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NORMAL GROSS AND HISTOLOGIC FEATURES OF THE GASTROINTESTINAL TRACT

THE NORMAL ESOPHAGUS

Anatomy

Gross Anatomy. The adult esophagus is a muscular tube measuring approximately 25 cm and extending from the lower border of the cricoid cartilage to the gastroesophageal junction. It lies posterior to the trachea and left atrium in the mediastinum but deviates slightly to the left before descending to the diaphragm, where it traverses the hiatus and enters the abdomen. The subdiaphragmatic esophagus lies against the posterior surface of the left hepatic lobe (1).

The International Classification of Diseases and the American Joint Commission on Cancer divide the esophagus into upper, middle, and lower thirds, whereas endoscopists measure distance to points in the esophagus relative to the incisors (2). The esophagus begins 15 cm from the incisors and extends 40 cm from the incisors in the average adult (3).

The upper and lower esophageal sphincters represent areas of increased resting tone but lack anatomic landmarks; they are located 15 to 18 cm from the incisors and slightly proximal to the gastroesophageal junction, respectively. The gastroesophageal junction is defined as the distal extent of the tubular esophagus and, in the normal state, roughly corresponds to the mucosal squamocolumnar junction, or Z-line (fig. 1-1). There are four areas of luminal narrowing: the upper esophageal sphincter, the areas where the esophagus crosses the aortic arch and left main bronchus, and the gastroesophageal junction. Left atrial enlargement can also impinge on the esophagus.

Vascular Anatomy. The upper esophagus is vascularized by branches of the inferior thyroidal artery. Branches of the bronchial arteries, aorta, and intercostal arteries penetrate the mid esophagus, and the distal esophagus is supplied by the

left gastric, left phrenic, and left hepatic accessory arteries. Veins in the proximal and mid esophagus drain into the systemic circulation, whereas the short gastric and left gastric veins of the portal system drain the distal esophagus. Linear arrays of large caliber veins are unique to the distal esophagus and can be a helpful clue to the site of a biopsy when extensive cardiac-type mucosa is present near the gastroesophageal junction (4).

Lymphatic vessels are present in all layers of the esophagus. They drain to paratracheal and deep cervical lymph nodes in the cervical esophagus, bronchial and posterior mediastinal lymph nodes in the thoracic esophagus, and left gastric lymph nodes in the abdominal esophagus.

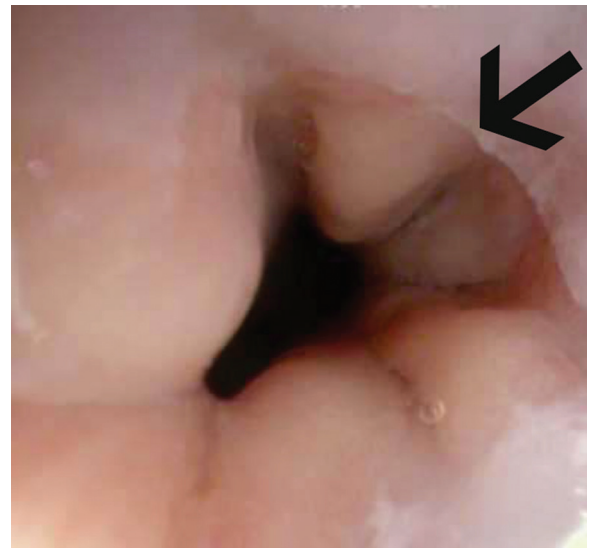


Figure 1-1

ENDOSCOPIC APPEARANCE OF THE GASTROESOPHAGEAL JUNCTION

The gastroesophageal junction normally corresponds to the squamocolumnar junction (arrow), which appears as an abrupt transition between the velvety mucosa of the rugal folds and the pink, pearly white squamous mucosa of the tubular esophagus.

Histology

The esophagus consists of mucosa, submucosa, and muscularis propria invested with adventitia, which is a nonperitonealized surface and important margin in cancer resection specimens. The left anterior aspect of the distal-most esophagus lies within the peritoneal cavity and is surfaced by mesothelium (i.e., serosa).

The pale pink, glistening esophageal mucosa is composed of multilayered, stratified nonkeratinizing squamous epithelium supported by lamina propria and muscularis mucosae (fig. 1-2A). The squamous epithelium contains a proliferative zone consisting of 2 to 3 cell layers at its base; epithelial cells in this area are ovoid with high nuclear to cytoplasmic ratios and scattered mitotic figures. Superficial squamous cells contain faintly eosinophilic cytoplasm and small nuclei with condensed chromatin arranged with their long axes parallel to the luminal surface (fig. 1-2B). Scattered CD8-positive T-lymphocytes are normally present in the peripapillary epithelium, particularly near the gastroesophageal junction, where they can number 40 to 60 per high-power field in asymptomatic patients (5).

The squamous mucosa contains occasional Langerhans cells and melanocytes (6–9). Rare eosinophils can be detected in otherwise normal biopsy samples from the gastroesophageal junction; their presence should be disregarded if unaccompanied by evidence of mucosal injury.

The lamina propria consists of loose connective tissue that supports thin-walled blood vessels, nerves, and inflammatory cells. Papillae penetrate approximately one-third of the squamous mucosal thickness. Bundles of longitudinally oriented smooth muscle cells comprise the muscularis mucosae and support the lamina propria. The muscularis mucosae is more pronounced in the distal esophagus and can be thickened or duplicated in chronic inflammatory conditions.

The submucosa contains blood vessels, lymphatic vessels, lymphoid follicles, superficial and deep nerve plexuses, and mucous glands supported by loose connective tissue. The Meissner plexus is located in the superficial submucosa and Henle plexus is present in the deep submucosa; each is composed of ganglion cells and associated nerve trunks. Smaller nerve

fibers stem from the plexuses, penetrating the submucosa and lamina propria.

Acid mucin-containing glands are distributed along the length of the esophagus and are most numerous in the proximal and distal regions; lobules of glands drain into ducts that empty onto the mucosal surface (fig. 1-2C). Esophageal ducts are lined by two layers of cuboidal cells in the deep submucosa and a single layer of squamous cells near the surface.

The muscularis propria consists of thick bundles of smooth muscle cells arranged in outer longitudinal and inner circular layers. The proximal muscularis propria contains skeletal muscle fibers derived from the cricopharyngeal and inferior pharyngeal constrictor muscles. The myenteric (i.e., Auerbach) plexus lies between the muscle layers and is intimately associated with the interstitial cells of Cajal, which emanate outward through the muscle layers (fig. 1-2D).

The esophagus is ensheathed by adventitia. This layer of loose connective tissue contains nerves, lymphoid tissue, and lymphatic and blood vessels, and merges with other support structures of the thoracic viscera.

THE NORMAL STOMACH

Anatomy

Gross Anatomy. The stomach is a saccular J-shaped organ located in the left upper quadrant of the abdomen that can hold up to 2 L in the average adult. It begins at the gastroesophageal junction and extends inferiorly to the pyloric sphincter just to the right of the midline. The superomedial and inferolateral aspects are termed the lesser curvature and greater curvature, respectively.

There are four anatomic subdivisions to the stomach. The cardia is an ill-defined region that extends 1 to 3 cm from the gastroesophageal junction. The fundus is a dome-shaped bulge that lies to the left and above the gastroesophageal junction. The gastric body (i.e., corpus) is the region between the fundus and the antrum. The antrum comprises the distal third of the stomach, above the pylorus (10). The incisura angularis is a notch in the lesser curvature that roughly coincides with the transition between the corpus and antrum.

The stomach is composed of four layers. The mucosal folds, or rugae, extend longitudinally

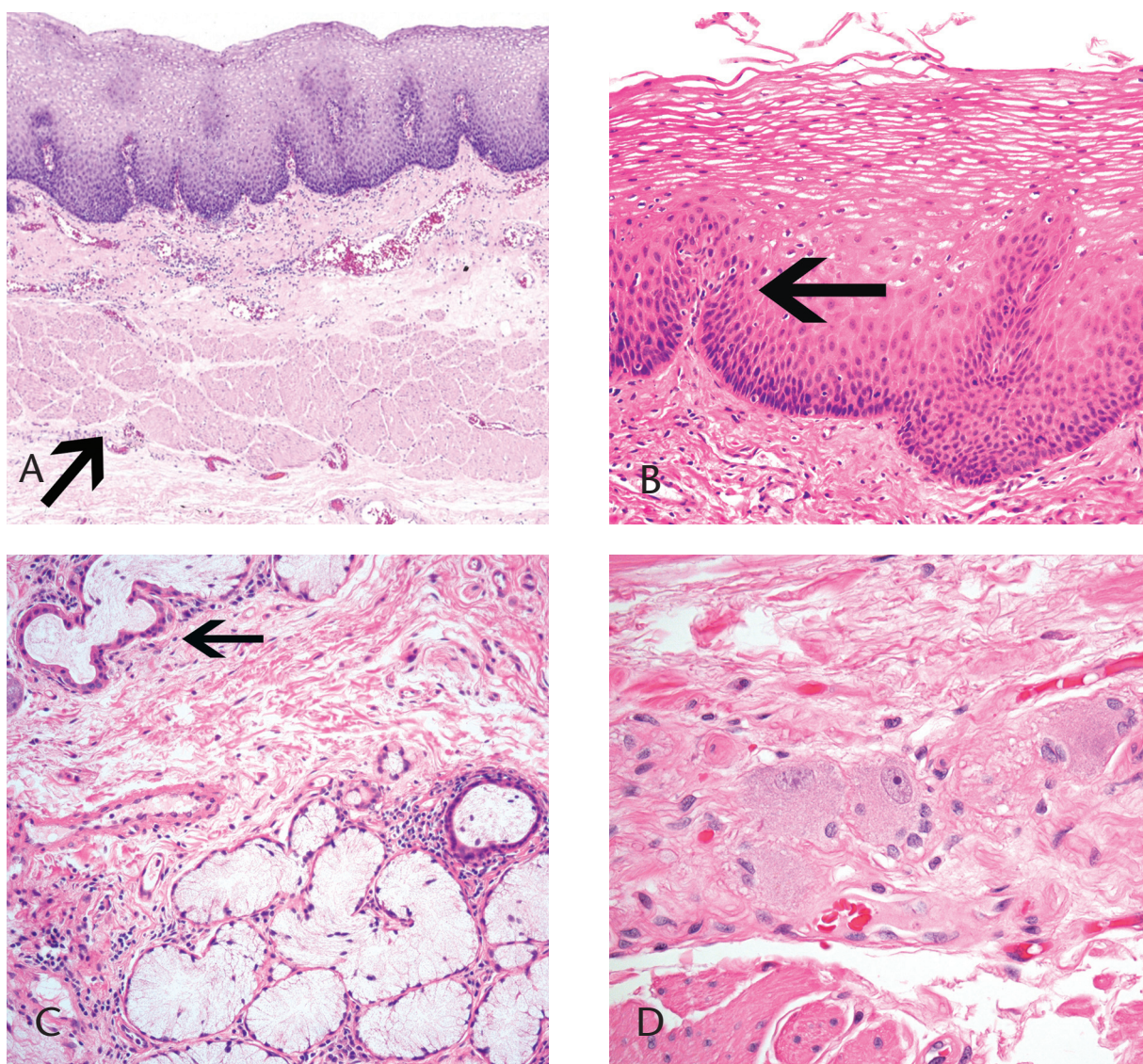


Figure 1-2

NORMAL HISTOLOGIC FEATURES OF THE ESOPHAGUS

The esophagus is lined by nonkeratinizing squamous epithelium supported by lamina propria connective tissue. The muscularis mucosae (arrow) is thickest in the distal esophagus and represents the deepest extent of the mucosa (A). Intraepithelial lymphocytes have convoluted nuclei and are most prominent around papillae (arrow). The cells in the deep mucosa comprise the proliferative zone and have higher nuclear to cytoplasmic ratios than the surface epithelial cells (B). Submucosal glands contain slightly basophilic mucin and are arranged in lobules. Their contents drain to the surface via ducts (arrow) lined by a combination of squamous and cuboidal epithelial cells (C). The myenteric plexus consists of nerve trunks and ganglion cells. The latter contain abundant amphophilic cytoplasm and large, eccentric nuclei with prominent nucleoli (D).

from the gastroesophageal junction to the pylorus and flatten with distension (fig. 1-3). The areae gastricae are shallow, horizontal grooves across the rugae. The submucosa is a loose layer of fat, collagen, and other supporting structures. The muscularis propria contains three muscle

layers: the inner oblique, middle circular, and outer longitudinal layers. The middle layer thickens distally to form the pyloric sphincter.

The stomach is almost entirely invested by the serosa, except where it attached to the omentum, mesocolon, and ligaments. It has no adventitia.

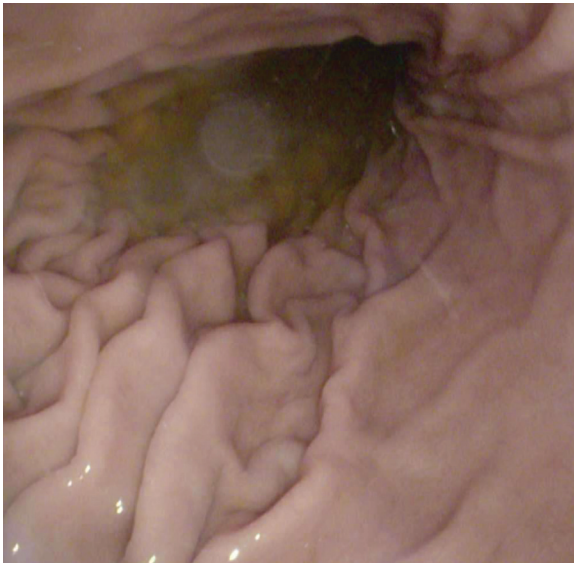


Figure 1-3

**NORMAL ENDOSCOPIC
APPEARANCE OF THE STOMACH**

The rugae are longitudinal mucosal folds that run from the gastroesophageal junction to the pylorus.

Vascular Anatomy. The gastric cardia is supplied by branches of the left gastric artery which arises directly from the celiac plexus. The greater curvature receives blood from branches of the splenic (left gastroepiploic and short gastric) and hepatic (right gastric and right gastroepiploic) arteries. The right gastric artery also supplies the lesser curvature. Anastomoses between branches of these vessels provide rich collateral circulation to the entire stomach, making ischemic gastric injury a rare event (11).

The left and right gastric veins run along the greater and lesser curvatures, respectively, and drain into the portal vein. The left and right gastro-omental and short gastric veins drain into the splenic vein, the largest tributary of the portal vein (10).

Most of the lymphatic drainage from the stomach reaches the celiac lymph nodes after passing through intermediaries. Lymphatics along the proximal greater curvature first drain to lymph nodes in the splenic hilum, whereas the distal greater curvature drains to the right gastroepiploic lymph nodes in the omentum and pyloric lymph nodes at the head of the pancreas. Lymphatics near the cardia and along the

lesser curvature pass through left gastric lymph nodes to the celiac trunk before reaching the para-aortic lymph nodes below the left renal vein. The pylorus drains through the right gastric and hepatoduodenal ligament lymph nodes en route to the celiac axis (12).

Histology

The stomach functions as a food reservoir, sterilizes luminal contents, and participates in early digestion. Not surprisingly, it is home to morphologically distinct areas and several epithelial cell types. Neutral mucin-containing glands predominate in the cardia and antrum, whereas oxyntic glands containing chief and parietal cells are located in the fundus and corpus. The entire mucosa is surfaced by a monolayer of columnar foveolar cells with small, basal nuclei and tall apical vacuoles of pale pink mucin (fig. 1-4A).

Foveolar cells secrete bicarbonate and mucin. They show strong immunohistochemical staining for mucin core protein-5AC (MUC5AC) and MUC1, as well as positivity for periodic acid-Schiff (PAS) stains. The gastric pits (i.e., foveolae) represent invaginations of the superficial mucosa and are lined by similar epithelial cells. The pits occupy approximately 50 percent of the mucosal thickness in the cardia and antrum compared with only 25 percent of the mucosal thickness in the body and fundus. Intraepithelial CD8-positive T-lymphocytes are normally present in the surface epithelium but number fewer than 20 per 100 epithelial cells (13).

Mucous neck cells are located between the pits and deeper glands, and represent the proliferative zone of the epithelium. They tend to have slightly larger nuclei than other mucinous epithelia in the stomach and contain both neutral mucin and acidic sialomucins. Thus, mucous neck cells stain with both PAS and Alcian blue (pH 2.5), and show MUC5AC and MUC6 immunopositivity.

Oxyntic mucosa contains tightly packed, tubular oxyntic glands that occupy approximately 75 percent of the mucosal thickness (fig. 1-4B) (10). Sectioned tangentially, oxyntic glands may appear as “cords” or stacks of individual glands. Chief (i.e., zygomantic) cells are present in higher numbers in the deep mucosa. These cells produce pepsinogen and contain blue-gray cytoplasm, basal nuclei, and small nucleoli. Parietal cells are more numerous in the mid-region of

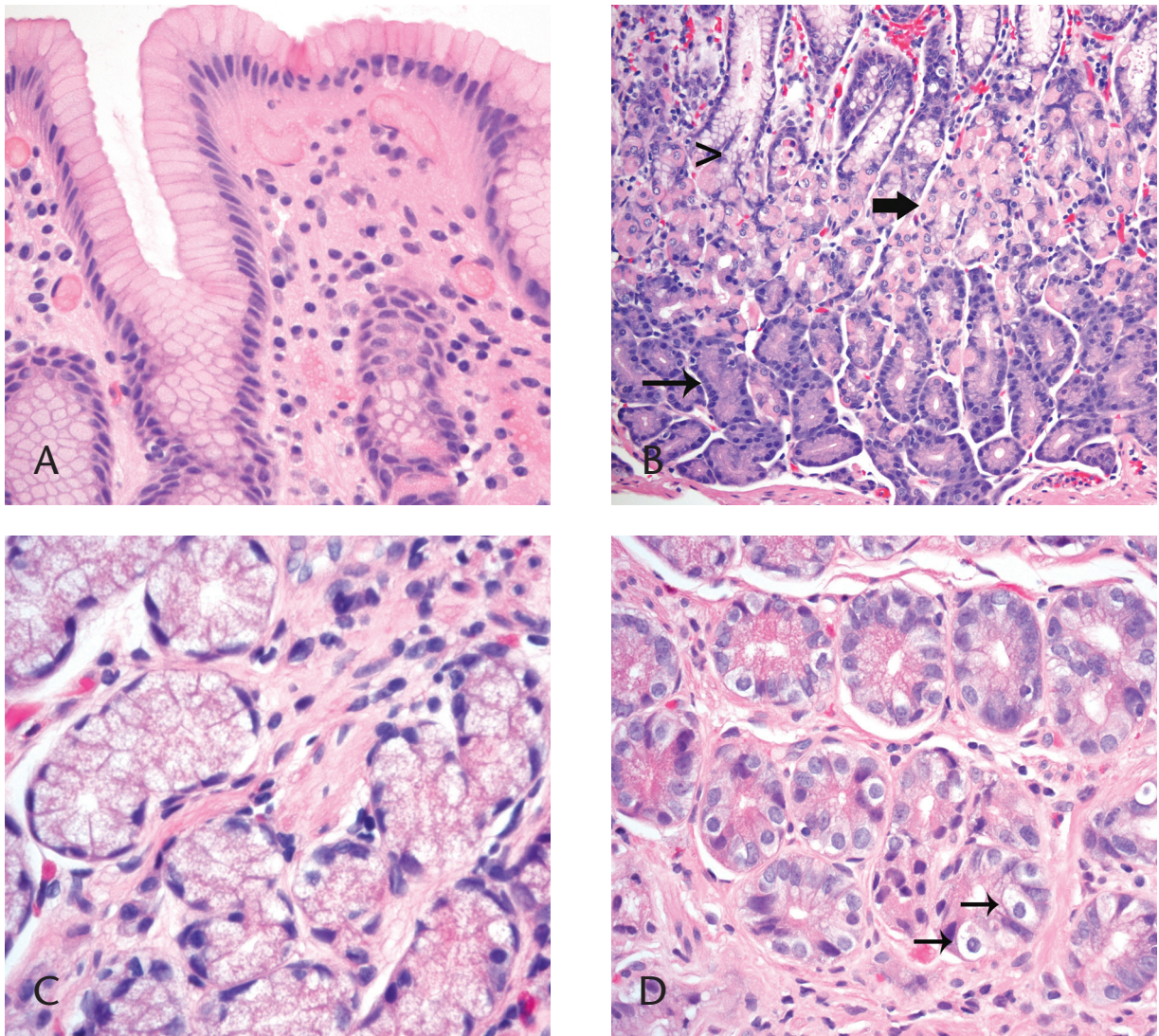


Figure 1-4

NORMAL HISTOLOGIC FEATURES OF THE STOMACH

The stomach is surfaced by a single layer of foveolar epithelial cells. These cells contain basally oriented uniform nuclei and a tall, apical mucin vacuole. The foveolar cells descend into the mucosa to form evenly spaced gastric pits (foveolae). The intervening lamina propria contains scattered inflammatory cells and capillaries (A). Oxyntic mucosa contains tubular glands that occupy 50 to 75 percent of the mucosal thickness. Chief cells are located deep in the glands and contain basophilic cytoplasm (arrow). Parietal cells have abundant eosinophilic cytoplasm and are most numerous in the mid-region (block arrow). The mucous neck cells (arrowhead) are found at the junction between the gastric pits and the oxyntic glands (B). Pyloric glands are found in the antrum and cardia. They contain pale, faintly eosinophilic, bubbly cytoplasm (C). Endocrine cells (arrows) are present throughout the stomach and are admixed with other types of epithelia in the gastric glands. They contain central nuclei and clear cytoplasm, resembling fried eggs (D).

the mucosa. They are pyramidal in shape and contain centrally located nuclei as well as abundant, granular, eosinophilic cytoplasm. Parietal cells maintain the acidity of gastric contents by releasing hydrochloric acid in response to

stimulation by gastrin and histamine. They also produce intrinsic factor, a glycoprotein that aids absorption of vitamin B₁₂. Chief, parietal, and mucous neck cells are frequently commingled in glands of the superficial mucosa.

The deep compartment of the antral mucosa is populated by loosely packed lobules of pyloric-type glands with abundant intervening lamina propria (fig. 1-4C) (9). Epithelial cells in these glands contain faintly eosinophilic, slightly bubbly mucin and show strong immunostaining for MUC6. Pyloric-type glands secrete mucus that, in combination with secretions from foveolar cells, form a protective layer that prevents acid-related injury to the gastric mucosa. Scattered parietal cells are commonly identified in the antrum, particularly at the transition point with the corpus, but chief cells are rarely present. The cardia also contains pyloric-type glands that are intimately associated with oxyntic glands in almost 50 percent of adults (14).

The stomach contains three main populations of endocrine cells: gastrin-producing G cells, enterochromaffin-like (ECL) cells that secrete histamine, and D cells that produce somatostatin (15). Endocrine cells of the stomach are ovoid with pale gray to clear cytoplasm and centrally located nuclei that impart a "fried egg" appearance with hematoxylin and eosin (H&E) stains (fig. 1-4D).

The G cells are most numerous, accounting for more than 50 percent of all endocrine cells in the stomach. They reside mostly in the antrum but may be scattered in small numbers in the oxyntic mucosa. ECL cells are located in oxyntic mucosae and tend to be most numerous in glands of the deep mucosa. Scattered D cells are dispersed throughout the stomach. They secrete somatostatin in response to low gastric pH, which, in turn, inhibits release of gastrin and histamine (16). Endocrine cells are most numerous in the gastric antrum, where they number between 20 and 50 in an entire gland; oxyntic glands contain fewer than 20 endocrine cells per gland.

The lamina propria contains a supportive network of collagen, reticulin, and elastic fibers, as well as blood vessels, fibroblasts, and scattered inflammatory cells, including macrophages, plasma cells, lymphocytes, and eosinophils. It is better visualized in the superficial mucosa. Basal lymphoid aggregates are normally present in the oxyntic mucosa; they often have a pyramidal configuration based on the muscularis mucosae. The muscularis mucosae is a thin bilayer of smooth muscle that forms the lower limit of the mucosa.

The submucosa contains loose connective tissue, blood vessels, and Meissner plexus. Each ganglion of the Meissner plexus consists of ganglion cells and parasympathetic nerves. Thick smooth muscle layers form the muscularis propria. Auerbach plexus lies between the middle circular and outer longitudinal layers and consists of sympathetic and parasympathetic nerves. Interstitial cells of Cajal are concentrated around the myenteric plexus and emanate through the muscle layers. A small amount of delicate collagen and adipose tissue lies between the muscularis propria and the single layer of mesothelial cells comprising the serosa.

THE NORMAL SMALL BOWEL

Anatomy

Gross Anatomy. The small intestine measures roughly 6 m in length and consists of the duodenum, jejunum, and ileum. The duodenum spans approximately 25 cm and is divided into four parts. The first part begins at the gastroduodenal junction and includes the duodenal bulb. The second part extends from the bulb to the level of the fourth lumbar vertebra on the right side of the spine where it descends a few centimeters. The ampulla of Vater is located on the medial aspect in the descending portion of the second part of the duodenum. Nearly 70 percent of healthy individuals have a minor ampulla that drains the accessory pancreatic duct of Santorini approximately 2 cm proximal to the ampulla of Vater. The third portion of the duodenum sweeps to the left across the spine to complete the C-shape that surrounds the pancreatic head and body. The fourth part rises slightly and terminates at the ligament of Treitz.

With the exception of its first portion, the duodenum lies in the retroperitoneum. The jejunum and ileum are entirely within the peritoneal cavity and supported by a mesentery. Most of the jejunum is located in the left upper quadrant; it transitions to the ileum in the mid-abdomen, and the latter passes obliquely into the right lower quadrant where it terminates at the ileocecal valve.

The small bowel consists of four layers: mucosa and muscularis mucosae, submucosa, muscularis propria, and serosa or adventitia. Mesenteric fat is normally confined to approximately 30 percent

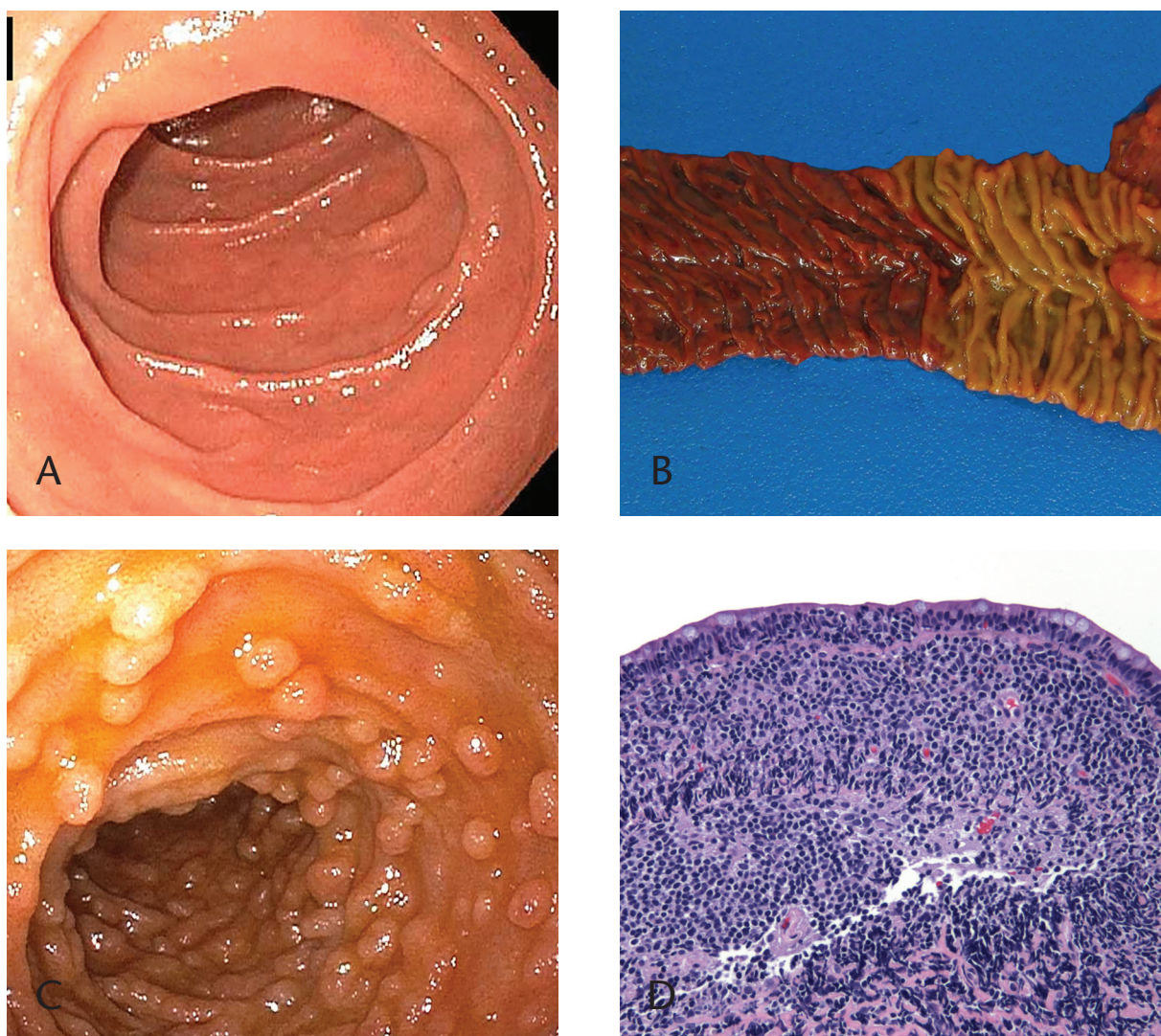


Figure 1-5

NORMAL ENDOSCOPIC APPEARANCE OF THE SMALL BOWEL

Circumferential mucosal folds are most prominent in the proximal small bowel (A). The proximal duodenum is surfaced by brown, velvety mucosa up to the region of the ampulla (right) but may have a dusky erythematous appearance more distally (B). Lymphoid aggregates impart a nodular appearance to the small intestine and are most numerous in the distal ileum (C). Lymphoid nodules extend into the lamina propria where they are surfaced by epithelium infiltrated by lymphocytes (D).

of the circumference of the jejunum and ileum. The luminal surface of the entire small intestine is arranged in transverse folds composed of mucosa and submucosa (i.e., valvulae conniventes, plicae circularis, folds of Kerckring); they are most prominent in the duodenum, which may normally show dusky discoloration compared with the proximal duodenum (fig. 1-5).

Lymphoid nodules are present throughout the small intestine and are most numerous in

the distal ileum where they coalesce to form Peyer patches. These appear as small nodules, often with central umbilication that simulate aphthous ulcers (fig. 1-5C,D). Lymphoid nodules are largest in children and adolescents but gradually involute in adulthood.

Vascular Anatomy. The proximal duodenum is supplied by branches of the superior pancreaticoduodenal arteries that create a complex network of feeder vessels. The small intestine

distal to the ampulla is vascularized by the superior mesenteric artery: the distal duodenum is supplied by the inferior pancreaticoduodenal arteries, and jejunal and ileal branches from the superior mesenteric artery supply the rest of the small bowel. The superior mesenteric artery courses through the mesentery and gives rise to branches from its convex aspect, forming rich, overlapping arcades (i.e., vasa recta). Short, straight branches from these arcades ramify in the serosa and penetrate the muscularis propria, ultimately terminating in arterioles that supply the villi (17). The small intestinal veins are paired with arteries in the small bowel and drain into the superior mesenteric vein of the portal venous system.

Lymphatic vessels of the duodenum drain to lymph nodes around the duodenum, pancreas, and distal stomach. Those of the jejunum and most of the ileum drain to lymph nodes in the mesentery, particularly around the superior mesenteric vessels, whereas the ileocolic lymph nodes receive lymph from the terminal ileum.

Histology

The small intestinal mucosa consists of epithelium and lamina propria arranged in villous projections into the lumen. Villi range from 0.3 to 1.0 mm in height; they are shortest in the proximal duodenum, particularly when associated with Brunner glands, reach their maximal height in the distal duodenum and jejunum, and become progressively shorter in the distal ileum (fig. 1-6). Each villus contains an arteriole, venule, central lymphatic vessel, capillaries, scattered nerve fibers, and rare, longitudinally oriented smooth muscle cells. Crypts of Lieberkühn are present in the deep mucosa near the muscularis mucosae. They are approximately 170 μ m in length and contain the proliferative compartment of epithelial stem cells (18,19). The latter give rise to daughter cells that differentiate into absorptive enterocytes, M cells, goblet cells, Paneth cells, and endocrine cells, as described below.

Enterocytes are tall columnar cells arranged in a monolayer along the villous surface and upper crypt region. They contain abundant eosinophilic cytoplasm and basally located nuclei, as well as a microvillous brush border that increases the cell surface area and enhances absorption. Microvilli are supported by internal

actin filaments that are cross-linked by villin and fimbrin, and tethered to the cytoplasmic membrane by myosin 1 and calmodulin. The microvillous brush border is immunopositive for CD10, EPCAM, and villin (20). Enterocytes produce glycoproteins that form a protective glycocalyx at the cell surface, as well as a variety of enzymes to break down carbohydrates and proteins. They also elaborate a secretory component, which facilitates translocation of IgA across epithelial cells.

The M cells are specialized epithelial cells overlying B-cell-rich regions of lymphoid nodules and Peyer patches. These cells play an important role in gut immunity by regulating presentation of luminal antigens to the mucosal immune system (21). Although they lack a well-developed brush border, M cells have a luminal membrane with a convoluted surface. They likely represent highly differentiated enterocytes but cannot be distinguished from other enterocytes by histochemical means (22).

Goblet cells are present throughout the small intestine, although their numbers and distribution vary in a site-specific fashion. They are more numerous in the crypt region than villous tips of the duodenum and jejunum, and increase in number toward the distal ileum. Goblet cells are distended by a large, lumenally oriented vacuole of cytoplasmic mucin. The mucin tends to be colorless or faintly basophilic, reflecting the presence of sialylated glycoproteins. Goblet cells are positive with Alcian blue and PAS histochemical stains, and they express MUC2.

Paneth cells and endocrine cells are confined to the deep crypt region. Paneth cells have a columnar shape, with basally oriented nuclei, and contain large, brightly eosinophilic cytoplasmic granules rich in growth factors and antimicrobial proteins (fig. 1-6D). Endocrine cells are pyramidal in shape and also contain eosinophilic serotonin-containing granules. However, the granules of endocrine cells tend to be finer and more purple than those of Paneth cells. They are also oriented such that nuclei are located at the cell apices and granules are near the basement membrane.

Similar to the lamina propria of the colon, that of the small bowel normally contains a mixed population of inflammatory cells with

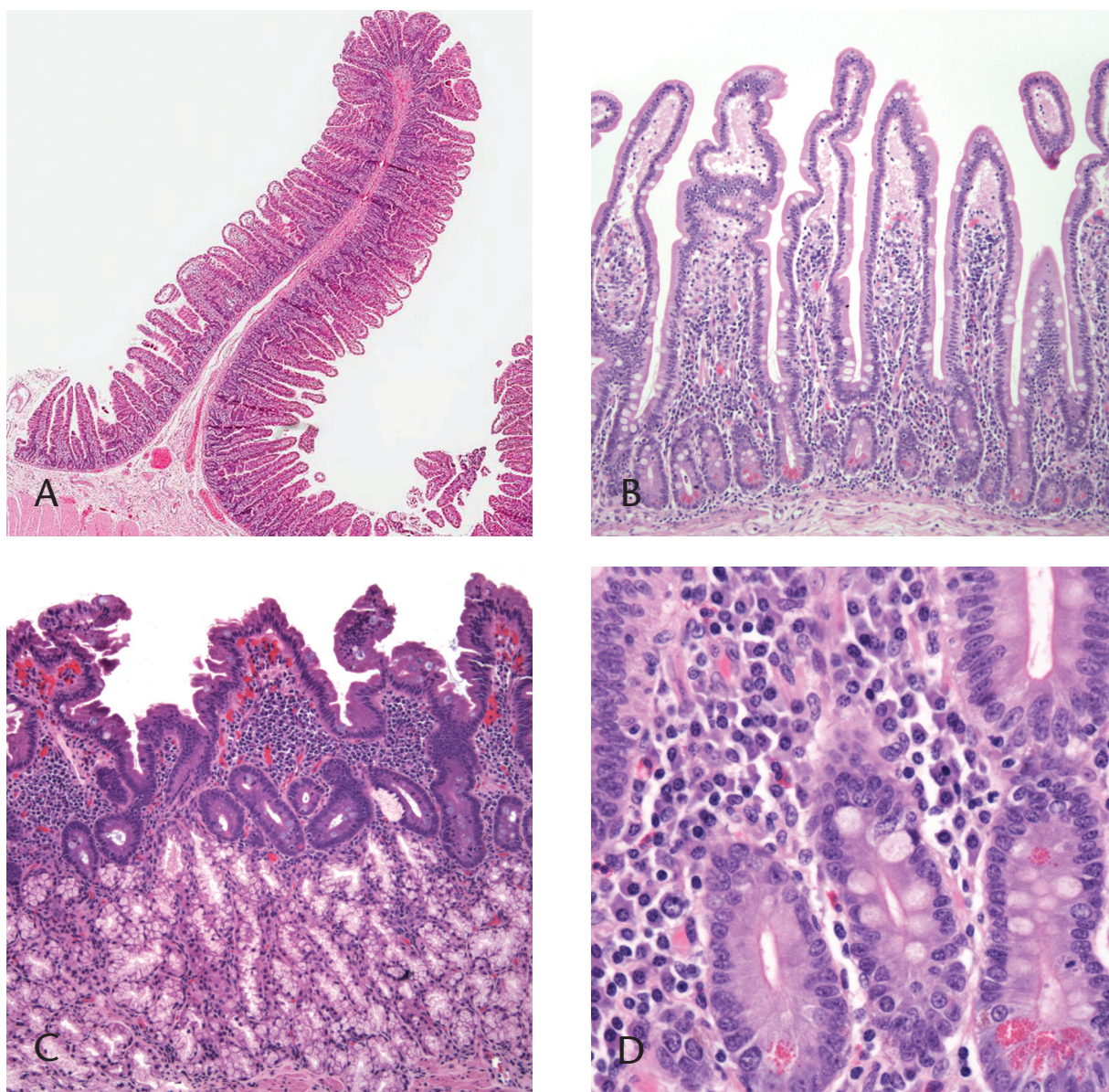


Figure 1-6

NORMAL HISTOLOGIC FEATURES OF THE SMALL BOWEL

The small bowel folds consist of submucosal projections surfaced by mucosa with a villous architecture (A). Long slender villi of the jejunum contain cellular lamina propria with small, scattered vessels and plasma cells; they are surfaced by absorptive enterocytes and interspersed goblet cells (B). Villi in the proximal duodenum are often shortened overlying Brunner glands (C). The crypts contain goblet cells and Paneth cells supported by plasma cell-rich lamina propria (D).

mononuclear cells, plasma cells, and occasional eosinophils. Neutrophils may be present, but are generally scattered and inconspicuous. Intraepithelial lymphocytes may be seen in villi of healthy patients; they number fewer than 25 per 100 enterocytes and tend to be most

numerous at the bases of the villi or along their lateral aspects.

The muscularis mucosae lies just below the crypt bases. It is composed of a slender, discontinuous band of smooth muscle cells arranged in inner circular and outer longitudinal layers.

The submucosa contains linear arrays of lymphoid aggregates that may transgress the muscularis mucosae and extend into the lamina propria. They are more prominent in the distal ileum where they may be circumferential, especially in children. Lobules of neutral mucin-containing glands (i.e., Brunner glands) are numerous in the duodenal bulb and periampullary duodenum. These lobules are mostly present in the submucosa, although they can extend into the lamina propria, especially in the duodenal bulb. Medium-sized arteries are accompanied by veins and are supported by loose connective tissue, fat, and collagen fibers. Submucosal nerve plexuses are also present.

The muscularis propria is composed of two thick layers of smooth muscle cells arranged in inner circular and outer longitudinal layers. The myenteric plexus lies between these layers and contains parasympathetic ganglion cells intimately associated with the interstitial cells of Cajal. A thin layer of loose connective tissue separates the muscularis propria from the mesothelium-lined serosal surface.

THE NORMAL COLORECTUM

Anatomy

Gross Anatomy. The large intestine measures up to 1.5 m in length and has a larger diameter proximally. It is composed of four anatomic regions: the right colon consisting of the cecum and ascending colon, the transverse colon, the distal colon (i.e., descending and sigmoid colon), and the rectum. The cecum is completely surfaced by peritoneum and contains the appendiceal orifice, which is located on its medial aspect slightly below the ileocecal valve. The ascending colon is approximately 20 cm long; it is surfaced by peritoneum anteriorly but lies on the posterior abdominal wall.

The colon acquires a mesentery at the hepatic flexure. This region marks the beginning of the transverse colon, which ranges from 30 to 60 cm in length and extends to the splenic flexure. At this point, the colon is adherent to the posterior abdominal wall, where it remains throughout the length of the descending colon. The sigmoid colon is again suspended on a mesentery as it crosses the pelvic brim.

The rectosigmoid junction is located at the level of the sacral promontory. The rectum

measures approximately 15 cm and extends to the dentate line. The upper third is surfaced by peritoneum on its anterolateral aspects but the remainder of the rectum is surrounded by perirectal fat and connective tissue. These soft tissues below the peritoneal reflection comprise the mesorectum, which is surfaced by adventitia, and represent the radial margin on rectal resection specimens.

Three evenly spaced longitudinal bands of smooth muscle are visible on the external surface of the entire colon. These teniae coli represent condensations of the outer layer of the muscularis propria. One of them lies adjacent to the insertion of the mesentery and the other two are located on the antimesenteric aspect of the colon. The longitudinal arrangement of teniae coli contributes to the formation of a series of saccular haustra between them, imparting a segmented appearance to the outer aspect of the colon, and producing the semilunar folds of the colonic mucosa (fig. 1-7A). The teniae coli coalesce at the base of the appendix and become progressively broader and thicker in the distal colorectum. Appendices epiploica are fatty protuberances arranged in two rows in the ascending and descending colon, and in a single row on the undersurface of the transverse colon.

Vascular Anatomy. The colon proximal to the splenic flexure is vascularized by the ileocolic, right colic, and middle colic branches of the superior mesenteric artery. The distal colon is supplied by the left colic and sigmoid branches of the inferior mesenteric artery. Anastomosing arcades link the superior and inferior mesenteric arteries through the marginal artery of Drummond, which courses parallel to the mesenteric surface of the colon. This vessel can be attenuated near the splenic flexure thereby predisposing it to ischemic injury. The vascular supply of the rectum consists of the superior rectal branch of the inferior mesenteric artery, the middle rectal arteries from the internal iliac vessels, and the inferior rectal arteries from the internal pudendal vessels. The colonic veins are paired with arteries; all of the colonic veins and those of the superior and middle rectum drain into the portal circulation, whereas veins from the distal rectum drain into the systemic circulation.

The lymphatic drainage of the colorectum is to paracolic and pararectal lymph nodes adjacent to

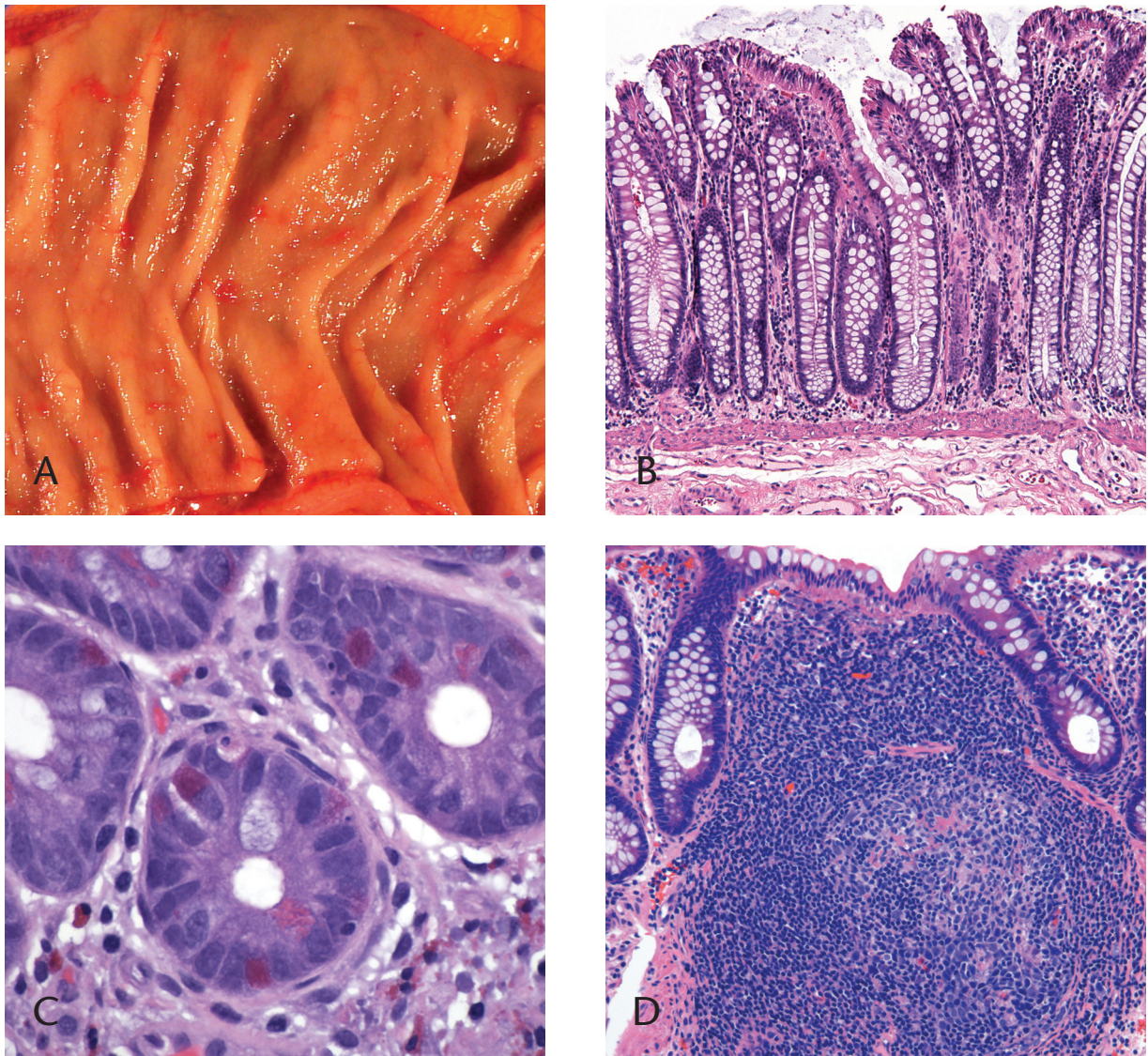


Figure 1-7

NORMAL GROSS AND HISTOLOGIC FEATURES OF THE COLON

The colonic mucosa is arranged in mucosal folds that incompletely surface the luminal circumference (A). The mucosa lacks villi, but shows an undulating surface and straight tubular crypts that extend to the muscularis mucosae (B). Deep crypts contain Paneth cells with lumenally oriented granules, as well as pyramidal endocrine cells with finer, more purple granules near the basement membrane (C). Lymphoid aggregates are centered in the submucosa and frequently extend into the lamina propria; the muscularis mucosae is often interrupted in these areas (D).

the bowel wall. Lymph nodes draining the colon and proximal rectum are also dispersed along mesenteric vessels, whereas the lower rectum drains to lymph nodes along the superior rectal artery and middle rectal vessels. Lower rectal lymph nodes ultimately drain to the internal iliac lymph nodes, or even to inguinal lymph nodes through presacral lymphatic vessels.

Histology

The colorectum consists of several layers: the mucosa and muscularis mucosae, submucosa, muscularis propria, and serosa or adventitia depending on whether it is surfaced by peritoneum. The colonic mucosa primarily functions to absorb water and electrolytes, reducing

approximately 1 L of liquid contents to 100 mL of feces each day. Thus, its mucosal architecture is different than that of the small intestine. The surface is flat with smooth undulations, and the epithelium is arranged in straight, regularly spaced crypts that extend to the muscularis mucosae (fig. 1-7B). Both the surface and crypts are lined by a predominance of goblet cells with interspersed absorptive cells. Colonic goblet cells are rich in sulfated or O-acetylated mucins that impart a slightly blue hue to their cytoplasm. Progenitor cells populate the lateral aspects of the deep crypts; endocrine cells are present at the crypt bases. Paneth cells are also scattered in the deep crypts of the ascending and proximal transverse colon but they should not be present in the distal colon (fig. 1-7C). The crypts of the rectal mucosa are shorter and tend to be irregularly dispersed in the lamina propria. They may also show a greater degree of crypt-to-crypt variability and occasional crypt branching.

The colonic lamina propria contains a mixed population of plasma cells, lymphocytes, and eosinophils; inflammatory cells are more numerous in the lamina propria of the proximal colon than the distal colon. The rectal lamina propria is similar, although it frequently contains mucin-filled macrophages that may be prominent in up to 40 percent of patients (23). Intraepithelial lymphocytes are commonly present in small numbers, especially overlying lymphoid aggregates. Small capillaries are normally present at all levels of the lamina propria but lymphovascular channels are limited to the deep mucosa near the crypt bases.

The muscularis mucosae is composed of slender fascicles of smooth muscle cells arranged in inner circular and outer longitudinal layers. It is discontinuous through lymphoid aggregates, often permitting herniation of mucosal elements beyond the level of the muscularis mucosae (fig. 1-7D). The submucosa contains Meissner plexus composed of parasympathetic ganglion cells and sympathetic neurons, arteries, and veins supported by loose connective tissue and fat.

The architecture of the colonic muscularis propria is slightly different than that of the small intestine. Like the small intestinal muscularis propria, it consists of inner circular and outer longitudinal layers between which lies the Auerbach plexus. Although the inner

circular layer is continuous throughout the colonic length and circumference, the outer layer is discontinuous. The latter appears as attenuated aggregates of smooth muscle cells that coalesce into three evenly spaced teniae coli. The outer colon is surfaced by a thin layer of loose connective tissue lined by mesothelium on its peritonealized surfaces.

THE NORMAL APPENDIX

Anatomy

Gross Anatomy. The tubular (or vermiform) appendix arises from the medial wall of the cecum. It reaches its maximum diameter by 4 years of age, ultimately averaging 9 cm in length and 0.7 cm in diameter. The teniae coli coalesce at the appendiceal base and completely invest it. The appendix becomes narrower with age, particularly after age 40, as lymphoid tissue decreases and fibrosis increases (24). Its location varies depending on the shape of the cecum and its positioning at the time of embryologic development and rotation (25–27). It most frequently lies 2 to 3 cm below the ileocecal valve posterior to the cecum or ascending colon; other locations include the retroileal space, pre-ileal space, pelvis, and hepatorenal recess. Abnormal positioning of the appendix can explain atypical manifestations of acute appendicitis (28).

Vascular Anatomy. The appendix is supplied by the posterior cecal branch of the ileocolic artery, which is derived from the superior mesenteric artery. Appendiceal venous drainage goes to the superior mesenteric vein. Both arterial and venous structures are supported by the mesoappendix, which is contiguous with the mesentery of the bowel. Small lymph nodes that drain to the pericolic and superior mesenteric lymph nodes are infrequently found within the mesoappendix.

Histology

The mucosa of the appendix is similar to that of the large bowel, although it contains a greater amount of lymphoid tissue, often with germinal centers, and is particularly prominent during childhood and adolescence (fig. 1-8A). The epithelium is composed of tall columnar absorptive cells, goblet cells, Paneth cells, and endocrine cells at the base of the mucosa (fig.

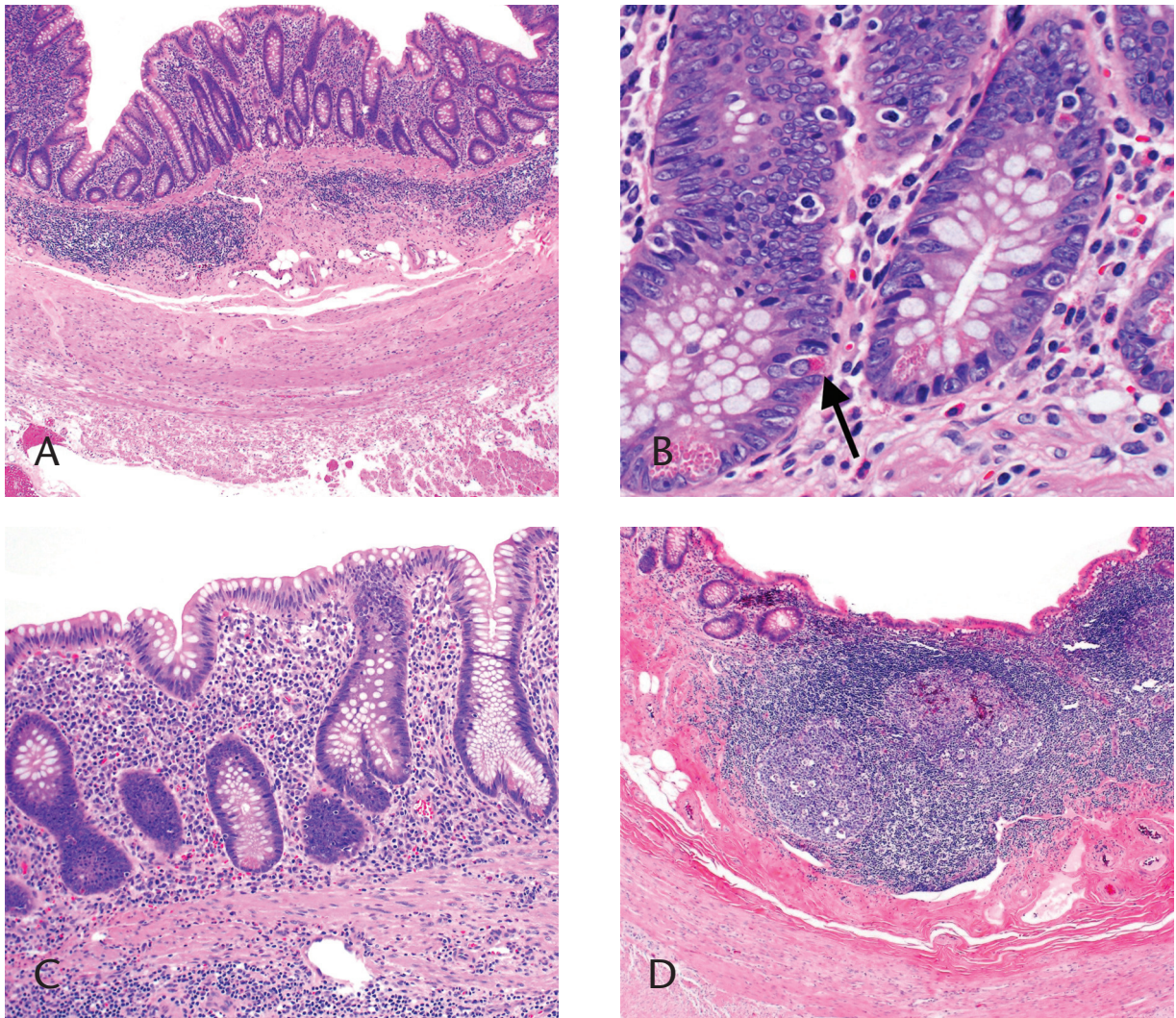


Figure 1-8

NORMAL HISTOLOGIC FEATURES OF THE APPENDIX

The appendiceal mucosa, submucosa, muscularis propria, and serosa are similar to those of the colon, although the appendix contains abundant lymphoid tissue and an irregularly thickened muscularis mucosae (A). The mucosa contains absorptive cells, goblet cells, endocrine cells (arrow), and occasional Paneth cells (B). The crypts are often irregularly distributed and show mild architectural distortion, but these features represent normal variants rather than evidence of appendicitis (C). Lymphoid tissue may be prominent and contains germinal centers with attenuated overlying epithelium; the muscularis mucosae is discontinuous through large lymphoid aggregates (D).

1-8B) (29). The lamina propria normally contains mononuclear cells and occasional eosinophils. The crypts typically display a slightly irregular distribution (fig. 1-8C) (30). Large lymphoid aggregates span the mucosal thickness and extend into the submucosa; disruption of the muscularis mucosae and attenuation of the overlying epithelium are often present (fig. 1-8D) (27,30).

The submucosa, muscularis propria, and serosa are qualitatively similar to analogous structures in the colon. Nerves and ganglion cells are not confined to a myenteric plexus; they are easily identified throughout the inner and outer layers of the muscularis propria (30). Aggregates of smooth muscle cells, particularly those of the inner muscularis propria, may rarely accumulate PAS-D–positive granular material in

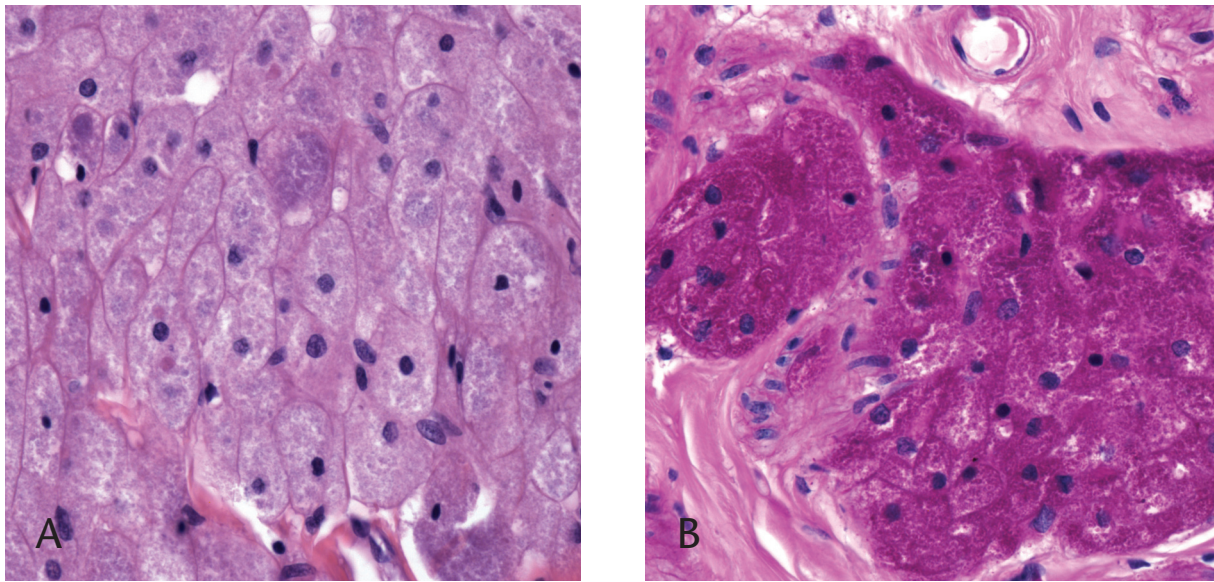


Figure 1-9

GRANULAR DEGENERATION OF THE MUSCULARIS PROPRIA

Some appendices feature abnormal smooth muscle cells in the muscularis propria, particularly its inner layers. Smooth muscle cells are enlarged and round. They contain abundant granular cytoplasm (A) that is strongly positive with PAS-D histochemical stains (B).

their cytoplasm that simulates an inflammatory process or neoplasm (fig. 1-9) (31). Prominent intravascular lymphocytosis in the appendix and meso-appendix is frequently present (fig. 1-10). The serosa is smooth, glistening, and transparent, and a thin layer of peritoneum covers the entire appendix.

THE NORMAL ANUS

Anatomy

Gross Anatomy. The surgical anal canal extends from the anorectal ring to the anal verge and spans approximately 4 cm in the adult. The proximal mucosa gives rise to 8 to 12 longitudinal mucosal folds (i.e., anal columns of Morgagni); pairs of these folds terminate at each of several circumferentially arranged semilunar folds of tissue (i.e. anal valves). The anal valves form the dentate, or pectinate, line and enclose the anal crypts that drain anal glands (32). The dentate line is composed of anorectal mucosa proximally and anodermal mucosa distally in young children, but these types of mucosae are separated by the anal transition zone in adults. The smooth mucosa distal to the dentate line

(i.e., pectin) terminates at the anal verge, which is wrinkled, slightly pigmented, and represents the transition from anoderm to perianal skin.

The internal anal sphincter is continuous with the circular layer of the rectal muscularis propria and terminates proximal to the anal verge. The intrinsic enteric nervous system of the myenteric plexus facilitates rhythmic contractions of the sphincter muscle; extrinsic autonomic control is derived from the hypogastric pelvic nerve plexus. The external anal sphincter is composed of alternating ring-like and elliptical layers of striated skeletal muscle that run from the perineal body to the coccyx. It surrounds the internal anal sphincter and extends caudally, terminating approximately 1 cm distal to the internal anal sphincter. The deep external sphincter is fused with the puborectalis muscle. Fibroelastic septa extend through the external sphincter into the perianal dermis, producing the characteristic folds of the perianal skin (33).

The external anal sphincter is innervated by the inferior rectal branch of the pudendal nerve and the perineal branch of S4. The puborectalis and levator ani form the pelvic diaphragm and

provide both sympathetic tonic contraction and voluntary control.

Vascular Anatomy. The anal canal above the dentate line is supplied by branches of the superior hemorrhoidal (rectal) artery. Draining venules coalesce into saccular venous plexuses in the submucosa in the anal cushions, which are most prominent in the right anterior, right posterior, and left lateral positions (34). The anal cushions compress the anal orifice, producing a “Y-shaped” opening and providing nearly 20 percent of the resting anal pressure at the level of the internal anal sphincter (35). The lymphatic vessels of the proximal anus drain to inferior mesenteric and internal iliac lymph nodes.

The anal canal below the dentate line is supplied by the middle and inferior hemorrhoidal arteries and drained by the portal venous system via the inferior mesenteric vein. Lymph flows through inferior rectal lymphatic channels to the superficial inguinal lymph nodes. The upper anal canal is richly innervated by pressure-sensitive fibers from the inferior rectal branch of the pudendal nerve, whereas pain fibers are present below the dentate line.

Histology

The anorectal junction is surfaced by mucosa similar to that of the rectum. A single layer of goblet cells, interspersed colonocytes, and occasional endocrine cells in the crypts are arranged along a basement membrane; the crypts are more irregularly shaped compared with the mucosa of the abdominal colon (36). The lamina propria contains delicate capillaries

and venules as well as scattered lymphocytes and plasma cells. Mucin-filled macrophages can be numerous and tend to aggregate in the superficial mucosa (fig. 1-10A). The muscularis mucosae is composed of longitudinally arranged aggregates of smooth muscle cells. The anal transition zone is lined by four to nine cell layers: polarized cuboidal cells are present in the deep layers, whereas surface cells may be flat, cuboidal, or columnar with apical mucin (fig. 1-10B). Histochemical stains demonstrate a predominance of sialomucins in this region (37).

Lobules of mucin-containing anal glands are located in the submucosa and commonly penetrate the internal sphincter. Cells in the neck region have a transitional appearance that gradually gives way to squamous cells at the gland orifice. The anal transition zone epithelium merges with the smooth, nonkeratinizing stratified squamous epithelium at the dentate line (fig. 1-10C). Scattered melanocytes, Langerhans cells, intraepithelial lymphocytes, and Merkel cells are often present (fig. 1-10D).

The perianal skin is surfaced by keratinizing epithelium with a granular cell layer, keratohyalin granules, and a cornified layer of keratin at the anal verge. Dermal papillae, hair follicles, and adnexal structures are present. The submucosa consists of loosely arranged collagen fibrils, fibroblasts, and scattered multinucleated stromal cells above the dentate line. The submucosa of the pecten is rich in elastic tissue and collagen fibrils that tether the mucosa to the underlying muscle. Elastic fibers are most prominent at the anal verge.

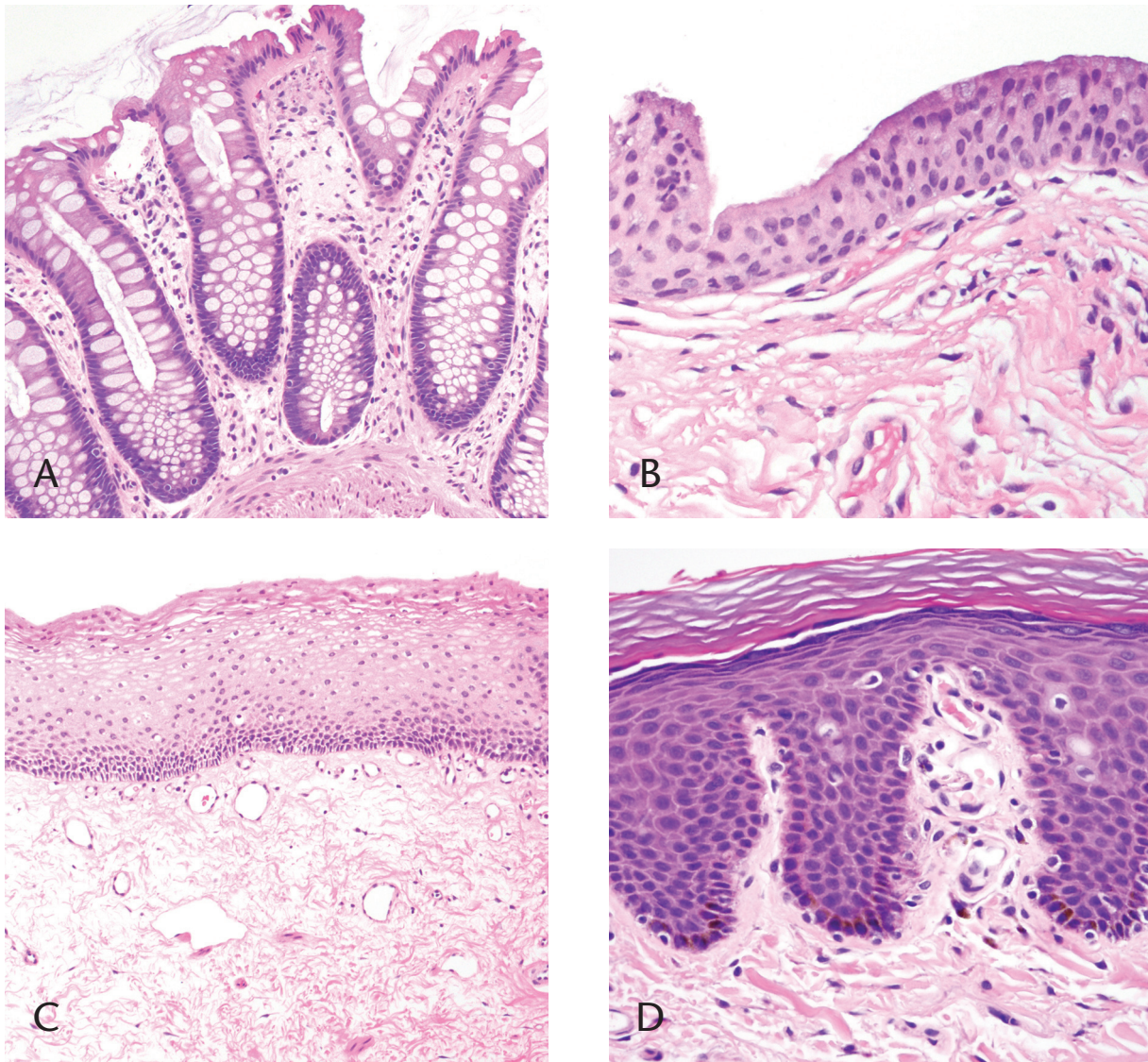


Figure 1-10

NORMAL HISTOLOGIC FEATURES OF THE ANORECTUM

The most distal rectal mucosa contains irregularly distributed colonic crypts with slight surface serration and aggregates of foamy macrophages in the lamina propria (A). Transitional mucosa consists of a multilayered epithelium composed of cuboidal, squamoid, and mucin-containing columnar cells (B). Nonkeratinizing stratified squamous epithelium is supported by loose connective tissue in the anal canal (C). The mucosa near the anal verge is surfaced by basket weave-type keratin with a granular cell layer. Scattered Langerhans cells and melanocytes are present in the epithelium, and basal keratinocytes show pigmentation (D).

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