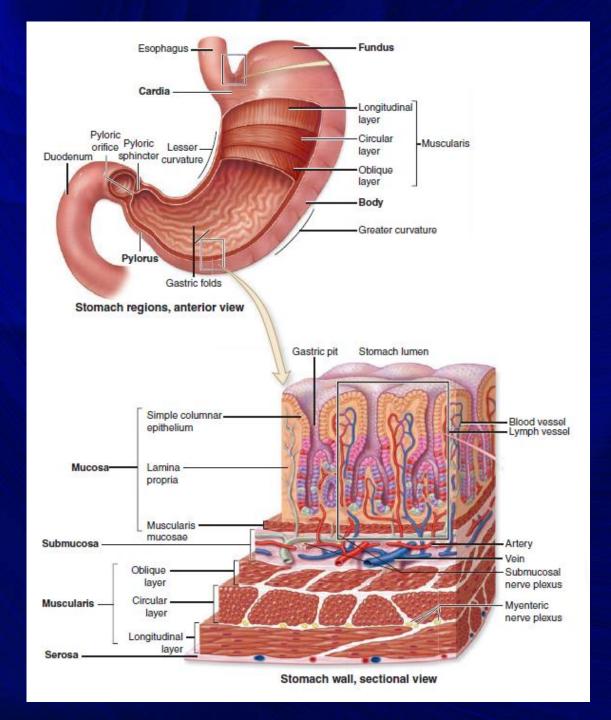
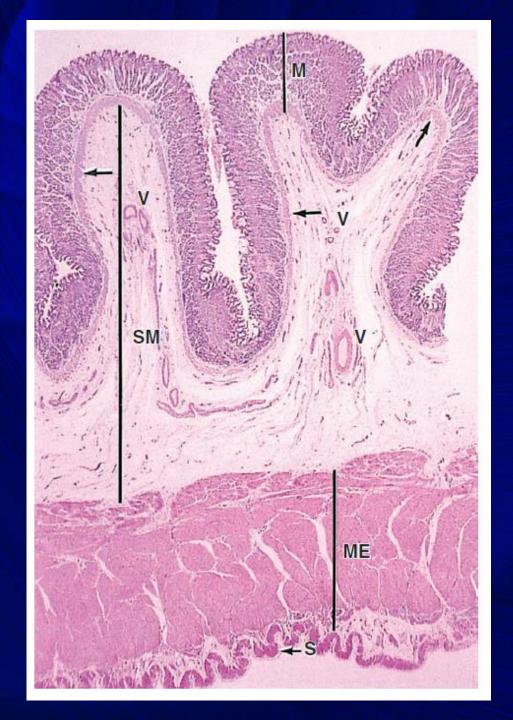
HISTOLOGY OF THE GIT HOLLOW ORGANS



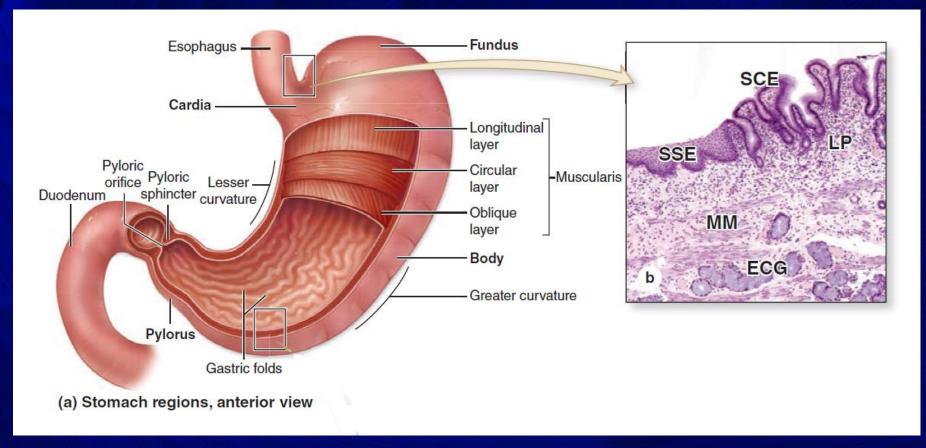


The wall in all regions of the stomach is made up of all *four* major layers.



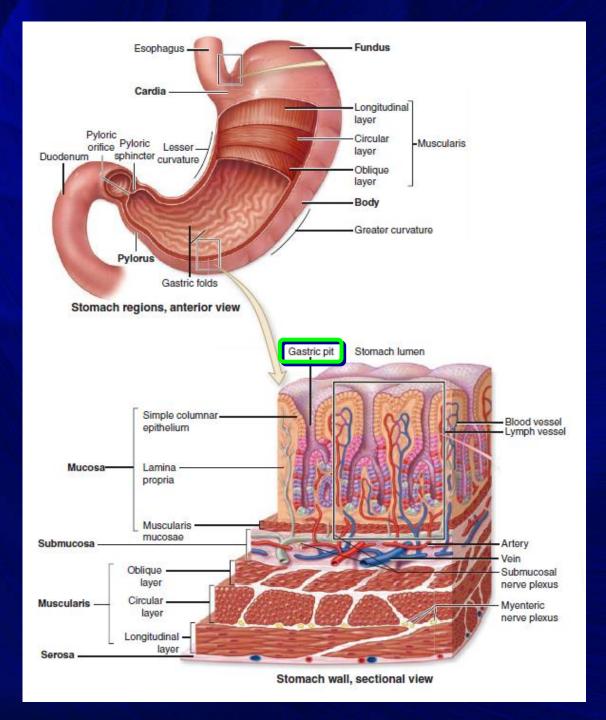
A low-magnification micrograph of the stomach wall at the fundus shows the relative thickness of the four major layers: the mucosa (M), the submu-cosa (SM), the muscularis externa (ME), and the serosa (S). Two rugae (folds) cut transversely and consisting of mucosa and submucosa are included. The mucosa is packed with branched tubular glands penetrating the full thickness of the lamina propria so that this sublayer cannot be distinguished at this magnification. The muscularis mucosae (arrows), immediately beneath the basal ends of the gastric glands, is shown. The submucosa is largely loose connective tissue, with blood vessels (V) and lymphatics. X12. H&E.

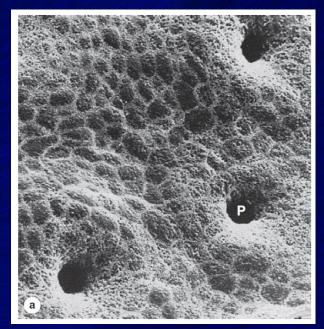




(a) The major stomach regions are the cardia, fundus, body, and pylorus, all with longitudinal gastric folds, or rugae. The muscularis has three layers. (b) At the esophagogastric junction, stratified squamous epithelium (SSE) lining the esophagus is abruptly replaced by simple columnar epithelium (SCE) of the stomach. Also seen here are the mucous esophageal cardiac glands (ECG) beneath the lamina propria (LP) and muscularis mucosae (MM). X60. H&E.

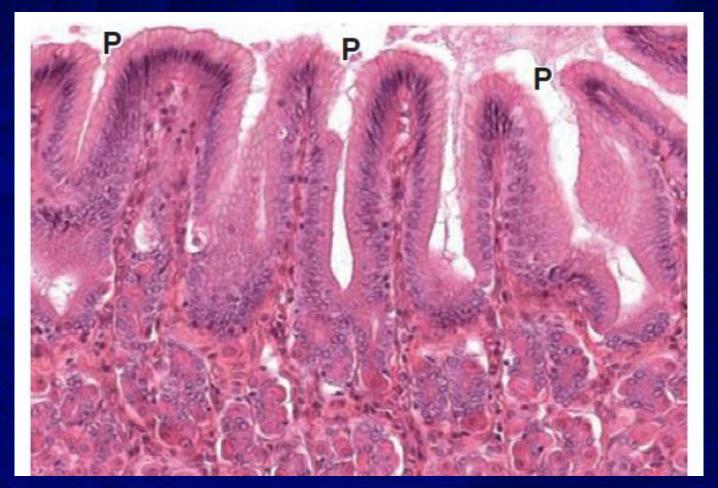
Changing abruptly at the esophagogastric junction, the mucosal surface of the stomach is a **simple columnar epithelium** (SCE) that invaginates deeply into the lamina propria.





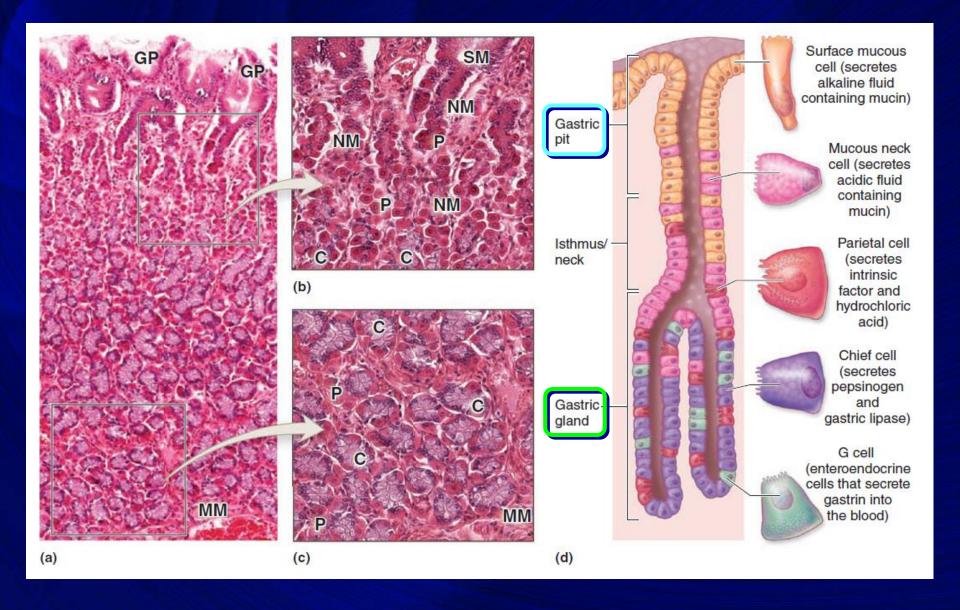
(a) SEM of the stomach lining cleared of its mucous layer reveals closely placed gastric pits (P) surrounded by polygonal apical ends of surface mucous cells. X600.

The invaginations form millions of gastric pits, each with an opening to the stomach lumen.

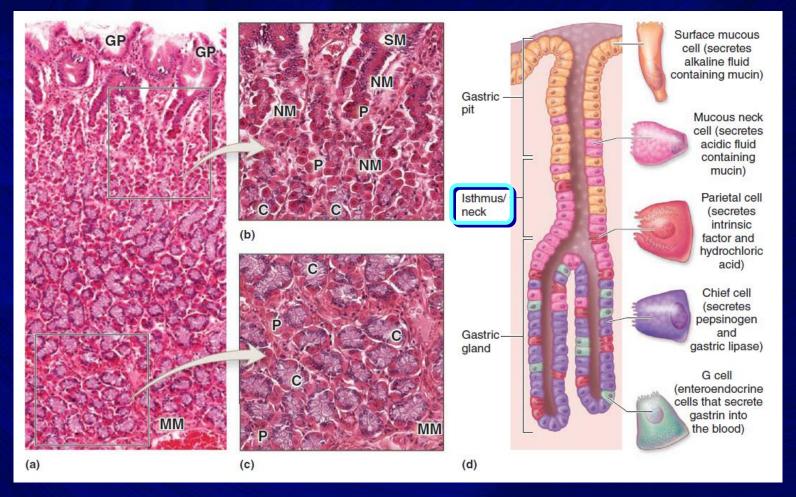


A section of the stomach lining shows that surface mucous cells are part of a simple columnar epithelium continuous with the lining of the pits (P). X200. H&E.

The surface mucous cells that line the lumen and gastric pits secrete a thick, adherent, and highly viscous mucous layer that is rich in bicarbonate ions and protects the mucosa from both abrasive effects of intraluminal food and the corrosive effects of stomach acid.

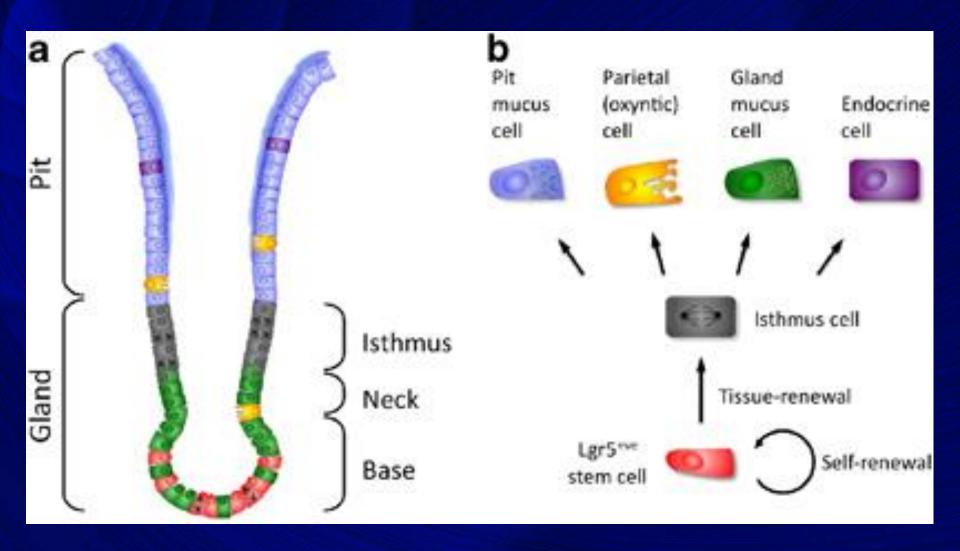


 The gastric pits lead to long, branched, tubular glands that extend through the full thickness of the lamina propria.

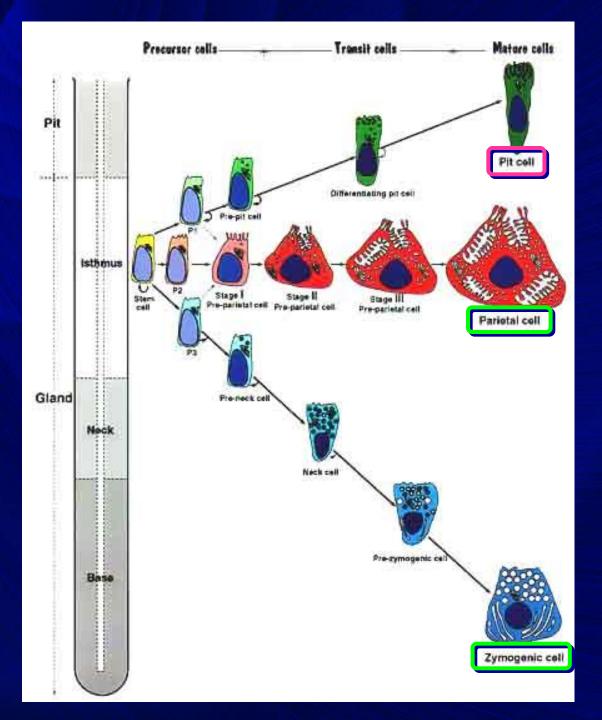


(b) In the neck of a gastric gland, below the surface mucous cells (SM) lining the gastric pit, are small mucous neck cells (MN), scattered individually or clustered among parietal cells (P) and stem cells that give rise to all epithelial cells of the glands.

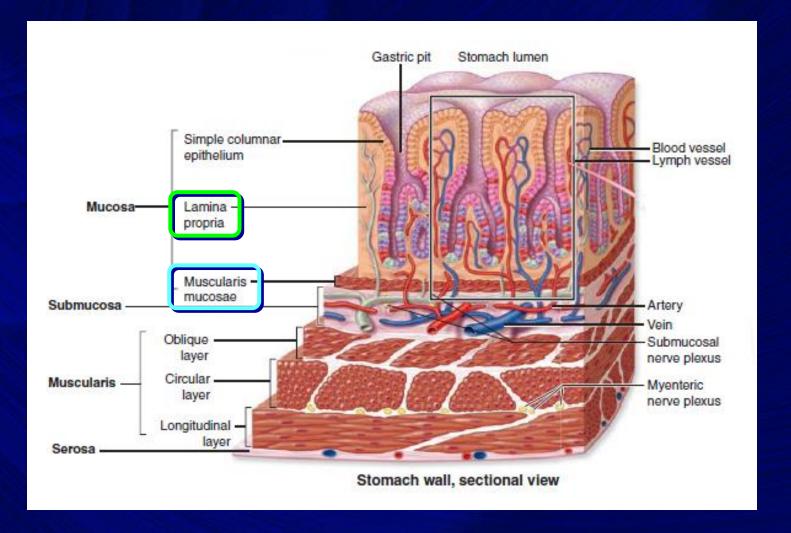
 Stem cells for the epithelium that lines the glands, pits, and stomach lumen are found in a narrow segment (isthmus) between each gastric pit and the gastric glands.



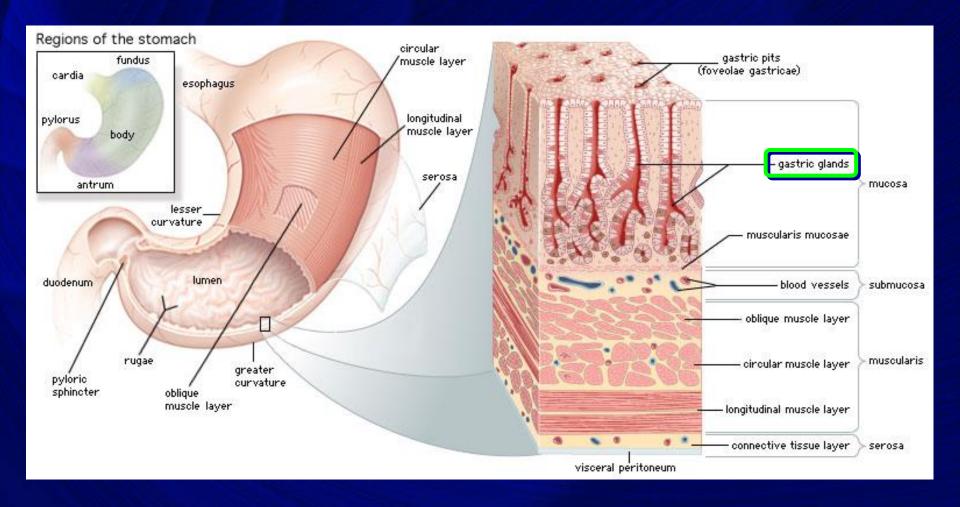
• The pluripotent **stem cells** divide asymmetrically, producing progenitor cells for all the other epithelial cells.



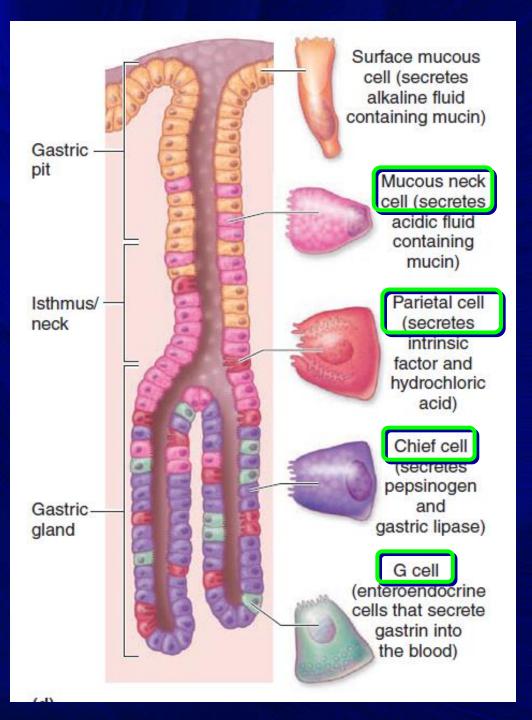
- Some of these move upward to replace surface mucous cells, which have a turnover time of 4 to 7 days.
- Other progenitor cells migrate more deeply and differentiate into the secretory cells of the glands that turn over much more slowly than the surface mucous cells.



- The vascularized lamina propria that surrounds and supports the gastric pits and glands contains smooth muscle fibers, lymphoid cells, capillaries, and lymphatics.
- Separating the mucosa from the underlying submucosa is a layer of smooth muscle, the **muscularis mucosae.**

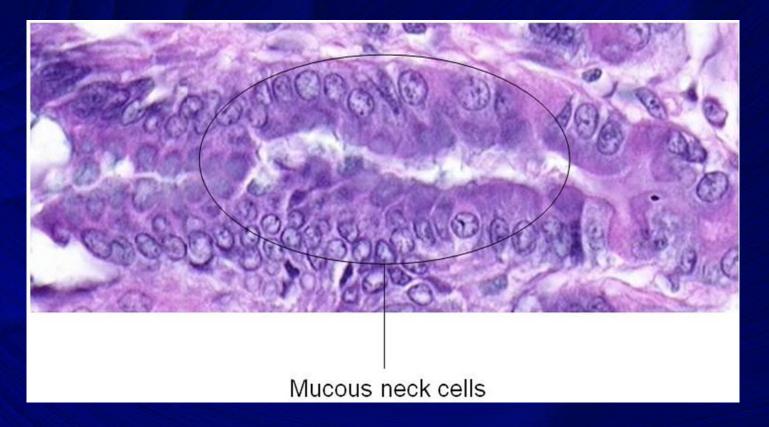


• In the fundus and body the gastric glands themselves fill most of the mucosa, with several such glands formed by branching at the isthmus or neck of each gastric pit.

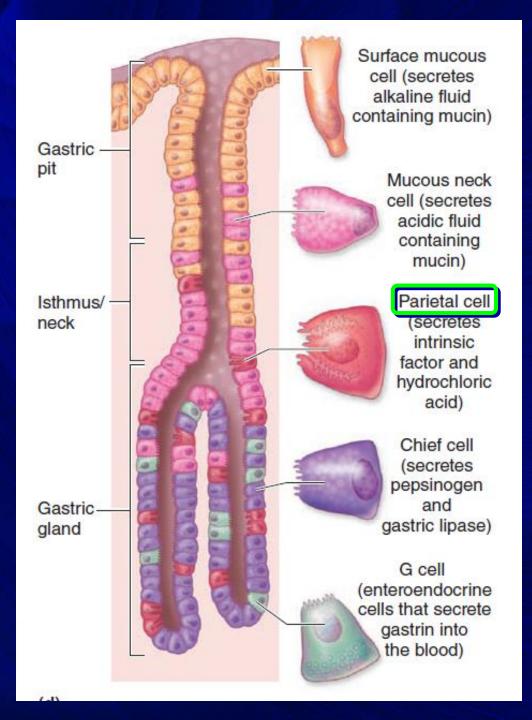


- These cells are of four major types and important properties of each are as follows:
 - Mucous neck cells >
 secretes acidic fluid
 containing mucin
 - Parietal (oxyntic) cells
 → secretes
 hydrochloric acid
 - Chief cells → secretes pepsinogen and gastric lipase
 - Enteroendocrine cells
 secretes gastrin into
 the blood

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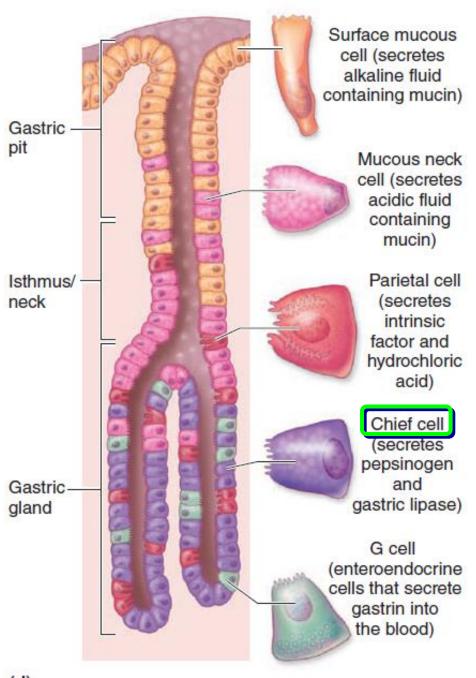


- Mucous neck cells are present in clusters or as single cells among the other cells in the necks of gastric glands and include many progenitor and immature surface mucous cells.
- Less columnar than the surface mucous cells lining the gastric pits.
- They have round nuclei and apical secretory granules
- Their mucus secretion is less alkaline than that of the surface epithelial mucous cells.

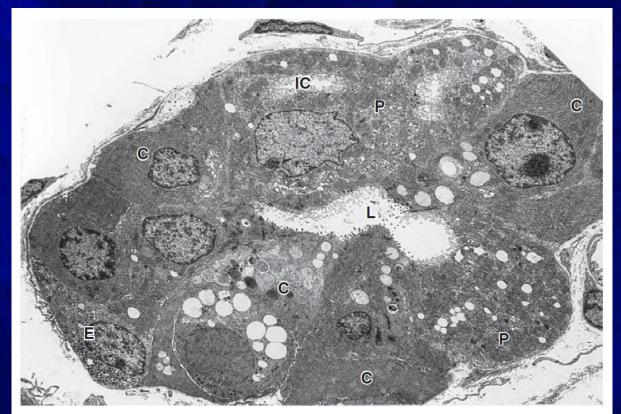


- Parietal (oxyntic) cells
 produce hydrochloric
 acid (HCl) and are present
 among the mucous neck
 cells and throughout
 deeper parts of the gland.
- They are large cells, usually appearing rounded or pyramidal, each with one (sometimes two) central round nucleus.
- The cytoplasm is intensely eosinophilic due to the high density of mitochondria.
- It also secretes Intrinsic factor combines with vitamin B12 to form a complex necessary for erythrocytes formation

17

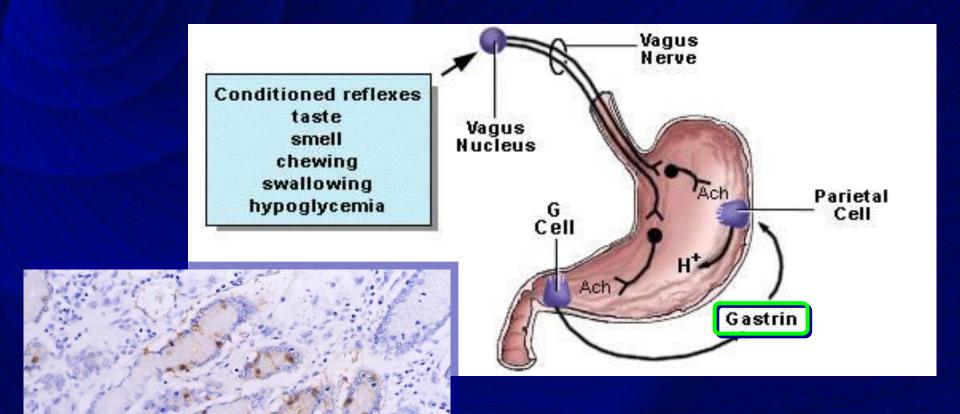


- chief (zymogenic) cells predominate in the lower regions of the gastric glands and
- have all the characteristics of active protein-secreting cells.
- Secrete pepsinogen which is converted into pepsin in an acid environment.
- > pepsin is an enzyme that breaks down proteins into small peptides.
- Chief cells also produce gastric lipase, which digests many lipids



TEM of a transversely sectioned gastric gland shows the ultrastructure of three major cell types. Parietal cells (P) contain abundant mitochondria and intracellular canaliculi (IC). Also shown are chief cells (C), which have extensive rough ER and apical secretory granules near the lumen (L). An enteroendocrine cell (E) shows dense basal secretory granules and is a closed type enteroendocrine cell; that is, it has no contact with the gland's lumen and secretes product in an endocrine/paracrine manner, X1200.

- Enteroendocrine cells are scattered epithelial cells in the gastric mucosa with endocrine or paracrine functions.
- <u>In the fundus</u> small enteroendocrine cells secreting serotonin (5-hydroxytryptamine) are found at the basal lamina of the gastric glands.



Gastrin immunostain

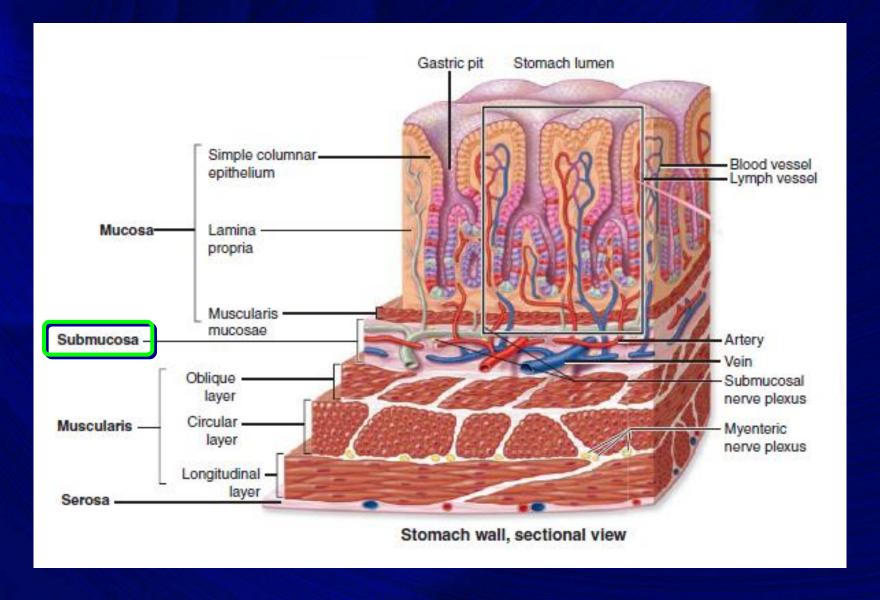
In the pylorus other enteroendocrine cells are located in contact with the glandular lumens, producing the peptide gastrin.



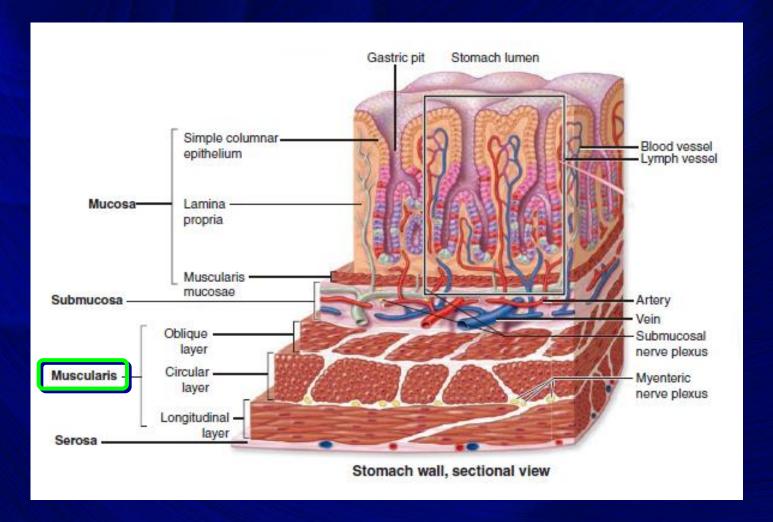
- regions of the stomach, the mucosa also contains tubular glands, with long pits, branching into coiled secretory portions, called cardial glands and pyloric glands.
- These glands lack both parietal and chief cells, primarily secreting abundant mucus.

The pyloric region of the stomach has deep gastric pits (P) leading to short, coiled pyloric glands (G) in the lamina propria (LP). Cardial glands are rather similar histologically and functionally. Cells of these glands secrete mucus and lysozyme primarily, with a few enteroendocrine G cells also present. The glands and pits are surrounded by cells of the lamina propria connective tissue containing capillaries, lymphatics and MALT. Immediately beneath the glands is the smooth muscle layer of the muscularis mucosae. X140. H&E.

Other Layers



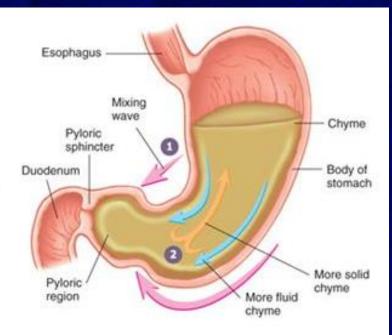
 In all stomach regions the submucosa is composed of connective tissue with large blood and lymph vessels and many lymphoid cells, macrophages, and mast cells.

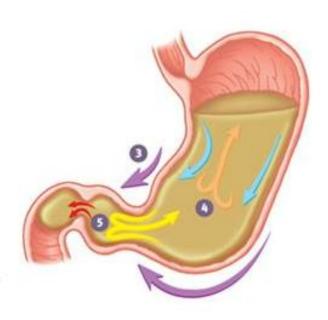


The muscularis has three poorly defined layers of smooth muscle:

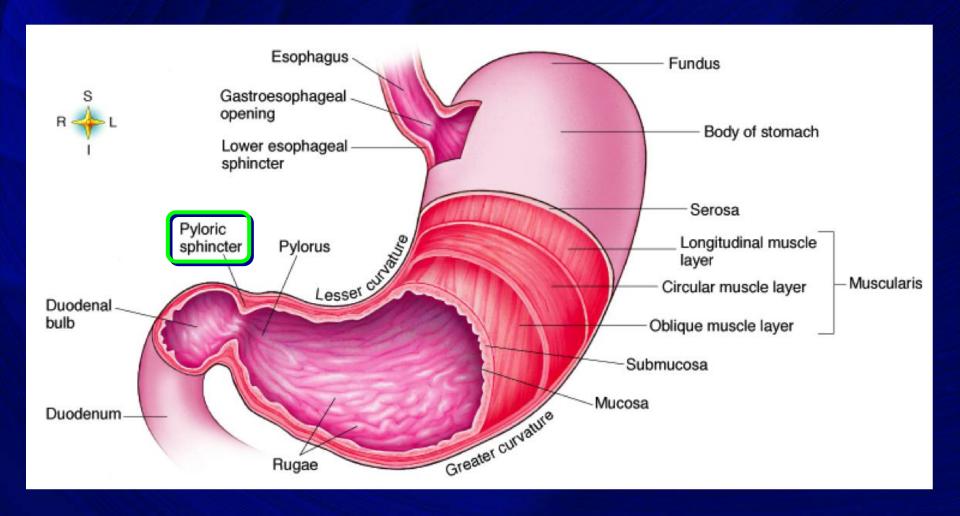
- an outer longitudinal layer,
- a middle circular layer, and
- an innermost oblique layer.

- A mixing wave initiated in the body of the stomach progresses toward the pyloric sphincter (pink arrows directed inward).
- The more fluid part of the chyme is pushed toward the pyloric sphincter (blue arrows), whereas the more solid center of the chyme squeezes past the peristaltic constriction back toward the body of the stomach (orange arrow).
- Peristaltic waves (purple arrows) move in the same direction and in the same way as the mixing waves but are stronger.
- Again, the more fluid part of the chyme is pushed toward the pyloric region (blue arrows), whereas the more solid center of the chyme squeezes past the peristaltic constriction back toward the body of the stomach (orange arrow).
- Peristaltic contractions force a few milliliters of the mostly fluid chyme through the pyloric opening into the duodenum (small red arrows). Most of the chyme, including the more solid portion, is forced back toward the body of the stomach for further mixing (yellow arrow).

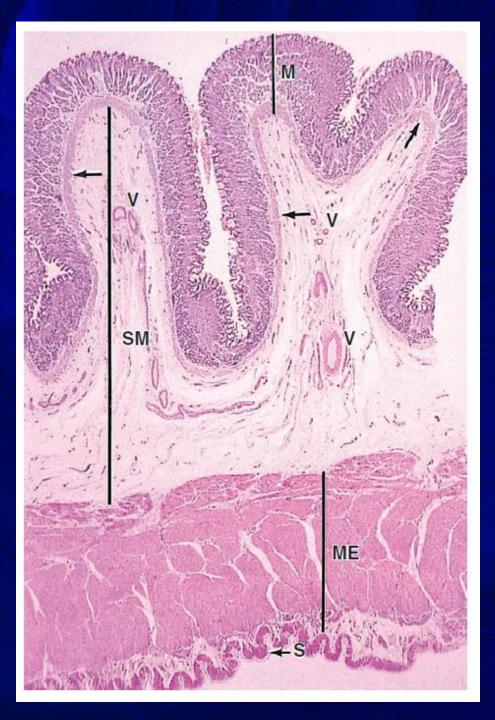




Rhythmic contractions of the muscularis thoroughly mix ingested food and chyme with mucus, HCl, and digestive enzymes from the gastric mucosa.



 At the pylorus the middle layer is greatly thickened to form the pyloric sphincter.

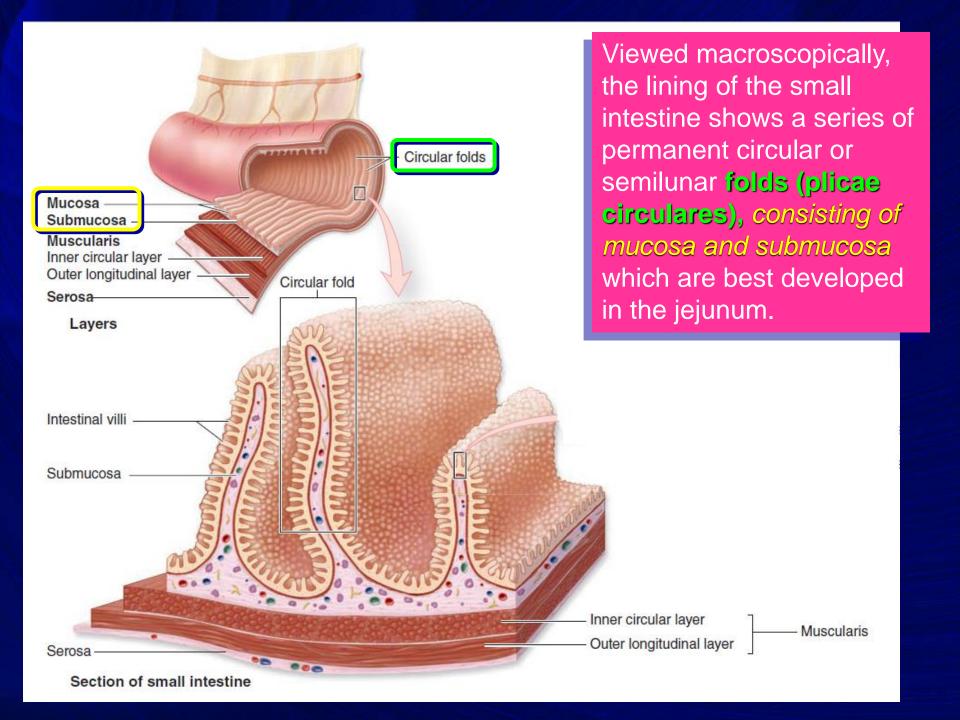


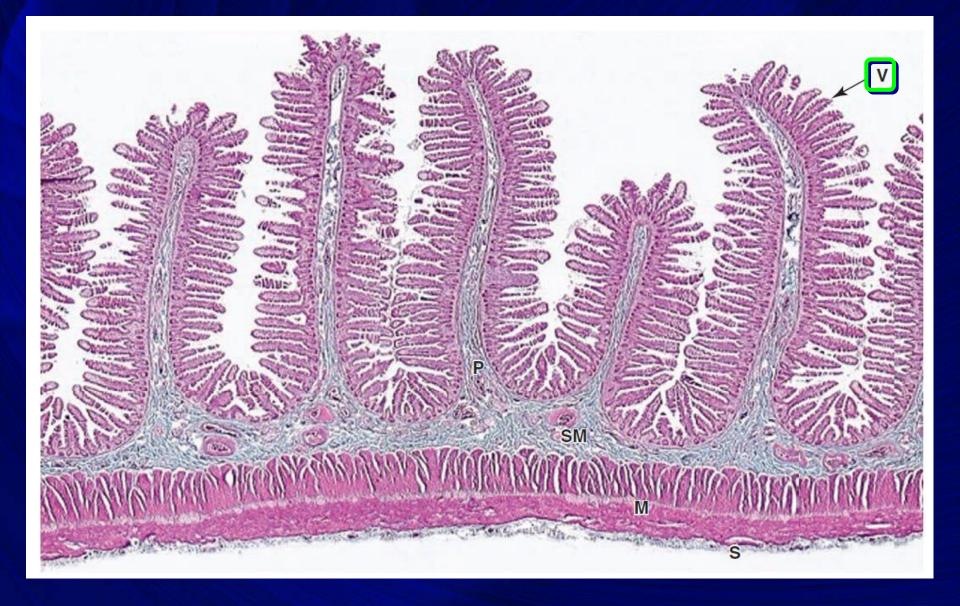
The stomach is covered by a thin **serosa** (consists of loose connective tissue covered by mesothelium)

A low-magnification micrograph of the stomach wall at the fundus shows the relative thickness of the four major layers: the mucosa (M), the submucosa (SM), the muscularis externa (ME), and the serosa (S). Two rugae (folds) cut transversely and consisting of mucosa and submucosa are included. The mucosa is packed with branched tubular glands penetrating the full thickness of the lamina propria so that this sublayer cannot be distinguished at this magnification. The muscularis mucosae (arrows), immediately beneath the basal ends of the gastric glands, is shown. The submucosa is largely loose connective tissue, with blood vessels (V) and lymphatics. X12. H&E.

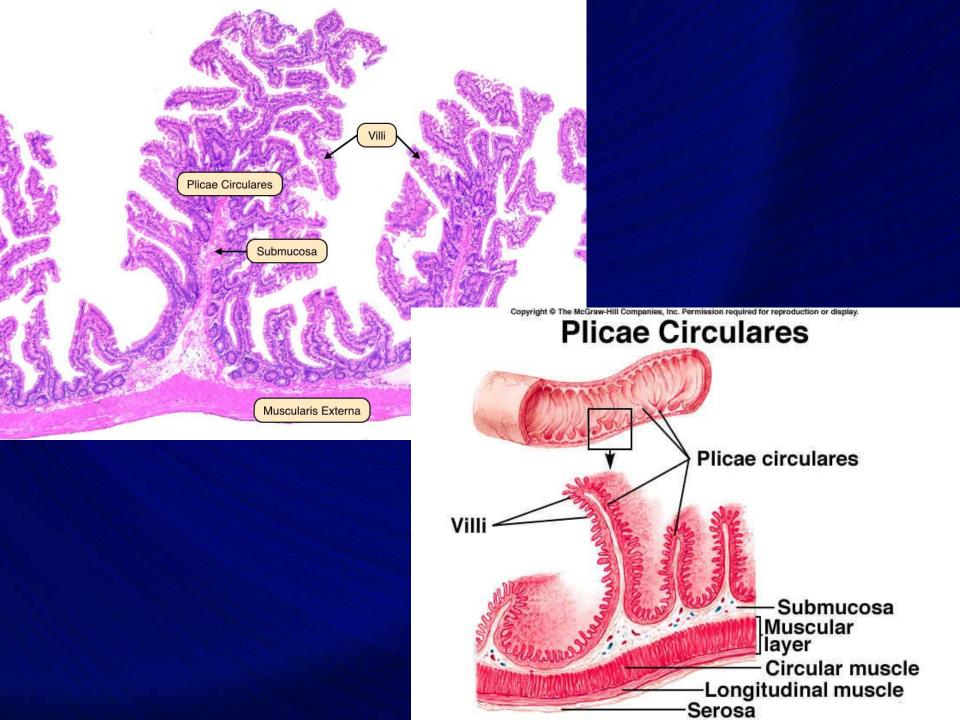
Small Intestine

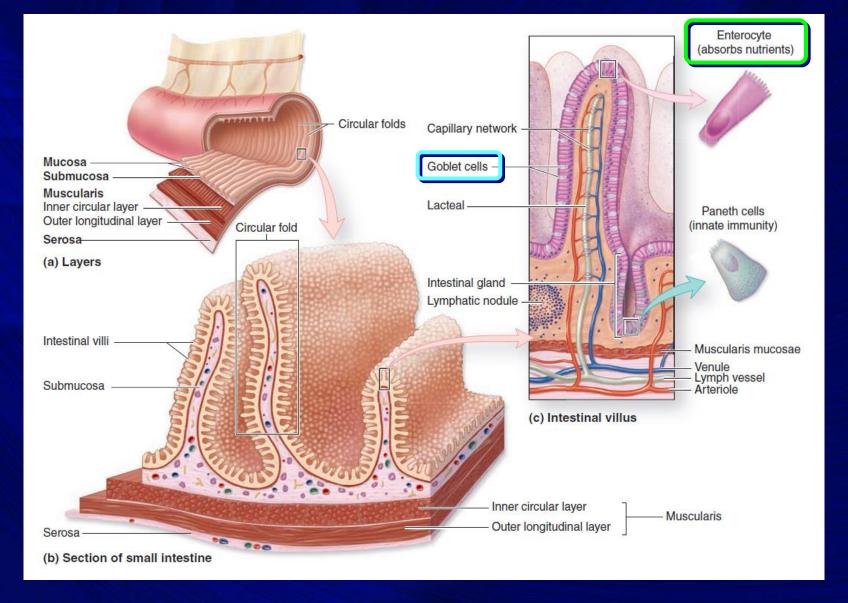




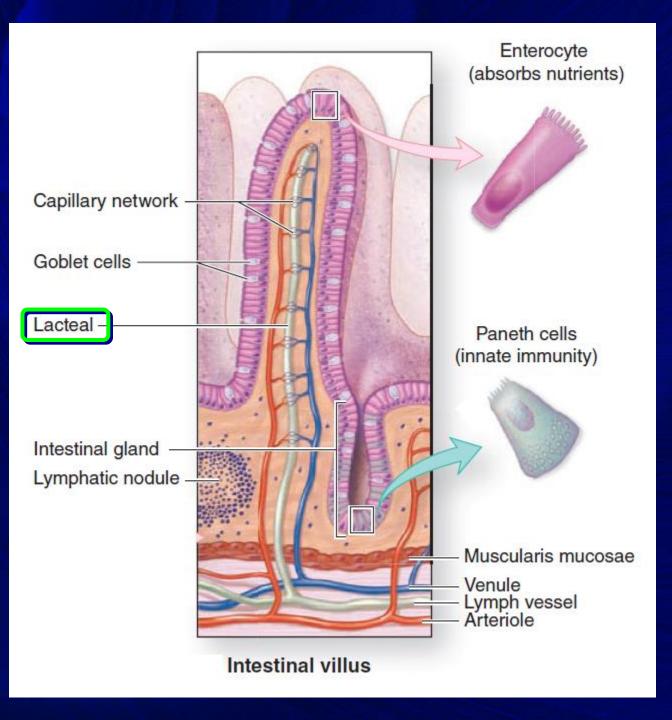


 Densely covering the entire mucosa of the small intestine are short (0.5- to 1.5-mm) mucosal outgrowths called villi that project into the lumen.

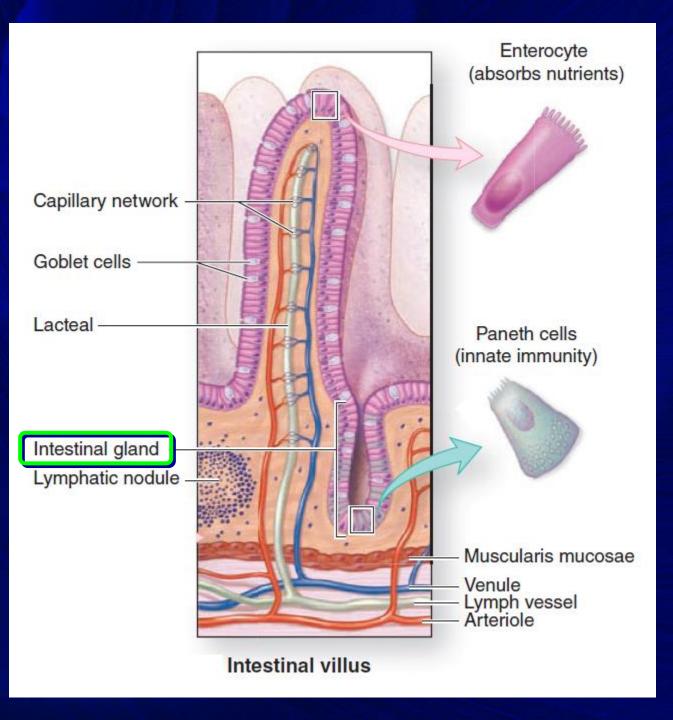




 These finger- or leaflike projections are covered by a simple columnar epithelium of absorptive cells called enterocytes, with many interspersed goblet cells.



- core of loose connective tissue that extends from the lamina propria and contains:
- √ fibroblasts,
- smooth muscle fibers,
- Iymphocytes
- ✓ plasma cells,
- fenestrated capillaries
- ✓ a central lymphatic called a lacteal.



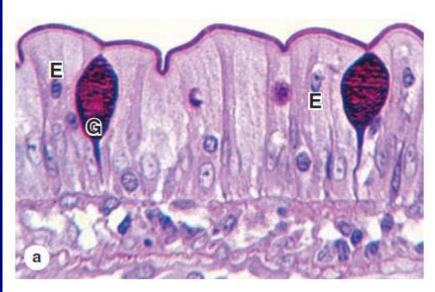
- Between the villi are the openings of short tubular glands called intestinal glands or crypts (or crypts of Lieberkuhn)
- The epithelium of each villus is continuous with that of the intervening glands.

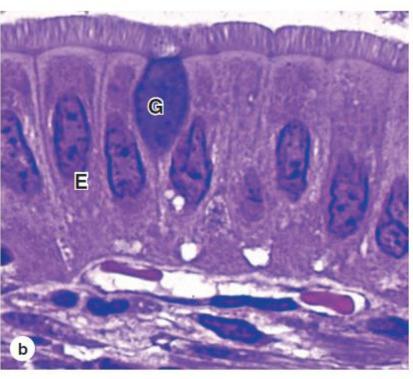


(a) Between villi (V) throughout the small intestine, the covering epithelium invaginates into the lamina propria (LP) to form short tubular glands called intestinal glands or intestinal crypts (IC). The lining near the openings of the crypts contains a population of stem cells for the entire epithelial lining of the small intestine. Daughter cells slowly move with the growing epithelium out of the crypts, differentiating as goblet cells, enterocytes, and enteroendocrine cells. These cells continue to move up each villus and within a week are shed at the tip. with billions shed throughout the small intestine each day. At the base of the crypts are many Paneth cells (P) with an innate immune function. The submucosa (S) has many lymphatics draining lacteals. X200. H&E.

The epithelium of the **intestinal glands** includes differentiating cells and pluripotent stem cells for all the cell types of the small intestine.

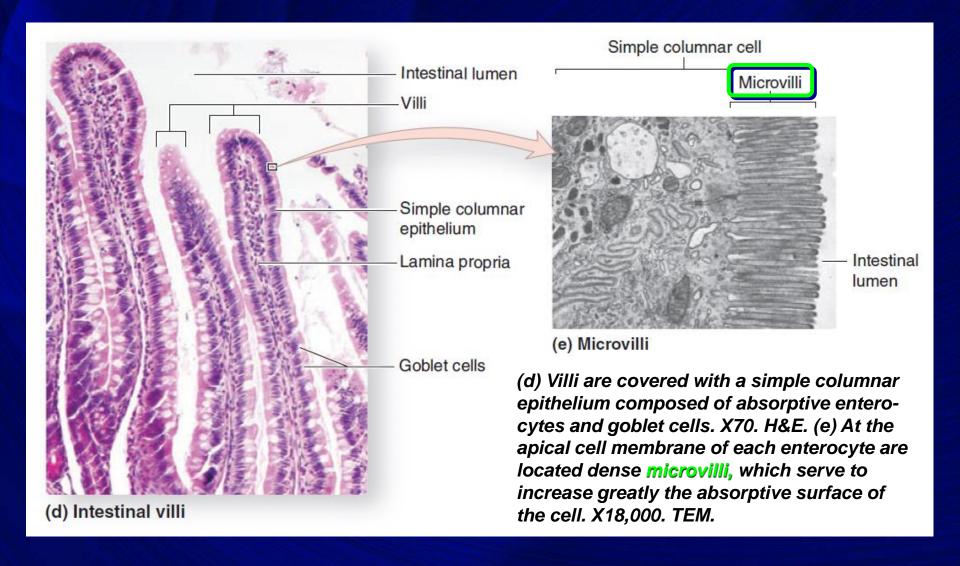
- These include the following:
 - 1. Enterocytes
 - 2. Goblet cells
 - 3. Paneth cells
 - 4. Enteroendocrine cells
 - 5. M (microfold) cells





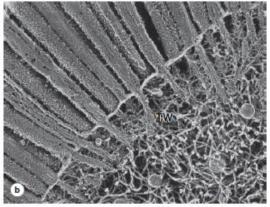
- Enterocytes, the absorptive cells, are tall columnar cells, each with an oval nucleus located basally.
- The apical end of each enterocyte displays a prominent ordered region called the striated (or brush) border.

(a) The columnar epithelium that covers intestinal villi consists mainly of the tall absorptive enterocytes (E). The apical ends of these cells are joined and covered by a brush border of microvilli. Covered by a coating of glycoproteins, the brush border, along with the mucus-secreting goblet cells (G), stains with carbohydrate staining methods. Other cells of the epithelium are scattered enteroendocrine cells, which are difficult to identify in routine preparations, and various immune cells such as intraepithelial lymphocytes. The small spherical nuclei of lymphocytes can be seen between the enterocytes. X250. PAS-hematoxylin. (b) At higher magnification individual microvilli of enterocytes are better seen and the striated appearance of the border is apparent. X500.



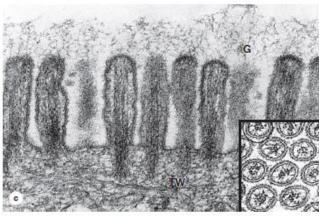
 Ultrastructurally the striated border is seen to be a layer of densely packed microvilli covered by glycocalyx through which nutrients are taken into the cells.





Formin and other proteins for

F-actin capping



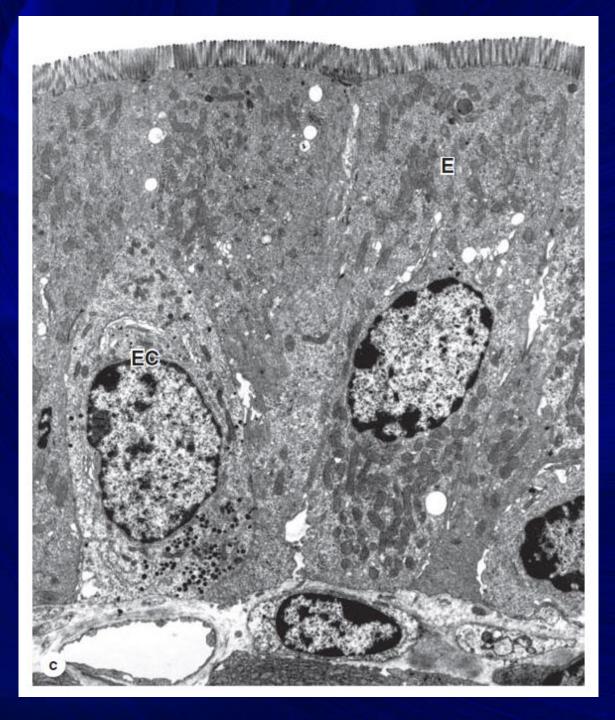
Fimbrin, villin (cross-linking F-actin to membrane)

Actin filaments (microfilaments)

Absorptive cells lining the small intestine demonstrate the highly uniform microvilli of a striated or brush border particularly well. (a) A high-magnification light microscope shows many parallel microvilli and their connections to the terminal web (TW) in the underlying cytoplasm. X6500. (b) SEM of a sectioned epithelial cell shows both the internal and surface structure of individual microvilli and the association with actin filaments and intermediate filaments of the terminal web (TW). X7000. (c) TEM of microvilli sectioned longitudinally and transversely (inset) reveals the microfilament arrays that form the core of these projections. The terminal web (TW) of the cytoskeleton is also seen. The glycocalyx (G) extending from glycoproteins and glycolipids of the microvilli plasmalemma contains certain enzymes for late stages of macromolecule disestion. X15,000.

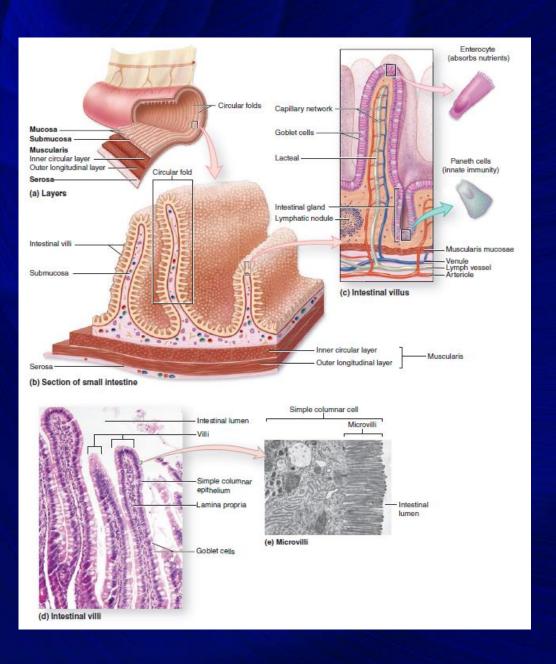
(d) The diagram shows a few microfilaments in a microvillus, with various actin-binding proteins important for F-actin assembly, capping, cross-linking, and movement. Like microfilaments in other regions of the cytoskeleton, those of microvilli are highly dynamic, with treadmilling and various myosin-based interactions. Myosin motors import various microvilli components along the actin filaments. (Figure 4–8b, with permission, from Dr John Heuser, Washington University School of Medicine, St. Louis, MO.)

Each microvillus is a cylindrical protrusion of the apical cytoplasm approximately 1 µm tall and 0.1 µm in diameter containing actin filaments and enclosed by the cell membrane.

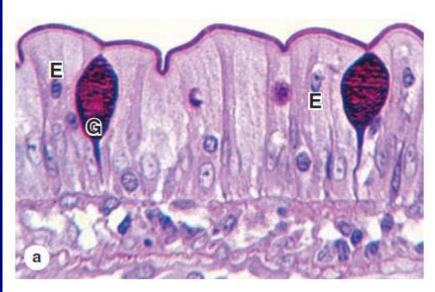


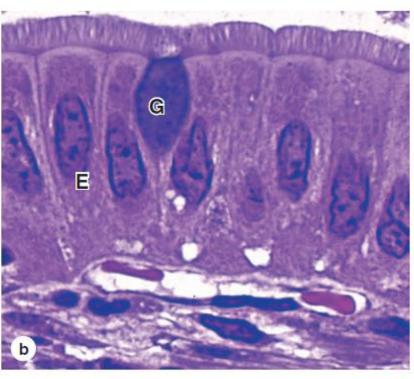
- Each enterocyte has an average of 3000 microvilli
- each 1 mm² of mucosal surface contains about 200 million of these structures.

(c) TEM shows microvilli and densely packed mitochondria of enterocytes (E), and enteroendocrine cells (EC) with basal secretory granules can be distinguished along the basal lamina. X2500.



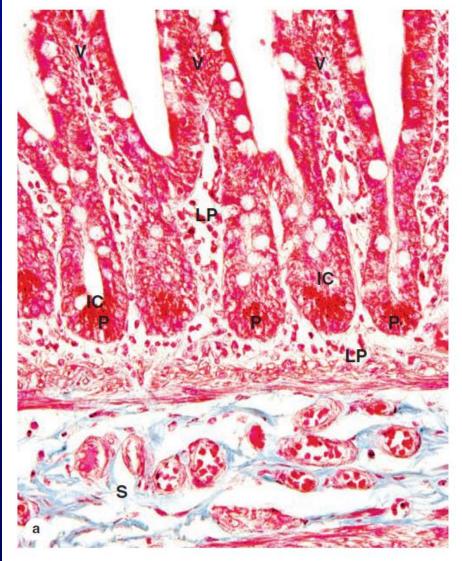
- Microvilli, villi, and the plicae circulares all greatly increase the mucosal surface area in contact with nutrients in the lumen, which is an important feature in an organ specialized for nutrient absorption.
- It is estimated that:
- plicae increase the intestinal surface area 3-fold,
- the villi increase it 10-fold, and
- the microvilli increase it another 20-fold,
 resulting in a total absorptive area of over 200 m² in the small intestine.

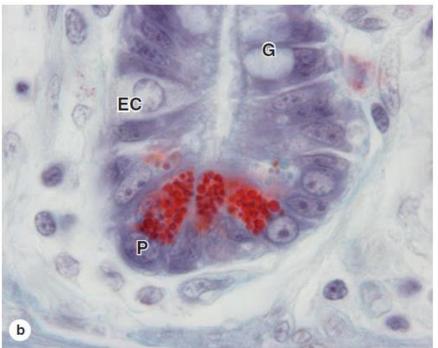




- Goblet cells are interspersed among the absorptive enterocytes.
- They secrete glycoprotein mucins that are then hydrated to form mucus, whose main function is to protect and lubricate the lining of the intestine.

(a) The columnar epithelium that covers intestinal villi consists mainly of the tall absorptive enterocytes (E). The apical ends of these cells are joined and covered by a brush border of microvilli. Covered by a coating of glycoproteins, the brush border, along with the mucus-secreting goblet cells (G), stains with carbohydrate staining methods. Other cells of the epithelium are scattered enteroendocrine cells, which are difficult to identify in routine preparations, and various immune cells such as intraepithelial lymphocytes. The small spherical nuclei of lymphocytes can be seen between the enterocytes. X250. PAS-hematoxylin. (b) At higher magnification individual microvilli of enterocytes are better seen and the striated appearance of the border is apparent. X500.





At the base of the crypts are many Paneth cells (P) with an innate immune function. The submucosa (S) has many lymphatics draining lacteals. X200. H&E.

(b) Higher magnification at the base of an intestinal gland shows the typical eosinophilic granules of Paneth cells (P), along with an open-type enteroendocrine cell (EC) and a differentiating goblet cell (G). X400. H&E.

Paneth cells, located in the basal portion of the intestinal crypts below the stem cells, are exocrine cells with large, eosinophilic secretory granules in their apical cytoplasm.



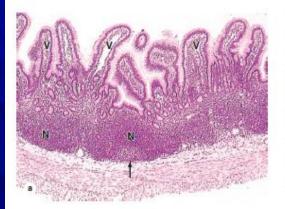
Paneth cells have an important role in innate immunity and in regulating the micro-environment of the intestinal crypts.

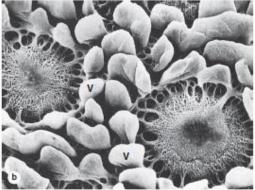
TABLE **15-1**

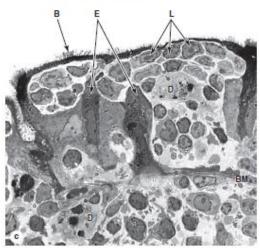
Principal enteroendocrine cells in the gastrointestinal tract.

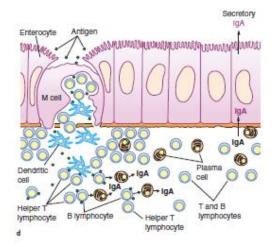
			Major Action	
Cell Type	Major Location	Hormone Produced	Promotes	Inhibits
D cells	Pylorus, duodenum, and pancreatic islets	Somatostatin		Secretion from other DNES cells nearby
EC cells	Stomach, small and large intestines	Serotonin and substance P	Increased gut motility	
G cells	Pylorus	Gastrin	Gastric acid secretion	
I cells	Small intestine	Cholecystokinin (CCK)	Pancreatic enzyme secretion, gallbladder contraction	Gastric acid secretion
K cells	Duodenum and jejunum	Gastric inhibitory polypeptide (GIP)		Gastric acid secretion
L cells	lleum and colon	Glucagon-like peptide (GLP-1)	Insulin secretion	Gastric acid secretion Sense of hunger
L cells	lleum and colon	Peptide YY	H ₂ O and electrolyte absorption in large intestine	Gastric acid secretion
Mo cells	Small intestine	Motilin	Increased gut motility	
N cells	lleum	Neurotensin		Gastric acid secretion
S cells	Small intestine	Secretin	Pancreatic and biliary bicarbonate and water secretion	Gastric acid secretion Stomach emptying

Enteroendocrine cells are present in varying numbers throughout the length of the small intestine, secreting various peptide hormones.









Peyer's patches are very large clusters of lymphoid follicles located in the wall of the ileum which allow close monitoring of microorganisms in the gut.

(a) A section through a Peyer patch shows a few lymphoid nodules (N), some with germinal centers (arrow). The mucosa of the small intestine is folded into many projecting villi (V). X100. H&E.

(b) With the surface epithelial cells removed, scanning electron microscopy (SEM) shows typical basement membrane over the villi (V) but reveals a highly porous covering over lymphoid nodules of the Peyer patch. This sieve-like basement membrane facilitates interactions between immune cells and M cells in the epithelium over the nodules.

(With permission, from Dr Samuel G. McClugage, Department of Cell Biology and Anatomy, Louisiana State University Health Sciences Center, New Orleans, LA.)

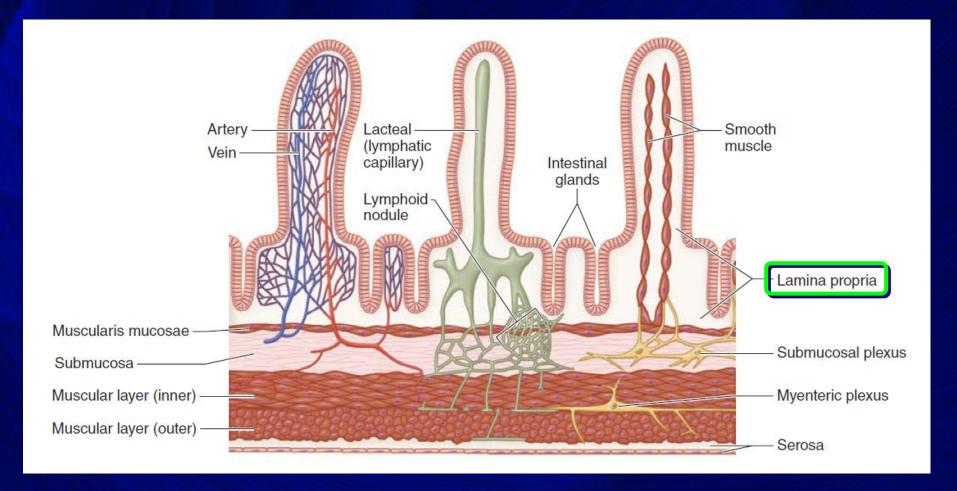
(c) The TEM shows that the epithelium directly over a Peyer patch lymphoid nodule has unique cells called M (microfold) cells with short apical folds but no brush border. The basal surface of M cells forms a large intracellular pocket that harbors a transient population of T and B lymphocytes (L) and dendritic cells (D) which move through the openings in the basement membrane (BM). Darker cytoplasm of adjacent entercytes (E) with brush borders (B) is also seen. X1000.

(With permission, from Dr Marian R. Neutra, Children's Hospital, Harvard Medical School, Boston, MA.)

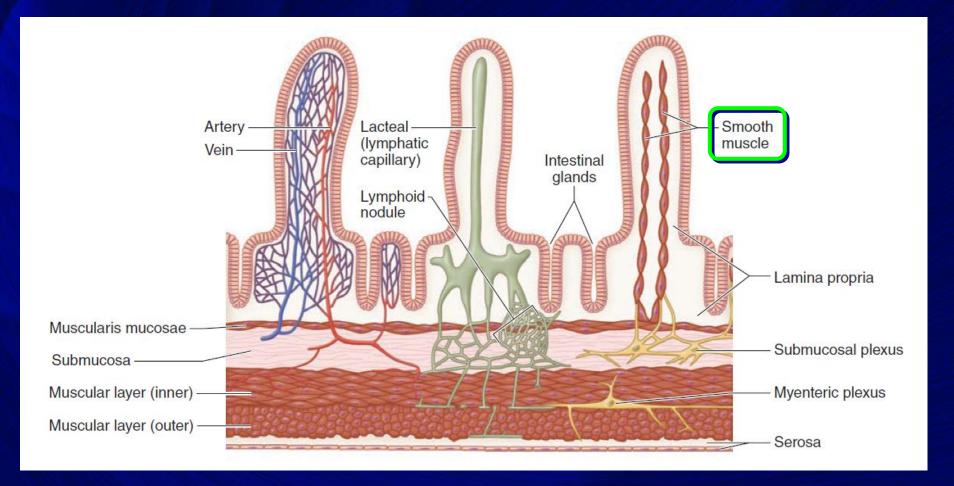
(d) A summary diagram showing that antigens in the gut lumen are bound by M cells and undergo transcytosis into their intraepithelial pockets where dendritic cells take up the antigen, process it, and present it to T helper cells. B lymphocytes stimulated by the Th cells differentiate into plasma cells secreting (gA antibodies. The IgA is transported into the gut lumen where it binds its antigen on the surface of microorganisms, neutralizing potentially harmful invaders before they penetrate the mucosa.

- M (microfold) cells are specialized epithelial cells in the mucosa of the ileum overlying the lymphoid follicles of Peyer patches.
- These cells are characterized by the presence of basal membrane invaginations or pockets containing many intraepithelial lymphocytes and antigen-presenting cells.

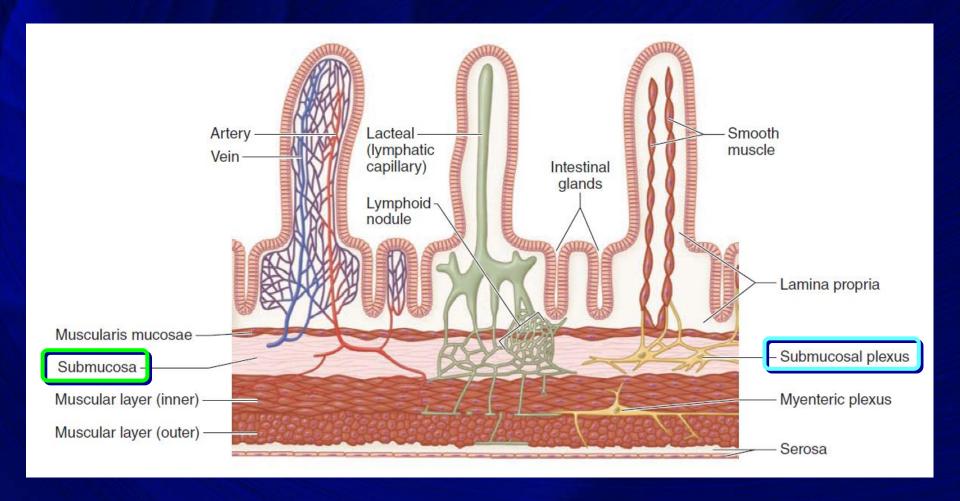
Other Layers



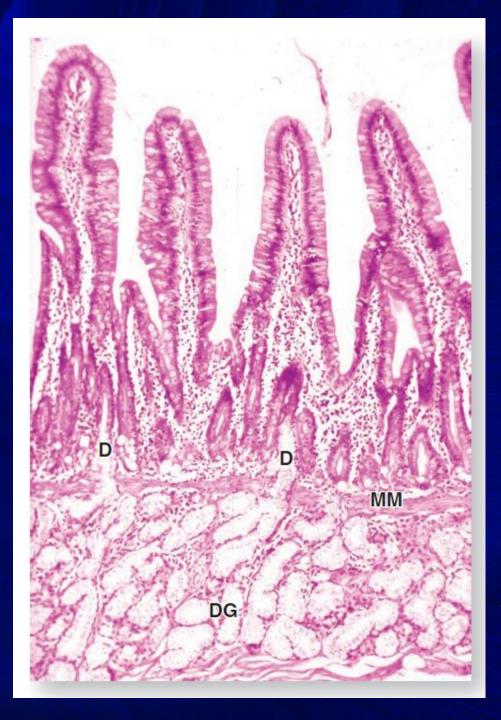
- Along the entire small intestine loose connective tissue of the mucosal lamina propria contains extensive blood and lymph microvasculature, nerve fibers, smooth muscle cells, and diffuse lymphoid tissue.
- The lamina propria penetrates the core of each intestinal villus, bringing with it microvasculature, lymphatics, and nerves.



- Smooth muscle fibers extending from the muscularis mucosae produce rhythmic movements of the villi that increase the absorption efficiency.
- muscularis mucosae also produce local movements of plicae
 circulares (→) that help propel lymph from the lacteals into submucosal
 and mesenteric lymphatics.

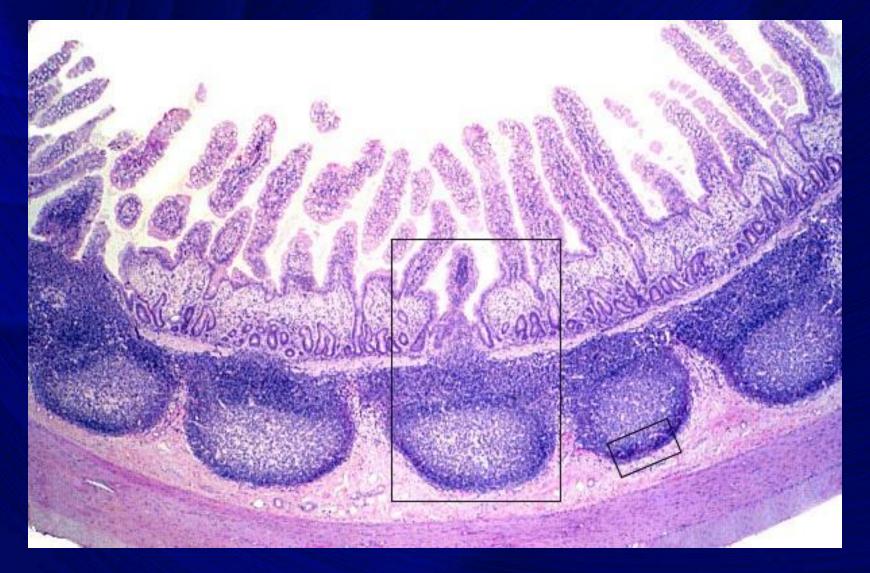


- The submucosa has:
- ✓ larger blood and lymph vessels and
- the diffuse, interconnected neurons of the submucosal (Meissner) nerve plexus.

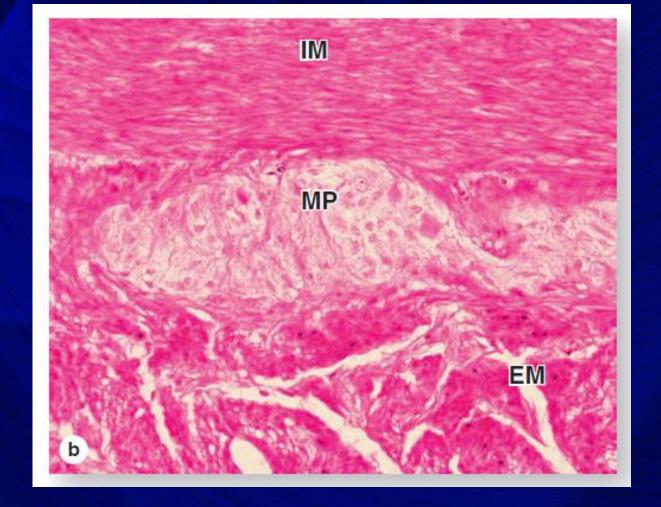


The proximal part of the duodenum has in the submucosa and mucosa large clusters of branched tubular mucous glands, the duodenal (or Brunner) glands (DG), with small excretory ducts opening among the intestinal crypts.

Concentrated in the upper duodenum are large masses of compound branched mucous glands, the duodenal glands (DG), with many lobules that occupy much of the submucosa and may extend above the muscularis mucosae (MM) into the mucosa. Many small excretory ducts (D) extend from these lobules through the lamina propria and empty into the lumen among the small intestinal crypts. Alkaline mucus from duodenal glands neutralizes the pH of material entering the duodenum and supplements the mucus from goblet cells in lubricating and protecting the lining of the small intestine. X100. H&E.

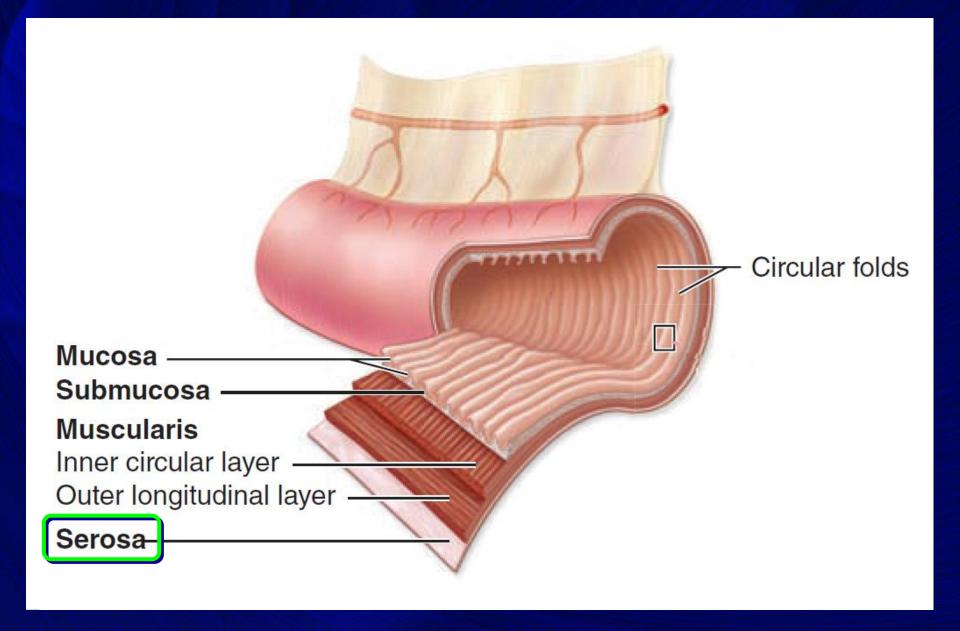


 In the ileum both the lamina propria and submucosa contain well-developed mucosa-associated lymphoid tissue (MALT), consisting of the large lymphoid nodule aggregates known as Peyer patches underlying the epithelial M cells.



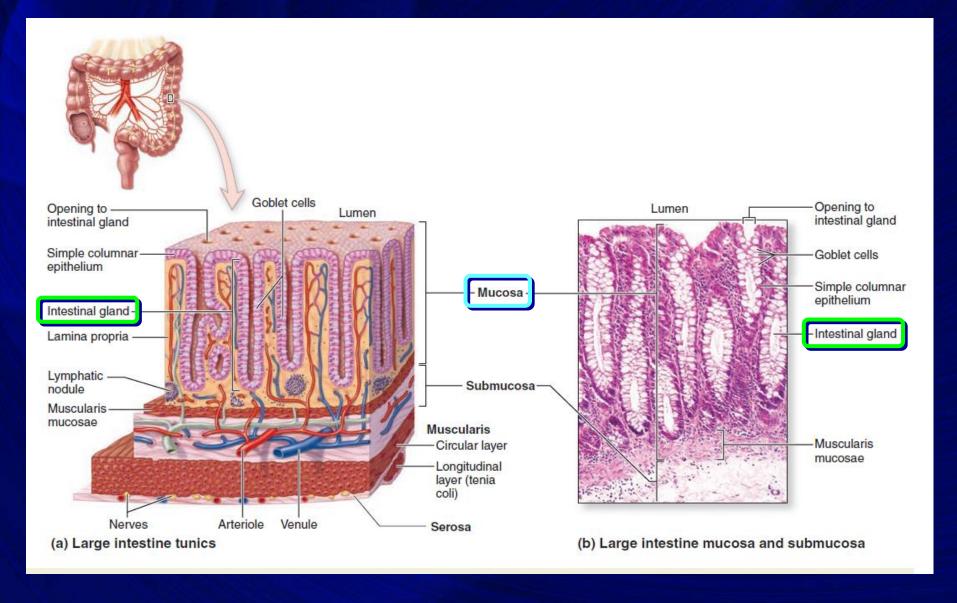
(b) Between the internal and external layers of muscularis (IM and EM) are ganglia of palestaining neurons and other cells of the myenteric plexus (MP).
X100. H&E.

- The muscularis is well developed in the small intestine, composed of:
- an internal circular layer
- an external longitudinal layer
- between them the neurons of the myenteric (Auerbach) nerve plexus (MP) which produce peristalsis.

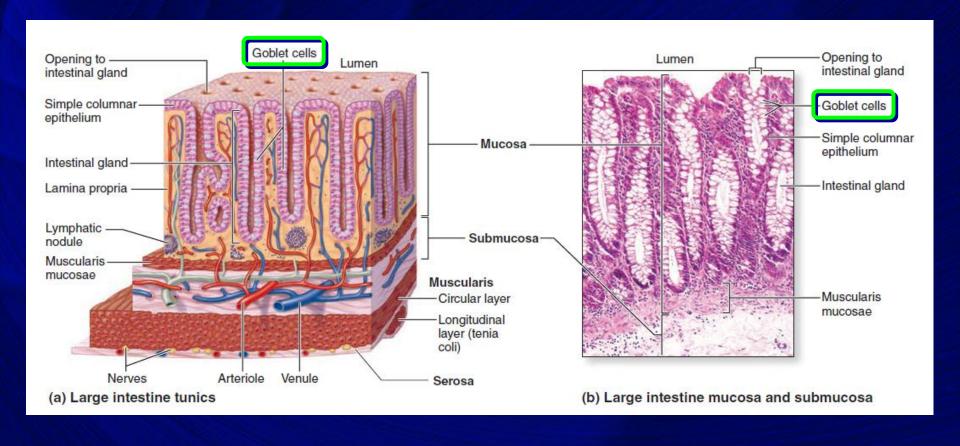


 The small intestine is covered by a thin serosa with mesothelium continuous with that of mesenteries.

Large Intestine

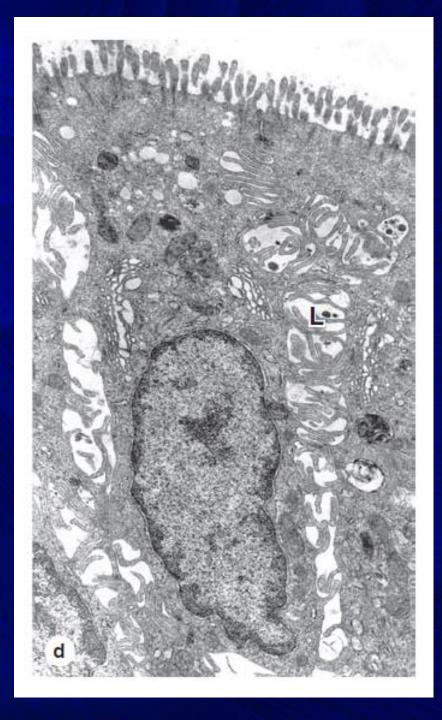


 The mucosa of the large bowel is penetrated throughout its length by tubular intestinal glands.



The intestinal glands and the intestinal lumen are lined by:

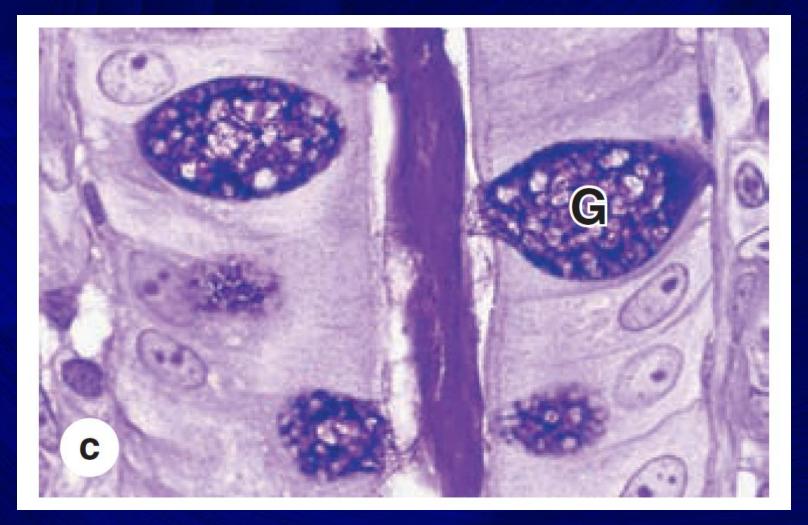
- ✓ goblet
- ✓ absorptive cells (colonocytes).
- ✓ with a small number of enteroendocrine cells.



The columnar absorptive cells or colonocytes have:

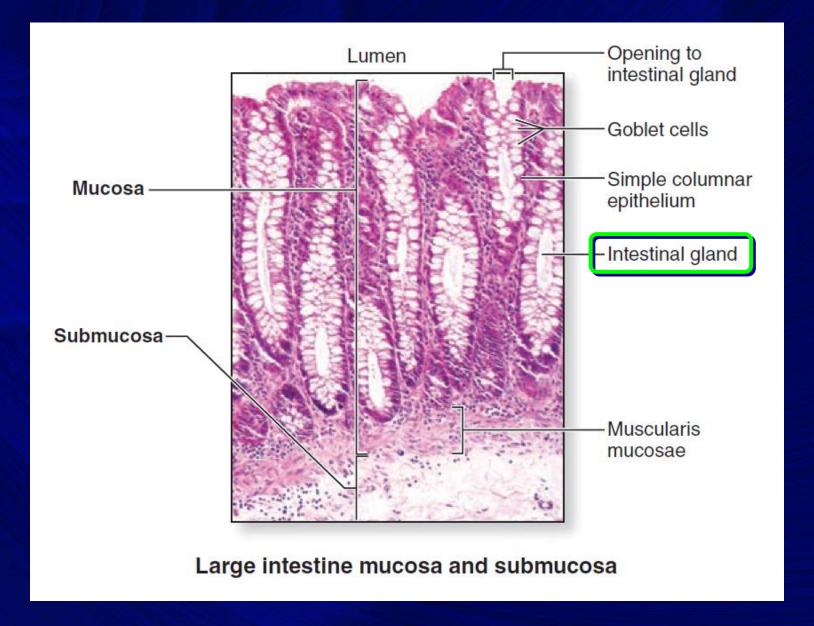
- ✓ irregular microvilli
- dilated intercellular spaces indicating active fluid absorption.

(d) TEM of the absorptive cells, or colonocytes, reveals short microvilli at their apical ends and dilated intercellular spaces with interdigitating leaflets of cell membrane (L), a sign of active water transport. The absorption of water is passive, following the active transport of sodium from the basolateral surfaces of the epithelial cells. X2500.

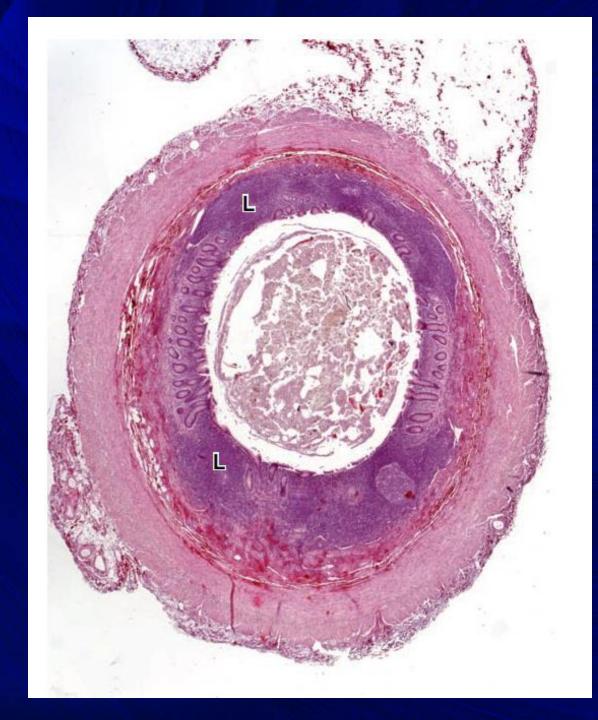


(c) Longitudinal section of one intestinal gland stained for glycoproteins shows mucus in the lumen and two major cell types in the epithelium: goblet cells (G) and the neighboring columnar cells specialized for water absorption. X400. PAS.

 Goblet cells producing lubricating mucus become more numerous along the length of the colon and in the rectum.

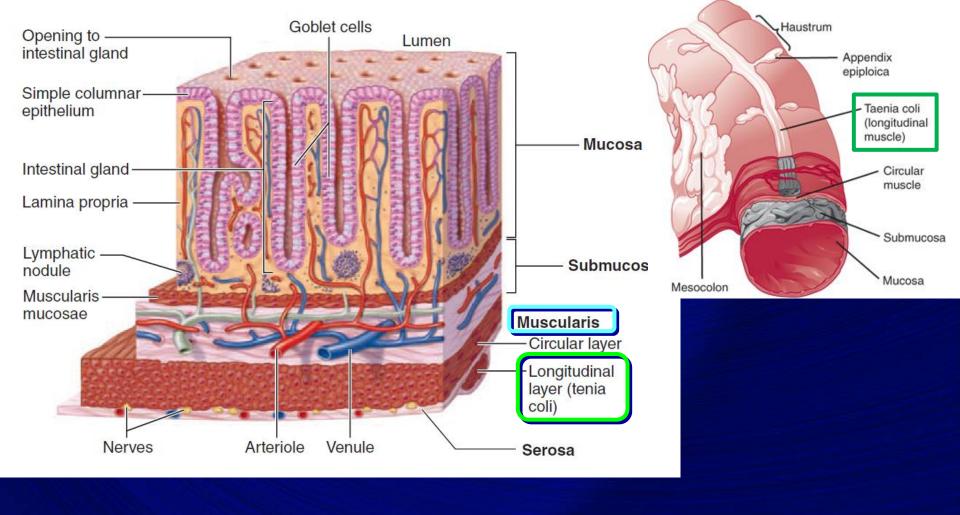


• Epithelial stem cells are located in the bottom third of each gland.

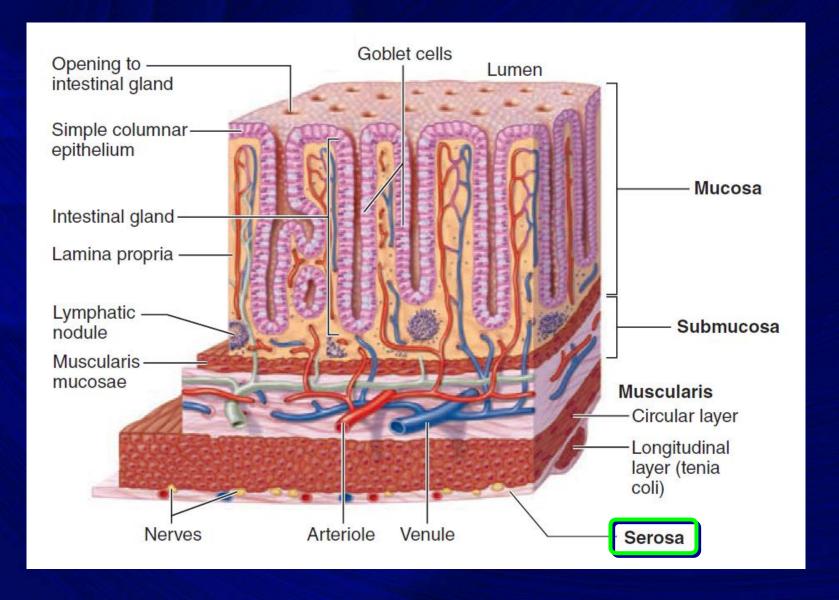


The appendix has little or no absorptive function but is a significant component of mucosa-associated lymphoid tissue (MALT).

A blind evagination off the cecum, the appendix is a significant part of the MALT with its lamina propria and submucosa filled with lymphocytes and lymphoid follicles (L). The small lumen contains a sample of the microbial flora of the intestine, along with undigested material. X20. H&E.

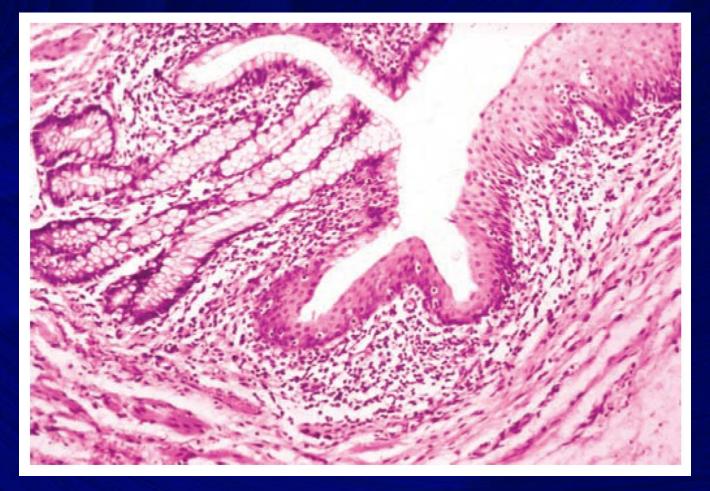


- The muscularis of the colon has longitudinal and circular layers but differs from that of the small intestine,
- with fibers of the outer layer gathered in three separate longitudinal bands called teniae coli.



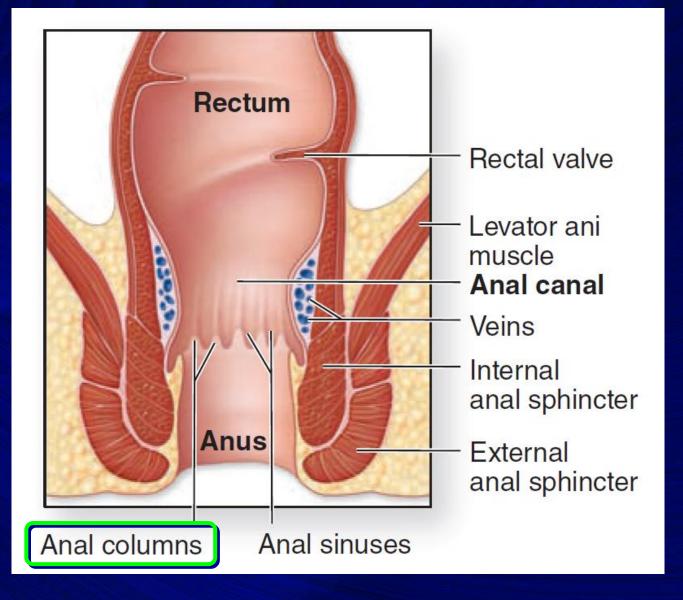
 Intraperitoneal portions of the colon are covered by serosa, which is characterized by small, pendulous protuberances of adipose tissue.

Anal Canal

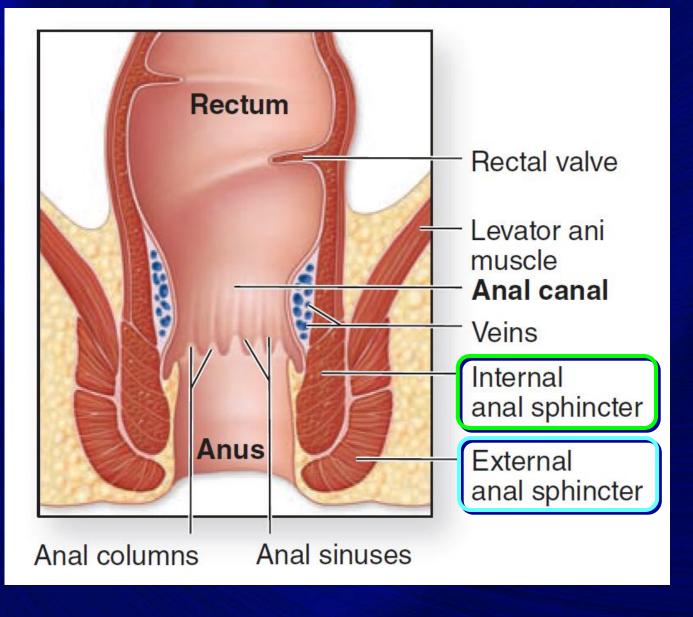


The simple columnar epithelium with tubular intestinal glands in the rectum (left side of photo) changes abruptly to stratified squamous epithelium in the anal canal (right side of photo), as seen in this longitudinal section. The connective tissue of the lamina propria is seen to contain many free lymphocytes. X40. H&E.

- The distal end of the GI tract is the anal canal, 3-4 cm long.
- At the rectoanal junction the simple columnar mucosal lining of the rectum is replaced by stratified squamous epithelium.



 The mucosa and submucosa of the anal canal form several longitudinal folds, the anal columns, in which the lamina propria and submucosa include sinuses of the rectal venous plexus.



Near the anus the circular layer of the rectum's muscularis forms the internal anal sphincter.

Defecation involves the action of voluntary muscle comprising the external anal sphincter.

Good Luck