INTRODUCTION

The gastrointestinal (GI) tract is a remarkable organ with many functions and several distinct functional regions: esophagus, stomach, small intestine, colon, and anus. Although the cell types in these various areas have many similarities, important regional histologic differences allow specific physiologic functions to be carried out in each area. The cellular rearrangements and migrations that accompany early embryogenesis play a critical role in organizing the eventual adult GI tract. Interactions between cell populations regulate subsequent patterns of gene expression and organ development (1).

The GI tract serves as the digestive organ of the body, taking in everything that is swallowed, converting it into nutrients, and discarding what is left over as waste. These processes begin in the mouth and terminate at the anus. While digesting everything to which it is exposed and breaking it down into smaller, absorbable chemical substances, the gut is itself able to withstand these processes and avoid autodigestion. Complex neuromuscular interactions move food and liquids from one section of the GI tract to the next, while at the same time controlling the passage of food in such a way that allows maximum digestion and absorption.

Not everything that enters the GI tract is healthy for the patient. The GI tract serves as a major interface between the outside world and other portions of the body. It is continuously exposed to toxins and infectious organisms, yet is often capable of eliminating these agents without any harm coming to the body. Not surprisingly, breakdown in these defense mechanisms often results in disease. This generally occurs when the integrity of the bowel wall becomes compromised, as is discussed in many of the following chapters. As a part of this mucosal defense, the GI tract serves as a major immune organ. It is the major site of the generation of mucosal immunity; hence the utility of oral vaccines.

GASTROINTESTINAL STRUCTURE

In general, the gut consists of four concentric layers as one progresses outward from the lumen: the mucosa, submucosa, muscularis propria, and serosa or adventitia (fig. 1-1). The mucosal features differ significantly from one region of the GI tract to another. The other layers share many of the same characteristics throughout the length of the gut, although some differences do occur.

Figure 1-1
FOUR TISSUE LAYERS OF COLON

Uppermost in the photograph is the mucosa, which is composed of the epithelium, a supporting lamina propria, and the muscularis mucosae. Deep to this layer is the submucosa, composed of connective tissue, vessels, and nerves. Next is the muscularis propria. The outermost layer in this case is the subserosa. This layer contains abundant adipose tissue underlying a mesothelial covering, the serosa.
Gastrointestinal Diseases

The mucosa consists of an epithelial lining, a supporting lamina propria composed of loose connective tissue rich in immune cells and capillaries, and the muscularis mucosae. The lamina propria is most visible in the stomach, large and small intestines, and appendix, and least visible in the esophagus and anus. The smooth muscle cells in the muscularis mucosae are predominantly arranged in a circular orientation, although some longitudinal muscle fibers are also present (fig. 1-2).

The character of the epithelium differs substantially in various regions of the GI tract, with differences reflecting the differing functions of each region. The squamous lining of the esophagus protects it from the passage of undigested food over its surface. Likewise, in the anus, the squamous epithelium protects the mucosa from the damaging effects of the passage of solid waste. In the stomach, the mucosa facilitates digestion by secreting acid. The epithelial lining of the small intestine is uniquely suited to the further digestion and absorption of nutrients along a gradient from the duodenum to the ileum. The colon predominantly reabsorbs water. The specific features of the various portions of the gut are discussed below.

The lamina propria represents the interglandular tissue of the mucosa. It consists of delicate, loose connective tissue containing lymphocytes, plasma cells (fig. 1-3), eosinophils, and mast cells. Most of the cells are plasma cells and lymphocytes. The majority of plasma cells secrete immunoglobulin (Ig)A; however, IgM-, IgG-, and IgE-secreting cells are also present. The lamina propria also contains large numbers of macrophages (55), which play an important role in mucosal immunity and immunoregulation (5,26,32, 45,52). Macrophages also engulf and remove apoptotic epithelial cells that are shed normally from the mucosal surface. As a result, lamina propria macrophages are sometimes immunoreactive with antibodies against epithelial-associated antigens, including carcinoembryonic antigen, BerEp4, and cytokeratin (34). The highest number of lamina propria macrophages is present in the colon and rectum (42).

Gut-associated lymphoid tissue (GALT) primarily lies within the lamina propria. It is distributed diffusely or appears as solitary (fig. 1-4) or aggregated nodules, which in the ileum and appendix are called Peyer patches. Larger aggregates contain germinal centers (fig. 1-4). Peyer patches often span the muscularis mucosae (fig. 1-5), creating gaps in this muscular layer. Solitary lymphoid nodules occur in the esophagus, gastric pylorus, and along the small and large intestines.
Mast Cells

Mast cells are an important, but heterogeneous, component of the lamina propria and submucosa. Mast cells are mononuclear and contain numerous cytoplasmic granules (fig. 1-6). The granules contain various mediators, including peptides, proteins, proteoglycans, and amines. The cytoplasmic granules stain with dyes, such as toluidine blue and Alcian blue. In addition, mast cells stain immunohistochemically with antibodies to CD117 (c-kit) and tryptase (fig. 1-7).

The relative proportion of mast cells differs between anatomic sites, and their recognition may be sensitive to formaldehyde fixation in
Mast cells are often adjacent to blood or lymphatic vessels, near or within nerves, and beneath epithelial surfaces, particularly those exposed to environmental antigens (3,19,33). Mast cell infiltrates are often associated with increased numbers of eosinophils. They degranulate after IgE-mediated stimulation. Following immunologic stimulation, mast cells release a variety of mediators that can contribute to inflammation, including histamine, leukotrienes, and cytokines. These mediators can recruit additional immune cells and activate other immune mechanisms.

**Figure 1-5**

PEYER PATCH

Above: Hematoxylin and eosin (H&E)-stained section shows a lymphoid aggregate that extends from the submucosa across the muscularis mucosae and into the mucosa.

Right: Immunohistochemical staining for actin demonstrates that the muscularis mucosae in this area is disrupted.

**Figure 1-6**

LAMINA PROPRIA

On routine H&E-stained sections, mast cells appear eosinophilic and have prominent cytoplasmic granules (arrow). The nucleus is not lobated like that of an eosinophil.

**Figure 1-7**

LAMINA PROPRIA

Mast cells in the lamina propria are easily recognized with the CD117 immunostain.

The intestinal mucosa (11,35,46). Mast cells are often adjacent to blood or lymphatic vessels, near or within nerves, and beneath epithelial surfaces, particularly those exposed to environmental antigens (3,19,33). Mast cell infiltrates are often associated with increased numbers of eosinophils. They degranulate after IgE-mediated stimulation. Following immunologic stimulation, mast cells release a variety of mediators that can contribute to inflammation, including histamine, leukotrienes, and cytokines. These mediators can recruit additional immune cells and activate other immune mechanisms.
activation via the IgE receptor, mast cells release cytokines, lipid-derived mediators, amines, proteases, and proteoglycans, all of which regulate adjacent cells and the metabolism of the extracellular matrix.

By virtue of their location and number, mast cells play a role in a wide variety of gastrointestinal abnormalities. The most important include food allergies, eosinophilic diseases, immunodeficiency syndromes, immediate hypersensitivity reactions, host responses to parasites and neoplasms, and immunologically nonspecific inflammatory and fibrotic conditions (4,30). Mast cells are also important in angiogenesis, wound healing, peptic ulcer disease, reactions to neoplasms, and other chronic inflammatory conditions, including graft versus host disease and inflammatory bowel disease (3,19,33).

**Eosinophils**

Eosinophils are commonly present within the lamina propria (fig. 1-8). Their brightly eosinophilic cytoplasmic granules and bilobed nucleus are characteristic identifying features. The cytoplasmic granules contain lysosomal hydrolases as well as many of the cationic proteins unique to eosinophils, including major basic protein (7,21) and eosinophil peroxidase. Eosinophils express receptors for IgG, IgE, and IgA on their plasma membranes (2,8,22,53). They also have receptors for complement components (9,20,23) and cytokines (29).

**Submucosa**

The submucosa is a more densely collagenous and less cellular layer than the mucosa (fig. 1-9). Major blood vessels, lymphatics, nerves, ganglia, and occasionally lymphoid collections are
located here. The submucosa may also contain adipose tissue in variable amounts.

**Muscularis Propria**

The muscularis propria is a continuous structure made up of two smooth muscle layers that extend from the upper esophagus to the anal canal (fig. 1-10). The only exception to this occurs in the stomach, where three layers are present. At the junctions between adjacent regions of the GI tract, the muscular coat rearranges to form sphincters (pharyngoesophageal, esophagogastric, pyloric, ileocecal, and anal sphincters). In the upper esophageal and anal sphincters, skeletal muscle fibers may be admixed with smooth muscle fibers (10). In the portion of the muscularis propria comprised of two layers, the inner muscular layer is arranged in a concentric circular fashion, while the outer muscle fibers are arranged longitudinally. In the cecum and in parts of the colon, the longitudinal muscle is attenuated except in the areas where it forms thick cords, the taeniae coli.

In the stomach, the arrangement of the musculature is more complex because in some areas there are three muscle layers. In the small intestine, the innermost portion of the circular layer consists of specialized muscle cells that are much smaller and more electron dense than the bulk of the circular muscle. A large number of nerve fibers run between the muscle layers, and it has been suggested that some of these are sensory fibers working in conjunction with the smooth muscle cells to function as stretch receptors (17,18).

The musculature also contains the interstitial cells of Cajal (ICCs), which share ultrastructural features with fibroblasts (38–40). ICCs are large, oval cells with light-staining nuclei and scant cytoplasm. They have two to five, long ramifying primary cell processes, giving them a spindled or stellate shape (fig. 1-11). They form a three-dimensional network and are closely associated with ganglion nerve bundles; they also extend over

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**Figure 1-10**

**MUSCULARIS PROPRIA**

Low-power view shows a distinct inner circular muscle layer and an outer longitudinal layer. The myenteric plexus contains nerve fibers and ganglion cells, and lies between the two layers of smooth muscle.

**Figure 1-11**

**INTERSTITIAL CELLS OF CAJAL**

Although difficult to identify on routine H&E-stained sections, immunostaining for CD117 highlights the interstitial cells of Cajal. The cells are associated with the myenteric plexus, appear somewhat spindled, and have scant cytoplasm. (Fig. 1-9A from Fascicle 32, 3rd Series.)
General Features of the Gastrointestinal Tract

the smooth muscle cells. The ICCs connect to both the circular and longitudinal cells via gap junctions, creating a network of interstitial cells that conduct electrical signals (27,28). ICCs have three major functions: they act as pacemakers for the gastrointestinal muscle (13–15,48); they facilitate active propagation of electrical events; and they mediate neurotransmission (15). They may also act as mechanoreceptors (13–15,48). These unique cells appear to require the c-kit gene or stem cell factor in order to develop (41), as well as to elicit their pacemaker activity (24).

The cells of the muscularis propria contain numerous receptors that allow them to respond to neural as well as other stimulatory and inhibitory signals during the digestive process. Contraction of the circular layer constricts the lumen; contraction of the longitudinal layer shortens the digestive tube.

Adventitia or Serosa

The adventitia is the outermost layer of the GI tract, and consists of loose connective tissue containing fat, collagen, and elastic tissue (fig. 1-12). If it is covered by mesothelium, the serosa, it is called the subserosa. A serosa and subserosa are present on the stomach, those parts of the small intestine that are not retroperitoneal, the appendix, and the large intestine above the peritoneal reflection.

Vasculature

The intestinal mucosa is a highly perfused organ. The largest arteries pass through the wall of the GI tract and are arranged longitudinally in a submucosal plexus. The submucosal plexus sends arterioles and capillaries into the mucosa, muscularis propria, and adventitia or serosa. The mucosa contains an irregular capillary plexus, often with its most terminal branches underlying the luminal surface epithelium (fig. 1-13). Veins arising in the mucosa anastomose in the submucosa and course with the arteries out of the intestine. Valves are present in the adventitia or subserosa.

The gut is richly supplied with lymphatic vessels, but their distribution, particularly in the mucosa, varies with the site within the GI tract. The richest lymphatic distribution occurs in the small intestine, where these vessels are intimately involved in nutrient absorption (fig. 1-14). Larger submucosal lymphatics branch freely and contain numerous valves. Smaller mucosal and submucosal lymphatics may be difficult to detect because they are often collapsed and blend in with the surrounding connective tissue. They are often difficult to distinguish from small capillaries.

Innervation

The enteric nervous system is the most complex portion of the peripheral nervous system. Three divisions of the nervous system
Gastrointestinal Diseases

(sympathetic, parasympathetic, and enteric) contribute to the neural control of at least four physiologic effector systems: 1) the visceral smooth muscle responsible for motility and sphincteric functions; 2) the mucosa responsible for gastric acid secretion and homeostasis of intestinal fluid and electrolytes; 3) the immune cells responsible for mucosal immunity; and 4) the vasculature. Complex reflex activities involving gastrointestinal motility, ion transport, and mucosal blood flow all occur in the absence of extrinsic autonomic and sensory input.

Functionally, the neurons of the enteric nervous system fall into five types: 1) motor neurons controlling smooth muscle tone in the wall of the gut; 2) vasomotor neurons controlling vascular muscle tone; 3) secretory neurons regulating exocrine and endocrine secretion; 4) sensory neurons carrying sensory information to the central nervous system; and 5) interneurons that provide communication between neurons and the gut wall (16). The interneurons intermingle in the myenteric and submucosal ganglia, making their identification difficult.

Gastrointestinal Endocrine System

Endocrine cells are widely distributed within the epithelium of the stomach, small and large intestines, the distal esophageal glands, and anus. Some are also present in the lamina propria in the stomach and the appendix. En-

docrine/paracrine cells differ in various parts of the gut in their overall density, contents, and structure. They are sensitive to chemical and mechanical stimuli, to which they respond by releasing extracellular mediators. The composition of enteroendocrine cells depends on their position along both the vertical and horizontal axes of the GI tract. At least 16 types of endocrine/paracrine cells inhabit the mucosa of the GI tract (Table 1-1).

Gastrointestinal endocrine cells have endocrine, paracrine, and neurotransmitter functions, constituting a complex system that regulates many functions of the GI tract. Some substances produced by enteroendocrine cells act as true peptide hormones. For example, gastrin, secretin, and cholecystokinin are secreted into the blood to reach their target organs (stomach, pancreas, and gallbladder) and soon after are metabolized and eliminated. Some peptides, such as somatostatin, are released from enteroendocrine cells into the local subepithelial connective tissue or directly on other types of cells via long basal cytoplasmic processes. This influences cells and tissues in the immediate vicinity via a paracrine mechanism.

Interactions exist between different components of the neuroendocrine system and the neural system. Neurons interact with endocrine cells, endocrine cells interact with other endocrine cells, and endocrine cells may influence neurons (47). In addition, many gastrointestinal hormones interact with the hypothalamic-pituitary axis to orchestrate the secretory activity and motility necessary for effective digestion (25, 36, 47). Gastrointestinal hormones and paracrine messengers control digestive processes such as acid secretion, bicarbonate secretion, enzyme secretion, and local blood flow. They also influence the immune system, metabolism, and gastrointestinal growth (49).

The circulating levels of the gastrointestinal peptides are influenced by numerous factors. For endocrine cells that lie in contact with the gastrointestinal lumen, such as gastrin cells (44), gastric inhibitory polypeptide cells (6), and secretin-producing cells (43, 51), direct contact with, and absorption of, nutrients and secretions are the most important stimuli. In contrast, peptides like pancreatic polypeptide and insulin, produced in cells outside of the
GI tract, depend on absorbed nutrients and stimulation by other peptides in the nervous system. Endocrine cells are also influenced by the nature of the intraluminal microflora (50).

Endocrine cells occur singly (fig. 1-15) or in discontinuous clusters. They appear as small, clear cells with a broad basal cytoplasm that contains electron-dense granules. Some endocrine

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**Table 1-1**

**GASTROINTESTINAL ENDOCRINE CELLS**

<table>
<thead>
<tr>
<th>Cell</th>
<th>Location</th>
<th>Product(s)</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>CCK*</td>
<td>Small intestine</td>
<td>Cholecystokinin</td>
<td>Stimulates pancreatic and biliary enzyme secretion</td>
</tr>
<tr>
<td>D</td>
<td>Stomach</td>
<td>Somatostatin</td>
<td>Inhibit secretion and motility</td>
</tr>
<tr>
<td></td>
<td>Small intestine Colon</td>
<td>Vasoactive intestinal polypeptide</td>
<td></td>
</tr>
<tr>
<td>EC</td>
<td>Stomach</td>
<td>Serotonin</td>
<td>Stimulate motility</td>
</tr>
<tr>
<td></td>
<td>Small intestine Appendix Colon</td>
<td>Motilin Substance P</td>
<td></td>
</tr>
<tr>
<td>G</td>
<td>Pylorus   Duodenum</td>
<td>Histamine</td>
<td>Stimulates acid secretion</td>
</tr>
<tr>
<td>GIP</td>
<td>Small intestine</td>
<td>Gastric inhibitory polypeptide</td>
<td>Inhibits gastric acid secretion</td>
</tr>
<tr>
<td></td>
<td>Colon</td>
<td>Glucagon-like peptides Peptide YY</td>
<td></td>
</tr>
<tr>
<td>M</td>
<td>Small intestine Colon</td>
<td>Motilin</td>
<td>Stimulates motility</td>
</tr>
<tr>
<td>N</td>
<td>Small intestine</td>
<td>Neurotensin</td>
<td></td>
</tr>
<tr>
<td>P/D</td>
<td>Stomach</td>
<td>Ghrelin</td>
<td></td>
</tr>
<tr>
<td>S</td>
<td>Small intestine</td>
<td>Secretin Serotonin</td>
<td>Stimulates pancreatic and biliary secretion</td>
</tr>
</tbody>
</table>

*CCK = cholecystokinin cell; EC = enterochromaffin cell; ECL = enterochromaffin-like cell; GIP = gastric inhibitory polypeptide cell.

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**Figure 1-15**

**ENDOCRINE CELLS**

Left: Gastric endocrine cells are difficult to visualize on routine H&E-stained slides. They are located in the neck of the gastric gland, and often have relatively clear cytoplasm and round, regular nuclei (arrows).

Right: A chromogranin stain highlights the endocrine cells.
Figure 1-16
ENDOCRINE CELL
An H&E-stained section demonstrates an endocrine cell in the base of a colonic crypt. The cell contains prominent subnuclear eosinophilic granules.

cells, particularly those in the colon, contain prominent eosinophilic granules (fig. 1-16). Endocrine cells may be identified histochemically using Grimelius or Fontana-Masson stains. Other markers of neuroendocrine differentiation include antibodies to neuron-specific enolase, protein gene product 9.5, synaptophysin, and chromogranin (fig. 1-17) (12,31,37,54). Specific peptide hormones can also be identified immunohistochemically.

NORMAL FEATURES OF INDIVIDUAL GASTROINTESTINAL SITES

Esophagus
The normal esophageal mucosa is readily recognizable by its squamous epithelial lining and submucosal glands (fig. 1-18). The basal layer of the squamous epithelium consists of cuboidal or columnar cells with central basophilic nuclei. This layer typically comprises no more than 10 to 15 percent of the total epithelial thickness, although distally the basal cell layer can be somewhat thicker, probably in response to physiologic reflux. Melanocytic or endocrine cells may be scattered among the basal cells (58). Cells in the basal layer give rise to daughter cells that migrate upward, differentiating as they approach the luminal surface. The most superficial layers may contain basophilic granules. The cells of the superficial or functional zone appear flattened, with their long axis parallel to the mucosal surface. Papillae, which are invaginations of vascularized lamina propria, extend into the epithelium. These usually do not penetrate more than two thirds of the way into the overlying mucosa (fig. 1-18). The height of a papilla (or rete ridge) is measured from the basal lamina of the surrounding squamous epithelium to the basal lamina at the top of the papilla. Nonepithelial elements include lymphocytes and antigen-presenting cells (56,57).

Submucosal glands lie in straight rows that extend outward from the esophageal lumen toward the muscularis propria (fig. 1-19). The glands lie both within the mucosa and the submucosa. The glandular lobules connect to the lumen via a straight duct. Mucous cells within the submucosal glands often have a pyramidal shape and contain numerous large, pale secretory granules. Myoepithelial cells lie between the secretory cells and the underlying basement membrane.

Although the esophageal mucosa is repeatedly exposed to potentially injurious materials that are ingested or that reflux into the distal esophagus, it is rare for injury to occur because preepithelial, epithelial, and postepithelial defenses protect against injury. Preepithelial defenses rely on intact neuromuscular function to maintain lower esophageal sphincter pressure and normal esophageal motility, thus minimizing gastroesophageal reflux and promoting clearance of esophageal luminal contents. Gravity and normal peristalsis move the intraluminal contents distally, thereby preventing prolonged mucosal contact and protecting against mucosal damage. The multilayered squamous epithelium also protects against damage from substances
General Features of the Gastrointestinal Tract

Figure 1-17

GASTRIC ENDOCRINE CELLS
Left: Endocrine cells within the neck region of the gastric glands are highlighted with the chromogranin immunostain.
Right: Antral glands contain scattered G cells, as demonstrated with this gastrin immunostain.

Figure 1-18

NORMAL ESOPHAGEAL HISTOLOGY
Left: The basal layer is only a few cells thick, and the papillae extend approximately to one third to half the thickness of the epithelium. The underlying muscularis mucosae is thicker in the esophagus than in other parts of the gastrointestinal tract.
Right: Higher-power view shows a basal cell layer composed of only a few layers of cells and short papillae. Only rare intraepithelial lymphocytes lie in the deep portion of the mucosa.
passing over it. When the protective mechanisms are overwhelmed, epithelial erosions or ulcers develop. Four general situations predispose to esophageal injury: 1) motility disturbances, 2) the presence of esophageal reflux, 3) infection, and 4) drug- or chemical-induced injury. Increased cell proliferation and secondary basal cell hyperplasia compensate for cells lost to injury.

**Stomach**

The stomach has three major histologic compartments: the gastric pits and surface lining, the mucous neck region, and the glands (fig. 1-20). Additionally, the stomach has four anatomic regions: the cardia, fundus, body, and antrypyloric region (fig. 1-21). The cardia, a narrow, ill-defined region, is not grossly distinctive and is histologically identified by the presence of cardiac glands. The fundus, the most superior part of the stomach, protrudes above a horizontal line drawn from the esophagogastric junction. It blends imperceptibly into the major portion of the stomach, called the body. Oxyntic mucosa lines the body and fundus. The antrum comprises the distal third of the stomach just proximal to the pyloric sphincter. It is a triangular zone that extends further along the lesser curvature than along the greater curvature.

Surface, or foveolar, cells line the surface and gastric pits; they are histologically identical throughout the stomach. Foveolar epithelium consists of tall, columnar, mucus-secreting cells (fig. 1-20) that form an integral part of the mucosal barrier. These cells have irregular, basally situated nuclei and apically, mucin-filled cytoplasm. The cardiac pits appear shorter than those in other regions of the stomach. The pits are deepest in the antrum. Mucous neck cells reside in the neck and isthmus in the middle and upper parts of the gastric glands. They merge with both the glandular epithelium below and the foveolar epithelium above.

In contrast to the foveolar and pit regions, the histology of the gastric glands, which empty into the base of the gastric pits, differs in different regions of the stomach. Cardiac glands share histologic features with esophageal submucosal glands (fig. 1-22) and with pyloric and antral glands. Oxyntic glands contain four cell types: mucous neck cells, endocrine cells, parietal (oxyntic) cells, and chief (zymogenic) cells (fig. 1-22). Parietal cells constitute approximately one third of the cells in the oxyntic mucosa and tend to be more numerous distally than proximally. This contrasts with chief cells, which are found in greater numbers in the proximal rather than the distal oxyntic mucosa. Parietal cells chiefly localize to the midportion of the oxyntic glands, whereas chief cells lie at the glandular bases. Some parietal cells are found in the antrum. The acid-secreting parietal cells are easily identified by their large size, pyramidal shape, large central
nuclei, and intensely eosinophilic cytoplasm (fig. 1-22). Chief cells, which make pepsinogen (fig. 1-22) and lipase, appear as triangular, low columnar cells containing a coarse, granular, pale, gray-blue, basophilic cytoplasm. The nucleus contains one or more small nucleoli.

The stomach contains a diverse population of endocrine cells. These are widely distributed in various regions of the gastric mucosa. At least seven distinct endocrine cell types exist: enterochromaffin, G, enterochromaffin-like (ECL), D, D1, P, and X cells. The predominant antral endocrine cell, the gastrin-producing G cell, causes ECL cell, parietal cell, and gastric mucosal growth. Somatostatin-secreting D cells are distributed uniformly throughout the antral and oxyntic mucosa. They inhibit the release of gastric acid, gastrin, intrinsic factor, and acetylcholine. ECL cells, the major endocrine cells of the oxyntic mucosa, are usually found in the fundus but they can occur more distally. They play a pivotal role in mediating gastrin-induced parietal cell secretion.

Small Intestine

The major functions of the small intestine are terminal digestion and absorption of nutrients. The anatomy of this region of the GI tract

**Figure 1-20**

**NORMAL GASTRIC MUCOSA**

Above: The gastric mucosa consists of surface epithelium, pits (in the upper mucosa), and glands (in the lower mucosa). The mucous neck region separates the two.

Right: Higher magnification of the foveolar epithelium that lines both the luminal surface and the gastric pits.
reflects these functions. Intestinal folds, known as plicae circulares, increase the surface area available for absorption. Innumerable villi stud the intestinal surface, further increasing the absorptive surface (fig. 1-23). The villi are unique to the small intestine, and are finger- or leaf-like mucosal evaginations. They are lined by epithelium overlying a connective tissue core that contains a highly cellular lamina propria, a capillary network, lacteals, and nerves. Simple
General Features of the Gastrointestinal Tract

tubular invaginations (crypts of Lieberkuhn) at the bases of the villi (fig. 1-24) extend downward toward the muscularis mucosae but do not penetrate it. The openings to several crypts empty into the intervillous basin.

Villi vary in height and form in different regions of the small intestine. The duodenum has the greatest villous variability. The villi in the proximal duodenum are shorter and broader than elsewhere; jejunal villi show little variation in their width from their base to their apex; and in the ileum, the villi are broader and shorter than in the jejunum.

Measurement of the ratio of villous height to crypt length is often required for the assessment of small intestinal absorptive function. Well-oriented sections allow optimal examination of the villous architecture. In adults, the villous height is approximately three or more times the depth of the crypts, whereas in children this ratio is lower, more typically 2 to 1 (fig. 1-25). The villous height is also lower in elderly patients (76). Villi are often stubby or absent overlying

Figure 1-23

SMALL INTESTINAL VILLI

Top: Long finger-like villi project upward into the lumen of the small intestine.

Bottom: Tangential sectioning demonstrates uniform, slender villous structures.

Figure 1-24

CRYPTS OF LIEBERKUHN

Straight crypts project downward from the base of the villi. In this case, two crypts empty into the intervillous space. Paneth cells are present in the crypt bases (arrow).