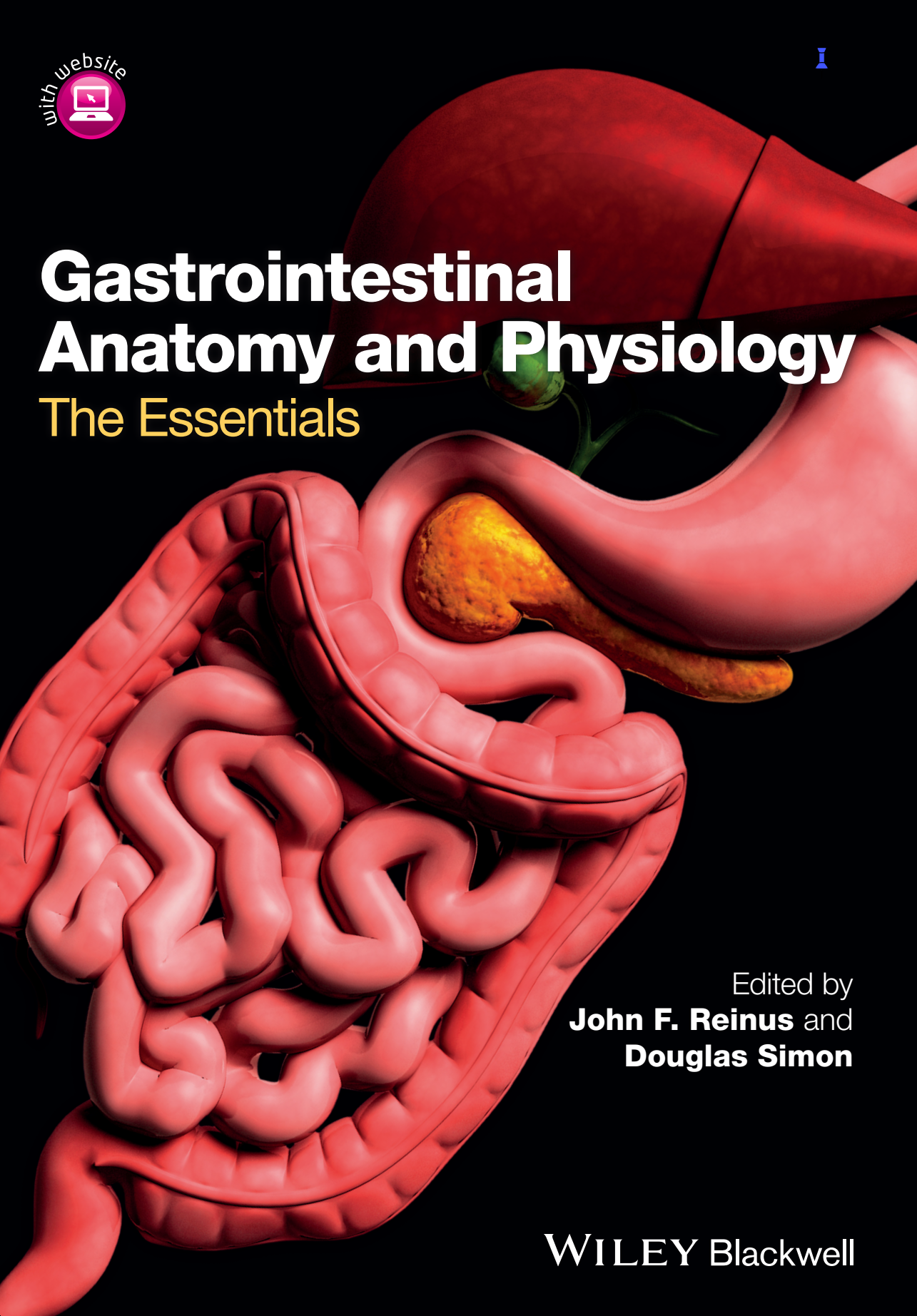

Gastrointestinal Anatomy and Physiology

The Essentials

Edited by
John F. Reinus and
Douglas Simon

WILEY Blackwell

Gastrointestinal Anatomy and Physiology

We dedicate this book to our teachers and students, and to our families, especially our wives: Enid and Doreen, this book is for you with our undying gratitude for your boundless love and support.

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The Essentials

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Preface

A relatively detailed understanding of normal organ structure and function is essential to adequately evaluate, diagnose, and manage disease. The American Board of Internal Medicine has endorsed this proposition by including questions about the normal anatomy and physiology of digestive organs in the Gastroenterology Certification Examination. According to a statement published by the Board, approximately 10% of the Certification Examination questions test knowledge of these subjects.

Many years ago, during our training, we had our first discussion of how best to learn about gastrointestinal anatomy and physiology. Predominantly regional organization made it difficult to acquire an overall understanding of many important topics by studying some standard texts: in these books, conceptually related information about microscopic anatomy, motility, absorption and secretion, and of other topics was divided among chapters principally devoted to major organs, for example, the stomach or the small bowel. In addition, the overwhelming quantity of information in reference works made finding and selecting the details that were relevant to clinical practice a near-impossible task, at least from the point of view of two novice practitioners.

Several years later, we were able to persuade the members of the Educational Affairs Committee of the American College of Gastroenterology to allow us to create a review course dedicated exclusively to the subjects of normal gastrointestinal structure and function. Until its recent discontinuation, this course was offered every other year at the College's annual meeting in conjunction with its regular board review. Hundreds of gastroenterologists have benefited from the excellent presentations made at the course by many of the same individuals who have contributed chapters to this book.

It is, therefore, with great pleasure that we have seized the opportunity offered us by the people at Wiley to address in book form the subject of basic gastrointestinal structure and function. Our intention is to create a review from the perspective of what is needed to practice clinical gastroenterology and to present it in chapters devoted to specific topics in anatomy and physiology. We hope you enjoy it.

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The Albert Einstein College of Medicine

About the companion website

Gastrointestinal anatomy and physiology has its own resources website:

www.wiley.com/go/reinus/gastro/anatomy

The website includes all figures from the book

CHAPTER 1

Structure and innervation of hollow viscera

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The tubular gastrointestinal (GI) tract consists of hollow organs composed of distinct tissue layers: mucosa, submucosa, muscularis propria, and serosa or adventitia. The mucosa of each GI organ has a unique cellular structure, whereas the other layers are similar throughout the GI tract. Innervation of the hollow viscera consists of postsynaptic sympathetic and presynaptic parasympathetic neurons with parasympathetic ganglion cells present in the myenteric (Auerbach's) and submucosal (Meissner's) plexi. It is important to note that there is more lymphoid tissue (mucosa-associated lymphoid tissue) in the GI tract than there is in all the rest of the body combined.

The mucosa

The mucosa is the innermost layer of the GI tract; its function will be discussed in detail in the succeeding text. The mucosa has three components:

1. The epithelium, which has protective and secretory or absorptive properties.
2. The lamina propria, a loose connective tissue zone supporting the avascular epithelium. In the esophagus, stomach, and small intestine, but not the colorectum, the lamina propria has many lymphatics, allowing mucosal tumors to easily invade the lymphatics of the upper GI tract. In the upper GI tract, there are fewer immune cells (lymphoid and plasma cells) in the lamina propria than there are in the lamina propria of the small bowel and colon.
3. The muscularis mucosae, a narrow double layer of inner circular and outer longitudinal smooth muscle separating the mucosa from the submucosa. The muscularis mucosae resembles the muscularis propria but in miniature.

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The submucosa

The submucosa is composed of connective tissue and contains Meissner's nerve plexus as well as large-caliber blood vessels.

The muscularis propria

The muscularis propria gives structural strength to the hollow viscera. It is composed of an inner circular and outer longitudinal layer of smooth muscle. Between these layers is Auerbach's nerve plexus.

Serosa or adventitia

The outermost layer of the GI tract is either a serosa or an adventitia. The latter is distinguished by its lack of a mesothelial membrane lining.

Parasympathetic ganglion cells are found in Meissner's and Auerbach's nerve plexi. The submucosal Meissner's plexi also contain neuronal cell bodies of the intrinsic sympathetic nerve system that function on the local area of the gut. These are the neurons that have chemoreceptors and mechanoreceptors. They synapse on both other ganglion cells and on muscle and secretory cells.

Esophagus

The esophagus is about 25 cm in length and consists of a cervical and upper-, mid-, and lower-thoracic segments. It is physiologically constricted by the cricoid cartilage, the aortic arch, the left atrium, and the diaphragm. The esophagus is unique among the hollow viscera in that it has skeletal (voluntary) muscle, which surrounds its upper portions. The vagus nerve provides the esophagus with parasympathetic innervation, whereas its sympathetic innervation is from the cervical and paravertebral ganglia.

Histologically, the squamous mucosa of the esophagus is heaped up in folds (Figure 1.1a and b). The mitotically active basal layer matures completely into a surface layer containing tonofilaments within 10 days. The basal layer comprises about 15% of the esophageal epithelial thickness. The cells become flatter and more eosinophilic as they approach the surface. The normal esophageal epithelium lacks a granular layer (present in skin) and does not keratinize. A small number of T lymphocytes are normally present in the epithelium.

Beneath the esophageal epithelium is the lamina propria, which contains numerous small capillary-sized blood vessels and lymphatics as well as elastic fibers. The esophageal lamina propria has very few lymphocytes and essentially no

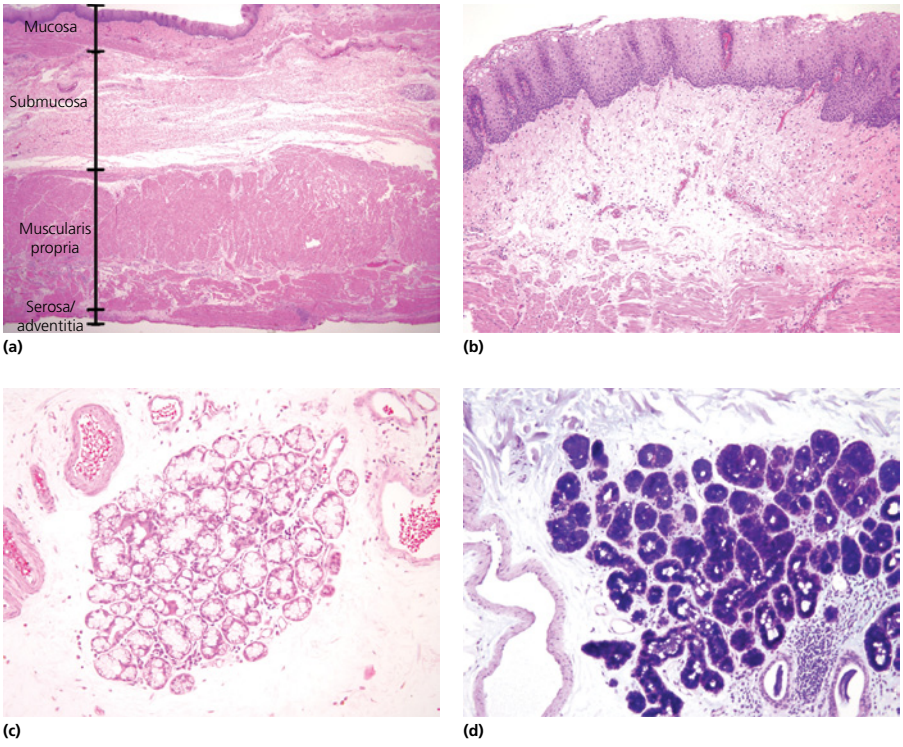

Figure 1.1 Normal histology of the esophagus. (a) Low-power image (H&E stain) of normal esophagus illustrating the characteristic layers of the wall – mucosa, submucosa, muscularis propria, and adventitia/serosa. A submucosal gland can be seen at the right side of the image. (b) Medium-power image (H&E stain) of the esophageal mucosa, with stratified squamous epithelium, lamina propria, and muscularis mucosae. Note the rich vascularity in the lamina propria. (c) High-power image (H&E stain) of an esophageal submucosal gland. (d) High-power image (PAS-AB stain) of an esophageal submucosal gland with characteristic dark blue color.

eosinophils or plasma cells. The lymphovascular network of the lamina propria facilitates spread of invading cancers, as do similar networks in the stomach and small intestine (but not the colon).

The muscularis mucosae of the esophagus is a slender layer that rapidly thickens in response to injury; resultant reduplication of this layer may make cancer staging difficult. Normally, the smooth muscle fibers of the muscularis mucosae are mostly longitudinal in orientation. There is no skeletal muscle in the esophageal muscularis mucosae (in contrast to the esophageal muscularis propria which contains skeletal muscle fibers). In the upper esophagus, the muscularis mucosae blends with the fibrous membrane of the hypopharynx, whereas in the lower esophagus, it merges with the muscularis mucosae of the stomach.

The submucosa of the esophagus is composed of loose connective tissue with abundant elastic fibers, a rich lymphovascular network that has well-developed venous plexi, scattered ganglion cells, and nerve fibers of Meissner's plexus.

The esophageal submucosa also contains glands (Figure 1.1c and d). These glands are composed of mucin-producing cells that are deeply alcianophilic on periodic acid–Schiff–Alcian blue (PAS-AB) staining. They may undergo various types of metaplasia in response to injury. Ducts lined by cuboidal epithelium convey mucus secreted by the glands to the luminal surface of the esophagus where it lubricates the passage of food.

The esophageal muscularis propria is composed of striated muscle in the upper esophagus, smooth muscle in the lower esophagus, and a mixture of the two in between. The amounts of smooth and striated muscle are said to become equal about 5 cm below the esophageal–pharyngeal junction. There is a well-developed neural plexus (Auerbach's plexus) between the inner circular and outer longitudinal muscle layers. The inner circular layer of the lower esophagus, or lower esophageal sphincter (LES), contracts or relaxes in response to gastrin or secretin. There are no specific histologic features that distinguish the LES from the rest of the muscularis propria.

The esophagus has an adventitia, a layer of coarse connective tissue that connects the esophagus to adjoining structures, in particular the mediastinum. The adventitia contains thick nerves, blood vessels, and lymphatics.

Stomach

The stomach has four parts, each with different mucosal features: the cardia (most proximal), fundus, body, and antrum (most distal). The cardia and antrum are histologically similar and have the function of protecting the esophagus (cardia) or duodenum (antrum) from the acid and enzymes present in the rest of the organ. The cardia expands, and may even be acquired, as a result of acid injury and other insults in the region of the gastroesophageal junction [1–5]. The stomach receives sympathetic innervation from the celiac plexus and parasympathetic innervation from the vagus nerve.

The luminal surface of the empty stomach has thick longitudinal folds, or rugae, with tiny surface invaginations called gastric pits, which allow gastric glandular secretions to reach the mucosal surface. These glands, regardless of their location in the stomach, have an isthmus, neck, and base and are complex, convoluted structures that are difficult to visualize in three dimensions based on their microscopic appearance in two dimensions (Figure 1.2a and b). The entire surface of the stomach, including the gastric pits, is lined by foveolar cells that secrete neutral mucin and appear pink on PAS stain (Figure 1.2c and d).

The glands of the gastric body and fundus are similar in structure. The most common cell type of the gland isthmus is the mucous neck cell. These cells also are found in the neck where parietal (oxyntic) cells are most numerous. The chief cell is found at the base of the gland. The areas of the gland with parietal and chief cells do not stain with PAS-AB because they do not contain mucin (Figure 1.2d).

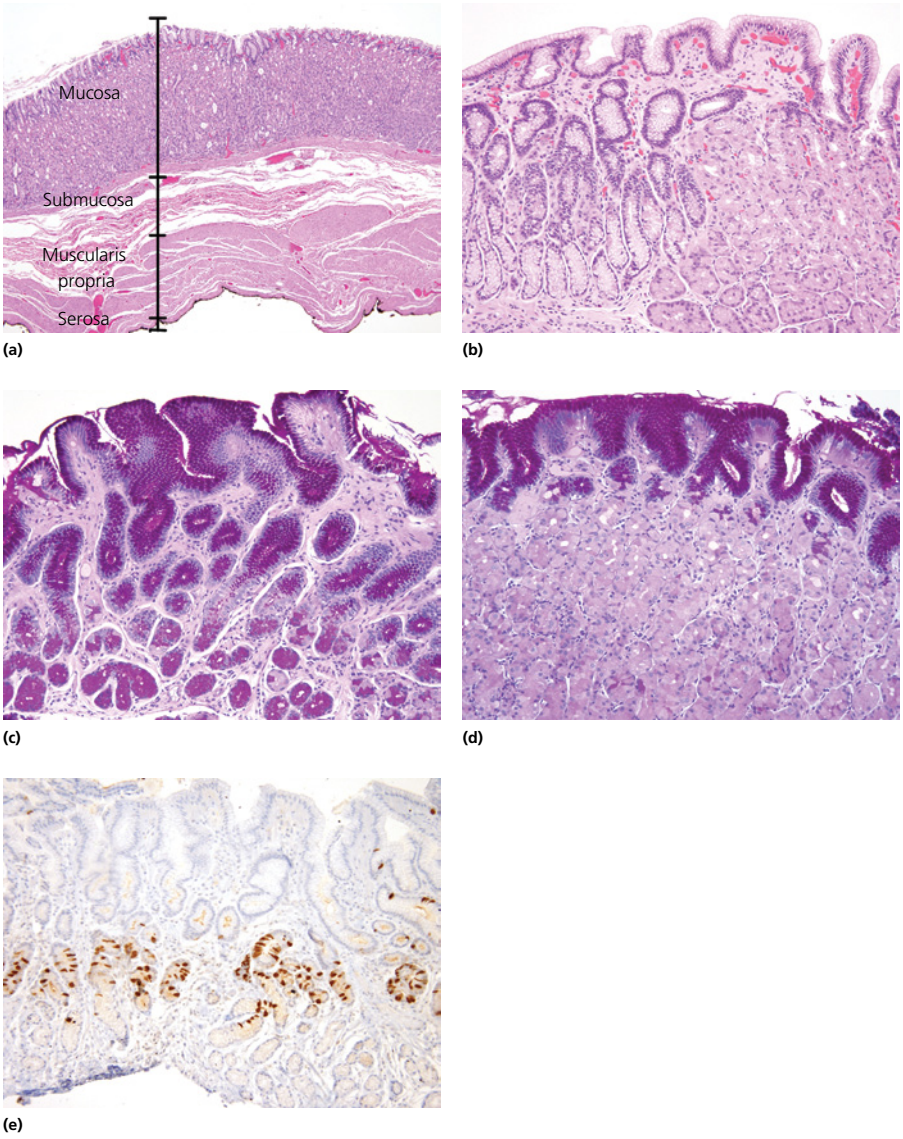

Figure 1.2 Normal histology of the stomach. (a) Low-power image (H&E stain) of normal stomach (body) illustrating the characteristic layers of the wall – mucosa, submucosa, muscularis propria, and serosa. (b) Medium-power image (H&E stain) of transitional gastric epithelium. On the right, oxyntic epithelium consists of surface foveolar cells overlying oxyntic glands with parietal and chief cells. On the left, antral epithelium consists of foveolar cells overlying mucin-producing antral glands. (c) Medium-power image (PAS-AB stain) of antral epithelium, illustrating the bright pink staining of both the foveolar cells and the antral glands. (d) Medium-power image (PAS-AB) stain of oxyntic epithelium, with bright pink staining of foveolar cells but lack of staining in the parietal and chief cells of the oxyntic glands. (e) Antral mucosa (gastrin immunohistochemical stain), illustrating the presence of gastrin-producing G cells in the antral glands. Gastrin immunohistochemical stain is negative in oxyntic mucosa and in cardiac mucosa.

Endocrine cells are found in the deep isthmus toward the gland base. The cardiac and antral glands are neutral mucin-producing glands that stain pink with PAS-AB (Figure 1.2c). The cardia and antrum are very similar histologically, but the antrum contains G cells, whereas the cardia does not (Figure 1.2e).

The G cells of the antrum secrete gastrin, which stimulates enterochromaffin-like cells of the gastric body and fundus to secrete histamine. Histamine in turn stimulates acid secretion by parietal cells of the gastric body and fundus. In addition, gastrin has a trophic effect on parietal cells. The antrum also contains D cells that secrete somatostatin, which inhibits G-cell gastrin secretion. All these endocrine interactions are important in disease states. For example, in autoimmune gastritis, patients have immune damage to parietal cells that results in hypergastrinemia, because antral G cells secrete excess gastrin in an attempt to stimulate acid production. Autoimmune damage to parietal cells, which produce intrinsic factor, results in pernicious anemia.

The lamina propria of the stomach contains small numbers of plasma cells, eosinophils, mast cells, and lymphocytes. Lymphatics and blood vessels are less numerous than they are in the lamina propria of the esophagus. Scattered lymphoid aggregates are present. Bacteria are absent from normal gastric mucosa, whereas mucosal bacteria are seen in the esophagus and ileocolon.

The muscularis mucosae of the stomach contains an inner circular and outer longitudinal layer of smooth muscle. In some instances, a third slim circular layer is present.

The submucosa of the stomach is formed of connective tissue with elastic fibers and has prominent blood vessels, as does the lamina propria of other parts of the tubular GI tract. Meissner's plexus is found in the gastric submucosa.

The gastric muscularis propria consists of three fairly indistinct layers: an inner oblique, middle circular, and outer longitudinal layer. The layers are somewhat randomly oriented and may be absent or poorly developed in some areas. This random arrangement of muscle fibers is typical of hollow organs that expel their contents (e.g., uterus, urinary bladder, gallbladder). The muscularis propria contains Auerbach's plexus and ganglion cells. Interstitial cells of Cajal (ICCs), also called "pacemaker" cells, can be readily identified in the muscularis propria using immunolabeling with antibodies directed against CD117 (c-kit protein).

The stomach is encased by a serosa that is composed of connective tissue and a lining of flat-to-cuboidal peritoneal cells, a unique type of modified epithelial cell. This contrasts with the connective tissue covering the esophagus.

Small bowel

The small bowel is divided into three major sections. The duodenum extends from the gastric pylorus to the ligament of Treitz and is formed sequentially of a bulb and descending, horizontal, and ascending portions. The duodenum is

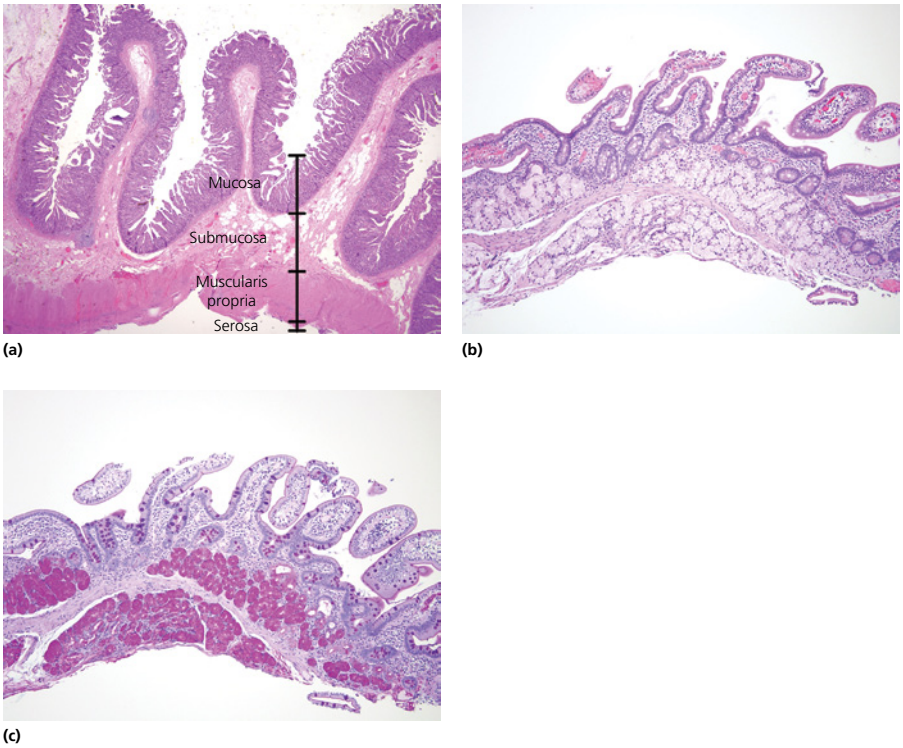

Figure 1.3 Normal histology of the small bowel. (a) Low-power image (H&E stain) of normal small bowel with plicae circulares and epithelial villi. The small bowel contains the same layers as the other organs of the tubular GI tract – mucosa, submucosa, muscularis propria, and serosa. (b) Medium-power image (H&E stain) of the duodenal mucosa and submucosa, illustrating the presence of Brunner's glands in the lamina propria and submucosa. Strictly speaking, Brunner's glands should be restricted to the submucosa, but most adult patients have Brunner's glands in the duodenal lamina propria, presumably a reparative change. (c) Medium-power image (PAS-AB stain) of the duodenal mucosa and submucosa, illustrating the bright pink staining of Brunner's glands. Note that the goblet cells contain alcianophilic purple-colored mucin, whereas the absorptive cells lack mucin.

mostly retroperitoneal, whereas the jejunum and ileum are intraperitoneal. The jejunum is distal to the ligament of Treitz and consists, somewhat arbitrarily, of the proximal third of the intraperitoneal small bowel. The jejunum narrows into the ileum, which is formed by the distal two-thirds of the intraperitoneal small bowel and joins the colon at the ileocecal valve. These sections of the small bowel receive parasympathetic innervation from the vagus nerves and sympathetic innervation from the celiac plexus.

Like the esophagus and stomach, the small bowel wall consists of layers: mucosa (epithelium, lamina propria, muscularis mucosae), submucosa, muscularis propria, and serosa or adventitia (Figure 1.3a). The unique gross and microscopic anatomy of the small bowel reflects its principal function, absorption of nutrients. Macroscopic plicae circulares and microscopic villous

projections of the epithelium and lamina propria give a tube 6–7-m long an absorptive surface of 200–500 m^2. Villi are broad in the duodenum and ileum and are long and thin in the jejunum. In between villi, the epithelium forms invaginations, or glands, referred to as "crypts of Lieberkühn." The villus-to-crypt height ratio is quite variable throughout the small bowel, ranging from 2–3:1 in the proximal duodenum to 4–5:1 in the jejunum.

Small bowel villi and crypts are lined mainly by absorptive cells that have a microvillus brush border consisting of numerous cytoplasmic projections that further expand the enterocyte's absorptive surface. Absorptive cells of the small bowel lack mucin, including the neutral mucin found in the foveolar cells of the stomach [6]. Although most epithelial cells are absorptive, the epithelium also contains scattered goblet cells with large vacuoles of acid mucin. There also are scattered Paneth cells in the crypts of the small bowel, with basal nuclei and red granular apical cytoplasm, as well as endocrine cells with apical nuclei and granular basal cytoplasm. These two cell types have a similar appearance but opposite orientation relative to the basement membrane, and the granules of endocrine cells are smaller than those of Paneth cells. Paneth cells have large eosinophilic granules containing growth factors and antimicrobial proteins, while endocrine cells have fine granules containing a variety of peptides and bioactive compounds.

The lamina propria of the small bowel contains numerous lymphocytes and plasma cells (primarily IgA-secreting) as well as scattered eosinophils. Capillaries and lacteals, blindly ending lymphatic vessels that absorb chylomicrons, are found in the lamina propria at the tips of the villi. The lamina propria of the villi also contains delicate strands of smooth muscle.

The small bowel muscularis mucosae consists of slim inner circular and outer longitudinal layers of smooth muscle. The crypt bases reach the top of the muscularis mucosae.

The small bowel submucosa is composed of loose connective tissue and contains large-caliber vessels and Meissner's nerve plexus of both parasympathetic ganglion cells and sympathetic neurons. In the duodenum, the submucosa is the site of Brunner's glands, mucin-producing glands that are unique to the duodenum and contain neutral mucin (Figure 1.3b and c). The submucosa also contains lymphoid aggregates, often with germinal centers. These lymphoid aggregates, or Peyer's patches (PPs), are present throughout the small bowel but are most numerous in the ileum. While they have a linear orientation in the duodenum and jejunum, they are arrayed circumferentially in the ileum where they create a potential for intussusception if they undergo hypertrophy. Numerous intraepithelial lymphocytes (IELs) are present in the epithelium overlying the PPs; these lymphocytes communicate with the rest of the lymphoid compartment through specialized epithelial cells known as M cells.

The muscularis propria is a thick double layer of inner circular and outer longitudinal muscle that generates the propulsive action of the bowel wall and