Esophagus, stomach, small and large intestine, appendix vermiformis

Professor Zbigniew Kmiec, MD, PhD

Structure of the GI Tract Tube

1. Mucosa

a. epithelium

b. lamina propria (loose CT)

c. muscularis mucosae (a thin layer of smooth muscle cells)

2. Submucosa

a thick layer of dense CT

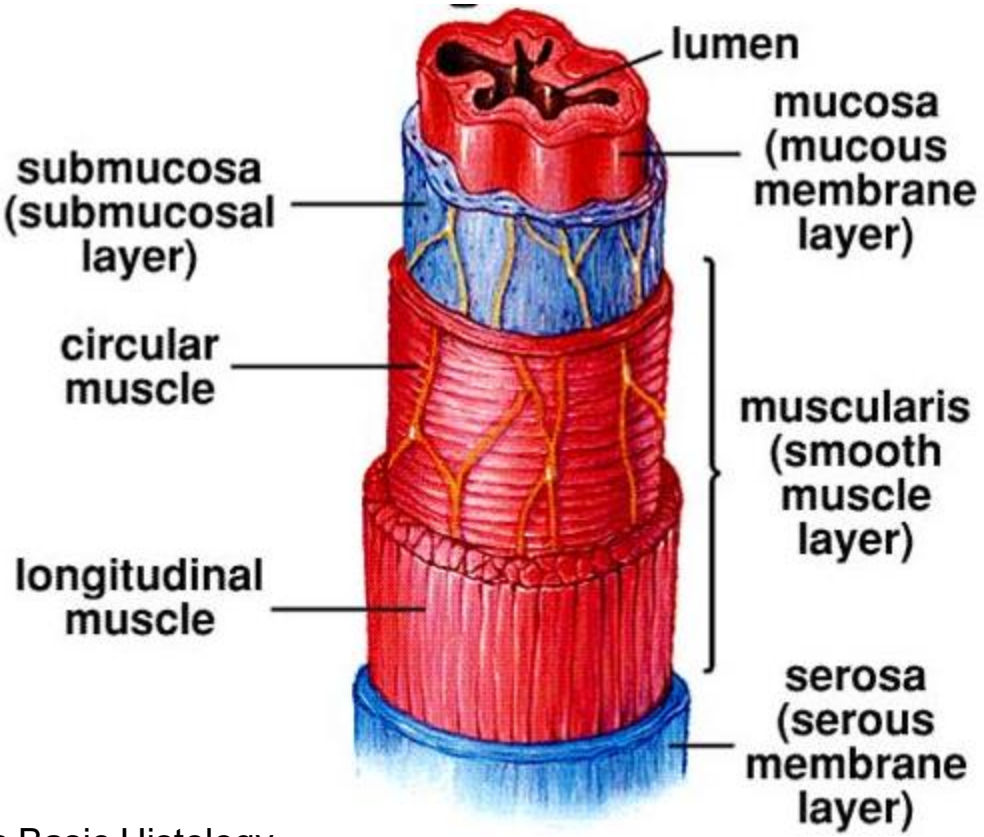
3. Muscularis externa

a. a circular layer of smooth muscle cells

b. a longitudinal layer of smooth muscle cells

c. an oblique layer of smooth muscle cells (***stomach***)

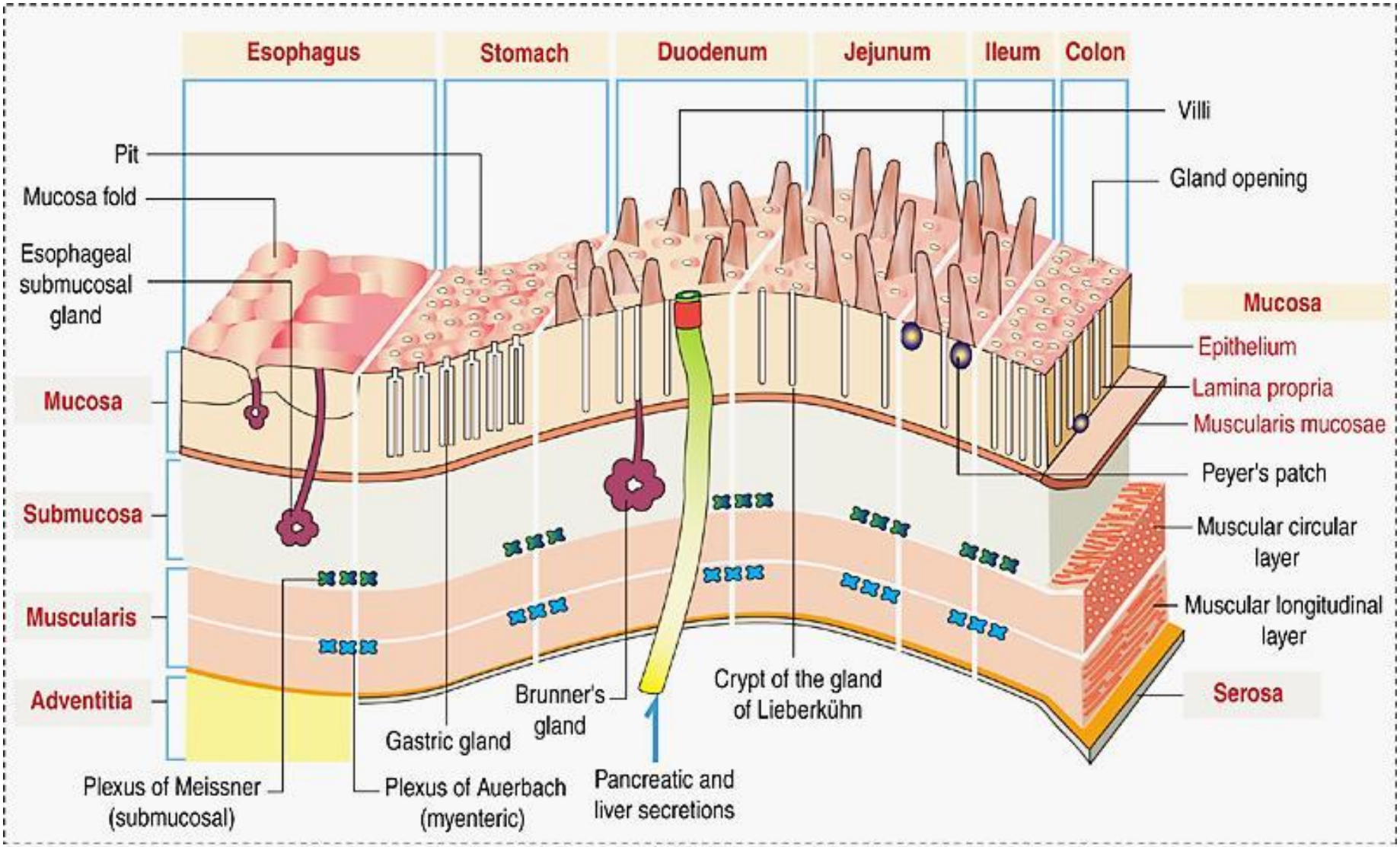
4. Serosa/Adventitia



Junqueira's Basic Histology, 12th ed, 2010

E

Upper part of the GI tract is lined up by stratified, squamous, nonkeratinized epithelium (SSnKE)



Klerszenbaum & Tres: Histology and Cell Biology: An Introduction to Pathology, 3e
Copyright © 2012 by Mosby, an imprint of Elsevier Inc. All rights reserved.

Middle and lower parts of GI tube stomach-colon (not anus) are lined by simple columnar epithelium

On cross section, the **lumen of esophagus** is in collapsed state and has a branched appearance because of longitudinal folds.
When a bolus of food passes through the esophagus, the lumen expands without mucosal injury.

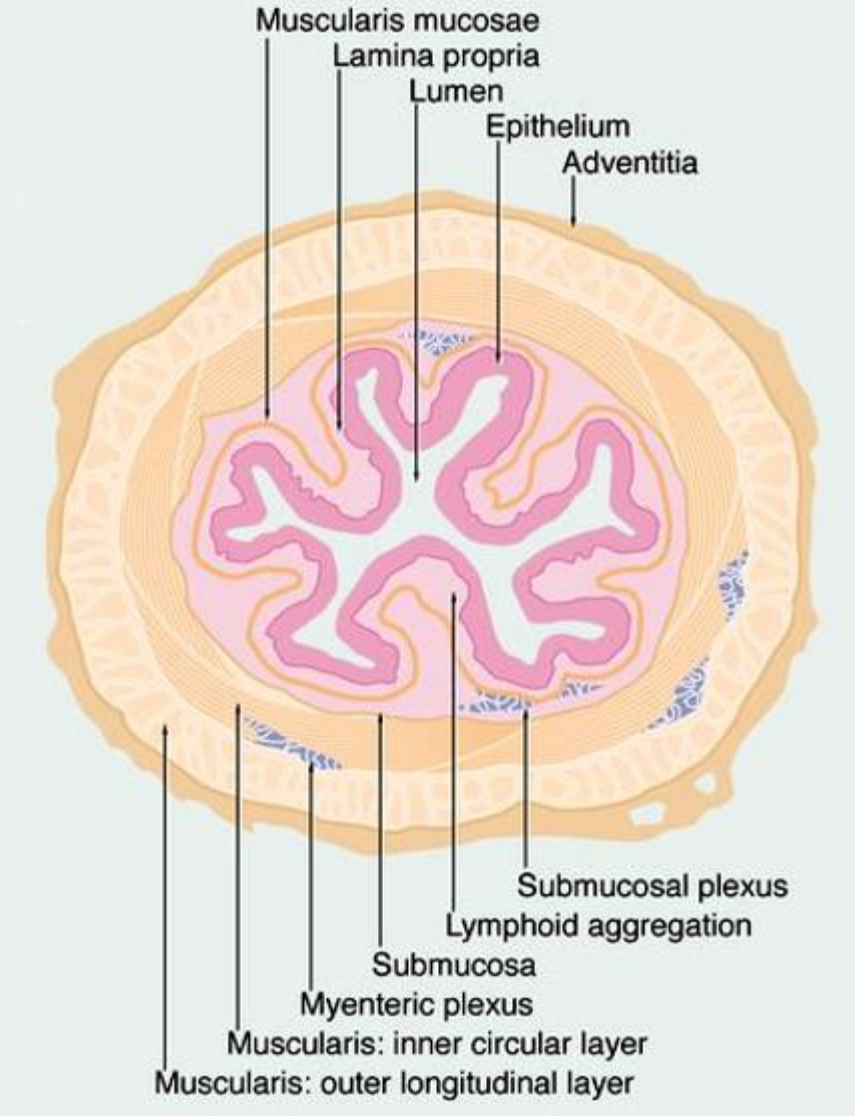
Mucosa: Thick stratifiedsquamous nonkeratinized epithelium (**SSnkE) protects against hard meal pieces.**

Muscularis mucosae has a loose structure.

Mucosa contains ESOPHAGEAL CARDIAC GLANDS. They are named for their similarity to the cardiac glands of the stomach. They are present in the terminal part of the esophagus although can be present also in its proximal part.

Submucosa has collagen and elastic fibers, and, in the lower part, venous plexus that drains both systemic and portal venous systems.

It contains tubuloacinar ESOPHAGEAL GLANDS PROPER: small, compound, tubuloalveolar glands **with mucous and serous cells.**



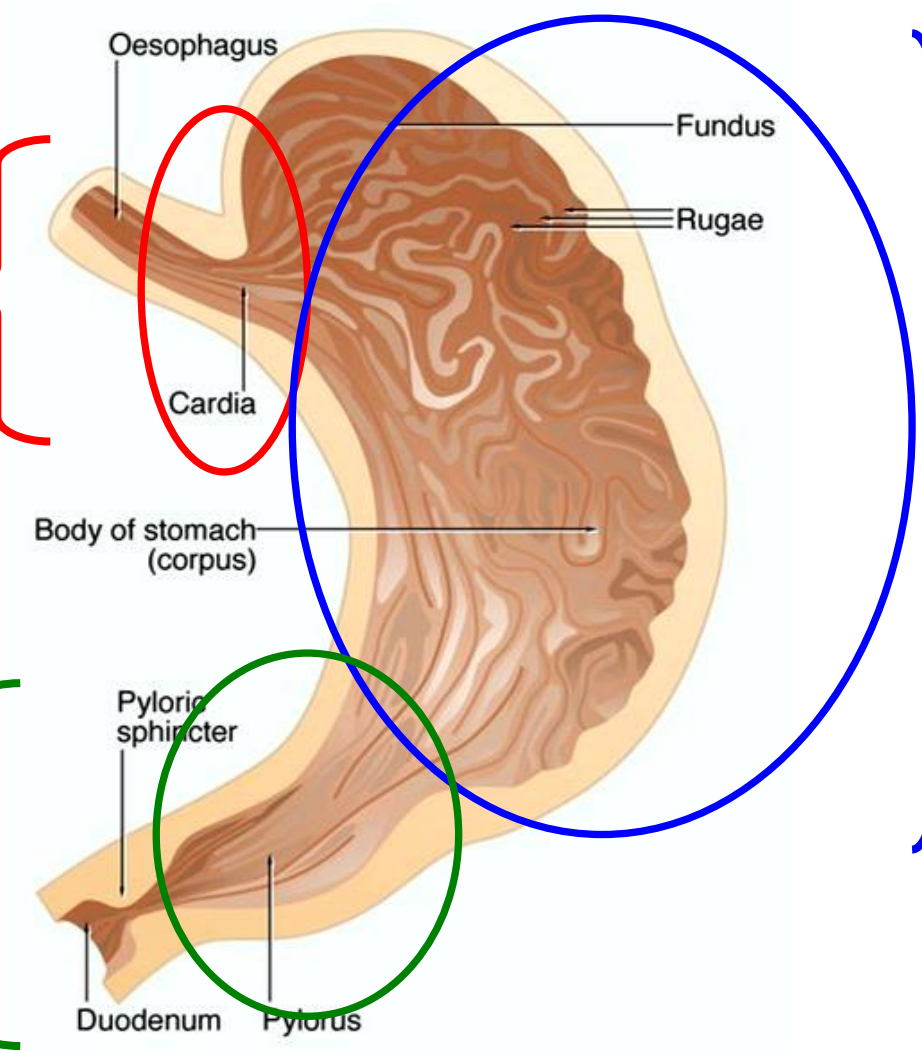
Functional Histology, 2004

The stomach is an expanded part of the digestive tube that lies beneath the diaphragm. It receives the bolus of macerated food from the esophagus.
Mixing and partial digestion of the food in the stomach by its gastric secretions produce a pulpy fluid mix called ***chyme***.
The chyme then passes into the small intestine for further digestion and absorption.

There are 3 different histological structures of stomach's mucosa

Cardiac portion

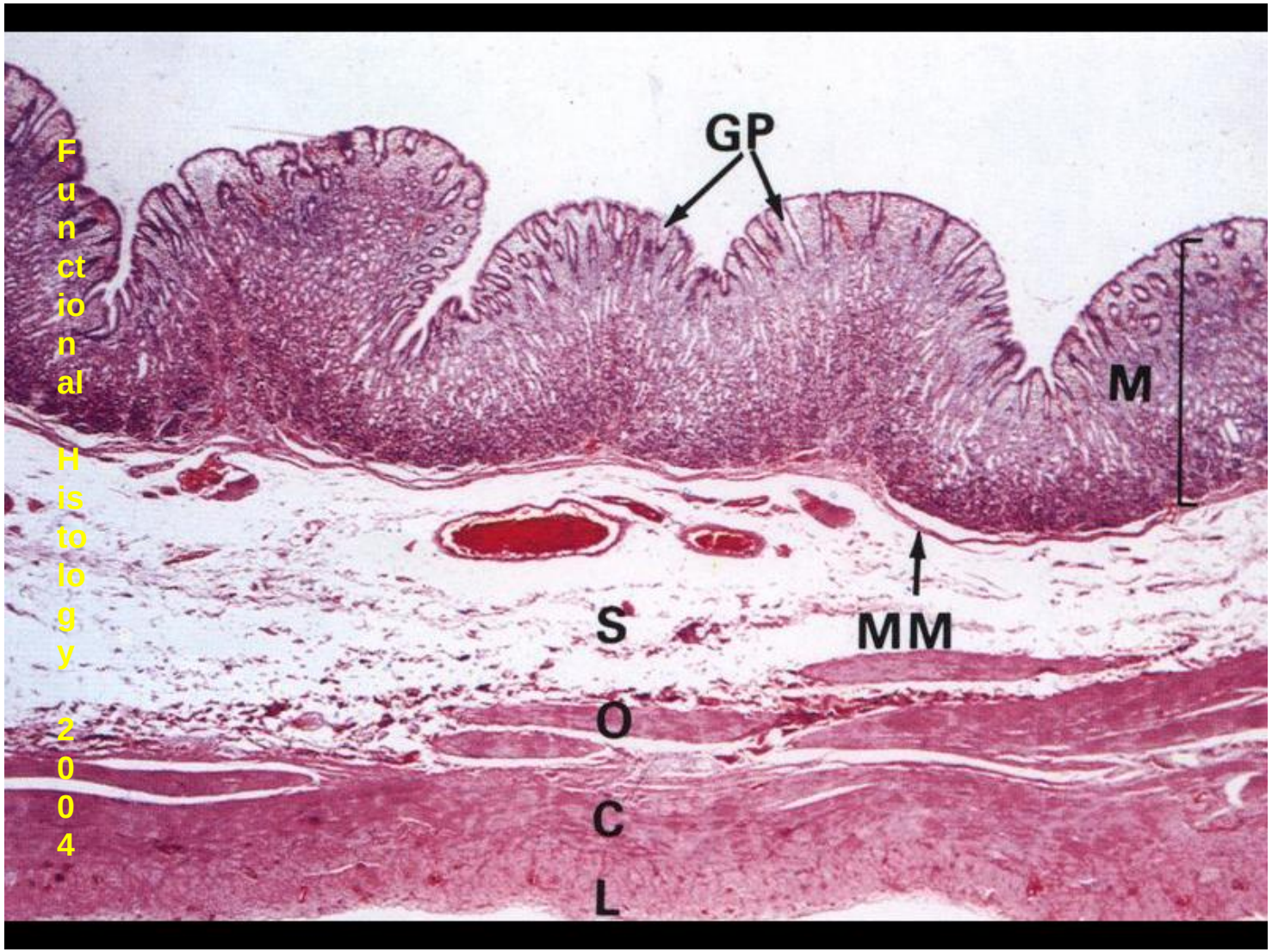
pylorus



Fundus and the body

Functional Histology, 2004

Stomach's wall layers



Gastric pits (GP): where 3-4 glands end up

Blood vessels in submucosa

O, additional oblique layer of muscles

STOMACH

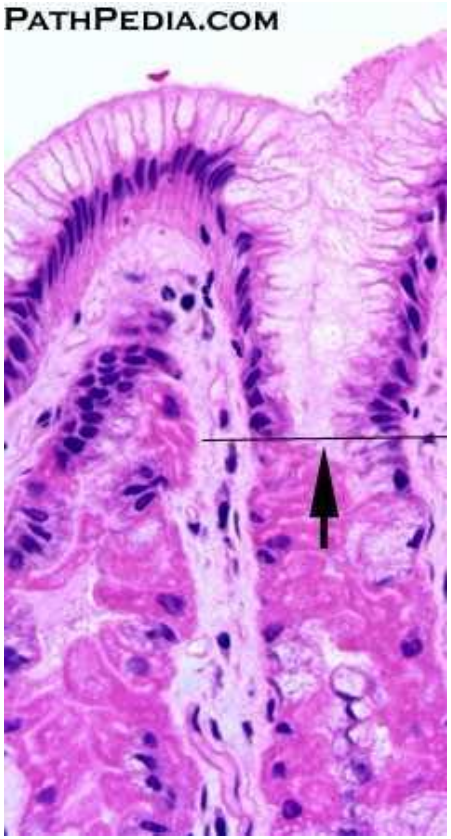
The inner surface of the **empty stomach** reveals a number of longitudinal folds or ridges called **rugae**. When the stomach is fully distended, the rugae, composed of the mucosa and underlying submucosa, virtually disappear. The rugae serve to accommodate expansion and filling of the stomach.

- **Mucosa**

Simple columnar epithelium with **surface mucous cells** (possesses a large, apical cup of mucinogen granules, creating a glandular sheet of cells. The mucous cup occupies most of the volume of the cell.

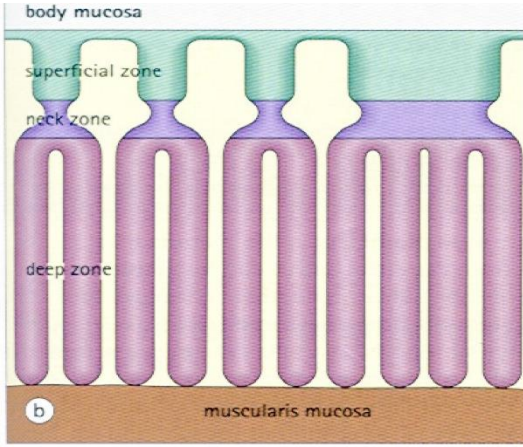
Fundic glands are composed of 5 different cell types:

- **Mucous neck** cells
- Chief cells
- Parietal cells, also called oxyntic cells
- Enteroendocrine cells (DNES)
- **Stem cells**

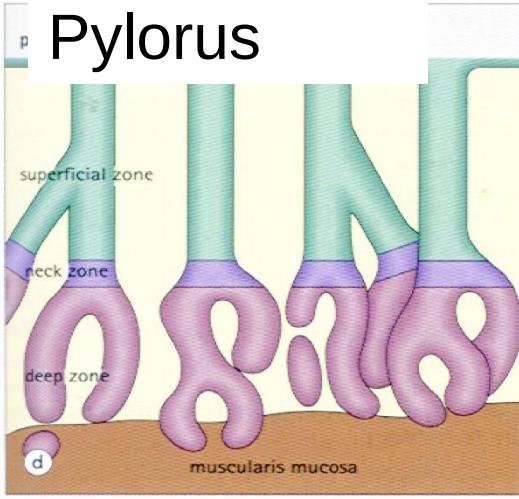


Arrow: bottom of gastric pit

Body and Fundus



Pylorus

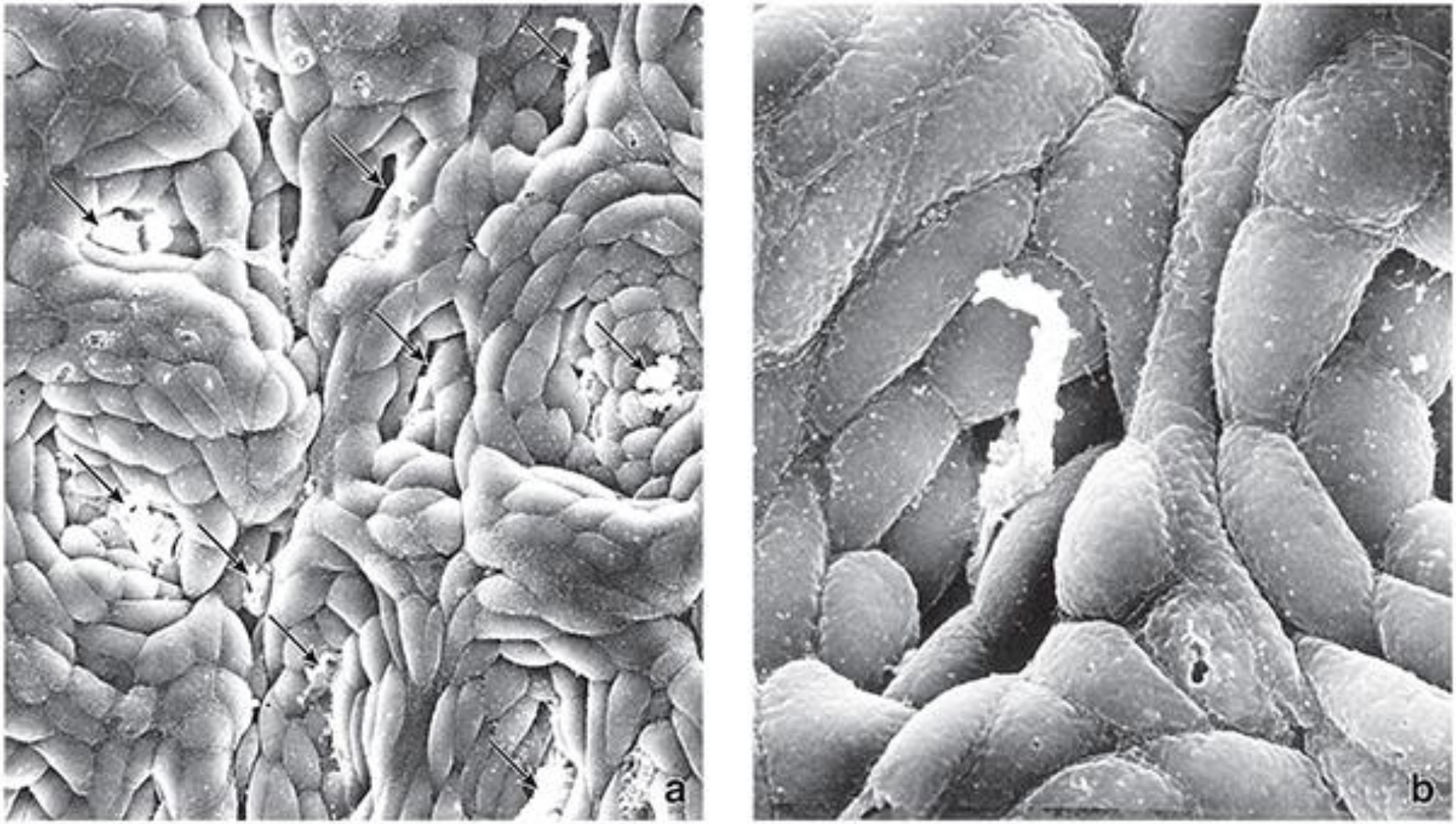


Gartner, 3rd. ed.

Histological structure of gastric mucosa

- **Cardiac glands contain mucous and endocrine cells and comprise less than 5% of the gastric gland area.**
- **Fundus and body OXYNTIC = fundic (gastric glands proper) make up 75% of the gastric gland area.**
- **They are responsible for HCl, pepsinogen and intrinsic factor secretion**
- **They contain parietal, chief, mucous neck, DNES (endocrine), and stem cells.**
- **Pyloric glands contain mucous, some parietal and endocrine cells of which the most important are G cells secreting gastrin.**

Mucosal surface of the stomach (SEM)



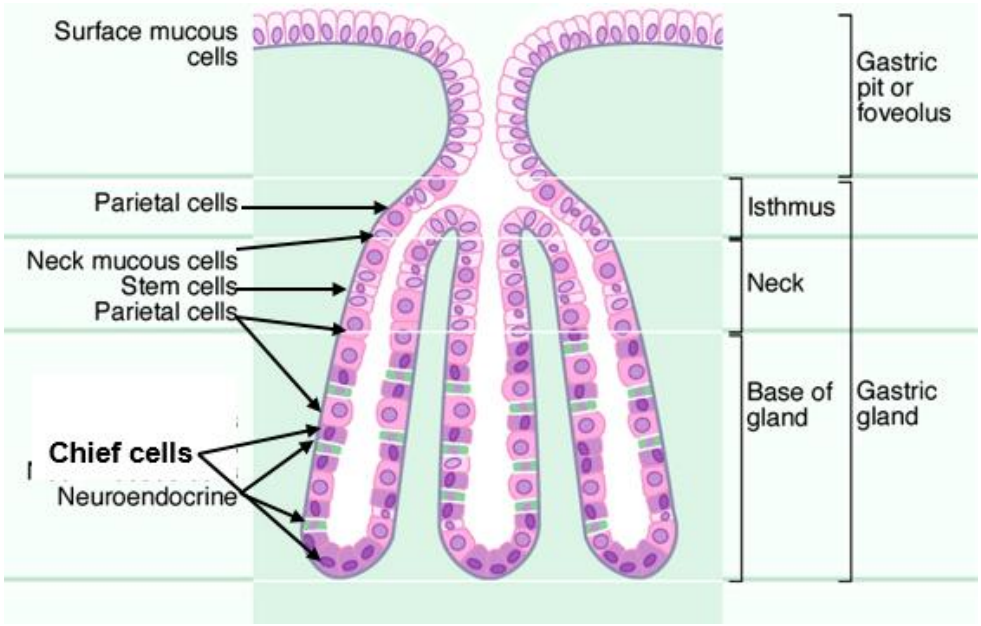
a. The gastric pits contain secretory material, mostly mucus (**arrows**). The **surface mucus** has been **washed away** to reveal the surface mucous cells. ×1,000. b. Apical surface of the elongated polygonal **surface mucous cells** that line the stomach and gastric pits. ×3,000.

Pawlina W, Ross MH. Histology: A Text and Atlas With Correlated Cell and Molecular Biology, 8th ed. Wolters Kluwer, 2016

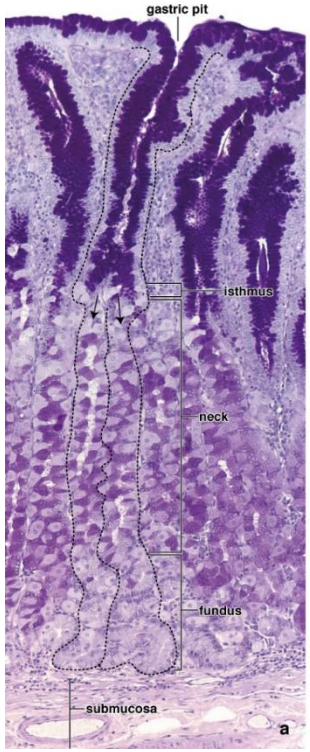
All mucous cells synthesize large amounts of mucin in prominent Golgi stacks, and these glycoproteins are transported by vesicles to form large apical mucous granules.

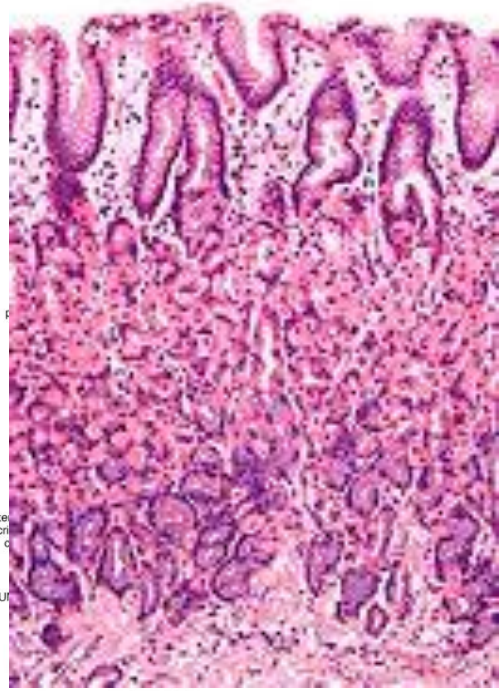
MUCOUS NECK CELLS contain acidic glycoproteins, called *soluble mucus*, whereas SURFACE MUCOUS CELLS contain a neutral glycoproteins called *visible mucus.*

Between them in gland's neck there are few columnar STEM CELLS *(regenerative cells)* which are precursors for all of the gastric epithelial cells. They have high proliferation rate.



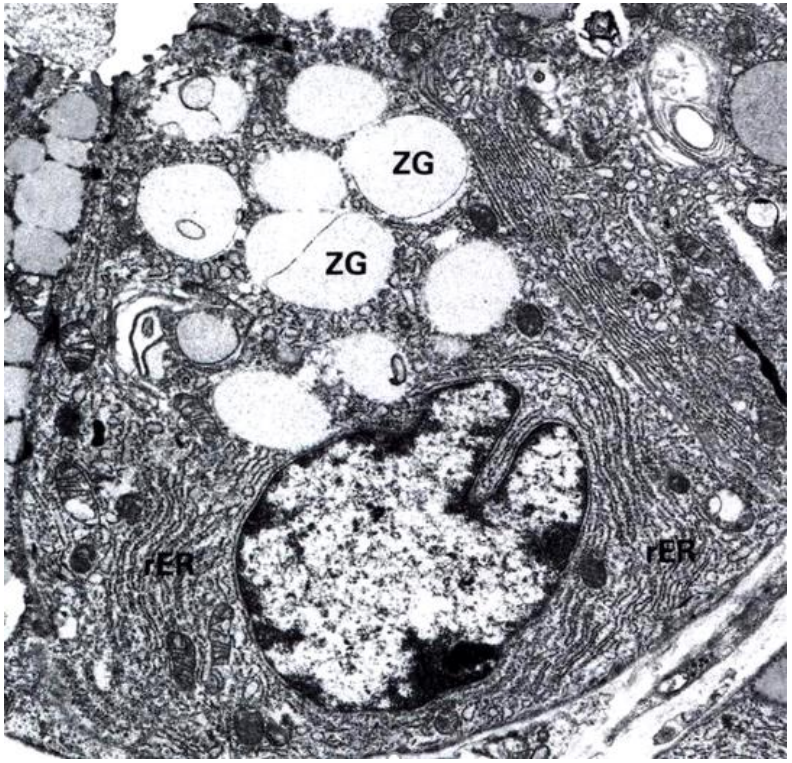
Functional Histology, 2004

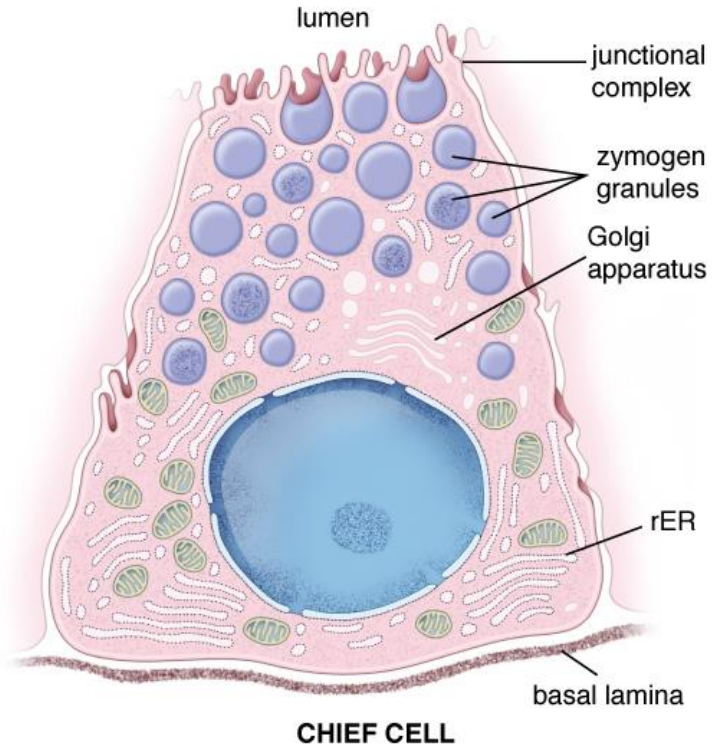




Histology, Pawlina 8th ed.

CHIEF (PEPTIC) CELL: strongly basophilic due to an abundant RER in the basal cell region (production of proenzymes: pepsinogen, prolipase, prorenin). Some of them secrete also leptin.





Many secretory granules called zymogen granules (ZG) located in the apical cytoplasm release their contents by exocytosis.

Apical membrane has a few short microvilli covered by a thin coating of glycoprotein or glycocalyx.

Parietal cell

Pyramidic or oval shape, eosiniphilic.

In the resting state there is a tubulovesicular system in the apical part of the cell

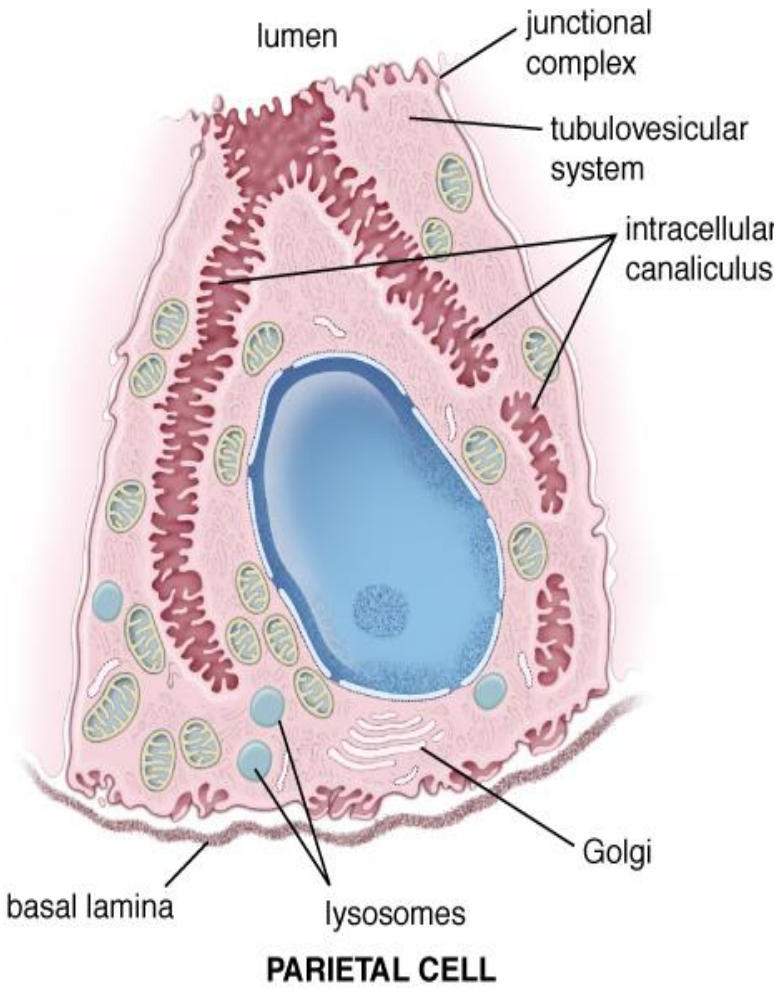
On stimulation, a dense meshwork of intracellular canaliculi that contain a large number of elongated microvilli rapidly forms.

Production of H^+ is due to carbonic anhydrase activity, secretion of H^+ by proton pump to the gland's lumen, and of HCO_3^- by facilitated diffusion across the basal domain of the cell membrane.

Carbonic anhydrase reaction:

$$H_2O + CO_2 \Leftrightarrow H^+ + HCO_3^-$$

Acid secretion is an active transport process and requires significant amount of ATP provided by numerous mitochondria, which account for 30% - 40% of total cellular volume.



Pawlina, Histology, 8th ed.

Other features of parietal cells (PCs)

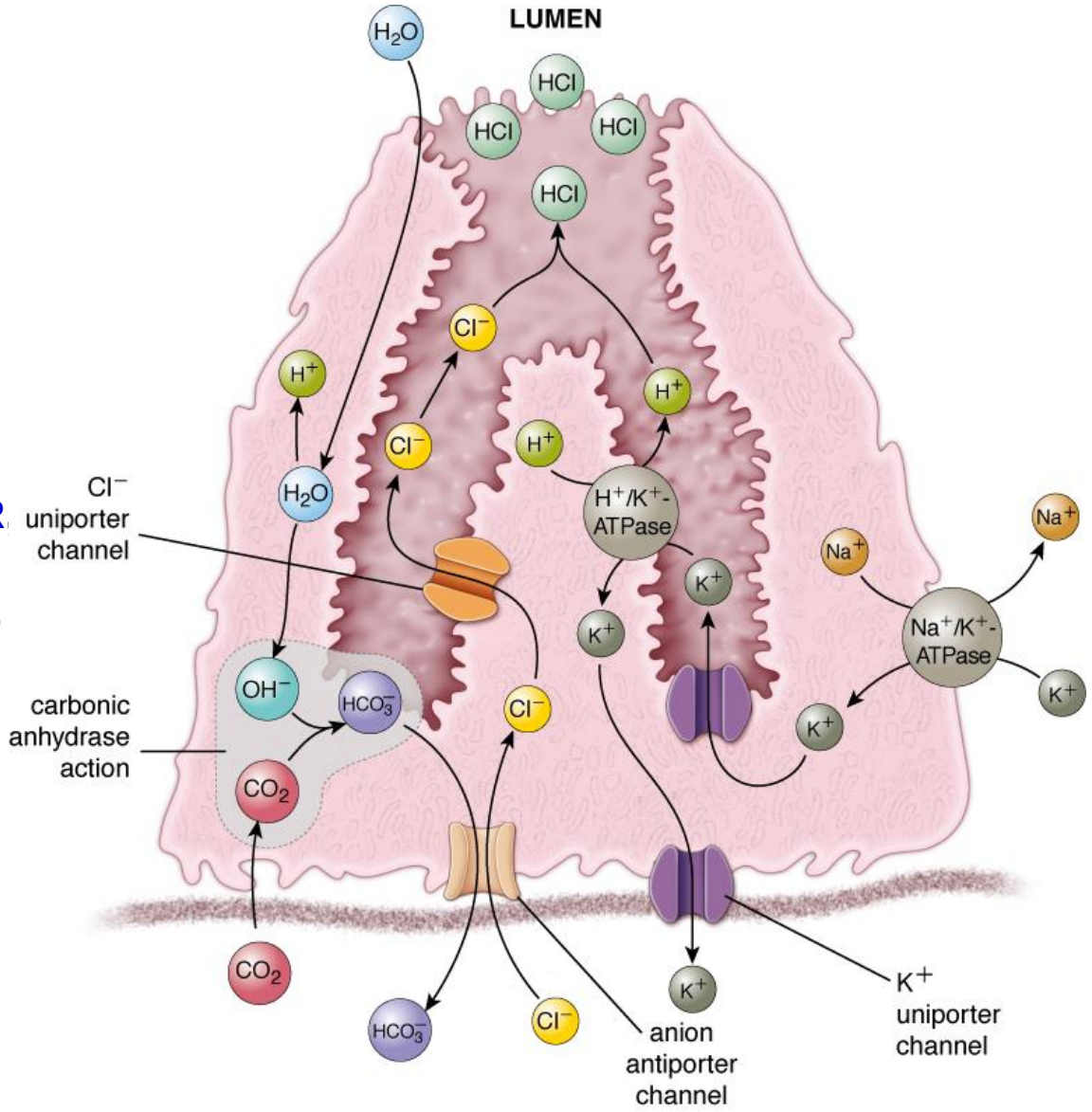
The 3 major activators of HCl production by PCs for which they have receptors in the basal domain of the cell membrane are:
- acetylocholine, - histamine, - gastrin

PCs lack microvillous glycocalyx that is present on other cells in the gastric glands.

PCs have numerous basolateral membrane folds that increase surface area for HCO_3^- exchange for Cl^- ions.

PCs produce INTRINSIC FACTOR a glycoprotein necessary for the jejunal absorption of vitamin B12 (which is cofactor of an enzyme necessary for erythroblasts' DNA synthesis).

LACK of vit. B12 leads to the disease: pernicious anemia.



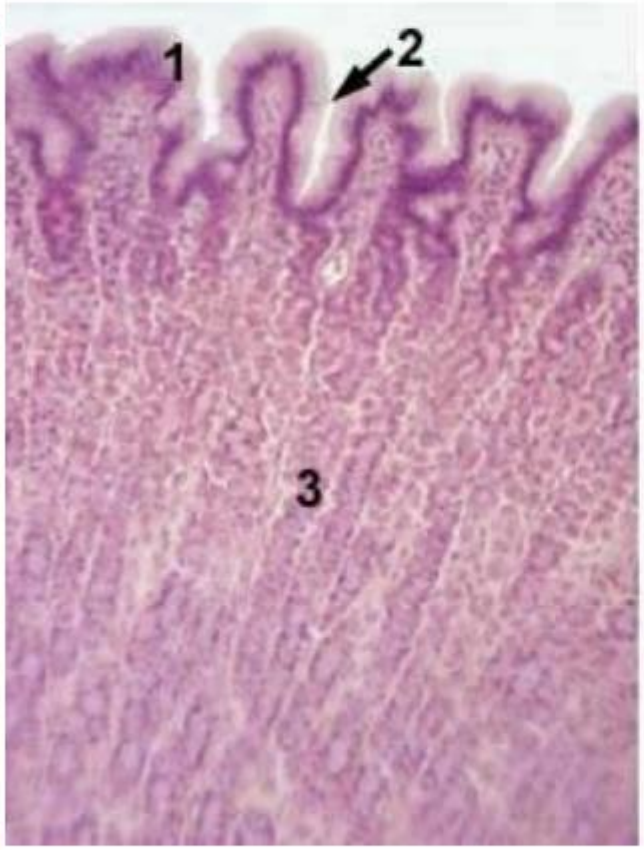
Pawlina, Histology, 8th ed.

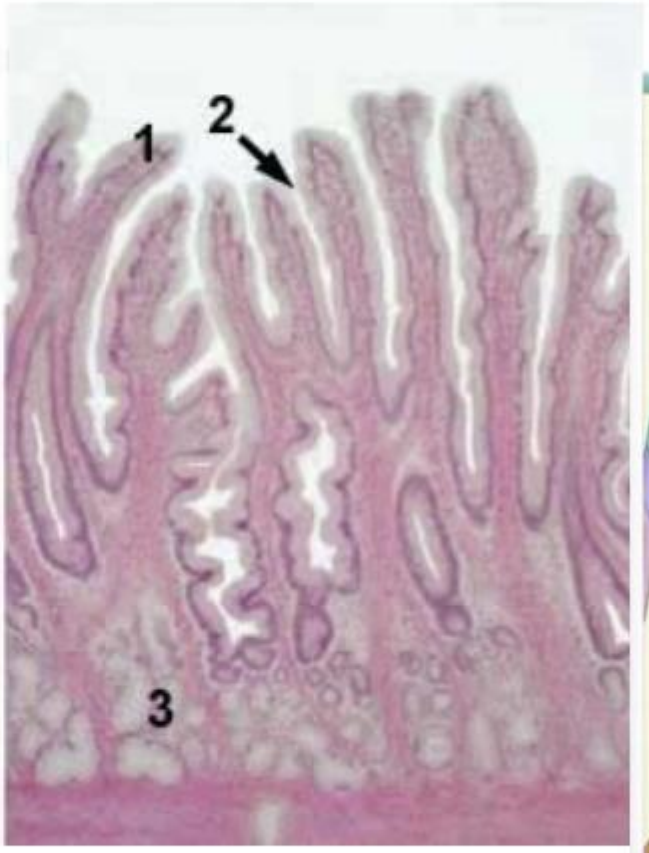
The pit occupies **1/3** of the height of the entire gland in the pylorus
Unbranched gland bottoms

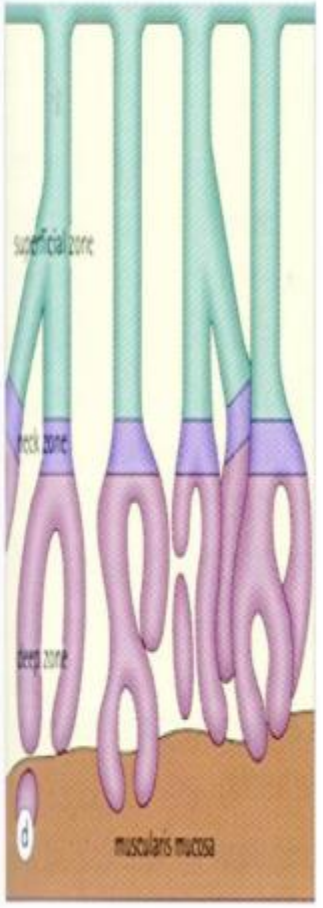
FUNDUS

The pit occupies **1/2** of the height of the entire gland in the pylorus
Branched bottoms of the glands

PYLORUS







1 – epithelium **2** – gastric pit **3** - gland

Functional Histology, 2004

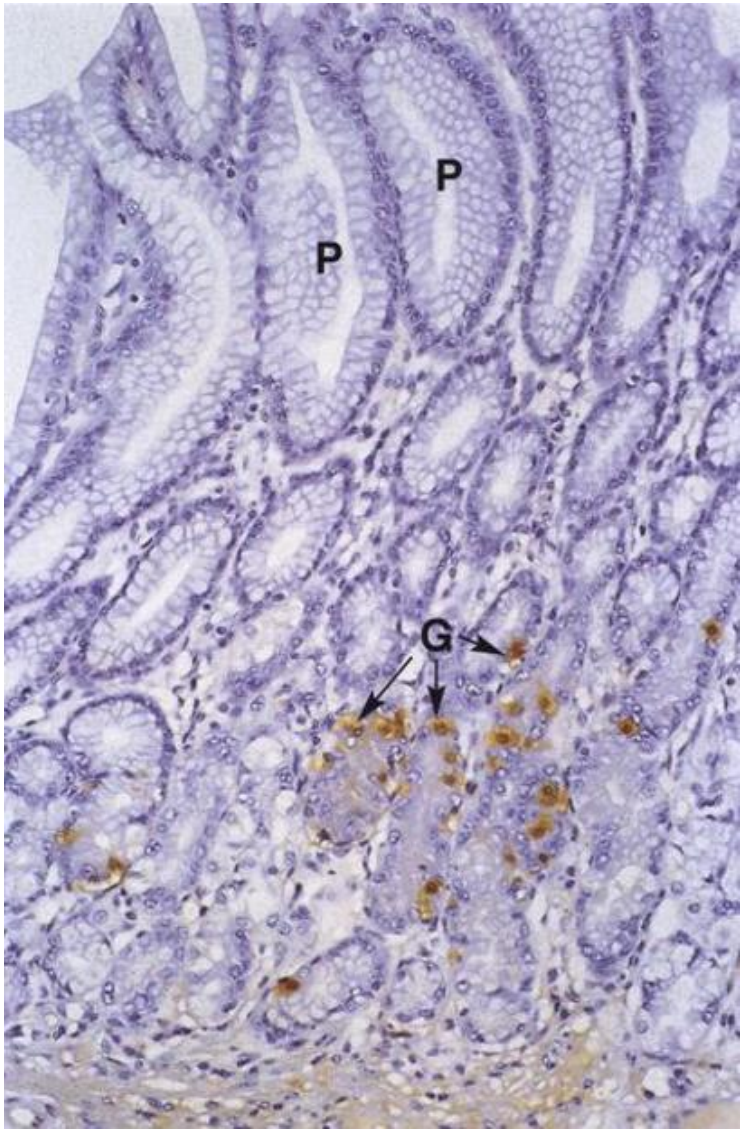
The pyloric glands cover gastric antrum and pylorus and contain:

- gastrin cells (G cells),
- mucous cells,
- some parietal cells.
- other types of endocrine cells.

Gastrin secreted into blood stimulates acid secretion by parietal cells of fundic glands.

Other enteroendocrine cells contribute to gastric secretion.

Gastrin secreting cells (G) in pyloric glands



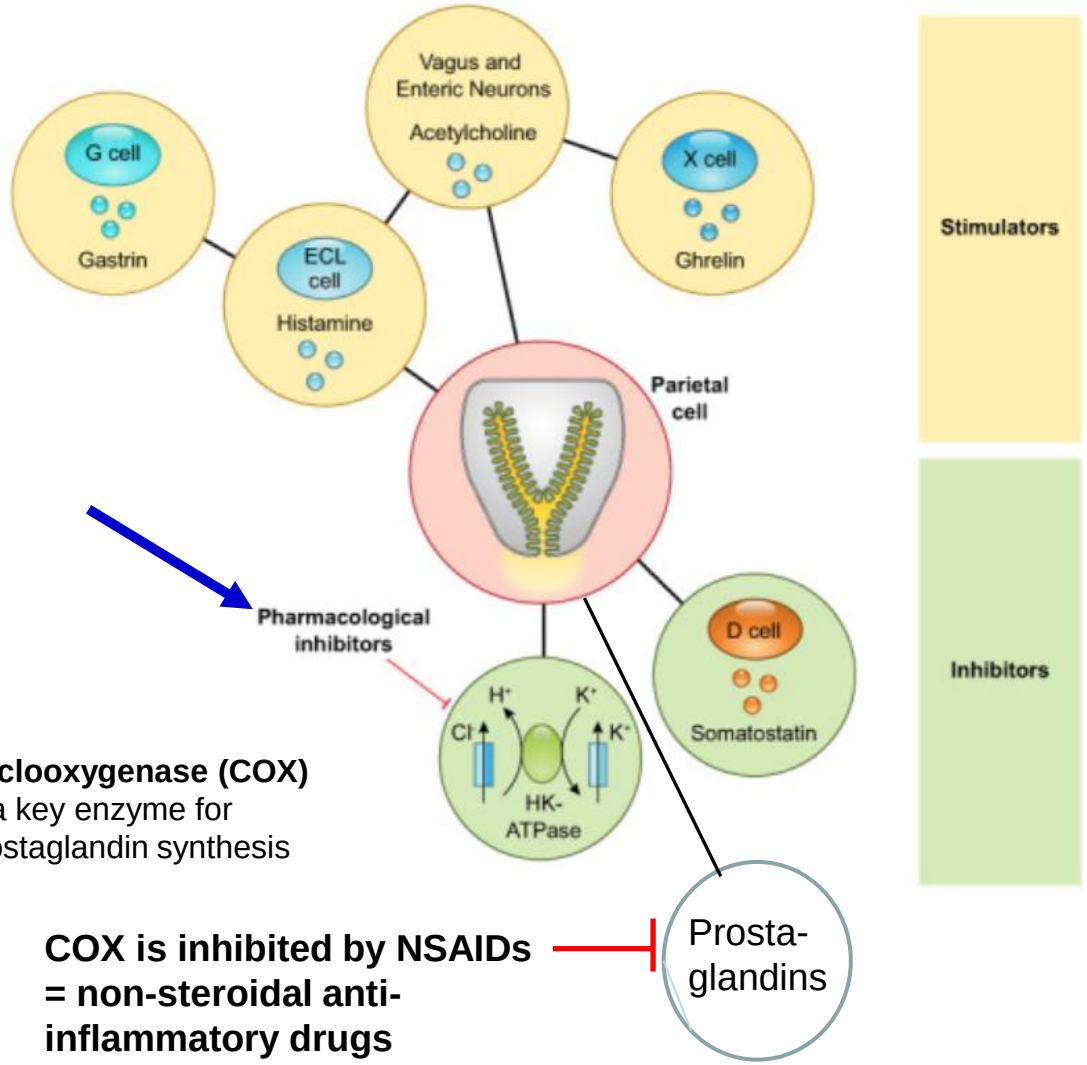
Functional Histology, 2004

The acctivators and inhibitors of gastric parietal cell secretion

Prazols = *proton pump inhibitors*;

histamine H2 receptor blockers (*ranitidine*);

parasympathetic NS antagonists (*atropine*);



Cyclooxygenase (COX) is a key enzyme for prostaglandin synthesis

COX is inhibited by NSAIDs = non-steroidal anti-inflammatory drugs

Prosta-glandins

Physiological Reviews

Physiol Rev. 2020 Apr 1; 100(2): 573–602.
Published online 2019 Oct 31.
doi: 10.1152/physrev.00016.2019

PMCID: PMC7327232
PMID: 31670611

The Physiology of the Gastric Parietal Cell

Amy C. Engevik, Izumi Kaji, and James R. Goldenring

Inhibition of Hydrochloric Acid Release

The hormones **somatostatin**, **prostaglandins**, and **gastric inhibitory peptide (GIP)** inhibit gastric HCl production.

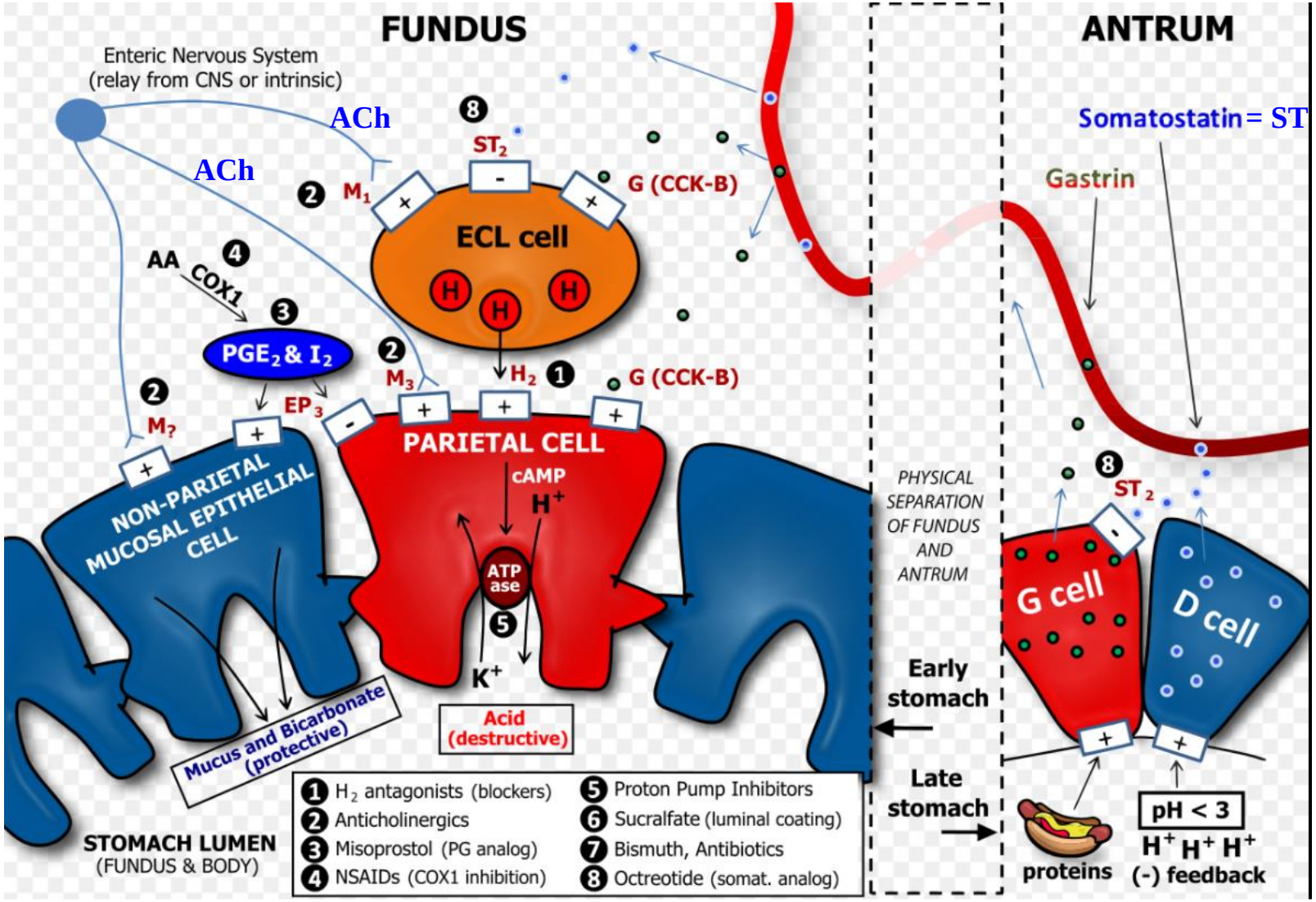
Somatostatin secreted by D cells acts on G cells and ECL cells, inhibiting their release of gastrin and histamine, respectively.

Prostaglandins and GIP act directly on parietal cells and inhibit their ability to produce HCl.

Additionally, **urogastrone (epidermal growth factor)**, produced by Brunner glands of the duodenum, acts directly on parietal cells to inhibit HCl production.

Major determinants of gastric acid secretion

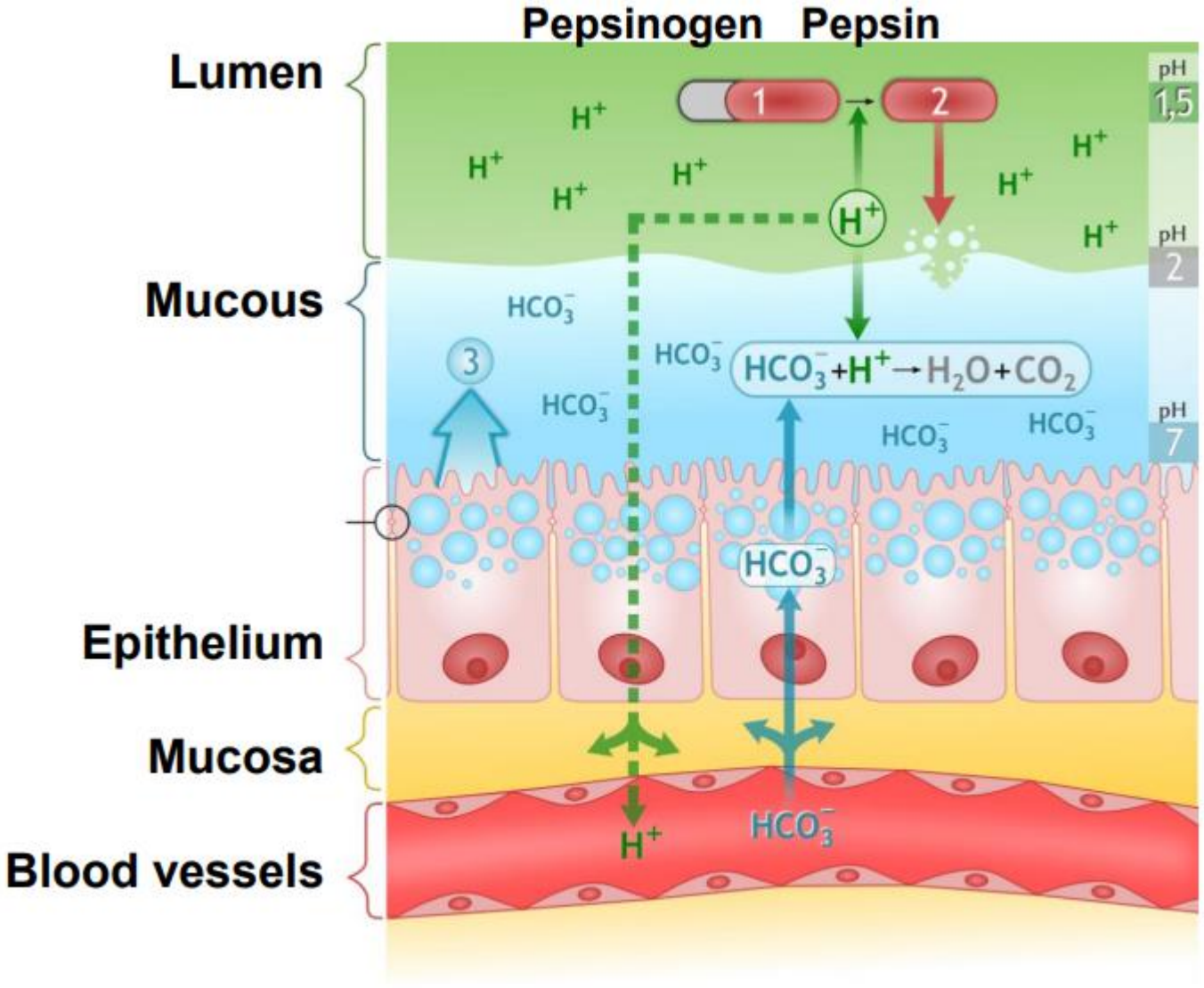
NON-OBLIGATORY



H – histamine; CCK-B cholecystokinin B; G – gastrin; ACh - acetylocholine

Wikipedia.com

How is surface epithelium protected from damage by HCl and pepsin?



Eroschenko VP, 2013

Structural basis of gastroprotection

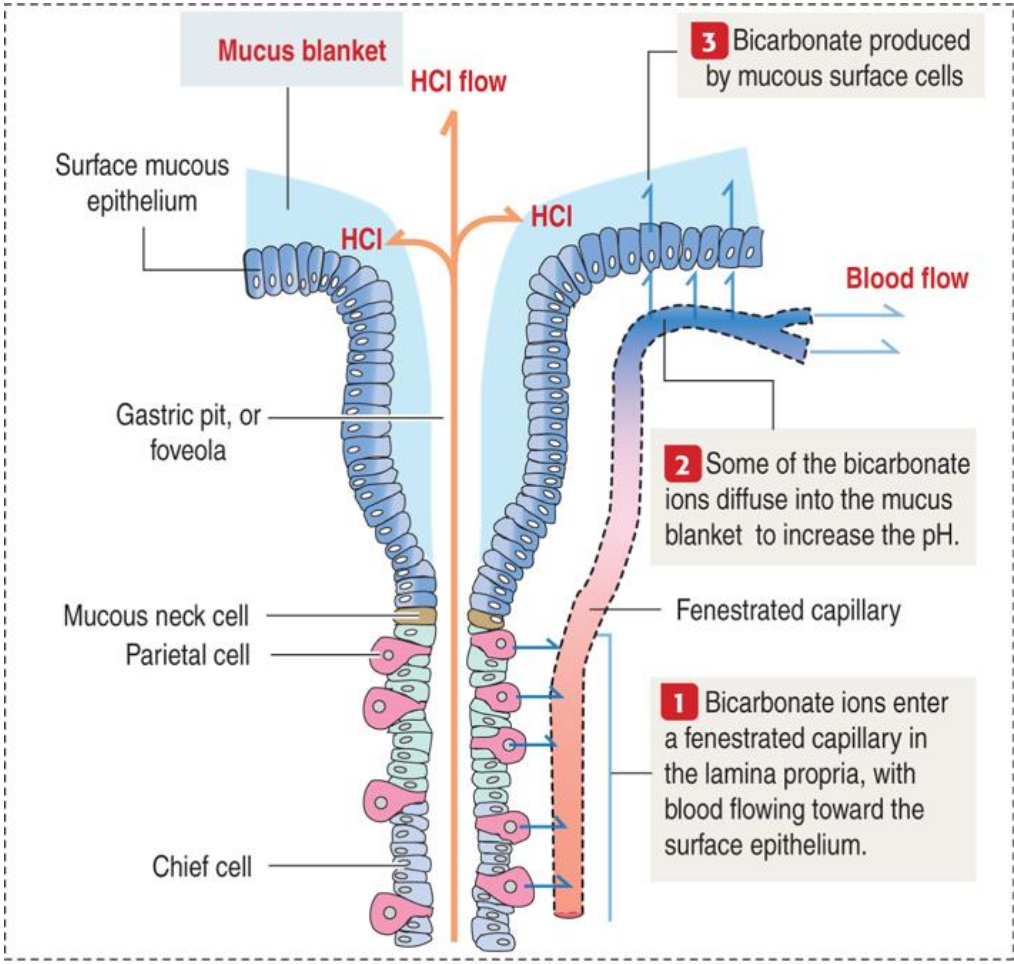
The pH of gastric acid is highly acidic (1-3) what enables the cleavage of the inactive proenzyme, pepsinogen, into the active peptidase, PEPSIN.

Surface mucous cells line the gastric pits and cover the entire lumenal surface of the stomach. They migrate up from the gastric pits and are replaced every 1 to 3 days.

They protect the stomach from injury by acid, pepsin, ingested materials, and pathogens by secreting mucus and HCO_3^- to form a 100 μm thick insoluble protective gel that contains 95% water + 5% of mucins = glycoproteins.

This mucus layer traps bicarbonate ions (HCO_3^-) that diffuse from venous blood and neutralize the microenvironment close to the apical cell surface to ca. pH 7.

Na^+, K^+, and Cl^- are additional components of the protective mucosal barrier.



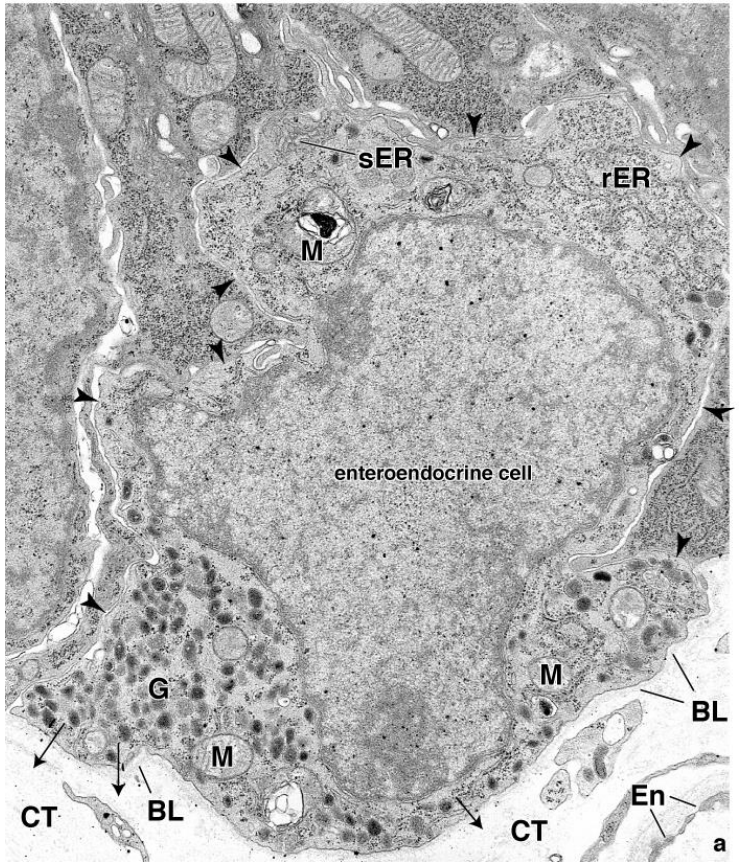
Kierszenbaum & Tres: Histology and Cell Biology: An Introduction to Pathology, 3e
Copyright © 2012 by Mosby, an imprint of Elsevier Inc. All rights reserved.

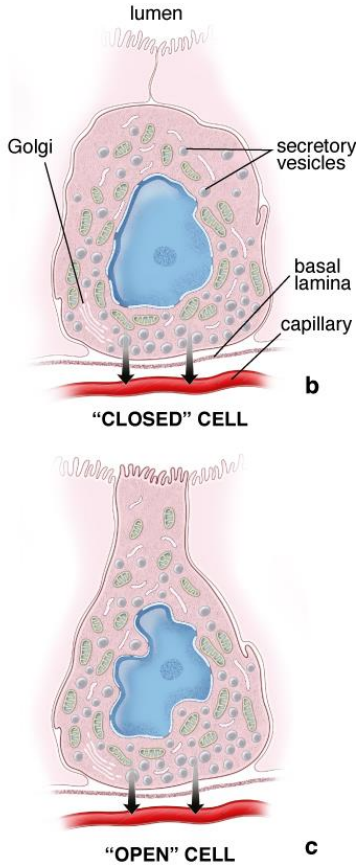
Gastrointestinal hormones (ca. 70) are secreted by enteroendocrine cells (EECs) that arise from embryonic endoderm, like pancreatic islets.

EECs are scattered among the epithelial cells of the mucosal lining of the gut.

EECs with an **open morphology** can sense the composition of chyme (fluid content of gut) and secretions of glands and epithelial cells since its apical membrane is **in a direct contact** with gland or gut lumen (eg. gastric G cells).

Hormones from the various EECs act in a coordinated manner to control gut motility, regulate secretion of enzymes, HCl, bile and other components for digestion, and produce the sense of satiety in the brain.





EEC with closed morphology facilitate sensing of the interstitial environment. Eg. **stomach's D cells** have long, slender processes that terminate on or near parietal and chief cells. These processes presumably mediate the paracrine effect of **somatostatin**.

Each hormone or neurotransmitter affects only those target cells that possess appropriate receptors on their surface.

Endocrine cells of the gastrointestinal tract (DNES cells) are characterized by IHC based on their secretory granule contents

G cells secrete gastrin (stimulates gastric acid secretion)

D cells secrete somatostatin (inhibits secretion)

EC cells secrete serotonin and substance P (stimulate motility in GI tract)

ECL (Enterochromaffin-like) cells secrete histamine, that stimulates gastric acid secretion.

S cells secrete secretin

I cells secrete cholecystokinin (CCK)

EG cells secrete enteroglucagon **NON-OBLIGATORY**

I cells secrete cholecystokinin (CCK)

K cells secrete Gastric Inhibitory Peptide (GIP)

L cells secrete Glucagon-like-Peptide 1 (GLP-1) and peptide YY

Leptin, an adipocyte's hormone that suppresses food intake, is also secreted into stomach's lumen by chief cells, and into blood by small endocrine cells dispersed between gastric pits.

Gastric leptin is involved in the short-term regulation of digestion, including delay of gastric emptying, absorption of nutrients by the intestinal wall and secretion of gastric, intestinal and pancreatic hormones.

Clinical Correlations

1. Possibly the most common cause of **ulcers** in in many developed countries is the prevalent use of the nonsteroidal anti-inflammatory drugs (NSAIDs) **ibuprofen** and **aspirin**. Both of these drugs inhibit the synthesis of prostaglandins, thus precluding their protective effects on the stomach lining.

2. The bacterium ***Helicobacter pylori***, which is localized in the mucus layer protecting the gastric epithelium, has also been implicated as a possible factor in ulcer formation.

3. Almost 12% of cancer-related fatalities are due to **gastric carcinoma**, one of the most common gastrointestinal (GI) malignancies. Although the cancer may be localized to any region of the stomach, usually the region of the lesser curvature and the pyloric antrum are the sites that are most generally involved.

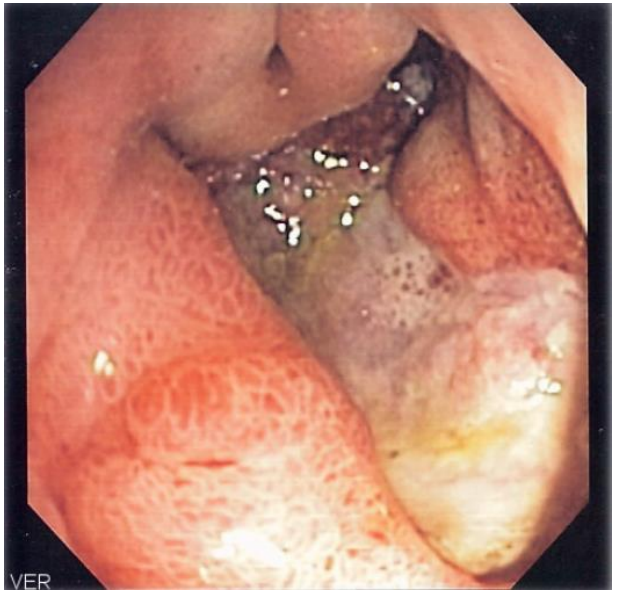
4. Many individuals who had type 2 diabetes and, **due to obesity** or other conditions, underwent **gastric bypass surgery**, experienced a quick reduction in their blood glucose levels. Currently, there is no explanation for this unexpected result, although it has been suggested that hormones released by the DNES cells of the GI tract may play an important role in this outcome.

Peptic ulcer disease (PUD) is a break in the inner lining of the stomach, the first part of the small intestine, or sometimes the lower esophagus.

The most common symptoms of a duodenal ulcer are waking at night with upper abdominal pain and upper abdominal pain that improves with eating. With a gastric ulcer, the pain may worsen with eating.

The pain is often described as a burning or dull ache.[1] Other symptoms include belching, vomiting, weight loss, or poor appetite.[1] About a third of older people have no symptoms.

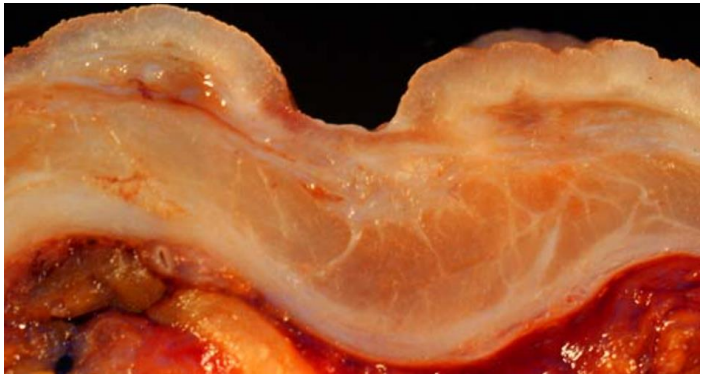
Complications may include bleeding, perforation, and blockage of the stomach. Bleeding occurs in as many as 15% of cases.



Deep gastric ulcer

Common causes include the bacteria *Helicobacter pylori* and non-steroidal anti-inflammatory drugs (NSAIDs). Other, less common causes include tobacco smoking, stress as a result of other serious health conditions, Zollinger–Ellison syndrome, Crohn's disease, and liver cirrhosis.[1][3] Older people are more sensitive to the ulcer-causing effects of NSAIDs.[1]

The diagnosis is typically suspected due to the presenting symptoms with confirmation by either endoscopy or barium swallow.[1] *H. pylori* can be diagnosed by testing the blood for antibodies, a urea breath test, testing the stool for signs of the bacteria, or a biopsy of the stomach.[1] Other conditions that produce similar symptoms include stomach cancer, coronary heart disease, and inflammation of the stomach lining or gallbladder inflammation.[1]



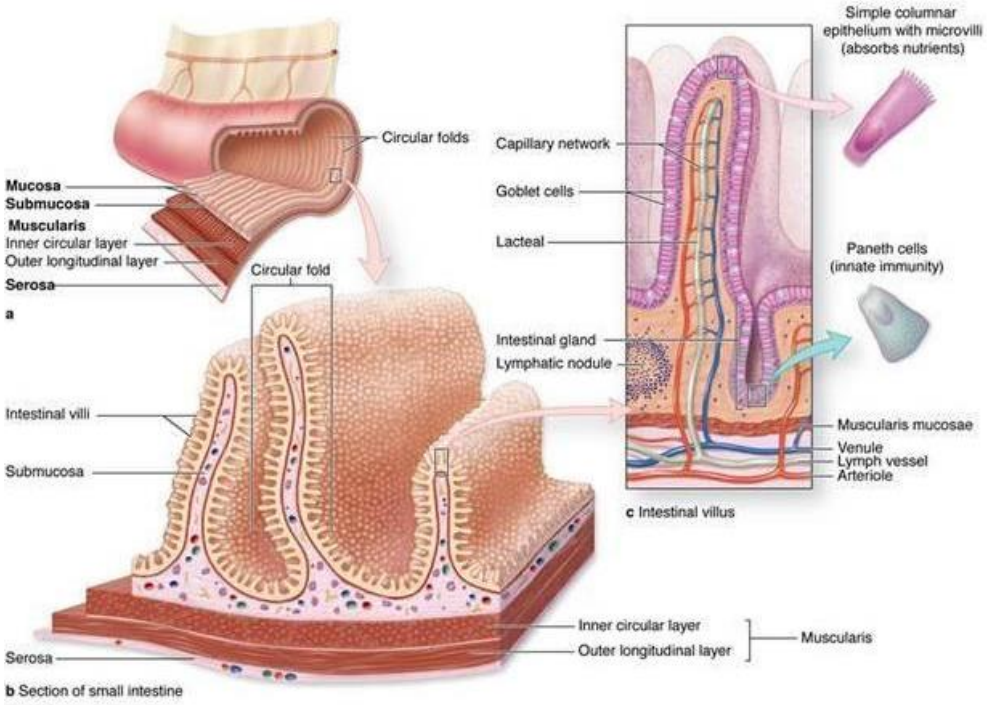
Ed Uthman, MD. - http://web2.airmail.net/uthman/specimens/index.html

SMALL INTESTINE is the longest component of the digestive tract, measuring over 6 m, and is divided into three anatomic portions:

- **Duodenum** (~25 cm long) is the first, shortest, and widest part of the small intestine. It begins at the pylorus of the stomach and ends at the duodenojejunal junction.

- **Jejunum** (~2.5 m long) constitutes the upper two-fifths of the small intestine. **It gradually changes** its morphologic characteristics to become the ileum.

- **Ileum** (~3.5 m long) constitutes the lower three-fifths of the small intestine. It ends at the ileocecal junction, the union of the distal ileum and cecum.



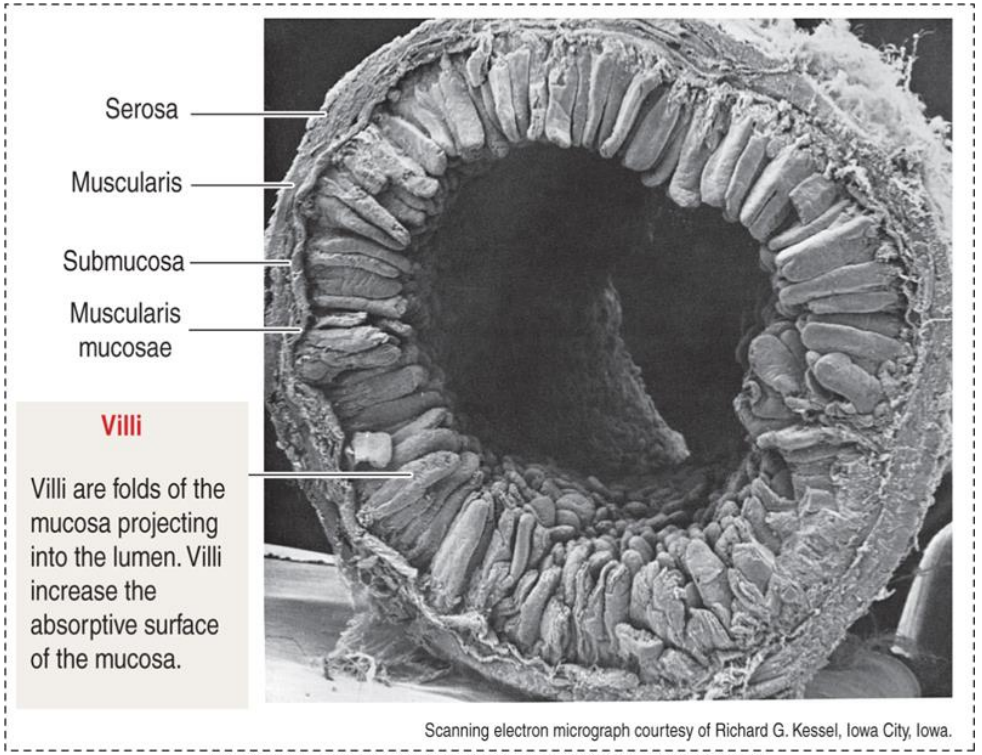
Junqueira's Basic Histology, 12th ed, 2010

The small intestine is the principal site for the digestion of food and absorption of the products of digestion. **Chyme** from the stomach enters the duodenum, where enzymes from the pancreas and bile from the liver are also delivered to continue the solubilization and digestion process.
Enzymes, particularly **disaccharidases and dipeptidases**, are also located in the **glycocalyx of the microvilli of the enterocytes**. These enzymes complete the breakdown of most sugars and proteins to monosaccharides and amino acids, which are then absorbed.

STRUCTURES THAT INCREASE ABSORPTION SURFACE IN A SMALL INTESTINE:

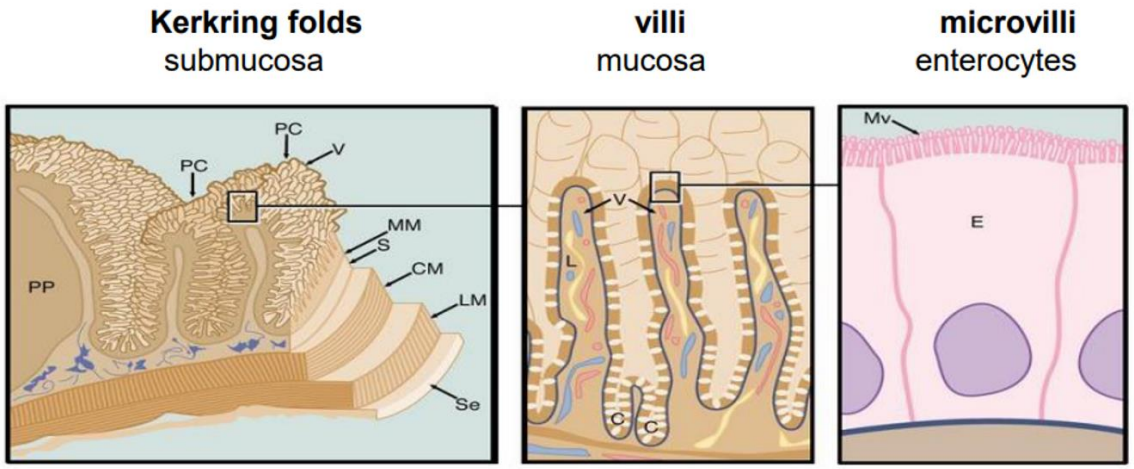
- plicae circulares (= Kerkring folds) made of submucosa) ,
- - villi (mucosa) and
- microvilli (invaginations of cell membrane.

They increase the absorption surface 2-3, 10, and 20 times, respectively.



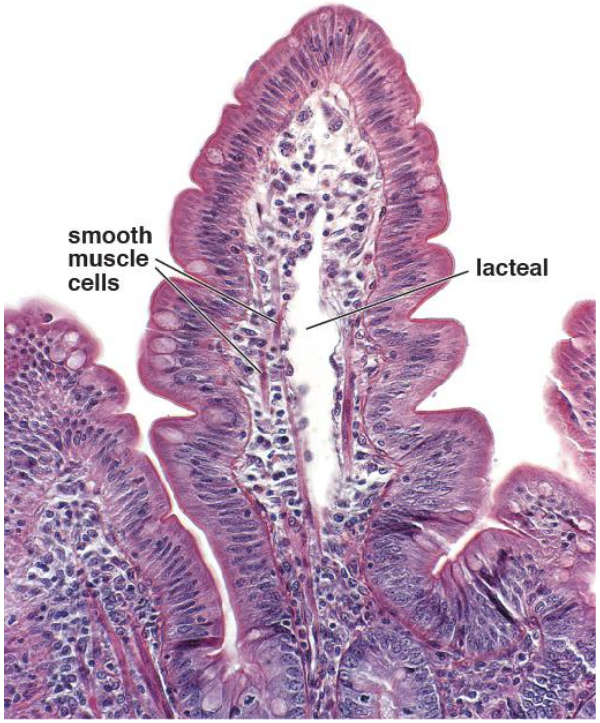
Scanning electron micrograph courtesy of Richard G. Kessel, Iowa City, Iowa.

Kierszenbaum & Tres: Histology and Cell Biology: An Introduction to Pathology, 3e
Copyright © 2012 by Mosby, an imprint of Elsevier Inc. All rights reserved.



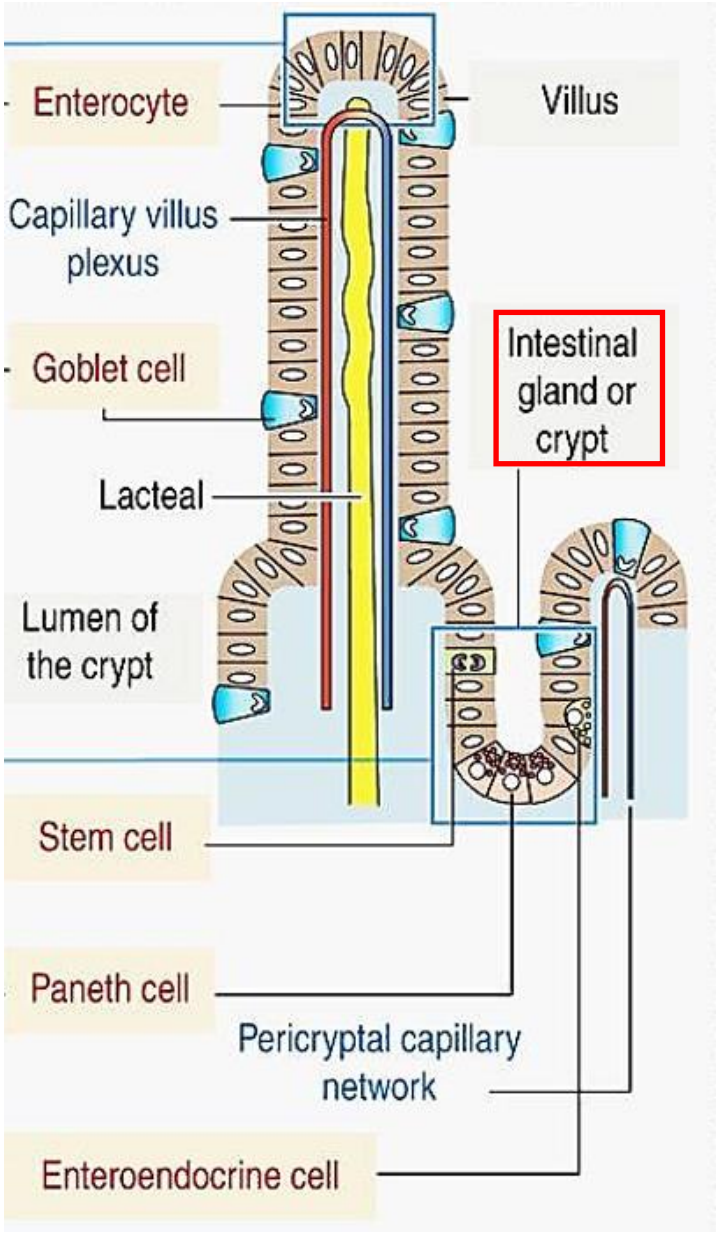
Eroschenko, 2013

There are 7 main cell types in the intestinal epithelium



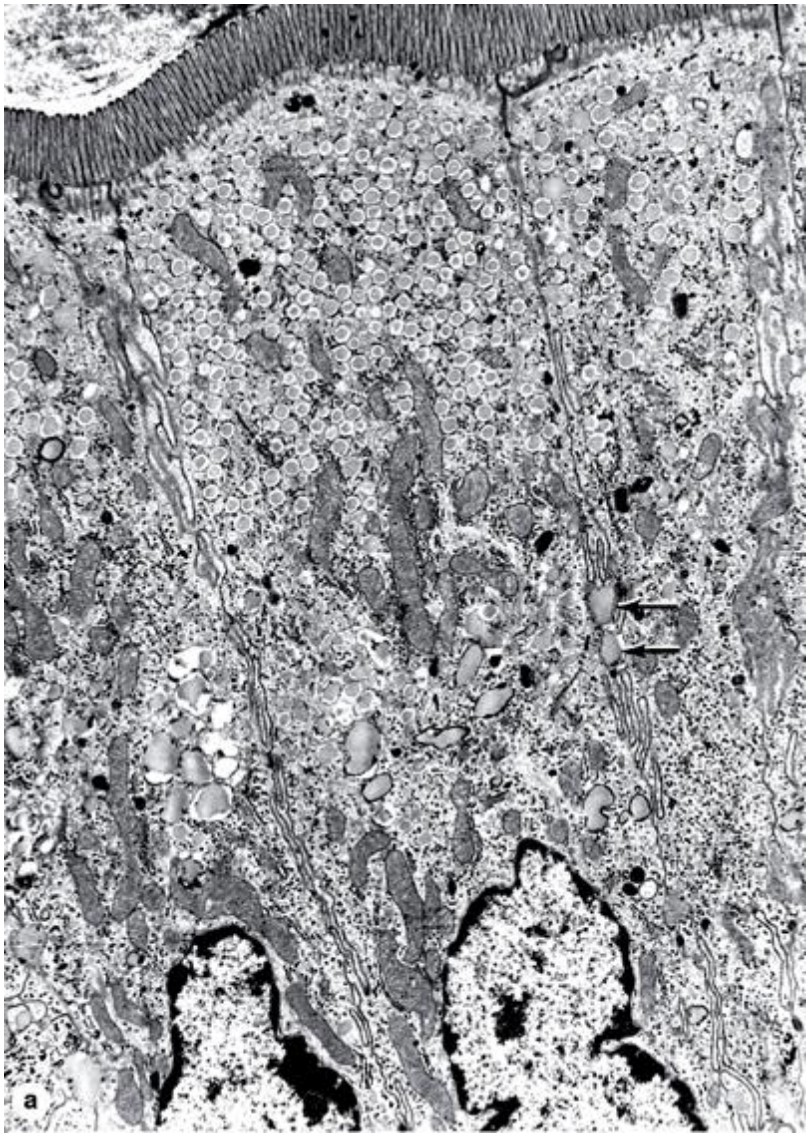
Pawlina, Histology, 8th ed.

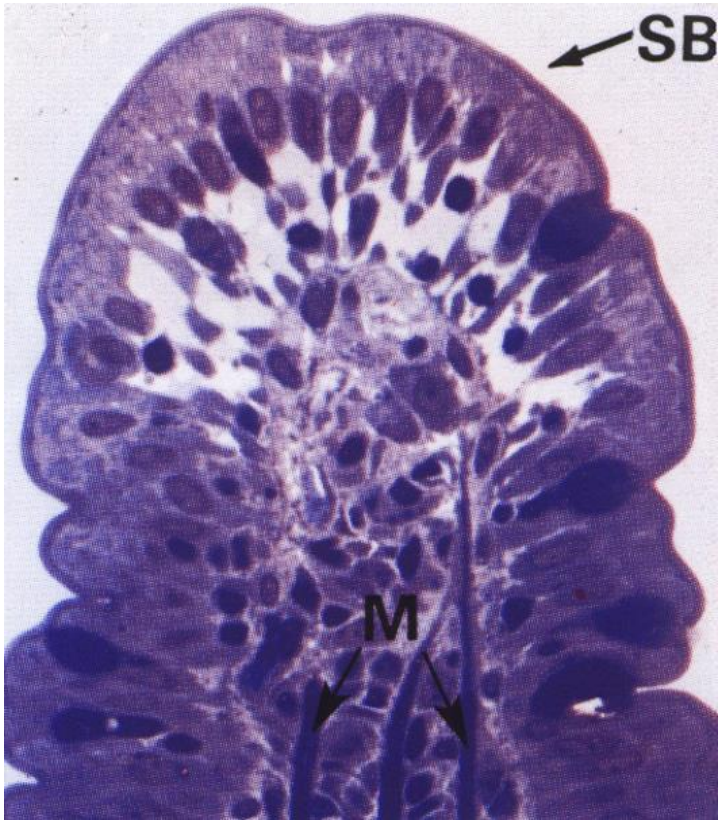
- Enterocytes
- Goblet
- Paneth
- Enteroendocrine (DNES)
- M (microfold) – antigen-transporting cells
- **Stem cells**
- Lymphocytes



Kierszenbaum, 3d ed.

- **Enterocytes are resorptive cells. They take up basic food components: simple sugars, amino acids, pyrymidines and purines, glycerol and fatty acis.**
- **They are tall columnar cells with numerous mitochondria, abundant SER, RER, and Golgi complex, and many endocytotic vesicles.**

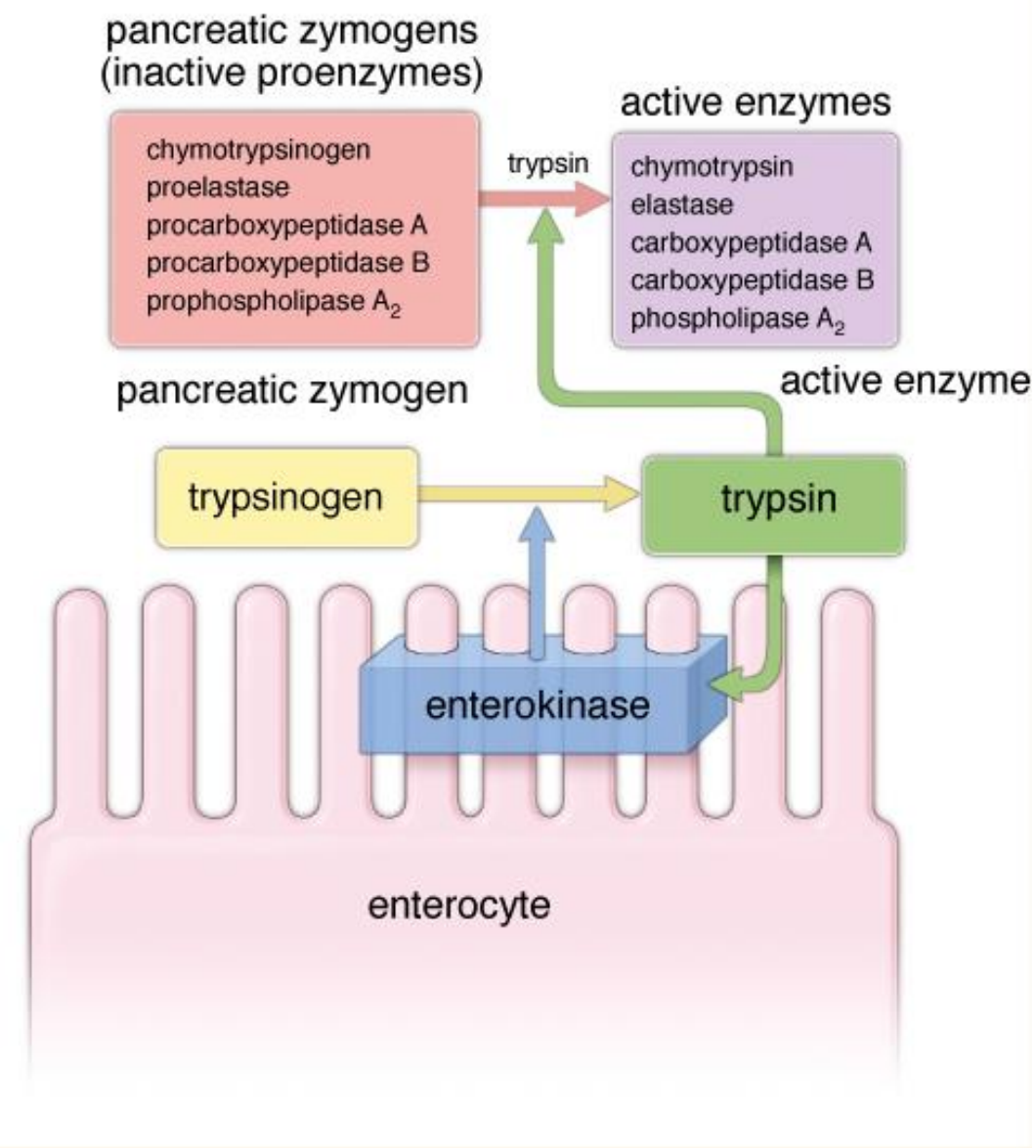




Functional Histology, 2004

STRIATED or BRUSH BORDER (SB) is a thin layer visible in light microscope. It is the uppermost part of enterocyte's cell membrane made by exceptionally long microvilli.

Enterokinase located in the plasma membrane of enterocytes' microvilli activates trypsinogen to trypsin which in turn activates other proenzymes present in the pancreatic juice

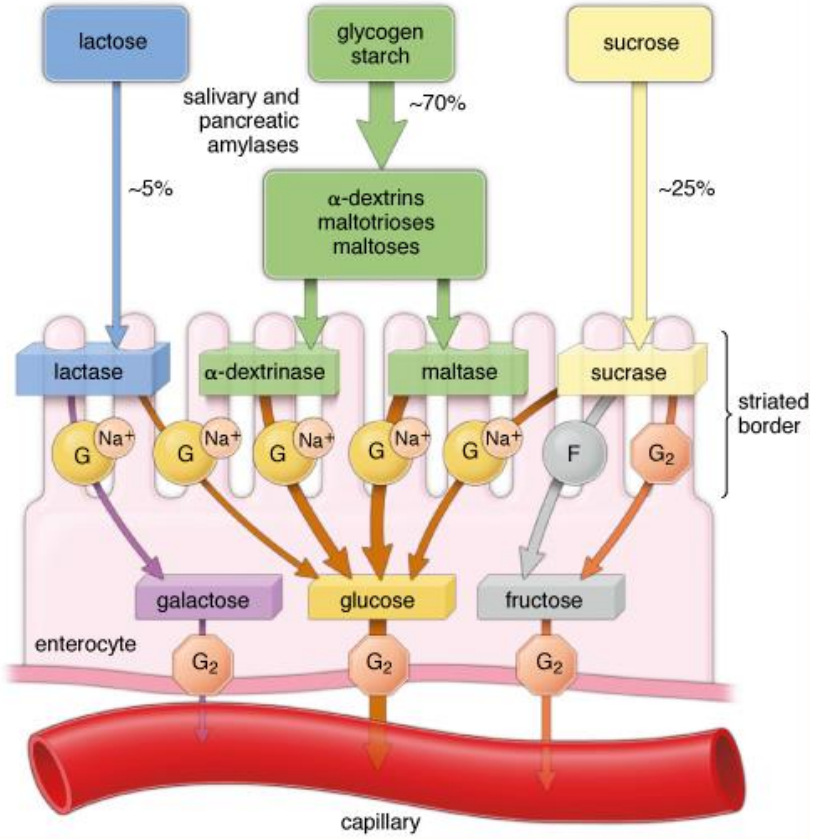


Pawlina, Histology, 7th ed.

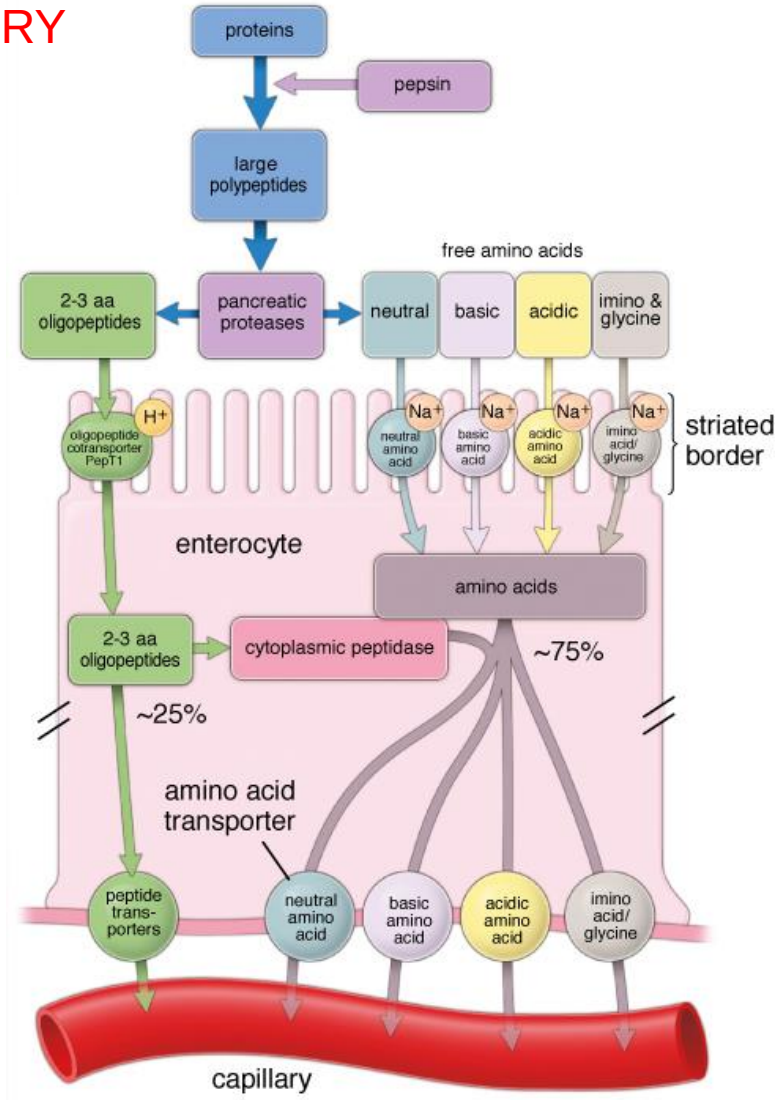
Digestive and Absorptive Functions of Enterocytes

NON-OBLIGATORY

Poly-, oligo- and disaccharides



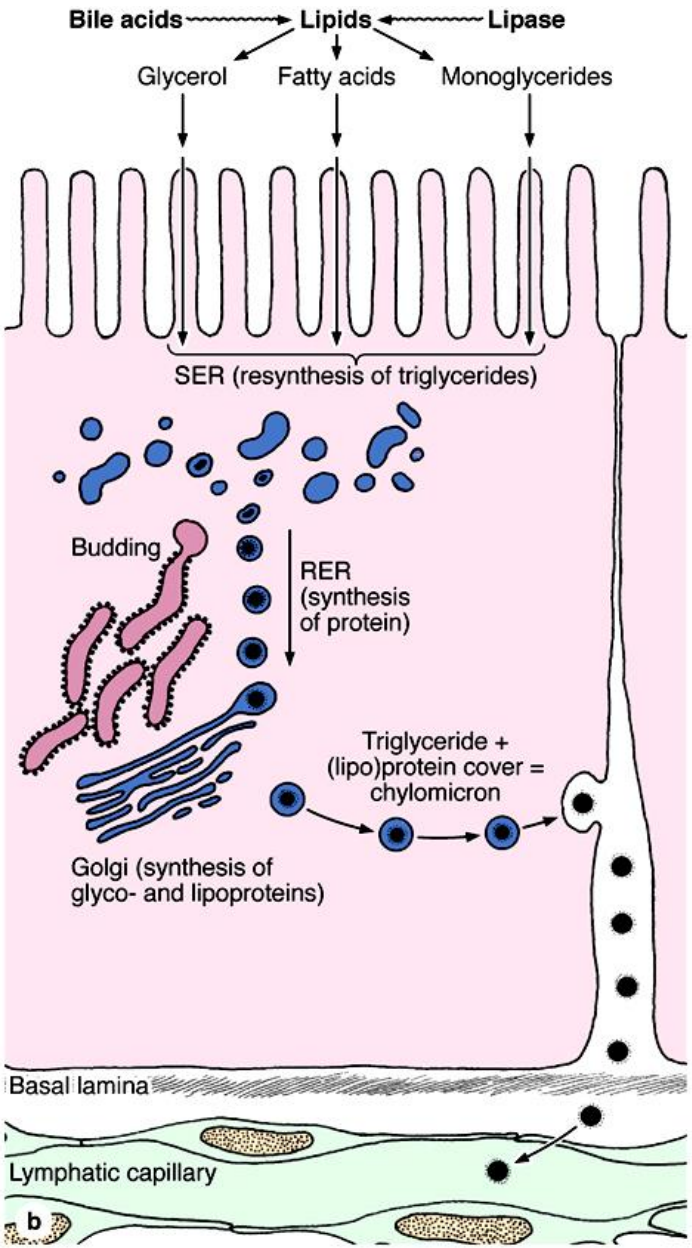
Proteins and peptides

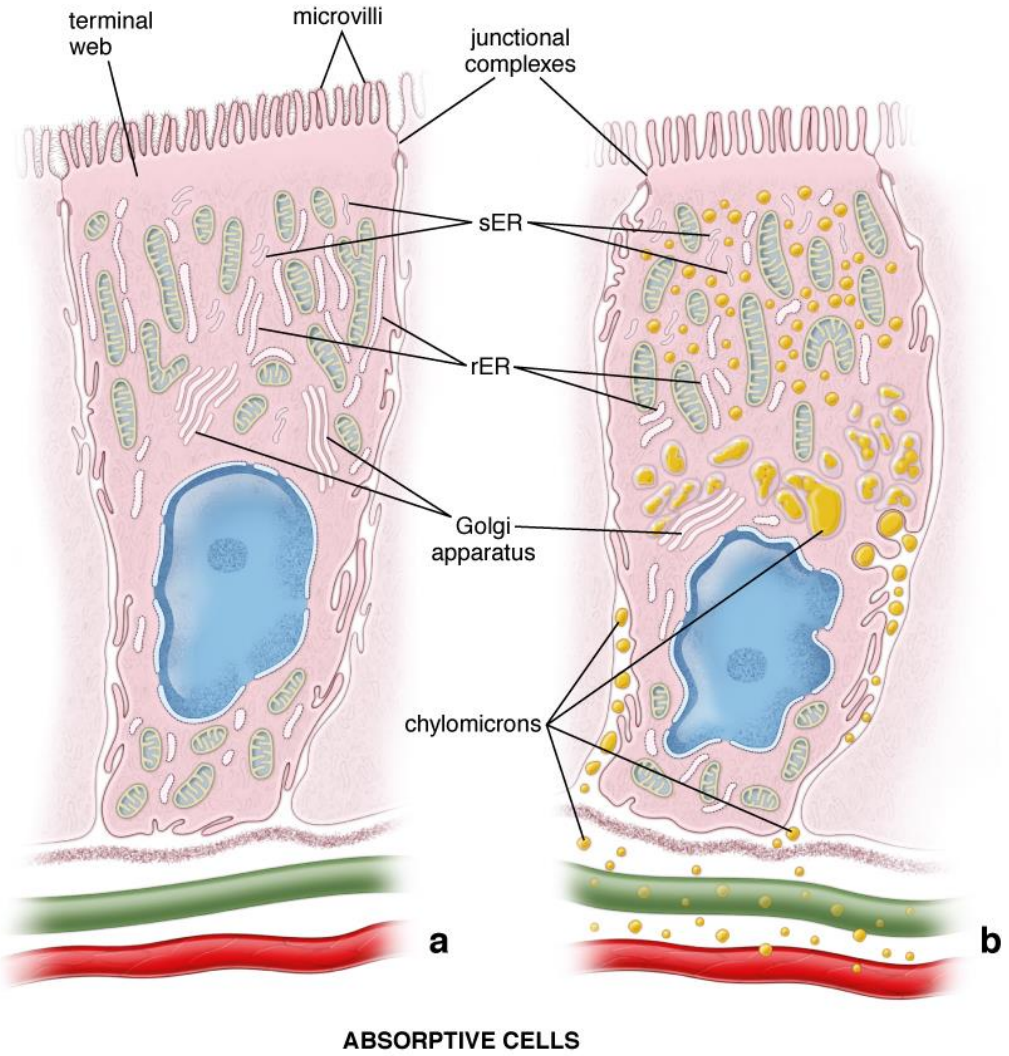


Pawlina, Histology, 7th ed.

G, SGLT1 Na+ dependent glucose and galactose transporters; F, GLUT5 fructose transporter, G2, GLUT2 transporters

The apical plasma membrane of the enterocytes bears at least four **Na^+-amino acid cotransporters**.
The **dipeptides and tripeptides** are transported across the apical membrane into the cell cytoplasm by the H^+-oligopeptide cotransporter (PepT1)





Fasted state

Resorptive state

Resorption of fat as **chylomicrons** into lymph

Lipid absorption and processing by enterocytes

Pawlina, Histology, 8th ed.

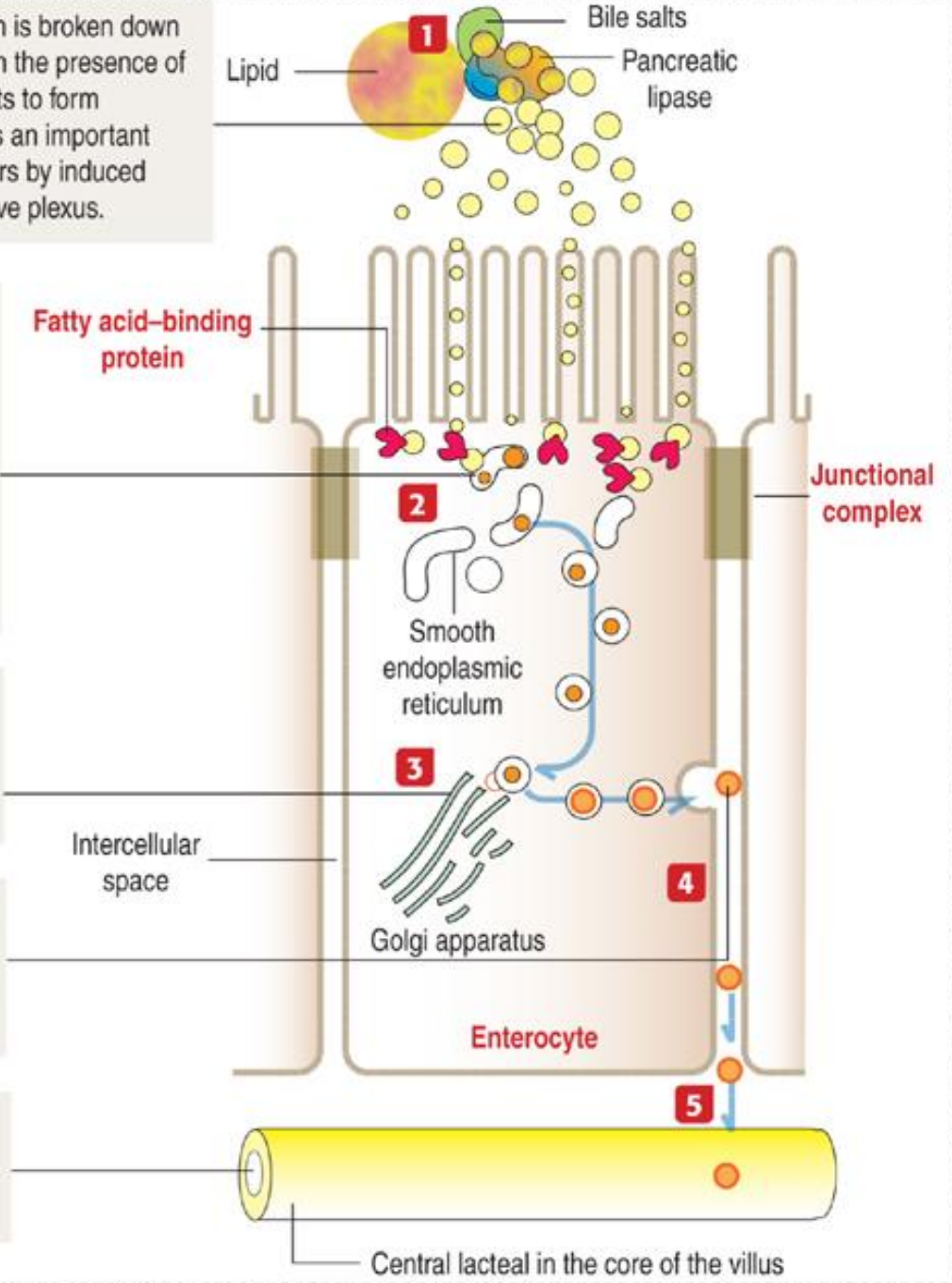
1 An emulsion of lipid droplets in the intestinal lumen is broken down to fatty acids and monoglycerides by pancreatic lipase in the presence of bile salts. Fat breakdown products combine with bile salts to form **micelles** (2 nm in diameter). The movement of the villi is an important part of the lipid absorption process. Villi movement occurs by induced contraction triggered by the submucosal Meissner's nerve plexus.

2 Fatty acids and monoglycerides diffuse into the microvilli and apical cytoplasm of the enterocyte —bound to **fatty acid–binding proteins (FABPs)**—where they are esterified to form triglycerides in the **smooth endoplasmic reticulum**. Enzymes required for the resynthesis of triglycerides (**acyl-CoA synthetase** and **acyltransferases**) are present in the membranes of the smooth endoplasmic reticulum.

3 Resynthesized triglycerides are transported to the **Golgi apparatus** for further conversion into **chylomicrons**, an **apoprotein-lipid complex**.

4 In the Golgi apparatus, chylomicrons are invested by a membrane that enables the vesicle to fuse with the plasma membrane of the basolateral domain of the enterocyte.

5 Chylomicrons are discharged into the intercellular space and into the **central lacteal**, a lymphatic vessel present in the lamina propria of the villus.

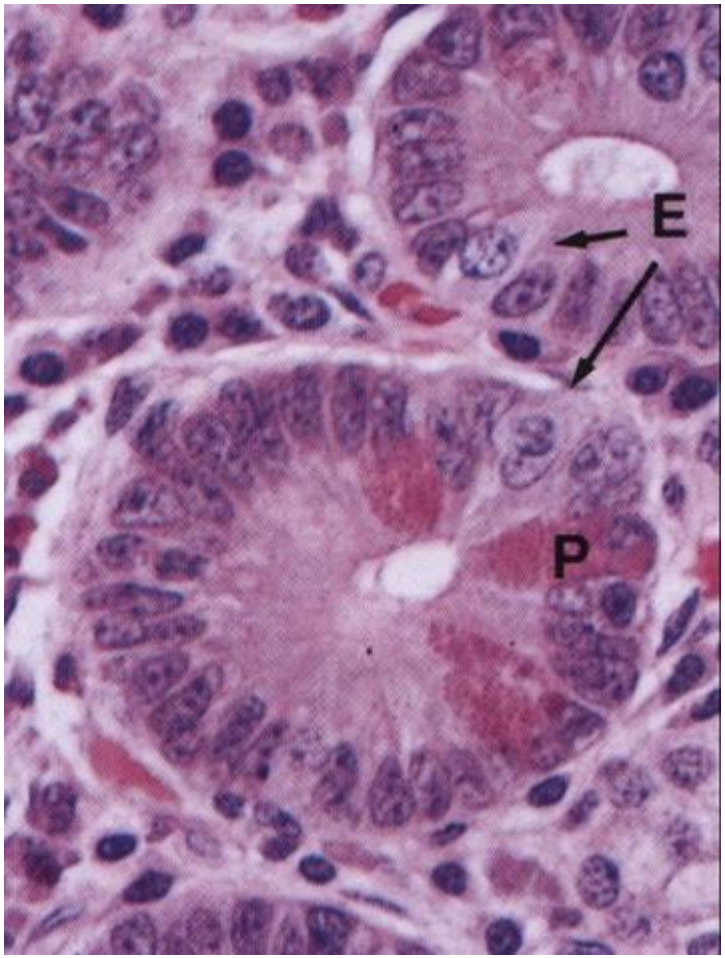


Kierszenbaum & Tres: Histology and Cell Biology: An Introduction to Pathology, 3e
Copyright © 2012 by Mosby, an imprint of Elsevier Inc. All rights reserved.

Intestinal crypts contain stem cells, located in the basal half of the crypts, that divide to replace themselves and the other types of epithelial cells.

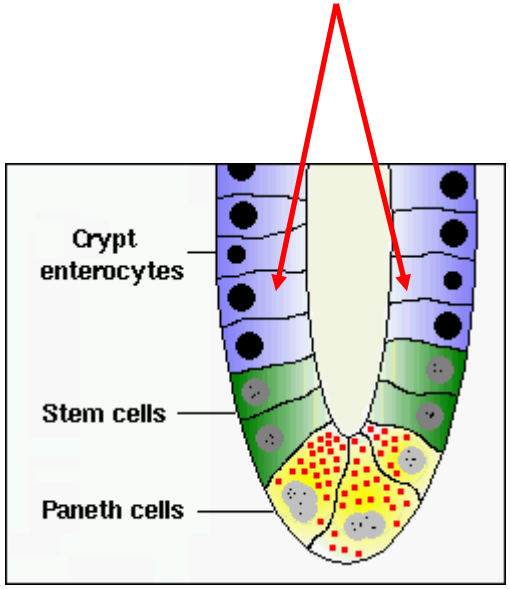
The largest population of crypt cells are highly proliferating *intermediate cells*.

They are localized UP the stem cells.



Functional Histology, 2004

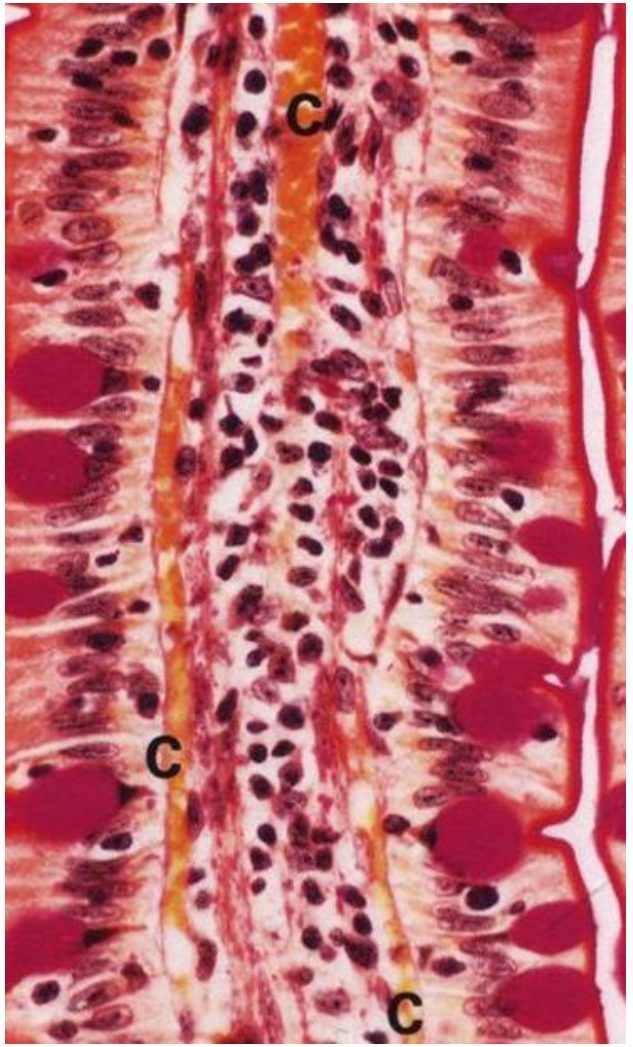
Endocrine (E) and Paneth's (P) cells at the bottom of two crypts.



Paneth cell granules contain antibacterial agents: defensins (small peptides), lysozyme, phospholipase A, and they secrete TNF (tumor necrosis factor), a proinflammatory cytokine.

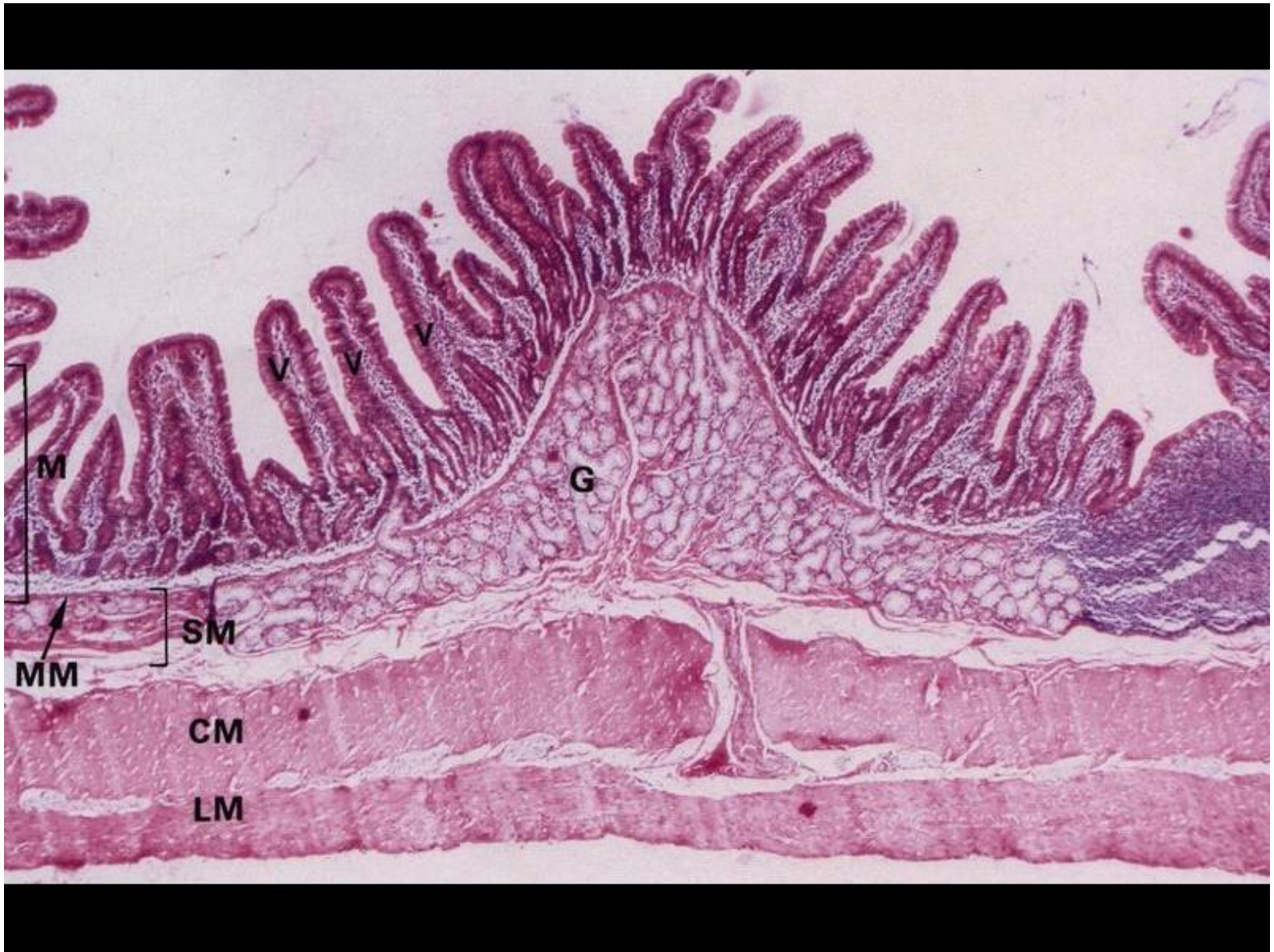
Villi's lamina propria contains:

- multiple plasmocytes that secrete IgA
- numerous lymphocytes
- macrophages
- fibroblasts
- mast cells
- myocytes
- nerve endings,
- blood and lymph vessels
- *lymphoid nodules*.



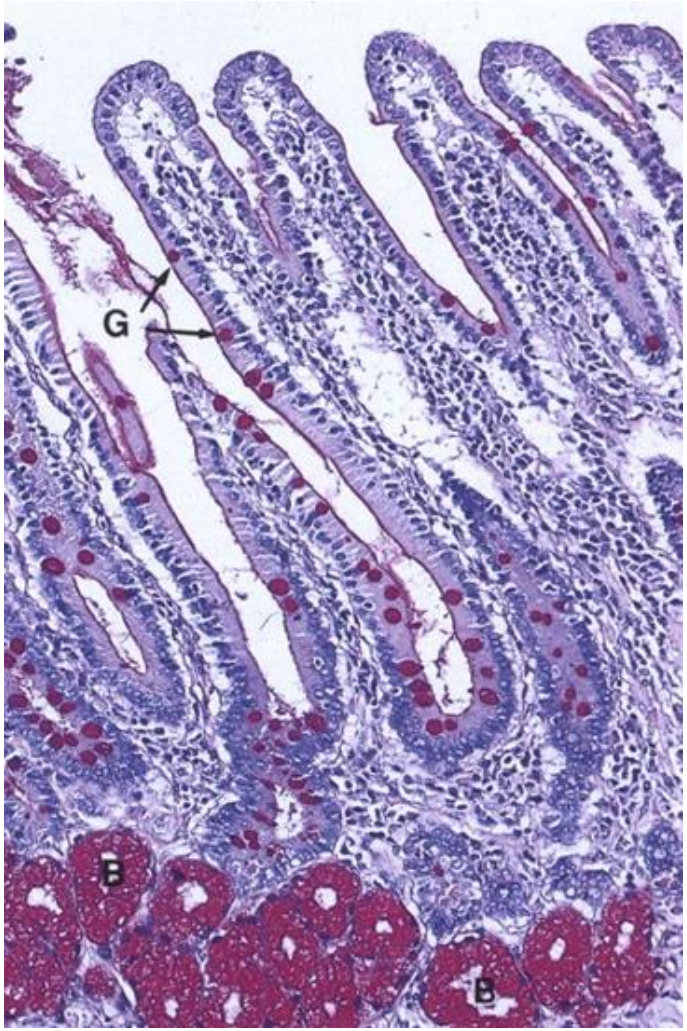
Functional Histology, 2004

Wall of the duodenum: villi made by mucosa, submucosa contains muco-serous Brunner glands, two muscle layers

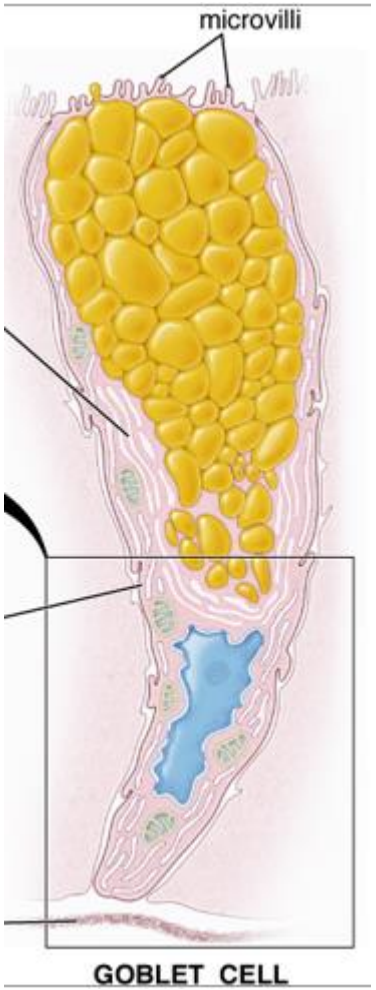


Functional Histology 2004

The number of goblet cells increases distaly in intestine's epithelium, there are only a few in duodenum. Goblet cells make majority of epithelial cells in colon. pAS staining + hematoxylin.



Functional Histology, 2004



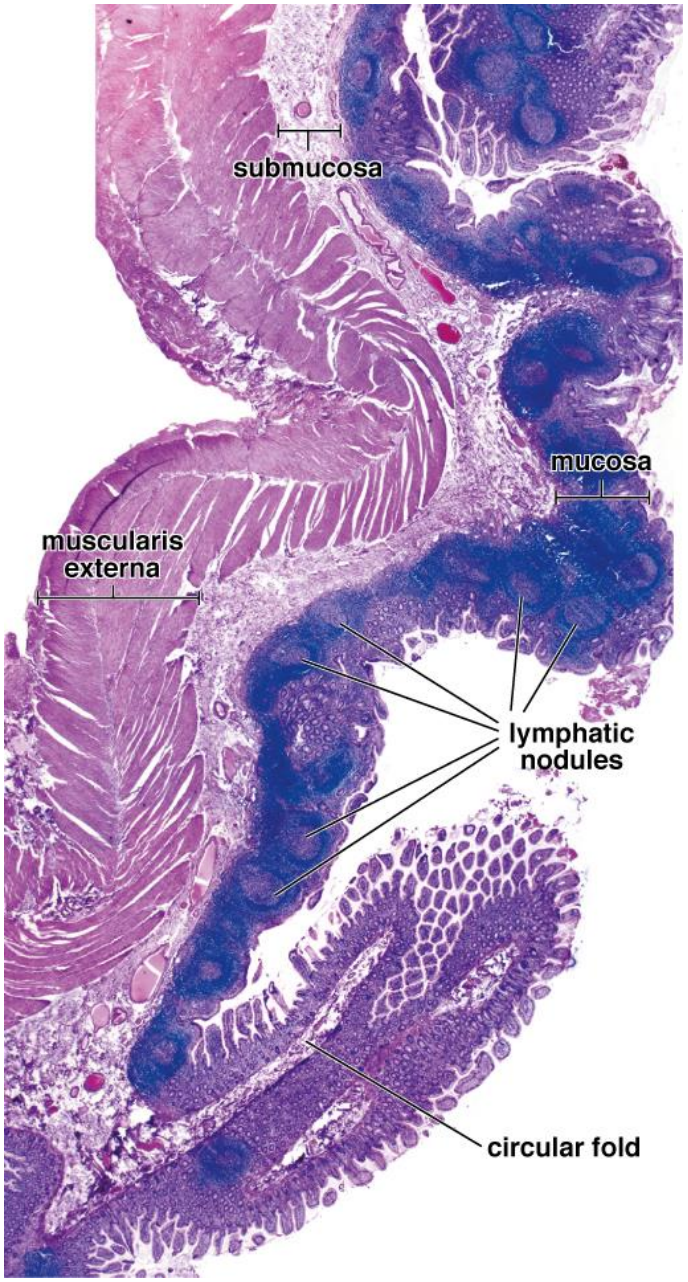
Peyer’s patches (PPs)

The **lamina propria** of the small intestine contains numerous **lymphatic nodules** that represent a major component of the GALT. Many of the nodules may extend into the submucosa.

They are particularly large and numerous in the **ileum** and are named **aggregated nodules** or **Peyer’s patches**. Besides, there are also **many lymphocytes** in the lamina propria and in epithelium.

Over the PPs there are none or only a limited number of villi, and the lining epithelium contains many antigen-transporting **M cells** (also enterocytes and goblet cells).

PPs are preferentially located on the side of the intestine opposite the mesenteric attachment.



Longitudinal section through the wall of a human ileum, 40x. Pawlina, 2020.

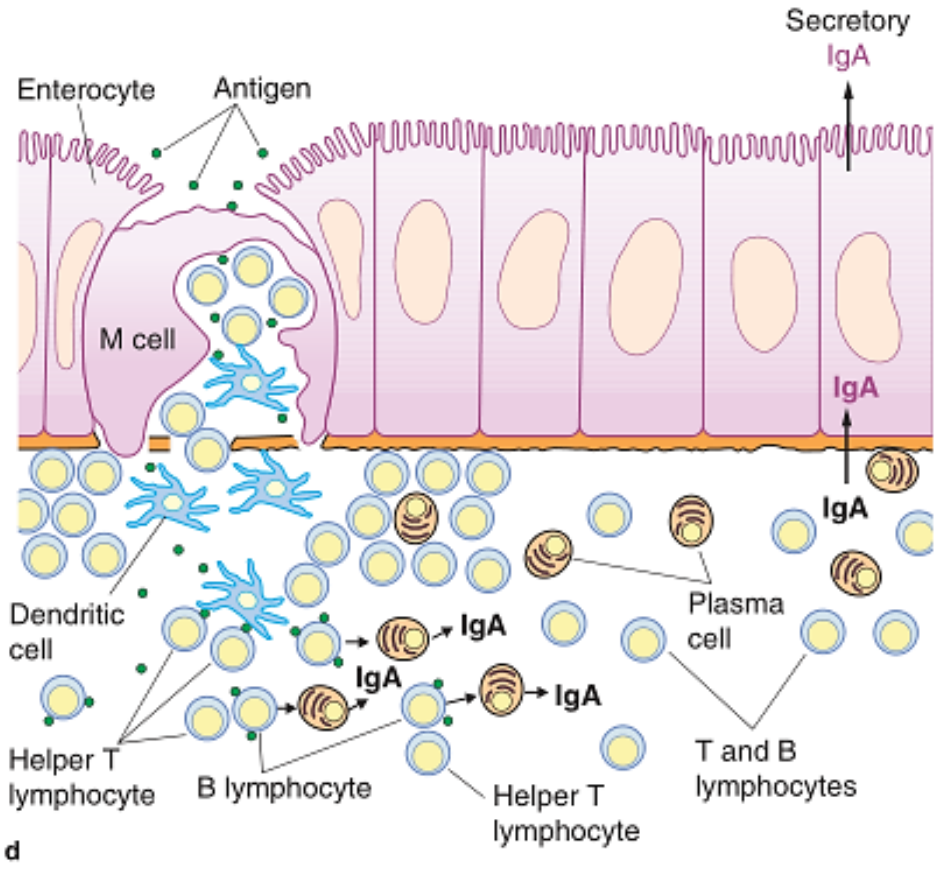
The role of antigen-transporting M cells in gut immunity

Antigens in the gut lumen are bound by M cells and undergo transcytosis into their intraepithelial pockets where dendritic cells/macrophages take up the antygen and process it. Then, these cells are transported with lymph into the **local intestinal lymph node**s.

Here, the antigens are present to **naive B and T helper cells**. The antigen-specific B cells return with blood into the intestinal mucosa and differentiate into antigen-specific plasma cells secreting IgA antibodies.

The **dimeric IgA** is taken up by gut epithelial cell by binding to its polymeric Ig receptor. The **secretory component (SC)**, part of the receptor's molecule, binds to IgA and in this form it is transported into the gut lumen.

Here it binds the specific antigen on the surface of microorganisms, neutralizing potentially harmful invaders before they penetrate the mucosa.

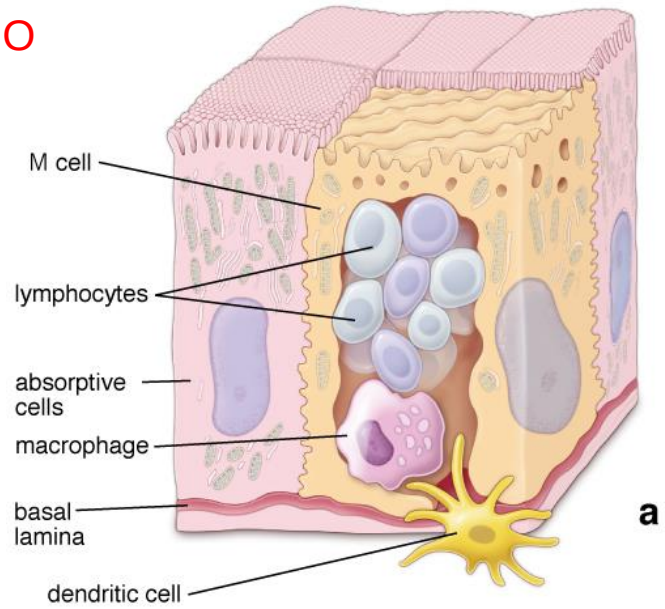


Gartner, 3rd ed.

M (microfold) cells are located in the epithelium that covers lymphatic nodules in the lamina propria. They convey microorganisms and other macromolecules from the intestinal lumen to Peyer's patches.

NON-OBLIGATORY = NO

SEM of a Peyer's patch lymphatic nodule bulging into the lumen of the ileum. **The area of the follicle covered by M cells** is surrounded by the finger-like projections of the intestinal villi. The surface of the M cells has a **smooth appearance**. The absence of absorptive cells and mucus-producing goblet cells in the area covered by M cells facilitates immunoreactions to antigens. ×80.



Pawlina, Histology, 8th ed.

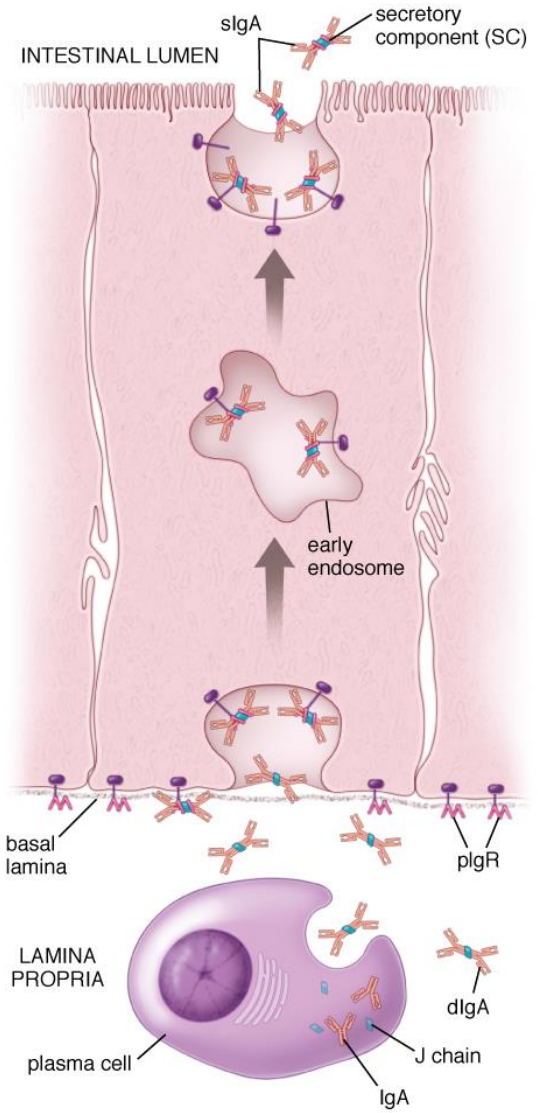
M cells have a characteristic shape because each cell develops a deep pocket-like recess connected to the extra-cellular space. Dendritic cells, macrophages, and T and B lymphocytes reside in this space. Due to this unique shape, the basolateral cell surface of the M cell resides within a few microns of its apical surface, greatly reducing the distance that endocytic vesicles must travel to cross the epithelial barrier. On their apical surface, M cells have **microfolds** rather than microvilli and a thin layer of glycocalyx. The apical surface expresses an abundance of glycoprotein 2 (GP2) receptors that bind specific macromolecules and Gram-negative bacteria, Substances bound to GP2 receptors are internalized in endocytic vesicles and transported to the basolateral cell surface of the pocket-like recess. Within the recess, the released contents are immediately transferred to immune cells residing in this space. Thus, M cells function as highly specialized **antigen-transporting cells** that relocate intact antigens from the intestinal lumen across the epithelial barrier. Antigens that reach the immune cells in this manner **will at the end stimulate antigen-specific response of B cells and plasmocytes as well as Th cells**.

Most of the plasma cells in the lamina propria of the intestine secrete dimeric **(dIgA) antibodies**. dIgA is composed of two monomeric IgA subunits and a polypeptide J chain. The dIgA molecules secreted by B cells/plasmocytes in the subepithelial lamina propria, bind to the **polymeric Ig receptor (pIgR)** located in the basal domain of the epithelial cells' plasma membrane.

The pIgR–dIgA complex is then endocytosed and transported via transcytosis to the apical surface of the enterocyte.
After the pIgR–dIgA complex reaches the apical surface, pIgR is proteolytically cleaved and the extracellular part of the receptor that is bound to dIgA is released into the gut lumen.

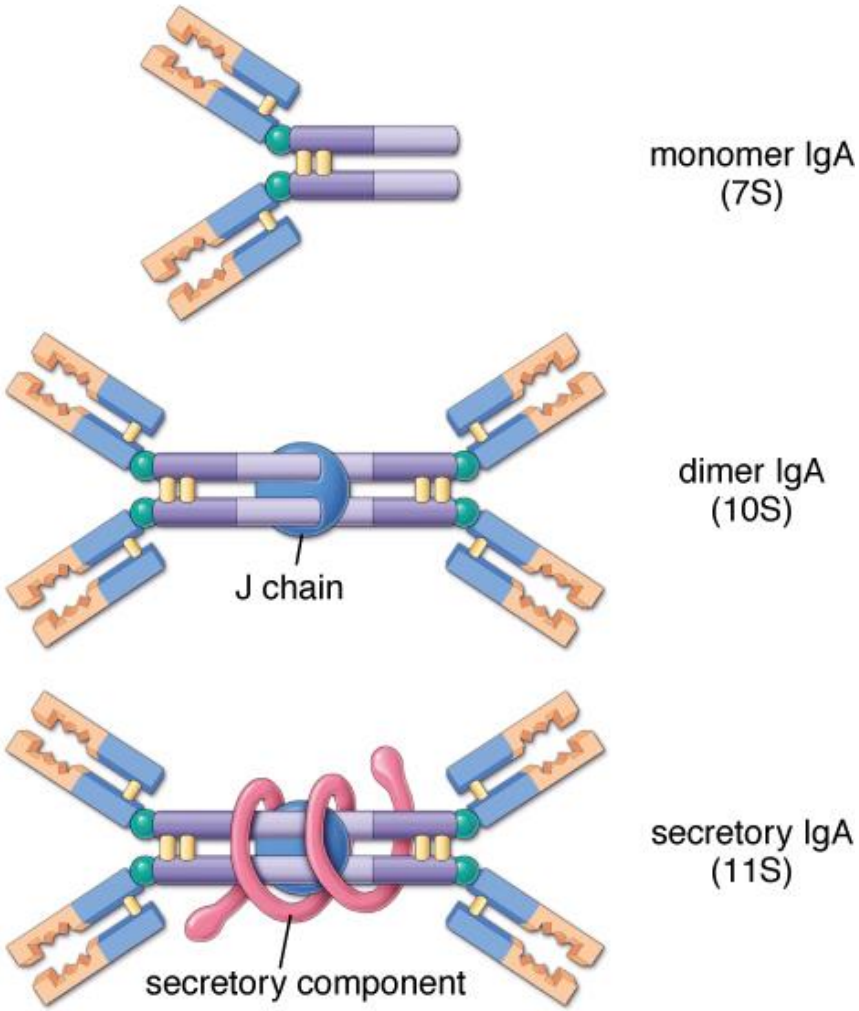
This cleaved extracellular binding domain of the receptor is known as the **SECRETORY COMPONENT (SC);** secreted dIgA in association with the SC is known as **SECRETORY IgA (sIgA)**.

The release of sIgAs is critical for proper **immunologic surveillance** by the mucosal immune system.
In the gut lumen, **sIgA binds to antigens, toxins, and microorganisms. Secretory IgA prevents the attachment and invasion of viruses and bacteria into the mucosa by either inhibiting their motility, causing microbial aggregation, or masking pathogen adhesion sites on the epithelial surface**.
For example, sIgA binds to a glycoprotein on the viral envelope of **HIV**, preventing its attachment, internalization, and subsequent replication in the cell.



Pawlina, Histology, 8th ed.

Diagram of different forms of immunoglobulin A (IgA)



Pawlina W, Histology, 2020

Monomer of IgA produced by B cells/ plasmocytes is shown at the *top*.

The dimer of IgA is a product of the plasma cell and contains a glycoprotein, **J chain (*J*)** connecting two monomers (*middle*).

The secretory component (*SC*), a product of a proteolytically cleaved pIgR (*polymeric Ig receptor present in the basal domain of epithelial cells*) is added to the dimer during its receptor-mediated endocytosis to form **secretory IgA (sIgA**; *bottom*).

sIgA is the main Ig present in the natural secretions of epithelial cells such as saliva, milk, and ‚intestinal juice'.

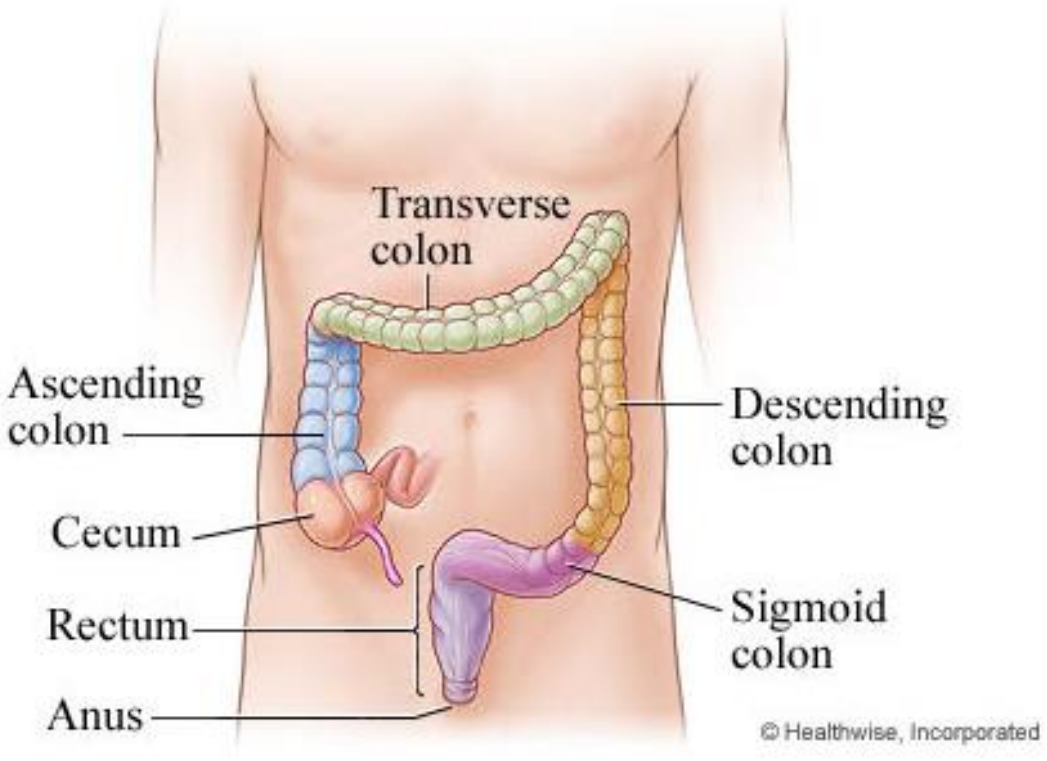
LARGE INTESTINE

The principal functions of the large intestine are **reabsorption of electrolytes and water and elimination of undigested food and waste**.

Elimination of **semisolid to solid waste materials** is facilitated by the **large amounts of mucus** secreted by the numerous goblet cells of the intestinal glands. Goblet cells produce mucin that is secreted continuously to lubricate the bowel, facilitating the passage of the increasingly solid contents.

The large intestine comprises:

- cecum with its projecting vermiform appendix,
- colon, which is further subdivided based on its anatomic locations:
  - ascending colon,
  - transverse colon,
  - descending colon,
  - sigmoid colon
- rectum,
- anal canal.



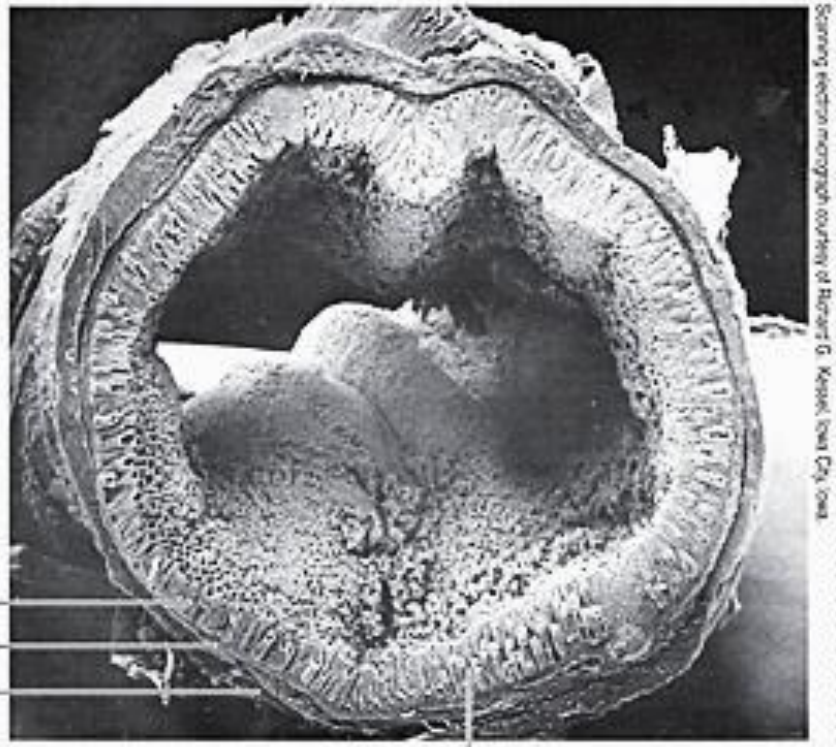
Pawlina W, Ross MH. Histology: A Text and Atlas With Correlated Cell and Molecular Biology, 8th ed. Wolters Kluwer, 2016

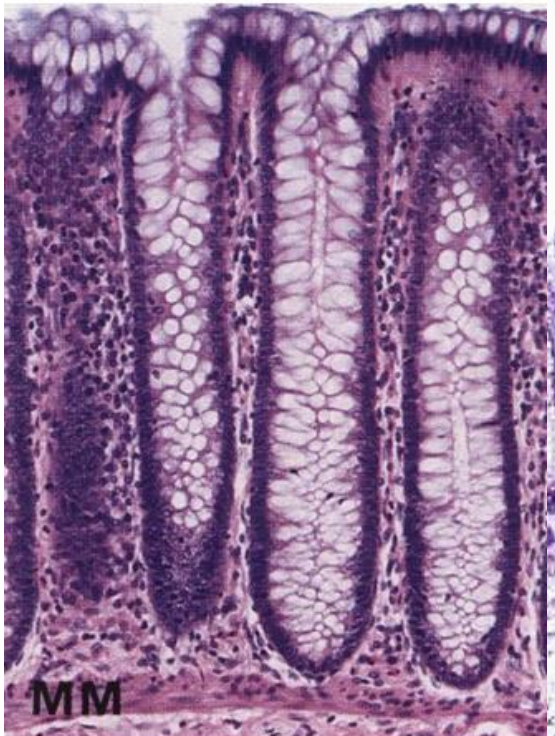
Large intestine

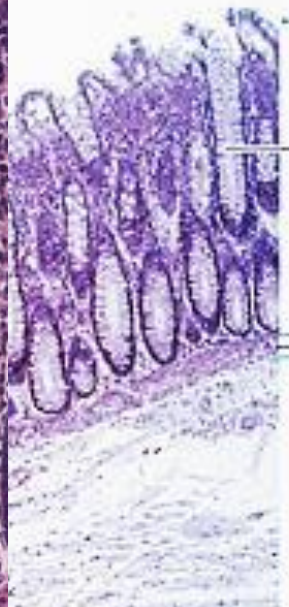
The layers of the large intestine are the same as those in the small intestine: mucosa, submucosa, muscularis, and serosa.

The **main function of the mucosa** is the absorption of water, sodium, vitamins, and minerals. The transport of sodium is active (energy-dependent), causing water to move along an osmotic gradient. As a result, the fluid chyme entering the colon is concentrated into semisolid feces. Potassium and bicarbonate are secreted into the lumen of the colon.

The absorptive capacity of the colon favors the uptake of many substances, including sedatives, anesthetics, and steroids. This property is of considerable therapeutic importance when medication cannot be administered through the mouth (for example, because of vomiting).







Tubular glands, or crypts of Lieberkühn, are oriented perpendicular to the long axis of the colon, are much deeper than in the small intestine, and have a higher proportion of goblet cells.

Mucosa

Muscularis mucosae

Mucosa of the large intestine

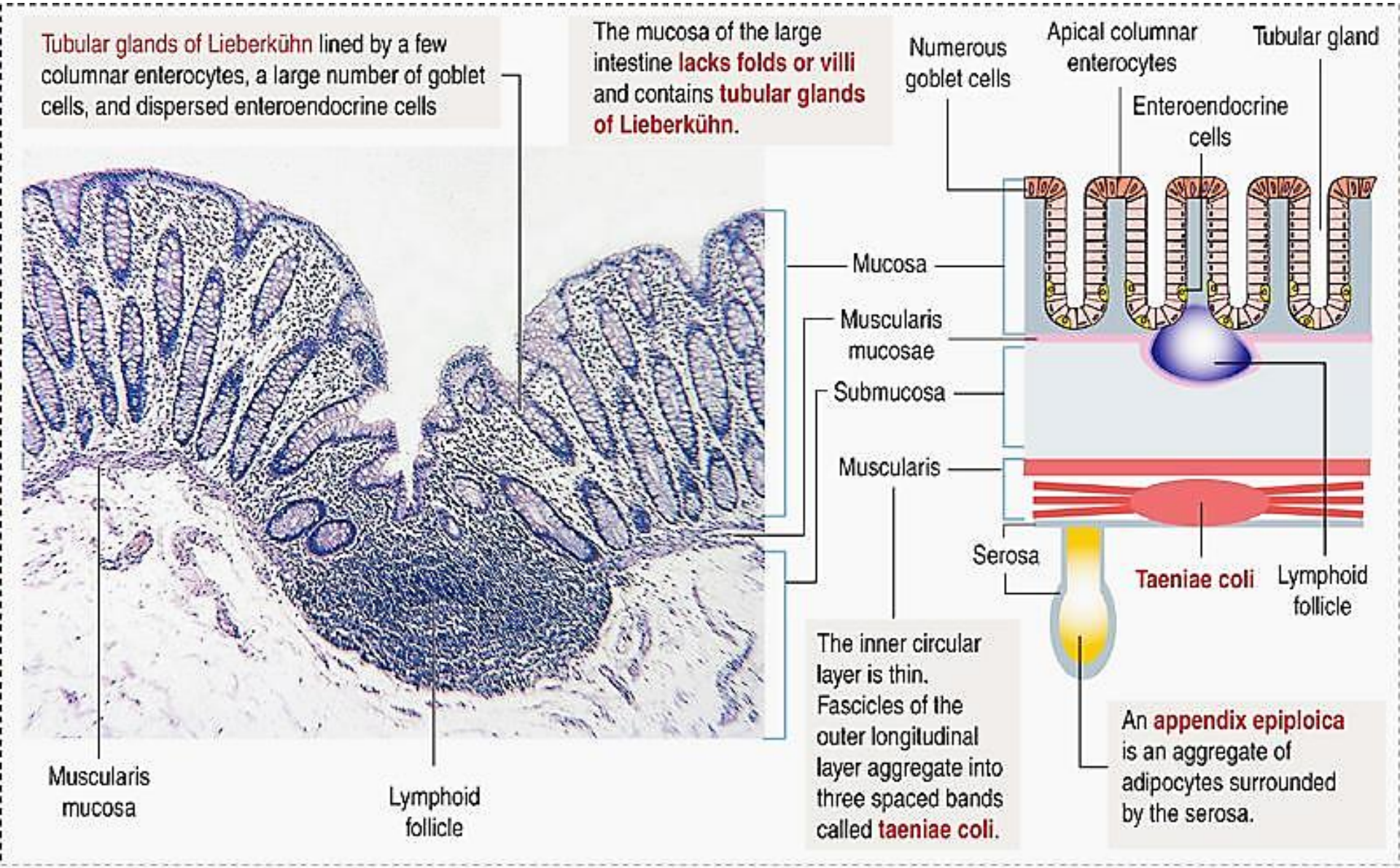
The mucosa of the colon is free of folds and villi.

Four cell types are present in the surface epithelium and tubular glands:

1. Simple columnar absorptive cells with apical microvilli

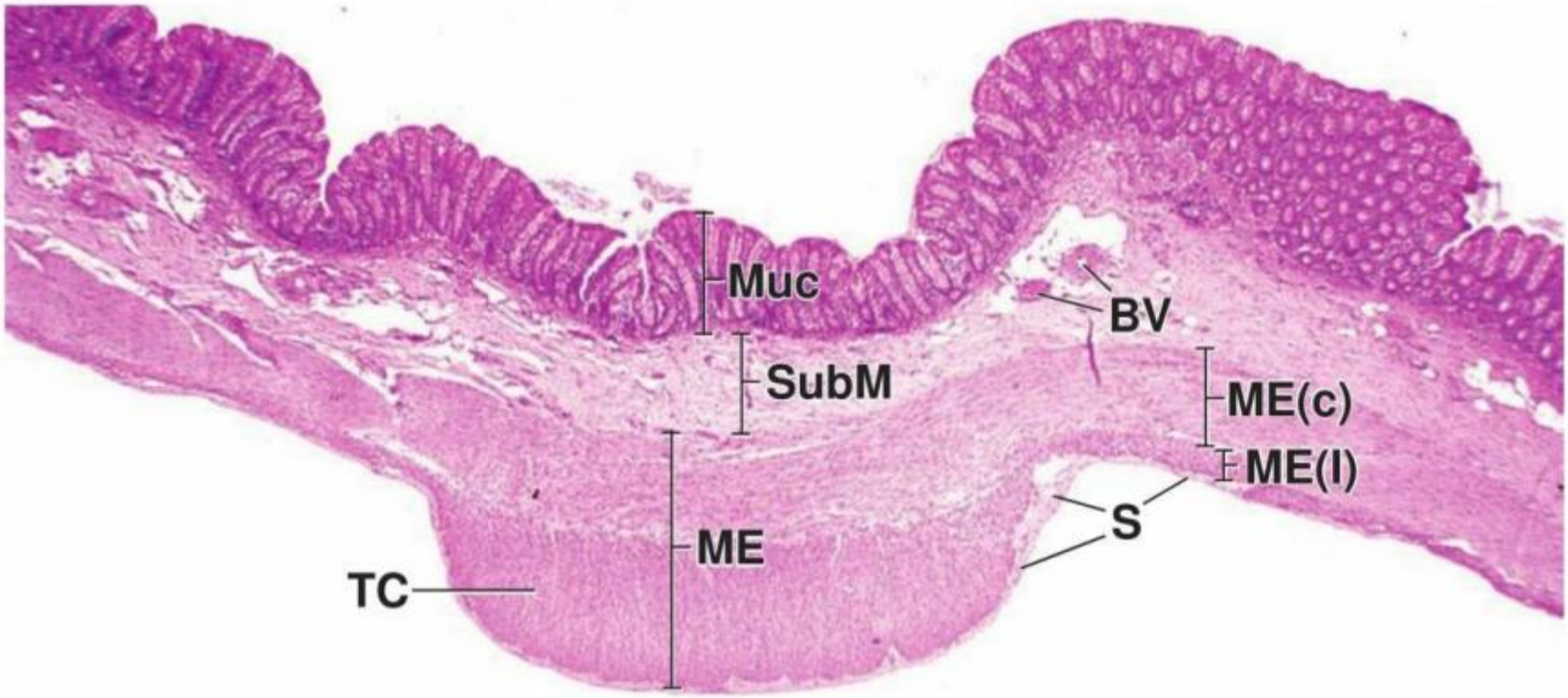
Kierszenbamum, 2012

Simple glands of colonic mucosa contain numerous goblet cells, there are no Paneth cells; lamina propria contains many lymphocytes, macrophages and neutrophils.
Colon produces abundant mucus, which lubricates its lining and facilitates passage and elimation of feces.



Klerszenbaum & Tres: Histology and Cell Biology: An Introduction to Pathology, 3e

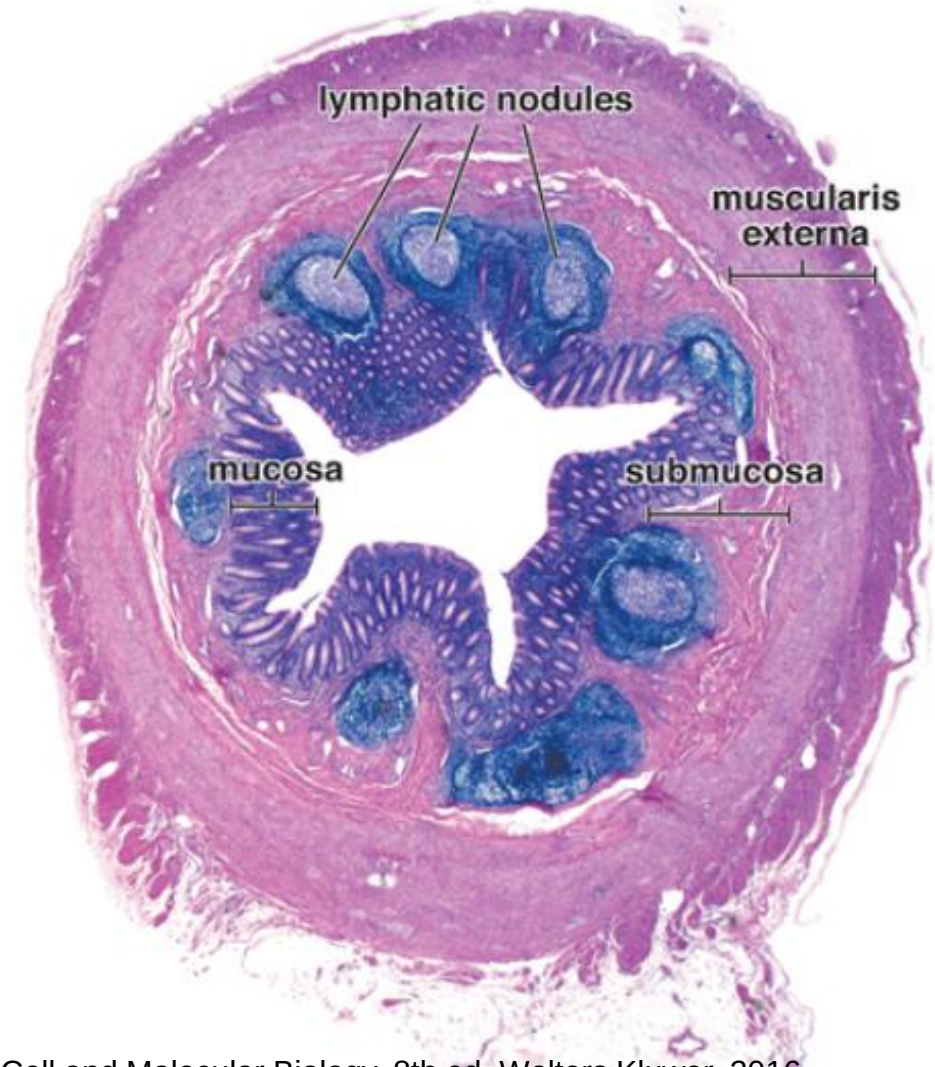
The wall of the large intestine has two layers of muscular membrane, circular and longitudinal. The longitudinal layer forms the three *taeniae coli* (ribbons of the colon).



APPENDIX VERMIFORMIS contains in mucosa the large number of lymphatic nodules that extend into the submucosa

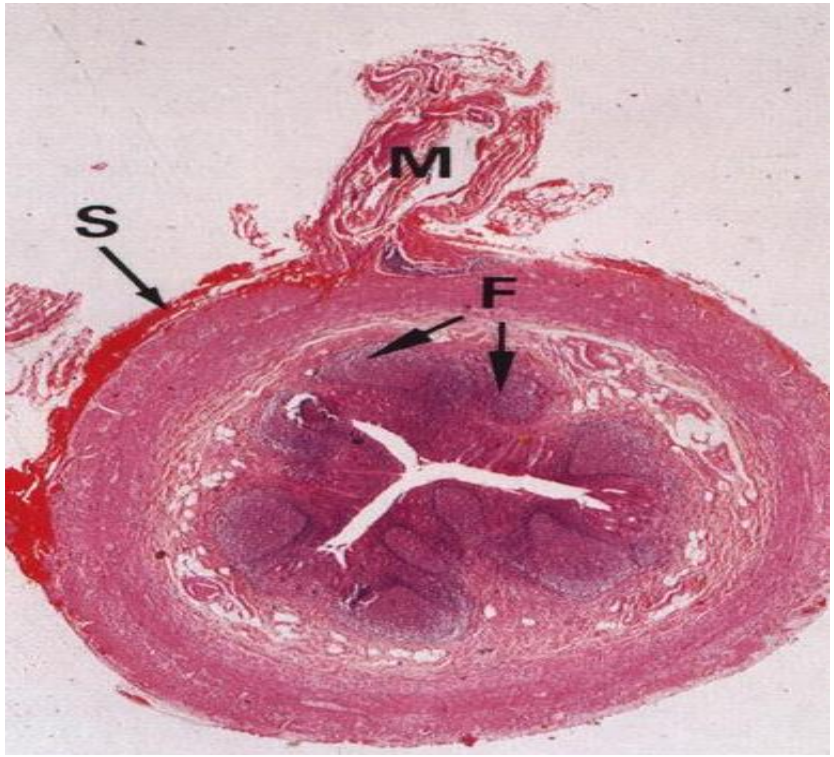
The **cecum** forms a blind pouch just distal to the ileocecal valve; the appendix is a thin, finger-like extension of this pouch. The histology of the cecum closely resembles that of the rest of the colon; the appendix differs from it in having a **uniform layer of longitudinal muscle** in the muscularis externa.

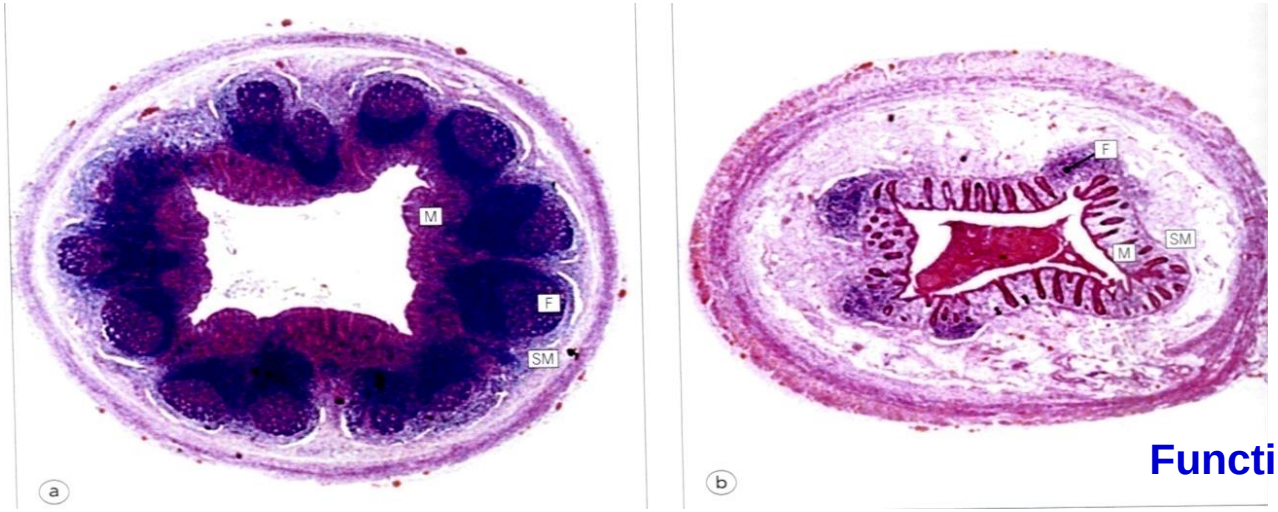
In the vermiform appendix, lymphatic nodules, often with distinct germinal centers are seen within the entire mucosa The muscularis externa is composed of a relatively thick circular layer and a much thinner outer longitudinal layer. The appendix is covered by a serosa that is continuous with the mesentery of the appendix (lower right). ×10.



Pawlina W, Ross MH. Histology: A Text and Atlas With Correlated Cell and Molecular Biology, 8th ed. Wolters Kluwer, 2016

Appendix (5x)





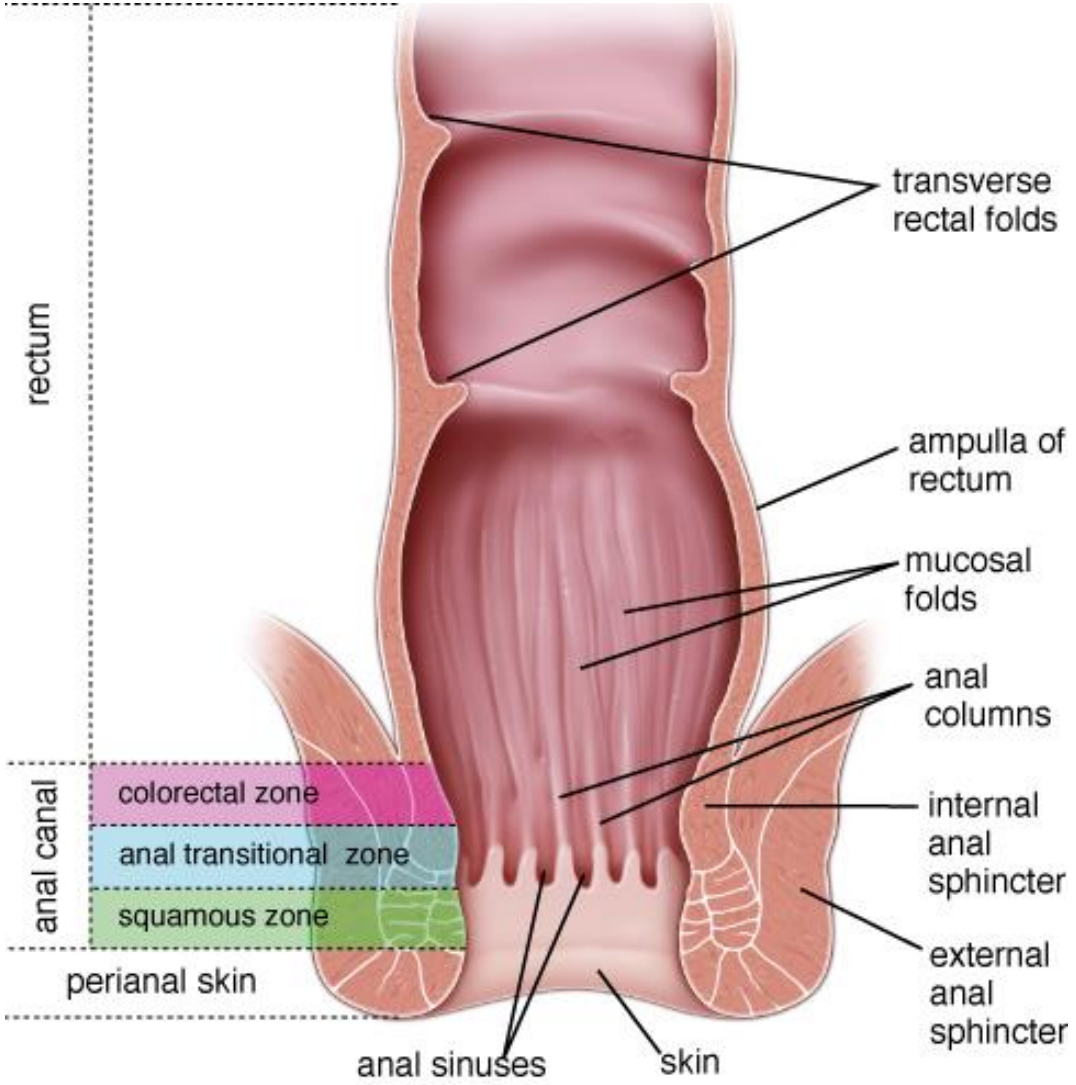
a) 10 year-old child dziecko

b) 36 year-old man

Recto-anal transition: quite abrupt change of the lining eoithelium: from simple columnar to SSnK epithelium

Anal transitional zone (ATZ), which occupies the middle third of the anal canal. The ATZ possesses a stratified columnar epithelium interposed between the simple columnar epithelium and the stratified squamous epithelium, which extends to the cutaneous zone of the anal canal.

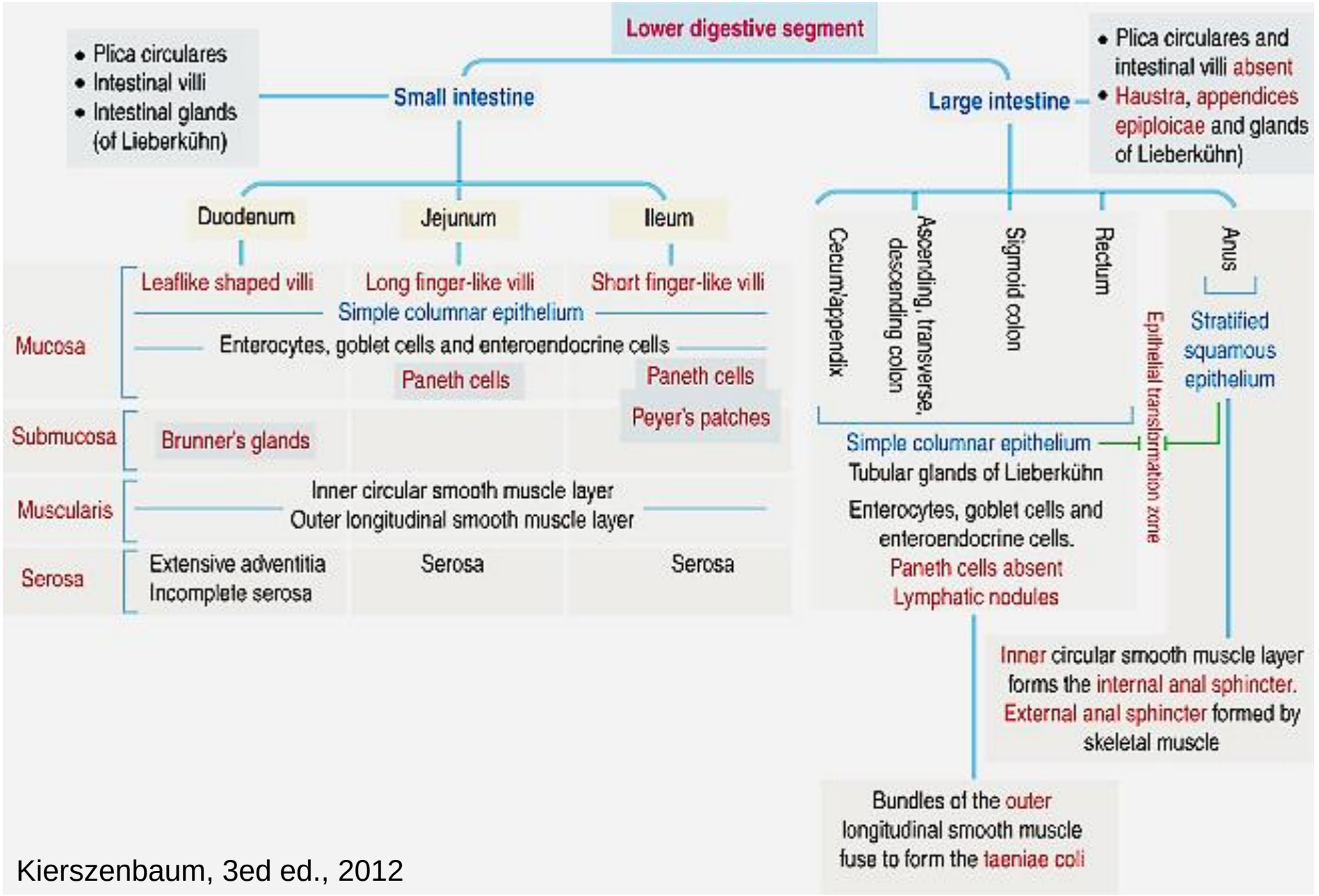
Squamous zone, in the lower third of the anal canal is lined with stratified squamous epithelium that is continuous with that of the perineal skin.



Pawlina, Histology, 8th ed.

The submucosa of the anal columns contains the terminal ramifications of the superior rectal artery and the **rectal venous plexus**. Enlargements of these submucosal veins constitute **internal hemorrhoids**, which are related to elevated venous pressure in the portal circulation (**portal hypertension**).

There are no teniae coli at the level of the rectum; the longitudinal layer of the muscularis externa forms a uniform sheet. The muscularis mucosae disappears at about the level of the ATZ, where the circular layer of the muscularis externa thickens to form the **internal anal sphincter**. The **external anal sphincter** is formed by **striated muscle** of the pelvic floor.



Kierszenbaum, 3ed ed., 2012