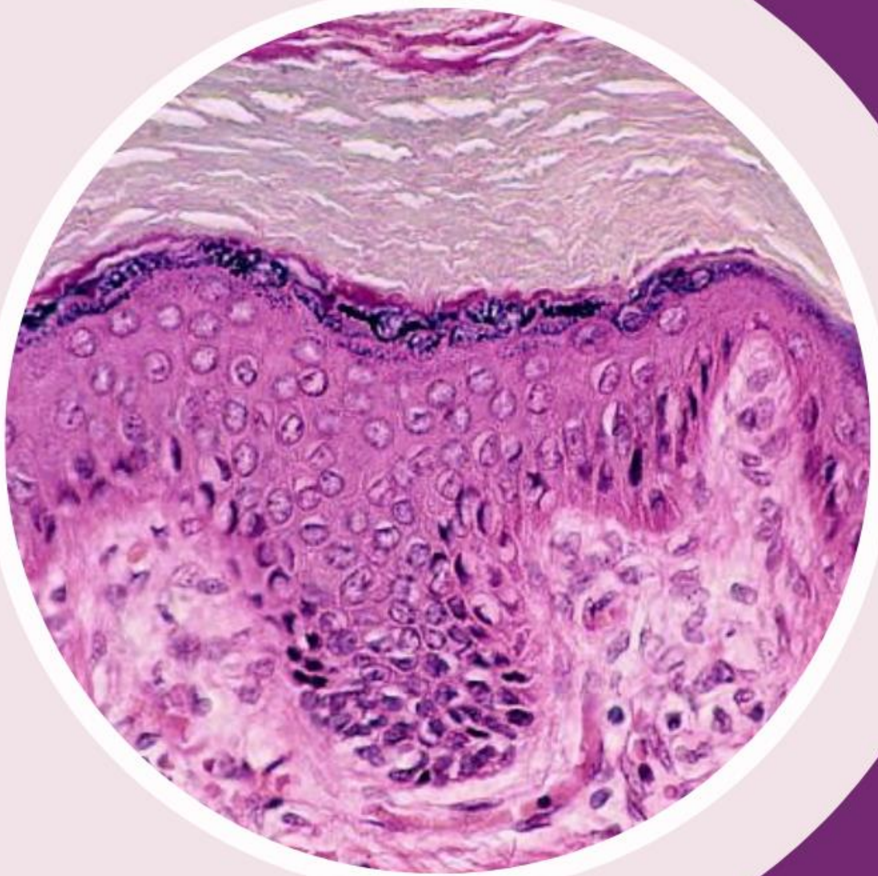
GI

Histology

LEC no. 1



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GI Histology 3

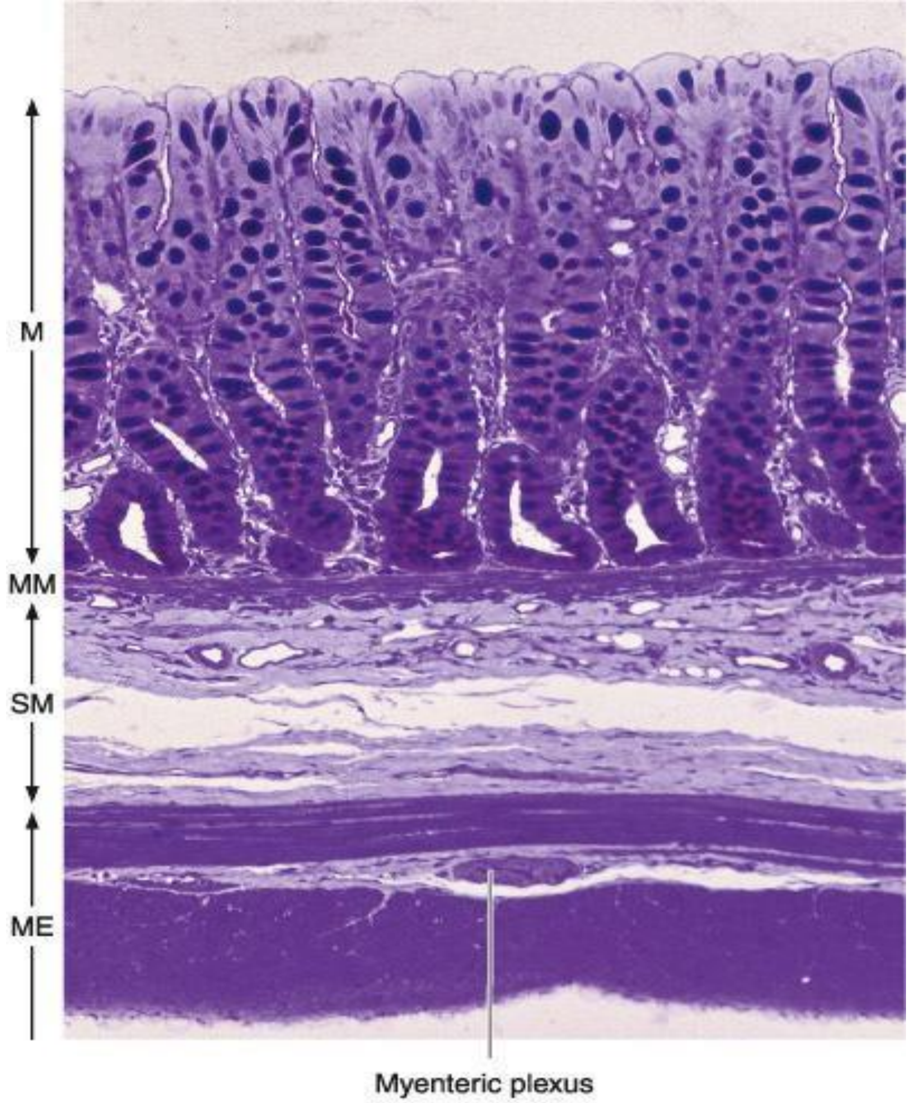
Large Intestine

- **<u>The large intestine consists of a mucosal membrane with no folds except in its distal (rectal) portion</u>**

- **As all GIT with many distinctive features, large intestine has 4 main layers mucosa, submucosa, muscularis externa with the myenteric plexus between the inner circular and the outer longitudinal layer and the last layer is adventitia.**

- **The esophagus and pharynx are lined with a stratified squamous non-keratinized epithelium**
- **The stomach is covered by a simple columnar epithelium without goblet cells.**
- **The small intestine is lined with a simple columnar epithelium with goblet cells.**
- **<u>The large intestine is lined with simple columnar epithelium with NUMEROUS goblet cells.</u>**

- **The main function of large intestine is water absorption and feces formation. To facilitate these processes, it is rich of goblet cells and intestinal glands such as the crypts of Lieberkühn. These structures produce lubricating mucus, essential for the smooth passage of feces.**



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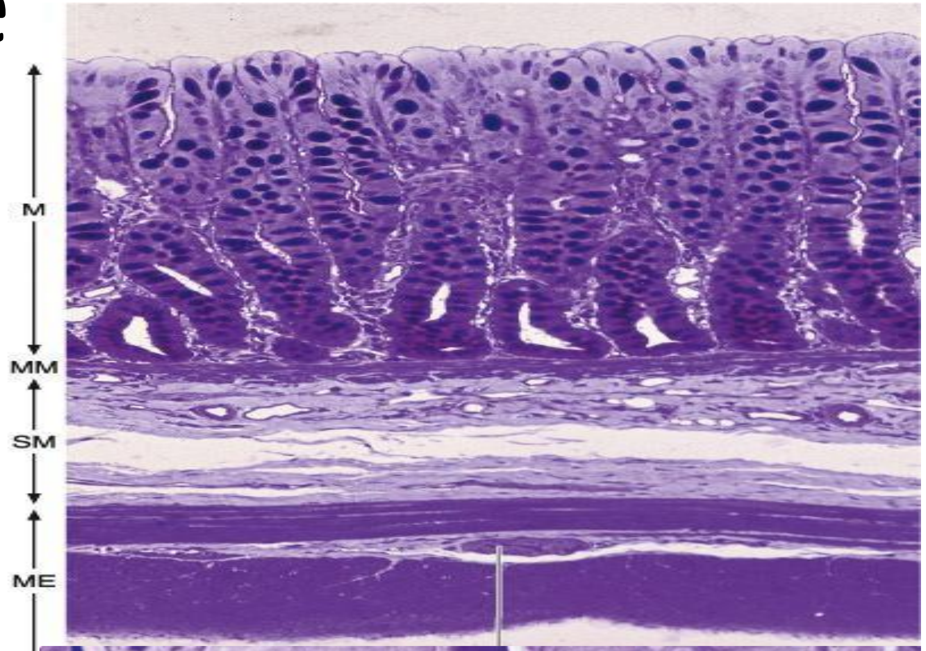
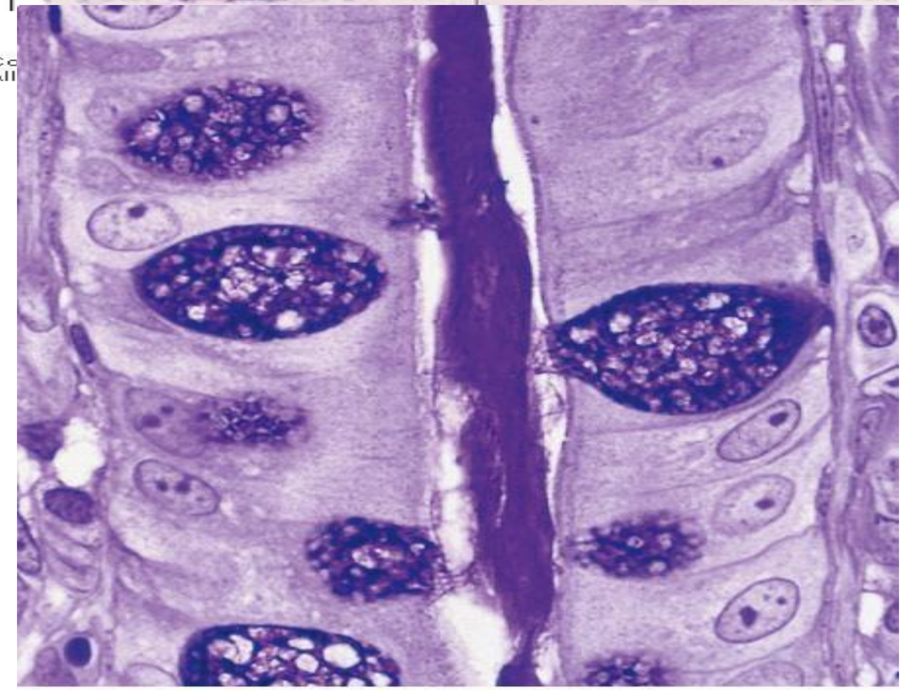
Large Intestine

No villi and folds are present in this portion of the intestine The intestinal glands are long and characterized by a great abundance of goblet and absorptive cells and a small number of enteroendocrine cells The absorptive cells are columnar and have short, irregular microvilli The large intestine is well suited to its main functions: absorption of water, formation of the fecal mass, and production of mucus.

Mucus is a highly hydrated gel that not only lubricates the intestinal surface but also covers bacteria that are commensal in large intestine to protect them and particulate matter.

The absorption of water is passive, following the active transport of sodium out of the basal surfaces of the epithelial cells.





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- The lamina propria is rich in lymphoid cells and in nodules that frequently extend into the submucosa

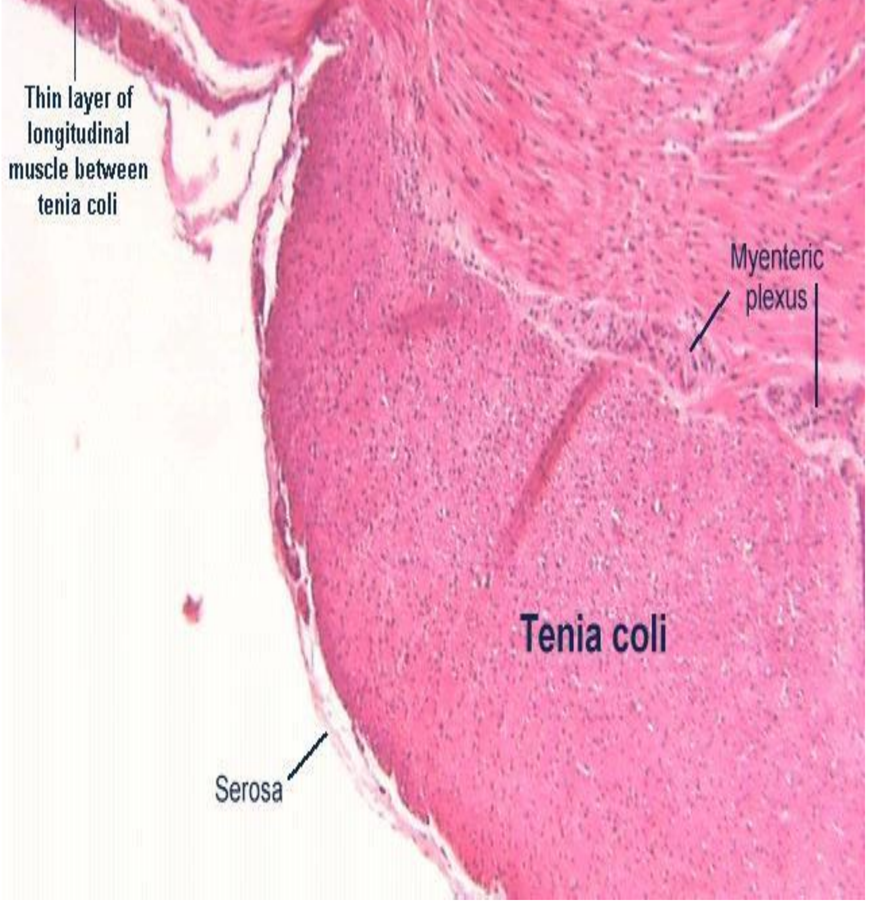
- This richness in lymphoid tissue (GALT) is related to the abundant bacterial population of the large intestine.

- The muscularis comprises longitudinal and circular strands

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

- Sometimes, the appendix lies in a retrocecal position, making it inaccessible during an endoscopic examination by a gastroenterologist. To locate it, the gastroenterologist may need to navigate along the taeniae coli until reaching the base of the cecum, where the appendix is situated.

- In the intraperitoneal portions of the colon, the serous layer is characterized by small, pendulous protuberances composed of adipose tissue (Mainly TAGs) —The appendices epiploicae which are lied on the surface of large intestine to provide required energy.



- **So the differences between the small and large intestine are :**

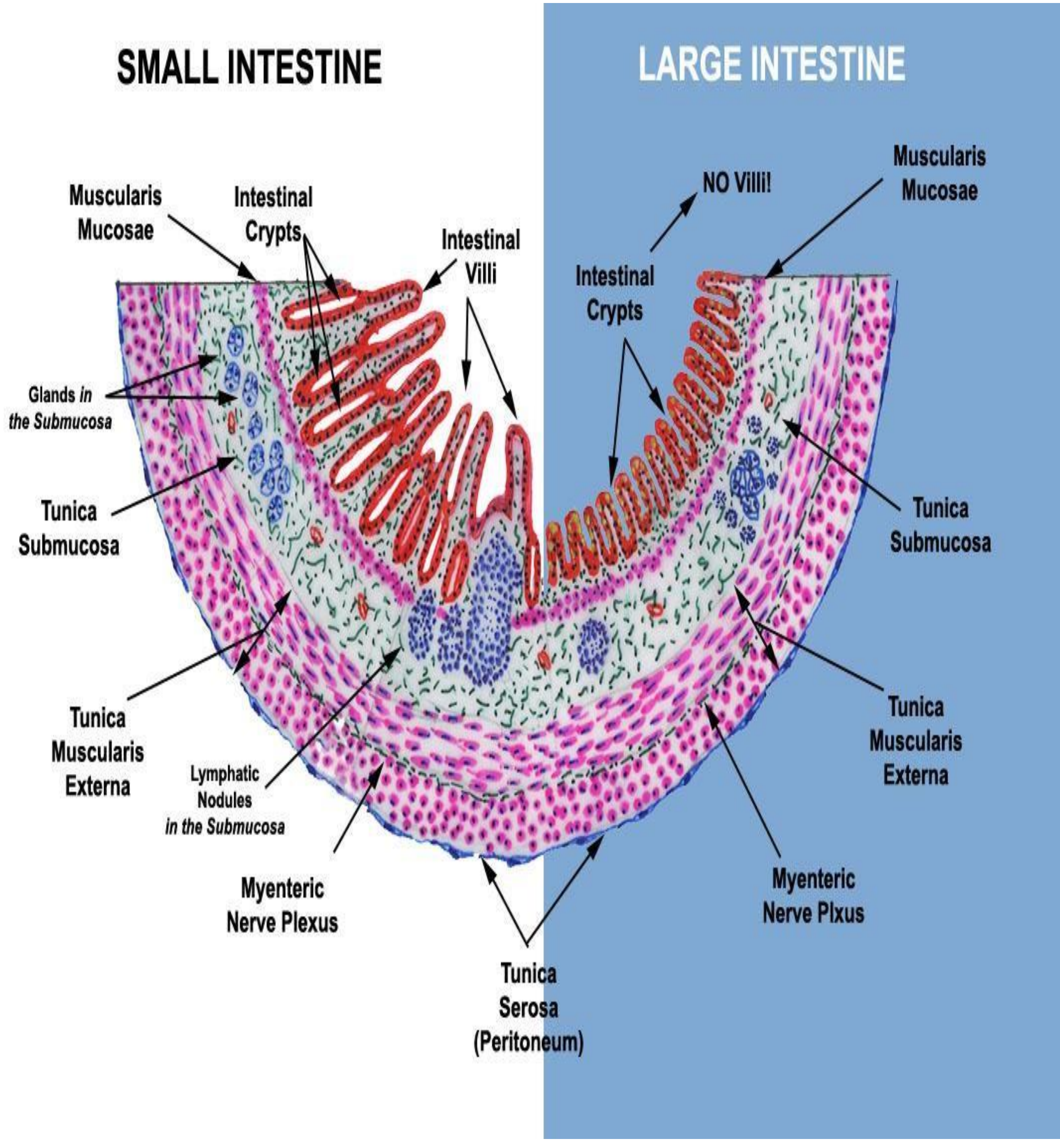
- **Mucosa is thicker and contains crypts but no Vili**

- **Simple columnar epithelium with an abundance of goblet cells**

- **Crypts are longer , more closely packed and there is no paneth cells**

- **Lamina propria is reduced, and it contains solitary lymph nodes.**

- **The muscualris layer is well developed (defined).**



بِقُوَّةِ الْعِلْمِ تَقْوَى شَوْكَةُ الأُمَمِ   فَالْحُكْمُ فِي الدَّهْرِ مَنْسُوبٌ إِلَى الْقَلَمِ

كَمْ بَيْنَ مَا تَلْفِظُ الأَسْيَافُ مِنْ عَلَقٍ   وَبَيْنَ مَا تَنْفُثُ الأَقْلامُ مِنْ حِكَمِ

	Large intestine	Small intestine
Mucosal lining	The large intestine is lined with simple columnar epithelium with numerous goblet cells.	simple columnar epithelium with goblet cells and microvilli.
Intestinal gland's lining	Simple tubular glands	Simple branched tubular glands
Villi and paneth cells	NO	YES
Appendices epiploicae & taenia coli	YES	NO
Lymph nodes appearance	Lymphatic nodules are present in the lamina propria till the submucosa, except in the appendix, where they appear as lymphatic follicles surrounding its lumen to fulfill its immunological function. The appendix plays no direct role in gastrointestinal function.	Aa all GIT, lymphatic cells
length	1.5-2.5 m	6 m
diameter	Larger	Smaller

- <u>In the anal region, the mucous membrane forms a series of longitudinal folds, the rectal columns of Morgagni</u>

- **The anal canal, 4 cm in length, is divided into two halves by the pectinate line. The upper half, 2 cm from the rectum, is lined with simple columnar epithelium without goblet cells. The lower half, 2 cm, is subdivided into upper cm and lower cm. The upper cm forms folds of mucosa, shaping the anal or rectal column and lined with stratified squamous nonkeratinized epithelium, while the lower cm lined with stratified squamous keratinized epithelium.**

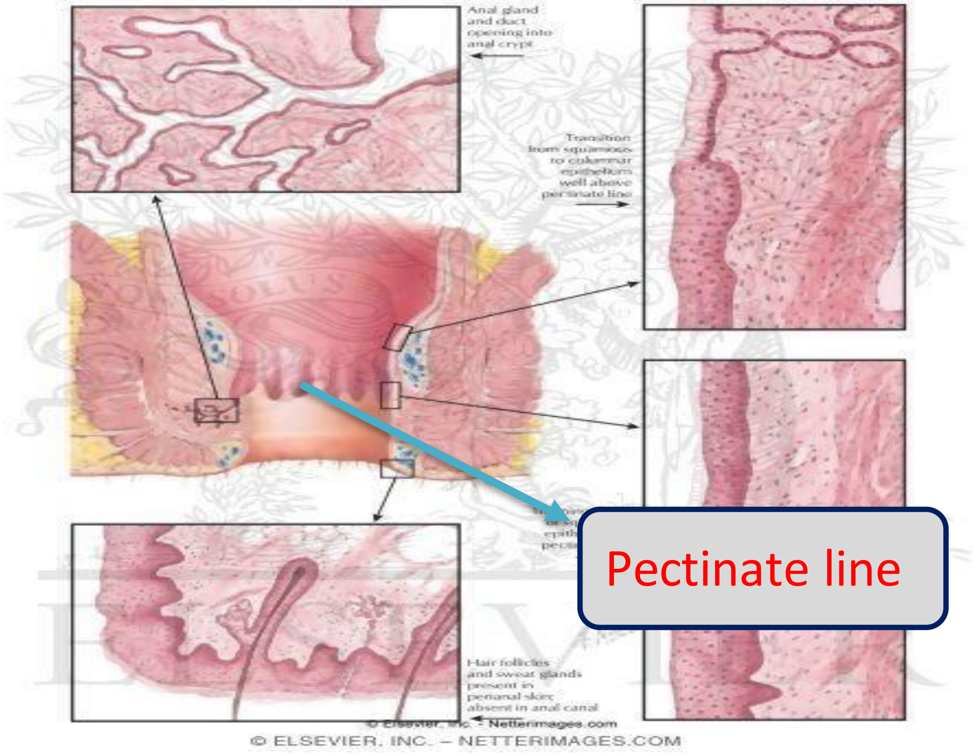
- <u>These columns connects to the anal orifice to form the anal valves and sinuses.</u>

- About 2 cm above the anal opening, the intestinal mucosa is replaced by stratified squamous epithelium

- In this region, the lamina propria contains a plexus of large veins that, when excessively dilated and varicose, produces hemorrhoids.

- The muscularis layer gives rise to the anal sphincter

- The adventitia layer connects the anal canal to the surrounding structures.



Appendix

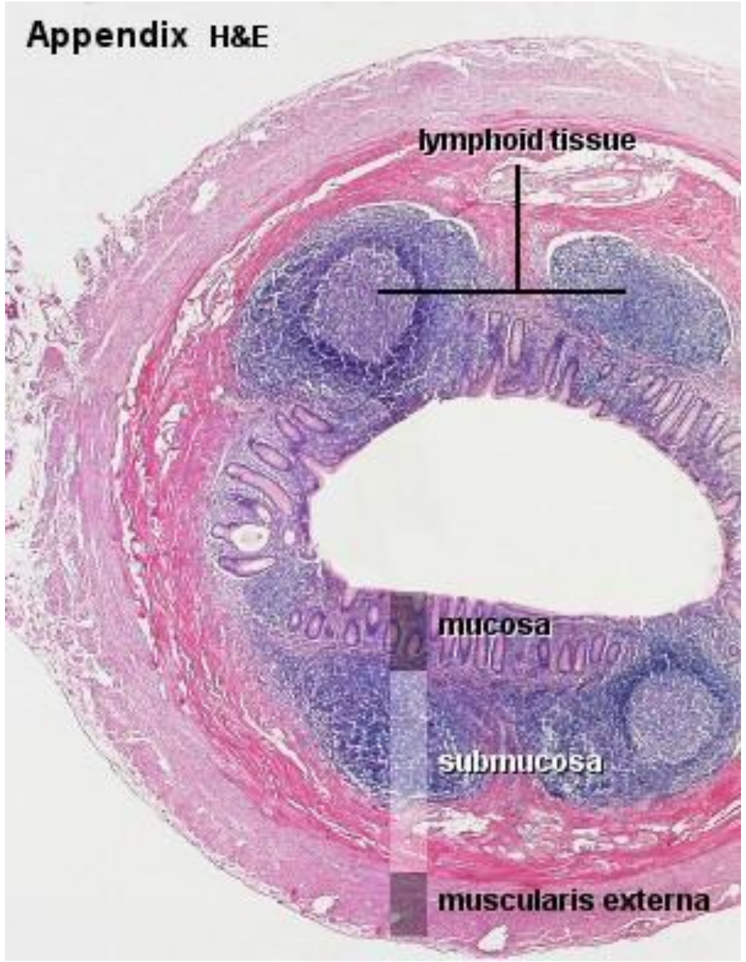
- **The appendix is a lymphatic tissue and an evagination of the cecum.**

- It is characterized by a relatively small, narrow, and irregular lumen and lined with simple columnar with a few goblet cells and numerous lymphoid follicles.
- caused by the presence of abundant lymphoid follicles in its wall , that form a circular layer in the mucosa and may infiltrate the submucosa.

- Although its general structure is similar to that of the large intestine (same epithelium) , it contains fewer and shorter intestinal glands and has no teniae coli.

- Covered entirely by serosa (mesoappendix)

Removing the appendix doesn't have a significant impact on the body's immunity because there are other lymphatic tissues. However, inflammation in the appendix can lead to closure of its narrow lumen, causing distension and potentially leading to rupture and maybe cause peritonitis. Therefore, if there's a 50% suspicion of appendicitis, patients are often observed closely. If the suspicion increases to 60%, indicating a higher risk of rupture, the appendix is usually surgically removed to prevent the development of fatal peritonitis.



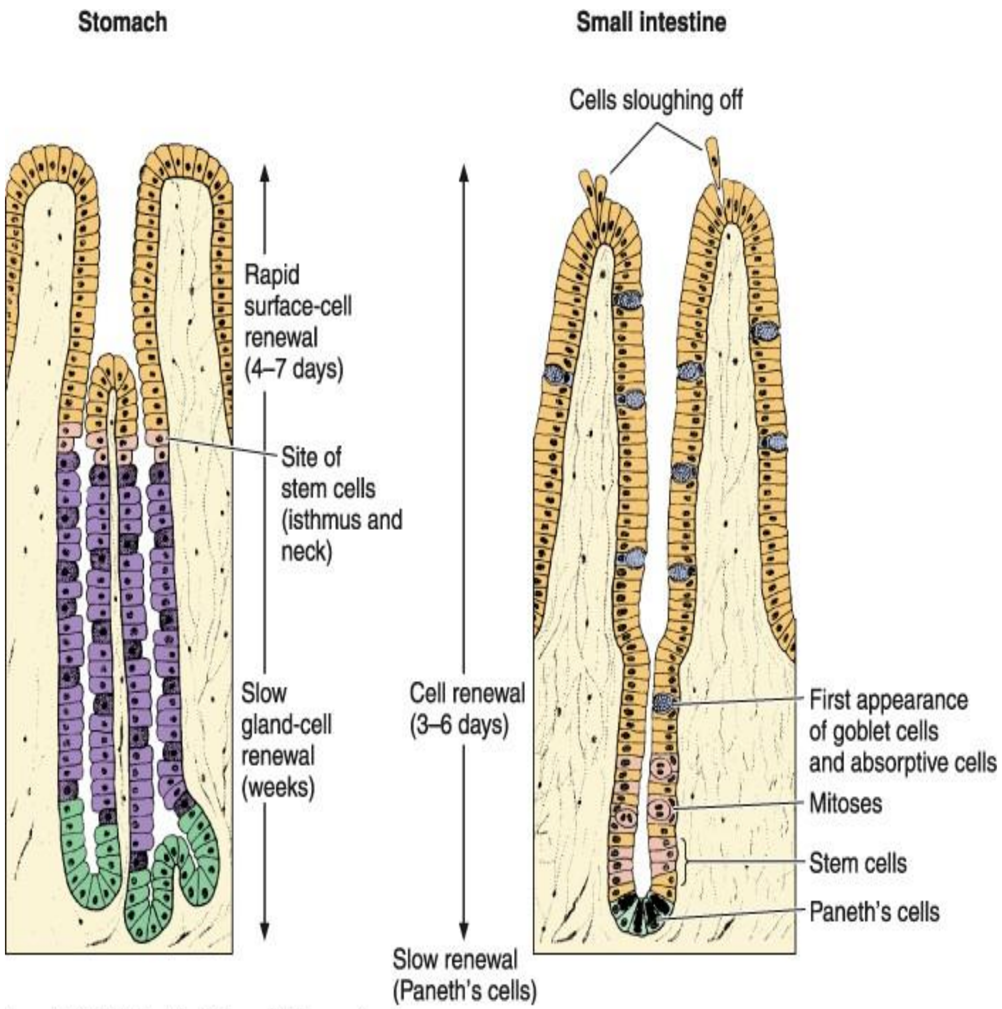
Cell Renewal in the Gastrointestinal Tract

- **<u>The epithelial cells of the entire gastrointestinal tract are constantly being cast off and replaced with new ones formed through mitosis of stem cells</u>**

- **<u>These stem cells are located in the basal layer of the esophageal epithelium, the neck of gastric glands, the lower half of the intestinal glands and the bottom third of the crypts of the large intestine</u>**

- **<u>From this proliferative zone in each region, cells move to the maturation area, where they undergo structural and enzymatic maturation, providing the functional cell population of each region</u>**

- **In the small intestine the cells die by apoptosis in the tip of the villi or are sloughed off by mechanical action during function.**



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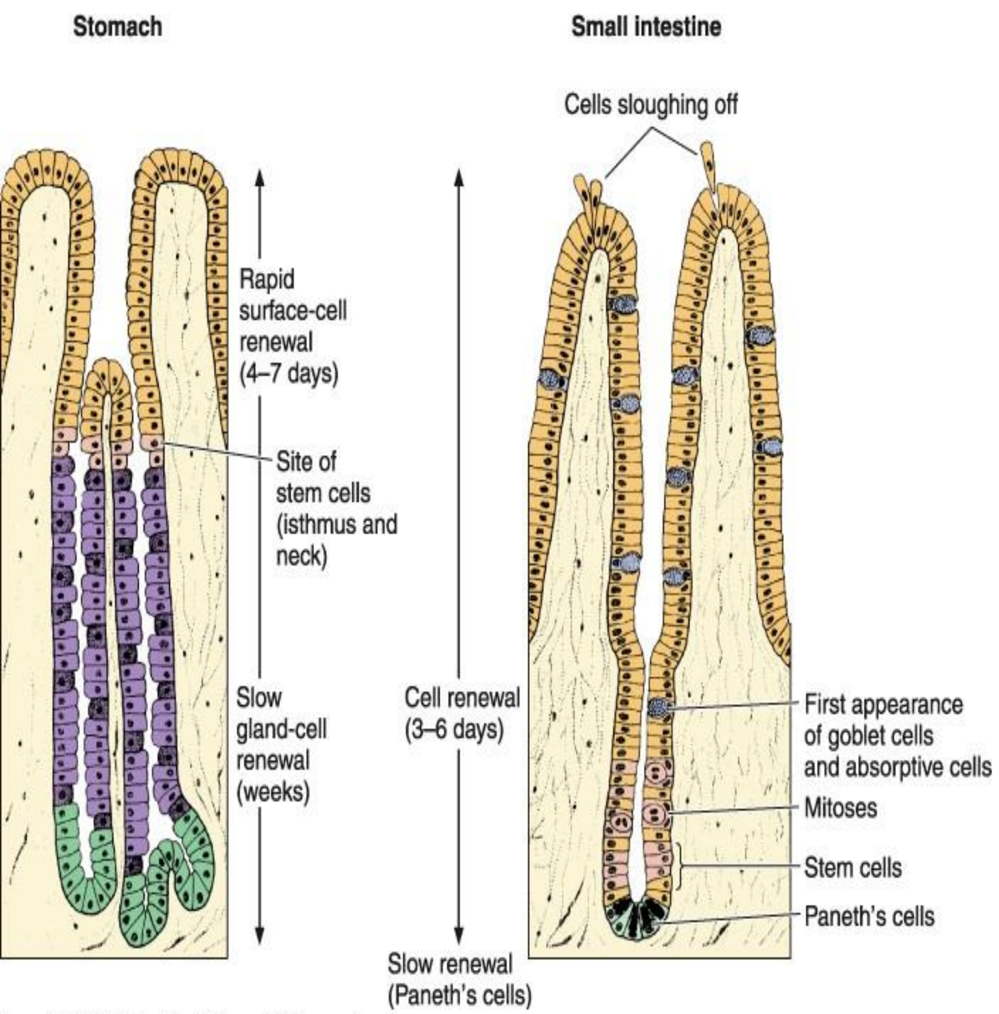

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	stomach	Small intestine
Lining epithelium	**Simple columnar without goblet cells.**	**Simple columnar with goblet cells.**
Site of stem cells	**Middle between the surface and the base.**	**Distal to the surface and proximal to the base.**
Cell renewal	**4-7 days.**	**3-6 days.**

You should study the structure of the liver because the doctor will bring a question about it in the practical EXAM!!

Liver

The characteristics of hepatocytes, Kupffer cells, blood sinusoids, and portal triads are very important.

- **The liver is the second-largest organ of the body (the largest is the skin) and the largest gland, weighing about 1.5 kg**

- **More active in children**
- **Weight = 1/20 of body weight**

- **The liver is the organ in which nutrients absorbed in the digestive tract are processed and stored for use by other parts of the body**

- **It is thus an interface between the digestive system and the blood**

- **Most of its blood (70-80%) comes from the portal vein, arising from the stomach, intestines, and spleen; the smaller percentage (20-30%) is supplied by the hepatic artery**

- **All the materials absorbed via the intestines reach the liver through the portal vein, except the complex lipids (chylomicrons), which are transported mainly by lymph vessels which goes to liver.**

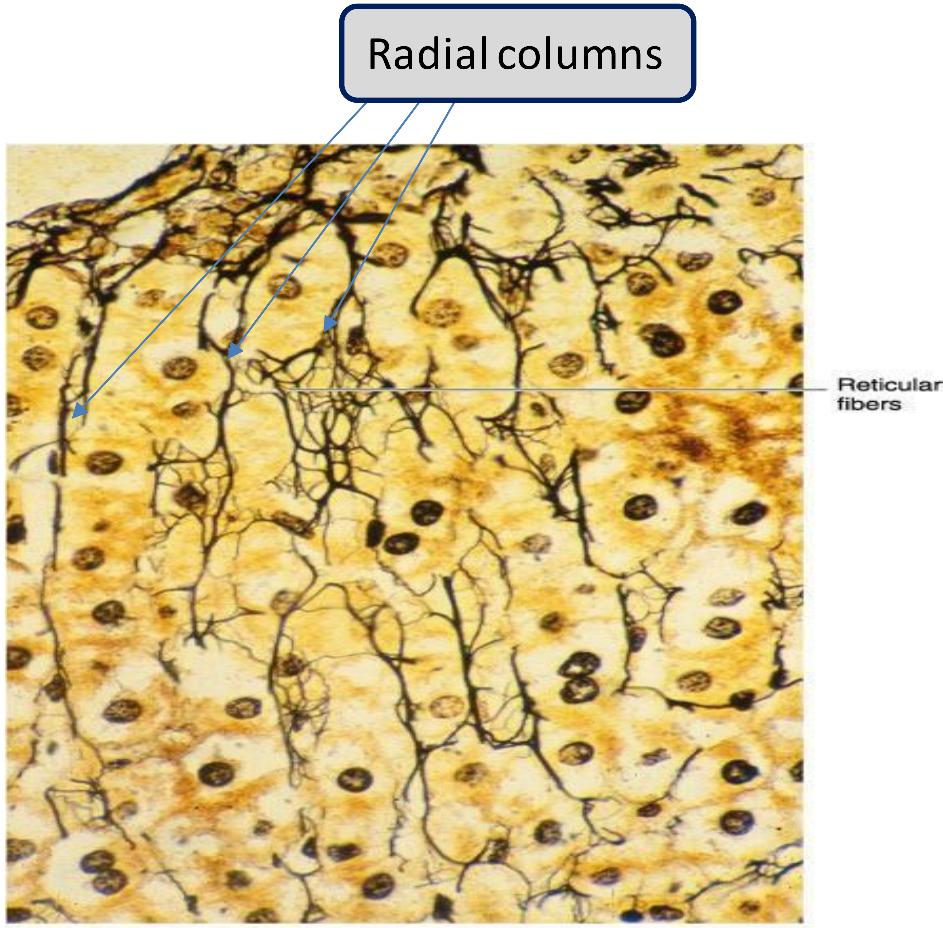
- The position of the liver the circulatory system is optimal for gathering, transforming, and accumulating metabolites and for neutralizing and eliminating toxic substances.
- Elimination occurs in the bile, an exocrine secretion of the liver that is important for lipid digestion
- The liver also has the very important function of producing plasma proteins, such as albumin, other carrier proteins, coagulation factors, and growth factors.

Stroma

Central vein

(Venous drainage of hepatocyte)

- **The liver is covered by a thin connective tissue capsule (Glisson's capsule)**
- **Hexagonal lopes**
- **becomes thicker at the hilum, where the portal vein and the hepatic artery enter the organ and where the right and left hepatic ducts and lymphatics exit**
- **These vessels and ducts are surrounded by connective tissue all the way to their termination (or origin) in the portal spaces between the liver lobules.**
- **At this point, a delicate reticular fiber network that supports the hepatocytes and sinusoidal endothelial cells of the liver lobules is formed.**



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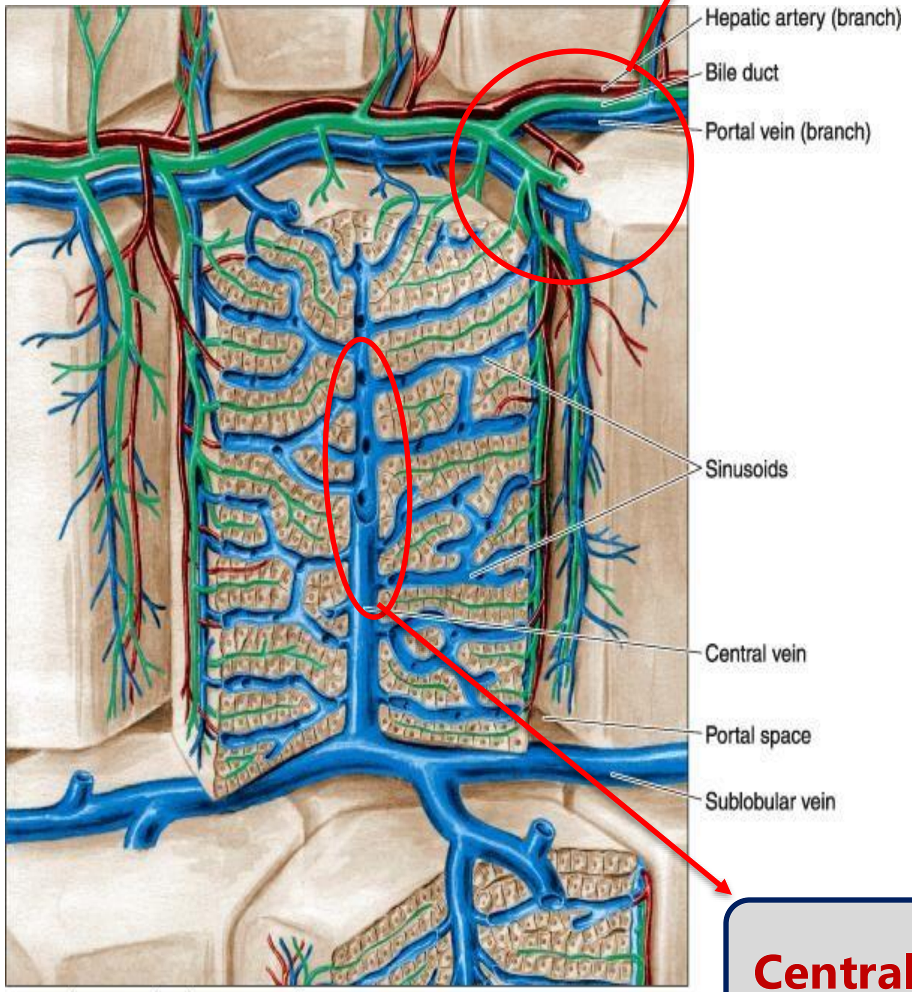
The Liver Lobule

- <u>**The basic structural component of the liver is the liver cell, or hepatocyte**</u>
- **These epithelial cells are grouped in interconnected plates and constitute two-thirds of the mass of the liver**
- **All Venous drainage go to central vein**
- **In light-microscope sections, structural units called liver lobules can be seen**
- **The liver lobule is formed of a polygonal mass of tissue about 0.7 x 2 mm in size**
- **with portal spaces at the periphery and a vein, called the central or centrolobular vein, in the center**
- **Blood sinusoid is channel for both portal blood (carrying absorbed material from the GITto hepatocytes) and hepatic blood (providing oxygen to hepatocytes). Absorptive substances from the portal blood enter the hepatocytes, while secretions from hepatocytes are directed towards the hepatic ducts.**

Portal triad which contains branches from hepatic artery and bile duct and portal vein.



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Central vein

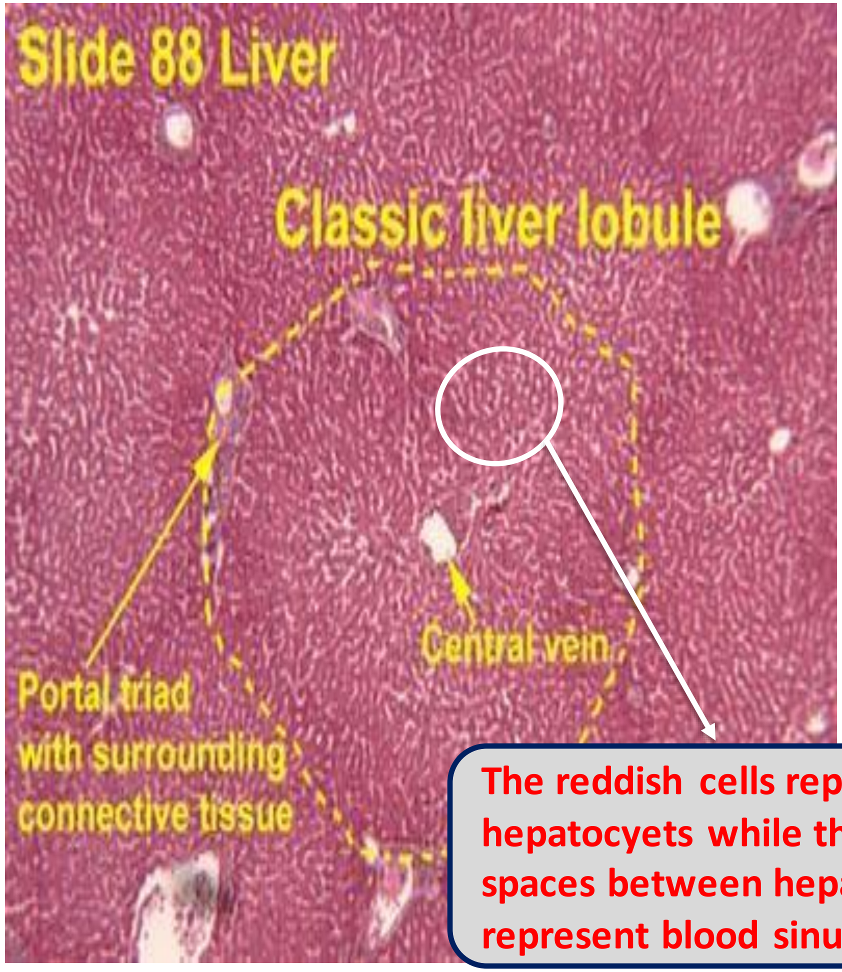
- Portal spaces, regions located in the corners of the lobules, contain lymphatic vessels, nerves, reticular fibers, branch of hepatic artery, branch of portal vein and bile duct

- The human liver contains three to six portal spaces per lobule, each with a venule (a branch of the portal vein),
- an arteriole (a branch of the hepatic artery),
- a duct (part of the bile duct system),
- and lymphatic vessels

- The venule contains blood coming from the superior and inferior mesenteric and splenic veins, and it's the largest structure.

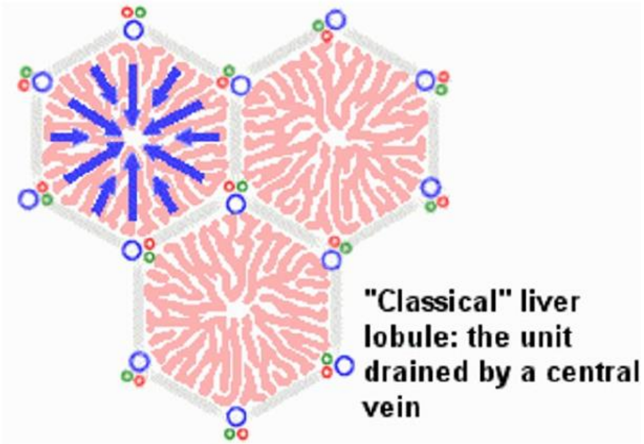
- The arteriole contains oxygen-rich blood coming from the celiac trunk of the abdominal aorta.

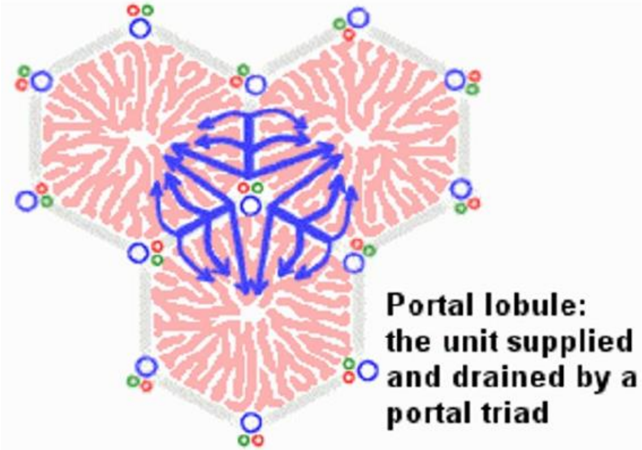
- The duct, lined by cuboidal epithelium, carries bile synthesized by the hepatocytes and eventually empties into the hepatic duct

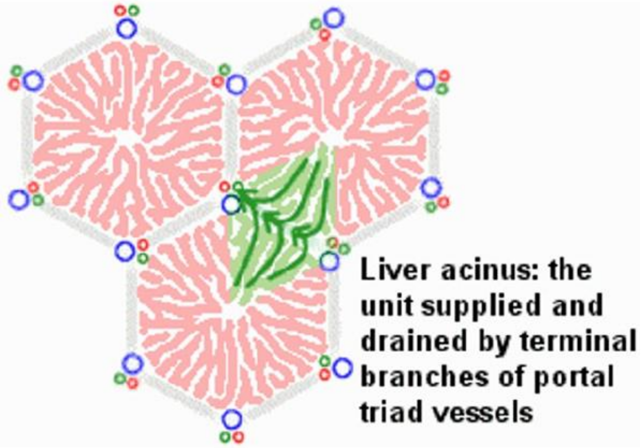


The reddish cells represent hepatocyets while the white spaces between hepatocytes represent blood sinusoids

There are 3 functional ways to describe the liver lobules







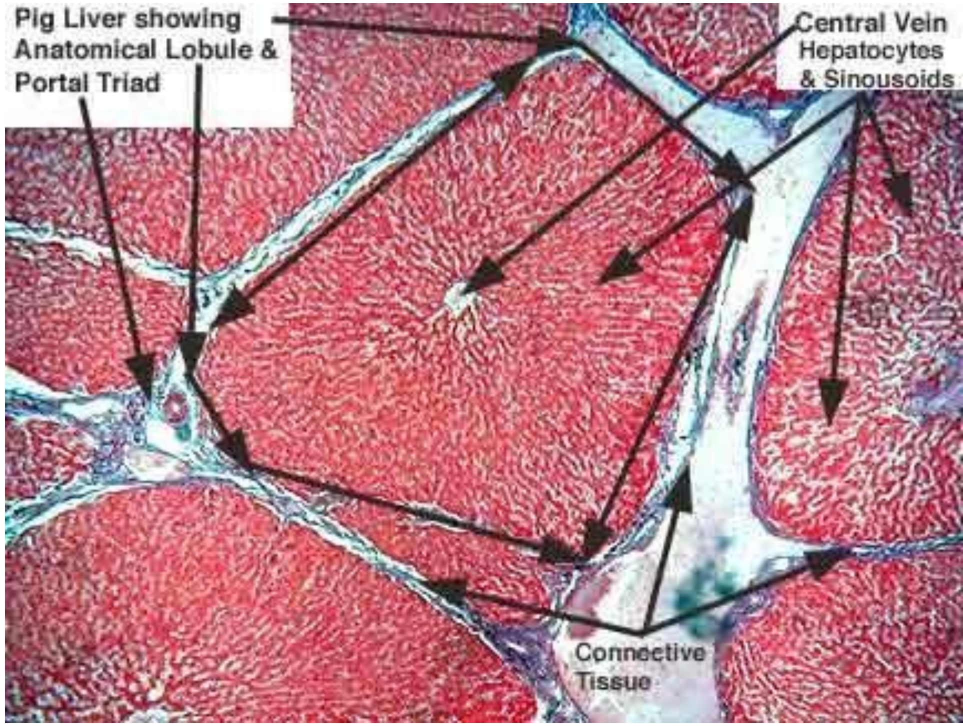
Classical lobules: Hexagonal in shape with central vein in the center and portal triad on each angle. (the drainage goes to the center)

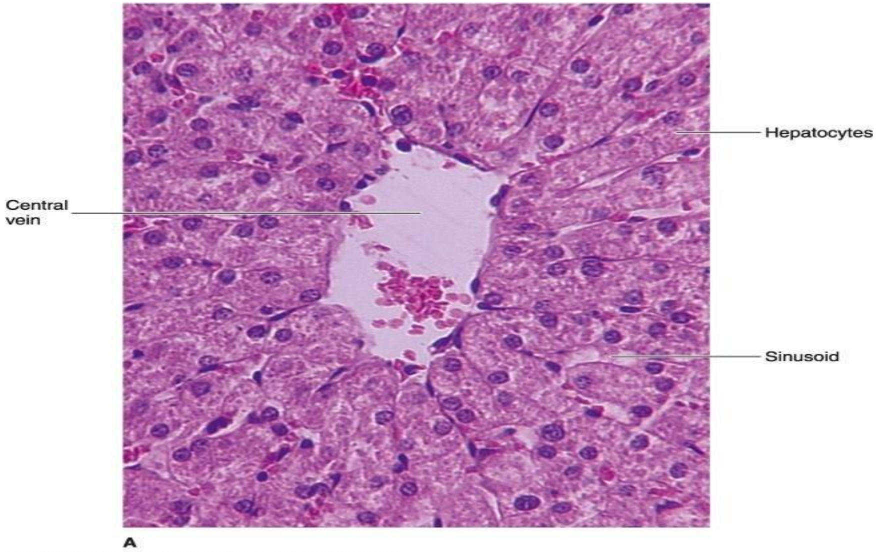
Portal lobule: triangular in shape with the portal triad in the center and central vein on each angle. (the drainage goes from the middle between the 3 classical lobules to the center)

Liver Acinus: diamond in shape and its between two central veins and two portal triads that function to collect the oxygen, so the functionality depend on the level of the oxygen. It is the most place has oxygen in it because having the arterial blood.

In this slide ask yourself why we use the pig as an example?
Because the boundaries are clear because they have more connective tissue

- **In certain animals (eg, pigs), the lobules are separated by a layer of connective tissue, while in human it is ill-defined.**
- **This is not the case in humans, where the lobules are in close contact along most of their length, making it difficult to establish the exact limits between different lobules.**
- **The hepatocytes in the liver lobule are radially disposed and are arranged like the bricks of a wall**
- **These cellular plates are directed from the periphery of the lobule to its center and anastomose freely, forming a labyrinthine and spongelike structure**





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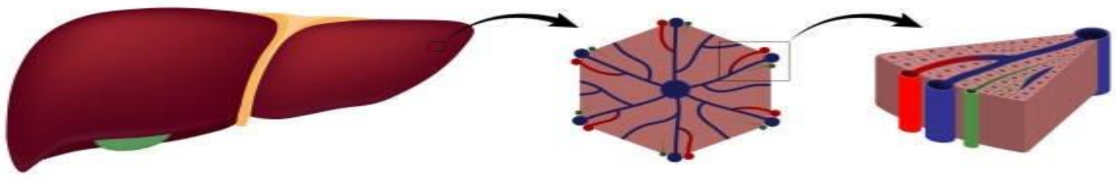
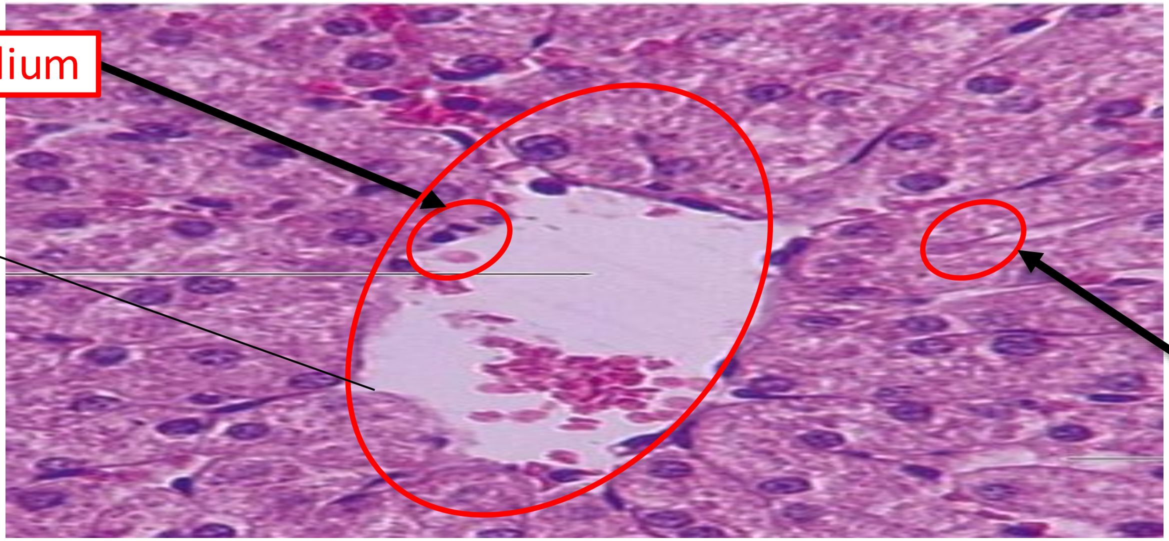
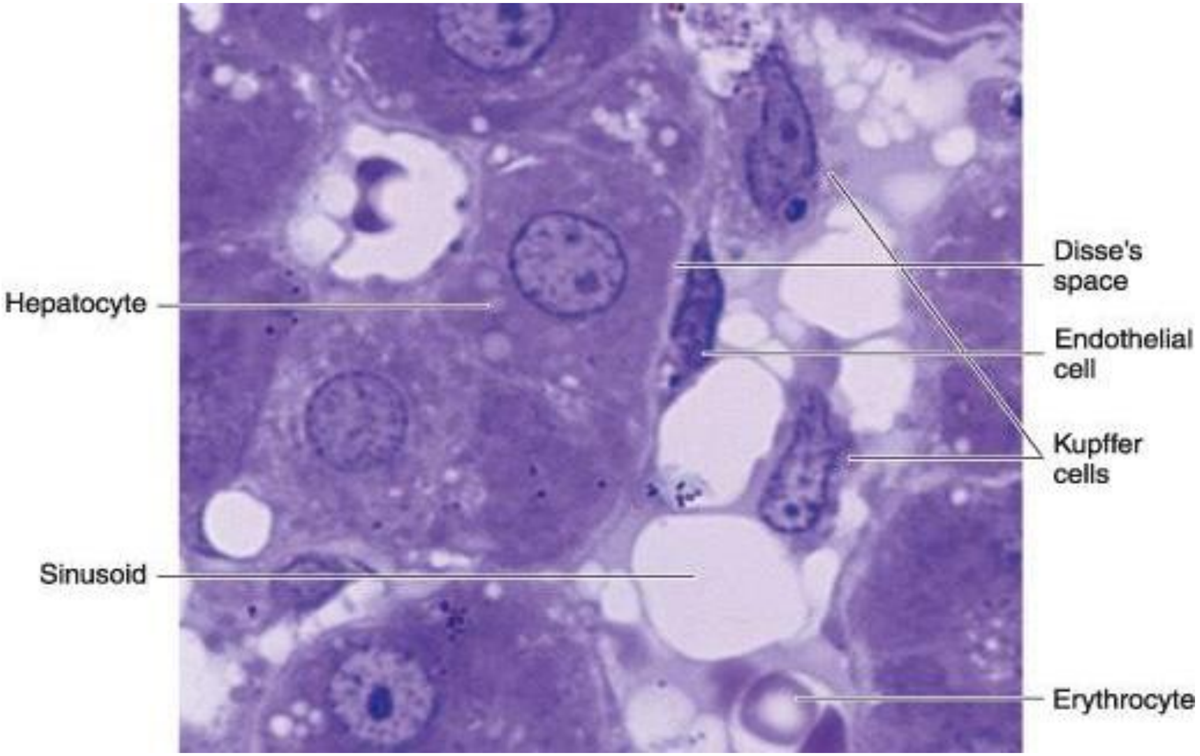
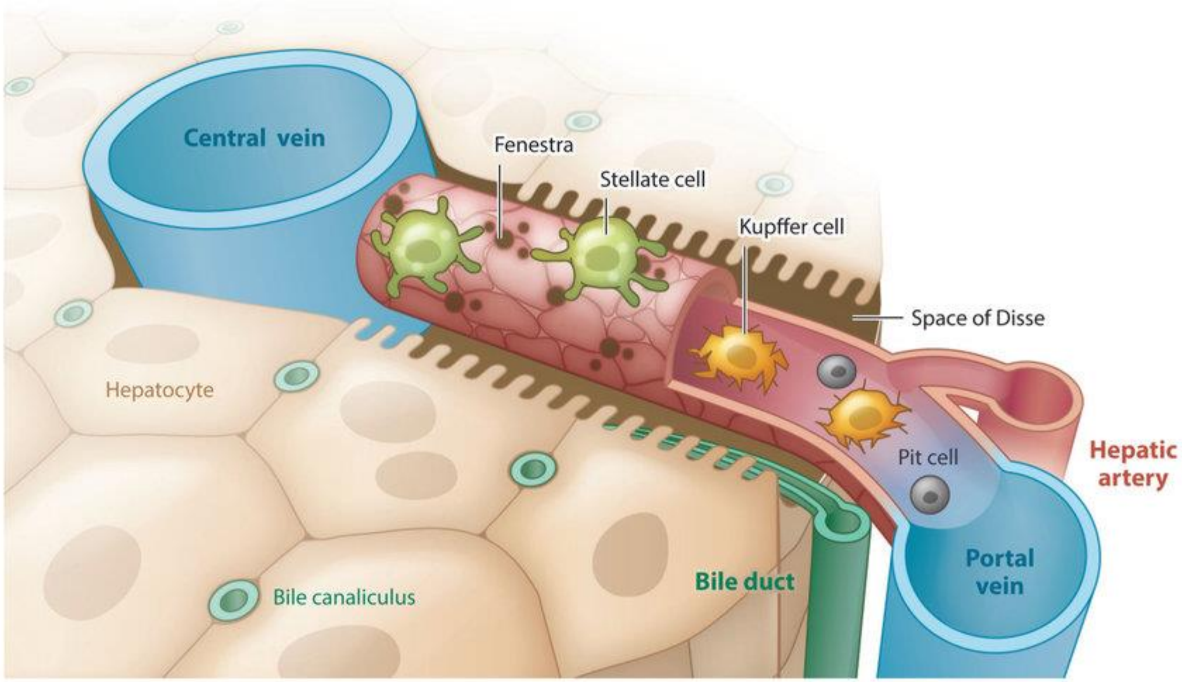




- **The space between these plates contains capillaries, the liver sinusoids**
- **sinusoidal capillaries are irregularly dilated vessels composed solely of a discontinuous layer of fenestrated endothelial cells.**
- **The sinusoid is surrounded and supported by a delicate sheath of reticular fibers**
- **The fenestrae which is the spaces that extend to the basal lamina, and helps in transporting materials from blood sinusoids to the hepatocytes are about 100 nm in diameter, have no diaphragm, and are grouped in clusters**
- **There are also spaces between the endothelial cells, which, together with the cellular fenestrae and a discontinuous basal lamina (depending on the species), give these vessels great permeability.**



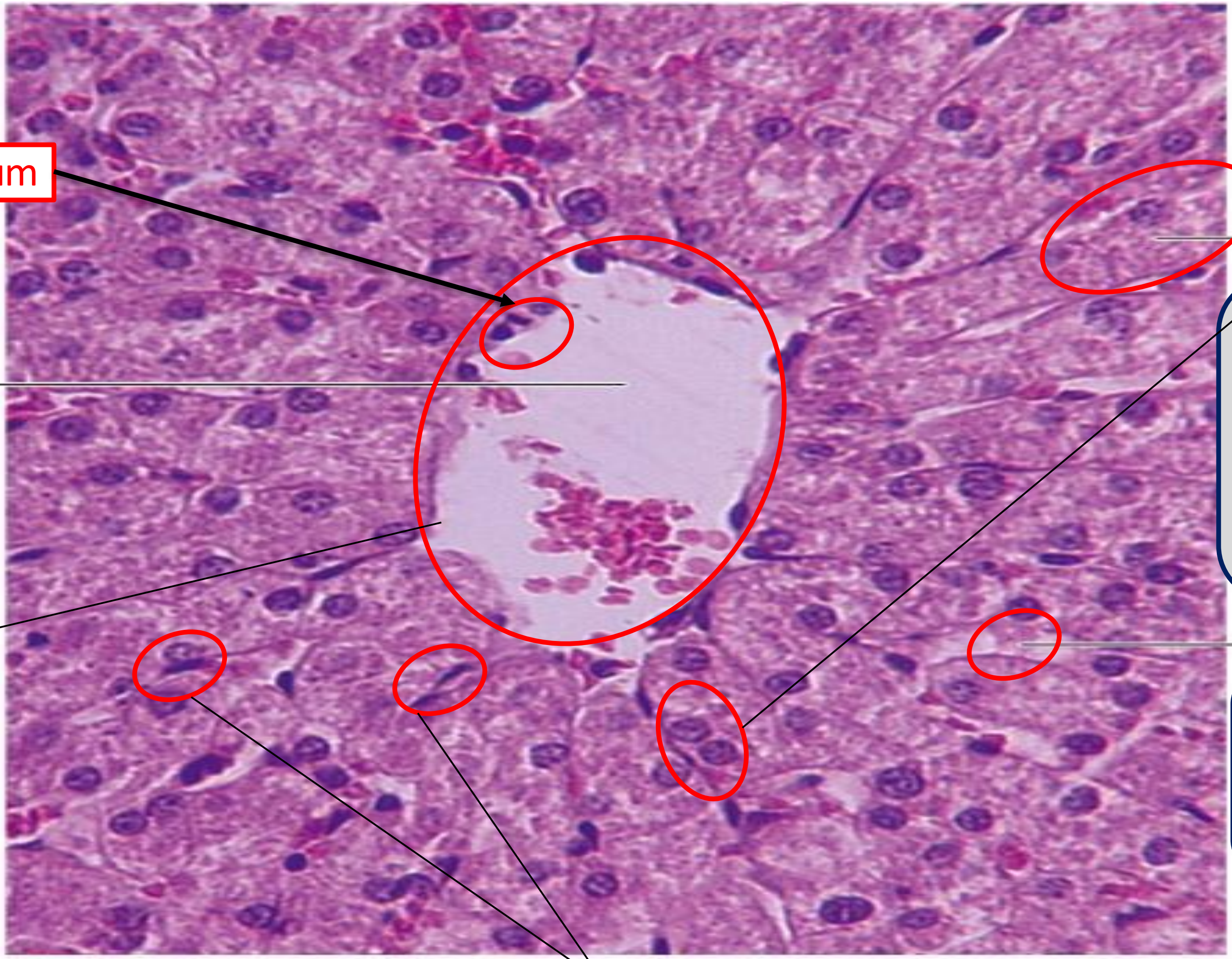


- **The sinusoids between hepatocytes contain macrophages called Kupffer cells.**

- **These cells are black cells found on the luminal surface of the endothelial cells, within the sinusoids**

- **Their main functions are to metabolize aged erythrocytes, digest hemoglobin, secrete proteins related to immunological processes, and destroy bacteria that eventually enter the portal blood through the large intestine**

- **Kupffer cells account for 15% of the liver cell population. Most of them are located in the periportal region of the liver lobule, where they are very active in phagocytosis**



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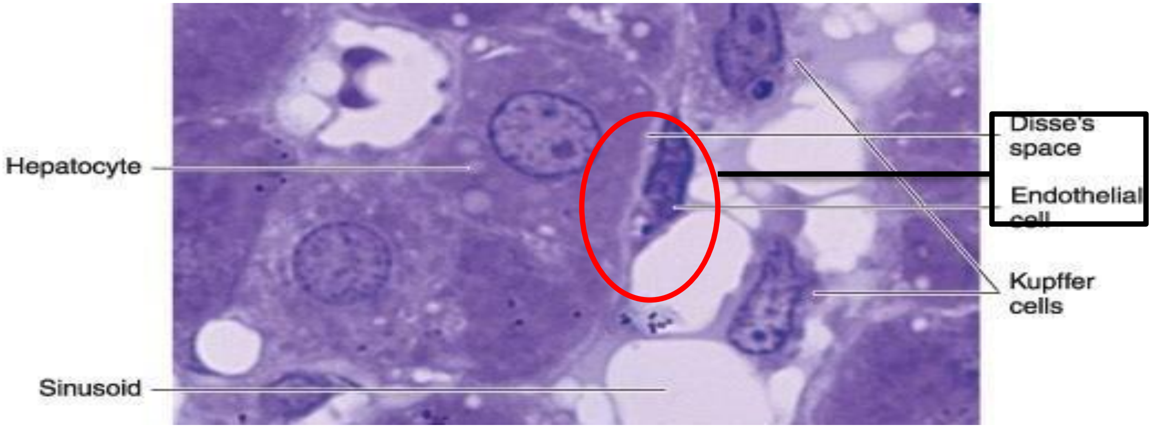
The Hepatocyte has a projection of a micro villi to help in absorption of absorptive material and enter it to make it function



- A subendothelial space known as the space of Disse separates the endothelial cells from the hepatocytes

- The fenestrae and discontinuity of the endothelium allow the free flow of plasma cells and small particles but not of cellular elements into the space of Disse which is a delicate shape of Reticular fibers.

- Thus permitting an easy exchange of molecules (including macromolecules) from the sinusoidal lumen to the hepatocytes and vice versa

- Which allows the release of the large number of macromolecules (eg, lipoproteins, albumin, fibrinogen) secreted into the blood by hepatocytes and also it enables the liver takes up and catabolizes many of these large molecules

- The basolateral side of the hepatocyte, which lines the space of Disse, contains many microvilli and demonstrates endocytic and pinocytic activity.

ITO'S CELLS

- <u>In the space of Disse (perisinusoidal space), fat-storing cells, also called stellate or Ito's cells, contain vitamin A rich lipid inclusions</u>

- In the healthy liver, these cells have several functions, such as

- uptake, storage, and release of retinoids

- synthesis and secretion of several extracellular matrix proteins and proteoglycans

- secretion of growth factors and cytokines, and the regulation of the sinusoidal lumen diameter in response to different regulators (eg, prostaglandins, thromboxane A_2).

The Hepatocyte

- **Hepatocytes are polyhedral, with six or more surfaces, and have a diameter of 20-30 um**

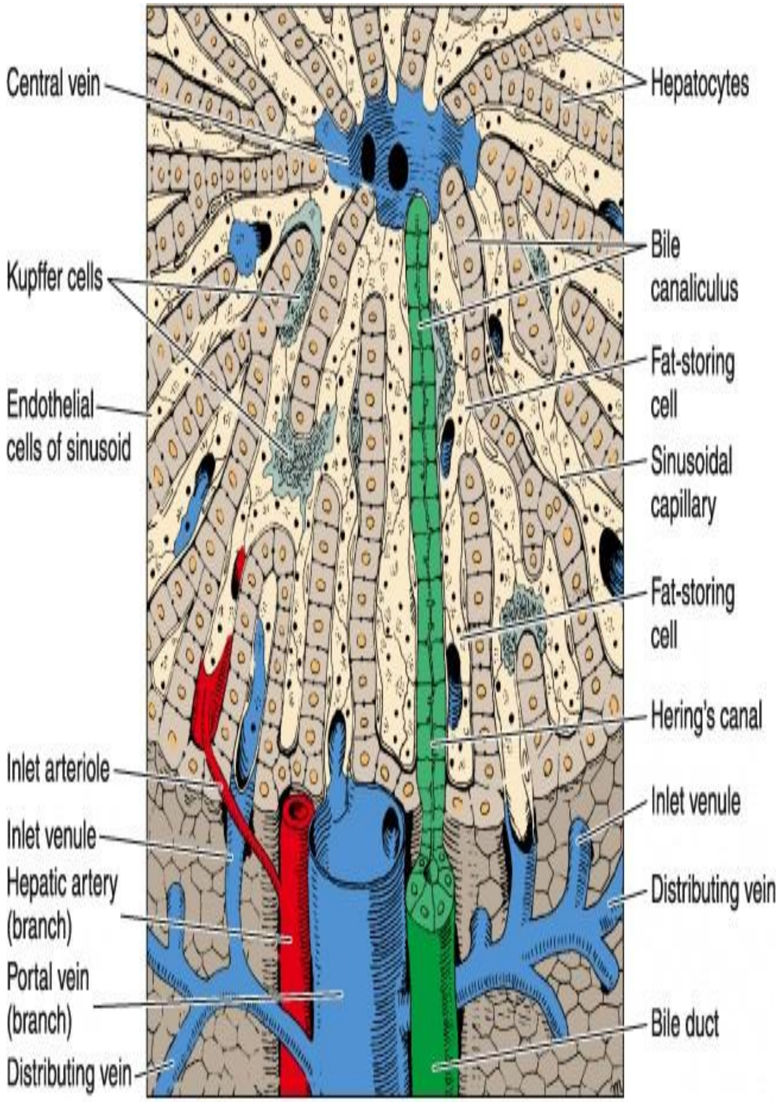
- **the cytoplasm of the hepatocyte is eosinophilic, mainly because of the large number of mitochondria and some smooth endoplasmic reticulum**

- **Hepatocytes located at different distances from the portal spaces show differences in structural, histochemical, and biochemical characteristics**

- **The surface of each hepatocyte is in contact with the wall of the sinusoids, through the space of Disse, and with the surfaces of other hepatocytes**

- **<u>Wherever two hepatocytes abut, they delimit a tubular space between them known as the bile canaliculus</u>**

- **At the periphery, bile enters the bile ductules, or Hering's canals composed of cuboidal cells**



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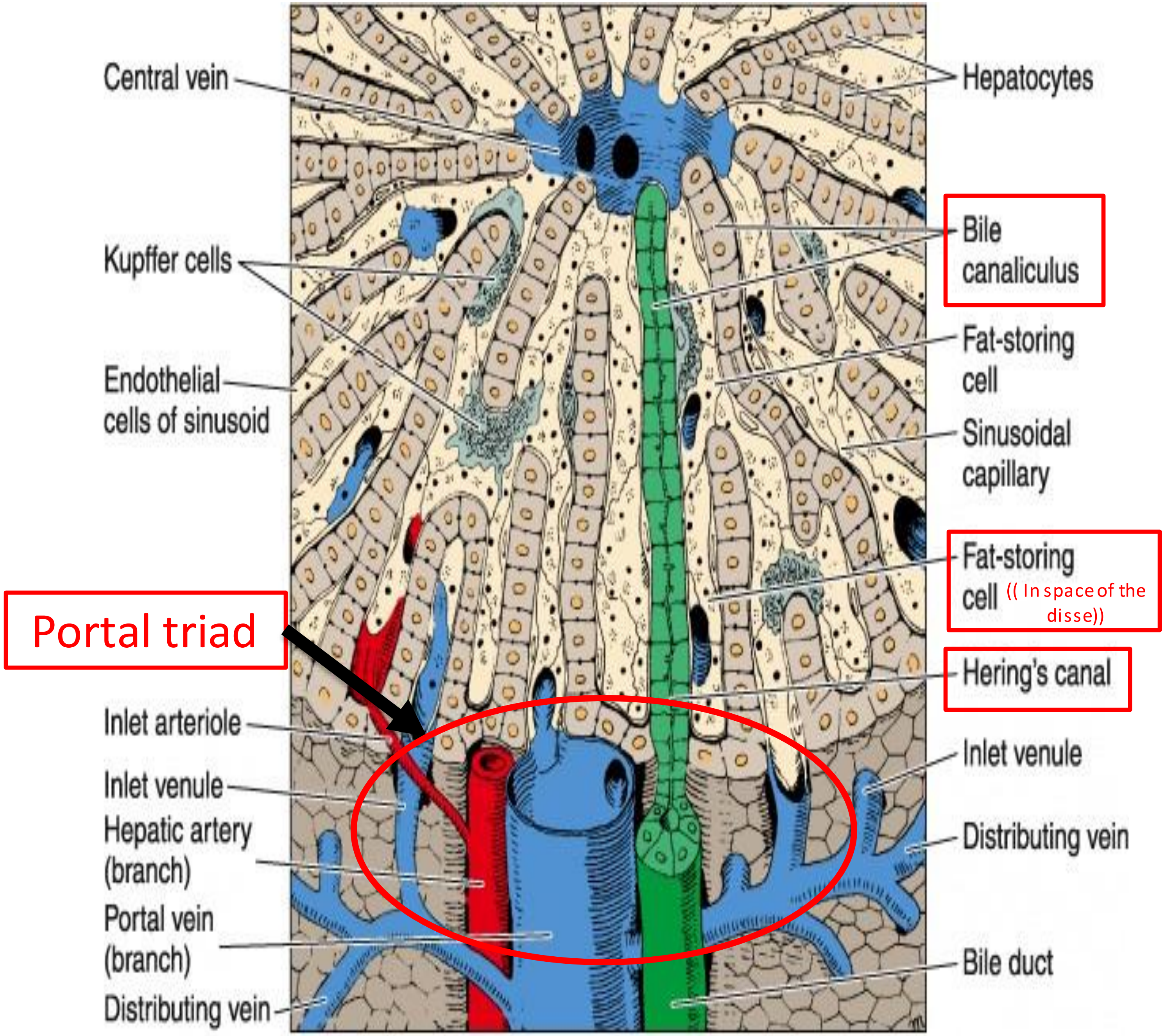

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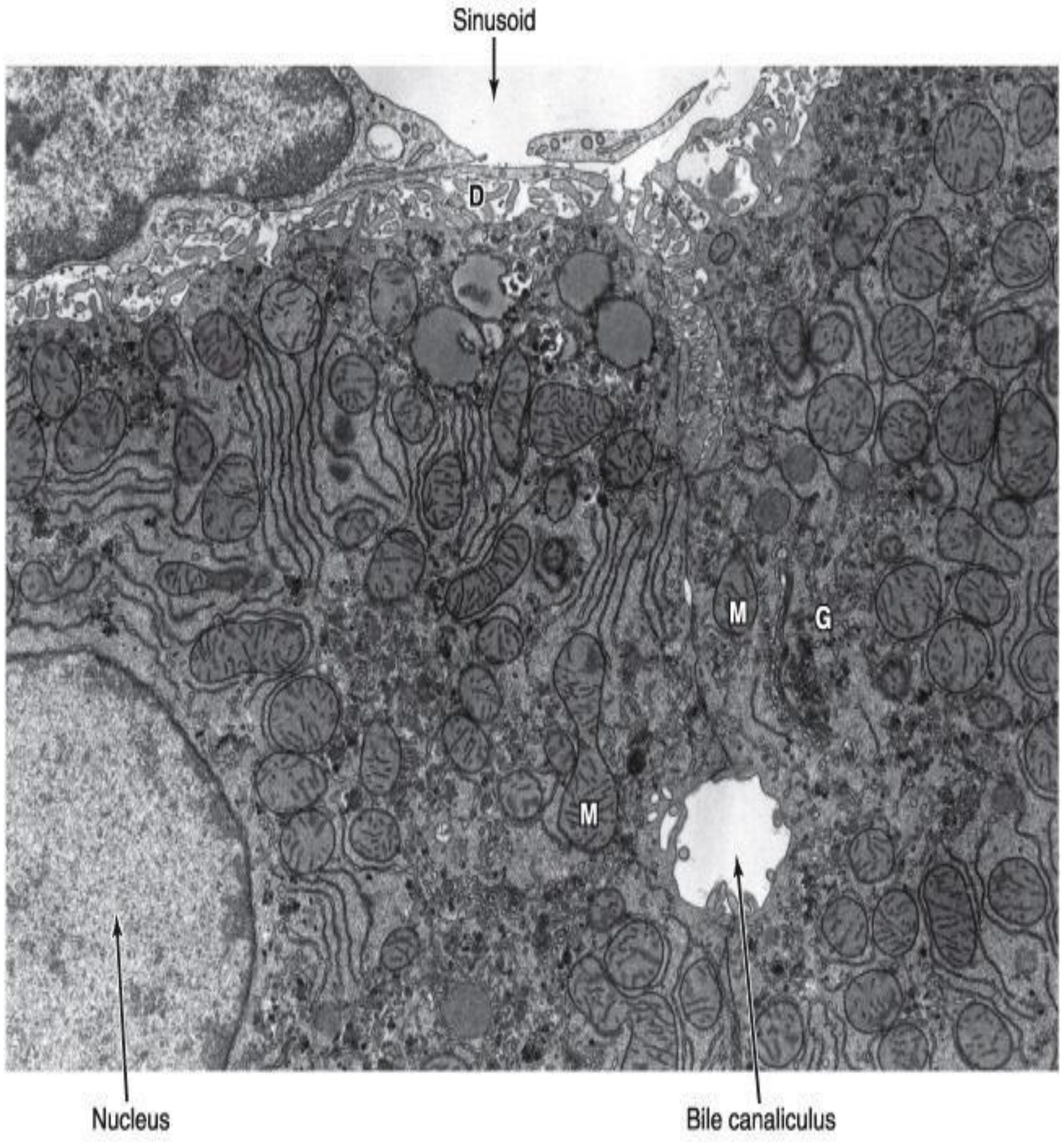
The doctor asked:
Where the bile duct started?

the bile started in between 2 adjacent hepatocytes (canaliculus)

then the Hering's canal

Then it will enter the portal triad and form portal duct

- The canaliculi, the first portions of the bile duct system, are tubular spaces 12 um in diameter
- They are limited only by the plasma membranes of two hepatocytes and have a small number of microvilli in their interiors
- The cell membranes near these canaliculi are firmly joined by tight junctions
- Gap junctions are frequent between hepatocytes and are sites of intercellular communication
- The bile flow therefore progresses in a direction opposite to that of the blood, ie, from the center of the lobule to its periphery.



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- The surface of the hepatocyte that faces the space of Disse contains many microvilli that protrude into that space, but there is always a space between them and the cells of the sinusoidal wall

- The hepatocyte has one or two rounded nuclei with one or two nucleoli

- Some of the nuclei are polyploid

- In the hepatocyte, the rough endoplasmic reticulum forms aggregates dispersed in the cytoplasm; these are often called striated basophilic bodies in the base, and in the apex, there is acidophilic bodies.

- Several proteins (eg, blood albumin, fibrinogen) are synthesized on polyribosomes in these structures

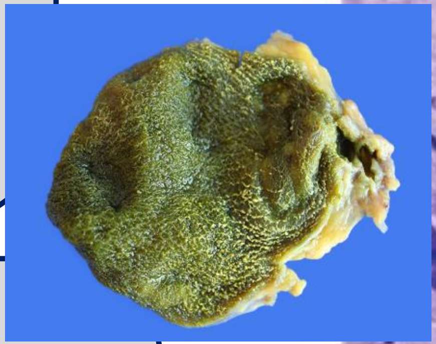
- the smooth endoplasmic reticulum is responsible for the processes of oxidation, methylation, and conjugation required for inactivation or detoxification of various substances before their excretion from the body.

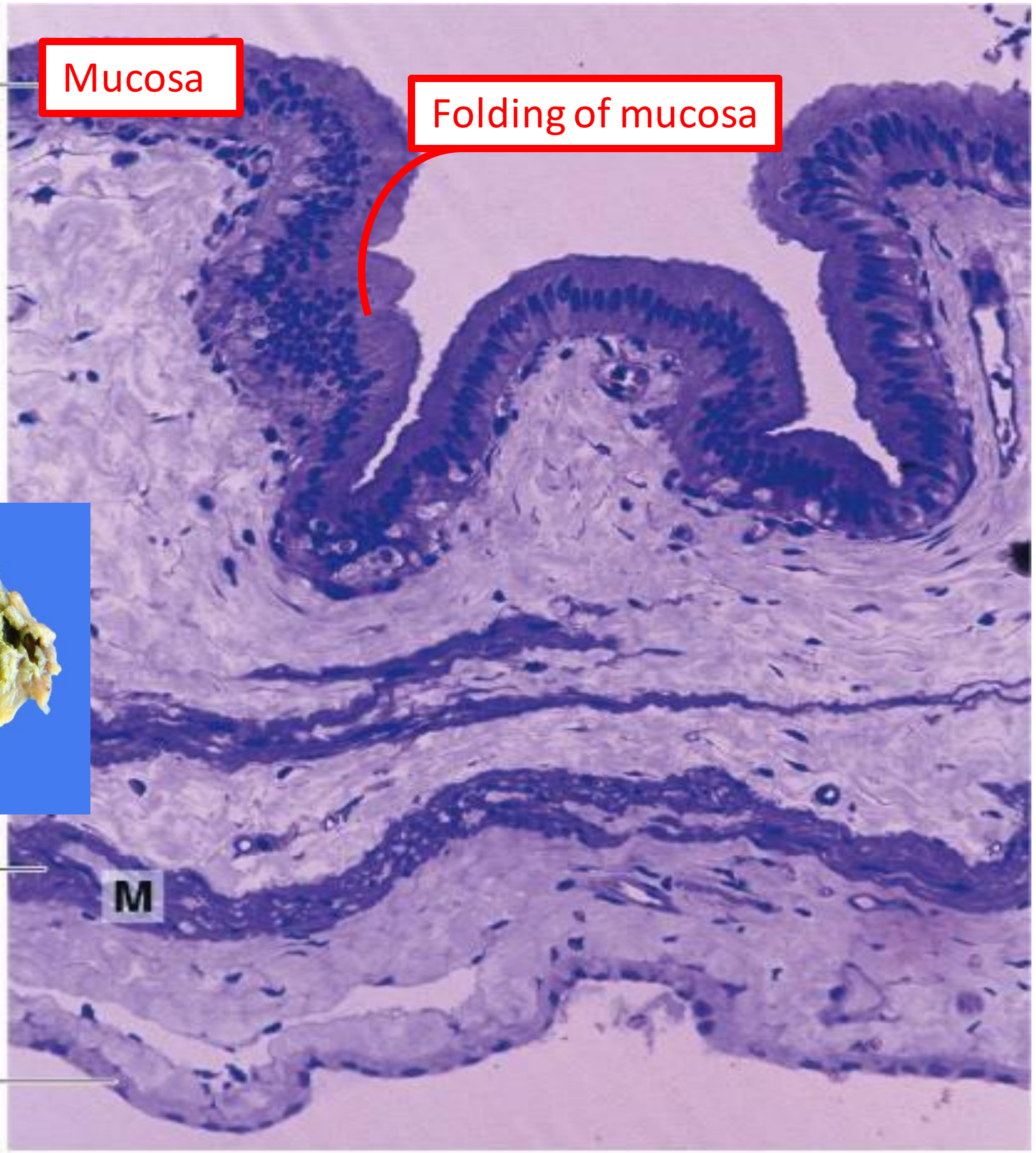
Gallbladder

- **The gallbladder is a hollow, pear-shaped organ attached to the lower surface of the liver**
- **Its primary function is to concentrate bile, increasing its potency by up to 20 times. When bile is required for digestion, only a small amount of concentrated bile is needed. Patients who undergo a cholecystectomy (gallbladder removal) may face difficulties during fat digesting due to the absence of concentrated bile. The physicians often advise these patients to eat smaller meals with intervals in between. They may also prescribe specific medications to aid in fat digestion.**
- **It can store 30-50 mL of bile.**
- **The gallbladder wall is composed of a mucosa that is lined with simple columnar epithelium without goblet cells or the muscularis mucosa. The lamina propria is often poorly defined, with minimal gland presence due to their limited function and it is composed of patches. Muscularis externa consists of patches of smooth muscle. Surrounding these layers are a perimuscular connective tissue layer and a serous membrane.**
- **The mucosa has abundant folds that are particularly evident when the gallbladder is empty**
- **The epithelial cells are rich in mitochondria**
- **All these cells are capable of secreting small amounts of mucus**
- **Tubuloacinar mucous glands near the cystic duct are responsible for the production of most of the mucus present in bile(no goblet cells).**

What is the difference between the gallbladder and other GIT organs in the lining epithelium?

the lining epithelium of gallbladder is a simple columnar epithelium without Goblet cell as the stomach and it characterized by the abundant folding that look like honeycomb appearance





The gallbladder is considered interperitoneal because a portion of it is covered by the liver, and its anterior aspect is enveloped by serosa (peritoneum) such as the liver and uterus.

- The main function of the gallbladder is to store bile, concentrate it by absorbing its water, and release it when necessary into the digestive tract

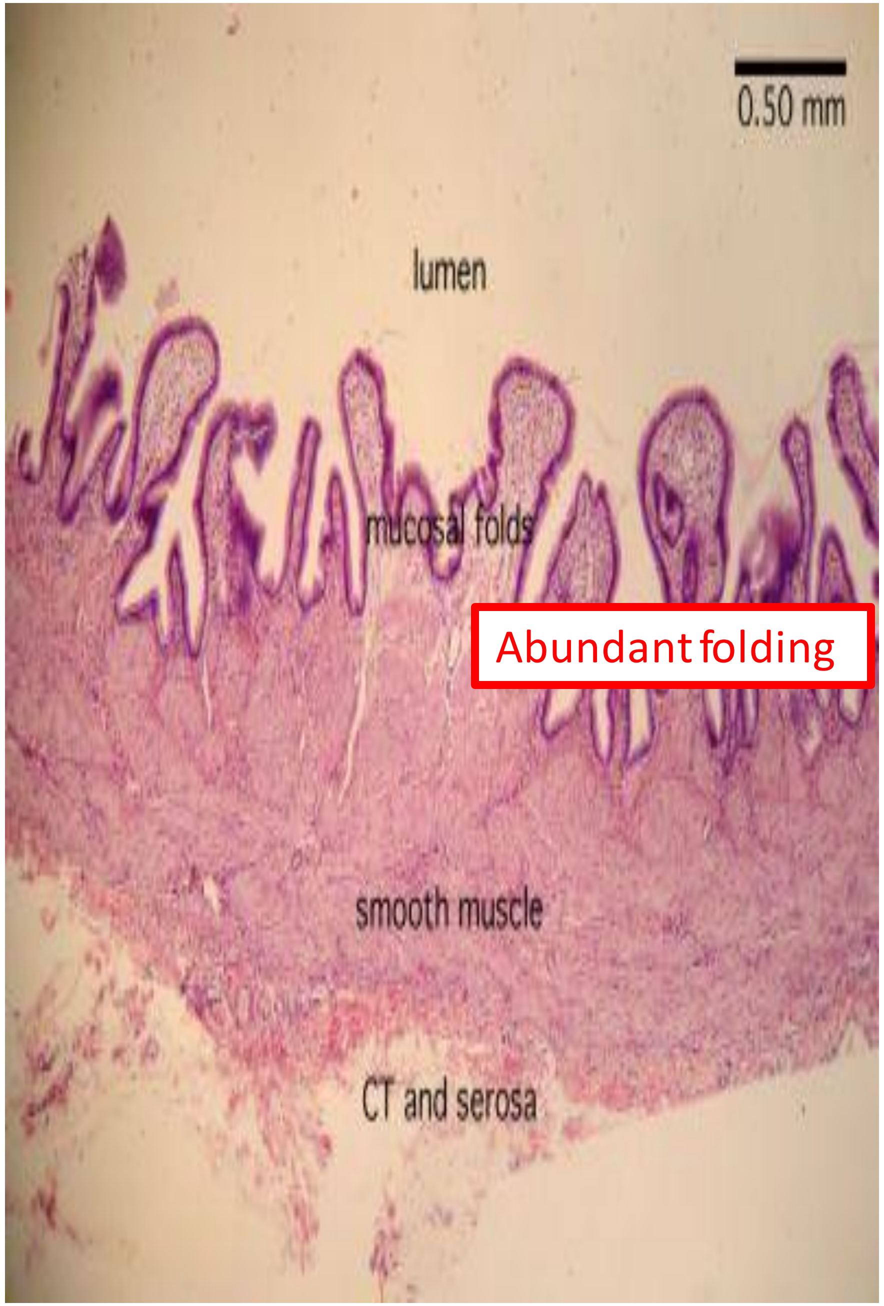
- Contraction of the smooth muscle of the gallbladder is induced by cholecystokinin, a hormone produced by enteroendocrine cells located in the epithelial lining of the small intestine

- Release of cholecystokinin is, in turn, stimulated by the presence of dietary fats in the small intestine.

- No muscularis mucosa or submucosa

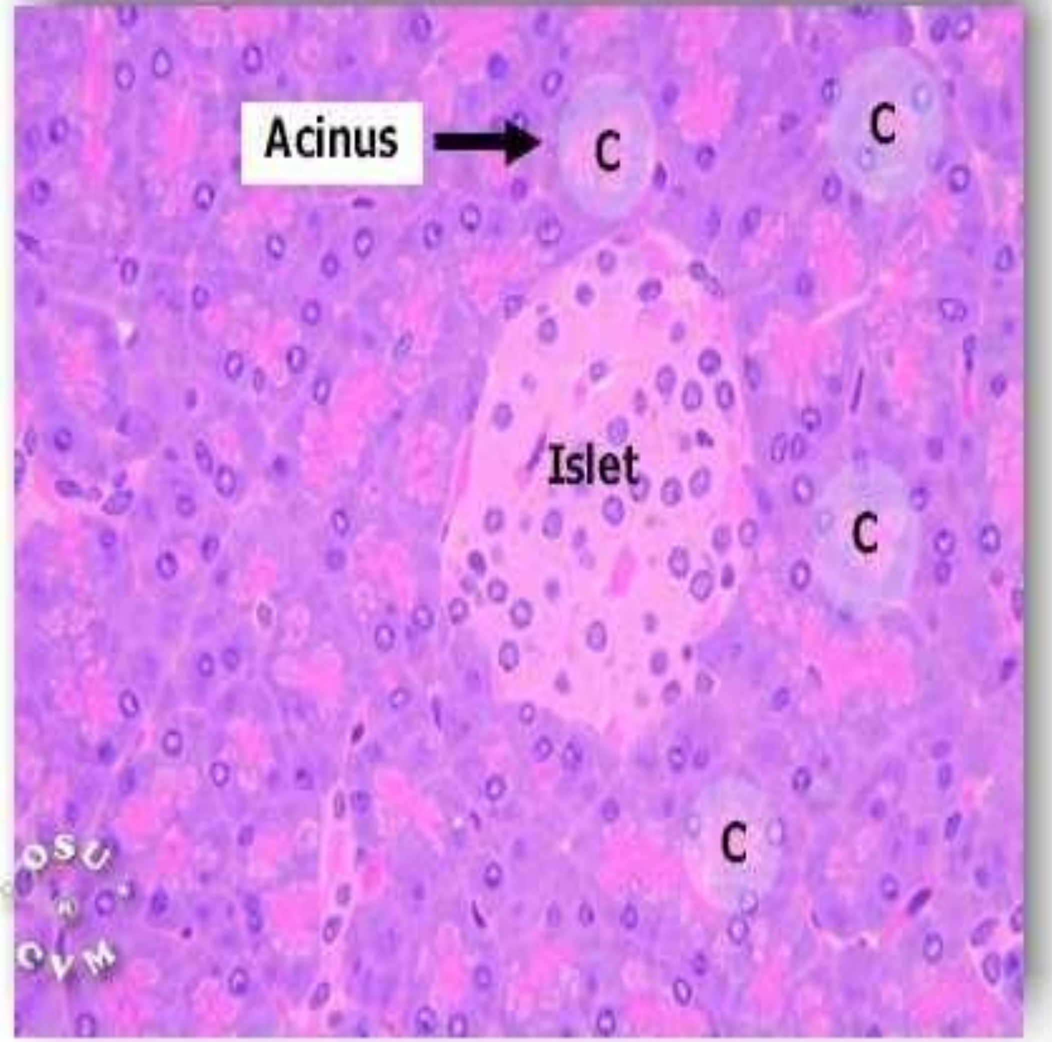
- The muscularis externa is composed of irregular(oblique) smooth muscles with collagen and elastic fibers in between.

- No peristaltic movements.



Pancreas

- <u>The pancreas is a mixed exocrine- endocrine gland that produces digestive enzymes and hormones</u>
- The enzymes are stored and released by cells of the exocrine portion, arranged in acini
- The hormones are synthesized in clusters of endocrine epithelial cells known as islets of Langerhans they contains 4 types of cells; alpha, beta, gamma and delta.
- Alpha secrets glucagon.
- Beta secret insulin.
- <u>exocrine portion of the pancreas is a compound acinar gland, similar in structure to the parotid gland</u>
- Acini consist of a cluster of cells bounded by a basement membrane, surrounding a central lumen.



Differences between the parotid and the pancreas

- **In histological sections, a distinction between the two glands can be made based on the absence of striated ducts and the presence of the islets of Langerhans in the pancreas.**

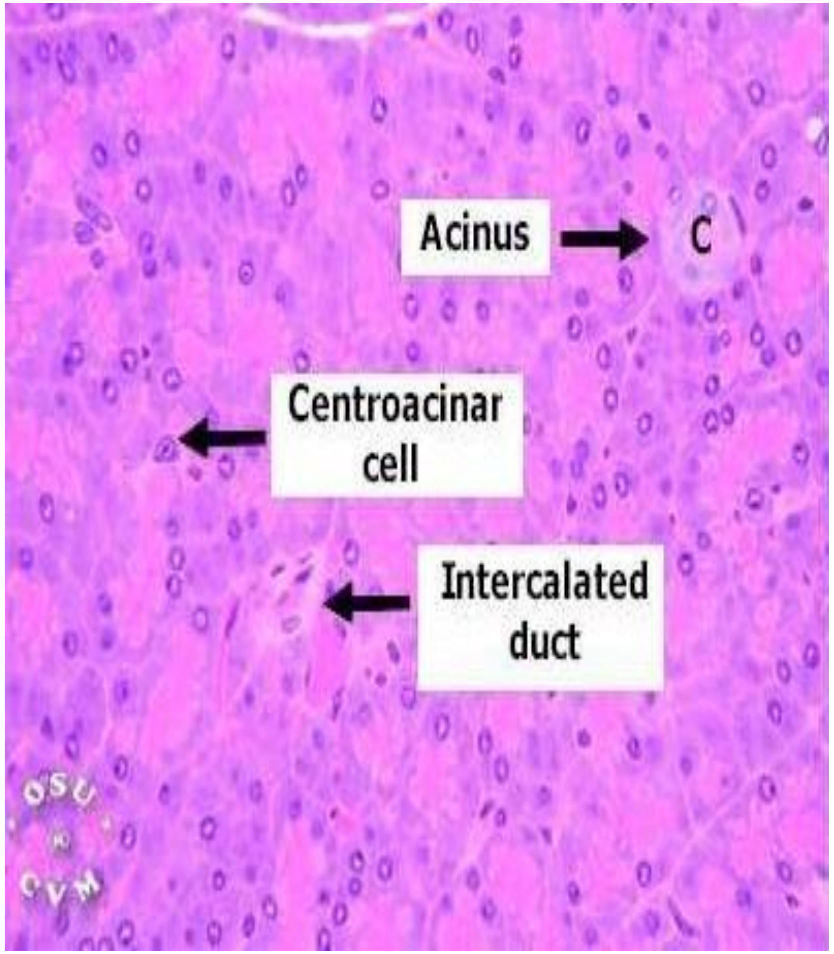
- **Another characteristic detail is that in the pancreas the initial portions of intercalated ducts penetrate the lumens of the acini**

- Nuclei, surrounded by a pale cytoplasm, belong to centroacinar cells that constitute the intraacinar portion of the intercalated duct

- These cells are found only in pancreatic acini

- Intercalated ducts are tributaries of larger intralobular ducts that, in turn, form larger interlobular ducts lined by columnar epithelium, located within the connective tissue septa.

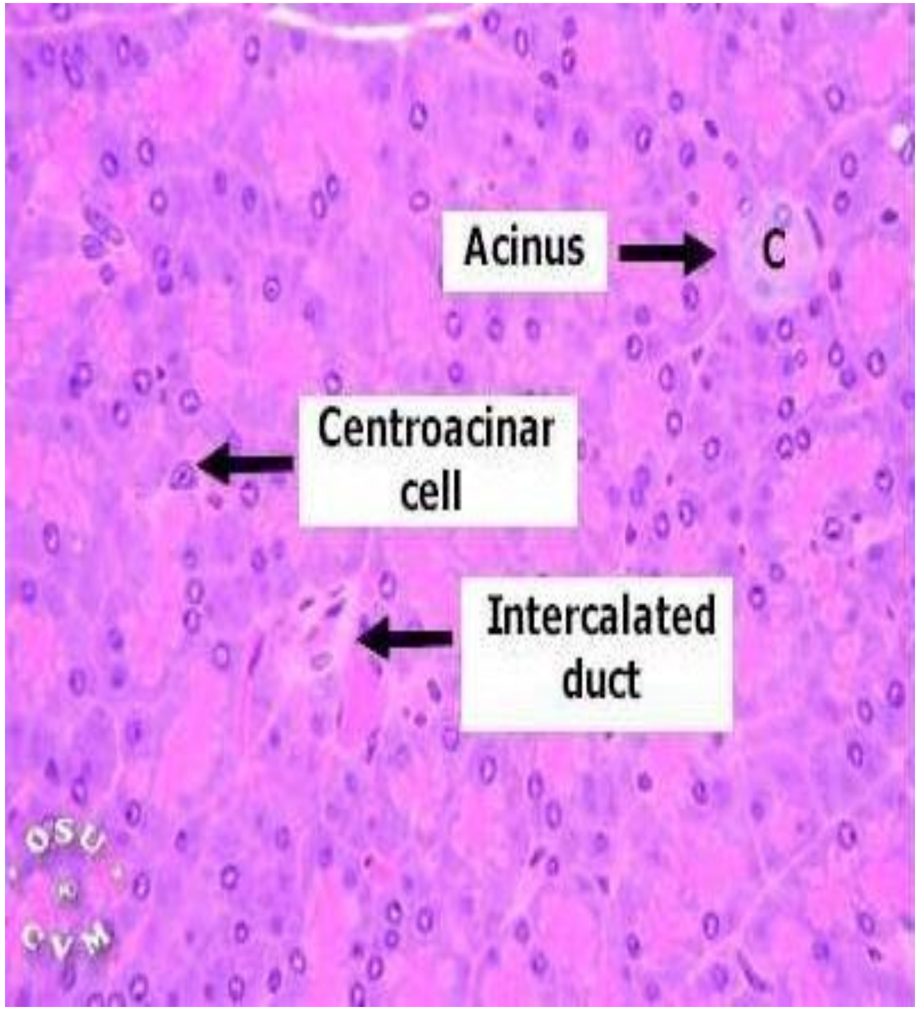
- There are no striated ducts in the pancreatic duct system.



Differences between the parotid and the pancreas

IMPORTANT

parotid	pancreatic
1)Serous acini	1) Centroacinar cells ((large cuboidal cell))
2)Striated duct	2) NO Striated duct
3)Intercalated duct	3)Intercalated duct (lined with simple cuboidal and presence to collect the secretion and send it to the pancreatic duct)



- The exocrine pancreatic acinus is composed of several serous cells surrounding a lumen

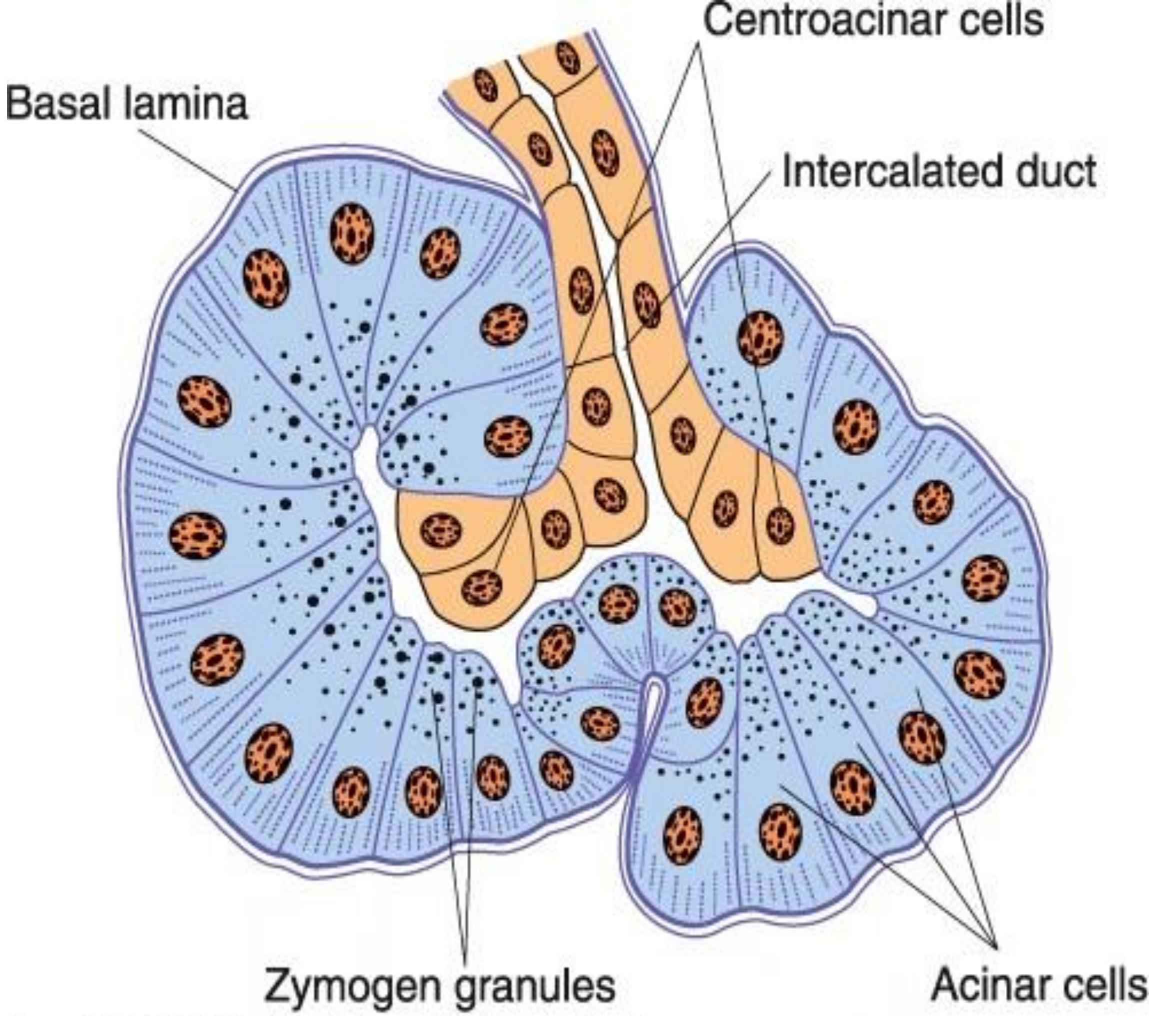
- These pancreatic cells are highly polarized, characterized by their basophilic basal rounded nucleus at the base and an acidophilic apex. They contain Zymogen granules which is typical protein-secreting cells, storing pancreatic enzymes for secretion.

- The number of zymogen granules present in each cell varies according to the digestive phase and attains its maximum in animals that have fasted

- thin capsule of connective tissue covers the pancreas and sends septa into it, separating the pancreatic lobules

- The acini are surrounded by a basal lamina that is supported by a delicate sheath of reticular fibers.

- The pancreas also has a rich capillary network, essential for the secretory process.



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- The exocrine pancreas secretes 1500-3000 mL of isosmotic alkaline fluid per day containing water, ions, and several proteases

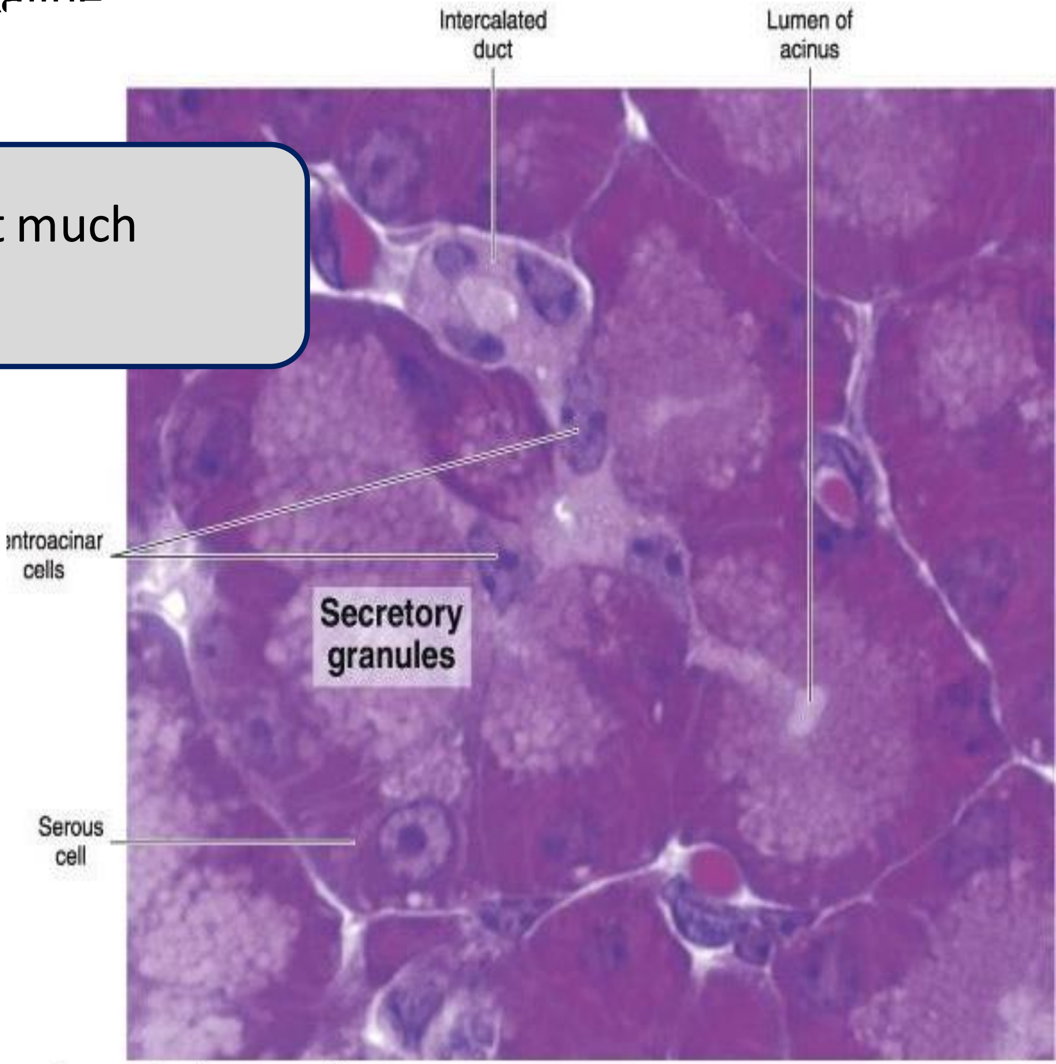
- **trypsinogens 1, 2,** and **3,**
- **chymotrypsinogen,**
- **proelastases 1** and **2, protease E**
- **, kallikreinogen,**
- **procarboxypeptidases A1, A2, B1,** and **B2**),
- **amylase, lipases** (**triglyceride lipase, colipase,** and **carboxyl ester hydrolase**), **phospholipase A_2,**
- and **nucleases** (**deoxyribonuclease** and **ribonuclease**)

Biochemistry part isn't much importance

- The majority of the enzymes are stored as proenzymes in the secretory granules of acinar cells, being activated in the lumen of the small intestine after secretion

- Enterokinase, an intestinal enzyme, cleaves trypsinogen to form trypsin, which then activates the other proteolytic enzymes in a cascade.

- Pancreatic secretion is controlled mainly through two hormones **secretin** and **cholecystokinin** that are produced by enteroendocrine cells of the intestinal mucosa (duodenum and jejunum



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اللَّهم ثبّت قلوب المجاهدين في غزة
وانصرهم على من عاداهم من اليهود و أعوانهم
الظّالمين، ردّ كيد الكائدين، نجعلك اللهم في
نُحورهم، ونعوذُ بكَ من شُرورهم

V2: Slide 28

Interperitoneal not Intraperitoneal

Slide 27

We add a line under the sentence that start with Tubuloacinar mucous

V18 edils :3 and (der ton etihw si roloc diosunis)20