Histopathology of Chronic Constipation
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In 2005, the Journal of Pathobiology (vol. 72) published a review about the pathohistology of motility disorders of the gut. This publication about the morphology of chronic constipation had a remarkable echo. Now, 7 years later, it seemed to be the time to write an update so as to incorporate the new data which has become available since that review. This book represents more than 40 years of experience in rectocolic biopsy diagnostics of gut motility disorders. Pathologists will find much diagnostic information in the field of chronic constipation, often considered as a functional disease without a morphological substrate.

It became obvious that not only an aganglionosis (Hirschsprung’s disease), but also a lack or atrophy of the tendinous collagen net in circular and longitudinal muscles may cause an aperistaltic syndrome.

Enzyme histochemistry has proven to be the pathophysiological technique of choice in the pathology of chronic constipation. This method provides insights into gastrointestinal motility disorders by the cholinergic nervous system and the dehydrogenase activity of nerve cells in the submucous and myenteric plexus. The dehydrogenases of the citric circle selectively stain nerve cells in the intestinal wall. Nitroxide synthase helps the pathologist in immediate sections for microscopic examination under surgery to reliably inform the pediatric surgeon whether the planned resection margin is aganglionic, hypoganglionic, or normal innervated.

Enzyme histochemistry overcomes the often frustrating results of classical histological stainings in formalin-fixed biopsies. Besides classical Hirschsprung’s disease, it is also possible to differentiate in mucosal biopsies ultrashort Hirschsprung’s disease, immaturity of the enteric nervous system, and neuronal dysplasia.

A laboratory guide provides instructions on how to prepare colorectal biopsies or surgical specimens, and how to transport them to the histopathological laboratory over long distances. The most important enzyme histochemical reactions in the diagnosis of gastrointestinal biopsies are also described. A final section briefly outlines immunohistochemical techniques in paraffin sections of formalin-fixed tissue. Immunohistochemistry is a static staining technique like any other histological staining (e.g. hemalum-eosin staining). It is less reliable than the enzyme histochemical technique.

It is the hope of the authors that the technical advice and the many pictures of characteristic anomalies in the gut may be helpful in the understanding and diagnosis of the different intestinal diseases which cause chronic constipation.
Preface

The first edition of the book on pathology of chronic constipation was drafted as an atlas folio. It enjoyed a brisk demand and sold out in the first year. This encouraged us to prepare the second edition 7 years later.

It has been demonstrated that enzyme histochemistry of native seromuscular intestinal biopsies allows the evaluation of nerve cell size and their dehydrogenase activity to recognize plexus immaturity in babies and inborn hypoplasia of the myenteric plexus in adults.

The acetylcholinesterase (AChE) activity of nerve fibers in circular and longitudinal muscles provides information about the motility performance of a particular intestinal part. This is important as it tells the surgeon whether an intestinal section is unable to transport its content properly, and it is a possible indication for resection in cases of negative findings. The nerve cell supply of the myenteric plexus and the parasympathetic tonus (AChE activity) of a proximal resection edge is a reliable source of information that the surgeon needs for a successful curative therapy.

Mucosa suction rectum biopsies offer a reliable diagnosis of an inborn aganglionosis (Hirschsprung’s disease) by the pathological increased AChE activity in parasympathetic nerves of mucosa and muscularis mucosae.

The use of native seromuscular intestinal biopsies, cut in a cryostat, avoids shrinking artefacts in circular muscles of the intestinal wall as is usually observed in formalin-fixed tissue. Shrinking artefacts of circular muscles prevents the pathologist from recognizing the extension of an atrophy or myopathy in circular muscles.

The heretofore neglected tendinous collagen net in the muscularis propria and plexus layer, which operates intestinal peristalsis, provides information about its stenotic effect if this structure is atrophied by inflammation or X-ray lesion. Crohn’s disease, diverticulitis, and ulcerative colitis destroy, via leukocytic collagenases, the tendinous net in muscularis propria and plexus layer, causing a stenotic symptomatology.

Architectural abnormalities of the muscularis propria as a doubling of the plexus layer explain focal stenotic symptoms. Smooth muscles myopathies are rare but serious reasons of an aperistaltic syndrome.

This book offers insights into many functional disturbances of intestinal motility, which are often not recognizable in formalin-fixed and standard HE-stained sections. It increases our diagnostic spectrum in chronic constipation. Histopathology of Chronic Constipation is an important reference book for pathologists in the diagnosis of chronic constipation; however, surgeons, gastroenterologists, and pediatricians will also find it important for understanding the reasons behind intestinal transport problems.

Acknowledgments

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We sincerely thank Thomas Schürch of the photographic unit of the institute for the invaluable help in preparing and printing the illustrations.
Introduction

Chronic constipation is a fairly frustrating matter in classical histopathology as hemalum-eosin staining allows only a limited diagnostic statement. This, however, has changed in recent decades. Today, the foundation of histopathological diagnosis of gastrointestinal motility disorder is enzyme histochemistry. Many different gut diseases have been clearly diagnosed by enzyme histochemical techniques, such as Hirschsprung’s disease (HD), ultra-short rectum aganglionosis, hypoganglionosis, immaturity of the enteral nervous system, intestinal neuronal dysplasia, and atrophic alterations of the lamina propria [1, 2].

Compared to enzyme histochemistry, immunohistochemistry in paraffin-embedded formalin-fixed tissue is presently only of limited value. The diagnosis of HD was a breakthrough for enzyme histochemistry. It is possible to diagnose HD reliably in rectum mucosa biopsies with the aid of an acetylcholinesterase reaction [3–5], which has become the gold standard in the diagnosis of HD [1, 6–8]. Today, enzyme histochemistry is the technique of choice in experimental pathology, as well as in the histopathological differential diagnosis of chronic constipation [9].