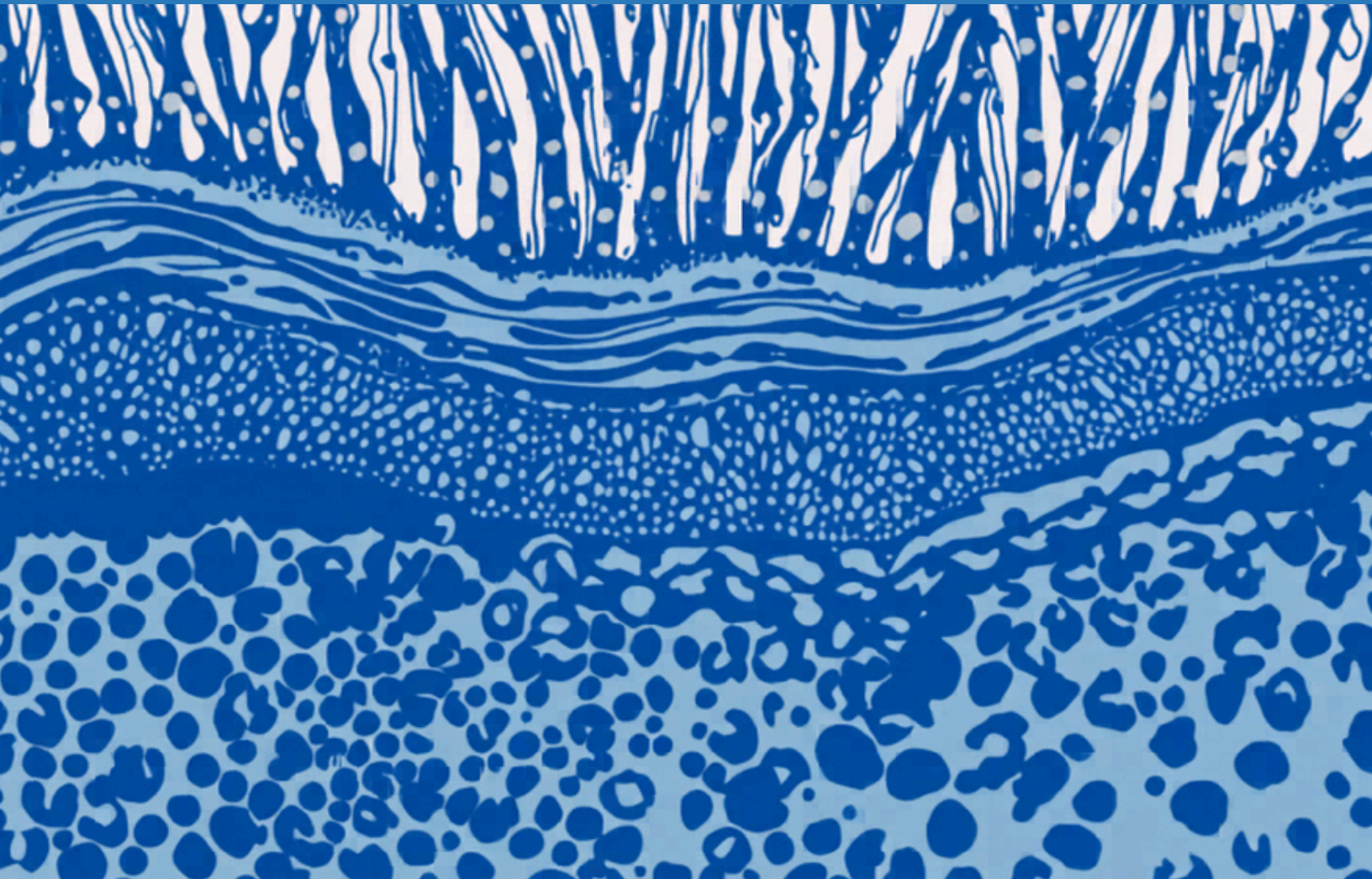


Histology



**Second Year Students
UJ-GIG GI Booklet**



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The University of Jordan
Gastroenterology Interest Group (UJ-GIG)
Booklet

Histology

Upper GI Tract Histology

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Edited by: Rawan Fratekh

Reviewed by: Amr Abdallah

[Overview]

→ Outline of upper GI tract histology:

- 1) Introduction
 - a. Recap of essential cells in the GI tract
 - b. General structure of the digestive tract
- 2) Basic mucosal forms in the GI tract
 - a. The oral cavity
 - b. The tongue
- 3) Salivary glands

[Introduction]

The digestive system consists of the **digestive tract** (oral cavity, esophagus, stomach, small and large intestines, rectum, and anus), **and its accessory organs/glands** (salivary glands, liver, gallbladder, and pancreas)

Functions of the gastrointestinal system:

- 1) The primary function is to break down ingested food into smaller molecules that can be absorbed from the GI tract to the liver through the portal system, to be metabolized and used by the body for growth, maintenance, and energy needs.
- 2) It is a **protective barrier** between the content of the tract's lumen and the internal milieu of the body.

General structure of the digestive tract

The digestive tract is a hollow tube composed of a lumen that varies in diameter, surrounded by a wall made up of four main layers: **mucosa, submucosa, muscular layer, and serosa/adventitia.**

Mucosa

Also called the "mucous membrane", this is the innermost layer that lines the digestive tract, and it consists of 3 layers:

- 1) **Lining epithelium**, which differs depending on the organ and site (*more on this later*).
- 2) **Lamina propria** → formed by loose connective tissue, rich in blood vessels, lymphatics, and smooth muscle cells.
- 3) **Muscularis mucosa** → consists of a thin inner circular layer and an outer longitudinal layer of smooth muscle cells. Its primary function is to change the shape and movement of the mucosa.

Submucosa

Consists of **dense connective tissue, lymphatic vessels, and blood vessels.**

It also contains the **submucosal nerve plexus** (called **Meissner's plexus**).

The plexus contains both **sympathetic and parasympathetic innervation.**

The **parasympathetic** system in Meissner's plexus has a **secretomotor** function that:

- 1) stimulates the secretion of the gland
- 2) the movement of the GI tract.

Important note: The duodenum and esophagus contain glands in their submucosal layer. These glands produce secretions that neutralize stomach acid. Example: Brunner's glands in the duodenum.

Muscular layer

Which is located outside the submucosa, and it's formed by:

- 1) **Circular layer:** inner layer (closer to the lumen). This layer is **thick** and highly innervated. Cell contraction decreases the diameter of the GI tract.

2) **Longitudinal layer:** outer layer. This layer is **thin** and less innervated. Contraction of its cells shortens the GI tract.

This layer contains nervous structures that supply the digestive tract and aid its function:

- 1) The **myenteric nerve plexus** (called **Auerbach's nerve plexus**), which is situated between the inner and outer layers.
- 2) Parasympathetic innervation through the **vagus nerve**. It has a secretomotor function.
- 3) Sympathetic innervation through postganglionic fibers.

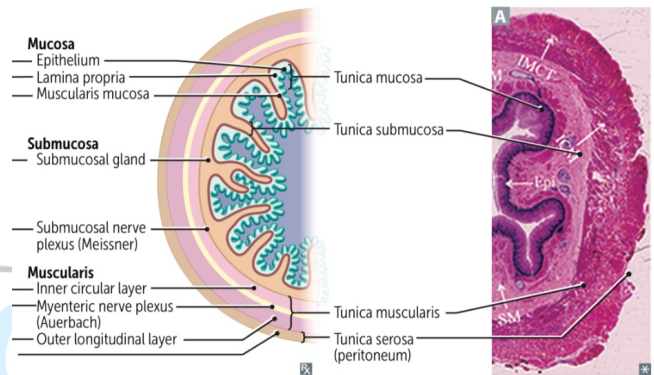
The myenteric (Auerbach's) and submucosal (Meissner's) nerve plexuses form what is known as the **Enteric Nervous System**.

The prefix *enter* refers to the GI tract (enteric nervous system, enterocytes, etc.).

Adventitia/ serosa

Consists of **loose connective tissue** (vs dense CT in the submucosa). Rich in blood vessels, lymphatic vessels, and adipose tissue.

The serosa is continuous with the mesenteries and the peritoneum. If a layer of connective tissue surrounded it, it's called **adventitia**.

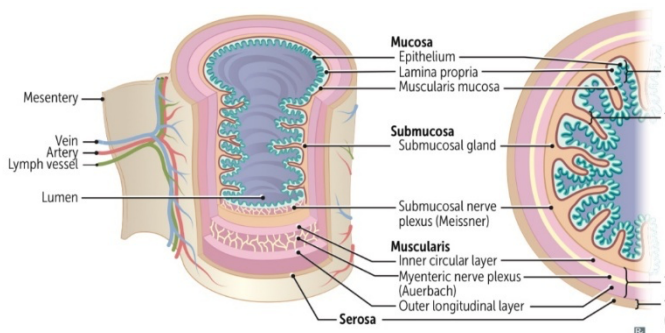


[Basic mucosal forms in the GI tract]

As mentioned earlier, the mucosa is the layer that lines the entire digestive tract. The epithelial lining is the innermost part of this layer, and its type varies depending on its function.

- 1) **Protective**
 - Epithelial lining: **stratified squamous epithelium, non-keratinized**.
 - Location: oral cavity, pharynx, esophagus, anal canal
- 2) **Secretory**
 - Epithelial lining: **simple columnar with or without goblet cells, with long, closely packed tubular glands**.
 - Location: the stomach, duodenum
- 3) **Absorptive**
 - Epithelial lining: **finger-like projections called villi with intervening short glands called crypts of Lieberkühn**.
 - Location: Small intestine
- 4) **Absorptive/protective**
 - Epithelial lining: **Simple columnar with goblet cells**.
 - Location: the large intestines.

Serosa	Adventitia
Surrounded by peritoneum	Surrounded by connective tissue
Simple squamous epithelium (mesothelium)	—
Example: Esophagus below the diaphragm, and in places where the tract is bound to other organs.	Example: Esophagus in the thorax and neck



The Oral Cavity

The mucosa of the oral cavity is formed by **stratified squamous epithelium** that can be keratinized, partially keratinized, or nonkeratinized, depending on the region.

Keratinization protects against trauma and damage during mastication.

- 1) **Keratinized** stratified squamous epithelium: lines the **gums and hard palate**. In these areas, the lamina propria rests directly on the underlying bone.
- 2) **Nonkeratinized** stratified squamous epithelium: lines the **soft palate, cheeks, floor of the mouth, and the pharynx**.

The **lamina propria** contains multiple invaginations between the mucosa and the submucosa called papillae.

The oral cavity has a **thick submucosa** that contains many **minor salivary glands**, which secrete continuously to keep the mucosal surface moist, as well as **diffuse lymphoid tissue**.

The lips

The **lips** are considered a transition zone, and their lining differs depending on the part.

- 1) The **internal mucous** surface is lined with **thick nonkeratinized** epithelium with minor labial salivary glands
- 2) The **red vermilion zone** is covered by very **thin keratinized epithelium**, which transitions between the oral mucosa and skin. This area lacks salivary and sweat glands and is kept moist by saliva from the tongue. It is **rich in sensory innervation and blood capillaries**.
- 3) The outer surface consists of **skin**, and it's rich in **sebaceous glands, sweat glands, and hair follicles**.

Its muscular layer is well-developed to aid in ingestion, speech, and other forms of communication.

The tongue

The tongue is a mass of striated muscle covered by a mucous membrane, which is closely adherent to it. Connective tissue between the small muscle fascicles is **penetrated by the lamina propria**, which is why the mucous membrane is adherent to the muscular core.

The muscle fibers cross one another in all directions, allowing high mobility.

Its primary function is to **manipulate and move food** during mastication to aid in swallowing and digestion.

Lining epithelium:

- 1) Dorsal (upper) surface: Para-keratinized stratified squamous epithelium.
- 2) Ventral (lower) surface: nonkeratinized stratified squamous epithelium.

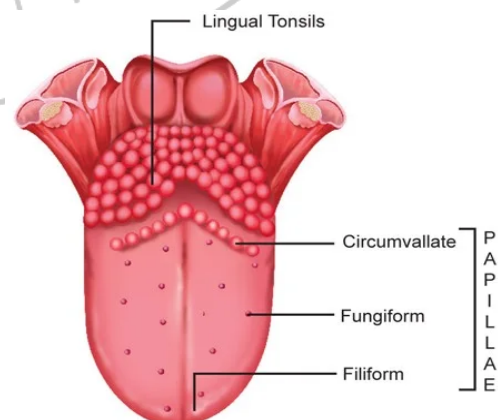
The mucous membrane is **smooth** on the lower (ventral) surface and **irregular** on the upper (dorsal) surface, with a bunch of small eminences called **papillae** on its anterior two-thirds, and the **lingual tonsils** on the posterior third.

The posterior one-third of the dorsal surface of the tongue is separated from the anterior two-thirds by a V-shaped boundary, called **the sulcus terminalis**.

Behind this boundary, the surface of the tongue shows small bulges composed mainly of two types of small lymphoid aggregations:

- 1) Small collections of lymphoid nodules.
- 2) Lingual tonsils, where lymphoid nodules aggregate around invaginations (crypts) of the mucous membrane.

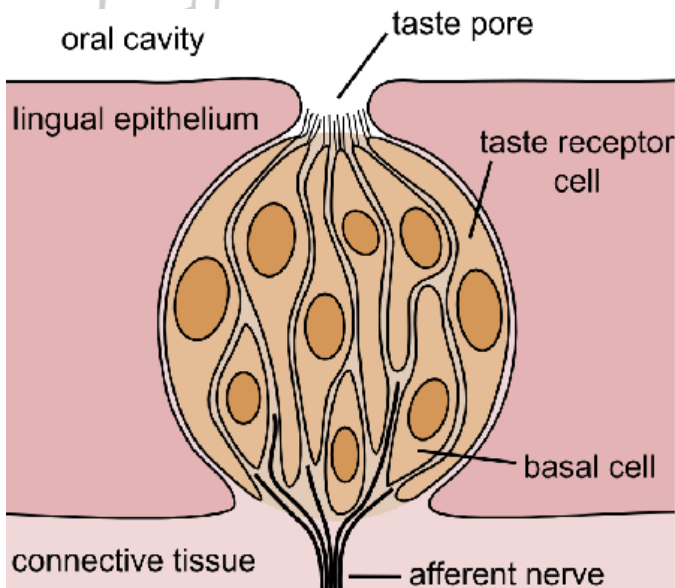
Papillae are elevations of the oral epithelium and **lamina propria** that assume various forms and functions.



There are four types of papillae on the tongue:

Type	Shape	Location	Notes
Filiform	Elongated conical shape	All over the tongue (numerous)	Keratinized epithelium, no taste buds
Fungiform	resemble mushrooms (<i>fungi</i>) in that they have a narrow stalk and a smooth-surfaced, dilated upper part	irregularly interspersed among the filiform papillae.	contain scattered taste buds on their upper surfaces
Foliate <i>poorly developed in humans</i>	consists of two or more parallel ridges and furrows	on the dorsolateral surface of the tongue	It contains many taste buds
Circumvallate	7–12 extremely large circular papillae whose flattened surfaces	They are distributed in the V region in the posterior portion of the tongue	Explained below

Each papilla is composed of multiple cells surrounding a small pore through which secretions pass. These pores also contain **bipolar** cells that **transmit taste signals via filaments of the chorda tympani nerve**.



→ Why are these glands important?

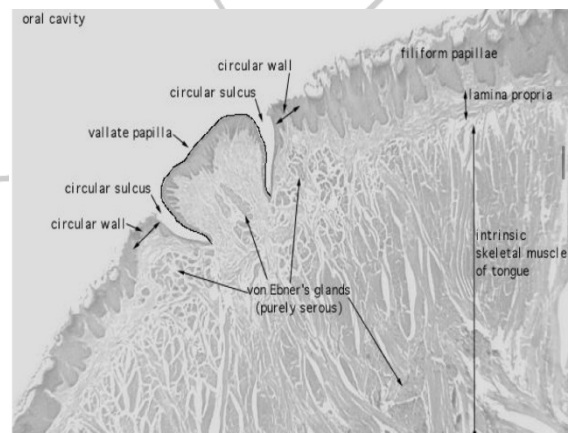
This flow of secretions from these glands is essential for **removing food particles** from the vicinity of the taste buds, allowing them to receive and **process new gustatory (taste) stimuli**. The glands also **secrete a lipase** that likely prevents the formation of a **hydrophobic layer** over the taste buds, thereby hindering their function.

Remember: In addition to this local role, lingual lipase is active in the stomach and **can digest up to 30% of dietary triglycerides**.

Other small mucous salivary glands dispersed throughout the lining of the oral cavity act in the same way as the serous glands associated with this type of papilla **to prepare the taste buds in other parts of the oral cavity, such as the anterior portion of the tongue, to respond to taste stimuli**.

Circumvallate papillae

Numerous serous (von Ebner's) glands drain their contents into the deep groove that encircles the periphery of each papilla. This provides a **continuous flow of fluid** over a significant number of taste buds present along the sides of these papillae.



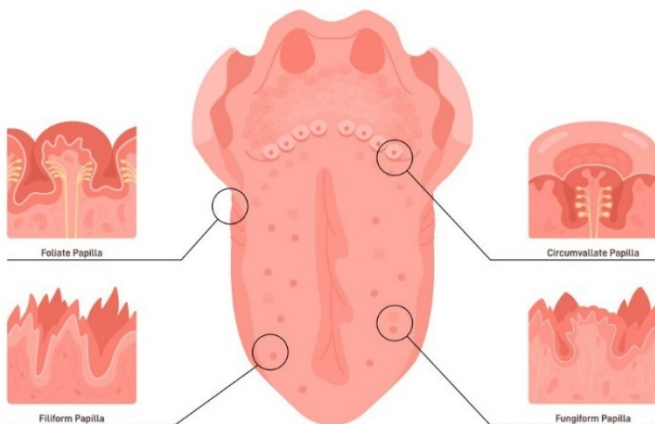
Notice how the Von Ebner's glands surround the circumvallate gland in the groove around it. The taste buds are located **lateral to the circumvallate papillae** but **medial to the ridge/groove**.

In this histology slide, notice the location of the taste buds on the foliate papillae.



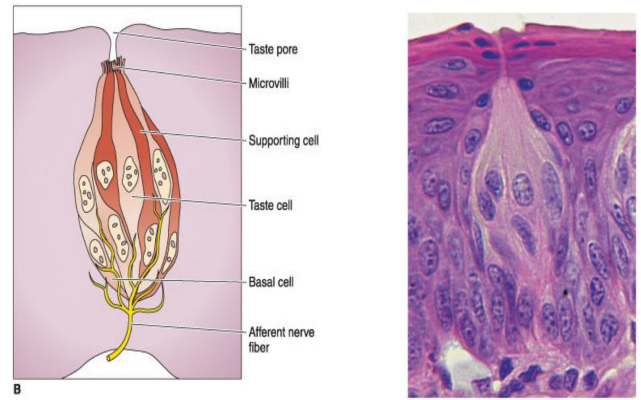
Notice the shape and locations of different papillae; the circumvallate papillae are behind the V ridge separating the anterior 2/3rd and posterior 1/3rd of the tongue.

Locations And Types Of Human Lingual Papillae



Taste buds

Are ovoid structures within the stratified epithelium on the tongue's surface, which samples the general chemical composition of ingested material.



Taste buds are composed of:

- 1) **Gustatory** (taste) cells: 50-100 elongated cells that turn over every 7-10 days.
- 2) **Supportive** cells
- 3) **Stem** cells: immature, slowly dividing cells that give rise to other cell types
- 4) **Taste pore**: an opening at the center of each taste bud.

Taste buds rest on the basal lamina, which is penetrated by sensory axons that form synapses with gustatory cells. Gustatory cells have **microvilli** that project through the taste pores and interact with dissolved molecules (tastants) in saliva.

[The salivary glands]

These are **exocrine glands** in the mouth that produce **saliva**, which has **digestive, lubricating, and protective** functions. Saliva has a pH of 6.5-6.9.

There are many small salivary glands and three large ones:

- 1) Parotid gland
- 2) Submandibular gland
- 3) Sublingual gland

In humans, the minor salivary glands secrete 10% of the **total saliva volume** but account for approximately 70% of the **mucus** secreted.

General structure of salivary glands

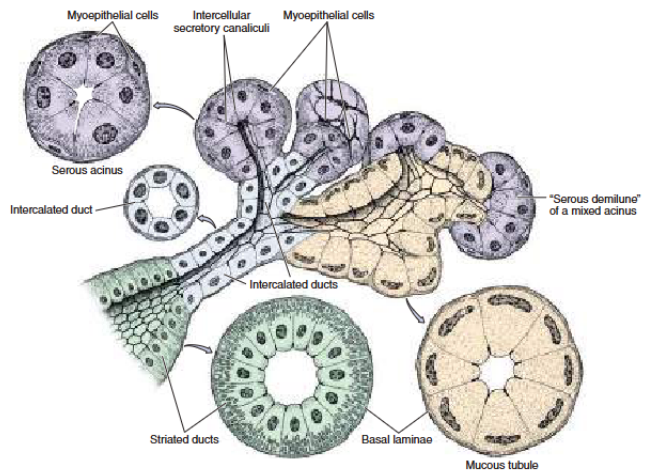
→ **Capsule:** composed of connective tissue rich in collagen fibers, surrounds the large salivary glands. The connective tissue **protects the gland** and **extends between its branches, forming septa** that divide it into lobes and lobules. The septa contain **nerve endings, blood, and lymphatic vessels**.

→ **Parenchyma:** consists of secretory units on a branching duct system arranged in lobules, separated by septa of connective tissue

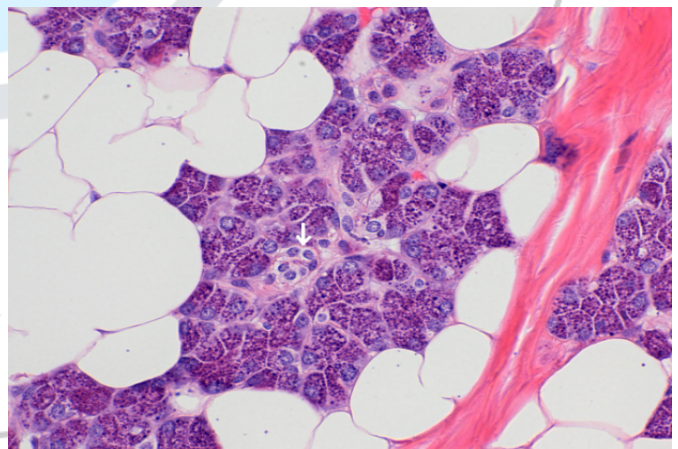
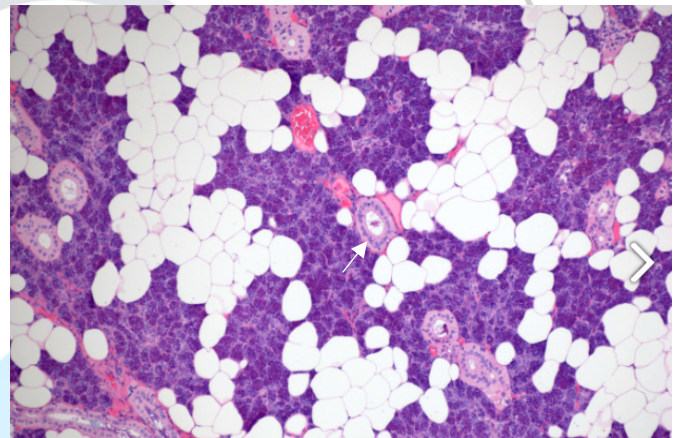
Secretory end pieces: may be mucous- or serous-secreting.

Serous cells: polarized, protein-secreting cells that are pyramidal in shape with round nuclei. They're joined by tight and adherent junctions, **forming round units called acini**. They **secrete enzymes**.

Mucous cells: columnar in shape with compressed basal nuclei. They're organized into **cylindrical tubules** and **secrete mucins to lubricate**. They appear foamy.



The following slides demonstrate sections of the parotid glands with the serous acini (white arrows).

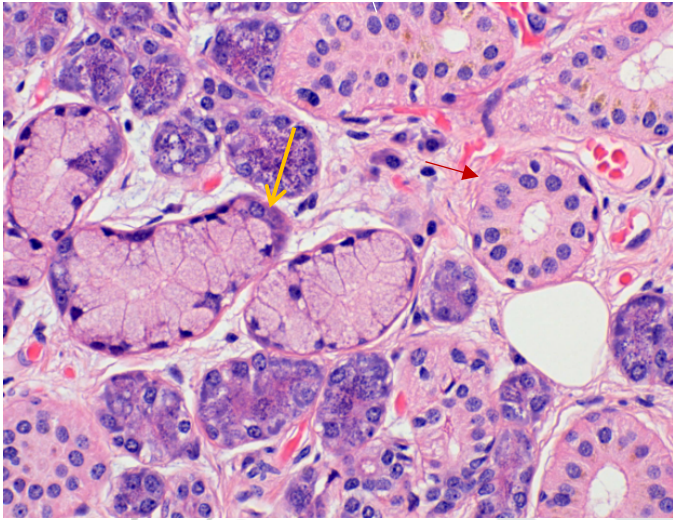


Parotid glands are **purely serous**.
Submandibular glands are mixed but mainly **serous**.
Sublingual glands are mixed but mainly **mucous**.

Serous cells	Mucous cells
Pyramidal in shape with a broad base and a narrow apical surface	Cuboidal to columnar in shape, with oval/ flattened nuclei near the base of the cell
Short microvilli facing the lumen	They secrete the glycoproteins mucins, which lubricate saliva.
Organized as acini with a narrow lumen	Organized as tubules with a wide lumen
More myoepithelial cells	Fewer myoepithelial cells
They appear more blue	They look foamy

- 1) Acini: sac-like structures formed by **serous cells** surrounding a lumen where the secretions are released. They **secrete enzymes**. E.g., **parotid** glands.
- 2) Tubules: cylindrical structures formed by mucous cells, which secrete mucus for lubrication.
- 3) Tubuloacinar: a mix of both.
- 4) Serous demilune: serous cells overlying mucous cells in a crescent-shaped arrangement

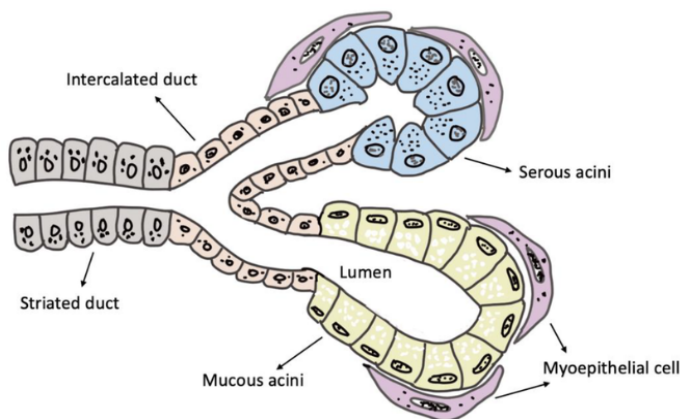
Compare the shape of the cells and nuclei in serous acini, **rounded and central** (red arrow), vs the mucous tubules, which have **compressed, basal** nuclei (yellow arrow).



Myoepithelial cells: small, flattened cells found between the basal lamina and the basal plasma membrane of cells. They resemble smooth muscle cells and share many of their characteristics, especially **contractility**. They're connected through **desmosomes**.

They can either surround the secretory portions (acini) or the ducts:

- 1) Around the acini and tubules: they are **well-developed and branched** cells called **basket cells**.
- 2) Around the intercalated ducts: they are **spindle-shaped** and lie parallel to the length of the duct.



Functions of the myoepithelial cells:

- 1) **Prevention of end-piece distention** during secretion caused by increased intraluminal pressure – primary function.
- 2) **Accelerate the secretion of saliva**.

The duct system

This is where the secretory units empty their secretions.

- 1) Secretory endpieces empty into the **intercalated ducts**, which are lined by cuboidal epithelial cells. *These cells can differentiate into secretory and ductal cells.*
- 2) The intercalated ducts join to form the **striated ducts**. These are lined by more columnar cells characterized by radial striations extending from the base of the cell to the central nuclei. Under electron microscopy, these striations appear to consist of infoldings of the basal plasma membrane, with numerous elongated mitochondria aligned parallel to the infolded membranes, a characteristic of **ion-transporting cells**.

The intercalated ducts and striated ducts are called **intralobular ducts**.

- 3) The striated ducts drain into **the interlobular or excretory ducts**, which are located in the connective tissue septa. The proximal part is lined by pseudostratified or stratified cuboidal epithelium. Distal parts are lined by stratified columnar epithelium containing a few mucus-secreting cells.
- 4) The interlobular ducts drain into the **main salivary duct**, which is lined by nonkeratinized stratified squamous epithelium.

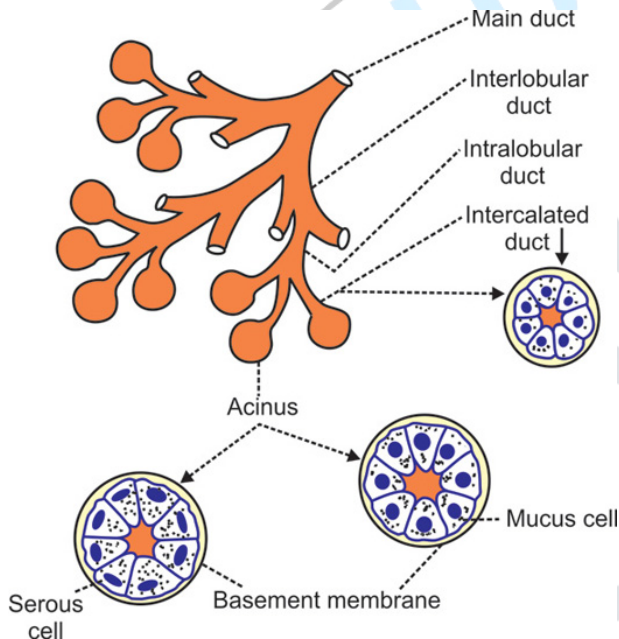
Vessels and nerves enter the large salivary glands at the hilum and gradually branch into the lobules.

The capillaries surrounding the secretory endpieces are very important for the secretion of saliva, stimulated by the **autonomic nervous system**.

Sympathetic stimulation: small amounts of viscous saliva, rich in organic material.

Parasympathetic stimulation: promotes vasodilation and copious watery secretions.

In large glands, the connective tissue surrounding the intralobular ducts contains **the immunoglobulin IgA**, which forms a complex with the secretory component synthesized by the acini and ducts. It's transferred to the oral cavity and protects against oral pathogens.



Major salivary glands

→ The parotid glands

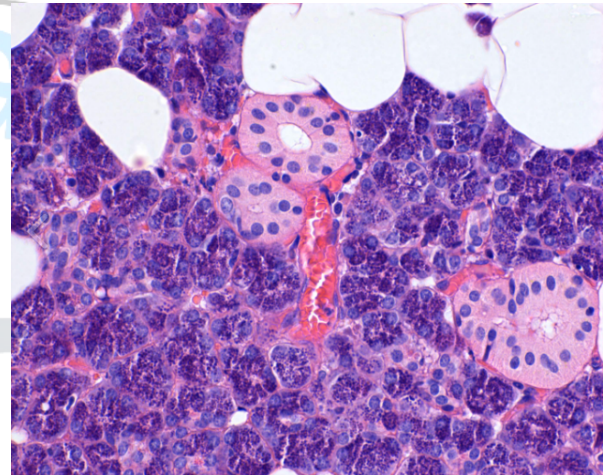
We have two parotid glands, one on each cheek.

- Structure: It's a branched, acinar **gland composed purely of serous cells**.
- Secretions: secretes secretory granules **rich in proteins and amylase**, which is responsible for the digestion of carbohydrates.

Amylase cycle: carbohydrate digestion begins in the mouth and continues briefly in the stomach before stomach acid inactivates the enzyme.

- Notes: **the intercalated and striated ducts are easily observed** within the lobules due to their length, Their connective tissue **contains the immunoglobulin IgA**, which is protective against oral pathogens.

Histology of the parotid gland

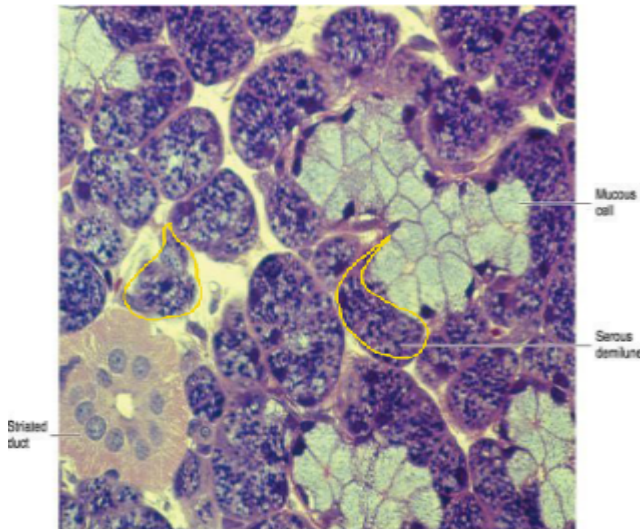


→ The submandibular glands

- Structure: a branched tubuloacinar gland that **contains both serous (mainly) and mucous cells**. 90% consists of serous acini. 10% consists of mucous tubules and serous demilunes.
- Secretions:
 - 1) Serous acini: serous secretion with **weak amylolytic activity**
 - 2) Serous demilunes: secrete the enzyme **lysozyme**, which hydrolyzes the wall of certain bacteria
 - 3) Some acini and intercalated ducts: secrete **lactoferrin**, which binds iron, an essential nutrient for bacterial growth.
- Notes: **The striated ducts are easily observed** within the lobules due to their length, but the intercalated ducts are very short.

Histology of the submandibular gland showing its mixed structure.

Minor salivary glands



- Location: these small, non-encapsulated glands are distributed **throughout the oral mucosa and submucosa**.
- Secretion: usually **mucous** secretions produced by small groups of secretory units and conducted to the oral cavity by short ducts with little modification of their content.

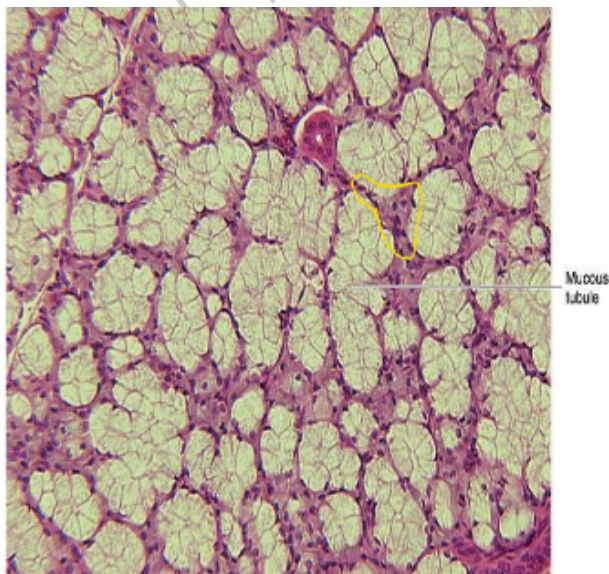
Except for **von Ebner's glands**, which are small **serous** glands present **in the posterior region of the tongue**.

- Notes: lymphocytic aggregates are commonly observed within these glands, associated with IgA secretion.

→ The sublingual gland

- Structure: a branched tubuloacinar gland formed of **mucous (mainly) and serous cells**. Serous cells are almost exclusively found on demilunes of mucous tubules.
- Secretions: the demilunes secrete **lysozyme**.
- Notes: **The intralobular ducts are less developed** compared to the other major glands.

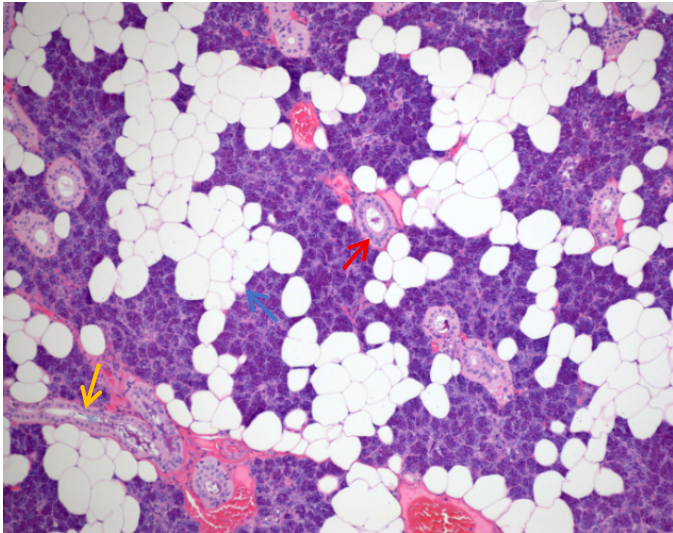
The mucous-secreting cells appear foamy white.



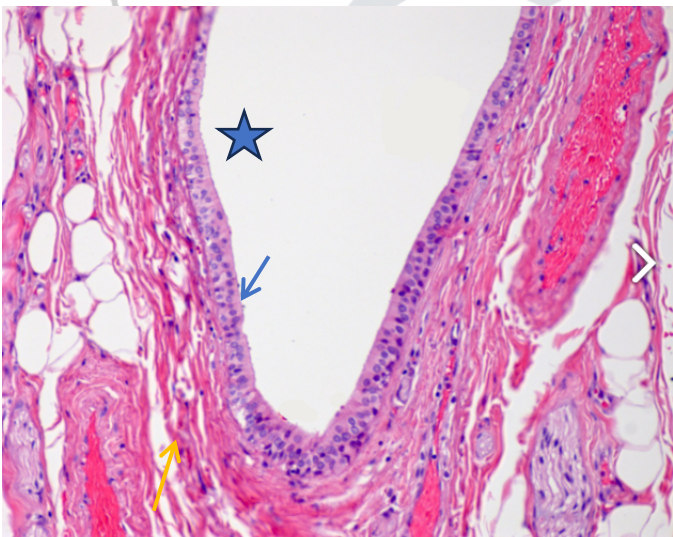
EXTRA HISTOLOGY SLIDES TO GET FAMILIAR WITH THEM

PAROTID GLAND

The parotid gland with serous acini (red arrow), intercalated ducts (yellow arrow), and adipose tissue (blue arrow).

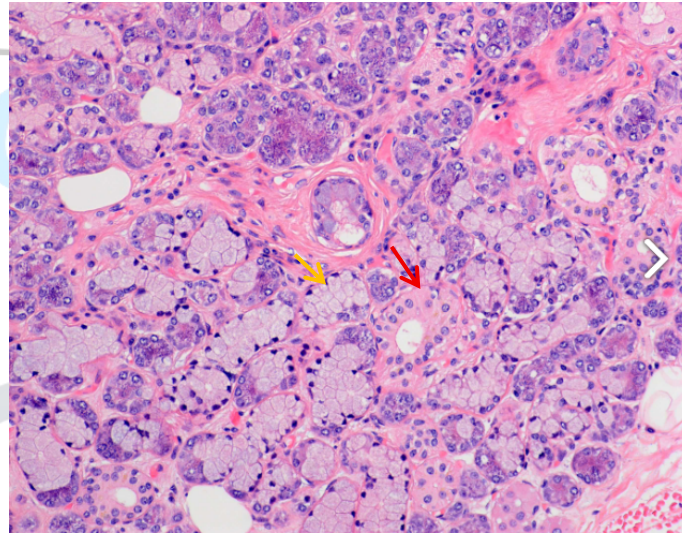


A slide showing the intercalated duct (star) lined with pseudostratified columnar epithelium (blue arrow), located within connective tissue septa (yellow arrow).



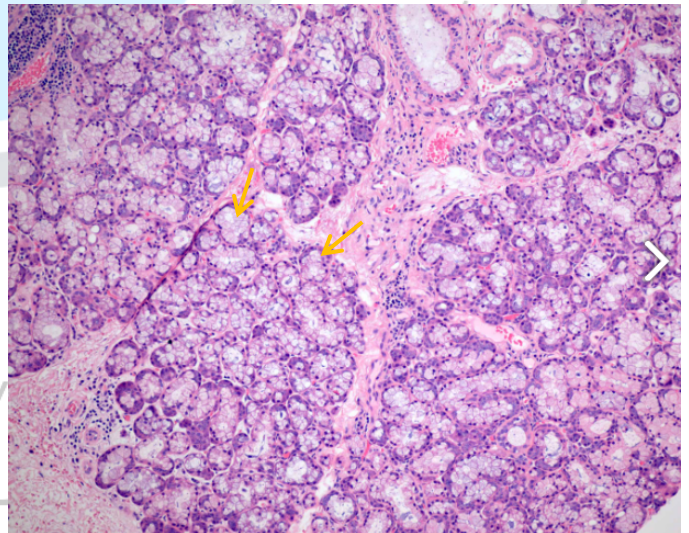
SUBMANDIBULAR GLAND

The submandibular gland has mixed glands, serous acini (red arrow) appear bluer because they secrete proteins, mucous tubules (yellow arrow) appear foamy and lighter in color.

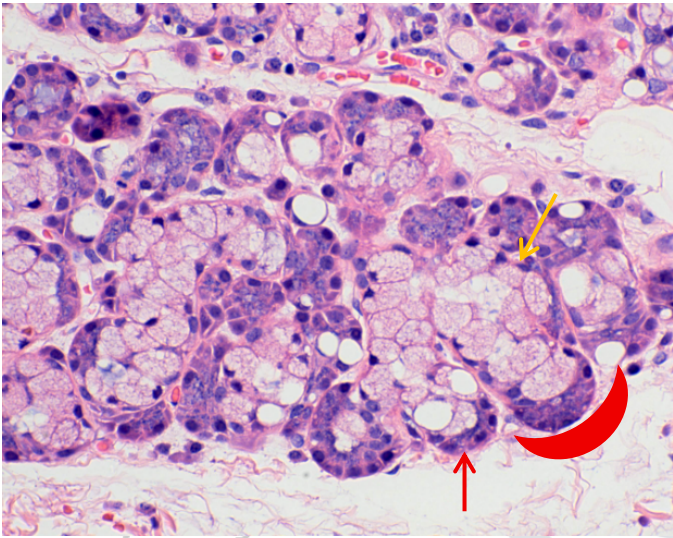


SUBLINGUAL GLAND

Mixed histology with mucous predominance (yellow arrows)



This slide clearly demonstrates the demilunes, which represent serous cells forming a crescent shape (red arrow) on top of mucous cells (yellow arrow) – lunar means moon/crescent 🌙





The University of Jordan
Gastroenterology Interest Group (UJ-GIG)
Booklet

Histology

Lower GI tract histology

Written by: Yasmin Al Subaihi

Edited by: Rawan Fratekh

Reviewed by: Amr Abdallah

[Overview]

→ Outline of lower GI tract histology:

- 1) Esophagus
- 2) The stomach
 - a. The mucosa
 - b. Other layers of the stomach
- 3) The small intestines
 - a. The mucosa
 - b. Other layers of the intestines
- 4) The large intestines
- 5) Vessels and lymphatics

[Esophagus]

It is a muscular tube that extends from the pharynx to the cardia of the stomach, measuring about 25 cm (45 cm from the incisors).

The functions of the esophagus are:

1) Transport of food from the mouth to the stomach

This is achieved through peristaltic contractions and the relaxation of the esophageal sphincters (upper and lower), which are controlled by reflexes and the autonomic nervous system.

2) To prevent the retrograde flow of gastric contents

Through the lower esophageal sphincter.

The esophagus has the same four layers as the rest of the digestive tract.

→ Mucosa

- Lining epithelium: **nonkeratinized stratified squamous epithelium**.
- Lamina propria: formed by loose connective tissue that contains blood vessels, lymphatics, and **esophageal cardiac glands**, which are more prominent in the distal part near the cardia of the stomach. They **secrete mucus**, which **lubricates and protects the esophageal mucosa**.
- Muscularis mucosa: inner circular and outer longitudinal.

→ Submucosa

- Formed by **dense connective tissue** that contains blood vessels, lymphatics, the **submucosal (Meissner's)** nerve plexus, and the esophageal glands. These **secrete mucus** to **lubricate and protect the mucosa and facilitate the transport of foodstuffs**.
- Only the duodenum and esophagus have glands in the submucosa to secrete the mucus that protects against the harsh stomach acid.

→ Muscular layer (*muscularis externa*)

- Consists of inner, thick circular and outer, thin longitudinal muscle layers
- Contains the **myenteric (Auerbach's)** nerve plexus between the two layers.
- Muscle type varies along the levels of the esophagus:
 - 1) **Upper 1/3**: only striated muscle cells (*under voluntary control*). Innervated by the **somatic** nervous system.
 - 2) **Middle 1/3**: mixture of striated and smooth muscle cells.
 - 3) **Lower 1/3**: Only smooth muscle cells. Innervated by the **autonomic** nervous system. These cells form the **lower esophageal sphincter** near the stomach.

Remember, striated muscles (skeletal and cardiac) have organized sarcomeres, giving them a striped look, and are for voluntary movement (skeletal) or involuntary pumping (cardiac).

Smooth muscles lack sarcomeres, appear smooth, and control involuntary functions, such as digestion, in hollow organs.

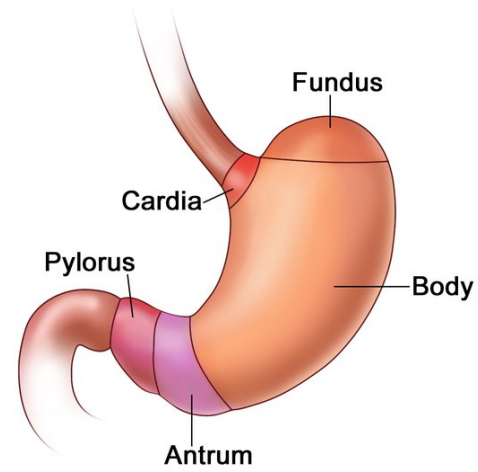
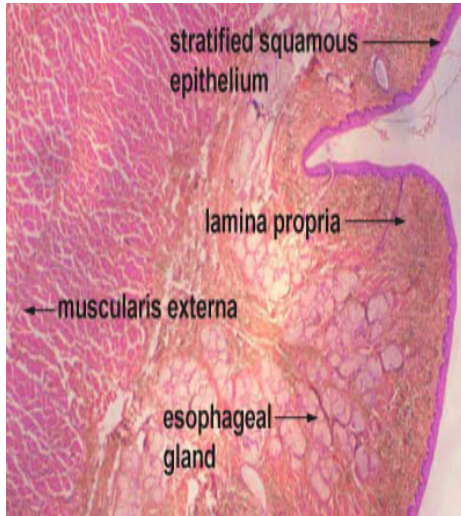
→ Serosa/adventitia

- Adventitia: covers the esophagus **from the neck to the thorax**.
- Serosa: covers the short abdominal **segment below the diaphragm** (~1.3 cm).

Remember

Serosa is only present when near the peritoneum; otherwise, it is called adventitia.

The layers of the esophagus, as identified under the microscope:



[Stomach]

The stomach is a dilated segment of the GI tract, which, like the small intestine, is considered a mixed exocrine-endocrine organ that digests food and secretes hormones.

Its main functions are:

- 1) Continues the digestion of carbohydrates initiated by amylase in the saliva.
- 2) Secretes acid (HCl), which mixes with ingested food to form chyme.
Chyme: the acidic fluid which passes from the stomach to the small intestines, consisting of gastric juices and partly digested food.
- 3) Begins the digestion of triglycerides by secreted lipase.
- 4) Promotes initial digestion of proteins by the enzyme pepsin.

The stomach consists of four regions upon gross inspection:

1. **Cardia** → which is the narrow, transitional zone (physiological sphincter) between the esophagus and the rest of the stomach.
2. **Fundus**
3. **Body**
4. **Pylorus** → a funnel-shaped region that opens into the small intestines.

Mucosa of the stomach

The mucosa that lines the stomach has three main layers:

- 1) Surface epithelium
- 2) Lamina propria
- 3) Muscularis mucosa

→ The surface epithelium

- Simple columnar epithelium cells without goblet cells
- It invaginates into the lamina propria, forming **gastric pits**. The tubular (cardiac, gastric, and pyloric) glands empty into these pits.
- The lining epithelium is **the primary source of the alkaline mucus** secreted by the stomach. Its composition reflects its function.
→ **protects the mucosa from gastric acid.**

→ The lamina propria

- Composed of loose connective tissue interspersed with smooth muscle and lymphoid cells, blood capillaries, and lymphatics.
- It contains **gastric glands**. Depending on the histological section, they can appear circular, oblique, or coiled.

→ The muscularis mucosa

- A thin layer of smooth muscle cells that separates the mucosa from the submucosa.

→ Gastric mucus

- Composition: **water (95%), lipids, and glycoproteins** → form a [hydrophobic](#) protective gel.
- It contains **bicarbonate**, secreted by the epithelial cells, which forms a **pH gradient** ranging from 1 at the gastric luminal surface to 7 along the epithelial cell surface.
- Epithelial cells form a vital defense line because they:
 - 1) Secrete mucus
 - 2) Have tight junctions and ion transporters that maintain intracellular pH and bicarbonate secretion.

The mucosal composition across the various stomach regions.

→ Cardia

- It is a narrow circular band, 1.5–3 cm in width, at the transition between the esophagus and the stomach.
 - **Composition:** the epithelium is simple columnar epithelium without goblet cells that contains [simple or branched tubular cardiac glands](#) that are coiled at the terminal portion (check the figure).
- Cells that can be found in the cardia:
- 1) Mucus cells → secrete mucus
 - 2) Parietal cells → secrete HCl
 - 3) Enteroendocrine cells → secrete gastrin
 - 4) Chief cells → secrete pepsinogen
 - 5) Stem cells → precursors to other cells

Parietal and chief cells are less abundant in the cardia compared to the body.

- Secretions:

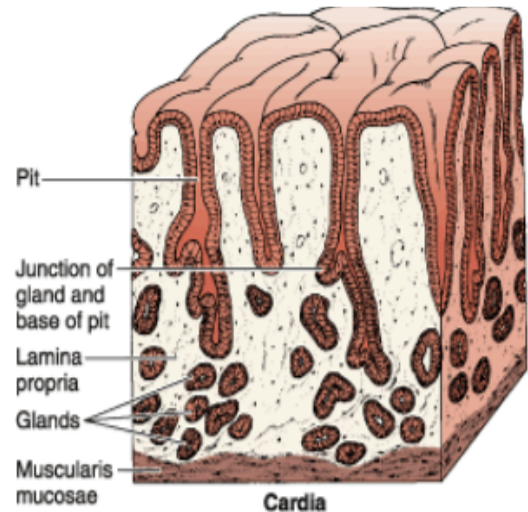
- 1) secretory cells produce mucus and **lysozyme** (an enzyme that attacks bacterial walls),
- 2) Parietal cells that secrete H⁺ and Cl⁻ (which will form HCl in the lumen) can be found.

- Note:

- 1) These glands are structurally similar to the cardiac glands in the terminal portion of the esophagus.

- 2) The thickness of the gastric pit and gland is equal.

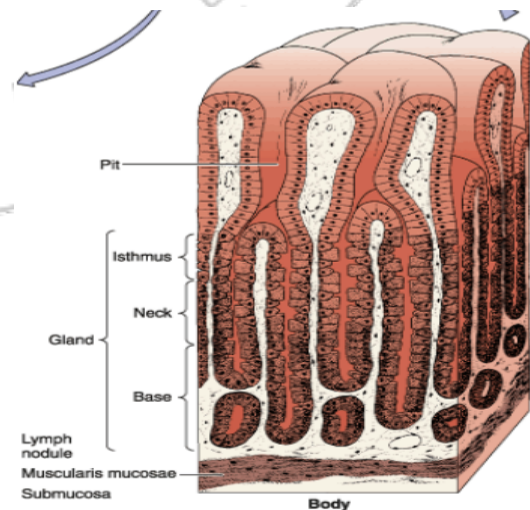
Notice the histological composition of the cardia.



→ Body/ fundus

- The body's primary role is digestion, which requires abundant glandular secretions.
- **Composition:** The lamina propria of the fundus and body is filled with [branched, tubular gastric \(fundic\) glands](#), three to seven of which open into the bottom of each gastric pit.
- **Note:** the pits appear wider and shorter than the glands, reflecting their central role in digestion.

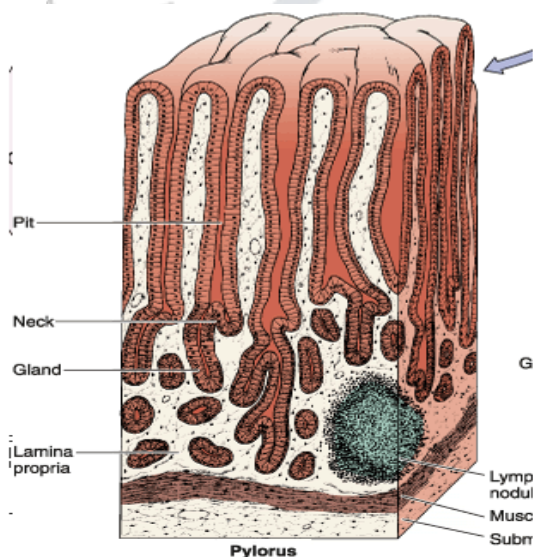
Notice the histological composition of the body.



→ The pylorus

- It is the most distal area of the stomach that contains: the antrum, pyloric canal, and pyloric sphincter.
- **Composition:** it has deep gastric pits into which the branched, tubular pyloric glands open. The myenteric and Meissner's plexus supply the glands and smooth muscle. Cells that can be found in the pylorus include:
 - 1) The pyloric glands have **mostly mucous cells** → they secrete mucus, which helps neutralize chyme before it enters the duodenum. They also secrete the enzyme lysozyme.
 - 2) G cells → secrete gastrin. The presence of food nutrients (amino acids) stimulates these cells to secrete gastrin, which in turn stimulates parietal cells to secrete HCl.
 - 3) D cells → secrete somatostatin, which inhibits the secretion of other hormones. Its secretion is stimulated by HCl.
- Note: the pylorus doesn't have a major role in digestion, and the pits are longer and narrower than the glands.

Notice the histological composition of the pylorus.



How do these cells interact with each other?

Nutrients such as amino acids and amines in the stomach, and distention of the stomach wall, → stimulates the parasympathetic system → which stimulates the G cells to secrete gastrin → gastrin stimulates the parietal cells to increase acid secretion → acid stimulates D cells to secrete somatostatin, which inhibits the release of some other hormones, including gastrin and acid (negative feedback)

Gastric glands

These glands fill the gastric mucosa and are concentrated in the body and fundus.

Each gastric gland has three distinct regions:

- 1) **Isthmus:** closest to the gastric pit. Contains differentiating stem cells
- 2) **Neck:** contains stem, mucous, parietal, and enteroendocrine cells.
- 3) **Base:** contains parietal, chief (zymogenic), and enteroendocrine cells,

The distribution of epithelial cells in the gastric glands is not uniform

- 1) **Mucous cells:** throughout the gland, but **most numerous in the neck.**
- 2) **Chief cells and enteroendocrine cells:** in **the base.**
- 3) **Parietal cells:** in the **neck and upper part of the body.**
- 4) **Stem cells:** in the **middle (isthmus),** and when mitosis occurs, they migrate upwards and downwards to replace the damaged cells.

Gastric gland cells

→ Stem cells

- **Histology:** low columnar cells with oval nuclei near the bases of the cells.
- **Location:** found in **the isthmus and neck** region, but few in number.
- **Function:** have a high mitosis rate (turnover time of 4-7 days) and **replace damaged cells.**

It can differentiate into mucous, parietal, chief, or enteroendocrine cells.

→ Mucous neck cells

- **Histology:** irregular in shape and has a nucleus near the base of the cell and secretory granules near the apical membrane.

Have a **foamy appearance** under the microscope due to mucus dissolution.

- **Location:** present in clusters between parietal cells in the neck of the gland.
- **Function:** their mucus is different from surface epithelial mucous cells.

→ Oxyntic (parietal) cells

- **Histology:** they are rounded or pyramidal in shape with a centrally located nucleus (sometimes binuclear) and an eosinophilic cytoplasm.

Under an electron microscope, **active cells** have **abundant mitochondria and deep, circular invaginations** of the apical plasma membrane, forming intracellular canaliculi.

In the **resting state**, several **tubulovesicular structures** are visible in the apical region below the plasma membrane, and they have few microvilli. When stimulated, the **tubulovesicles fuse with the cell membrane to form the canaliculus and additional microvilli**, thereby increasing the cell membrane surface area.

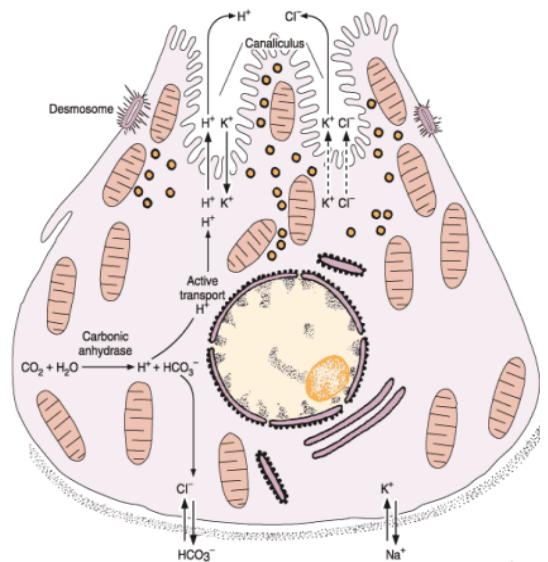
- **Location:** They are mainly present in the upper half of the gastric gland.
- **Function:** secrete hydrochloric acid and intrinsic factor.

HCl secretion →

- 1) H^+ originates from the dissociation of H_2CO_3 by the action of **carbonic anhydrase**.
- 2) The active cells also **secrete** K^+ and Cl^- in the lumen.
- 3) K^+ is **exchanged** for H^+ by the action of H^+/K^+ pump.
- 4) H^+ joins Cl^- to form HCl.

- **Notes:** The number of mitochondria reflects the **level of metabolic activity**, because the **exchange pumps require energy**. Acid secretion is stimulated by **histamine and gastrin**, which are secreted by the gastric mucosa (more on this in physiology).

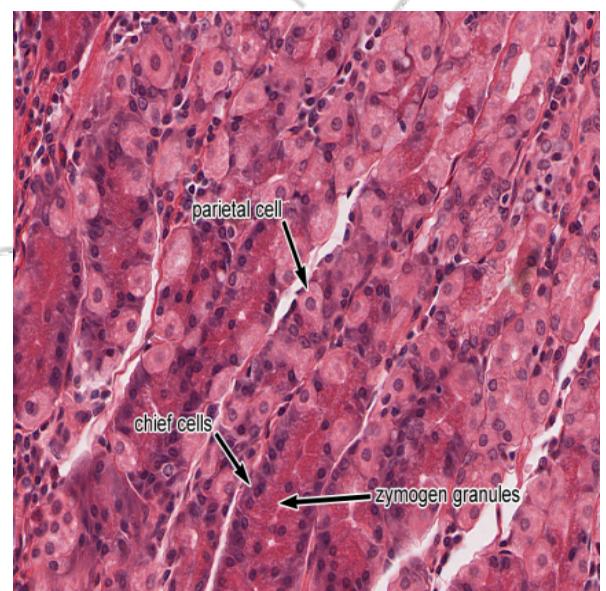
Notice the shape and organelles in the active parietal cell.



→ Chief cells

- **Histology:** they have abundant **endoplasmic reticulum**, which gives the cytoplasm a **basophilic appearance**, characteristic of protein-synthesizing and exporting cells.
- **Location:** the lower region of the gland.
- **Function:** they synthesize **pepsinogen**, which converts to the active enzyme pepsin, which is **responsible for protein digestion**. They can also secrete **lipase**. Humans have 7 different pepsins, which are endoproteases that function at $pH < 5$.

Notice how darker the chief cells appear bluer compared to the parietal cells.



- Enteroendocrine cells
- **Histology:** they're characterized by a **large nucleus**, and their secretions appear as **granules** under the electron microscope.
- **Location:** in the **neck and bases** of gastric glands.
- **Function:**
 - 1) In the fundus → they secrete **5-hydroxytryptamine (serotonin)**
 - 2) In the pylorus → G cells secrete **gastrin**, which stimulates gastric acid secretion and gastric mucosal growth.

Other layers of the stomach

→ Submucosa

Composed of dense connective tissue containing blood and lymph vessels, it is infiltrated by lymphoid cells, macrophages, and mast cells.

Rugae: longitudinal folds formed by the mucosa and submucosa of the empty stomach, which flatten when the stomach fills with food.

→ Muscular layer

Composed of smooth muscle fibers oriented in three main directions.

1. The external layer is longitudinal.
2. The middle layer is circular.
*Note that at the pylorus, the middle layer is greatly **thickened to form the pyloric sphincter**.*
3. The internal layer is oblique, **absent in the pyloric canal and sphincter**.

→ Serosa

The stomach is lined by a thin serosa. Remember, when in contact with the peritoneum, the outer layer is called serosa.

[Small intestine]

The small intestine is the site for terminal food digestion, absorption, and endocrine secretion. It is a relatively long tube (5 meters) that consists of three segments:

- 1) Duodenum
- 2) Jejunum
- 3) Ileum

Generally, the epithelial lining is simple columnar epithelium with goblet cells, and as we go distally, the number of goblet cells increases.

The mucosa

Special structures

Multiple histological structures set the small intestine apart from the rest of the GI tract, optimizing its primary role in digestion and absorption.

→ Plicae circularis (Kerckring valves)

A series of **permanent folds** consisting of mucosa and submucosa in the small intestine.

They are primarily developed and present in the jejunum.

→ Intestinal villi

They are 0.5- to 1.5-mm-long outgrowths of the mucosa (epithelium plus lamina propria) projecting into the lumen of the small intestine.

They're covered by simple columnar epithelial cells called **enterocytes**. With many interspersed goblet cells.

- In the duodenum -> they are leaf-shaped.
- Jejunum and ileum -> gradually turn into a fingerlike shape.

Enterocytes are simple columnar epithelial absorptive cells with a prominent apical region called the **brush border (microvilli)**.

Villi have a **core of loose connective** tissue that contains fibroblasts, smooth muscle fibers, lymphocytes and plasma cells, blood capillaries, and a central lymphatic called **lacteal**.

The plica circularis, villi, and microvilli greatly increase the absorptive surface.

→ Intestinal glands (crypts), or glands of Lieberkühn

These are simple tubular glands in the small intestines. They are lined with simple columnar epithelium with goblet cells, The epithelium of the glands is continuous with that of the villi.

- They contain **stem cells, some absorptive cells, goblet cells, Paneth's cells, enteroendocrine cells, and mucus cells**.

The glands' openings are located between the villi.

Notice the lining of the small intestine.

Epithelial lining & the small intestinal cells

→ Absorptive cells (enterocytes)

- **Structure:** tall columnar cells, each with an oval nucleus in the basal half of the cell. At the apex of each cell is a homogeneous layer called the **striated (brush) border**. Under the electron microscope, the striated border appears as a layer of densely packed **microvilli**.

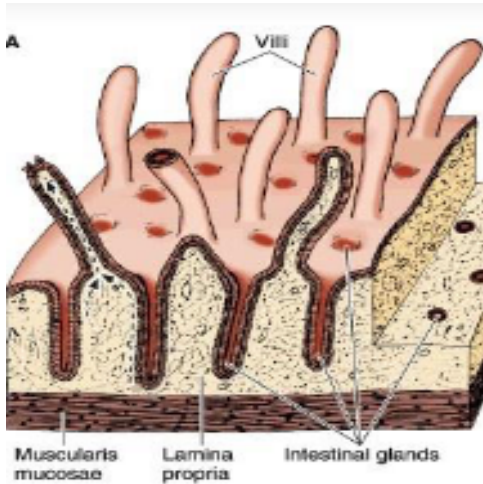
Each absorptive cell is estimated to have an average of 3000 microvilli, and 1 mm² of mucosa contains about 200 million of these structures

Function of the microvilli

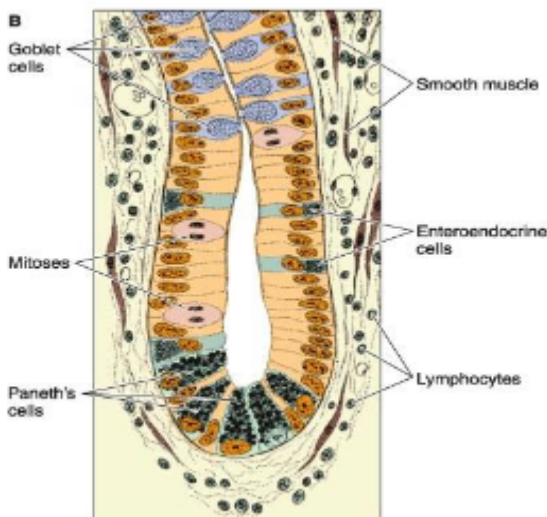
Increase the area of contact between the intestinal surface and the nutrients.

Microvilli components

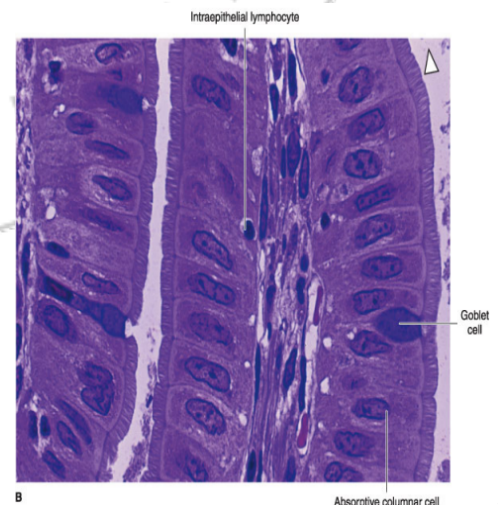
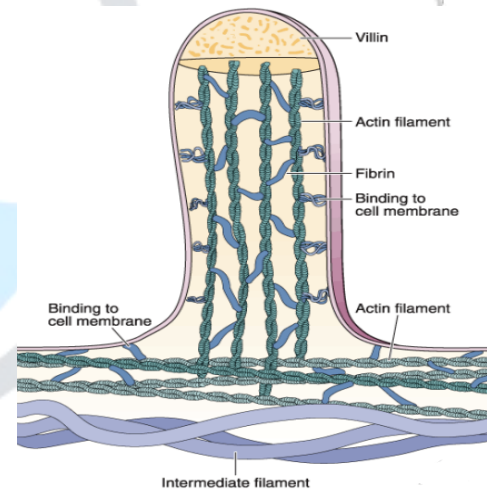
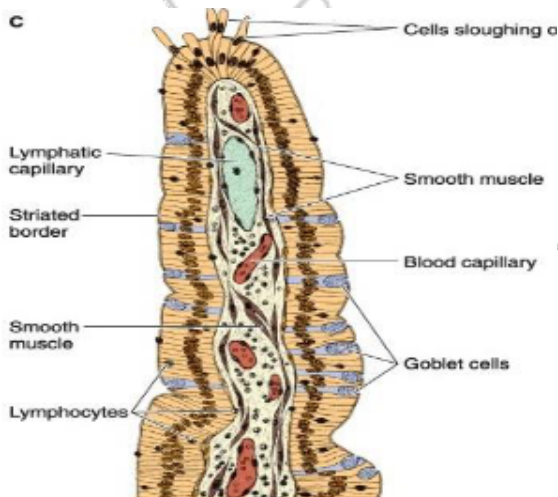
Consists of the cell membrane enclosing a core of actin microfilaments associated with other cytoskeletal proteins.



The intestinal crypts

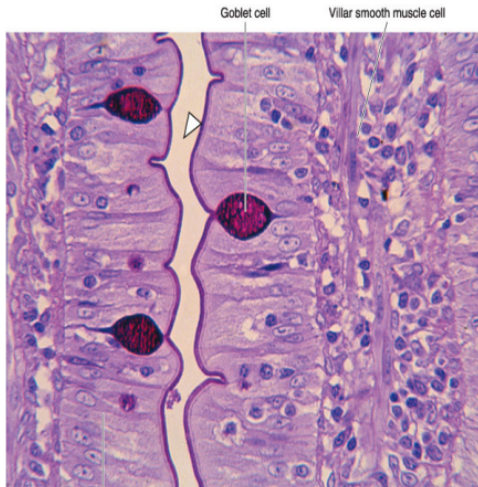


The structure of the villi.



→ **Goblet cells**

- **Location:** interspersed between the absorptive cells. They are less abundant in the duodenum and increase in number as they approach the ileum.
- **Function:** they produce acid glycoproteins to form mucus, whose primary function is to **protect and lubricate the lining of the intestine.**



A Absorptive columnar epithelium

→ **Paneth's cells**

These are **acidophilic** exocrine cells with secretory granules in their apical cytoplasm.

- **Location:** in the **basal portion of the intestinal glands**, most prominent in the **Jejunum.**
- **Function:** they secrete **lysozyme**, an enzyme that digests the cell walls of bacteria. It also plays a role in controlling the intestinal flora.

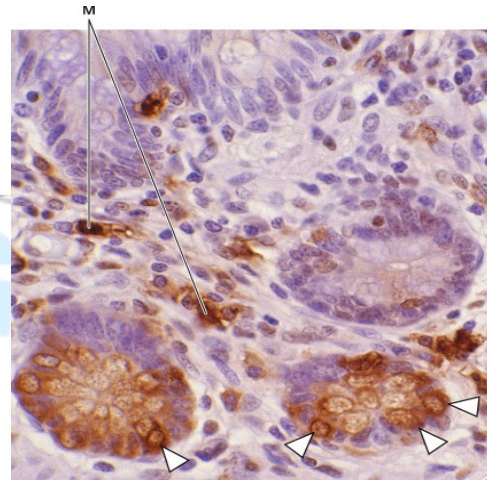
→ **M (microfold) cells**

They are specialized epithelial cells overlying the lymphoid follicles of Peyer's patches.

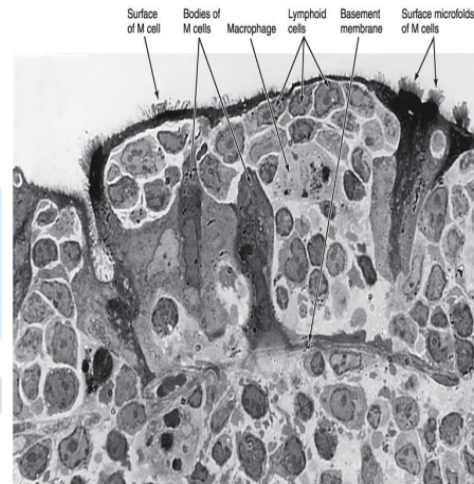
- **Location:** Prominent in the **ileum.**
- **Structure:** they have **numerous basal membrane invaginations (pits)** that contain lymphocytes and macrophages.
- **Function:** M cells represent an essential link in the **intestinal immunological system.**

M cells can **endocytose antigens** and transport them to the underlying **macrophages** and **lymphoid cells**, which then migrate to other compartments of the lymphoid system (nodes).

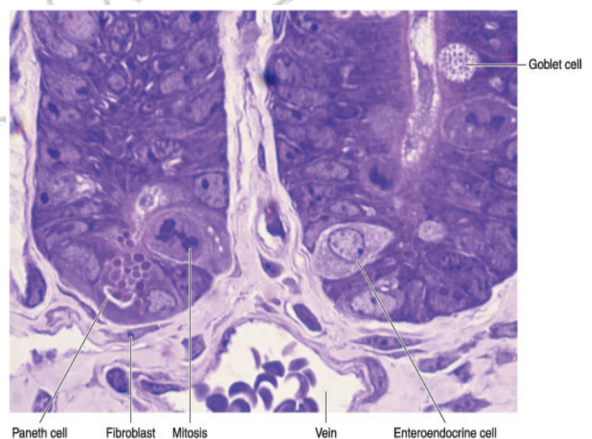
Notice the appearance of M cells under the light and electron microscope.



The basement membrane under M cells is not continuous (**separated**), facilitating transit of lymphocytes and macrophages between the lamina propria and M cells.



Notice the differences in histological appearance between the different cell types.

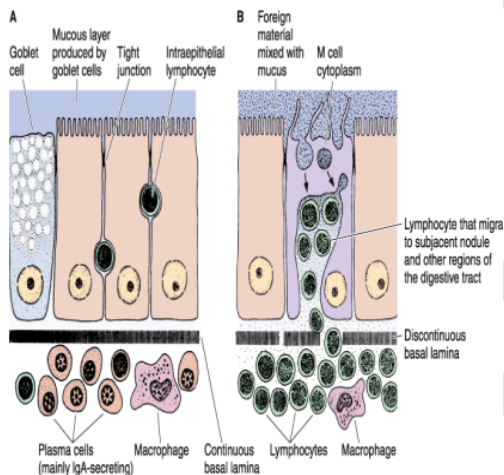


The importance of immune cells within the digestive tract

The huge mucosal surface of the gastrointestinal tract is exposed to many potentially invasive microorganisms.

The GI tract protects itself through many mechanisms:

- 1) **IgA immunoglobulins:** secretory immunoglobulins of the **IgA** are the first line of defense.
- 2) **Tight junctions:** the intercellular tight junctions that make the epithelial cells a barrier to the penetration of microorganisms.
- 3) **Other immune cells:** It also contains antibody-secreting **plasma cells**, **macrophages**, and a vast number of **lymphocytes** located in both the mucosa and the submucosa. Together, these cells are called **gut-associated lymphoid tissue (GALT)**.



Lamina propria

- Structure: composed of **loose connective tissue with blood and lymph vessels, nerve fibers, and smooth muscle cells**.
- It penetrates the core of the intestinal villi

Muscularis mucosa

- Contain smooth muscle cells that extend into the villi and are responsible for their **rhythmic movements**, which are essential for absorption.

Other layers of the small intestine

→ Submucosa

- It contains larger blood and lymph vessels and the submucosal nerve plexus.
- It also contains **Brunner's glands**. Function of the glands: **secretes a thick, alkaline mucus** that:
 - 1) Protects the duodenal lining from the stomach's acidic chyme
 - 2) Neutralizes the acid with bicarbonate and lubricates the intestine
 - 3) Provides an optimal environment for digestive enzymes, also contributing to immune defense and cell growth.

Peyer's patches

Aggregates of lymphoid nodules. They are an essential component of GALT.

- **Location:** in both the **lamina propria and submucosa**. Peyer's patches are most prominent in the **ileum**.
- **Structure:** each patch consists of 10–200 nodules and is visible to the naked eye as an oval area on the **antimesenteric** side of the intestine. The **area is devoid of microvilli** and topped by an M cell.
- **Notes:** There are about 30 patches in humans, most of them in the ileum.

→ Muscular layer

- Well-developed in the small intestines with an internal circular layer and external longitudinal layer.
- Between them is the myenteric plexus.

[The large intestines]

The large intestine mainly absorbs water and electrolytes from feces and has the following regions:

- 1) Cecum
- 2) Ileocecal valve
- 3) Appendix
- 4) Ascending, transverse, and sigmoid colon
- 5) Rectum

The mucosa

- Lacks villi and folds, except in the rectum.
- Contains tubular intestinal glands and **colonocytes**, which have irregular microvilli and dilated intracellular spaces, indicating active fluid absorption.
- Contains goblet cells that produce lubricating mucus.

The muscular layer

- It has longitudinal and circular layers.
- The outer longitudinal layer is gathered in three separate bands called **teniae coli**.

The wall

- The wall of the colon is puckered into a series of large sacs called **haustra**.

[Vessels and lymphatics]

→ Vascularity

- The blood vessels of the intestine form a large plexus in the **submucosa**; they pierce through the muscularis mucosa and lamina propria to reach the villi.
- The amount of blood supply is proportionate to the size of the villus. Bigger villi receive more blood.
- At the tips of the villi, one or more venules arise from these capillaries and run in the opposite direction, reaching the veins of the submucosal plexus. These capillaries are called **lacteals**.

Lacteals

- **Location & structure:** Lacteals run to the region of the lamina propria above the muscularis mucosae, where they form a plexus. From there, they are directed to the submucosa, where they surround lymphoid nodules. They anastomose multiple times and leave the GI tract along with blood vessels.
- **Function:** **absorption of lipids**, because blood circulation does not easily accept the lipoproteins produced by the absorptive cells during this process.

→ Innervation

The innervation of the intestines is formed by:

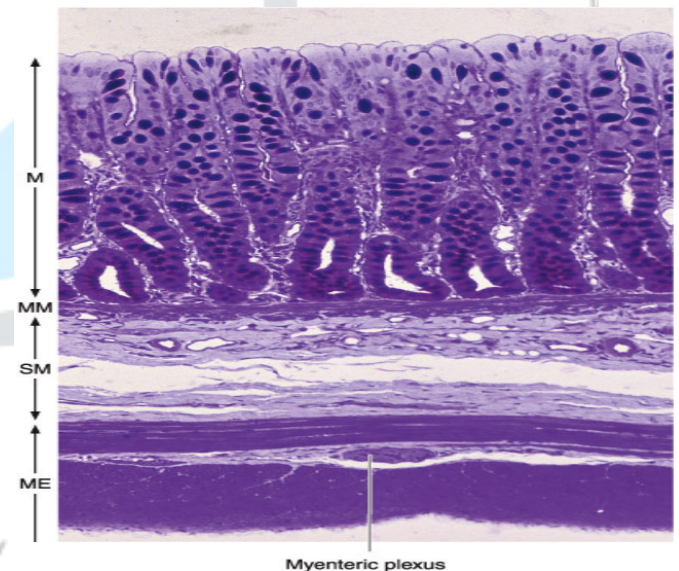
Intrinsic component (Enteric nervous system)

- 1) **Myenteric** (Auerbach's) nerve plexus, which is located between the outer longitudinal and inner circular layers of the muscularis. Contains axons, Schwann cells, and neuronal cell bodies.
- 2) **Submucosal** (Meissner's) plexus in the submucosa.

They contain both sensory and motor innervation.

- They contain sensory neurons that receive information from nerve endings near the epithelial and smooth muscle layers. These stimuli include:
 - 1) Chemical stimuli (food content)
 - 2) Mechanical stimuli (distension)

The intrinsic innervation formed by these plexuses is responsible for the intestinal contractions that occur in the total absence of extrinsic innervation.



Extrinsic component (autonomic nervous system)

1) **Parasympathetic** cholinergic nerve fibers, mainly through the vagus nerve.

- **Preganglionic** fibers: travel via the **vagus** nerve and synapse with the neurons in the **myenteric plexus**.
- **Postganglionic** fibers: **very short fibers** directed at the smooth muscle cells and glands.
- **Result:** **increase** smooth muscle contract and overall GI secretions.

2) **Sympathetic** adrenergic nerve fibers

- **Preganglionic:** originates **in the spinal cord (T5-T12)** and synapses in the paravertebral ganglia (celiac, superior mesenteric, etc.)
- **Postganglionic fibers:** **long**, to the smooth muscle cells and glands.
- **Result:** **inhibit** GI movement and overall secretions





The University of Jordan
Gastroenterology Interest Group (UJ-GIG)
Booklet

Histology

Lower GI tract histology 2

Written by: Yasmin Al Subaihi

Edited by: Rawan Fratekh

Reviewed by: Amr Abdallah

Large Intestines

The large intestine has 3 main functions:

1. absorption of water
2. Formation of the fecal mass
3. Production of mucus.

Due to these functions, the large intestine differs from the small intestine in these features:

1. mucosal membrane with no folds except in its distal (rectal) portion
2. No villi are present in this portion of the intestine
3. The glands are long and characterized by a great abundance of **goblet and absorptive cells** and a small number of enteroendocrine cells

Layers of the large intestines:

1) Mucosal layer:

-lining epithelium: **simple columnar epithelium with absorptive cells (enterocytes) containing microvilli.**

-lamina propria: rich in lymphoid cells and in nodules that frequently extend into the submucosa. Why is it rich in lymphoid tissue? This richness in lymphoid tissue (GALT) is related to the abundant bacterial population of the large intestine.

2)Submucosa:

Contains **solitary lymph nodes**

3)muscular layer:

1. Outer layer: longitudinal
2. Inner layer: circular

This layer differs from that of the small intestine, because fibers of the outer longitudinal layer congregate in three thick longitudinal bands called **teniae coli.**

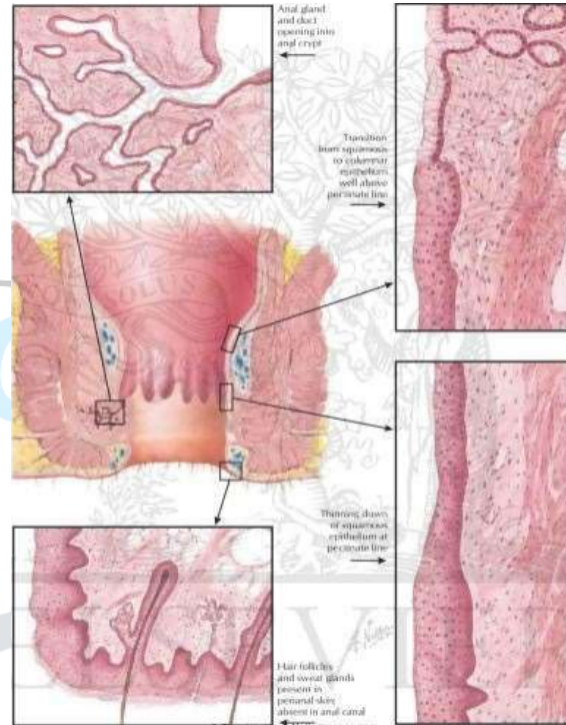
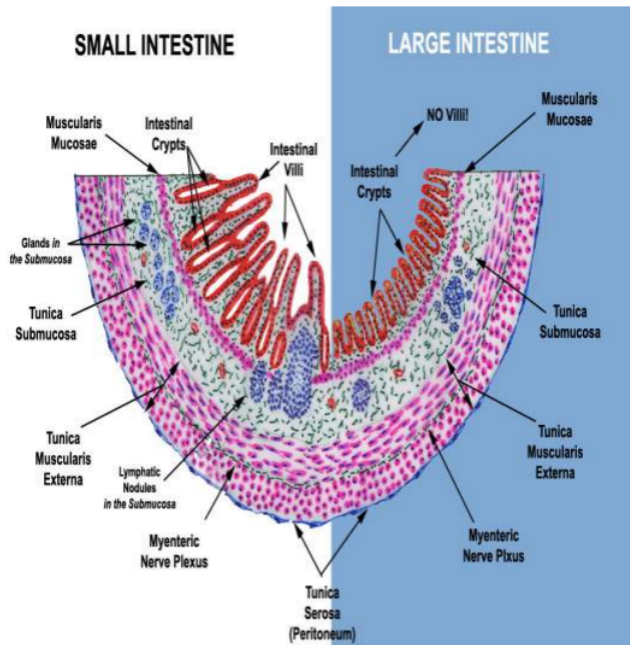
4)Serosa/ Adventitia:

In the intraperitoneal portions of the colon, the serous layer is characterized by small, pendulous protuberances composed of adipose tissue—the **appendices epiploicae.**

Main Differences between the small and large intestine:

Feature	Small Intestine	Large Intestine
Mucosa Structure	Presence of Intestinal Villi and Intestinal Crypts	NO Villi; contains only intestinal crypts
Mucosa Thickness	Standard thickness	Thicker mucosa
Epithelium	Simple columnar epithelium	Simple columnar epithelium with an abundance of goblet cells
Intestinal Crypts	Present as shorter glands	Longer, more closely packed, and no Paneth cells
Submucosa Content	Contains glands and lymphatic nodules; these glands are branched	Contains solitary lymph nodes
Lamina Propria	Standard distribution	Reduced in size
Muscularis Layer	Standard development	Well developed
Primary Function	Digestion and nutrient absorption	Water/electrolyte absorption and waste storage
Average Length	~6-7 meters (Longer)	~1.5 meters (Shorter)
Average Diameter	~2.5-3 cm (Narrower)	~6-7 cm (Wider)

Muscularis Externa	Complete longitudinal layer	longitudinal layer forms Teniae Coli
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Anal canal:

-Mucous Membrane: Forms a series of longitudinal folds known as the **rectal columns of Morgagni**

Epithelium Transition: About 2 cm above the anal opening, the intestinal mucosa is replaced by **stratified squamous epithelium**. The proximal 2 cm have the same epithelial lining as the rectum.

-Anal Orifice Structure: Rectal columns connect to the anal orifice to form **anal valves and sinuses**

-Lamina Propria: Contains a **plexus of large veins**; excessive dilation of these veins produces hemorrhoids

-Muscularis Layer: This layer gives rise to the **anal sphincter**.

-Adventitia Layer: Connects the anal canal to the surrounding anatomical structures.

Appendix:

Origin: An evagination of the cecum

-Epithelium: similar to that of the large intestine.

-Lumen: Characterized by a relatively small, narrow, and irregular lumen. That is why, once obstructed, it can easily rupture.

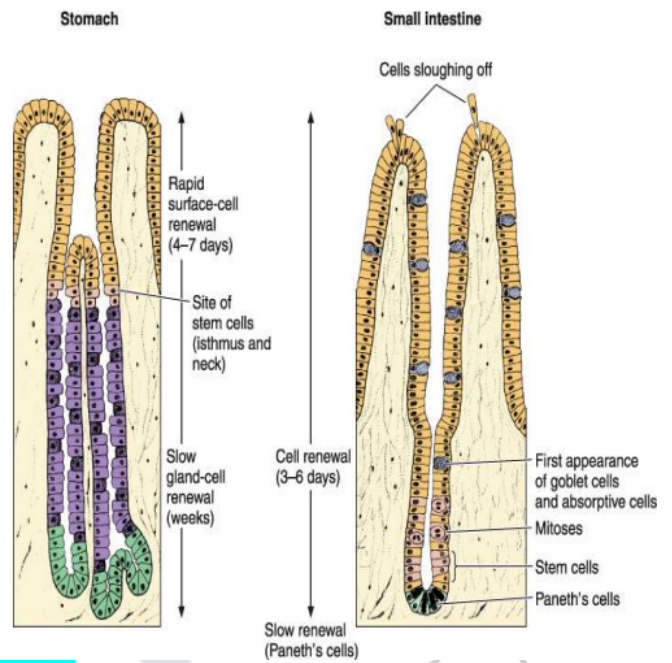
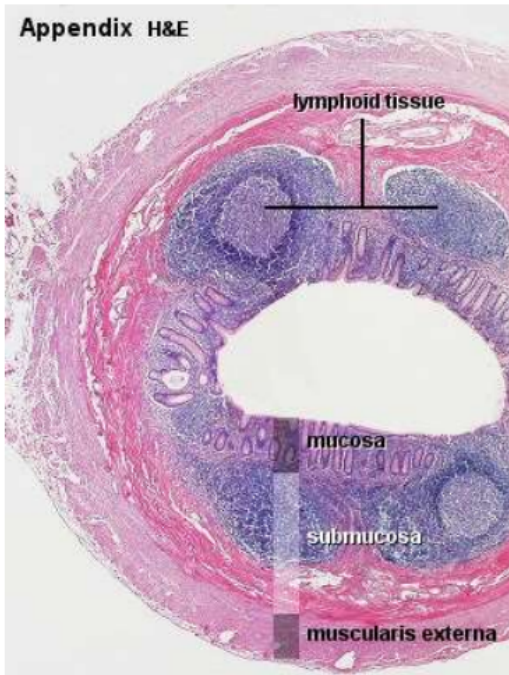
-Lymphoid Tissue: Contains abundant lymphoid follicles in its wall, forming a circular layer in the mucosa that may infiltrate the submucosa.

-Glands: Contains fewer and shorter intestinal glands compared to the large intestine

-Muscularis Externa: Lacks teniae coli, unlike the general structure of the large intestine.

-Outer Covering: Covered entirely by serosa, specifically the **mesoappendix**.

Appendix H&E



Liver:

The liver is categorized as the second-largest organ in the human body, surpassed only by the skin, and is the body's largest gland. It typically weighs approximately **1.5 kg**.

Function

The liver serves as a critical **interface** between the digestive system and the blood. Its primary roles, as outlined on this page, include:

- **Processing Nutrients:** It processes nutrients that have been absorbed from the digestive tract.
- **Storage:** It stores these processed nutrients for later use by other parts of the body.

Dual Blood Supply

The liver's position in the circulatory system is unique due to its **dual blood supply**, which allows it to receive nearly all materials absorbed by the intestines.

Cell Renewal in the Gastrointestinal Tract

-Core Process: Epithelial cells of the entire tract are constantly cast off and replaced by new ones formed through mitosis of stem cells.

-Stem Cell Locations in the entire GI tract:

- Basal layer of esophageal epithelium.
- Neck of gastric glands.
- Lower half of the intestinal glands.
- Bottom third of the crypts of the large intestine.

-Maturation Process: Cells move from the proliferative zone in each region to the maturation area (upwards and downwards in the stomach, only upwards in the small intestine), where they undergo structural and enzymatic maturation to provide the functional cell population.

-Small Intestine Cell Death:

Cells die by apoptosis at the tip of the villi or are sloughed off by mechanical action during function.

Blood Source	Percentage of Total Supply	Origin/Purpose
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Portal Vein	70% – 80%	Arises from the stomach, intestines, and spleen. It carries all materials absorbed via the intestines to the liver.
Hepatic Artery	20% – 30%	Supplies oxygenated blood to the liver tissue.

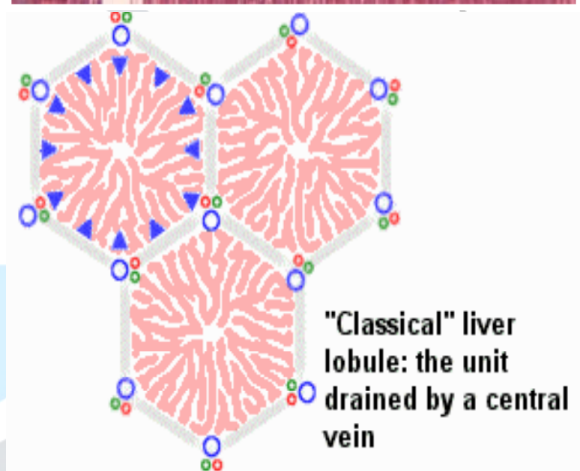
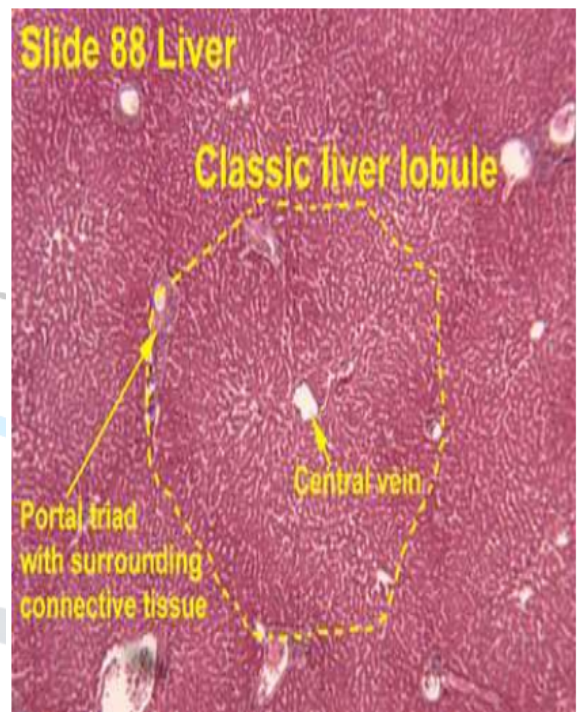
Note on Lipid Transport: Complex lipids, specifically chylomicrons, are an exception to this rule; they bypass the portal vein and are transported mainly through **lymph vessels**

Architecture

- **External Structure:** It is covered by a thin connective tissue capsule called **Glisson's capsule**, which becomes thicker at the hilum. The capsule forms the lobes and lobules.
- **Liver Lobule:** The basic structural unit, consisting of a polygonal mass of tissue.
- **Hepatocytes:** Epithelial cells that make up two-thirds of the liver mass, arranged in interconnected plates. It could be binucleated.
- **Central Vein:** Located at the center of each lobule.
- **Portal Spaces:** Located at the corners of the lobules.

Route of drainage:

Portal vein---> hepatic vein---> inferior vena cava

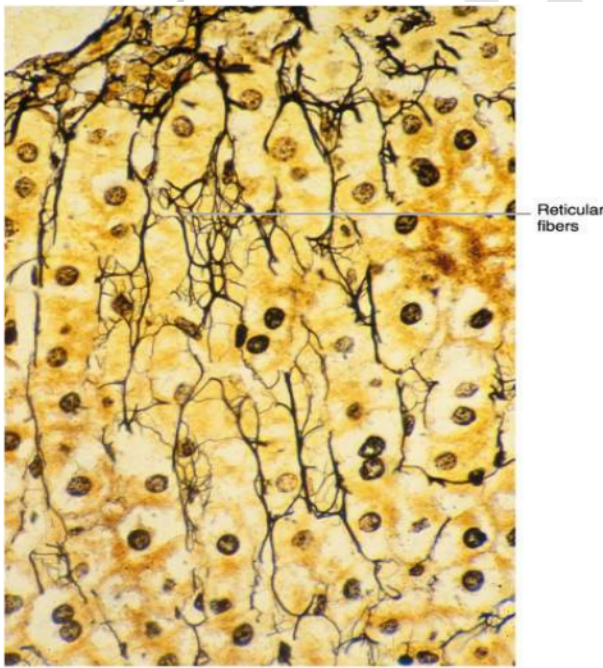
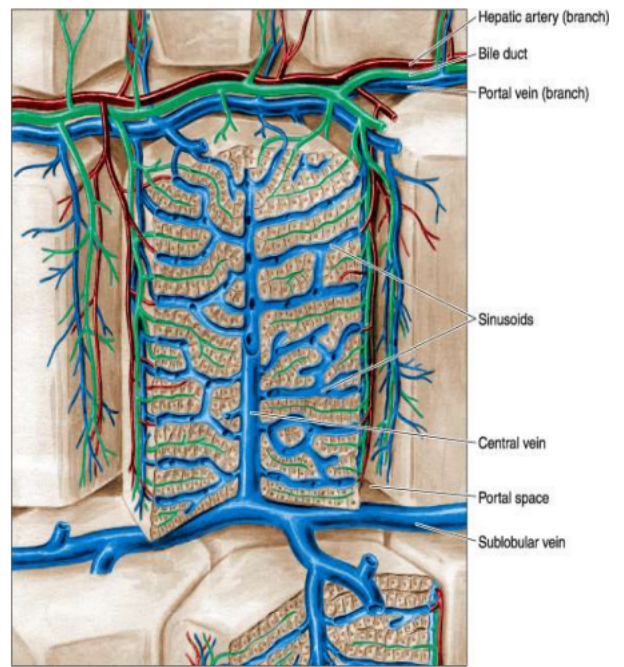


Liver Cytology and Microcirculation

The liver contains specialized cells and spaces that facilitate the exchange of macromolecules and immune defense.

- **Sinusoids:** Discontinuous, fenestrated capillaries that run between hepatocyte plates. Oxygenated blood and nutrients accumulate here.
- **Space of Disse (Perisinusoidal Space):** Located between endothelial cells and hepatocytes; it allows for the free flow of plasma and the exchange of nutrients/waste.

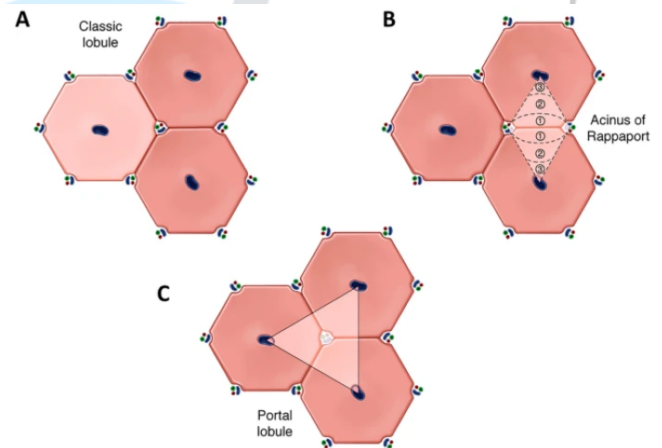
- **Kupffer Cells:** Macrophages found within the sinusoids; they metabolize aged red blood cells and destroy bacteria.
- **Ito (Stellate) Cells:** Located in the space of Disse; their primary roles are **Vitamin A storage** and the production of extracellular matrix proteins.
- **The Portal Triad (found in portal spaces):**
 - **Venule:** A branch of the portal vein.
 - **Arteriole:** A branch of the hepatic artery.
 - **Bile Duct:** Lined with cuboidal epithelium.
 - **Lymphatic Vessels.**
 - **Reticular fibers**



Notice that there are two rows of cells with sinusoids (takes nutrients and oxygen to form bile) on one side and bile ducts on the other.

Types of liver lobules:

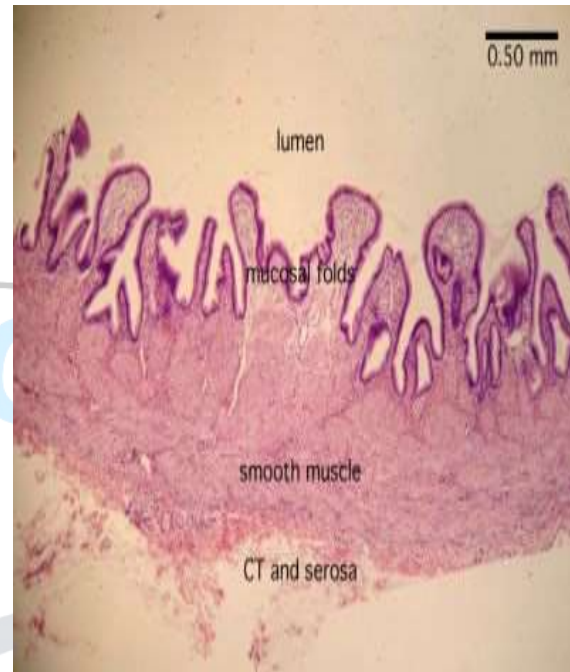
A: classic lobule B: acinus C: portal lobule



Notice the reticular fibers that fill the stroma of the liver. It supports the sinusoids and hepatocytes.

Type of Lobule	Shape / Structure	Central Landmark	Corner Landmarks	Primary Focus
Classic Hepatic	Hexagonal	Central Vein	Portal Triads	Blood flow direction (periph

Lobule				ery to center)
Portal Lobule	Triangular	Portal Triad	Central Veins	Bile drainage (center to periphery)
Hepatic Acinus	Diamond / Oval	Vascular Backbone (Distributing Vessels)	Central Veins & Portal Triads	Metabolic activity and oxygen gradient



Gallbladder

A pear-shaped organ that stores and concentrates bile.

- **Mucosa:** Simple columnar epithelium with abundant folds; **no goblet cells.**
- **Unique Structure:** Lacks a muscularis mucosa and submucosa.
- **Regulation:** Contraction is induced by **cholecystokinin (CCK)**, released by the small intestine in response to dietary fats.

Notice the lack of muscularis mucosa and submucosa

Pancreas

A mixed gland with both exocrine and endocrine functions.

- **Exocrine Portion:** A compound acinar gland that secretes digestive enzymes (proteases, amylase, lipases).
- **Endocrine Portion:** Clusters of cells known as Islets of Langerhans that produce hormones.
- **Centroacinar Cells: Unique to the pancreas;** these are the initial cells of the intercalated ducts found inside the acini.
- **Duct System:** Unlike the parotid gland, the pancreas has no striated ducts.
- **Activation:** Enzymes are stored as inactive proenzymes; they are activated in the small intestine by enterokinase.

Difference between pancreas and parotid duct:

Feature	Pancreas	Parotid Gland
Striated Ducts	Absent	Present
Islets of Langerhans	Present (Endocrine portion)	Absent
Centroacinar Cells	Present (Intraacinar portion of duct)	Absent
Gland Type	Mixed (Exocrine and Endocrine)	Exocrine (Serous)

