for anal and colorectal cancers
Topography	International Documentation System (IDS) for colorectal cancer UICC: TNM classification	WHO: International classification of diseases for oncology (ICD-O), 3rd edn	Soreide et al. (1997); UICC (2003); Fritz et al. (2000)
Histomorphology (typing, grading)	WHO: Histological classification of tumours		Hamilton and Aaltonen (2000); Hennan et al. (1996); Fritz et al. (2000)
Anatomic extent before treatment	UICC: TNM classification	–	UICC (2002, 2003, 2005)
Anatomical extent after treatment	UICC: Residual tumour (R) classification	–	

before treatment by physical examination, imaging, endoscopy, biopsy and surgical exploration
  - pTNM (histopathological classification): Based on evidence acquired prior to treatment, supplemented or modified by the additional evidence from histopathological examination
- TNM is essential to select the therapy; pTNM provides the most precise data to estimate prognosis and calculate end results.
- Based on T, N and M and/or pT, pN and pM categories the cases are grouped into stages and substages, e.g. I, II, IIIA, IIIB, etc. These should, as far as possible, be more or less homogenous in respect of biological behaviour and survival.
- The classification of *anatomical extent following neoadjuvant therapy* is described with the prefix "y" as yTNM (clinical) and ypTNM (pathological). For the latter only viable tumour cells are considered and not signs of regressed tumour tissue such as scars, fibrotic areas, fibrotic nodules, granulation tissue, mucin lakes, etc.
- *Isolated tumour cells* (ITC) are single tumour cells or small clusters of tumour cells not more than 0.2 mm in greatest dimension. Their presence in regional lymph nodes or at distant sites should not be classified as metastasis. ICT are usually detected by immunohistology or molecular (non-morphological) methods. Respective findings are indicated in parentheses to pN0 and pM0, respectively:
  - (i−): Negative morphological (mostly immunohistological) findings
  - (i+): Positive morphological (usually immunohistological) findings
  - (mol−): Negative molecular (non-morphological) findings
  - (mol+): Positive molecular (non-morphological) findings
- *Recurrent tumours* after a disease-free interval may be classified according to TNM. Such classifications are indicated by the prefix "r", e.g. rT2N0M0 or rT0N1M0 or rT0N0pM1.
- *Telescopic ramifications* of TNM: For orderly development and expansion of TNM allowing improvements in prognostic evaluation and planning treatment the mechanism of optional telescopic ramification is provided. T, N and M as well as pT, pN and pM categories may be subdivided, e.g. T3 into T3a, 3b, and 3c. This allows the collection of additional data without altering the definition of the existing TNM categories.

9.5.1.4 General Rules of TNM

- *Doubtful findings*: If there is doubt concerning the correct (p)T, N or M category to which a particular case should be allotted, than the lower (i.e. less advanced) category should be chosen.
- *Multiple simultaneous primary tumours in one organ*: The tumour with the highest T/pT category should be classified and the multiplicity, e.g. T2(m), or the number of tumours, e.g. pT2(3), should be indicated in parentheses.
- *Regional lymph node metastasis*:
  - Direct extension of the primary tumour into lymph nodes is classified as lymph node metastasis.
  - A tumour nodule in the adipose tissue of a lymph drainage area without histological evidence of residual lymph node in the nodule is classified as regional lymph node metastasis if the nodule has the form and smooth contour of a lymph node.
  - If the nodule has an irregular contour, it should be classified in the pT category (discontinuous spread) and also as venous invasion (V1 microscopic, V2 macroscopic).
  - Cases with micrometastasis only, i.e. no metastasis larger than 2 mm, can be identified by the addition of "(mi)", e.g. pN1(mi).
- *Sentinel lymph nodes:* The findings of sentinel lymph node assessment are described as pN with the adjunct of "(sn)", e.g. pN0(sn) or pN1(sn).
- *Optional descriptors:*
  - Lymphatic invasion:
    - LX: Lymphatic invasion cannot be assessed
    - L0: No lymphatic invasion
    - L1: Lymphatic invasion
  - Venous invasion:
    - VX: Venous invasion cannot be assessed
    - V0: No venous invasion
    - V1: Microscopic venous invasion
    - V2: Macroscopic venous invasion (includes macroscopic involvement of the vein wall without tumour within the vein)

9.5.1.5 Site-specific Classifications

The classification of histomorphology and that of anatomical extent before treatment (TNM and pTNM) are site-specific for the following groups:

- Anal canal cancer
- Perianal (anal margin) cancer
- Colorectal cancer

In contrast, the classification of anatomical extent after treatment (residual tumour R classification) follows the same rules for all included cancer entities.

9.5.2 Topography Classification

9.5.2.1 Anal Cancer (Topography Codes C21.1 and C44.5)

Two different entities are included (Fig. 9.5.1):

1. Anal canal cancer (topography code C21.1): The centre of the tumour is located between the linea anorectalis and the linea anocutanea.
2. Perianal (anal margin) cancer (topography code C44.5): The centre of the tumour is located beyond the linea anocutanea, but not more than 5 cm from the latter.

9.5.2.2 Rectal Cancer (Topography Code C20.9)

- A cancer is classified as rectal if its lower margin lies 16 cm or less from the anal verge when measured from below with a rigid sigmoidoscope. In case of missing sigmoidoscopy a cancer is considered rectal if any part of it is located at least partly within the supply of the superior rectal artery.
- When differentiation between rectal and sigmoid cancer according to the above rules is not possible, the tumour is classified as rectosigmoid (C19.9).
- *Attention*: In USA rectal cancer is usually defined as cancer with lower margin lying 12 cm or less from the anal verge when measured from below with a rigid sigmoidoscope.
- Because of differences in treatment and prognosis the rectum may be subdivided into three parts according to the distance of the lower margin of the tumour from the anal verge:
  - Upper third/upper rectum: 12–16 cm
  - Middle third/middle rectum: 6 to < 12 cm
  - Lower third/lower rectum: < 6 cm

9.5.2.3 Colon Cancer (Topography Codes C18.1–18.8)

- Anatomical subsites and topography codes are shown in Table 9.5.2.
- A tumour located at the border between two subsites is registered as a tumour of the subsite that is more involved.
- If two subsites are involved to the same extent, the lesion is classified as an overlapping lesion of the colon (C18.8).
- Carcinomas of the appendix are classified according to the TNM system, but should be analysed separately from other colon cancers.

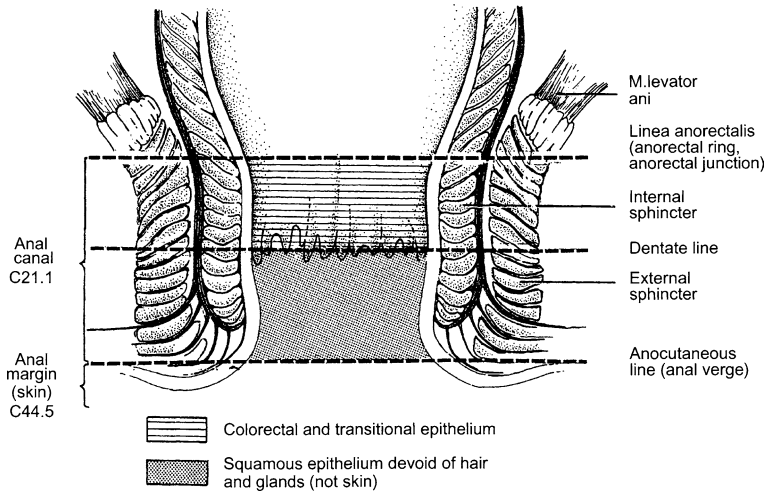


Fig. 9.5.1 Topography of the anal region. Modified from UICC (2005)/AJCC

Table 9.5.2 Topography codes for subsites in the colon

Anatomical subsites	Topography code
Appendix	C18.1
Caecum	C18.0
Ascending colon	C18.2
Hepatic flexure	C18.3
Transverse colon	C18.4
Splenic flexure	C18.5
Descending colon	C18.6
Sigmoid colon	C18.7

9.5.2.4 Multiple Simultaneous Tumours

- For the classification of such tumours in "one organ" (see *General Rules of TNM*) the following definitions should be applied: Colon and rectum (C18–20) / anal canal (C21.1)/perianal skin (anal margin) (C44.5).

9.5.3 Histomorphology and TNM Classification of Anal Canal Cancers

9.5.3.1 Histological Typing

- Carcinoma in situ (high-grade intraepithelial neoplasia, dysplasia): Either at the margin of invasive carcinoma or synchronous lesion separated from an associated carcinoma or isolated lesion without invasive carcinoma ("precursor"). Most cases are squamous carcinoma in situ (8077/2).
- Invasive carcinomas (excluding exocrines): Squamous cell carcinoma (8070/3) (75–80%); adenocarcinoma (8140/3) (15–20%) arising from the mucosa above the dentate line, anal glands or anorectal fistulae; others (very rare): mucinous adenocarcinoma (8490/3), undifferentiated carcinoma (8020/3).
- Squamous cell carcinoma: The pathology report should include the proportions (in per cent) of squamous, basaloid and ductal differentiation and should identify the presence of one of the "subtypes" with unfavourable prognosis as squamous cell carcinoma with mucinous microcysts (formerly described as mucoepidermoid carcinoma, at present code number not yet assigned) or small cell non-keratinising squamous cell carcinoma (8073/3).
- Squamous cell carcinoma frequently associated with human papilloma virus (HPV), in young patients with human immunodeficiency virus (HIV).
- Endocrine (neuroendocrine) tumours of the anal canal are usually classified as rectal (see Histomorphology and TNM Classification of Colorectal Cancers)
- Malignant melanoma (4%) is most frequently mucosal lentiginous (8746/3).
- Non-epithelial malignant tumours (1%): Malignant fibrous histiocytoma (8830/3), leiomyosarcoma (8890/3), Kaposi sarcoma (9140/3) (predominantly HIV-associated), malignant lymphomas (predominantly B cell, often HIV-associated).

9.5.3.2 Grading

- Recommended in tumour excision specimens only, not on biopsies.
- Squamous cell carcinoma: Low grade and high grade.
- Small-cell non-keratinising squamous cell carcinoma and squamous cell carcinoma with mucinous microcysts: G4.
- Adenocarcinoma: G1–4 as in colorectal adenocarcinoma (see *Histomorphology and TNM Classification of Colorectal Cancers*)
- Malignant melanoma: No grading.

9.5.3.3 TNM Classification

- Applicable only to carcinomas.
- Regional lymph nodes: The regional lymph nodes are the perirectal, the bilateral internal iliac (including obturator) and the bilateral inguinal lymph nodes.

Definitions of TNM/pTNM Categories

- T/pT:
  - (p)TX: Primary tumour cannot be assessed
  - (p)T0: No evidence of primary tumour
  - (p)Tis: Carcinoma in situ
  - (p)T1: Tumour 2 cm or less in greatest dimension
  - (p)T2: Tumour more than 2 cm but not more than 5 cm in greatest dimension
  - (p)T3: Tumour more than 5 cm in greatest dimension
  - (p)T4: Tumour of any size invades adjacent organ(s), e.g. vagina, urethra, bladder (direct invasion of the rectal wall, perirectal skin, subcutaneous tissue or the sphincter muscle(s) is not classified as T4)
- N/pN
  - (p)NX: Regional lymph nodes cannot be assessed
  - (p)N0: No regional lymph node metastasis
  - (p)N1: Metastasis in perirectal lymph node(s)
  - (p)N2: Metastasis in unilateral internal iliac and/or unilateral inguinal lymph (node(s))

  - (p)N3: Metastasis in perirectal and inguinal lymph nodes and/or bilateral internal iliac and/or bilateral inguinal lymph nodes

Requirements for pN0: Histological examination of a regional perirectal-pelvic lymphadenectomy specimen ordinarily including 12 or more lymph nodes and/or histological examination of an inguinal lymphadenectomy specimen ordinarily including 6 or more lymph nodes. If the lymph nodes are negative, but the number ordinarily examined is not met, classify as pN0 and state the number of examined nodes.

- M/pM
  - (p)MX: Distant metastasis cannot be assessed
  - (p)M0: No distant metastasis
  - (p)M1: Distant metastasis
  - Optional ramification:
    - (p)M1a: Metastasis in non-regional lymph nodes only
    - (p)M1b: Metastasis in viscera (excluding peritoneal and pleural metastasis)
    - (p)M1c: Peritoneal and/or pleural metastasis

Stage grouping: See Fig. 9.5.2.

9.5.4 Histomorphology and TNM Classification of Perianal (Anal Margin) Cancers

9.5.4.1 Histomorphology

- Malignant tumours of the perianal region are similar to skin tumours of other sites. Most invasive carcinomas (90%) are squamous cell carcinomas, basal cell carcinomas and other types are rare.
- Perianal squamous cell carcinoma has a better prognosis than squamous cell carcinoma of the anal canal (lymph node metastasis uncommon).
- Basal cell carcinoma metastasis is extremely rare.
- Verrucous carcinoma (8051/3) (formerly described as giant malignant condyloma Buschke-Loewenstein): Uncommon well-differentiated exophytic and endophytic destructive growth with squamous cell morphology, no metastasis.
- Non-invasive epithelial lesions:
  - Carcinoma in situ (high-grade anal intraepithelial neoplasia (AIN), high-grade squamous dysplasia): Most cases incidental findings in surgical excisions of benign lesions.
  - Bowen's disease (8081/2): Non-invasive (intraepithelial) squamous epithelial lesion, sometimes in continuity with dysplastic lesions in the anal canal, sometimes HPV-associated, strong tendency to recurrence after local excision, but only a few per cent will progress to squamous cell carcinoma.
  - Extramammary Paget's disease (8542/3): Uncommon intraepithelial lesion of the perianal skin. About 50% associated with synchronous or metachronous malignant tumours, most often colorectal adenocarcinoma (so-called pagetoid extension of colorectal cancer). In cases not associated with other malignancies high local recurrence rate and progression to invasive carcinoma possible.
- Malignant melanoma of the perianal skin uncommon, behaviour as other melanomas of the skin.
- Non-epithelial malignant tumours extremely rare, only few cases of leiomyosarcoma, rhabdomyosarcoma and fibrosarcoma reported.

<table>
<tr><td rowspan="2"></td><td colspan="3">M0</td><td rowspan="2">M1</td></tr>
<tr><td>N0</td><td>N1</td><td>N2,3</td></tr>
<tr><td>Tis</td><td>St.0</td><td colspan="3">----------</td></tr>
<tr><td>T1</td><td>St.I</td><td rowspan="3">St.IIIA</td><td rowspan="4">St.IIIB</td><td rowspan="4">St.IV</td></tr>
<tr><td>T2</td><td rowspan="2">St.II</td></tr>
<tr><td>T3</td></tr>
<tr><td>T4</td><td>St.IIIA</td><td colspan="2"></td></tr>
</table>

Fig. 9.5.2 Stage grouping for anal canal carcinoma

9.5.4.2 Grading

- Basal cell carcinoma and malignant melanoma: No grading.
- Other carcinomas: Grading as for respective tumours of the anal canal.

9.5.4.3 TNM Classification

- Perianal carcinomas and perianal malignant melanomas are classified like the respective tumours of the skin.
- Regional lymph nodes are the inguinal lymph nodes (ipsilateral or in case of midline involvement bilateral).

9.5.5 Histomorphology and TNM Classification of Colorectal Cancers

9.5.5.1 Histological Typing

- Carcinoma in situ: In the rectum and colon, carcinoma in situ (high-grade intraepithelial neoplasia or dysplasia, pTis) includes intraepithelial carcinoma as well as cases with invasion of the lamina propria (including the muscularis mucosae, but not the submucosa), i.e. intramucosal carcinoma.
- Invasive non-endocrine carcinomas:
  - 80–90% adenocarcinoma (8140/3)
  - 10–15% mucinous adenocarcinoma (8480/3)
  - Rare carcinomas (< 5%): Medullary carcinoma (8510/3), undifferentiated carcinoma (8020/3)
  - Very rare (< 1%): Squamous cell carcinoma (8070/3), adenosquamous carcinoma (8560/3), signet-ring-cell carcinoma (8490/3)
- Endocrine carcinomas (< 1%):
  - Well-differentiated L cell carcinoma (malignant enteroglucagonoma) (8157/3)
  - Well-differentiated EC cell carcinoma (malignant EC cell carcinoid) (8241/3)
  - Small cell carcinoma (8041/3)
  - Large cell neuroendocrine carcinoma (8013/3)
  - Mixed endocrine-exocrine carcinoma (mixed carcinoid-adenocarcinoma, composite carcinoid, combined carcinoid and adenocarcinoma) (8244/3)
- Malignant melanoma (8720/3): In the rectum extremely uncommon
- Malignant mesenchymal tumours (< 1%): Leiomyosarcoma (8890/3), malignant gastrointestinal stromal tumour (GIST) (8936/3), angiosarcoma (9120/3), Kaposi sarcoma (9140/3)
- Malignant B cell lymphomas (< 1%), predominantly mucosal-associated lymphoid tissue (MALT) lymphoma (8699/3)

9.5.5.2 Grading

- For adenocarcinoma, see Table 9.5.3.
- Signet-ring-cell carcinoma, undifferentiated carcinoma: G4
- Medullary carcinoma: No grading (morphologically undifferentiated, but prognosis more favourable than for undifferentiated carcinoma or G3 adenocarcinoma)
- Subdivision of carcinomas limited to submucosa (early carcinoma, pT1) according to the risk of positive lymph node status:
  - Low risk (lymph node metastasis < 3%): G1,2 and no lymphatic invasion (L0)
  - High risk (lymph node metastasis > 10–20%): G3,4 or lymphatic invasion (L1)

9.5.5.3 TNM Classification

Applicable only to carcinomas, including small cell and mixed exocrine-endocrine carcinoma, but not to low-grade endocrine carcinomas (malignant carcinoid tumours).

Regional Lymph Nodes

- The regional lymph nodes for the various anatomical subsites are detailed in Table 9.5.4.
- In tumours with involvement of two subsites the lymph nodes for both subsites are considered as regional.
- In case of direct invasion of small intestine, lymph nodes in the mesentery of the invaded intestinal loop are considered as regional lymph nodes.

Definitions of TNM/pTNM Categories

- T/pT
  - (p)TX: Primary tumour cannot be assessed
  - (p)T0: No evidence of primary tumour
  - (p)Tis: Carcinoma in situ: intraepithelial or invasion of lamina propria (intramucosal) (with no evidence of extension through muscularis mucosae into submucosa)
  - (p)T1: Tumour invades submucosa
  - (p)T2: Tumour invades muscularis propria

Table 9.5.3 Grading for colorectal adenocarcinoma

Proportion (%) of glands	Hamilton and Aaltonen (2000)	Compton (2000)
> 95	G1	Low grade
50–95	G2	
5 to < 50	G3	High grade
< 5	G4	

Table 9.5.4 Regional lymph nodes for subsites in the colon and rectum

Anatomical subsites	Regional lymph nodes
Appendix	Ileocolic
Caecum	Ileocolic, right colic
Ascending colon	Ileocolic, right colic, middle colic
Hepatic flexure	Middle colic, right colic
Transverse colon	Right colic, middle colic, left colic, inferior mesenteric
Splenic flexure	Middle colic, left colic, inferior mesenteric
Descending colon	Left colic, inferior mesenteric
Sigmoid colon	Sigmoid, left colic, superior rectal, inferior mesenteric, rectosigmoid
Rectum	Superior, middle and inferior rectal, inferior mesenteric, internal iliac, mesorectal (paraproctal), lateral sacral, presacral, sacral promontory (Gerota)

- (p)T3: Tumour invades through muscularis propria into subserosa or into non-peritonealised pericolic or perirectal tissues (invasion of external sphincter is classified as (p)T3, invasion of levator muscle(s) (p)T4)
- Optional ramification according to the extent of invasion beyond the outer border of muscularis propria (histologically measured):
  - pT3a: ≤ 1 mm (minimal)
  - pT3b: > 1–5 mm (slight)
  - pT3c: > 5–15 mm (moderate)
  - pT3d: > 15 mm (extensive)
- (p)T4: Tumour directly invades other organs or structures (including invasion of levator muscle(s); invasion of other segments of the colorectum by way of the serosa, e.g. invasion of sigmoid colon by a carcinoma of the caecum; tumour that is adherent to other organs or structures, macroscopically, is classified T4; however, if no tumour is present in the adhesion, microscopically, the classification should be pT3)
- Optional ramification:
  - (p)T4a: Invasion to adjacent organs or structures without perforation of the visceral peritoneum
  - (p)T4b: Perforation of visceral peritoneum

- N/pN
  - (p)NX: Regional lymph nodes cannot be assessed
  - (p)N0: No regional lymph node metastasis
  - (p)N1: Metastasis in 1–3 regional lymph nodes
  - (p)N2: Metastasis in 4 or more regional lymph nodes

Requirements for pN0: Histological examination of a regional lymphadenectomy specimen ordinarily including 12 or more lymph nodes. If the lymph nodes are negative, but the number ordinarily examined is not met, classify as pN0 and state the number of examined nodes.

- M/pM
  - (p)MX: Distant metastasis cannot be assessed
  - (p)M0: No distant metastasis
  - (p)M1: Distant metastasis

Stage grouping: See Fig. 9.5.3.

	M0			M1
	N0	N1	N2	
Tis	St.0	----------		
T1	St.I	St.IIIA	St.IIIC	St.IV
T2				
T3	St.IIA	St.IIIB		
T4	St.IIB			

Fig. 9.5.3 Stage grouping for colorectal carcinoma

9.5.6 Residual Tumour (R) Classification

- The R classification deals with tumour status after definitive treatment. It reflects the effects of therapy, influences further therapeutic procedures and is a strong predictor of prognosis.
- In the R classification, not only local-regional tumour is to be taken into consideration, but also distant residual tumour in the form of remaining distant metastasis.
- The R classification following surgical treatment requires the cooperation between surgeon and pathologist in a two-stage process:
  - Clinical information on remaining local tumour and/or distant metastasis
  - Histopathological examination of resection specimens
- Definitions of R categories:
  - R0: No residual tumour
  - Optional ramification:
    - R0a: Negative markers
    - R0b: Persistently elevated marker level or rising marker levels within 4 months
  - R1 Microscopic residual tumour
  - R2 Macroscopic residual tumour (with statements on its location, i.e. local-regional and/or distant)
- Although there have been proposals from the UK to code a tumour R1 if the tumour is 1 mm or less from the resection margin, according to the UICC R1 is only used if the tumour is transected, otherwise it is R0. To allow comparison with the circumferential resection margin (CRM) status (see below) it is recommended to record cases with tumour within 1 mm or less from resection margin separately.
- In cases of locally incomplete resections of rectal cancer, tumour is found in more than 90% on the circumferential (radial, lateral, mesorectal) resection margin (CRM). In addition to the R classification the British description of the CRM status is useful for estimating prognosis:
  - CRM positive: CRM directly involved with tumour or minimal distance between tumour and CRM 1 mm or less
  - CRM negative: Minimal distance between tumour and CRM more than 1 mm
- The R classification after surgery following neoadjuvant therapy considers vital tumour only.
- Positive peritoneal lavage cytology using conventional staining techniques without any other evidence of residual tumour is classified as R1(cy+).
- The finding of isolated tumour cells in lymph nodes, bone marrow biopsies, other distant organs or blood does not affect the R classification. Such morphological (cytological, immunohistological) findings are indicated by the addition of (i+) and molecular pathological findings by the addition of (mol+), e.g. R0(i+) or R0(mol+).

9.5.7 Special Considerations

In addition to the classification of cancers in a narrow sense (see Table 9.5.1), in some defined situations the pathological examination includes additional assessments:

- After neoadjuvant treatment: Histological regression grading
- After rectal cancer surgery with total or partial mesorectal excision: Pathological assessment of quality of mesorectal excision
- After abdominoperineal excision: Pathological assessment of quality of this operation

9.5.7.1 Histological Regression Grading

The effect of neoadjuvant radiotherapy or radiochemotherapy is always assessed by the yTNM/ypTNM classification (see *Principles of TNM Classification*). In addition, a more detailed analysis by a histological regression grading may be useful to estimate prognosis. To date, there are no internationally accepted systems for histological regression grading, but some semiquantitative systems have been published since 1994:

- Applicable for colorectal and anal canal carcinoma: Japanese Society for Cancer of the Colon and Rectum (1997), Werner and Höfler (2000)
- Applicable for colorectal carcinoma only: Dworak et al. (1997)
- Applicable for anal cancer only: Klimpfinger et al. (1994)

9.5.7.2 Pathological Assessment of Quality of Mesorectal Excision

The results of rectal cancer surgery are decisively influenced by the quality of mesorectal excision. A formal classification for the assessment of quality of mesorectal excision by the pathologist has been developed by Quirke. It was used in a slightly modified form in British and Dutch studies and recommended for use in the USA by Compton in 2002. In this system three categories are distinguished:

- Grade 3 (complete/good): Intact mesorectum with only minor irregularities of the smooth mesorectal surface. No defect greater than 5 mm. No coning of the specimen. Smooth CRM on slicing the specimen.
- Grade 2 (moderate/nearly complete): Irregularity of the mesorectal surface. At no site is the muscularis propria visible with the exception of the area of insertion of levator muscles. Moderate coning of the specimen towards the distal margin allowed. Moderate irregularity of the CRM on slicing the specimen.
- Grade 1 (incomplete/poor): Little bulk to mesorectum. Defects in the mesorectum down to muscularis propria. Very irregular CRM on slicing of the specimen or pronounced coning.

9.5.7.3 Pathological Assessment of Quality of Abdominoperineal Excision

A system for the pathological assessment of the quality of abdominoperineal excision with mesorectal excision and removal of the levator/anal canal below the mesorectum has been used in two British studies (MERCURY, CORE) (Maughan & Quirke 2003):

- Grade 3 (complete/enhanced): Specimen with circumferential component of the levator muscles.
- Grade 2 (moderate/standard): No levator muscles attached to the specimen, resection margin on the muscularis propria.
- Grade 1 (poor/substandard): Areas of the muscularis propria are missing from the specimen or perforation of the area of tumour.

Suggested Reading

1. Compton CC for the members of the Cancer Committee, College of American Pathologist (2000) Updated protocol for the examination of specimens received from patients with carcinomas of the colon and rectum, excluding carcinoid tumors, lymphomas, sarcomas, and tumors of the vermiform appendix. Arch Pathol Lab Med 124:1016–1025
2. Compton CC (2002) Pathologic prognostic factors in the recurrence of rectal cancer. Clin Colorect Cancer 2:140–160
3. Dworak O, Keilholz L, Hoffmann A (1997) Pathological features of rectal cancer after preoperative radiochemotherapy. Int J Colorect Dis 12:19–23
4. Fritz A, Percy C, Jack A et al (2000) International classification of diseases for oncology (ICD-O), 3rd edn. WHO, Geneva
5. Hamilton SR, Aaltonen LA (eds) (2000) Pathology and genetics of tumours of the digestive system. WHO classification of tumours. IARC Press, Lyon
6. Heenan PJ, Elder DE, Sobin LH (1996) Histological typing of skin tumours. WHO international histological classification of tumours. Springer, Berlin
7. Japanese Society for Cancer of the Colon and Rectum (JSCCR) (1997) Japanese classification of colorectal carcinoma, 1st English edn. Kanahara, Tokyo

8. Klimpfinger M, Hauser H, Berger A, Hermanek P (1994) Aktuelle klinisch-pathologische Klassifikation von Karzinomen des Analkanals. Acta Chir Aust 26:345–351
9. Maughan NJ, Quirke P (2003) Modern management of colorectal cancer: a pathologist's view. Scand J Surg 92:11–19
10. Quirke P (1998) The pathologist, the surgeon and colorectal cancer – get it right because it matters. Progr Pathol 4:201–213
11. Soreide O, Norstein J, Fielding LP, Silen W (1997) International standardization and documentation of the treatment of rectal cancer. In: Soreide O, Norstein J (eds) Rectal cancer surgery. Optimisation – standardisation – documentation. Springer, Berlin, pp 405–445
12. UICC (Sobin LH, Wittekind C eds) (2002) TNM classification of malignant tumours, 6th ed. Wiley, New York
13. UICC (Wittekind C, Greene FL, Henson DE, Hutter RVP, Sobin LH eds) (2003) TNM supplement, 3rd edn. A commentary on uniform use. Wiley, New York
14. UICC (Wittekind C, Greene FL, Hutter RVP, Klimpfinger M, Sobin LH eds) (2005) TNM atlas, 5th edn. Springer, Berlin
15. Werner M, Höfler H (2000) Pathologie. In: Roder JD, Stein HJ, Fink U (eds) Therapie gastrointestinaler Tumoren. Springer, Berlin, pp 45–53

Stomas and Stomatherapy

10.1 Stomas and Stomatherapy

HARALD ROSEN

10.1.1 Introduction

Faecal diversion by construction of a stoma is still a common procedure in colorectal surgery. While formation of a stoma as a treatment for rectal cancer has decreased markedly due to the introduction of sphincter-saving techniques, there is still a variety of indications leading to the construction of intestinal stomas. While the first historical reports about the treatment of penetrating abdominal injuries are ranging back to the thirteenth century, the eighteenth and nineteenth centuries saw a change from mere exteriorisations of lacerations of the intestine to elective formations of ileostomies and caecostomies as well as left inguinal colostomies for large-bowel obstructions. Following the next "milestone" of the introduction of a rod by Maydl which led to the creation of a loop colostomy in 1884, it took more than 60 years until mucocutaneous sutures and the immediate opening of a stoma were accepted as the method of choice. Parallel to this, a German chemistry student, Koernig, suffering from the side effects of an ileostomy due to ulcerative colitis, developed a bag made of rubber and fixed it to the skin with a latex preparation, thus leading to the emergence of modern stoma appliances. While the principle of the "Koernig bag" remained a standard for many years, more effective sealing material, first Karaya and later Stomahesive or similar hydrocolloids, have led to the present state of the art of stoma appliances.

10.1.2 Definitions and Indications

Stomas may be *permanent* or *temporary* and can be created either as a *loop*, *double-barrel* or as an *end stoma* using a part of the small (ileostomy) or large (colostomy) bowel.

10.1.2.1 Indications for a Permanent Stoma

- Abdominoperineal (APR) excision of the rectum for rectal or recurrent anal cancer or severe inflammatory bowel disease of the anorectum
- Untreatable persistent faecal incontinence

10.1.2.2 Indications for a Temporary Stoma

Contrary to the applications in the past, when a temporary stoma was used as the first step of treatment in emergency situations (colonic obstruction, acute diverticulitis, fulminant ulcerative colitis), today most of these patients will be treated immediately by definitive surgical resection. Therefore, temporary stoma formation as a sole procedure should be reserved only for the few patients with massive obstruction and in such a general condition that they cannot tolerate a resection.

Formation of a temporary stoma will be limited to those patients in whom either a *primary anastomosis* might be not desirable (Hartmann procedure, double-barrel stoma following resection in selected patients) or in whom it should serve as the so-called *protective or covering stoma*. However, stoma reversion should be feasible in an acceptable time period.

Temporary stoma are used:

- For protection of low rectal or anal anastomoses
- When there is a need to delay primary anastomoses to a later time point (Hartmann procedure, double-barrel stoma)
- In complicated perianal and/or rectal fistula disease
- In penetrating colorectal injuries
- In extensive trauma of the pelvic floor
- In congenital malformations (anal atresia)

Efficacy of a Protective Stoma

There is controversy regarding the efficacy of a protective stoma today. Experimental as well as clinical data show evidence that the faecal stream has an important beneficial effect for anastomotic healing leading to a higher anastomotic strength as well as increased collagen synthesis. Since it is widely accepted that especially the formation of loop stomas does not result in a complete faecal exclusion of the bowel which should be covered, the use of a temporary stoma for protective purposes is more and more questioned. Furthermore, recent data are available showing the safety of elective colorectal surgery even without bowel preparation as well as with the introduction of early feeding and activation of peristalsis.

In contrast to these observations, low rectal anastomoses are regarded to be at higher risk for leakage, and

data from randomised trials suggest that although covering stomas do not influence the insufficiency rate, serious life-threatening infection might be prevented.

However, it must be taken into account that in large series only two thirds of all temporary stomas were closed while more than 30% of all patients kept their stoma permanently (due to the underlying primary disease, old age, bad general condition, etc.) or died before closure. In addition, closure of a stoma is not a procedure devoid of problems and the complication rate ranges from 16% to 35% with a mortality of 0–4%. The most common complications seen are wound infections, fistulas and incisional hernia, but also bowel obstruction as well as peritonitis have been observed.

In conclusion, the number of temporary stomas has markedly decreased in the recent past although a final conclusion about the necessity and the protective efficacy cannot be drawn at the moment.

Loop Ileostomy or Loop Colostomy?

In the 1980s many authors started to favour construction of loop ileostomies in order avoid problems associated with colostomies (i.e. higher incidence of parastomal hernias and/or stoma prolapse, incisional hernias following stoma closure, easier application of appliances with ileostomies). While some controlled studies with a limited number of patients showed evidence of a lower complication rate associated with the formation and following closure of ileostomies (lower rate of infections and incisional hernias) other data show a decrease in the number of obstruction problems following reversal of colostomies. Furthermore, it must be emphasised that for mere decompression of an obstructing process in the colon or rectum an ileostomy (if the ileocaecal valve is still competent) can sometimes be insufficient. However, especially in obese patients construction of a transverse loop colostomy or loop sigmoidostomy is technically so difficult that an ileostomy is the preferable procedure.

The choice of the type of loop stoma is, therefore, influenced by individual factors of the patient:

- Anatomical situation
- Weight and size
- Indication for the formation of a loop stoma
- Time span until stoma closure.

10.1.3 Stoma Construction

10.1.3.1 Stoma Site and Preoperative Counselling

The optimal location for the placement of a stoma is a prerequisite for satisfactory function and an acceptable application of stoma appliances. The site will depend on the anatomical position, type of the stoma, scars, the patient's build and clothing habits.

Anatomical sites of stomas (present surgical standard) are:

- Ileostomy: Over the right rectus muscle half way between the umbilicus and the anterior superior iliac spine, lying just below the midline and well away from the symphysis pubis and costal margin. If the right side is not accessible (e.g. scars after previous operations) a trephine can also be performed in the left rectus muscle.
- Transverse colostomy: Usually brought through the rectus muscle just right of the midline, well above the umbilicus but a safe distance from the costal margin.
- Sigmoidostomy: Through the left rectus muscle away from the inguinal ligament and midway between the umbilicus and the anterior superior iliac spine.

In elective stoma formation (or even when there is a possibility for the need of a stoma) it is mandatory to define the site preoperatively using ink and a stoma bag. The optimal position should be marked while sitting and standing as well as taking into account the usual clothing habits of the patients. A specialised stoma therapist should counsel the patient as well as the surgeon during this step in order to achieve an optimal position.

Preoperative counselling by a stoma therapist who will also follow the patient postoperatively and following hospital discharge is mandatory in order to reduce the negative effect of a stoma on quality of life (QOL). This includes introduction of stoma appliances, irrigation sets (if applicable) and dietary recommendations to the patient and to his/her relatives as well as communication with the patient, the family doctor and the surgeon in the further follow-up. Introduction of the patient to organised "patient stoma groups" is also possible in some countries and has been proven to be beneficial in order to influence the patient's concerns and fears preoperatively and to reduce postoperative problems, especially with regards to healthcare providers (e.g. insurance problems).

10.1.3.2 Surgical Techniques

Conventional (Open) Surgery

- Straight trephine through the abdominal wall (dimension: one thumb for an end stoma, two fingers for a loop stoma).
- Excise a cylinder of subcutaneous fat together with the skin.
- Division of the rectus sheath and the rectus muscle (parallel to the muscle fibres). For colostomies a cruciate incision of the rectus sheath may be advisable in order to create sufficient space for the sometimes bulky bowel. Avoid pulling the stoma lateral of the rectus muscle (increased risk of parastomal hernia).
- Division of the posterior rectus sheath and the peritoneum.
- Dissection of the ileum as close as possible to the ileocaecal valve for an end ileostomy (avoidance of high volume of secretion).
- Mobilisation of the stoma and its mesentery (vascular supply) through the abdominal wall without any tension.
- Closure of the lateral gutter with sutures between bowel wall, mesentery and the lateral peritoneum to prevent formation of an inner hernia (not uniformly accepted).
- Fixation of the stoma with absorbable mucocutaneous sutures and with a rod for loop stomas (all sutures, even if absorbable, must be removed after a period of 7–10 days in order to avoid inflammatory peristomal reaction as well as the formation of granulomas).

Laparoscopic Surgery

Laparoscopic stoma formation might be indicated either as part of a laparoscopically performed colorectal resection or (in rare cases) as a therapy on its own (Hartmann procedure for complicated fistula disease, faecal exclusion for severe pelvic soft tissue infection, palliative treatment of malignant colorectal obstruction). However, if indicated, laparoscopically constructed stomas have been shown to be beneficial with regard to a short hospital stay as well as an easier reversion of the stoma (if possible).

- Pneumoperitoneum can be created either by conventional technique (Veress needle) or by using the preparation of the trephine for an "open" approach.
- Trocar placement is performed as described for the technique for laparoscopic colorectal surgery (usually three 10- to 12-mm trocars).
- Ileostomies can be easily produced after identification of the terminal ileum by grabbing the bowel with an atraumatic Babcock clamp and pulling it through the abdominal wall while the trocar is retracted.
- Colostomies need more surgical preparation in terms of either mobilisation and/or dissection of the mesocolon in order to achieve stoma formation without tension.
- Hartmann's procedure needs the additional use of a laparoscopic stapling device for the closure of the rectal stump.
- Similar to "open" formation of a stoma, closure of the lateral gutter can be achieved.

10.1.4 "Continent" Stomas

There is no question that formation of a stoma will lead to a significant impairment of QOL and various studies have shown its negative impact on the different domains of daily life. Based on individual factors (social status, geographical origin, religion, lack of stoma therapists) this can lead to a complete deterioration of patient's QOL. Therefore, there have been continuous efforts to create stomas in which the evacuation of the bowel content can be voluntarily controlled by the patient; however, only those that have gained some role in the literature as well as in routine practice will be mentioned.

10.1.4.1 Stoma Irrigation

While irrigation of a colostomy has been accepted controversially by patients in the past, introduction of an easy-to-handle device has led to an increased popularity of this method in some countries. The great advantage of irrigation is that bulky appliances are not needed (the stoma is simply covered by cap) and it enhances the body image leading to an improvement in QOL. However, it requires a certain level of intelligence, toilet facility and stoma design as well as a certain training period with assistance of a specialised stoma therapist. Therefore, the acceptance of this effective method of bowel control varies among countries in Europe.

10.1.4.2 Colostomy Plug

A recently developed two-piece occlusive device is supposed to be able to occlude a stoma sufficiently and even absorb flatus. After first enthusiastic reports this method is mainly accepted by those patients who undergo irrigations in order to gain control of flatus (in more than 90%).

10.1.4.3 Total Anorectal Reconstruction (TAR)

The construction of a perineal colostomy ("neoanus") is a possibility especially for those patients in whom the body image ("abdomen without a bag") will be of the utmost importance. Various procedures have been described in the literature including mere stoma implant into the perineum, construction of a colonic conduit as well as formation of a muscle wrap ("neosphincter") around the perineal colostomy using skeletal muscles (gracilis or gluteus muscle). In order to achieve an acceptable continence these muscles have been additionally stimulated by an implanted neuromuscular stimulation system connected to a subcutaneous implanted pulse generator (dynamic graciloplasty). Since the major problem in patients following TAR was the problem of voluntary emptying of their neorectum, almost all patients will have to undergo regular irrigations, either retrograde via the perineal colostomy or antegrade via an appendicostomy or a colonic conduit (Malone procedure). Despite these and other problems (soiling, need of a pad) patients with a functioning TAR report a high degree of satisfaction as well as a marked improvement in their QOL. The future will show if the muscle wrap and/or the electrical stimulation will remain as necessary prerequisites for the functional success of this method.

10.1.4.4 Kock Ileostomy

In most patients surgical therapy will aim for a preservation of the anal canal, thus leaving the possibility for reconstruction by ileal pouch–anal anastomosis. However, some patients will have to undergo the formation of a permanent ileostomy. For these, the Kock ileostomy provides a possibility to overcome many of the problems associated with a permanent ileostomy. However, the construction is a technically demanding operation, revision rates for valve slippage range from 7% to 25% and serious complications such as obstruction, sepsis and fistula have also been reported. Although QOL (especially in young patients) is significantly improved by a functioning Kock stoma, metabolic problems, valve slippage and inflammation in the pouch are potential problems of this method.

10.1.5 Stoma Complications

10.1.5.1 Early Complications

Stoma Necrosis

Stoma necrosis is usually caused by impaired vascular supply due to technical problems during stoma formation or due to high tension and will occur within the first days following surgery. It must be distinguished from superficial focal necrotic areas around some mucocutaneous sutures in the mucosa of the stoma which have no clinical significance. However, total wall necrosis of stomas is a major problem since it will lead to retraction of the bowel wall back into the abdominal wall or even into the peritoneum. Early diagnosis and new formation of a well-vascularised stoma are the only therapeutic options.

10.1.5.2 Late Complications

Skin Excoriation and Infection

Skin excoriation is associated with liquid stomal effluent and/or badly fitting appliances (sometimes as a result of a bad stoma site). Patients with skin problems should be managed by cutting the wafer as close as possible to the circumference of the stoma in order to avoid any contact of the skin with bowel content. Sometimes it will also be necessary to fill selectively existing skin depressions with the wafer, thus leakage can be prevented.

Peristomal skin infection must be managed, depending on the extent of the problem, by local antibiotic ointments, local drainage, resiting of the stoma or formation of a more proximal "covering" stoma.

Stenosis

Stenosis rarely responds to dilatation. Refashioning will be the only solution in the long term.

Parastomal Hernia

A wide trephine in order to achieve a loop colostomy (especially in obese patients), obesity and/or increase of the intra-abdominal pressure, a stoma site lateral to the rectus muscle and delay of stoma closure in temporary loop stomas are the common reasons for the development of parastomal hernias. In temporary stomas stoma closure should be achieved as the most effective therapy. In permanent stomas parastomal hernias must be treated if appliances cannot fit appropriately anymore or if obstruction problems arise. The most successful strategy is resiting of the stoma on the contralateral abdominal side, however, local repair might be indicated in patients who are not candidates for a laparotomy or in whom the contralateral side is not appropriate for stoma placement (scars, infection). Direct repair of the defect in the abdominal wall and also mesh repair have been reported with varying results.

Prolapse

The aetiology of prolapse is not completely understood but it is thought to occur mainly in patients in whom the

bowel had been significantly dilated during stoma formation (e.g. due to obstruction). After reduction of the bowel size there remains a defect in the abdominal wall that allows the stoma to slip. While manual repositioning might be necessary in the acute situation, definitive surgical treatment is indicated in most of the patients in the long term. Local reduction of the prolapsed bowel (amputation, colopexy) should be reserved only for people not fit or willing to undergo new stoma formation as the long-term results are unsatisfactory.

Ileostomy Flux

Ileostomy flux is characterised by water fluid discharge with a total volume more than 1.5 l/24 h and requires repeated emptying of the stoma bag in order to avoid leaking. The aetiology of ileostomy flux can be a too proximal small-bowel stoma (jejunostomy), short-bowel syndrome, intra-abdominal sepsis, gastroenteritis, intestinal obstruction and, in many patients, completely unknown. Since this complication can be very quickly life-threatening due to dehydration and insufficient absorption of necessary medications, early admission and intravenous fluid replacement are recommended. Oral intake of water, sweet drinks and salt aggravate the secretion and, therefore, the consumption of isotonic electrolyte drinks up to a total volume of 1 l/day should be recommended. Additionally, drugs such as codeine and somatostatin analogues are helpful in special situations.

Suggested Reading

1. Boman-Sandelin K, Fenyo G (1985) Construction and closure of the transverse loop colostomy. Br J Surg 69:19–22
2. Deen K, Madoff R, Goldberg S et al (1998) Surgical management of left colonic obstruction: The University of Minnesota experience. J Am Coll Surg 187:573–576
3. Gonzales R, Falimirski M, Holevar M (2000) Further evaluation of colostomy in penetrating colon injury. Am Surg 66:342–346
4. Gooszen AW, Geelkerken RH, Hermans J et al (1998) Temporary decompression after colorectal surgery: randomized comparison of loop ileostomy and loop colostomy. Br J Surg 85:76–79
5. Hardy KJ (1989) Evolution of the stoma. Aust N Z J Surg 59:71–77
6. Kairaluoma M, Rissanen H, Kultti V, Mecklin JP, Kellokumpo I (2002) Outcome of temporary stomas. Dig Surg 19:45–51
7. Kehlet H, Willmore DW (2005) Fast-track surgery. Br J Surg 92:3–4
8. Lasser P, Dube P, Guillot JM, Elias D (2001) Pseudocontinent perineal colostomy following abdominoperineal resection: technique and findings in 49 patients. Eur J Surg Oncol 27:49–53
9. Livingstone DH, Miller FB, Richardson JD (1989) Are the risks after colostomy closure exaggerated? Am J Surg 158:17–20
10. Miettinen R, Laitinen S, Makela J (2000) Bowel preparation with oral polyethylene glycol electrolyte solution vs. no preparation in elective open colorectal surgery. Prospective, randomised study. Dis Colon Rectum 43:669–675
11. Oliveira L (2003) Laparoscopic stoma creation and closure. Sem Laparoscop Surg 10:191–196
12. Pakkastie TE, Ovaska JT, Pekkala ES et al (1997) A randomised study of colostomies in low colorectal anastomoses. Eur J Surg 163:929–933
13. Patey DH (1951) Primary epithelial apposition in colostomy. Proc R Soc Med 44:423–9
14. Rosen HR, Schiessel R (1999) Das Deviationsstoma. Chirurg 70:650–655
15. Sprangers MAG, Taal BG, Aaaronson NK et al (1995) Quality of life in colorectal cancer: stoma vs nonstoma patients. Dis Colon Rectum 38:360–369
16. Uden P, Blomquist P, Jiborn H et al (1988) Influence of proximal colostomy on healing of a left colon anastomosis: an experimental study in the rat. Br J Surg 75:325–330
17. Williams NS, Nasmyth DG, Jones D (1986) Defunctioning stomas: a prospective controlled trial comparing loop ileostomy with loop transverse colostomy. Br J Surg 73:566–572

Endoscopy

11.1 Diagnostics, Therapeutic, Surveillance, New Techniques

SØREN MEISNER

11.1.1 Introduction

Endoscopy means looking inside and refers to an examination of the interior of a canal or hollow organ by means of an endoscope. Flexible endoscopy of the colon and rectum was introduced in 1963. The procedure is a primary diagnostic and therapeutic tool for evaluation and treatment of colorectal diseases.

11.1.2 Diagnostic Endoscopy of the Colon and Rectum

11.1.2.1 Flexible Sigmoidoscopy

Flexible sigmoidoscopy is direct examination of the rectum, sigmoid and descending colon (≤ 70 cm) by means of a flexible endoscope.

Indications

Common indications include:

- Evaluation of patients with lower gastrointestinal (GI) bleeding
- Evaluation of suspected lower GI pathology
- Evaluation of suspected inflammatory disease of the colon and rectum
- Decompression of sigmoid volvulus
- Cancer surveillance after surgical resection/endoscopic resection (rule out local intraluminal recurrence)
- Screening for colorectal cancer

Contraindications

There are few absolute contraindications. Flexible sigmoidoscopy should be avoided in:

- Severe diverticulitis (unless carcinoma is highly suspected)
- Acute peritonitis
- Toxic megacolon/toxic colitis
- Severe cardiopulmonary disease (acute or recent myocardial infarction)
- Signs of intestinal perforation
- Massive GI bleeding
- Severe coagulopathy
- If clear indication for full colonoscopy

Patient Preparation

- Informed consent on the basis of information given to the patient:
  - Goals
  - Technique
  - Risks
  - Alternatives
- Bowel preparation (several options are possible): 90% adequate bowel preparation is obtained by a single phosphosoda enema administered several minutes before the procedure.
- Sedatives, narcotics or anaesthetics are not necessary in the majority of patients
- After the examination patients can resume their prior level of activity

Complications

Sigmoidoscopy is safe and complications are rare. Reported complications are:

- Local pain
- Bleeding
- Bacteraemia
- Cardiac arrhythmia
- Bowel perforation (≤ 0.01%)

Technique

The endoscopy report should include:

- Indication for endoscopy
- Type of instrument
- Adequacy of bowel preparation
- Depth of scope insertion
- Appearance of the mucosa
- Abnormalities found:
  - Anorectal abnormalities
  - Polyps
  - Pseudopolyps

  - Mucosal fissures
  - Neoplasia
  - Ulcers
  - Friable regions
  - Blood
  - Pus
  - Diverticula
  - Others
- Therapeutic procedures performed
- Biopsy sites
- Intraoperative complications
- Recommendations/plan

11.1.2.2 Colonoscopy

The designation "diagnostic" or "therapeutic" procedure can only be assigned after the procedure. It is generally unacceptable to perform diagnostic procedures without the skill to perform therapeutic manoeuvres that are likely to be indicated. All colonoscopists must be trained in polypectomy and perform colonoscopy with intent to clear the colon of polyps at initial examination.

Indications

In clinical practice, opinions differ regarding indications for colonoscopy. Standard indications are:

- Evaluation of an abnormality seen on barium enema or virtual colonoscopy
- Evaluation of unexplained gastrointestinal bleeding:
  - Melaena after upper GI source has been excluded by gastroscopy
  - Presence of faecal occult blood (FOBT positive)
  - Unexplained iron-deficiency anaemia
- Follow-up/surveillance after polypectomy of adenomas
- Follow-up/surveillance after resection of colorectal cancer
- Clearing the colon of synchronous neoplasia (polyps or cancer) in patients with colorectal cancer
- After identification of adenomas by sigmoidoscopy
- Follow-up/surveillance of ulcerative pancolitis
- Follow-up/surveillance of Crohn's colitis
- Colorectal cancer screening
- Chronic inflammatory bowel disease of the colon (more precise diagnosis, determination of extent and/or activity of disease)
- Significant diarrhoea of unexplained origin
- Intraoperatively to localise a lesion not apparent at surgery

Generally Accepted Non-indications/ Relative Indications

- Irritable bowel syndrome
- Acute self-limited diarrhoea
- Stable inflammatory disease (exception of cancer surveillance)
- Melaena with a clear suspicion of upper GI source
- Haematochezia with a clearly identified anorectal source seen on sigmoidoscopy

Contraindications

- Severe diverticulitis (unless carcinoma is highly suspected)
- Acute peritonitis
- Toxic megacolon/toxic colitis
- Severe cardiopulmonary disease
- Signs of intestinal perforation
- Massive GI bleeding
- Severe coagulopathy
- Patients unable to cooperate and cannot be adequately sedated

High-risk Situations (Relative Contraindications)

- Uncontrolled lower GI bleeding (haemodynamic instability)
- Recent colorectal anastomosis
- Multiple previous pelvic operations
- Severe chronic obstructive pulmonary disease (COPD) or severe arteriosclerotic heart disease (ASHD)
- Acute or recent myocardial infarction/pulmonary embolism
- Large and/or symptomatic abdominal aortic aneurysm
- Pregnancy in third trimester

Patient Preparation

Informed Consent on the Basis of Information Given to the Patient

- Goals
- Technique and possibility of biopsy, polypectomy or other applicable procedure
- Related risks
- Alternatives

Bowel Preparation

Thorough bowel cleaning is mandatory. There are a wide variety of methods using diet restrictions with various purgatives and laxatives. Three normally used options are:

- *Diet and cathartics:* Clear liquids for 72 h or a low residual diet for 1–3 days. Cathartics such as magnesium citrate and Bisacodyl. Tap-water enema the evening or morning before procedure.
- *Gut lavage:* Peroral gut lavage with osmotically balanced electrolyte solutions such as polyethylene glycol electrolyte lavage solution (PEG-ELS). Volume 2–4 l (lavage rate 1.5 l/h). Several adverse experiences have been reported and include disagreeable taste, hypothermia, fullness, nausea, bloating, aspiration, reactivation of bleeding, oesophageal tear, perforation, malabsorption of medication, allergic reaction (angiooedema, urticaria, anaphylaxis).
- *Phosphates:* Available in solutions or tablets they are an attractive alternative as less volume needs to be ingested. Oral sodium phosphates 45 ml diluted with water to 90 ml evening before and repeated 4 h prior to colonoscopy. The solution is very hypertonic. Adverse experiences have been reported and include: electrolyte disturbances, hyperphosphataemia, hypocalcaemia, vomiting, dehydration, colonic aphthous ulceration, seizures.

Contraindications for colonoscopy bowel preparation:
- If gastric or bowel obstruction is suspected
- Gut lavage should be avoided in gastroparesis

Increased risk exists in patients with:
- Congestive heart failure
- Ascites
- Renal insufficiency
- Dehydration
- Debility
- GI obstruction
- Gastric retention
- Colitis
- Megacolon
- Ileus
- Diuretics or medications affecting electrolytes

Premedication and Sedation

Based on tradition, culture and economics, acceptance of colonoscopy can differ from country to country. Sedation and analgesia are commonly provided for the performance of colonoscopy. The goal is to increase patient tolerance for the procedure and to increase satisfaction for both patient and endoscopist. Standard sedation is safe and effective when administered by the endoscopist.
- Combination of narcotic and benzodiazepine.
- Unsedated colonoscopy can be done in selected patients.
- Propofol is an excellent sedative, however, it can cause profound apnoea and needs to be administered by an anaesthesiologist or others with special/similar training.

Special Considerations

The risk for bacteraemia during colonoscopy is low. There is no consensus on the need for antibiotic prophylaxis for bacterial endocarditis for patients undergoing colonoscopy. In patients with prosthetic valves, history of endocarditis, rheumatic valvular disease or other high-risk cardiac disease it is common to administer antibiotics. Several accepted regimen can be used depending on local guidelines.

Complications

Major complications:
- Perforation (estimated at 0.14–0.8%)
- Haemorrhage (negligible, 0–0.5%)
- Respiratory depression (oversedation, especially in patients with chronic lung disease)
- Bacteraemia (incidence varies from 0% to 0.5%)

Other complications:
- Vasovagal reactions
- Splenic laceration
- Transient ECG changes
- Dehydration resulting from the bowel cleansing
- Volvulus
- Explosion of combustible gases in the colon (H_2, methane) when in contact with an electric spark

Technique

The endoscopy report should include:
- Indication
- Type of instrument
- Adequacy of bowel preparation
- Premedications used, antibiotic prophylaxis if given
- Most proximal bowel segment examined
- Appearance of the mucosa
- Abnormalities:
  - Anorectal abnormalities identified
  - Polyps (number, size, appearance)
  - Pseudopolyps
  - Haemorrhagic areas
  - Ulcers/fissures
  - Neoplastic or obstructing lesions
  - Diverticula
  - Friable regions
  - Lipomas
  - Telangiectasia
  - Spasm
  - Competence of ileocaecal valve

  - Blood
  - Pus
  - Others
- Therapeutic procedures performed
- Biopsy sites
- Complications
- Recommendations/plan

Alternatives to Diagnostic Colonoscopy

Virtual Colonoscopy

Computed tomography (CT) for image acquisition is the most preferred method. Some centres use magnetic resonance imaging (MRI). Bowel preparation with complete cleaning of the colon together with colonic insufflation of gas is needed for CT virtual colonoscopy.

Indications/clinical role of virtual colonoscopy:

- Evaluation of the colon proximal to an incomplete conventional colonoscopy
- Evaluation of the colon proximal to an obstructing neoplasm
- Evaluation in patients who are not fit for conventional colonoscopy due to:
  - Chronic obstructive lung disease
  - Bleeding diathesis
  - Allergic reactions to sedation
- Colorectal cancer screening
- Patients who refuse colonoscopy

Double-contrast Barium Enema (DCBE)

- Higher risk of missing colorectal cancer than colonoscopy
- Sensitivity of 50% for adenomas < 1 cm in diameter
- Biopsy or treatment is not possible
- Rectum and anal canal not adequately visualised

Barium enema is most appropriate if imaging of the colon is necessary:

- Under 50 years old
- No family history of colorectal cancer
- Non-bleeding symptoms

11.1.3 Therapeutic Endoscopy

11.1.3.1 Polypectomy

The ability to find and remove colon polyps is one of the major reasons for colonoscopy and removal of polyps has made an impact on the incidence, morbidity and mortality of colorectal cancer.Safe polypectomy means:

- Removal of the polyp
  - Transection with a snare loop
  - Sufficient biopsies to excise
- Achieving haemostasis
  - Heat/coagulation
- Maintaining the integrity of the colon wall

Snare Loops

There are a wide variety of shapes and sizes available. The operator should be familiar with a few types only.

Polypectomy Technique

There are a few important steps:

- Mark the handle at the point that the snare is just closed at the tip
  - Possible to estimate tissue volume in the closed snare
- Check for a smooth "feel" when moving the handle open and closing the snare
  - Maximum feedback to the assistant controlling the snare
- Be aware of snare-wire thickness
  - Greatly affects the speed of electrocoagulation and transection of the polyp
- Be aware of the squeeze pressure
  - If squeeze pressure is inadequate, transection relies on high-power cutting, increasing the risk for bleeding due to insufficient coagulation of stalk vessels

Additional Devices

Hot Biopsy Polypectomy Forceps

These are used to destroy small polyps up to 5 mm in diameter, enabling simultaneous cautery of a polyp base while obtaining a biopsy specimen. The rationale for diminutive polyp eradication is to destroy neoplastic tissue and possibly prevent colon cancer. However, convincing data are lacking. Complications of hot biopsy include haemorrhage, perforation and postcoagulation syndrome. Tissue injury is deeper with monopolar hot biopsy forceps than bipolar forceps. The right colon is particularly susceptible to transmural injury and perforation.

Polyp Retrieval

Devices designed for polyp retrieval include:

- Multipronged grasping forceps

  - Consists of two to five wires with angled ends contained within a plastic sheath
- Baskets
- Nylon net
  - The Roth retrieval net device is comprised of a gauze net over a retractable loop that captures the polyp after snare polypectomy
- Polyp suction trap
- The polypectomy snare may be employed to lasso the severed polyp

Injection Needles

Injection needles have multiple uses and are a ubiquitous feature of endoscopic practice.

- Resection of sessile polyps may be aided by the injection of saline solutions (physiological saline or hypertonic saline, with or without epinephrine) into the submucosa, raising the polyp and facilitating polypectomy.
- Submucosal injection of India ink to tattoo the colon has been used to mark lesions for subsequent surgical identification and to mark polypectomy sites for follow-up.
- Bleeding areas, such as colonic diverticula, have been successfully treated with epinephrine injection. Epinephrine injection has been used to help control postpolypectomy haemorrhage.
- Strictures associated with Crohn's disease have been treated with steroid injection and balloon dilation.

Dye-spray Cannulas

Chromoendoscopy (see *Chromoendoscopy*)

Clipping Devices

The mechanism of haemostasis is mechanical compression by a metallic clip. Clips are loaded onto the fixing device and drawn into a sheath. At the target lesion, the clip is advanced out of the sheath, oriented with the rotational handle, and then deployed.

- Haemostasis after polypectomy

Nylon-loop Devices

A detachable nylon loop can be deployed to ensnare target tissue. Uses include:

- Strangulation of polyp stalk (prevent bleeding)
- Treatment of postpolypectomy bleeding

Complications to Polypectomy

Bleeding

Bleeding is relatively rare, less than 1.5%. In comparison, bleeding after diagnostic colonoscopy is around 0.1%.

Immediate Bleeding

- Bleeding is usually a slow ooze but can be an arteriolar spurt.
- Treatment is usually done by injection of adrenalin-saline solution.
- Stalk bleeding can be treated by resnaring the remnant stalk.
- Haemostatic clips can be applied to the polyp transection area.

Secondary (Delayed) Haemorrhage

- It can occur up to 2 weeks after polypectomy, particularly after removal of larger polyps.
- It usually is self-limiting but may require re-endoscopy and haemostatic treatment.

"Postpolypectomy Syndrome"

Incidence is between 0.5 and 1%. It is defined by fever, pain and localised signs of peritonitis/peritonism. It represents a "closed perforation" with full-thickness heat damage to the bowel wall. Conservative treatment with bed rest and antibiotics is indicated and the syndrome very rarely leads to surgical intervention.

Perforation

Perforation is very rare, between 0.1 and 0.3%. Management may be conservative, depending on the site of the polyp. Free air on x-ray is not an absolute indication for laparotomy. A surgeon should always be consulted. Occasionally, laparoscopy and suturing of a small perforation in a well-prepared bowel is possible.

11.1.3.2 Balloon Dilation

Balloon dilators deliver a dilating force radially and simultaneously over the entire length of a stenosis rather than progressively from its proximal to its distal extent (compared to bougienage where dilation is accomplished by the radial vector of an axially directed force). Since little or no axial force is exerted with balloons, shear stress is significantly reduced.

Two basic types of balloons are available:
- One type designed for fluoroscopic placement over a guidewire
- One type designed to be passed through the working channel of an endoscope directly or over a guidewire

In the colon and rectum, most strictures dilated with balloons have been anastomotic. Symptoms of obstruction and pain are relieved in most patients. Over 75% of patients normally need redilation after 4 weeks, and then most remained asymptomatic for 1–2 years. Diverticular, inflammatory, ischaemic and malignant strictures can also be an indication.

11.1.3.3 Argon Plasma Coagulation

The argon plasma coagulator (APC) is a device intended for non-contact thermal coagulation of tissue with many potential uses. The APC is a non-contact electrocoagulation device that uses high-frequency monopolar current conducted to target tissues through ionised argon gas (argon plasma). Coagulation depth is dependent on generator power setting, flow rate of the argon gas, duration of application and distance of the probe tip to the target tissue.

Vascular Ectasias

The APC has been used successfully to treat vascular ectasia of the upper and lower digestive tract including gastric antral vascular ectasia syndrome (GAVE), sporadic angiodysplasia, haemorrhagic telangiectasia and radiation-induced enteropathy and proctopathy.

Polyps and Remnant Adenomatous Tissue After Polypectomy

The APC can be used for ablation of intestinal polyps as well as for ablation of residual adenomatous tissue after colonic polypectomy.

Tumour Destruction and Palliation

The APC may also be used to treat T1 tumours of the rectum in patients deemed unsuitable for surgical excision. APC has also been used to recanalise occluded or overgrown metal stents or to cut displaced metal stents.

Complications

The APC is widely used and is safe. Reported complication rates range from 0% to 24% and include:
- Gaseous distension
- Pneumatosis intestinalis
- Pneumoperitoneum
- Pain at the treatment site
- Chronic ulceration
- Stricture
- Bleeding
- Transmural burn syndrome
- Perforation

11.1.3.4 Self-expanding Metal Stents

- Self-expanding metal stents (SEMS) are used for the non-surgical relief of malignant colorectal obstruction.
- Emergency operation is associated with a high morbidity and mortality and often results in stoma construction. SEMS are becoming more widely used to avoid emergency operations and to reduce the need for a stoma.
- They may be used as a bridge to surgery, allowing decompression of an obstructing lesion and formal resection as a elective procedure at a later date.
- Lastly, SEMS may be used in a palliative procedure in patients with unresectable local or metastatic disease.

SEMS: Techniques for Placement

Radiological Placement

- The obstruction is located fluoroscopically using water-soluble contrast medium.
- The stricture is then traversed with a guidewire, over which the stent is inserted and released under fluoroscopic guidance.

Combined Endoscopic/Fluoroscopic Placement

- If the obstruction cannot be passed with the scope, the length and configuration of the stenosis are demonstrated fluoroscopically by injecting water-soluble contrast.
- After this, the obstruction is negotiated with a guidewire.
- The stent delivery system can now be inserted through the scope, and the stent is released under both endoscopic and fluoroscopic guidance.
- In 85–100% of patients the stents effectively palliated obstruction for more than 1 year.

Complications of SEMS

Complications may occur during the procedure, soon after (early complications) or late after placement. Major

complications such as perforation (< 4%) and bleeding (< 5%) are rare. Mainly two types of complications are seen (late complications):

- Reobstruction (10%) due to tumour ingrowth; it can be treated with restenting
- Distal stent migration (10%) may be completely asymptomatic, but, if obstructive symptoms occur, a new stent can be placed in the tumour stricture. The procedure-related mortality is very low (0.5–1%).

11.1.4 Surveillance

11.1.4.1 Postpolypectomy Surveillance

After removal of benign adenomas/adenomatous polyps, there is a 30–50% likelihood of developing a metachronous adenoma. Removal of colon polyps will, to a large extent, protect the patient from developing carcinoma by interrupting the adenoma-carcinoma sequence. Not all patients have the same likelihood of developing metachronous adenomas, therefore follow-up colonoscopic examinations need to take into account the individual patient's risk for developing metachronous adenomas. Postpolypectomy surveillance strategies should be tailored accordingly and patients should be stratified into high- and low-risk groups (Table 11.1.1).

Recommendations for Benign Polypectomy

- Complete colonoscopy should be performed at the time of the initial polypectomy to detect and resect all synchronous adenomas.
- Additional clearing colonoscopies may be required after resection of large sessile adenoma if there is uncertainty that all adenomas have been found and removed.
- Surveillance colonoscopy according to a risk stratification, see Table 11.1.1.
- Selected patients at low risk for metachronous advanced adenomas may not require follow-up.
- After one negative follow-up surveillance colonoscopy intervals may be increased to 5 years.
- If surveillance colonoscopy is not feasible/possible, flexible sigmoidoscopy followed by a double-contrast barium enema or virtual colonoscopy is an acceptable alternative.
- It is important to individualise follow-up surveillance according to the age and comorbidity of the patient.

Recommendations for Malignant Polyps

- Because the risk for local recurrence or of lymph node metastasis from invasive carcinoma in a endoscopically resected polyp is less than the risk for death from colonic resection, no further treatment is indicated after endoscopic resection of a malignant polyp if the endoscopic and pathological criteria listed below are fulfilled:
  - The polyp is considered completely excised by the endoscopist and is submitted complete for pathological examination.
  - The cancer is not poorly differentiated.
  - There is no vascular or lymphatic involvement.
  - The margin of the excision is not involved.
- Follow-up endoscopic examination should be performed in 3 months to check for residual abnormality at the polypectomy site (it can be useful to mark the polypectomy site with India ink).
- After one negative examination, standard surveillance as recommended for benign polyps.

Table 11.1.1 Recommended surveillance strategies

Risk group	Inclusion criteria	Surveillance strategy
High risk	Removal of large (> 1 cm) or multiple (> 2) adenomas	Colonoscopy interval 3 years
	Adenoma with the advanced pathological features of villous change, high-grade dysplasia or invasive carcinoma	
	Family history of colorectal cancer	
Low risk	Less than 3 small (< 1 cm) tubular adenoma	Colonoscopy interval 5 years
	High-grade dysplasia absent	
	Absent family history of colorectal cancer	

11.1.4.2 Colonoscopy Surveillance After Colorectal Cancer Resection

- All patients must have complete imaging of the large bowel in the perioperative period to detect synchronous cancer and adenomas.
- If that examination is normal, subsequent colonoscopy should be offered after 2 and 5 years and, if normal, every 5 years.
- There is no evidence for shorter intervals and it is not indicated to use colonoscopy to detect intraluminal local recurrent cancer.
- Anastomotic recurrences are rare and are often not resectable for cure.

11.1.5 New Techniques

Efforts are directed to the earlier diagnosis of GI neoplasia at the dysplasia level. A limitation of conventional white light endoscopy is that it cannot detect occult dysplasia, differentiate hyperplastic from adenomatous polyps or easily detect recurrence at the scar site of previously snared flat, spreading villous adenomas. The following are the imaging light-based technologies that are now being studied for dysplasia detection:

- Chromoendoscopy
- Magnifying colonoscopy (with chromoendoscopy)
- Spectroscopic:
  - Fluorescence
  - Raman spectroscopy
  - Light-scattering spectroscopy
- Optical coherent tomography (OCT)
- Narrow-band imaging (NBI)

11.1.5.1 Chromoendoscopy

Chromoendoscopy (CE) is a technique in which tissue stains or dyes are applied to the gastrointestinal mucosa. It may or may not be combined with magnification endoscopy (ME) or high-resolution endoscopy (HE). Tissue stains can be classified into three categories:

- Absorptive stains (vital stains) identify specific epithelial cell types or cellular constituents
- Reactive stains identify cellular products
- Contrast stains are not absorbed by epithelial tissue and highlight tissue topography

11.1.5.2 Magnifying Colonoscopy

Magnifying endoscopy, with or without dye spraying, has been developed to allow fine topographical details to be seen. Magnification has been primarily studied in the colon using dye spraying to clarify abnormalities already seen by conventional endoscopy. The combination of chromoendoscopy and magnifying colonoscopy is used for classification of adenomas and experts can differentiate adenomatous versus hyperplastic polyps.

11.1.5.3 Spectroscopic Endoscopy

Changes in tissue may be detected by measuring light scattering or absorption. There are several new techniques under evaluation that may allow more accurate detection of adenomatous or dysplastic changes in gastrointestinal mucosa.

11.1.5.4 Narrow-band Imaging (NBI)

A newly developed endoscope lighting system called a narrow-band imaging system emphasises certain histological features such as capillary and crypt patterns. Conventionally, enhancement of surface patterns is achieved by dye staining (chromoendoscopy), which can be laborious, especially in the colon, where large areas should be stained. NBI may eliminate the need for dye staining. However, background inflammation may be a confounding factor, especially in surveillance of dysplasia in inflammatory bowel disease.

11.1.6 Summary

- Endoscopy is a valuable procedure in the diagnostics and in the treatment of diseases in the colon and rectum.
- Diagnostic endoscopy remains the golden standard for investigation of the large bowel. New developments will increase the sensitivity and specificity in diagnosis.
- Therapeutic endoscopy has evolved with availability of new technologies. Techniques for endoscopic removal of large polyps and stent placement have obviated the need for surgical intervention in selected patients.

Suggested Reading

1. American Society For Gastrointestinal Endoscopy (1998) Colonoscopy in the screening and surveillance of individuals at increased risk for colorectal cancer. Gastrointest Endosc 48:676–678.
2. Bond JH (2000) Polyp guideline: diagnosis, treatment, and surveillance for patients with colorectal polyps. Am J Gastroenterol 95:3053–3063
3. Cotton PB, Williams CB (eds) (2003) Practical gastrointestinal endoscopy: the fundamentals. Blackwell Science, Edinburgh
4. DaCosta RS, Wilson BC, Marcon NE (2004) Optical techniques for the endoscopic detection of dysplastic colonic lesions. Curr Opin Gastroenterol 21:70–79
5. Dekker E, Fockens P (2004) New endoscopic tools for the IBD physician. Inflamm Bowel Dis 10(suppl 1):S7–S10
6. Waye JD, Rex D, Williams CB (eds) (2004) Colonoscopy, principles and practice. Blackwell Science, Edinburgh
7. Winawer S, Fletcher R, Rex D, Bond J, Burt R, Ferrucci J, Ganiats T, Levin T, Woolf S, Johnson D, Kirk L, Litin S, Simmang C (2003) Colorectal cancer screening and surveillance: clinical guidelines and rationale. Update based on new evidence. Gastroenterology 124:544–560

Emergencies

12.1 Anal and Rectal Trauma

DONATO F. ALTOMARE

12.1.1 Introduction

Anal and rectal traumas are relatively rare, except as a result of iatrogenic damage, thanks to the anatomical position of the anorectum (protected by the pelvic bones, the sacrum and pelvic floor muscles). Owing to its relatively superficial position the anus is more frequently injured, but traumas involving the extraperitoneal rectum although more rare, are often more severe and extend to the neighbouring organs. The aim of surgery, as in any trauma, is to preserve life followed by controlling infections and, in these cases, to preserve the patient's faecal continence and evacuation function.

12.1.2 Aetiology

- *Blunt (closed) trauma:* Rarely affect the anus or the rectum without involving the pelvic bones and is usually a consequence of motor vehicle accidents or accidental falls from stairs and scaffolding.
- *Childbirth:* Cephalopelvic disproportion during delivery can lacerate the vagina, tearing the perineal body. Midline episiotomy can facilitate the progress of the laceration through the sphincters, anal canal and rectum and should be avoided.
- *Ingested foreign bodies:* Several small sharp particles ingested voluntarily (such as nails in psychiatric patients), or accidentally (fish or chicken bones, walnut husk, fragments of glass, toothpicks, dentures) can reach the rectum and become entrapped in the rectal wall or sphincter muscles, leading to perforation or abscess formation. A new type of ingested foreign body includes drugs wrapped in plastic packets. Breakage of the package during endoscopic or surgical attempts to remove it may cause a life-threatening drug overdose.
- *Foreign bodies introduced per anum:* An amazing variety of oblong objects (phallic-like objects) have been introduced into the rectum and remained trapped above the anal sphincters, the most frequent being bottles, plastic dildos and vibrators, vegetables, electric light bulbs, pens, glasses, etc. usually in an attempt at autoerotism or during sexual assault. Sometimes thermometers can get lost in the rectum when taking the temperature in children and may break causing penetrating injuries to the rectal wall.
- *Sexual assault per anum:* In both men and women it may be the result of too vigorous an anal sex act voluntarily accepted by both partners or may be a criminal act sometimes performed on children (particularly young boys).
- *Pneumatic injuries:* Explosion of the rectum and colon provoking severe abdominal pain and shock can be caused by a sudden increase of the intrarectal pressure if compressed air is injected through the anus as a foolish and criminal joke.
- *Iatrogenic diagnostic/therapeutic injuries:* These can be due to:
  - Enema (the enema nozzle may cause mucosal laceration and rectovaginal fistulas, or using too hot water can cause severe mucosal burns)
  - Barium enema
  - Rectal biopsy, which can cause bleeding and perforation
  - Diathermy polypectomy, which can cause explosion of the colonic gases (methane, hydrogen sulphide, hydrogen)
  - Rectoscopy, sigmoidoscopy
  - Surgery for anal fissures, haemorrhoids, fistulas and abscesses
  - Surgery for prostate, bladder and uterine diseases
- *Penetrating injuries:* Sharp anorectal injuries due to stab or gunshot wounds. These should be classified as intraperitoneal (more frequent) and extraperitoneal wounds.
  - Stab wounds involving the anus or the extraperitoneal rectum are rare in western countries but may arise as part of a complex anoperineal trauma in car or motorcycle accidents. Penetrating stab wounds involving the intraperitoneal rectum may be produced by knives or daggers and need to be treated like any colonic injury.
  - Gunshot wounds are relatively frequent in wartime due to the prone position assumed by soldiers while firing, and the rectal damage depends on the ballistic properties of the projectile. High-velocity

bullets (military) produce a small entrance hole but extensive tissue damage, multiple perforations and a large exit wound, whilst low-velocity bullets (civilian use) are often retained in the tissues.

- *Rectal impalement:* This was used to torture and kill enemies in ancient times, but can still be observed following unfortunate falls onto pointed objects. This may happen, for example, in agricultural workers during accidental falls onto agricultural tools or a picket fence with the legs astride, or in an accidental fall in sports involving climbing or jumping. The penetrating trauma can involve the anus, the anal sphincters and the rectal wall, but can also extend to the sacrum and coccyx, the perineum, the prostate, the urethra and the bladder, as well as intraperitoneal organs, especially small and large bowel. Such a severe trauma has also been described as the outcome of a criminal act.

12.1.3 Diagnosis

- Enquiry into the patient's history and an exploration of the perineum and abdomen are the first steps in any anorectal trauma. Sometimes patients are reluctant to admit anal intercourse or autoerotism resulting in retention of foreign bodies. Perianal ecchymosis or laceration are usually present in any sexual assault, and sometimes sperm may also be found. Due to legal issues, special care is taken to prove the assault with photographs or stains, allowing eventually identification after rape for instance.
- A retained foreign body may be felt by lubricating anal digital exploration, although in most cases the foreign body migrates distally into the rectosigmoid colon. An abdominal X-ray can usually assist diagnosis. A colonoscopy could be necessary for diagnosis and treatment of a retained foreign body.
- Abdominal pain, tenderness, ileus and high temperature after a rectal trauma should suggest perforation and peritonitis.
- Minor anorectal trauma and retention of foreign bodies may cause anal and abdominal pain and rectal bleeding, and reflex urinary retention. The occurrence of perianal-perirectal abscess formation induces a high temperature and severe pain, sometimes leading to general sepsis.

The type of management and the prognosis depend on the severity of the disease. An attempt to quantify the severity of the anal trauma was made by the American Association for the Surgery of trauma who proposed the Rectal Injury Scaling System (RISS) with five degrees of severity. A simpler classification of rectal injuries was made by McGrath at al. between intraperitoneal and extraperitoneal rectal trauma on the basis of rectal anatomy.

12.1.4 Management

- Severe anorectal trauma must be managed like any other trauma (Fig. 12.1.1): control of bleeding and immediate resuscitation of the patient are the first steps in emergency treatment.
- Recommended in anorectal trauma examination under anaesthesia (EUA): Control of infection by the so-called 4-D treatment is mandatory in cases of severe penetrating (stab or gunshot) wounds
  - Distal rectal wash-out
  - Diversion of the faecal stream
  - Drainage
  - Damage repair
- The necrotic tissue, foreign bodies and faeces must be accurately removed from the wounds which also need to be irrigated with antiseptic solutions. The perirectal spaces must be drained with a Penrose or a suction drainage and a diverting left colostomy should be performed immediately.
- Full-dose antibiotic therapy including anti-gram-negative anaerobe bacteria antibiotics (metronidazole, tobramycin) and tetanus antitoxin should be started as soon as possible because of the considerable risk of severe infections. Administration of general analgesics can be necessary.
- Major anorectal trauma with impalement or destruction of the perineum and external herniation of the small bowel (Fig. 12.1.2) may require complex recon-

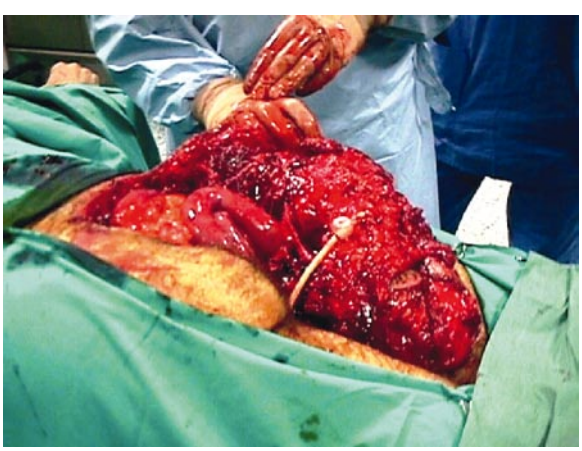


Fig. 12.1.1 Management of anorectal trauma

structive surgery with a left colostomy, anorectal resection, urinary tract repair and complete closure of the perineum.

- Rectal perforation can be sutured and a protective left colostomy should be performed. A distal rectal washout using dilute povidone-iodine solution through a mucous fistula or per anum is recommended.
- Anorectal endoscopy is necessary in every case of anorectal trauma to evaluate and control rectal bleeding, facilitate cleaning of the faeces and damaged tissues, and locate foreign bodies. It should not, however, be performed if perforation of the extraperitoneal rectum is suspected.
- The patient should be positioned in the lithotomy position except for selected cases of posterior trauma involving the sacrum and coccyx where the prone position could provide better exposure of the traumatised area.
- Local anaesthesia may be sufficient in minor anal traumas but spinal or general anaesthesia is generally preferred for most anorectal traumas.
- Placement of a urinary catheter is mandatory in order to exclude lesions of the urinary tract. Sometimes multislice MRI, or, if not available, water-soluble contrast (Gastrografin, Hypaque) enema, and i.v. urography may aid in the recognition of extrarectal organ and tissue involvement.
- In cases of suspected intraperitoneal perforation laparoscopy (in stable patient) could be performed as a preliminary step.
- Laparotomy may be necessary in cases of disseminated peritoneal contamination, bleeding and perforation. These complex cases may need a multidisciplinary approach including urologists, vascular surgeons, radiologists and bone surgeons (fixation of pelvic fractures).
- Isolated anal sphincter lesions could be managed by primary suture (using re-absorbable material such as polyglycolic acid sutures) if the risk of infection is low. Primary suture of the sphincter muscle seems to yield better functional results than delayed suture provided infection can be prevented. In such cases, vigorous antibiotic prophylaxis and sigmoidostomy should be performed at the same time.
- Minor anal trauma can be managed conservatively with antibiotics, local medication and analgesics.

12.1.4.1 Treatment of Foreign Bodies in the Rectum

- Extraction of foreign bodies from the rectum should be achieved through the anus whenever possible.
- After maximal anal dilation has been obtained under anaesthesia, several instruments have been proposed to assist extraction, such as Foley catheter placed above the foreign body and pulled downward after inflation of the balloon, obstetric forceps, long haemostatic forceps, an endoscope, etc.
- A rectosigmoidoscopy should also be repeated after retrieval of the foreign body to evaluate any possible mucosal lesion or perforation.
- Laparotomy with rectal opening to extract the foreign body should be performed only in cases of failure of transanal attempts.

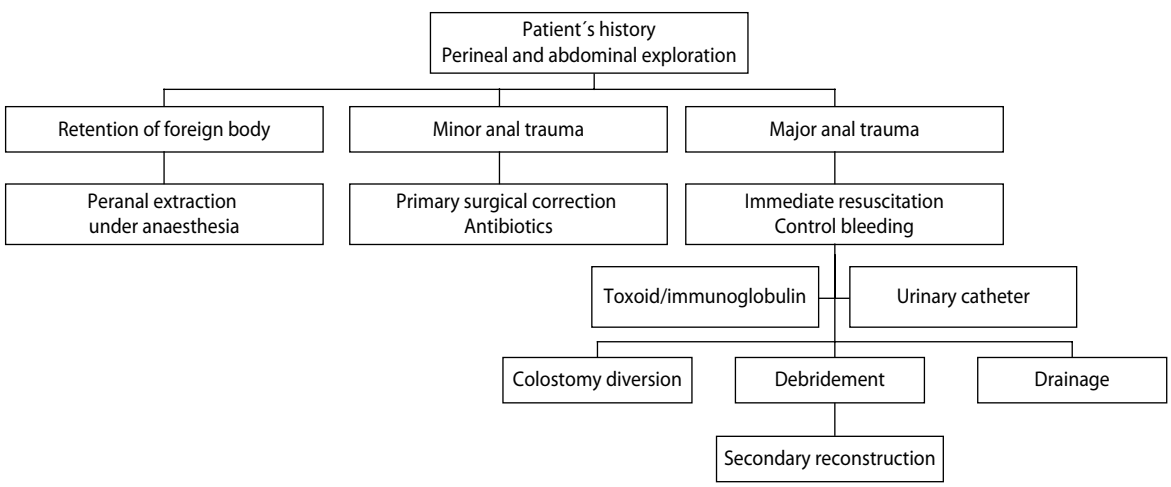


Fig. 12.1.2 Severe anoperineal trauma involving the anus, sphincters, rectum, prostate and urethra with small bowel herniation following a car accident

12.1.5 Functional Sequelae Following Anorectal Trauma

- Several disabling conditions can follow anorectal traumas, the most frequent being faecal incontinence. But also defaecation problems can arise as a consequence of strictures or rectal denervation.
- Sexual assaults, particularly in childhood, usually leave profound psychological problems and, frequently, anismus or pelvic dyssynergia causing obstructed defaecation.
- The persistence of abdominal colostomy is not rare after these trauma with the obvious disabling consequences on the patient's social and emotional life.
- More severe traumas, involving sacral nerves and the anterior perineum can lead to more severe problems including impotence, urinary incontinence or retention requiring permanent catheterisation. Major surgery, with multidisciplinary approach (urologists, plastic surgeon, colorectal surgeon and neurologist) can sometime help these patients.

Suggested Reading

1. Kouraklis G, Misiakos E, Dovas N, Karatzas G, Gogas J (1997) Management of foreign bodies of the rectum: report of 21 cases. J R Coll Surg Edinb 42:246–247
2. Levine JH, Longo WE, Pruitt C et al (1996) Management of selected rectal injuries by primary repair. Am J Surg 172:575–579
3. McGrath V, Fabian TC, Croce MA, Minard G, Pritchard FE (1998) Rectal trauma: management based on anatomic distinctions. Am Surg 64:1136–1141
4. Moore EE, Cogbill TH, Malangoni MA et al (1990) Organ injury scaling, II: pancreas, duodenum, small bowel, colon, and rectum. J Trauma 30:1427–1429
5. Morgado PJ, Morgado PJ Jr (1995) Anorectal trauma. In: Wexner SD, Varnava III AM (eds) Clinical decision making in colorectal surgery. Igaku-Shoin Medical, New York
6. Morken JJ, Kraatz JJ, Balcos EG et al (1999) Civilian rectal trauma: a changing perspective. Surgery 126:693–700
7. Smith L (1999) Traumatic injuries. In: Keighley MRB, Williams NS (eds) Surgery of the anus, rectum and colon. Saunders, London, pp 2227–2244
8. Vitale GC, Richardson JD, Flint LM (1983) Successful management of injuries to the extraperitoneal rectum. Am Surg 49:159–162

12.2 Colonic/Rectal Obstruction

JOAO PIMENTEL

12.2.1 Introduction

- Colonic/rectal obstruction, also known as large-bowel obstruction (LBO), is a serious impairment or complete arrest of the passage of intestinal contents caused by mechanical or functional blockage.
- It is an emergency condition that requires early recognition and prompt therapeutic intervention to obviate the potential risk of serious complications or death.
- It is much less common than small-bowel obstruction, representing less than 20% of all cases of intestinal obstruction.
- According to its presentation, colonic/rectal obstruction can be classified in several ways:
  - Acute or chronic
  - Partial or complete
  - Open loop or closed loop
- The pathophysiology depends on the competence of the ileocaecal valve:
  - If competent, a closed loop obstruction occurs, with the risk of perforation and gangrene
  - If incompetent the intestinal contents can reflux into the small intestine

Recent technological innovations have changed therapeutic strategy, with a marked benefit for patient outcome. Understanding them and the various aetiological hypotheses, as well as the clinical presentation and the use of appropriate tests make it possible to choose the best treatment option.

Table 12.2.1 Aetiology of colonic/rectal obstruction

Mechanical	Non-mechanical
Tumours	Ogilvie's syndrome
Volvulus	Paralytic ileus
Diverticulitis	Constipation
Faecal impaction	Dysfunction
Anastomotic structure	
Ulcerative/Crohn's colitis	

12.2.2 Aetiology

The aetiology of obstruction may be mechanical or non-mechanical (Table 12.2.1):

- Mechanical factors can be anything that produces narrowing of the colonic lumen and can be:
  - Intraluminal
  - Mural
  - Extrinsic
- Non-mechanical factors include those that interfere with the muscle action or innervation of the bowel

12.2.3 Symptoms

- Symptoms of colonic/rectal obstruction depend on a number of factors, in particular the aetiology, degree of obstruction (partial or total) and how it presents (acute or chronic, closed or open loop, with a competent or incompetent ileocaecal valve).
- Symptoms may appear suddenly, suggesting an acute obstruction, such as that seen in sigmoid or caecal volvulus, or they may come on progressively, which makes colorectal cancer a more plausible cause.
- The most frequent clinical presentation may include:
  - Changed bowel habit
  - Constipation
  - Abdominal pain which may be colicky
  - Nausea
  - Vomiting
- Severe, continuous abdominal pain, especially in the right iliac fossa, raises the suspicion of gangrene with imminent perforation.
- Systemic symptoms may be present, usually less serious than those of obstruction of the small intestine, including:
  - Weight loss, fatigue, anorexia and anaemia suggesting a neoplastic lesion

  - Fever, chills, feeling unwell associated with an inflammatory disorder such as diverticulitis or colitis.
- A history of chronic constipation, straining to pass faeces, pneumaturia or faecaluria would reveal diverticulitis or carcinoma, and a change in calibre of the stools is very indicative of the latter.
- If colonic ischaemia may be present, signs and symptoms of acute toxicity could be found, and septic shock is possible.

12.2.4 Diagnosis

- Initial physical examination must evaluate the severity of the patient's clinical condition:
  - Begin with the acquisition of a careful and comprehensive patient history.
  - Then make a complete physical examination. This must include the evaluation of vital signs, general physical appearance and mental status.
- Continue with a focused abdominal examination:
  - Significant abdominal distension will be found in the vast majority of patients. Colonic distension may be extremely large, as in the case of a closed loop obstruction or with a competent ileocaecal valve, where the risk of ischaemia or perforation, mainly caecal, is higher.
  - Hyperresonance will be noted on percussion.
  - Palpation will reveal tenderness, while rebound tenderness in the right lower quadrant suggests ischaemia or perforation of the caecum, which needs urgent surgical intervention. Perforation can also occur at the obstruction site (tumours or diverticulitis). Eventually, a mass elucidating a carcinoma, an acute diverticulitis or a markedly dilated caecum can also be palpated.
  - At auscultation, in the initial phase, bowel sounds may be hyperactive or normal, becoming diminished or absent in cases of longstanding obstruction, colonic ischaemia or colonic pseudo-obstruction.
  - Digital rectal examination should always be performed, making possible the identification of a rectal or lower pelvic. The rectum is usually empty of faeces. The presence of blood suggests a carcinoma.
- Routine laboratory studies are needed to evaluate fluid and electrolyte imbalance, chronic blood loss and/or sepsis:
  - Obtain blood for a complete blood count, prothrombin time, crossmatch, electrolyte levels, creatinine and liver function tests.
  - Arterial blood gas determination should be performed must also be done.
  - An elevated white blood cell count suggests bowel ischaemia/necrosis.
- Imaging:
  - A standard plain abdominal radiographic series (flat and upright or left lateral decubitus films) may distinguish small-bowel from large-bowel obstruction, making the diagnosis of colonic obstruction in 60–80% of cases. They also are useful for defining where the obstruction is located, showing distension of the colon proximal to the lesion, or by suggesting the cause, as in caecal or sigmoid volvulus. If the caecal diameter is more than 12 cm there is a risk of rupture and urgent surgery is indicated. An erect chest radiograph or an upright abdominal film may reveal free air if perforation has occurred. If in doubt over diagnosis—mechanical versus non-mechanical obstruction (Ogilvie's syndrome)—or site of obstruction, carry out a water-soluble contrast enema.
  - Colonoscopy may also help in this setting and also as a therapeutic procedure in reducing a sigmoid volvulus or in decompressing the colon in Ogilvie's syndrome. Be careful with this procedure because of the risk of perforation.
  - Computed tomography (CT), nowadays used in a more expeditious way, may be useful for a complete, one-venue, assessment of the condition. In cases of diverticulitis CT scans can be used also as part of a therapeutic procedure.
  - Other diagnostic tools such as ultrasound play a limited role, with a low accuracy due to the presence of major gaseous distension.

12.2.5 General Management

- Patient resuscitation must begin immediately. This includes volume resuscitation, correction of electrolyte imbalances and transfusion if necessary. Since intravascular volume is usually depleted, early intravenous crystalloid fluid rehydration is required (isotonic saline or Ringer's lactate solution), sometimes by means of a central venous catheter. To monitor urinary output insert a urethral catheter.
- When bowel obstruction is partial, these measures should precede or accompany intestinal decompression efforts, which can be attempted by the insertion

of large-bowel or nasogastric tubes or by means of several enemas. Nasogastric tubes are also needed if the patient has been vomiting, revealing in some cases a faecal content. Consider prophylactic antibiotics.

- Appropriate treatment depends on the aetiology of the colonic/rectal obstruction (Fig. 12.2.1). Each situation including its prognosis is described below.
- In cases of potential stoma formation, patient consent should be obtained and the potential site marked before surgery.
- Patient's informed consent about management options should be obtained whenever it is possible.

12.2.6 Neoplastic Colorectal Obstruction

12.2.6.1 Aetiology/Epidemiology

- Colonic/rectal carcinoma is responsible for approximately one third (UK) to one half (USA) of all cases of colorectal obstruction.
- About 15% of all patients with colorectal carcinoma present with obstruction.
- Most patients are aged over 70 years.

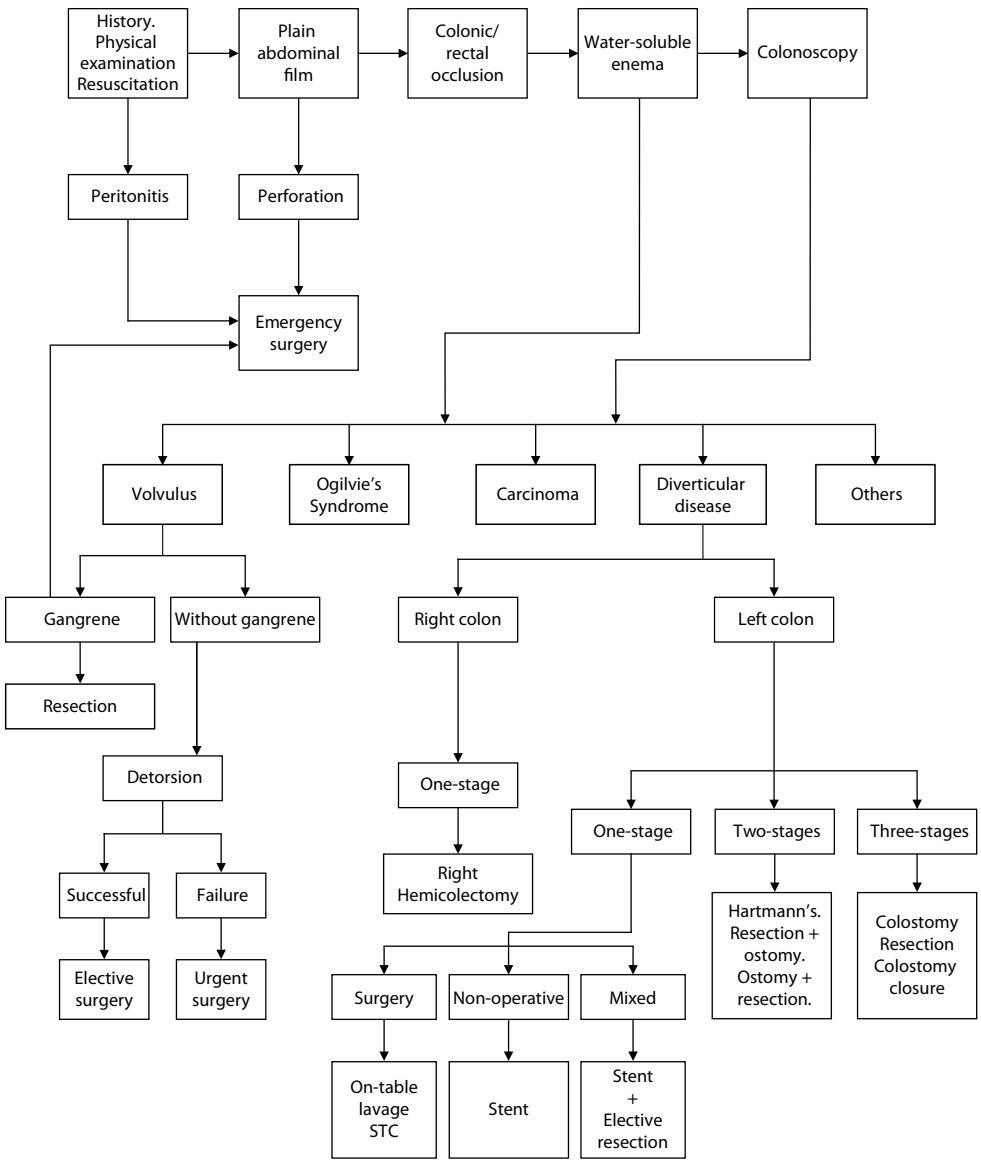


Fig. 12.2.1 Management of colonic/rectal obstruction

- The risk of obstruction is greater in the left colon, most often in the sigmoid and splenic flexure, whereas rectal carcinoma has less tendency to obstruct.
- It is usually found at a more advanced stage of the disease, with 25% having already metastasised when diagnosis is made.

12.2.6.2 Symptoms

The onset of symptoms caused by an obstructive tumour may be insidious or acute. Most patients report symptoms evolving over a 3- to 6-month period, while acute obstruction occurs as the first symptom in 15–20% of carcinomas of the left colon. Symptoms are non-specific and are often ignored until complete obstruction occurs:

- Inability to pass gas and faeces, colicky abdominal pain and abdominal distension
- Anorexia
- Asthenia
- Bloody stools or rectal bleeding
- Changes in bowels habits and diameter of faeces, tenesmus
- Abdominal mass
- Marked weight loss, jaundice, ascites, cough raising suspicion of a possible metastatic disease

Whether the tumour is located in the right or left colon can also affect the clinical picture: the first presents with a picture of obstruction of the small intestine and the second of the large intestine.

12.2.6.3 Diagnosis

- The step procedures already mentioned above for general diagnosis are followed. A patient's history will usually reveal a drawn-out evolution, with a change in bowel habits for several months. Results of physical examination depend mainly on tumoral stage and duration of symptoms: signs of cachexia, malnutrition, dehydration can be found or, on the contrary, general health status may be good. Initiate prompt resuscitation if it is necessary.
- Abdominal distension is usually present with loud borborygmi. In some cases a mass can be palpated, corresponding to the site of the tumour. Remember that rebound tenderness in the right lower quadrant can be caused by caecal gangrene. Digital rectal examination may identify the tumour.
- Laboratory studies (including carcinoembryonic antigen determination) and plain abdominal films are always needed. Consider a water-soluble contrast enema in cases of a dubious diagnosis. Colonoscopy may also be used if the colon distal to the obstruction can be cleaned with enemas. CT scans can have some benefits in the case of a large-bowel obstruction due to a colorectal cancer, helping in the clinical staging or in the differential diagnosis with diverticulitis.

12.2.6.4 Treatment

In case of partial colonic/rectal obstruction due to colorectal cancer, patients can be initially managed conservatively, with appropriate reanimation and preoperative bowel preparation, allowing an elective surgical procedure. Complete obstruction, with higher morbidity and mortality and worse survival rates, implies early and urgent treatment. Surgical procedures are mostly used, but non-surgical procedures such as endoscopic stents are also useful. There is no consensus, however, about the most appropriate therapeutic options to select. Several options that are currently available permit one-stage procedures, avoiding the inconveniences of the past directly related to multistaged procedures that required at least one temporary stoma. Such procedures are, however, far from being abandoned.

Conservative Treatment

In order to minimise the risks associated with the surgical treatment of patients with LBO, there has been a trend towards decompression of the colon before surgery, allowing an emergency situation in a non-stabilised patient to be converted into a more elective one and also avoiding the need for a stoma. This can be accomplished by laser tumoral ablation or by endoscopic stent placement to canalise a neoplastic obstruction.

Stent insertion is nowadays the most commonly used non-surgical endoluminal technique, since the need for repeated treatment sessions and the risk of complications has limited the widespread acceptance of laser dilatation. Stents have been increasingly applied in recent years, bridging patients from emergency to elective surgery, by re-establishing the intestinal lumen and allowing a thorough bowel preparation prior to surgery. Bowel function is restored immediately after stent insertion, with regularisation of the pathophysiological changes associated with obstruction. Colonic stents are also used as a palliative and definitive treatment in patients where surgery should be avoided, such as those with significant comorbidities, with incurable malignancies or with non-resectable neoplasias. The technical success of stent placement is around 92% with a clinical success rate between 82% and 97%. Total mortality is less than 1% (figures rising

to 10–13% when results from the subsequent surgery are also included). Procedure-related complications are few, less than 10% (colonic perforation: 2–4%; stent migration: 4–10%, re-obstruction: 3–10%). Colonic stent placement compares favourably with emergency surgery, with a reduction in mortality and morbidity. Endoluminal stent insertion is a cost-effective technology, with a higher success rate in relieving obstruction in the vast majority of patients.

Surgical Treatment

Right-side colonic obstructive cancers (caecal, ascending and transverse colonic lesions proximal to the splenic flexure) are usually treated with a resection and a primary anastomosis (right hemicolectomy). This is the procedure of choice, except in cases with perforation or gangrene (where a primary anastomosis is contraindicated) which are best managed by resection, end ileostomy and exteriorisation of the proximal colon, with subsequent re-establishment of intestinal continuity.

It is difficult to formulate recommendations for the surgical treatment of left-side lesions; the discussion has centred on those who favour multiple-staged operations or those who argue for the one-stage procedure as the preferred approach. Colonic obstruction in this location has been managed for years by multistaged surgical procedures (three- and two-staged): initial diversion followed by a staged procedure or resection without primary anastomosis followed by re-establishment of colonic continuity. Recently there has been an increasing trend towards a single-stage procedure (segmental resection and primary anastomosis after intraoperative colonic lavage or subtotal colectomy), conceptually the ideal surgical strategy, if performed safely.

Three-stage Procedure

Since a three-staged procedure involves three operations (construction of a defunctioning colostomy, resection with anastomosis, closure of the colostomy) and a prolonged total hospital stay, it is nowadays almost abandoned. Eventually, this strategy could still have a role in cases of high-risk patients or with less experienced surgeons.

Two-stage Procedure

A two-stage procedure always implies a creation of a stoma: primary resection with creation of an end colostomy—Hartmann's procedure—followed by re-establishment of the intestinal transit, or primary resection with anastomosis and creation of a defunctioning stoma, followed by stoma closure. As an alternative, a proximal diversion can be done (usually a transversostomy) allowing for adequate patient resuscitation and colonic lavage followed by an early elective resection with a primary anastomosis. Unfortunately, in cases of a primary resection without anastomosis, the intestinal continuity is restored only in 70% of patients.

Single-stage Procedure

When the option is for a single-stage procedure, the goal is best accomplished by on-table lavage followed by segmental resection and anastomosis. A subtotal colectomy, due to the increased number of bowel movements seen after this type of operation, should be reserved for patients with caecal ischaemia/perforation or with right-sided concomitant neoplasias, and must be avoided in cases of compromised faecal continence. The indication for a single-stage procedure remains controversial and debatable, with multistaged procedures still being used, mainly for severely ill patients, with associated conditions, or in the face of bowel gangrene or faecal peritonitis (ASA III–IV patients).

Current Treatment Recommendations

See Table 12.2.2.

12.2.6.5 Prognosis

- Both the perioperative and long-term survival are adversely affected in these patients.
- Perioperative mortality is highest in patients with obstruction operated on in emergency conditions (15–30%) than in those with non-obstructive carcinomas (< 10%), regardless of tumour stage at the time of surgery. It appears to be a result of the increased surgical risk present in these circumstances.
- The same is also true for crude overall survival at 5 years, which is approximately 30%, being around 35% in those patients undergoing curative surgery. Only 40–50% of tumours in obstruction are operated on with a view to cure, far from the 70% without obstruction.
- Although acute complete obstruction might not be a major prognostic factor, it is nonetheless independent of prognosis. Other variables affect the prognosis for patients with obstruction, some common to non-obstructive colorectal carcinomas. These include: colonic perforation, advanced stage tumour, poor tumour differentiation, mucinous characteristics and vascular and neural invasion.

Table 12.2.2 Current recommendations for surgical treatment of neoplastic colorectal obstruction

Right-side lesions	Left-side lesions
One-stage procedure:	One-stage procedure:
Resection with primary anastomosis (right hemicolectomy)	Resection with primary anastomosis (on-table lavage)
	Resection with primary anastomosis (subtotal colectomy)
	Colonic stenting followed by elective surgery (resection with primary anastomosis)
Two-stage procedure:	Two-stage procedure:
Resection with end ileostomy, re-establishment of intestinal continuity (if gangrene or perforation)	Resection with colostomy, re-establishment of intestinal continuity (Hartmann's procedure)
	Resection with anastomosis with diversion ostomy, closure of ostomy
	Proximal diversion, resection with primary anastomosis

12.2.7 Colonic Volvulus

12.2.7.1 Definition

Colonic volvulus is caused by an abnormal twisting of an affected segment of bowel along its longitudinal mesenteric axis. This creates partial or total intestinal obstruction and significant vascular compromise, possibly leading to ischaemia and gangrene of the colon. It may occur in any colonic segment but is most common in the sigmoid colon (75–80%) and the caecum (15–20%), followed by other sites (2–3%).

12.2.7.2 Epidemiology/Aetiology

- Volvulus is an important cause of colonic occlusion worldwide.
- The incidence varies considerably, according to the population studied, being extremely prevalent (50–80%) in the Middle East, Africa and parts of Europe and Brazil (the so-called Volvulus Belt), with a minor incidence in western Europe and USA (1–5%).
- It is very rare in children and adolescents, being mostly a disorder of the elderly. Sigmoid volvulus occurs predominantly in 70-year-olds, while caecal volvulus arises on average 10 years earlier.
- Fifty per cent of patients have had a previous episode.

There is no clear aetiology, but certain factors are known to predispose to colonic volvulus. In sigmoid volvulus the presence of a long, mobile, redundant loop of sigmoid is assumed, with a narrow mesentery base (inferior mesenteric artery). It is usually acquired rather than congenital, and facilitates twisting of the mesentery, usually clockwise. For caecal volvulus to occur, retroperitoneal fixation must be incomplete or absent in the caecum and ascending colon. This suggests a congenital defect caused by twisting of the mesentery of the ileocolic artery or by it folding upwards (caecal bascule). Other possible causative factors may include a high-fibre diet (Volvulus Belt), constipation, a sedentary lifestyle, psychotropic drugs, residence in psychiatric institutions or nursing homes for the elderly, Parkinson's disease and its treatment, Chagas' disease, Hirschsprung's disease, and pregnancy (caecal volvulus).

12.2.7.3 Symptoms

Signs and symptoms vary according to whether:

- The occlusion is complete or not
- The ileocaecal valve is competent or not (closed loop)
- Ischaemia or intestinal necrosis is present or not

The patient may present with pronounced abdominal distension and discomfort, and inability to pass gas and faeces, or complain of constant pain indicating necrosis with peritonitis. Vomiting occurs in caecal volvulus if the clinical picture is maintained. Fever, dehydration, haemodynamic changes, abdominal defence and shock suggest ischaemia or secondary perforation of the volvulus. Gangrene must be prevented as this increases the mortality rate by three or four times.

12.2.7.4 Diagnosis

- On physical examination, abdominal findings are generally non-specific. Besides marked distension, intestinal meteorism with visible peristalsis may be observed, and bowel sounds may be intensified and have a metallic tone. Peritoneal signs suggest colonic gangrene.
- Plain abdominal radiographs are diagnostic or highly suggestive (70–90%), especially in sigmoid volvulus. Images resemble a bent inner tube, in sigmoid volvulus, with the apex pointing towards the left iliac fossa, or a coffee bean, in caecal volvulus. Volvulus in the caecum also usually reveals distended loops of the small intestine. Diagnosis is confirmed by a water-soluble contrast enema, with the typical finding of the "bird-beak" appearance of the sigmoid at the point of torsion of the volvulus' neck.
- If volvulus of the sigmoid or left colon is suspected, flexible sigmoidoscopy or colonoscopy will be diagnostic and usually therapeutic. This should not be performed if colonic perforation is suspected. About 15–25 cm from the anal verge, the examination will detect a twist of folds of the mucosa, indicating the disorder. Bloody fluid and ischaemic mucosa suggest gangrene.
- Computed tomography can be an additional diagnostic aid. It can reveal intestinal distension and the level of obstruction, and can demonstrate the mesenteric twist, visualised as a mass of soft tissue in the shape of a "whirl" ("whirl" sign).

12.2.7.5 Therapy

Sigmoid Volvulus

The timing and nature of therapy will be different depending on whether signs of gangrene or colonic perforation are present or not or sigmoidoscopy detorsion will be effective or not. If signs of perforation are found, surgery is obligatory and urgent. The procedure will consist of segmental resection with ostomy (Hartmann's procedure). When this serious complication is not present, strategy is based on decompression and detorsion of the affected segment, followed by elective surgery, in most cases. Detorsion via endoscopy is successful in 80–90% of cases. Rigid proctoscopy or flexible sigmoidoscopy may be used, but the latter procedure is preferred as it gives better visualisation and can treat volvuli higher up the bowel. Detorsion may succeed or fail. If it fails, surgery is indicated: either resection of the sigmoid with primary anastomosis, following on-table lavage, or segmental resection with ostomy (Hartmann's procedure).

The question arises as to how to proceed after successful detorsion. If nothing more is done, the recurrence rate is over 50%, and so surgery is recommended for most patients with this disorder. Several surgical procedures are possible. Non-resection procedures, which include simple detorsion, detorsion with colopexy or mesosigmoidoplasty, result in lower morbidity/mortality, but a higher rate of recurrence. Thus, whenever the general state of the patient permits, the option should be for a resection procedure: either segmental resection with primary anastomosis or subtotal colectomy with ileorectal anastomosis in cases of associated megacolon.

Caecal Volvulus

Colonoscopic detorsion of the caecal volvulus may be attempted, but it is not usually successful. Contrast enema carried out for diagnostic purposes may occasionally be therapeutic. Since gangrenous changes are often seen during surgery (20–40%), these procedures are therefore contraindicated for therapeutic routine. Surgery is frequently needed, due to ischaemia, and should not be delayed. It involves resection of the colon with primary anastomosis (right hemicolectomy). Anastomosis is only avoided in cases of faecal peritonitis, in which the option will be for resection with terminal ileostomy. In the absence of ischaemia, resection procedures with primary anastomosis are preferred, given their obvious advantages over the non-resectional methods of simple detorsion, detorsion with caecopexy and detorsion with caecostomy, with respect to the lower rate of recurrence and complications.

Current Treatment Recommendations

For caecal volvulus the recommendations are:

- Resection with primary anastomosis (right hemicolectomy)
- Resection with terminal ileostomy (faecal peritonitis)

For sigmoid volvulus see Fig. 12.2.2.

12.2.8 Other Conditions

Other conditions which may cause colorectal obstruction are:

- Acute colonic pseudo-obstruction (Ogilvie's syndrome)
- Diverticular disease
- Inflammatory bowel disease
- Radiation damage
- Faecal impaction
- Endometriosis

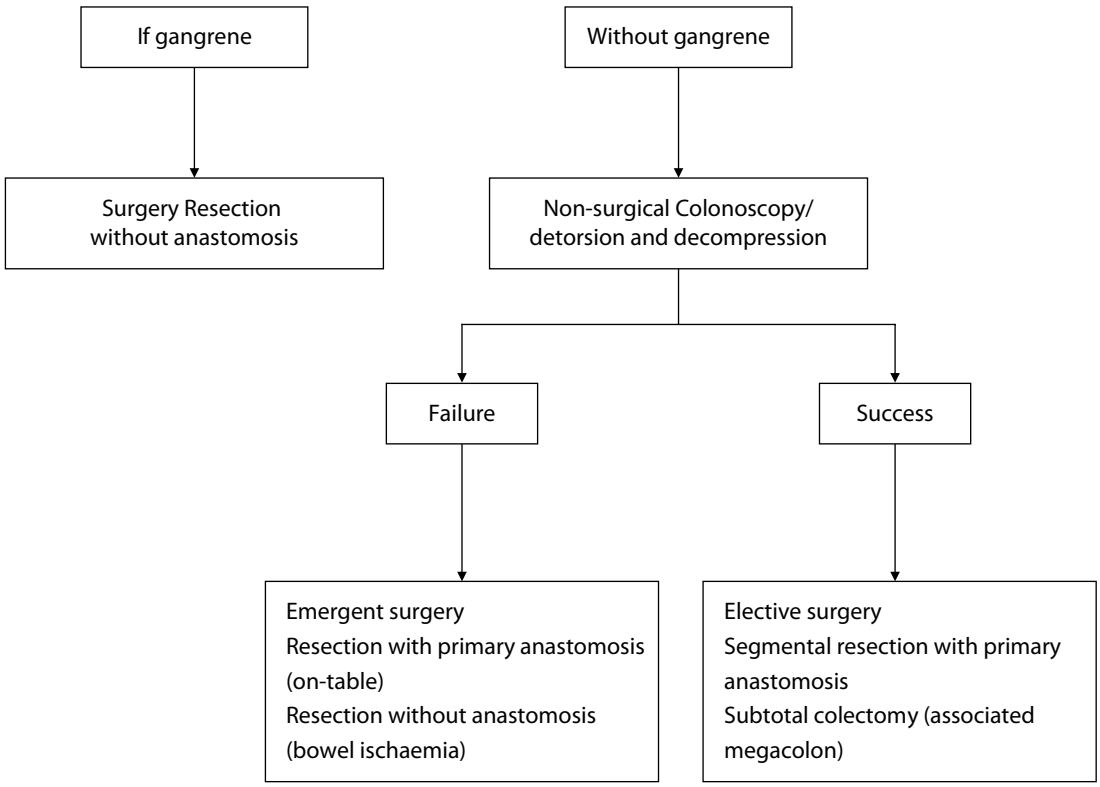


Fig. 12.2.2 Current treatment recommendations for sigmoid volvulus

- Extrinsic lesions (ovarian, bladder, prostate cancers, non-colonic metastatic lesions)

12.2.9 Summary

- Colonic/rectal obstruction is much less frequent than small-bowel obstruction.
- Colorectal cancer is the main cause in western countries.
- Colonic/rectal obstruction is a serious condition that needs careful and prompt diagnostic and therapeutic measures to obviate harmful complications or even death (gangrene and perforation should be avoided).
- Recent technological innovations have changed therapeutic strategy, with a marked benefit for patient outcome (on-table lavage, colonic stents).
- There is now a trend towards single-stage procedures instead of a multistaged approach, the rational being to reduce the morbidity inherent to the latter.
- Multistaged procedures should remain, however, the preferable option for severely ill patients, with associated conditions, or in the face of bowel gangrene or faecal peritonitis.
- The preferred approach should be selected on an individual basis and tailored to the particular situation.
- Understanding the various aetiological hypotheses, as well as the clinical presentation and the use of appropriate tests make it possible to choose the best treatment option.

Suggested Reading

1. Cataldo PA (2001) Large bowel obstruction. Semin Colon Rectal Surg 12:140–153
2. Douglas JM, Stahl TJ (2001) Obstructing cancer: overview and prognosis. Semin Colon Rectal Surg 12:154–157
3. Khot UP, Wenk Lang A, Murali K et al (2002) Systematic review of the efficacy and safety of colorectal stents. Br J Surg 89:1096–1102

4. Lopez-Kostner F, Hool GR, Lavery IC et al (1997) Management and causes of acute large-bowel obstruction. Surg Clin North Am 77:1265–1290
5. Meisner S, Hensler M, Knop FK et al (2004) Self-expanding metal stents for colonic obstruction: experiences from 104 procedures in a single center. Dis Colon Rectum 47:444–450
6. Pahlman L, Enblad P, Rudberg C et al (1989) Volvulus of the colon. A review of 93 cases and current aspects of treatment. Acta Chir Scand 155:53–56
7. SCOTIA Study Group (1995) Single-stage treatment for malignant left-sided colonic obstruction: a prospective randomised clinical trial comparing subtotal colectomy with segmental resection following intraoperative irrigation. Br J Surg 82:1622–1627
8. Watson AJM, Shanmugam V, Mackay I et al (2005) Outcomes after placement of colorectal stents. Colorectal Dis 7:70–73
9. Williams NS (1999) Large bowel obstruction. In: Keighley MRB, Williams NS (eds) Surgery of the anus, rectum and colon. Saunders, London, pp 1823–1866

12.3 Lower Gastrointestinal Bleeding

ZORAN KRIVOKAPIC, GORAN BARISIC

12.3.1 Definition

Lower gastrointestinal bleeding (LGIB) is defined as any haemorrhage occurring distal to the ligament of Treitz.

- *Acute LGIB* is defined as bleeding of less than 3 days duration that results in haemodynamic compromise, anaemia or the need for blood transfusion. Massive bleeding results in a haematocrit less than 30%, haemodynamic instability that requires resuscitation or transfusion requirements of more than 3 units of blood products.
- *Chronic LGIB* is defined as any bleeding of more than 3 days duration and includes:
  - *Occult LGIB:* Positive faecal occult blood testing and/or iron deficiency anaemia with no obvious evidence of gastrointestinal blood loss
  - *Obscure LGIB:* Bleeding of unknown origin that persists or recurs despite negative oesophagogastroduodenoscopy or colonoscopy.

This chapter focuses on aetiology, diagnosis and treatment modalities of LGIB, and deals principally with colorectal bleeding.

12.3.2 Incidence

The overall incidence of LGIB is largely unknown. In the USA it has been estimated to occur in 20/100,000 of the population per annum with male predominance. It accounts for approximately 0.7% of emergency surgical admissions. In most cases LGIB is a minor, self-limiting event with relatively low mortality ranging from 2% to 4%. Severe, life-threatening haemorrhage is rare.

12.3.3 Presenting Clinical Features

- The passage of maroon and/or red blood per anus, without a positive history or concomitant symptoms such as abdominal pain, is frequently the first symptom.
- In approximately 30% of patients syncope or orthostatic hypotension with signs of haemodynamic shock are the first presentation.

12.3.4 Aetiology and Differential Diagnosis

The vast majority of LGIBs are of colonic origin. Several pathological conditions can cause LGB.

- *Diverticular disease* is the most likely cause of LGIB in adults and accounts for as many as 40% of all LGIBs. The estimated risk of bleeding from diverticulosis ranges between 4% and 48%. Usually, the bleeding originates from a single diverticulum, more commonly on the right colon; in most cases it stops spontaneously and only 10–20% continue to bleed. The rebleeding rate after one episode of bleeding is approximately 25%, but increases up to 50% after two or more episodes of haemorrhage. Bleeding reoccurs in 9% of patients within 1 year, in 10% within the second year, 19% in the third year and 25% in the fourth year. The cause of diverticular bleeding remains unknown, however it is thought that thinning of the vasa recta predisposes to intraluminal rupture from a local trauma, such as might result from the presence of a faecalith. Operative intervention for recurrent bleeding is indicated if interventional procedures are not amenable or have failed. Usually a resection of the relevant colonic segment is performed.
- *Arteriovenous malformations (angiodysplasia).* Angiodysplasia may be isolated or multiple. The cause is arteriovenous communications in the submucosa or mucosa; they are mostly acquired (being associated with renal failure, von Willebrand's disease and Osler-Weber-Rendu syndrome) and appear as vascular tufts in the submucosa and mucosa of the colon. Angiodysplasia is a cause of significant LGIB in 1–4% of cases. The incidence rises in patients older than 60 years. Bleeding is usually chronic and intermittent, but approximately 15% of patients will experience severe

bleeding. Rebleeding may occur in up to 85% if left untreated. Angiography is the diagnostic procedure of choice and offers the treatment potential of embolisation or infusion of a vasoconstrictor.

- Inflammatory bowel disease (IBD), including ulcerative colitis and Crohn's disease is a common cause of LGIB, but massive bleeding is uncommon. There is usually an associated change in bowel habit with diarrhoea. During the course of the disease approximately 6% of patients with IBD will experience severe, life-treating bleeding.
- *Neoplasms*, benign and malignant, located in the colon are a frequent cause of LGIB, but in most cases bleeding is not severe. Colorectal neoplasia accounts for between 7% and 33% of cases of severe LGIB.
- *Ischaemic colitis* is a rare cause of severe LGIB. Bloody diarrhoea after rapid onset of abdominal pain is almost indicative of this condition; severe bleeding is very unlikely.
- *Aorto-enteric fistula* is as rare and is usually associated with previous abdominal vascular surgery. Usually this condition results in massive bleeding. It is associated with high mortality.
- *Anorectal disease*, such as haemorrhoids and anal fissure, can occasionally present as a significant LGIB. They account for approximately 11% of LGIB.
- *Varices*, colonic, anorectal and peristomal, can cause painless severe LGIB. The overall incidence of colonic varices is unknown but in patients with portal hypertension the incidence of anorectal varices ranges between 78% and 89%.
- *Coagulopathy* can result in severe LGIB. It remains unclear whether severe bleeding in patients with coagulopathy originates from the intact mucosa and is caused by the coagulopathy or whether it is due to an identifiable mucosal lesion with bleeding due to coagulopathy. Severe gastrointestinal bleeding due to coagulopathy must be taken into consideration with platelet counts less than 20,000 mm^3. Several regimens are used for long-term anticoagulant and antiplatelet therapy for underlying cardiovascular conditions. The long-term risk of bleeding on anticoagulant therapy with warfarin is considered to be approximately 22%.
- *The small intestine*, although constituting 90% of the gastrointestinal mucosal surface area is a relatively rare source of bleeding and constitutes approximately 3–5% of all LGIB. The most common cause of bleeding is angiodysplasia, accounting for 70–80% of all cases. Neoplasia, inflammatory bowel disease, Meckel's diverticulum, non-steroidal anti-inflammatory drugs (NSAID) and backwash ileitis in patients with colitis are potential causes.
- *Upper gastrointestinal haemorrhage* (proximal to the ligament of Treitz) most commonly presents with melaena and haematemesis. In approximately 10–15% of patients, especially in patients with severe bleeding and rapid exsanguination, upper gastrointestinal bleeding can present with massive rectal bleeding and passage of bright red blood and blood clots. Upper gastrointestinal bleeding should always be considered in the differential diagnosis of LGIB.

12.3.5 Evaluation

12.3.5.1 Basic

The course of evaluation is determined by the extent and severity of the haemorrhage. Accurate diagnosis of the cause and location of acute bleeding is challenging due to limitations in diagnostic options. Once the diagnosis of severe LGIB is established, it is of paramount importance to calculate approximate blood loss and bleeding intensity at the time of admission.

- Resuscitative measures should be initiated:
  - Haemodynamic stabilisation: Crystalloid solutions to correct volume deficit, correction of red blood cell deficiencies and oxygen delivery.
  - Diagnostic procedures should be started depending and according to the patient's condition. The history should focus on any prior episodes of gastrointestinal bleeding and chronic diseases such as peptic ulcer, gastritis, varices, cirrhosis, liver disease, previous radiation, coagulopathy, malignant diseases, inflammatory bowel disease, previous operations and recently used drugs (aspirin, NSAIDs, warfarin, etc.). Physical examination should include careful inspection of the nasopharynx, the abdomen and the perianal region. Specific signs such as spider nevi, "caput medusae", jaundice, etc. can facilitate establishing the site of bleeding. Digital rectal examination followed by proctoscopy are mandatory.
  - As most of all LGIB spontaneously stop (85%), physical examination of the massively bleeding patient is in many cases unrewarding. However, one should try to identify the source of bleeding as soon as possible.
- Differentiation from upper GI bleeding:
  - Nasogastric tube: Gastric aspirate containing bile without blood considerably reduces the likelihood of the upper gastrointestinal bleeding. However, in approximately 16% of cases, gastric aspirate will be normal despite bleeding in the upper gastrointestinal tract.
  - Oesophagogastroduodenoscopy needs to be considered as in all patients with severe gastrointesti-

nal bleeding, even in those with well-documented LGIB.
- Confirmation of lower GI bleeding:
  - Once an upper gastrointestinal bleeding is excluded, an anorectal source of bleeding should be examined by:
    - Digital rectal examination
    - Proctoscopy

If the bleeding site is still unidentified, more refined diagnostic techniques need to be applied to locate the bleeding site in the colon or small intestine. As there is an overlap in diagnostic value and specific limitation in the various diagnostic techniques, some of these diagnostic procedures can be used sequentially. Application of these techniques depends on the condition of the patient, the extent and severity of the bleeding, and especially whether it ceases spontaneously.

12.3.5.2 Advanced

Colonoscopy

Urgent colonoscopy is the diagnostic procedure of choice in acute LGIB, if the patient is in a stable condition and especially if the bleeding is self-limiting.
- The safety, tolerability and clinical effectiveness of urgent colonoscopy after a rapid oral purge within the first 24 h after initial diagnosis are now well established.
- The overall diagnostic accuracy for bleeding site detection is between 74% and 89%. Tattoo marking of the bleeding site may be helpful for potential future surgery, as later correct intraluminal determination of the bleeding site may be difficult.
- Colonoscopy carries the potential for immediate intervention by various techniques:
  - Thermal methods such monopolar/bipolar cautery
  - Heater probe
  - Injection therapy, such as epinephrine, alcohol, cyanoacrylate glue, ethanolamine, thrombin, fibrin glue, polidocanol, hypertonic saline
  - Combination injection/thermal therapy
  - Laser therapy
  - Mechanical devices such metallic clips and rubber band ligation

  Definitive endoscopic haemostasis has been reported in up to 67% of patients.

- Potential disadvantages of urgent colonoscopy have to been taken into account:
  - Increased risk of perforation
  - Diagnostic delay to adequately prepare the bowel; rapid oral purge

  Despite these potential disadvantages colonoscopy is strongly recommended as the diagnostic procedure of choice in cases of LGIB but should be performed only in a haemodynamically stable patient. No one of the interventional therapeutic methods has been shown to be superior and in most cases the choice will depend on the underlying pathology and preference of the endoscopist.

If the source of bleeding has not been identified by upper GI endoscopy and colonoscopy, either selective angiography or nuclear scintigraphy should be performed to determine the bleeding site.

Angiography

Direct selective, sequential catheterisation of the superior mesenteric, inferior mesenteric arteries and celiac trunk is accomplished by femoral access using the Seldinger technique.
- Angiography can be diagnostic and therapeutic.
- Angiography is indicated in major ongoing haemorrhage.
- Angiography can detect the bleeding site only if the rate of haemorrhage is 0.5–1 ml/min or more. If the bleeding ceases or is less than 0.5 ml/min at the time of injecting contrast, the test will be negative. A positive examination is extravasation of contrast into the bowel lumen, arteriovenous malformation and/or early mesenteric venous filling.
- Angiography can be useful in accurately locating a bleeding site detected with nuclear scintigraphy.
- The sensitivity of angiography to identify a bleeding site is 40–78%.
- The overall complication rate is approximately 2%.
- Once the bleeding site is identified, angiographic intervention such as arterial embolisation by coils, polyvinyl articles or pledgets, or highly selective, intra-arterial vasopressin infusion can be considered. Embolisation controls bleeding in up to 93%. The rebleeding rate varies depending on the underlying condition, and is up to 75% in angiodysplasia. Vasopressin infusion controls bleeding in up to 91%, but relapse of the bleeding is around 50%. Both techniques carry the risk of intestinal ischaemia or infarction.

Nuclear Scintigraphy

- Nuclear scintigraphy is a more sensitive diagnostic tool for detecting haemorrhage than angiography, but location of the bleeding site is less accurate.
- It has the potential to detect a bleeding site even when the haemorrhage rate is 0.1 ml/min.

- Two methods are in use: technetium sulphur-colloid scintigraphy (Tc 99m) and technetium (Tc 99m)-labelled red blood cells.

Technetium Sulphur-Colloid Scintigraphy

- This method requires no preparation and can be performed immediately. The active site of bleeding appears as a "hot spot" on gamma camera scan. It detects brisk bleeding, not sporadic bleeding.
- Technetium sulphur-colloid half-life is very short (2–3 min) because the agent is rapidly cleared by the reticuloendothelial system. Thus this technique is only justified in cases of severe, life-treating GIT haemorrhage of unknown origin, immediately before the emergency operation in order to identify the bleeding site.

Tc 99m-Labelled Red Blood Cell Scanning

- This is the preferred scintigraphic method.
- This technique permits identification of a haemorrhage of lesser intensity because red blood cells are not rapidly cleared and are available to produce positive scans up to 24 h after injection.
- Sensitivity to detect active and intermittent bleeding is 80–98%.
- The accuracy in locating the precise site of haemorrhage is variable with reports of false-positive localisation ranging from 3% to 59%. In most institutions it is performed in patients with major, self-limiting, intermittent LGIB as a screening tool before angiography in order to confirm the presence of active bleeding. The timing of the positive blush is highly predictive of the success of a subsequent angiography: a blush that occurs within 2 min after scanning will be associated with a positive angiogram in approximately 60% of patients; if no early blush is seen, angiography will be negative in 93%.
- In patients with severe, life-treating bleeding, Tc 99m-labelled red blood cell nuclear scintigraphy is not recommended because it is time consuming and may delay therapy.

Video Capsule

Video capsule endoscopy is a new, promising technique in evaluating LGIB. Experience with this technique is limited as yet, but the preliminary results are promising. It is rarely indicated in cases of colorectal bleeding. At this time, video capsule endoscopy is limited for those cases where all previously described diagnostic tools have failed to identify a bleeding source, particularly when bleeding from the small bowel is suspected.

Enteroscopy

Push enteroscopy should be performed in a minority of patients who have persistent bleeding but in whom no definite bleeding source can be found by the techniques noted above. The procedure is performed with a special enteroscope passed orally. A diagnostic yield of 25% has been reported.

Computed Tomographic Scanning and Magnetic Resonance Imaging

With the development of advanced, thin-sliced computed tomographic scanning the role of CT in the diagnosis of LGIB is evolving. Current CT use focuses on indirect signs of a bleeding such as observing hyperdensity of the peribowel fat, contrast enhancement of the bowel wall and vascular extravasation of the contrast medium. However, with advanced technology and three-dimensional reconstruction techniques, the accuracy of detection and localisation of the bleeding source will further improve.

Similar developments are expected with MRI especially with the use of contrast enhancement techniques.

12.3.6 Treatment

An algorithm for the treatment of the patient with severe LGIB is shown in Fig. 12.3.1. Resuscitation measures and initial treatment are uniform regardless the cause of LGIB. Definite treatment is started as soon as the diagnosis is established and the bleeding site identified.

12.3.6.1 Bleeding from Colonic Diverticulosis

Colonoscopy may reduce the need for surgery and should be performed within 24 h of admission to hospital after rapid oral purge.

- The endoscopic approach to a bleeding diverticulum depends on the physical characteristics, location and size of the diverticulum.
- In most cases diluted (1:20,000) epinephrine can be injected in four quadrants around the diverticulum opening to control the bleeding.
- Non-bleeding visible vessels located at the edge of the diverticulum can be treated with bipolar coagulation with 10–15 W of power in 1-s pulses.
- If bleeding originates from within a diverticulum, 5–10 ml of diluted (1:20,000) epinephrine can be injected inside the diverticulum to raise the mucosa away from the submucosa.

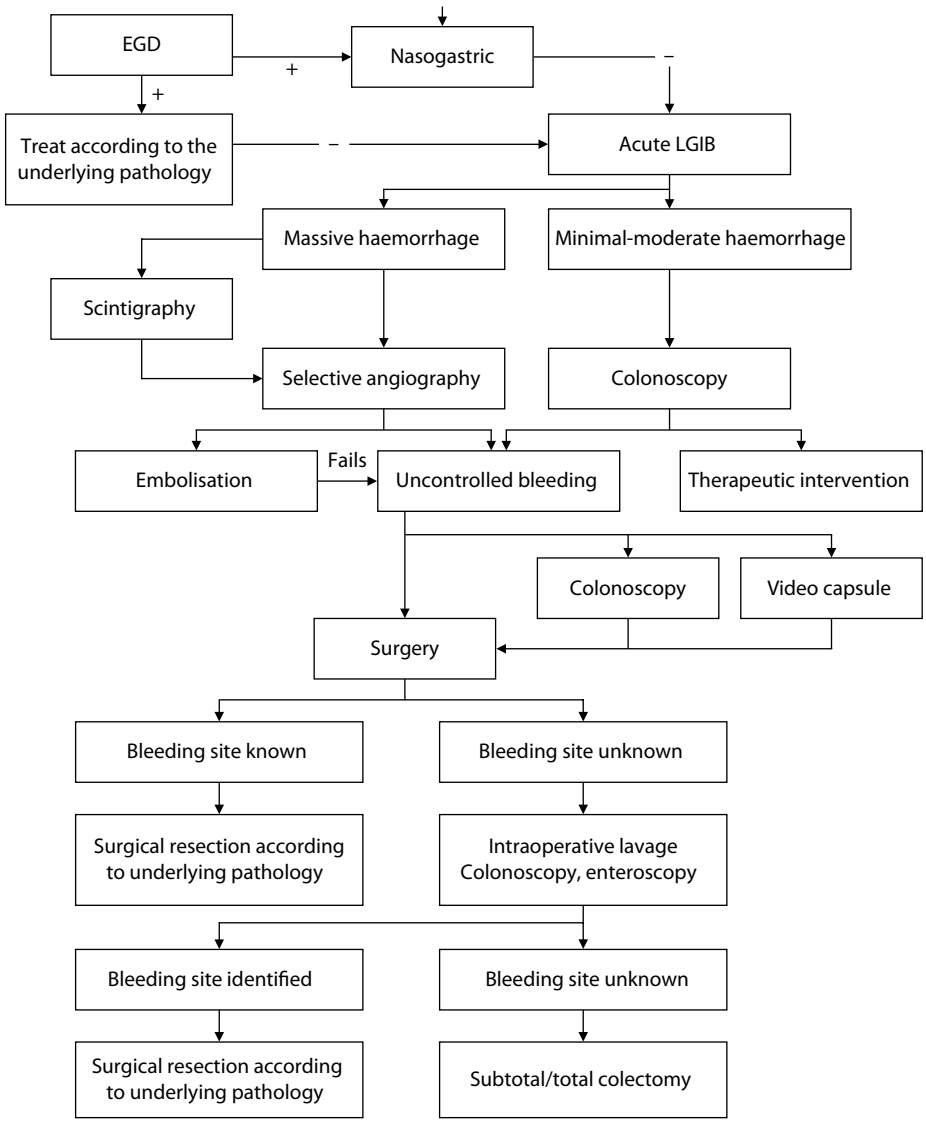


Fig. 12.3.1 Management of acute LGIB

- Non-bleeding adherent clots can be injected with epinephrine (1:20,000).

12.3.6.2 Bleeding from Angiodysplasia

Active bleeding from angiodysplasia can successfully be treated endoscopically using injection therapy, monopolar or bipolar coagulation, heater probe, argon plasma coagulation or Nd:YAG laser.

- The main therapy remains thermal with the success rate ranging between 50% and 87%.
- Various drug treatments have been tried in patients with bleeding from colonic angiodysplasia. The outcome of treatment with oestrogen is variable. Octreotide, 0.1 mg administered subcutaneously three times daily for up to 6 months has been reported to be of benefit.
- If mesenteric angiography is necessary to identify the exact site of bleeding, infusion of vasopressin or embolisation can be performed once the bleeding site is identified.

12.3.6.3 Perianal Conditions

Perianal conditions rarely present with severe bleeding. Treatment needs to be directed according to the underlying condition.

12.3.6.4 Surgical Treatment

- Emergency surgery is indicated in 10–25% of patients with LGIB, usually for continuing haemorrhage unresponsive to non-surgical treatment.
- In general, patients who have required repeated transfusion (critical point is considered beyond 8 units of blood) should undergo an operation.
- Operative intervention is associated with a reported mortality rate of up to 35%.
- Whenever the bleeding point has been identified preoperatively, the surgeon should perform a tailored resection according to the underlying pathology (ranging form segmental resection to total colectomy).
- In cases of "unknown" bleeding origin, intraoperative colonoscopy and enteroscopy should be performed and every attempt should be made to identify the bleeding site: "blind" segmental resection has a high risk of rebleeding (up to 75%) and mortality (up to 50%) and should be avoided. If the bleeding site remains unidentified after all available diagnostic procedures, subtotal colectomy with terminal ileostomy or ileorectal anastomosis is advisable.

12.3.7 Prognosis

- Approximately 80% of acute severe LGIBs stop spontaneously.
- Surgical treatment is inevitable in 10–25% of cases.
- When the bleeding source is preoperatively identified, a rebleeding rate of 8% and mortality of up to 15% can be expected.
- In cases with an unknown bleeding site, limited resections have a rebleeding rate of 20% with high mortality; when "blind" subtotal colectomy and ileostomy is performed, the risk of rebleeding is 2% and mortality is 15%.

Suggested Reading

1. Bounds BC, Friedman LS (2003) Lower gastrointestinal bleeding. Gastroenterol Clin 32:1107–1125
2. Finne CO III (1992) The aggressive management of serious lower gastrointestinal bleeding. Probl Gen Surg 9:597
3. Jensen DM, Machicado GA (1997) Colonoscopy for diagnosis and treatment of severe gastroenterological bleeding. Routine outcome and cost analysis. Gastrointest Endoc Clin North Am 7:477–493
4. Landefeld CS, Goldman L (1989) Major bleeding in outpatients treated with warfarin: incidence and prediction by factors known at the start of outpatient therapy. Am J Med 87:144–152
5. Longstreth GF (1997) Epidemiology and outcome of patients hospitalized with acute lower gastrointestinal hemorrhage: a population-based study. Am J Gastroenterol 92:241–252
6. Ng DA, Opelka FG, Beck DE et al (1997) Predictive value of technetium Tc 99m-labeled red blood scintigraphy for positive angiogram in massive lower gastrointestinal hemorrhage. Dis Colon Rectum 40:471–477
7. Ure T, Vernava AM, Longo WE (1994) Diverticular bleeding. Semin Col Rect Surg 5:32

Pain Syndromes

13.1 Chronic Pelvic Pain

GUILLAUME MEURETTE, JEAN-JACQUES LABAT

13.1.1 Definition

Chronic pelvic pain may be defined as on going pelvic pain or discomfort that results in suffering with psychological and social consequences for a period of more than 6 months. For the purposes of this chapter it does not include pain due to primary, secondary or recurrent malignant disease.

13.1.2 Introduction

Chronic perineal pain is not well described in the surgical literature. It affects a heterogeneous group of patients who may be disabled for prolonged periods. Patients are often subjected to a series of negative investigations and unsuccessful medical treatments. This situation leads to a debilitating condition with severe psychological consequences. The underlying causes are many and management usually requires multidisciplinary involvement to include coloproctological, urogynaecological and neurophysiological assessment alongside input from a specialist in pain management.

13.1.3 Clinical Features

In the assessment of chronic pelvic pain the clinical history is of paramount importance. It is important to characterise the distribution (topography) and the nature of the pain. Three anatomical distributions of pain are frequently recognised (Fig. 13.1.1):

- The pudendal nerve area
- The iliohypogastric area
- The inferior cluneal (perineal) nerve area

The nature of the pain may be characterised as mechanical or inflammatory. These may be distinguished as follows (Table 13.1.1):

- Mechanical: the pain is influenced by the position of the patient (sitting or standing position) and may be improved by the decubitus position.
- Inflammatory: the pain is worse at night with sleep loss. No position eases the pain. Medications can be effective in controlling the pain.

13.1.4 Investigation

Investigation of chronic pelvic pain must include a comprehensive series of clinical, endoscopic and physical examinations to exclude anatomical abnormalities and malignant or inflammatory disease of the pelvic organs. Computed tomography (CT) or magnetic resonance imaging (MRI) of the lumbosacral spine is required to identify anatomical abnormalities of the spine or compression of the cauda equina or roots of the sacral plexus. Particular attention must be paid to exclude tumours in the presacral space. Bone metastases, particularly from breast or prostatic primary tumours, must be considered. An isotope bone scan may be helpful. However, in the majority of patients with chronic pelvic pain the radiological findings are normal.

Neurophysiological studies are helpful to identify abnormalities of nerve conduction. Pudendal nerve terminal motor latency, external anal sphincter electromyogram (EMG) and the bulbospongiosus or clitoroanal reflex allow assessment of both motor and sensory function. Of these tests, EMG is quite invasive. Interpretation of results can be difficult and must be in the context of the clinical features.

13.1.5 Classification

13.1.5.1 Pain Influenced by the Sitting Position

Pudendal Nerve Entrapment

The most frequent and best known cause of chronic pelvic pain, pudendal nerve entrapment, is characterised by a median or unilateral pain localised between the penis and the anus in men and the clitoris and the anus in women. The pain does not usually involve the scrotum or

Fig. 13.1.1 Management of chronic pelvic pain

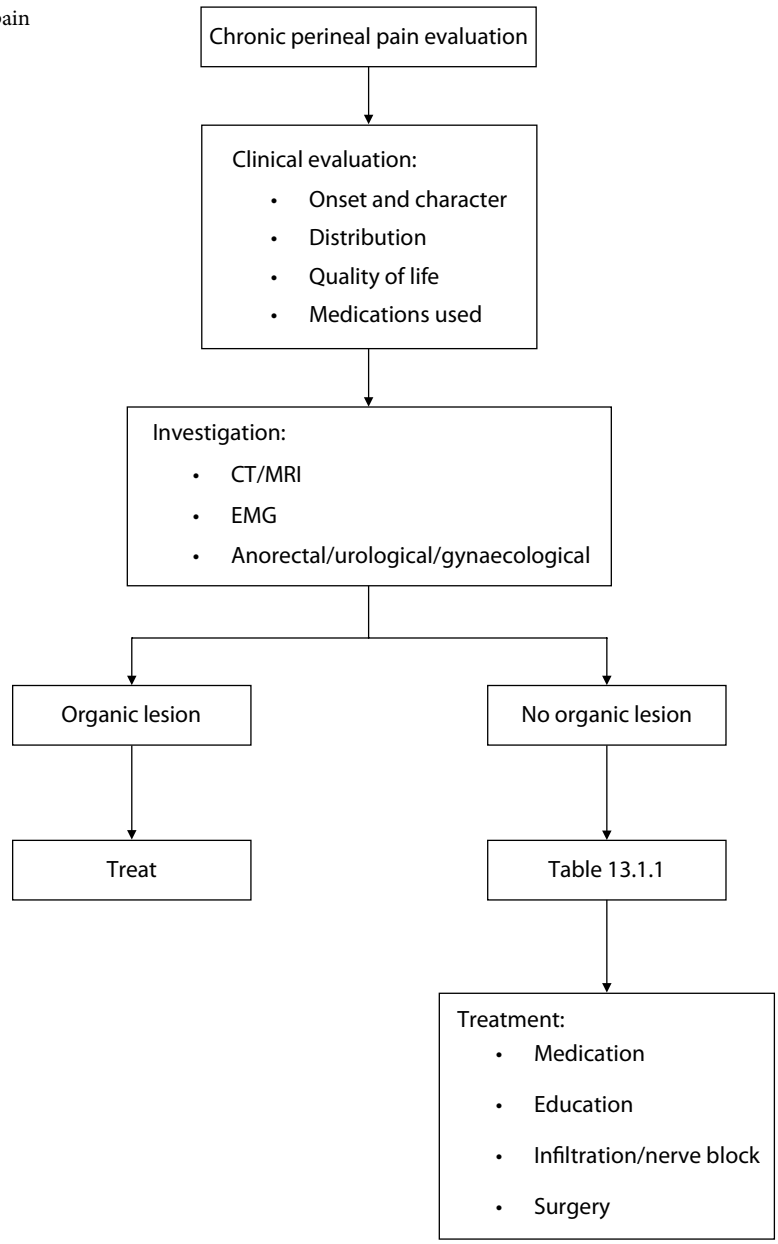


Table 13.1.1 Aetiology of chronic pelvic pain

Pain influenced by sitting position	Pain not influenced by sitting position
Pudendal nerve entrapment	Sacral nerve irritation
Piriformis muscle syndrome	Abdomino-genital pain
Coccygodynia	Vulvodynia
Obturator internis muscle syndrome	Urethral syndrome
Inferior cluneal (perineal) nerve syndrome	Paroxystic algias (proctalgia fugax)
Levator ani syndrome	Myofascial syndrome

testicles. The onset may be spontaneous or after an event, typically cycling.

The pain is described as a perineal burning or strangling pain which may be superficial or deep and continuous. It may be associated with hypersensitivity to local touch. The pain is usually worse on sitting and improves when the patient stands up. Typically, pain increases during the day. There may be a trigger point on rectal examination at the level of the ischial spine or the pain may be induced by simple pressure on the levator ani muscle.

The diagnosis is supported by finding prolonged pudendal nerve motor latency on electrophysiological studies and successful treatment by steroid infiltration of the nerve at the level of the ischial spine.

Piriformis Syndrome

The posterior cutaneous nerve of the thigh can be entrapped in the subpiriformis canal. This may result in chronic perineal pain, often associated with perineal radiation in distribution of the cluneal (perineal) or pudendal nerves.

Coccygodynia

The pain is situated in the midline over and anterior to the coccyx. The pain is usually reproduced by pressing the coccyx. The standing position may improve the pain. Clinical examination and dynamic x-rays may show excessive mobility of the sacrococcygeal joint. Relief of symptoms following injection of local anaesthetic and steroids into the joint confirms the diagnosis. Rarely excision of the coccyx is necessary.

Obturator Internis Syndrome

The gluteal part of the obturator internis muscle is in contact with the pudendal and obturator nerves. Hypertonicity of the muscle may explain chronic pain in the sciatic and the perineal areas. Clinical examination can be helpful in establishing the diagnosis as the pain can be evoked by deep pressure on the inside of the ischial tuberosity.

Inferior Cluneal (Perineal) Nerve Syndrome

The inferior cluneal (perineal) nerve has perineal ramifications with the posterior cutaneous nerve of the thigh. A lesion of this superficial nerve can produce pain on the posterior aspect of the thigh and under the buttock going towards the lateral perineal area. The pain usually does not involve the vulva or the anus.

Levator Ani Syndrome

The levator ani syndrome typically results in anorectal pain occurring in the sitting position with associated tenesmus. Defaecation disorders are often associated with the pain.

13.1.5.2 Pain Not Influenced by the Sitting Position

Sacral Nerve Irritation

Sacral radiculopathy is usually associated with compression or irritation of the nerves of the cauda equina or sacral plexus. Loss of perineal sensation or difficulty with either defaecation or micturition are serious clinical findings and should prompt urgent investigation with MRI scanning of the lumbosacral spine to identify nerve compression.

Abdomino-Genital Pain and Myofascial Syndrome

Compression or entrapment of the ilioinguinal or iliohypogastric nerves can cause chronic pain, often associated with dysaesthesia or anaesthesia in the inguinal, and scrotal or labial cutaneous distribution of the nerve. The usual cause is surgical injury often during inguinal hernia repair. A local anaesthesic block in the line of the surgical scar can confirm the diagnosis.

Vestibulodynia (Vulvar Vestibulitis)

A burning sensation localised at the vestibule represents the typical description of the pain. The wearing of tight clothes may be uncomfortable. Dyspareunia and vulvar hyperaesthesia are usual and typically, in younger women, have profound effects on sexual function with significant emotional consequences.

Urethral Syndrome

Pain occurs during micturition or ejaculation. The syndrome can be related to interstitial cystitis or chronic prostatitis.

Paroxystic Algia and Proctalgia Fugax

The diagnosis is based on symptoms only, but is well characterised. The pain is located in the anal canal, with no radiation. The pain is of sudden onset, is severe, lasts for several minutes and abruptly stops. The whole painful period is usually less than 15 min. A spasm of the internal anal sphincter or levator ani is often given as the explanation of this syndrome. There is no specific treatment, although many patients find that by bearing down or straining in an attempt to defaecate will relieve the

pain. Rarely it is associated with obstructed defaecation syndrome.

13.1.6 Treatment

- Treatment of chronic perineal pain is challenging partly because of the heterogeneous group of underlying causes and partly because of the debilitation of chronic pain syndromes.
- The main objective is to help the patient manage the pain together with its psychological and social consequences. This often requires the assistance of a specialist in chronic pain management and occasionally psychological or even psychiatric support.
- The first steps are:
  - Explanation and reassurance regarding the nature of the problem
  - Evaluation of the severity of the pain
  - Initiation of analgesic medication according to the severity of pain.
- Invasive procedures such as local nerve blocks or steroid infiltration or surgical neurolysis may be useful when a focal lesion is identified.
- Pudendal nerve entrapment can be successfully managed by combining decompression and transposition of the pudendal nerve.
- Transcutaneous electrical stimulation may be helpful in reducing the intensity of pain and long-term implantable electrical stimulation devices are available to block noxious sensory input.

Suggested Reading

1. Goodson J (1981) Pudendal neuritis from biking (letter). N Engl J Med 304:365
2. Mavillon J, Thomas D, Leroi AM, Freger P, Michot F, Denis P (1999) Results of pudendal nerve neurolysis-transposition in 12 patients suffering from pudendal neuralgia. Dis Colon Rectum 42:186–192
3. Robert R, Prat-Pradal D, Labat JJ, Bensignor M, Raoul S, Rebai R, Le Borgne J (1998) Anatomic basis of chronic pain: role of the pudendal nerve. Surg Radiol Anat 20:93–98
4. Robert R, Labat JJ, Bensignor M, Glemain P, Deschamps C, Raoul S Hamel O (2005) Decompression and transposition of the pudendal nerve in pudendal neuralgia: a randomised controlled trial and long-term results. Eur Urol 47:403–408
5. Wald A (2001) Anorectal and pelvic pain in women. J Clin Gastroenterol 33:283–288

Subject Index