MD Program
UNIVERSITY OF TORONTO

Histology

The Small and Large Intestine

eMODULE TUTORIAL

CLICK TO BEGIN

H14 The Histology of the Small and Large Intestine

All images are from Junqueira's Basic Histology, 14th ed., © 2016 by Mescher, denoted by "J", a recommended resource, unless otherwise noted.

Recommended online resources:

Western University Virtual Slide Box

University of Michigan Virtual Microscopy

University of Minnesota Histology Guide

University of Leeds Histology Guide

University of Illinois Cell and Tissue Biology

When you have learned the material presented here, you will be able to:

- describe the basic structural organization of the walls of the gastrointestinal tract.
  This overview is repeated from H13, in order to remind you of the basic pattern of the digestive tract, on which the histology of each organ is based.
- describe the histological features that distinguish the duodenum, jejunum, ileum and large intestine.
- describe the structure of intestinal villi and the crypts of Lieberkuhn.
- describe the functional significance of the cells that make up the epithelium lining the small and large intestines.

The **digestive system** can be subdivided into the **digestive tract** and **accessory organs**.

The **digestive tract** consist of:

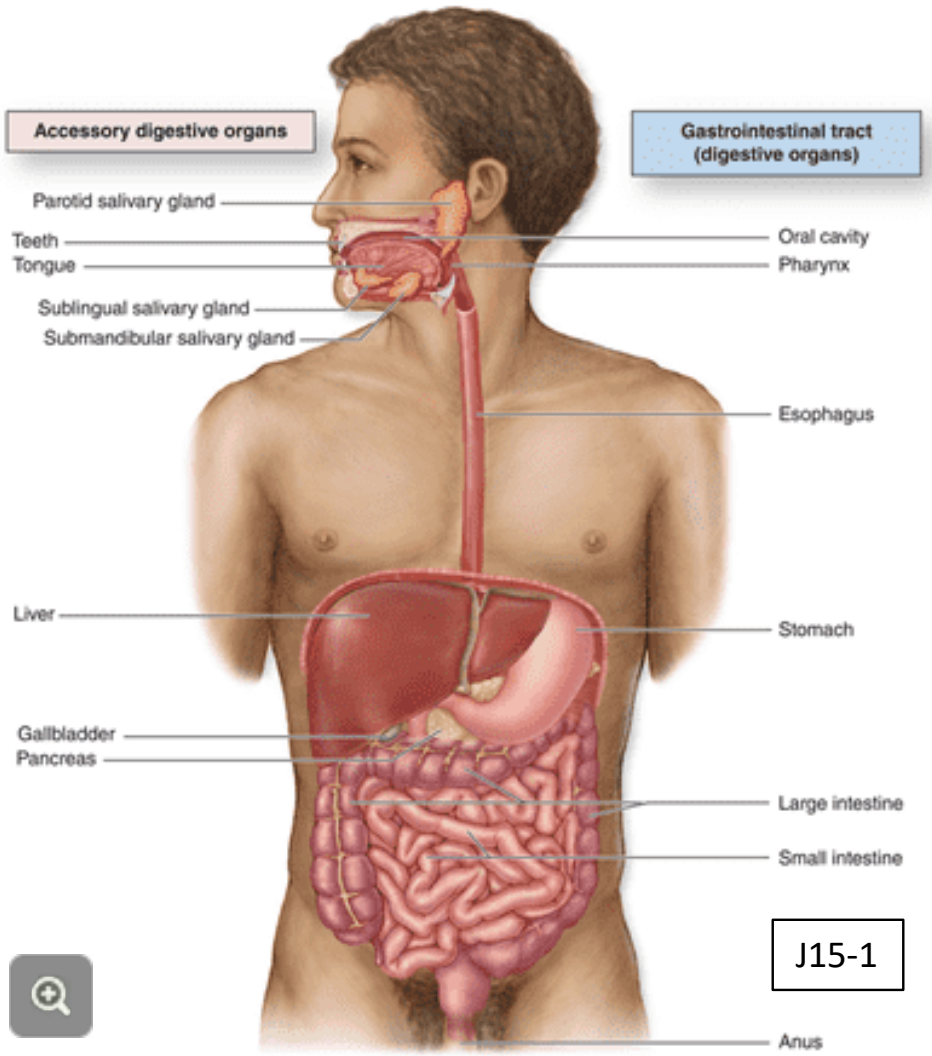
- the oral cavity
- pharynx
- esophagus
- stomach
- small intestine
- large intestine

H13 & H14 will discuss the esophagus, stomach, small and large intestine.

The **accessory digestive organs** are the:

- salivary glands, teeth and tongue
- liver
- gall bladder
- pancreas

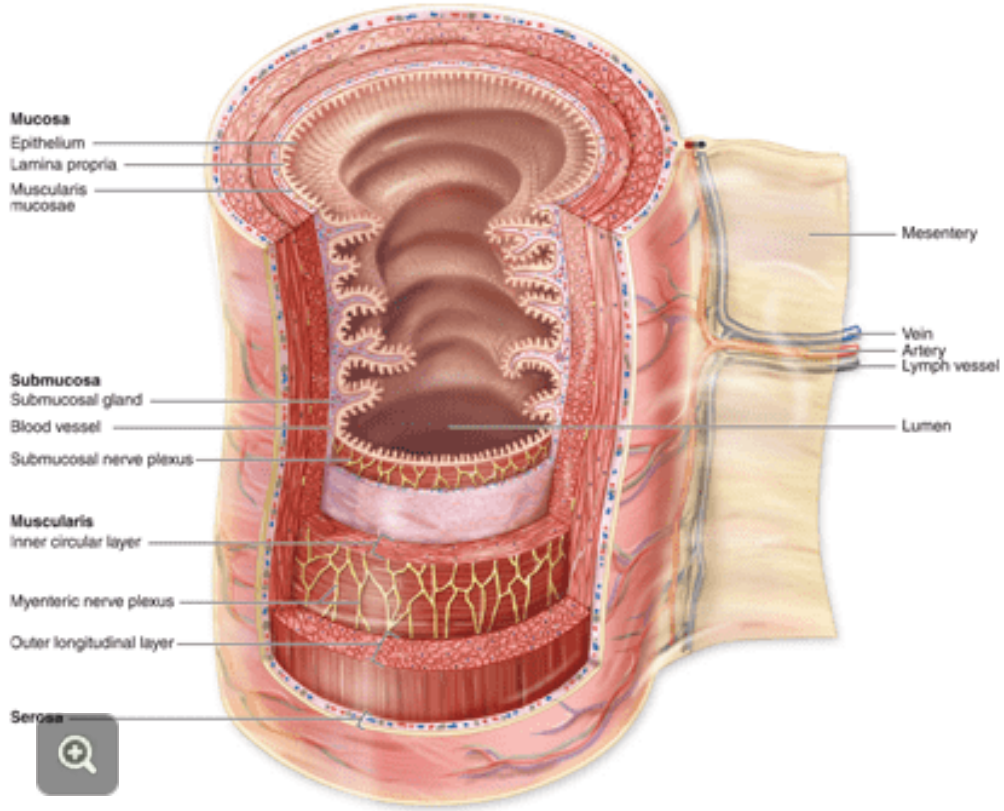
H15 will discuss the **liver, gall bladder and pancreas**.



The basic histological structure of the esophagus, stomach, small and large intestine is the same.

Each consists of **four layers**. From the lumen outward, these are the:

1. **mucosa** or mucous membrane
2. **submucosa**
3. **muscularis externa**
4. **serosa** OR **adventitia**



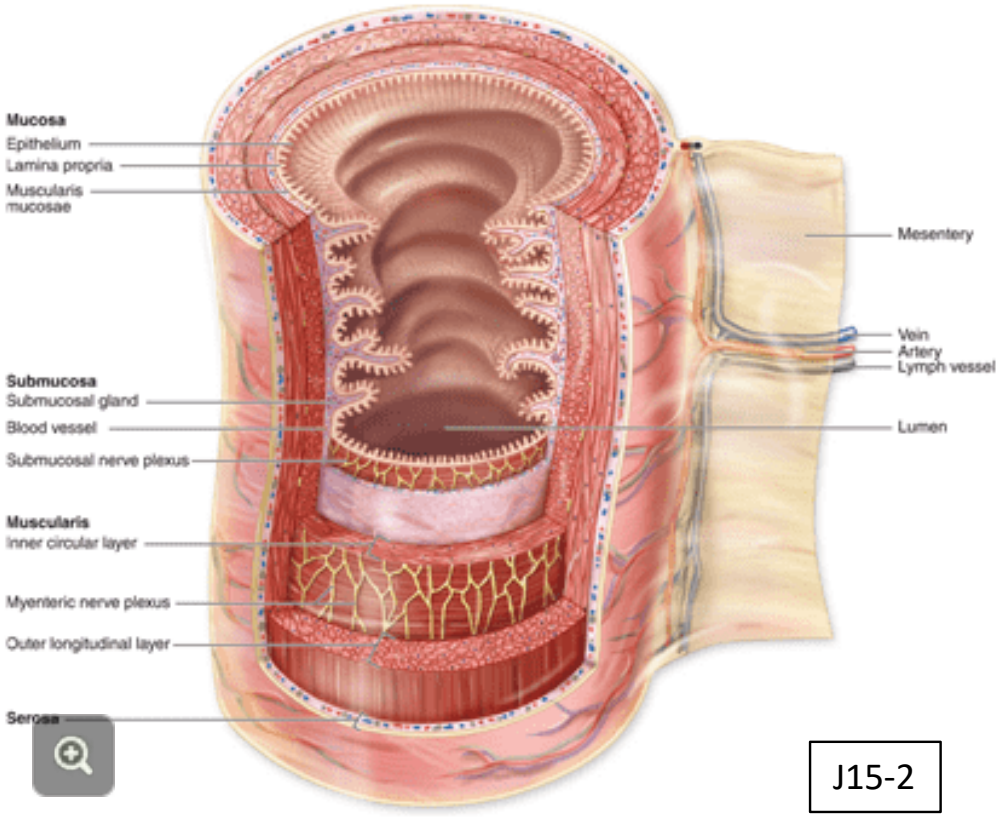
Mucosa

Remember: **mucous membranes line internal surfaces that open to the outside of the body**.
A mucous membrane consists of an **epithelium** and its underlying CT layer, the **lamina propria (LP)**.

The epithelial component of mucous membranes varies along the length of the digestive tract. It may be **simple or stratified**, it may be **squamous, cuboidal or columnar**. It often forms glands. Whatever its structure, **it is suited to the function of its location.**

The LP is loose CT; it contains blood vessels (BVs), nerves (Ns) and lymphatics (Ls). Because its overlying epithelium is the only thing separating it from the lumen, and therefore the harsh outside world (and its pathogens), the LP is **often heavily infiltrated with lymphocytes and plasma cells**.

The **muscularis mucosa** is composed of two thin layers of smooth muscle, inner circular and outer longitudinal.



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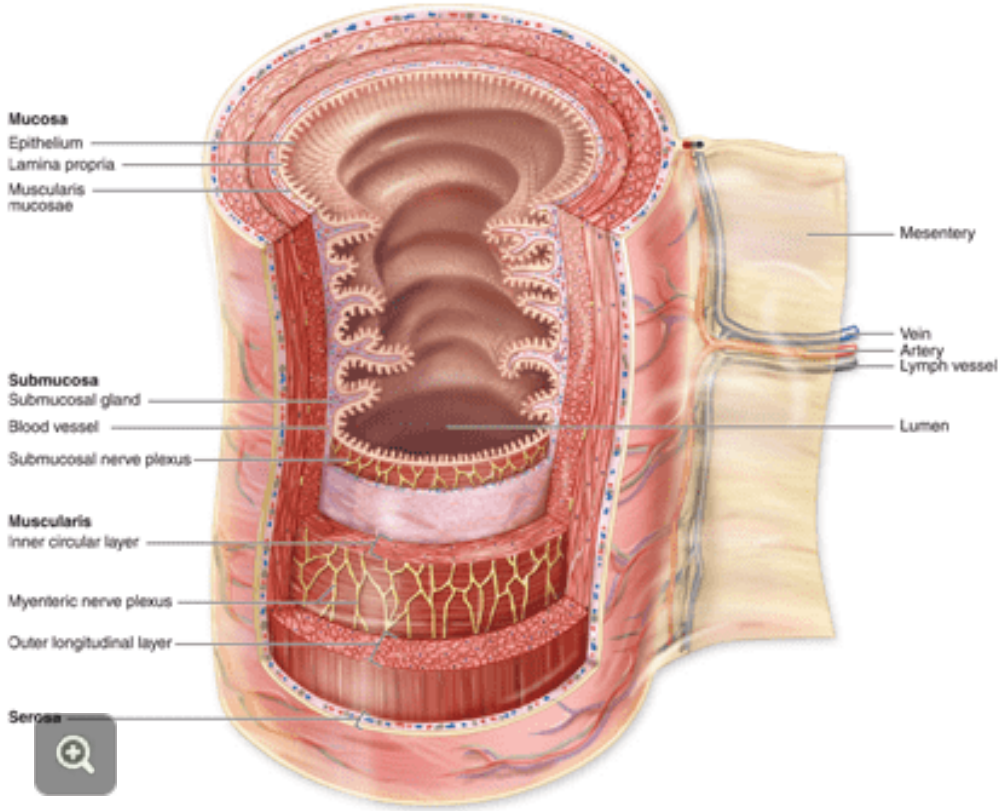
Submucosa

The submucosa is loose CT containing **blood and lymphatic vessels**. These are the parent vessels of those in the LP of the mucosa.

The submucosa also contains a **submucosal (Meissner's) nerve plexus** consisting of parasympathetic (PSy) neuronal cell bodies and sympathetic (Sy) postganglionic fibres. These fibres control the secretion of the mucosal and (if present) submucosal glands, as well as the motility of the mucosa via the muscularis mucosa.

In the **esophagus and duodenum only**, submucosal, mucous-secreting glands are present.



Muscularis Externa

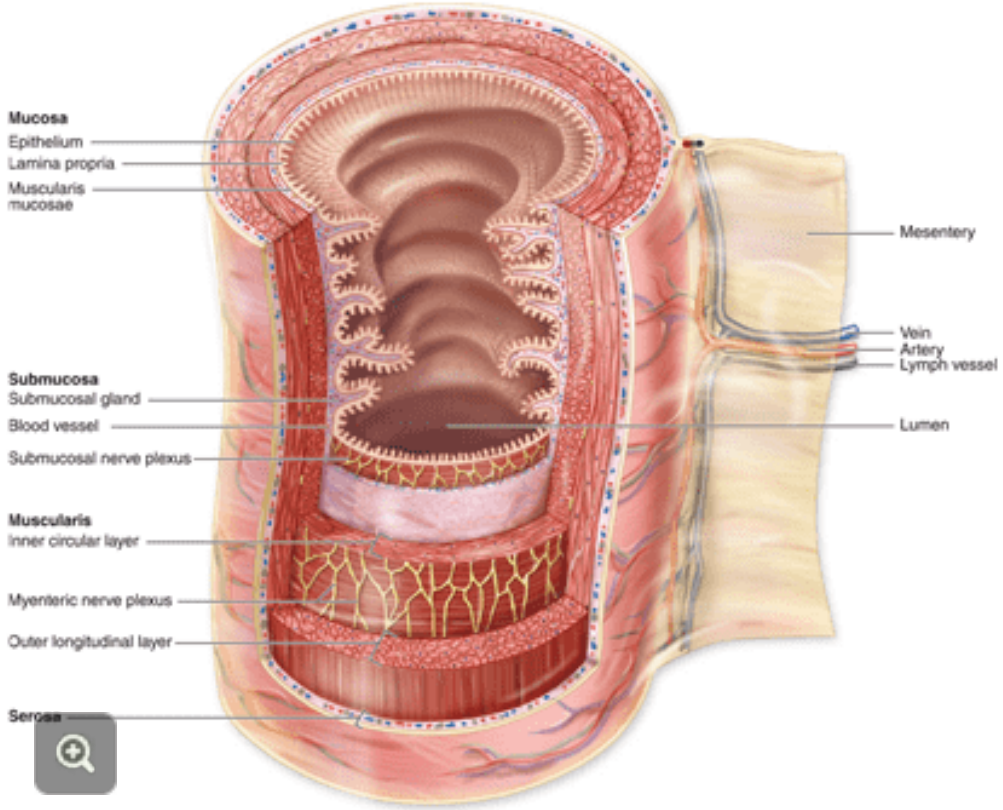
The muscularis externa usually consists of **two layers of smooth muscle**. They are thick, as compared to the muscularis mucosa. Like the muscularis mucosa, **the inner layer is arranged circularly, the outer layer longitudinally**. Their coordinated contraction causes **segmentation** and **peristalsis**.

Segmentation kneads the luminal contents, mixing it with glandular secretions from the gut wall.

Peristalsis has directionality; these wave-like contractions propel the luminal contents along the length of the gut tube.

Between the muscle layers is the **myenteric (Auerbach's) nerve plexus**, which, like the submucosal plexus, contains PSy neuronal cell bodies and Sy postganglionic fibres. It controls the motility of the gut wall, as described above.

BVs and Ls are also present between these layers of muscle.



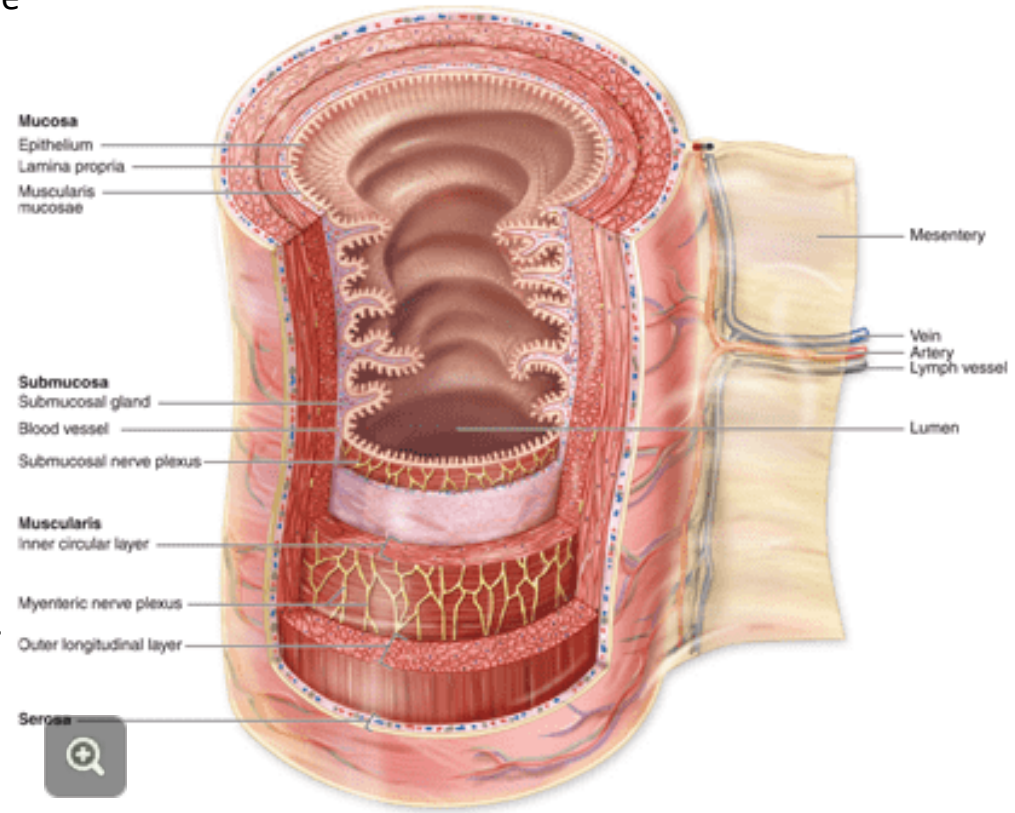
Serosa or Adventitia

Serous membranes line body cavities; i.e. they line internal surfaces that DO NOT open to the outside of the body. They consist of loose CT and adipose, with BVs, Ns and Ls, covered by **mesothelium**. Serous membranes in the peritoneal cavity are called **peritoneum**. On the surface of an abdominal organ is **visceral peritoneum**. Lining the wall of the peritoneal cavity is **parietal peritoneum**.

Thus, digestive organs facing the peritoneal cavity are covered by **serosa.**

A **mesentery** consists of **loose CT, adipose, BVs, Ns & Ls sandwiched between two layers of serous membrane**. They attach intraperitoneal organs to the body wall.

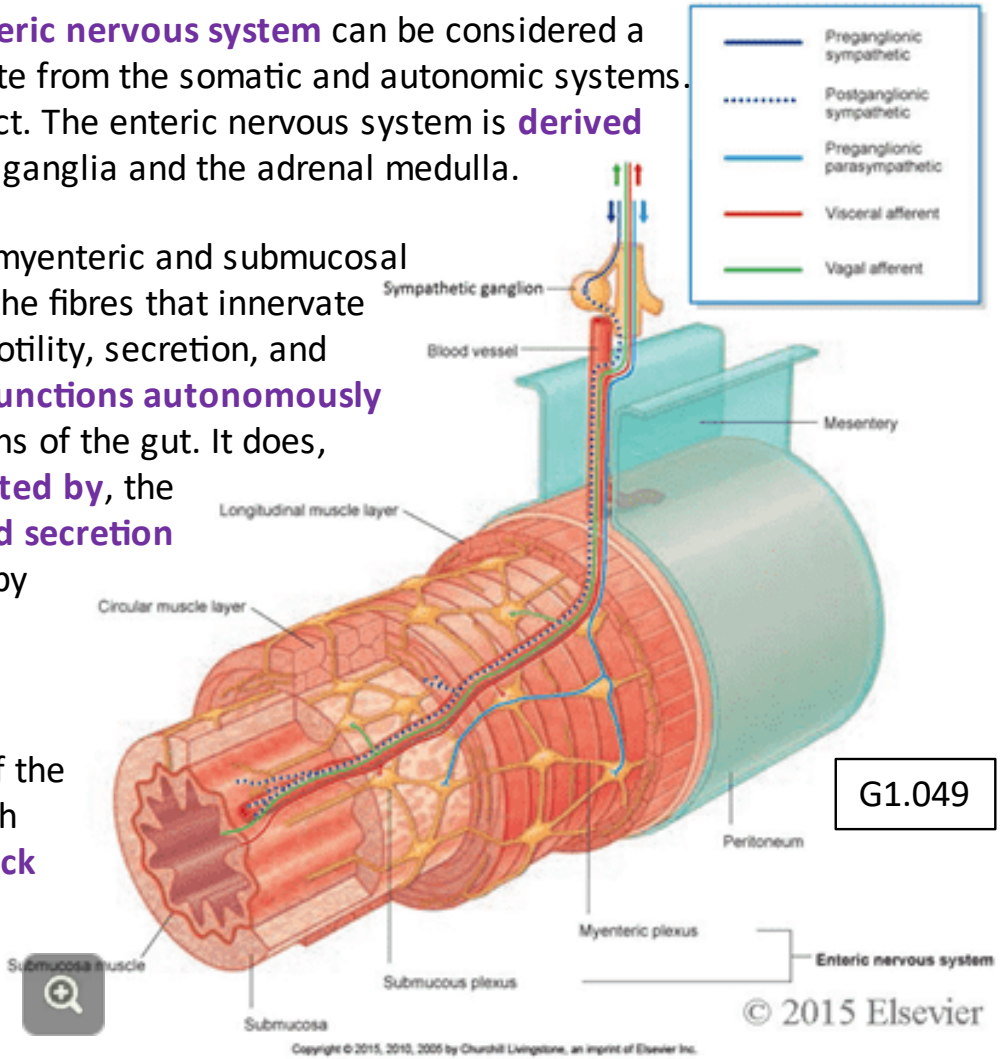
Portions of the digestive tract that do not face the peritoneal cavity are covered by an **adventitia**, a layer of loose CT that connects the organ to adjacent structures. An example is the esophagus in the posterior mediastinum, or the anal canal in the perineum.



Because it functions autonomously, the **enteric nervous system** can be considered a third division of the nervous system, separate from the somatic and autonomic systems. It is located in the walls of the digestive tract. The enteric nervous system is **derived from neural crest cells**, as are sympathetic ganglia and the adrenal medulla.

The enteric nervous system consists of the myenteric and submucosal plexuses, the fibres that connect them and the fibres that innervate the tissues of the gut wall. It controls gut motility, secretion, and vascular tone. The enteric nervous system **functions autonomously** to control activity within and between regions of the gut. It does, however, receive input from, and is **modulated by**, the autonomic nervous system. Gut **motility and secretion** are increased and decreased, respectively, by parasympathetic and sympathetic input.

Sensory information from the gut wall feeds back to the CNS. Along most of the length of the gut, **visceral pain** is conducted centrally with sympathetic efferents. **Homeostatic feedback** travels with parasympathetic efferents.



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The Histology of the Small Intestine

The small intestine is the site of **terminal food digestion** and **nutrient absorption**. By means of its **endocrine products**, it controls the function of other portions of the digestive tract and, indeed, accessory digestive organs such as the pancreas and gall bladder. The small intestine is 5 m in length and from proximal to distal, it is divided into the **duodenum, jejunum and ileum**.

The **serosa and muscularis** of the small intestine is typical, as described.

The **submucosa and mucosa** are folded **transversely** to form **plicae circulares**. These permanent features **increase luminal surface area for nutrient absorption by 3-fold**. They are best developed in the **jejunum**, where **the majority of nutrient absorption takes place**. In the **duodenum**, the submucosa contains numerous **mucous-secreting duodenal (Brunner's) glands**. The alkaline mucous buffers the chyme arriving from the stomach, which 1) protects the duodenal mucosa from corrosion and 2) brings the pH of the chyme up to a level at which pancreatic enzymes can function. In the **ileum**, the submucosa contains **mucosa-associated lymphoid tissue (MALT),** called **Peyer's patches**. These accumulations of lymphocytes in the ileum protect against systemic infection by the bacterial flora of the large intestine.

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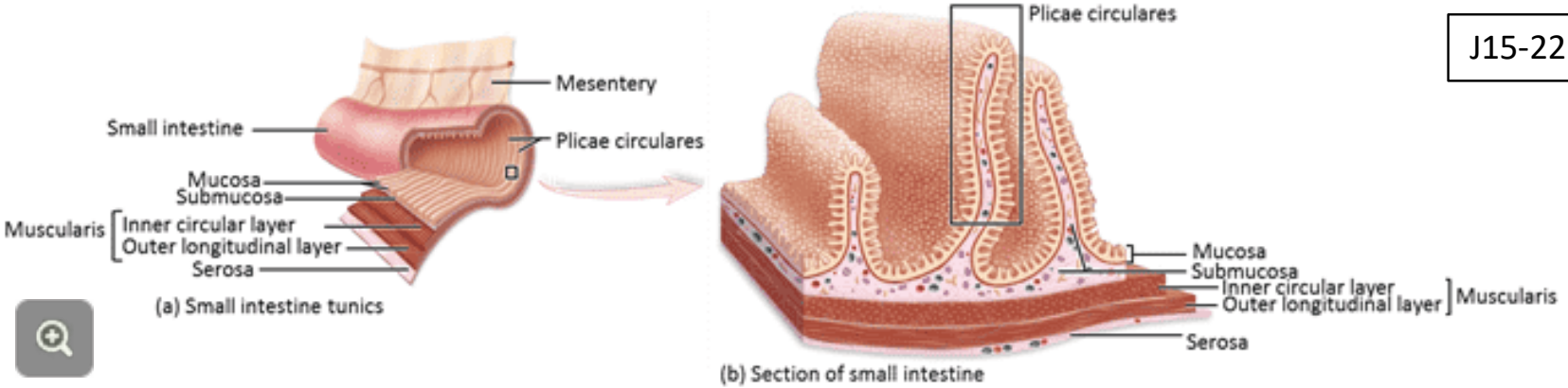

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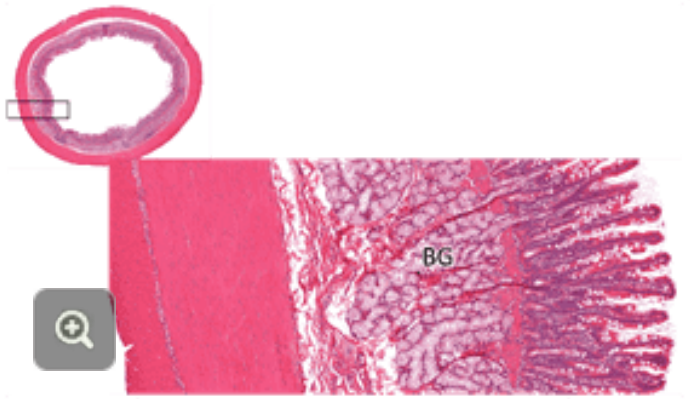

This histological section of the duodenum illustrates **duodenal (Brunner's) glands (BG)** within the submucosa.

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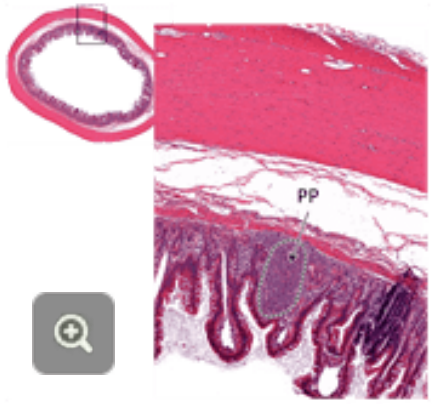


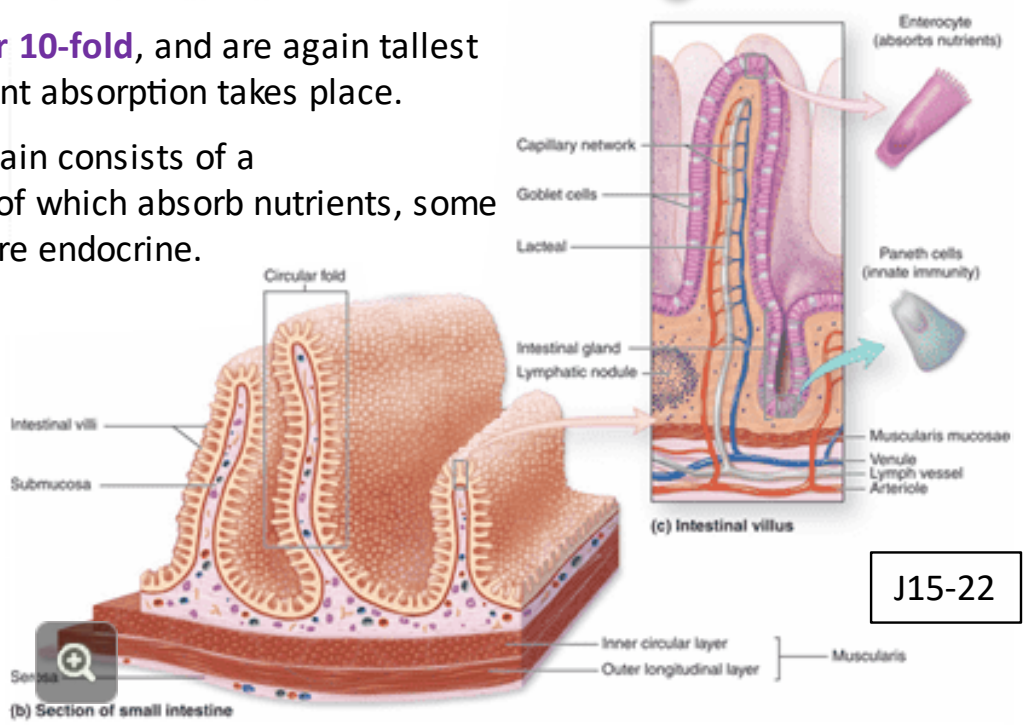
This histological section of the ileum illustrates **Peyer's patches** within the submucosa.

The **mucosa** of the small intestine forms **villi**, 0.5-1.5 mm tall finger-like projections into the intestinal lumen consisting of a **core of LP covered by a simple columnar epithelium**. At the base of the villi, the epithelium invaginates forming **intestinal glands** (crypts of Lieberkuhn).

The LP, including the core of the villus, contains fibroblasts, lymphocytes, plasma cells and bands of smooth muscle cells. Extending into the core of the villus are **fenestrated capillary plexuses** and blind-ended lymphatic capillaries called **lacteals**. In the lamina propria, and extending into the underlying submucosa are MALT, called Peyer's patches, which are most prominent in the ileum.

Villi increase luminal surface area another 10-fold, and are again tallest in the jejunum, where the majority of nutrient absorption takes place.

The epithelium lining the small intestine again consists of a **heterogeneous population of cells**, some of which absorb nutrients, some of which are exocrine, and some of which are endocrine.



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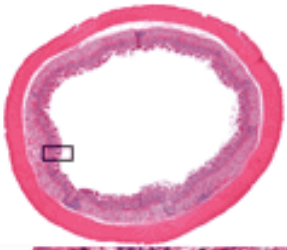
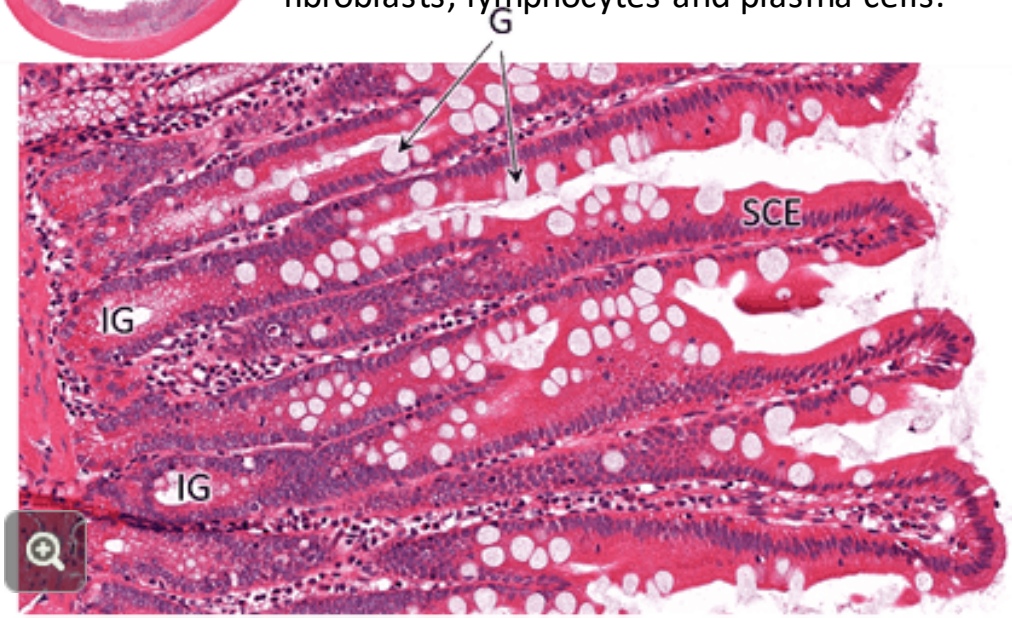
This histological image of the duodenum has been zoomed in on the mucosal layer.

Villi are composed of **simple columnar epithelium (SCE)** with **goblet cells (G)** interspersed, overlying a CT core.

The epithelial cells lining the small intestine are referred to as **enterocytes.** On the apical surface of enterocytes are densely packed **microvilli**, also referred to as a **"brush border"**. Microvilli further increase the absorptive surface area.

The CT core contains blood and lymphatic capillaries (lacteals) and numerous fibroblasts, lymphocytes and plasma cells.





At the bases of the villi, the epithelium forms **intestinal glands (IG)**, also referred to as **Crypts of Lieberkuhn** or **intestinal crypts**.

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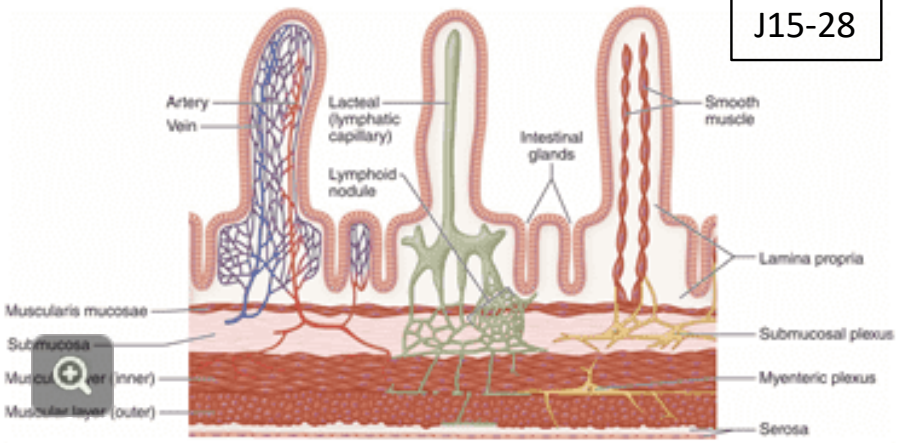
Microvasculature, Lymphatics and Muscle in Villi

J15-28



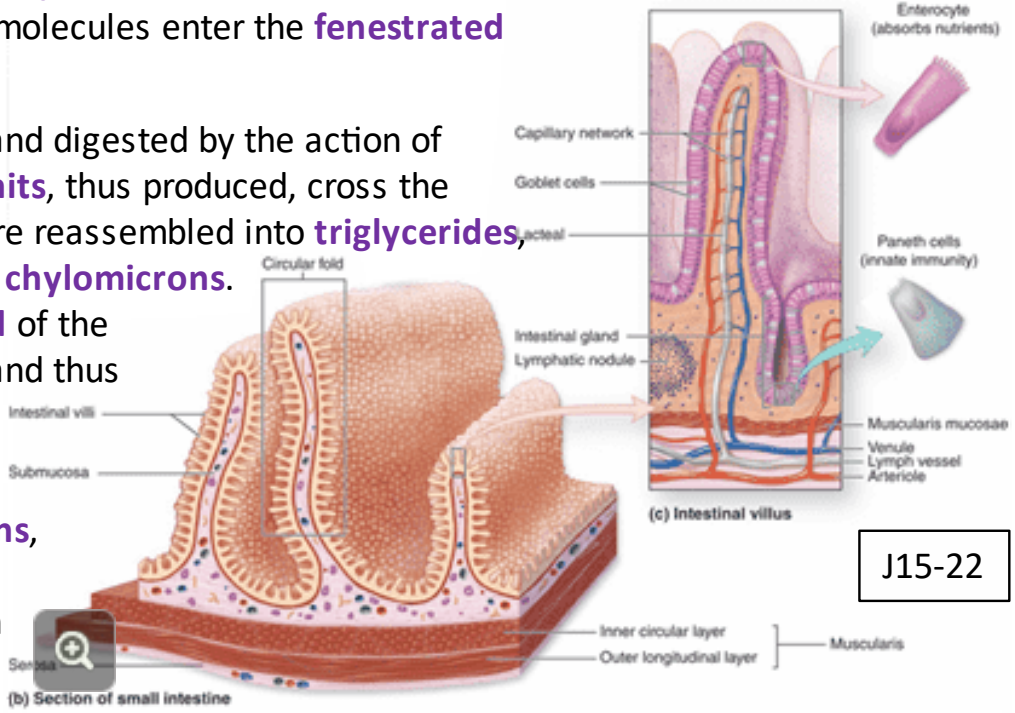
The simple columnar epithelium of the villus consists of **enterocytes** and **goblet** cells.

Enterocytes (surface absorptive cells) have the most well-developed **microvilli** in the body. Each enterocyte has ~3000 densely-packed microvilli. These ~1 µm tall, finger-like extensions from the apical surface of the cell increase luminal surface area by another 20-fold. Because microvilli are at the limits of resolution with the light microscope, they appear as a fuzzy apical cell surface, termed a **"brush border"**.

The **glycocalyx** covering the microvilli includes **enzymes** that aid in the **terminal digestion of dipeptides and disaccharides**, and the subsequent **absorption of amino acids and monosaccharides**. Once in the interstitial fluid of the underlying LP, these molecules enter the **fenestrated capillaries** of the villus.

Ingested **fats are emulsified by bile salts**, and digested by the action of **pancreatic and gastric lipases**. **Lipid subunits**, thus produced, cross the apical surface of enterocytes, where they are reassembled into **triglycerides**, and complexed with **proteins**, thus forming **chylomicrons**. These are secreted into the **interstitial fluid** of the sub-adjacent LP. **Most enter the lacteals**, and thus leave digestive surfaces via lymph.

Goblet cells are interspersed amongst the enterocytes on the villi. They produce **mucins**, which combine with water to form **mucous**. It forms a protective and lubricating coat on the luminal surface of the small intestine.



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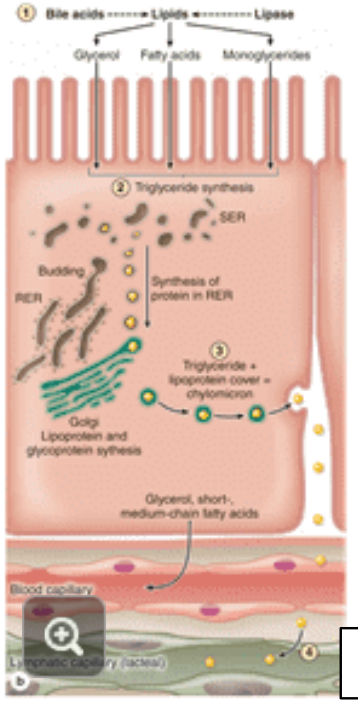


The Digestion and Absorption of Lipids

J15-25

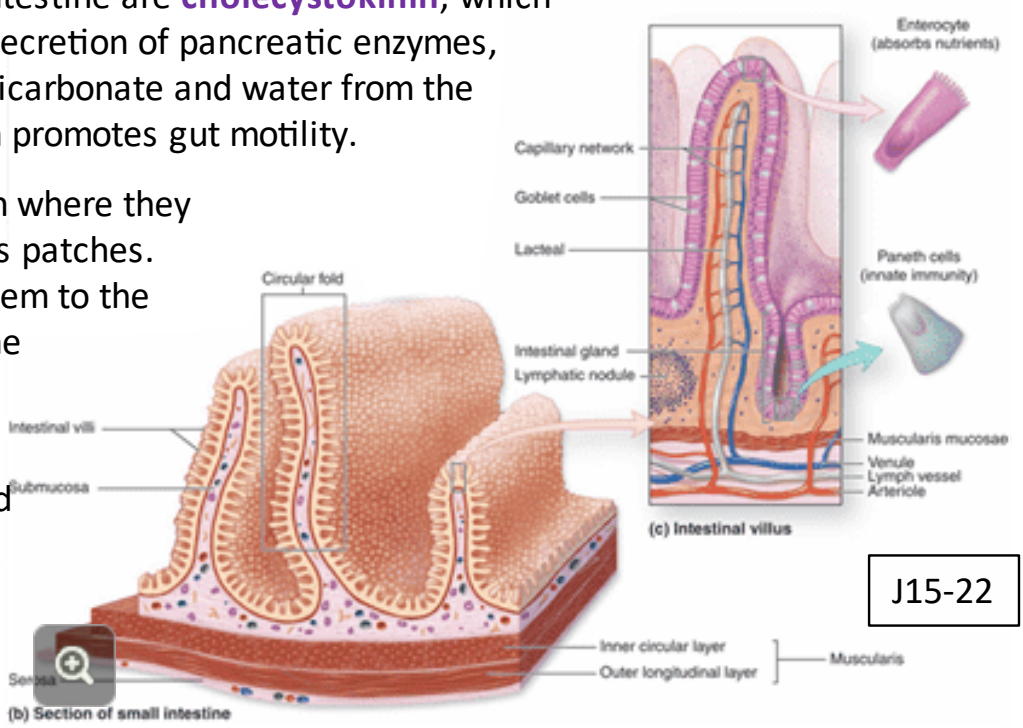
A variety of cell types line the intestinal glands.

Paneth cells play a role in innate immunity. They are exocrine, producing **antimicrobial peptides**, such as **lysozyme**, which they secrete into the intestinal lumen to destroy pathogens present in chyme.

Enteroendocrine cells are present in the intestinal glands, the specific population and their number varying in the different regions of the small intestine. Many **sample luminal contents via endocytosis at their apical aspect**, using this to **regulate hormonal release from their basal aspect into the underlying LP**. Major hormonal products of the small intestine are **cholecystokinin**, which promotes gall bladder contraction and the secretion of pancreatic enzymes, **secretin**, which promotes the secretion of bicarbonate and water from the pancreas and bile ducts, and **motilin**, which promotes gut motility.

M (microfold) cells are present in the ileum where they form an epithelial covering overlying Peyer's patches. They **endocytose antigens** and transport them to the lymphocytes and dendritic cells (APCs) in the underlying LP, which then migrate to lymph nodes to **initiate an immune response**.

This wide variety of cell types is replenished by the division of **stem cells** present in the bases of the intestinal glands. The transit time from "birth" to being shed from the tip of a villus is **3 - 5 days**.



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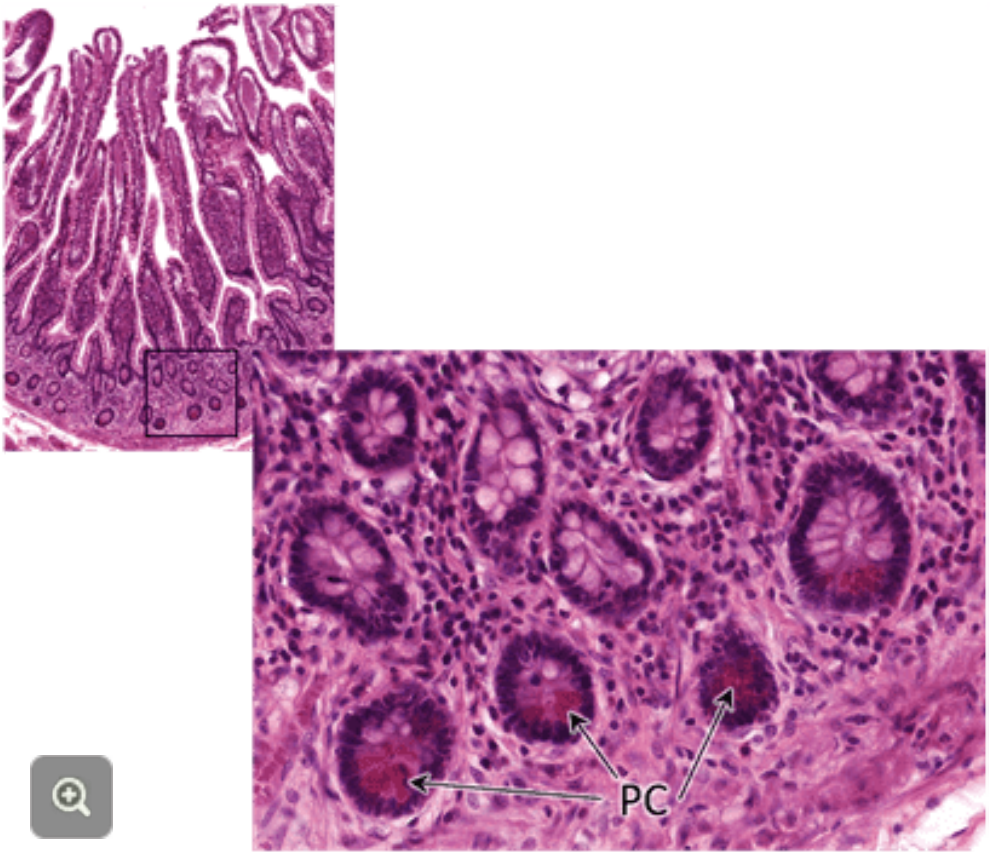


This histological section of the ileum shows **Paneth cells (PC)** within the intestinal glands of the mucosa. These cells heavily stain with eosin which make them look reddish-pink.

INFO

Celiac Disease

In **celiac disease**, an immune reaction to proteins in wheat and other grains causes inflammation and atrophy of the small intestinal mucosa (**predominantly duodenal mucosa**) and a loss of villus height, leading to **malabsorption**.

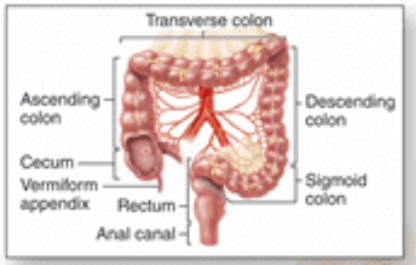
INFO

Crohn's Disease

In **Crohn's disease**, there is chronic inflammation that can involve any portion of the GI tract, although **most commonly affects the terminal ileum and/or colon**, classically presenting with **chronic non-bloody diarrhea, abdominal pain and weight loss**. The inflammation may penetrate deep into the gut wall. The cause is not clear; it may involve a combination of immune and genetic factors.

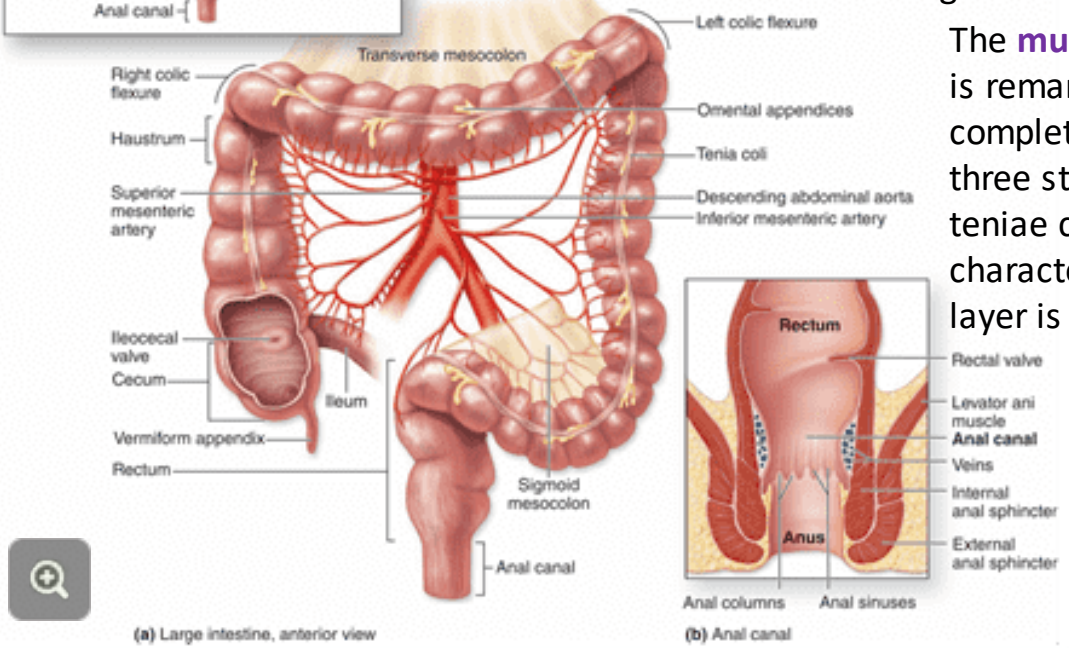
The Histology of the Large Intestine

The large intestine **absorbs water, electrolytes, and some vitamins**. It forms indigestible material into feces. It includes the cecum, the ascending, transverse, descending and sigmoid colon, and the rectum. While it is shorter in length than the small intestine, it is **larger in diameter**.



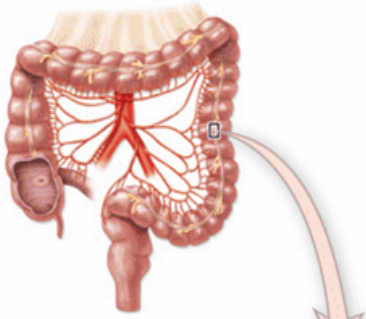
The cecum, ascending and descending colon are **secondarily retroperitoneal**; only their anterior surfaces are covered by serosa. The transverse and sigmoid colons are **intraperitoneal**, and therefore suspended by mesenteries. The serosae covering them is continuous with that of their mesenteries.

Epiploic (omental) appendages are accumulations of fat, covered by serosa that are characteristic of the large intestine.



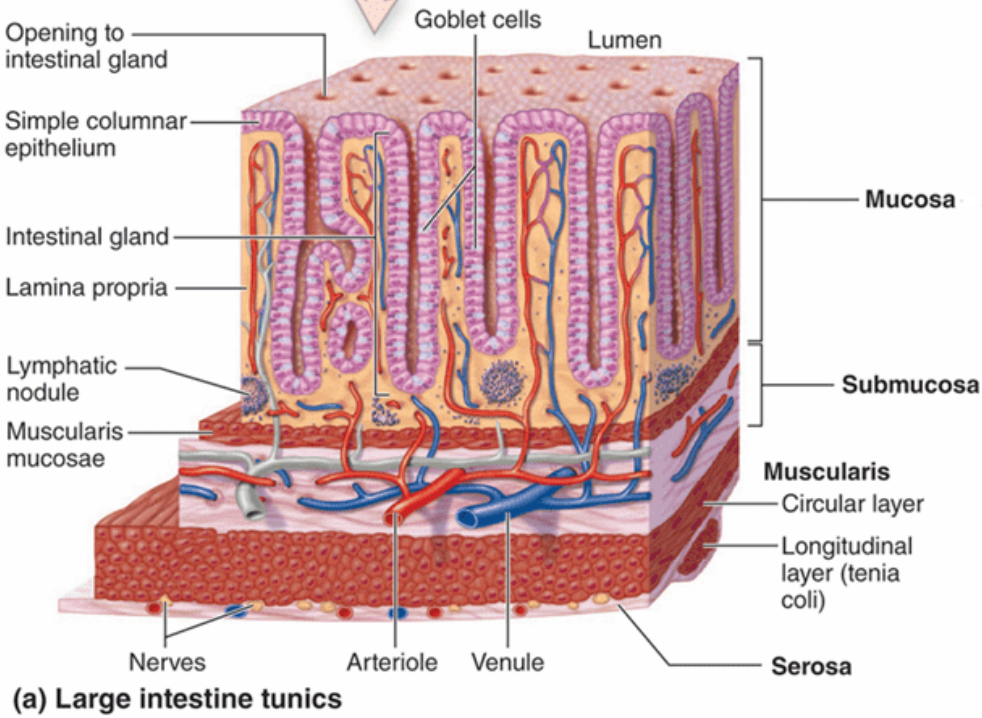
The **muscularis externa** of the cecum and colon is remarkable in that while its circular layer is complete, its longitudinal layer is reduced to three strips, the **teniae coli**. Tension in the teniae coli forms **haustra**, the sacculations characteristic of the bowel wall. This muscle layer is complete in the appendix and rectum.

The inner circular layer of muscle is thickened at each end of the large intestine to form the **ileocecal valve** and the **internal anal sphincter**. In the rectum, it also forms the **rectal "valves" of Houston.**



Lymphatic nodules of the LP **may extend into the submucosa**. Otherwise, the submucosa of the large intestine is typical, and therefore unremarkable. The large bacterial population in the large bowel necessitates the presence of this MALT.

The **mucosa** of the large intestine is distinctly different from that of the small intestine in that it **lacks villi**. It does form deep tubular invaginations into the LP, the **intestinal glands**. The epithelium is dominated by **absorptive cells** and **goblet cells**, and includes a small population of **enteroendocrine cells**.

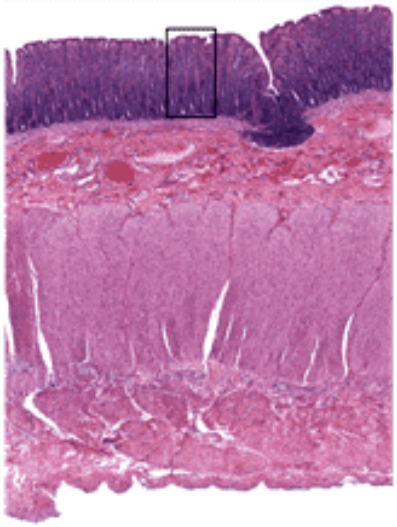


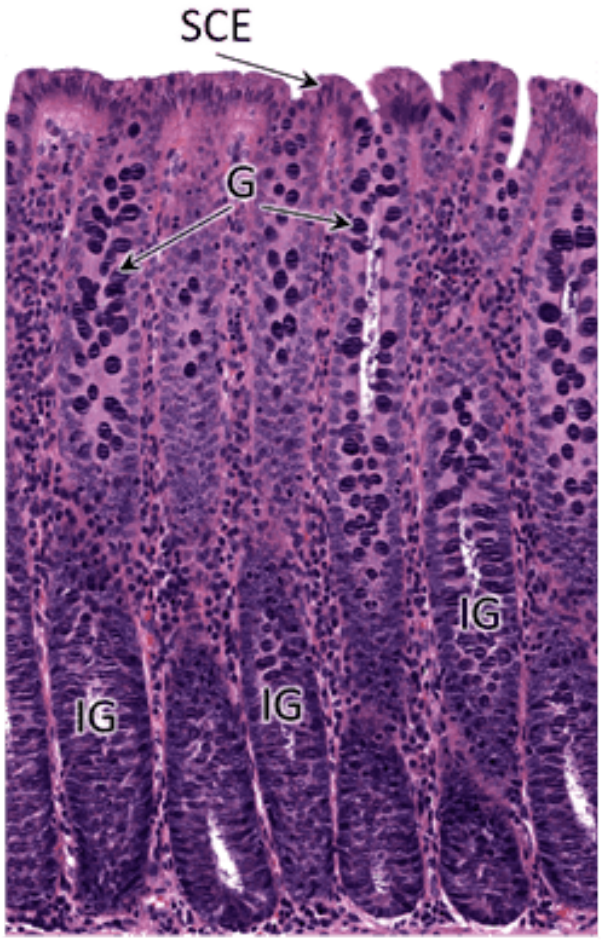
(a) Large intestine tunics

Goblet cells increase in number along the length of the large intestine, as the feces are dried out through the absorption of water, and lubrication of the intestinal wall becomes more necessary.

Stem cells in the bases of the intestinal gland divide to replace cells lost into the luminal contents.

There is an abrupt transition to **stratified squamous epithelium** at the rectoanal junction, and the mucosa is raised into longitudinal folds, the **anal columns**. The stratified squamous epithelium of the anal canal becomes **keratinized** at the anus.



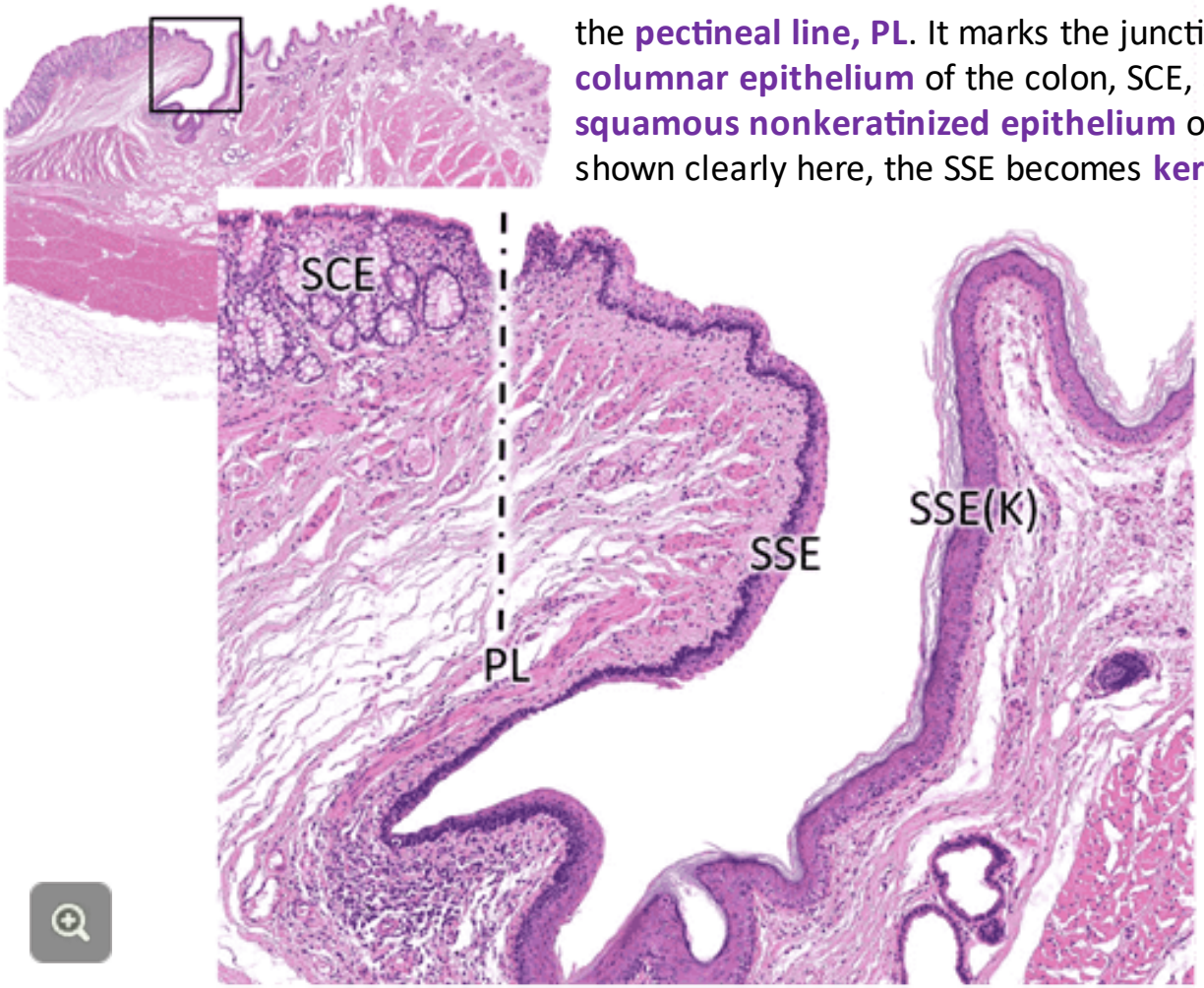


This histological section of the colon has zoomed in on the mucosal layer.

There are **no plicae circulares or villi**. **Goblet cells (G)** are more abundant.

The **intestinal glands (IG)** of the mucosa form deep, **tubular** invaginations into the lamina propria.

Remember, the epithelial lining along the intestine is composed of a **simple columnar epithelium (SCE)** with a brush border, and these cells are referred to as **enterocytes**.



The transition zone between the rectum and the anus is called the **pectineal line, PL**. It marks the junction between the **simple columnar epithelium** of the colon, SCE, and the **stratified squamous nonkeratinized epithelium** of the anal canal, SSE. As shown clearly here, the SSE becomes **keratinized**, SSE(K) at the anus.

INFO

Inflammatory Bowel Disease in the Colon

In **ulcerative colitis**, chronic active inflammation of the mucosa of the large intestine causes the formation of ulcers, which results in chronic bloody diarrhea. It typically starts at the rectum and proceeds proximally.

The inflammation in **Crohn's disease** can involve all layers of the intestinal wall, from mucosa to serosa. It is present as discontinuous patches throughout the GI tract, although commonly in the terminal ileum and large intestine (thus, it is mentioned here, as well as in the section on the small intestine). Crohn's disease presents with **chronic, non-bloody diarrhea, abdominal pain and weight loss**.

INFO

Rectal Varices

As described earlier, **portal-systemic anastomoses** connect veins of the **hepatic portal system**, which drains blood from the digestive tract to the liver, to **systemic veins**, which drain blood directly to the IVC or SVC. Recall that such a portal-systemic anastomosis occurs in the esophagus, and can lead to **esophageal varices**. **A portal-systemic anastomosis also occurs in the submucosa of the rectum.**

The superior rectal veins drain into the portal system. The middle and inferior rectal veins drain into the systemic system (the internal iliac veins, and from there into the IVC). These veins are connected by a portal-systemic anastomosis.

With **hepatic portal hypertension**, as may occur in **cirrhosis of the liver** secondary to alcoholic liver disease or viral hepatitis, veinous blood is diverted from the superior rectal vein to the tributaries of the middle and inferior rectal veins, located in the submucosa of the rectoanal junction. In response to the increased venous pressure, veins in the submucosa of the rectum dilate (**rectal varices**).

These are distinct from **hemorrhoids**, which are dilated vessels at the anorectal junction in the venous plexus associated with mucosa overlying the internal anal sphincter (internal hemorrhoids) and at the anus in the venous plexus associated with the skin overlying the external anal sphincter (external hemorrhoids). Hemorrhoids are not associated with portal hypertension, but, for instance, with a low fibre diet and the resultant straining associated with defecation.

Press **Next** to start the Quiz or **Skip** to end H14

H14 Question 1

Which of the following regions of the digestive tract include an adventitia?

- [ ] the esophagus
- [ ] the stomach
- [ ] the ileum
- [ ] the sigmoid colon

SUBMIT

Which of the following regions of the digestive tract has the largest accumulation of mucosa-associated lymphoid tissue (MALT)?

- [ ] stomach
- [ ] duodenum
- [ ] jejunum
- [ ] ileum

SUBMIT

H14 Question 3

In the large intestine, the teniae coli are a specialization of which layer?

- [ ] mucosa
- [ ] submucosa
- [ ] muscularis externa
- [ ] serosa

SUBMIT

Identify cell type A.

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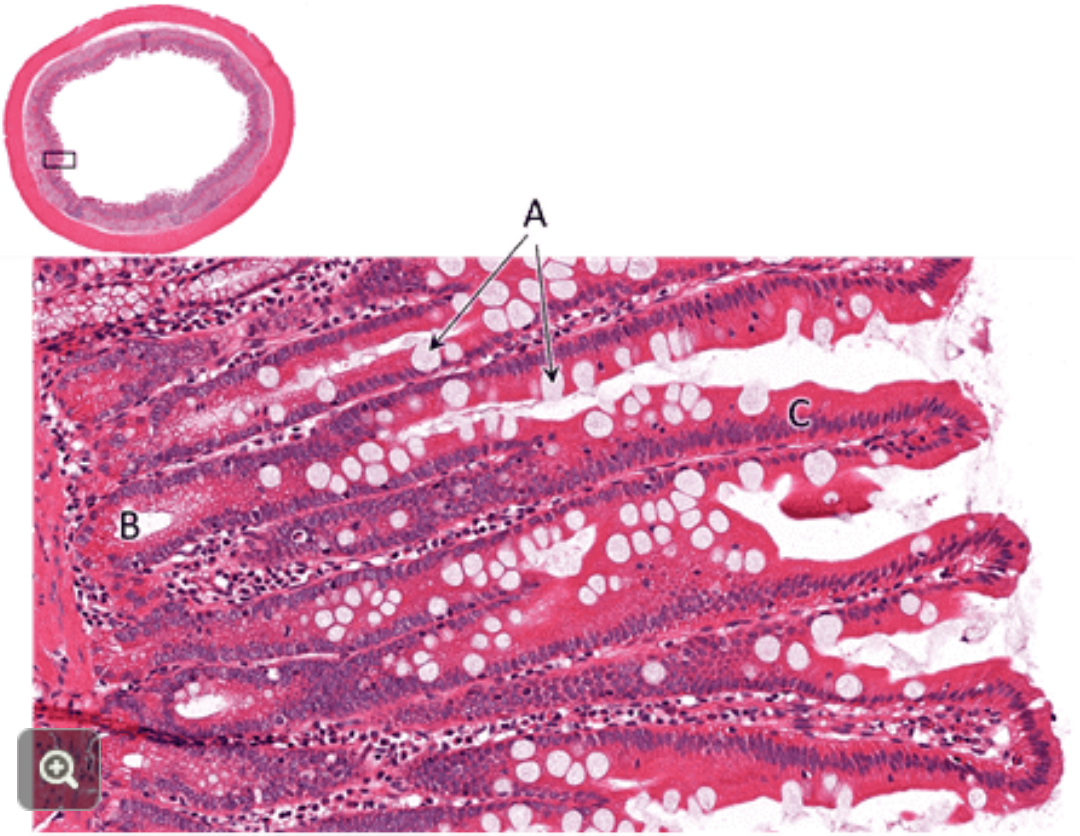
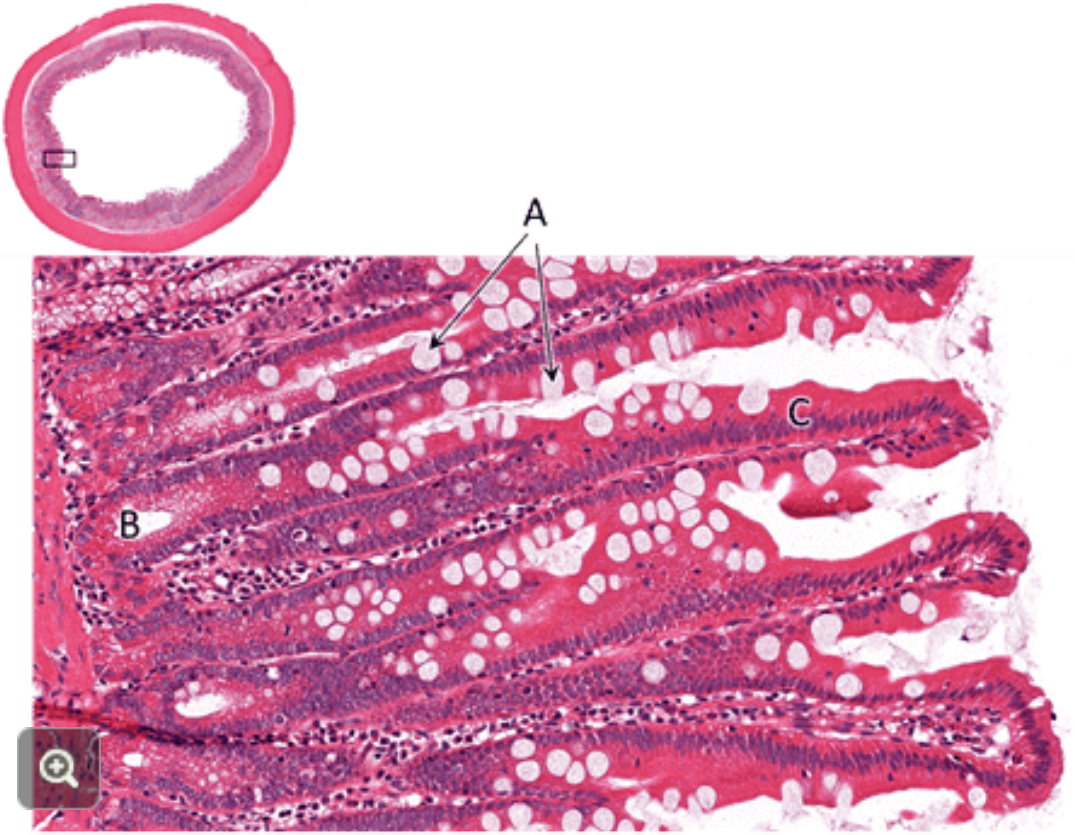


SUBMIT

Identify structure B.

type your text here



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Identify cell type C.

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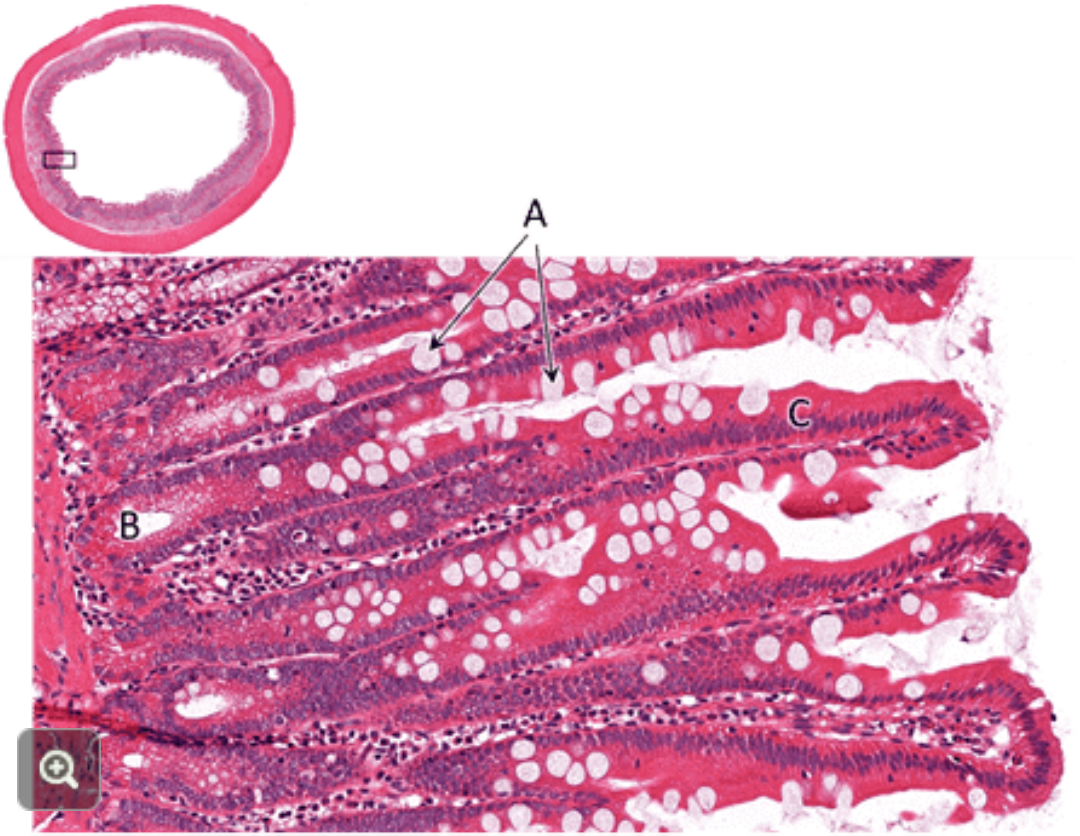
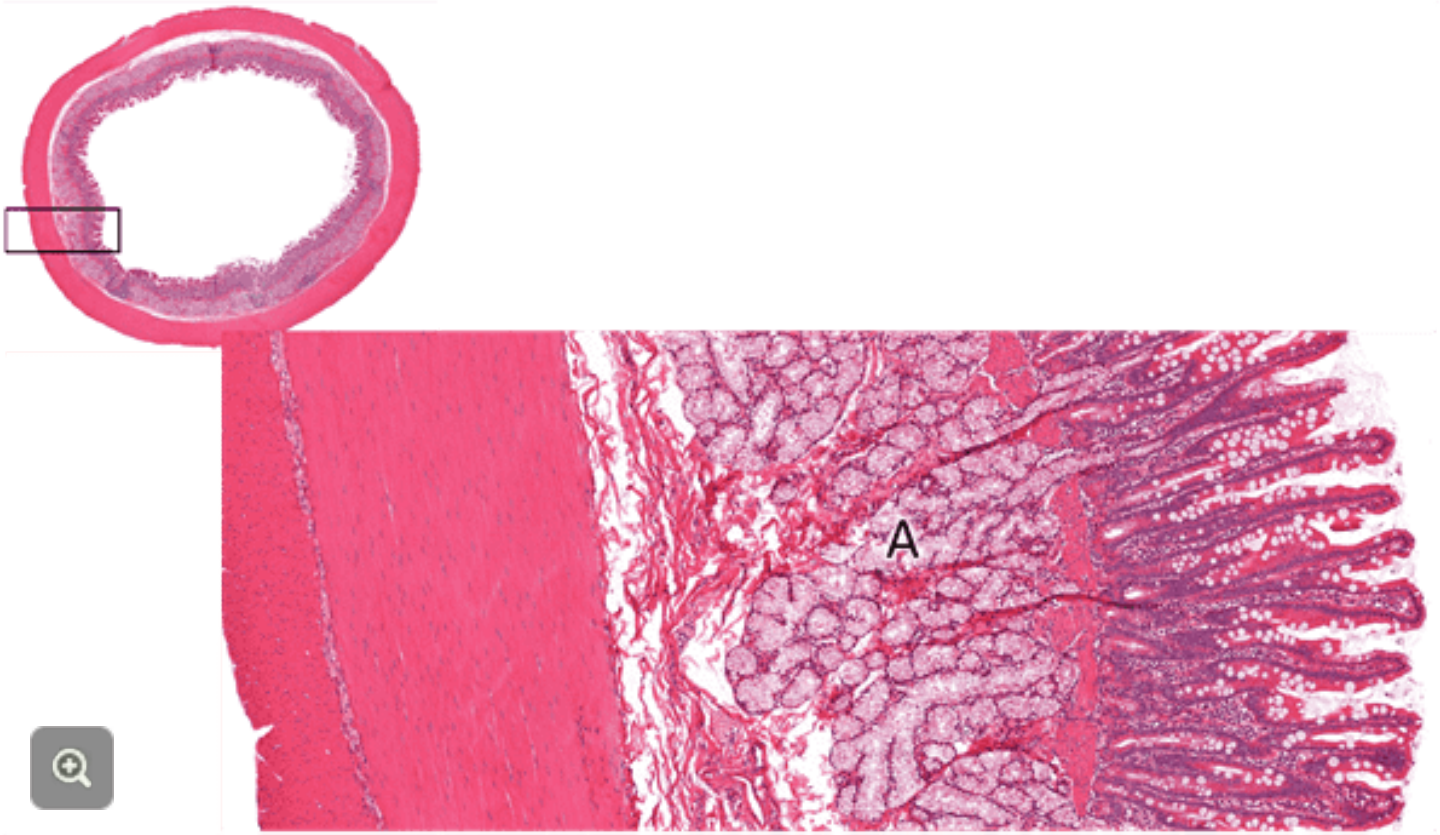


SUBMIT

Identify structures A.

type your text here

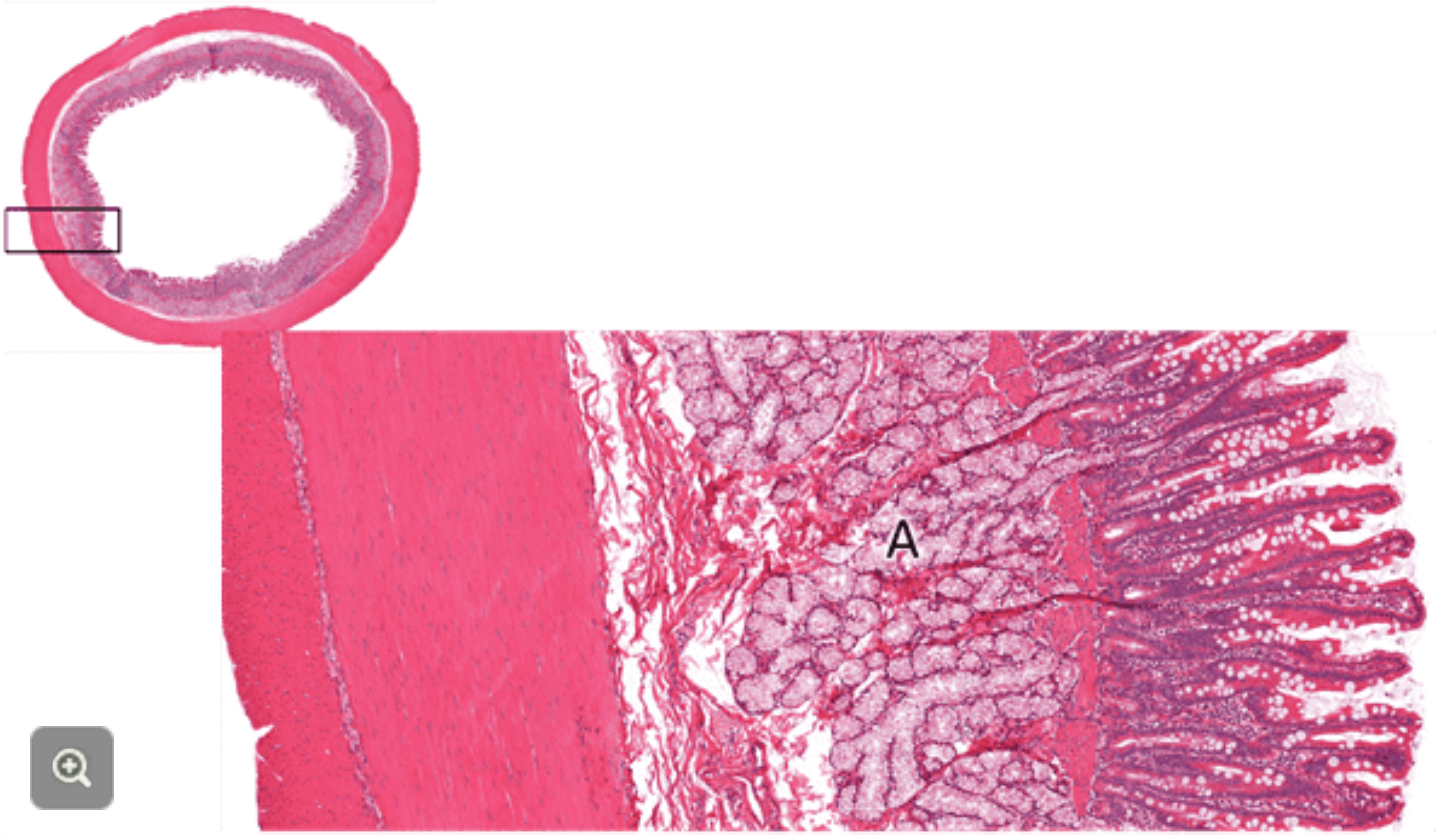


SUBMIT

H14 Question 8

In what subdivision of the small intestine are these glands found?

type your text here



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Identify cell type A.

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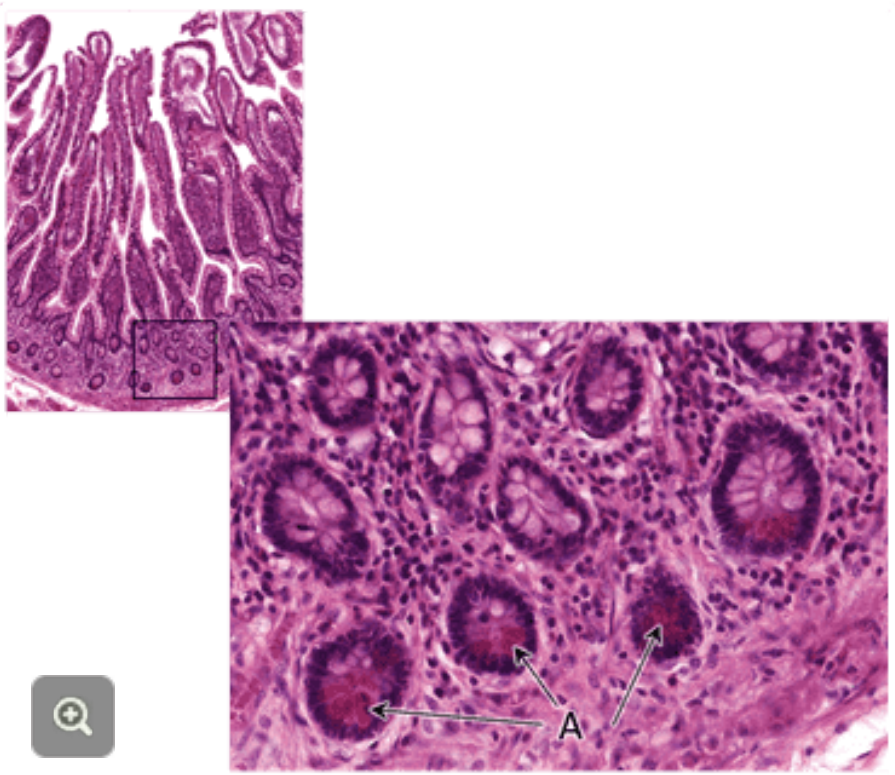

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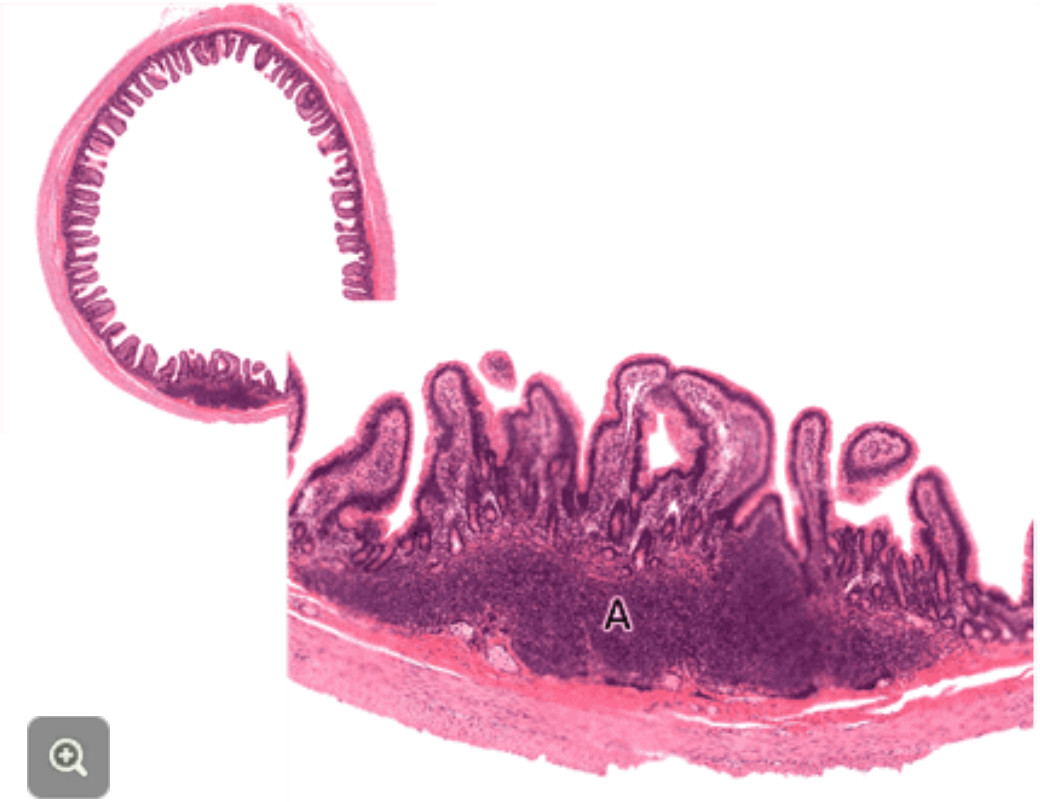
H14 Question 10

Identify structures A.

type your text here

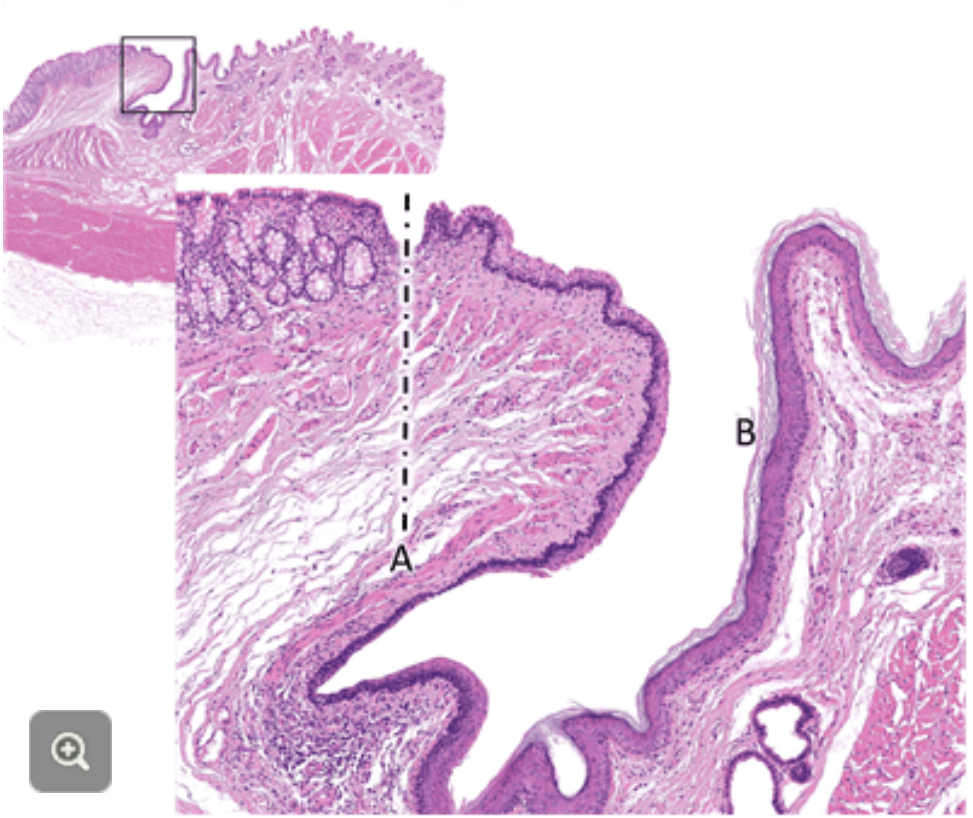


SUBMIT

H14 Question 11

Identify A.

type your text here

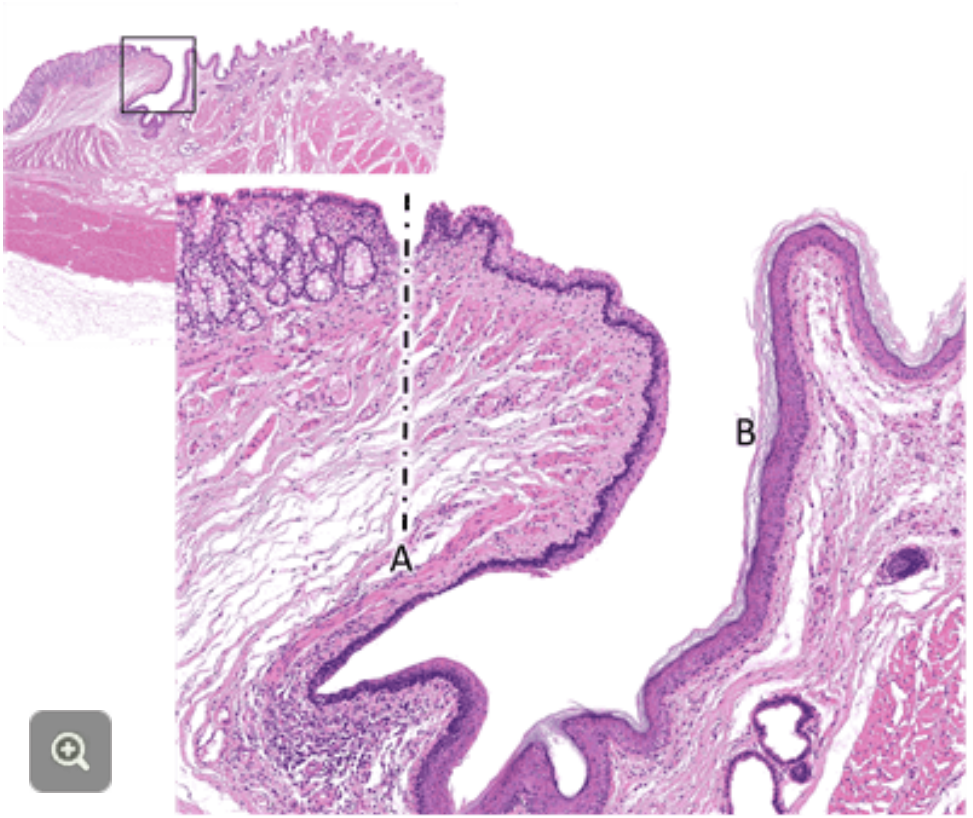


SUBMIT

H14 Question 12

Identify the class of epithelium B.

type your text here



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