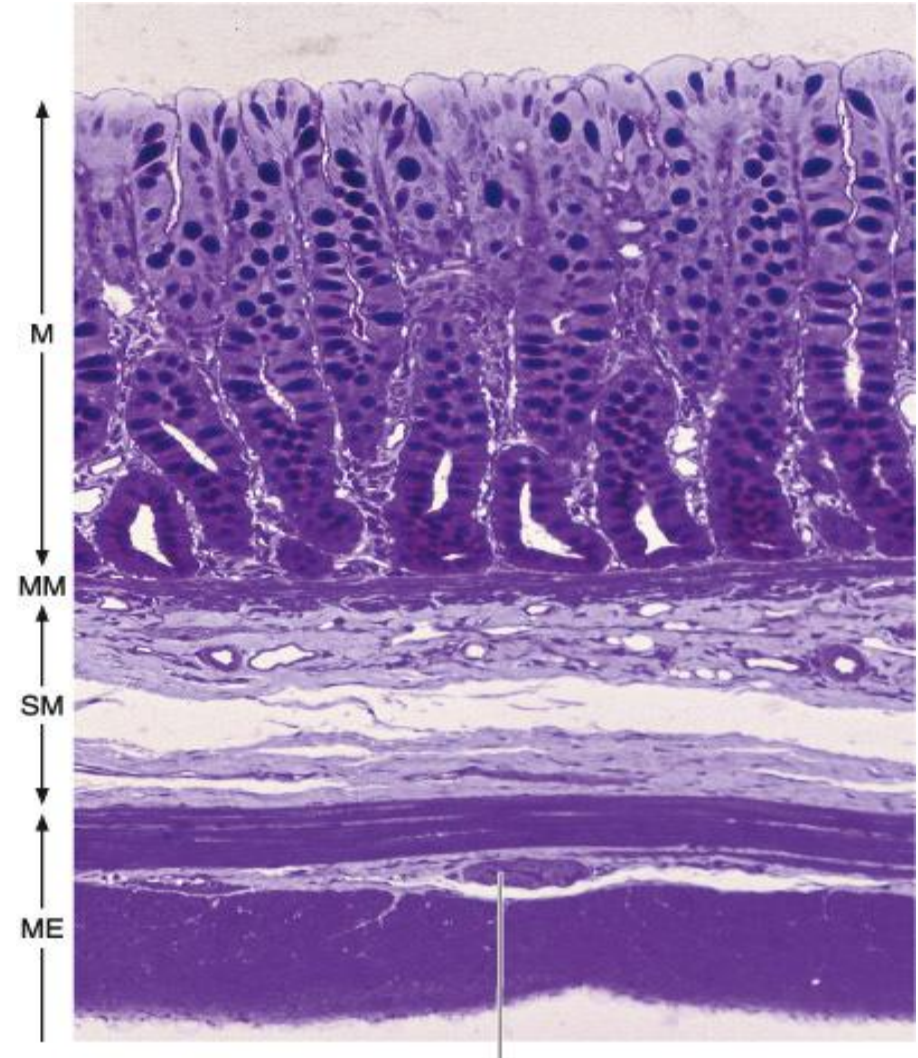


GI Histology 3

Large Intestine

- The large intestine consists of a mucosal membrane with no folds except in its distal (rectal) portion
- No villi 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.

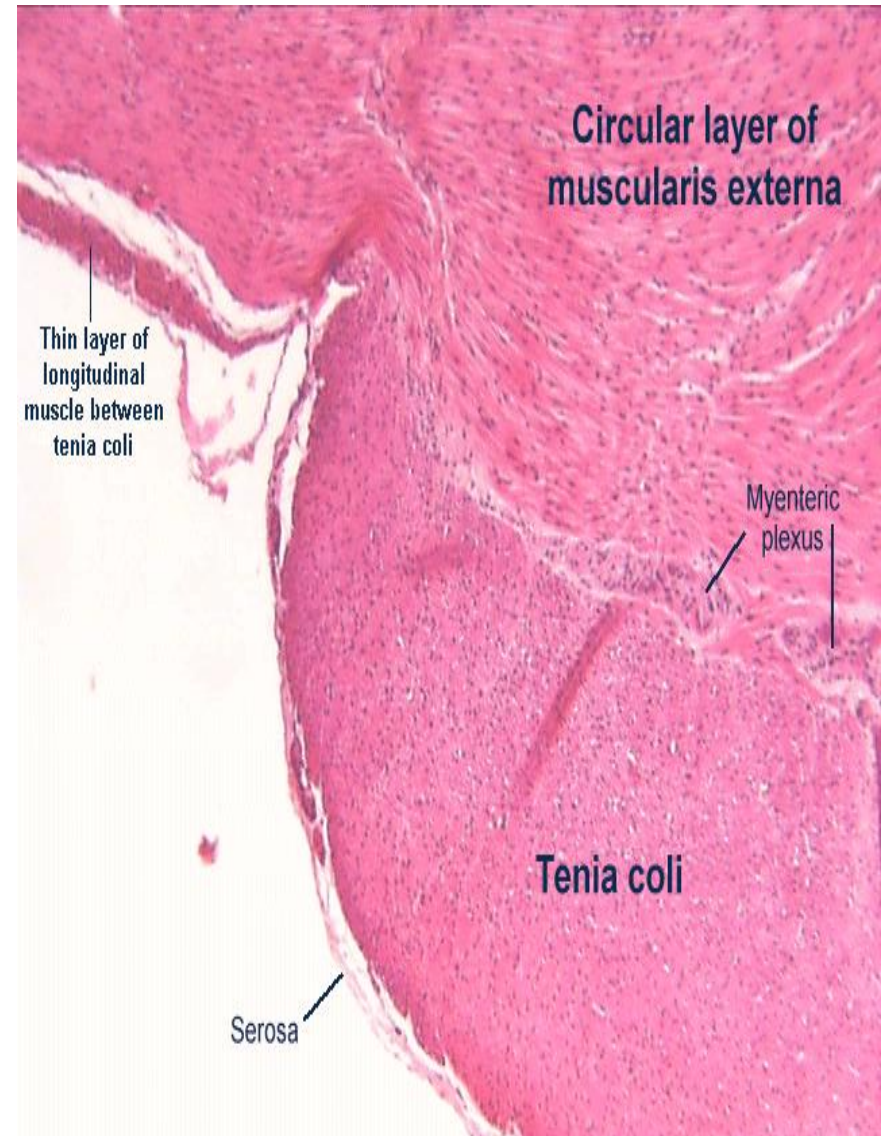


Myenteric plexus

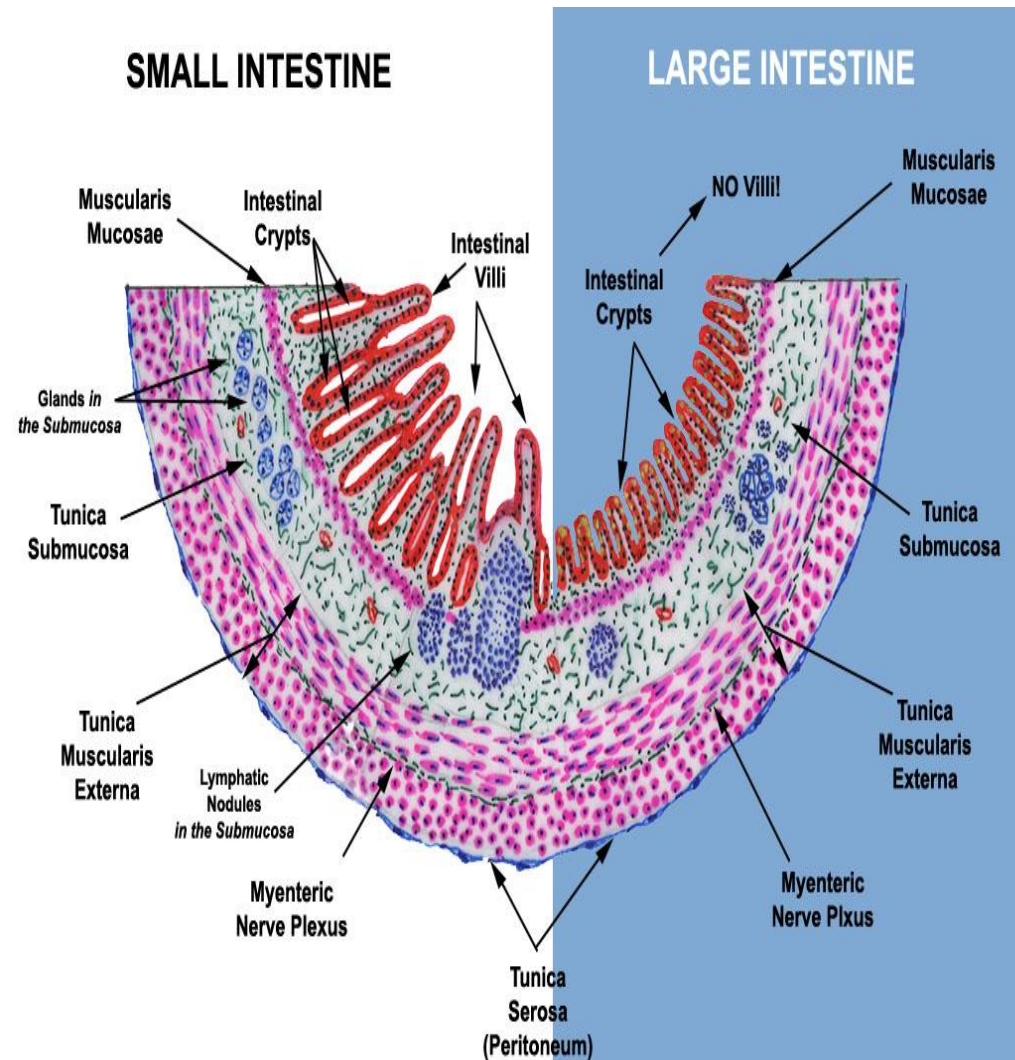
- Mucus is a highly hydrated gel that not only lubricates the intestinal surface but also covers bacteria and particulate matter.
- The absorption of water is passive, following the active transport of sodium out of the basal surfaces of the epithelial cells



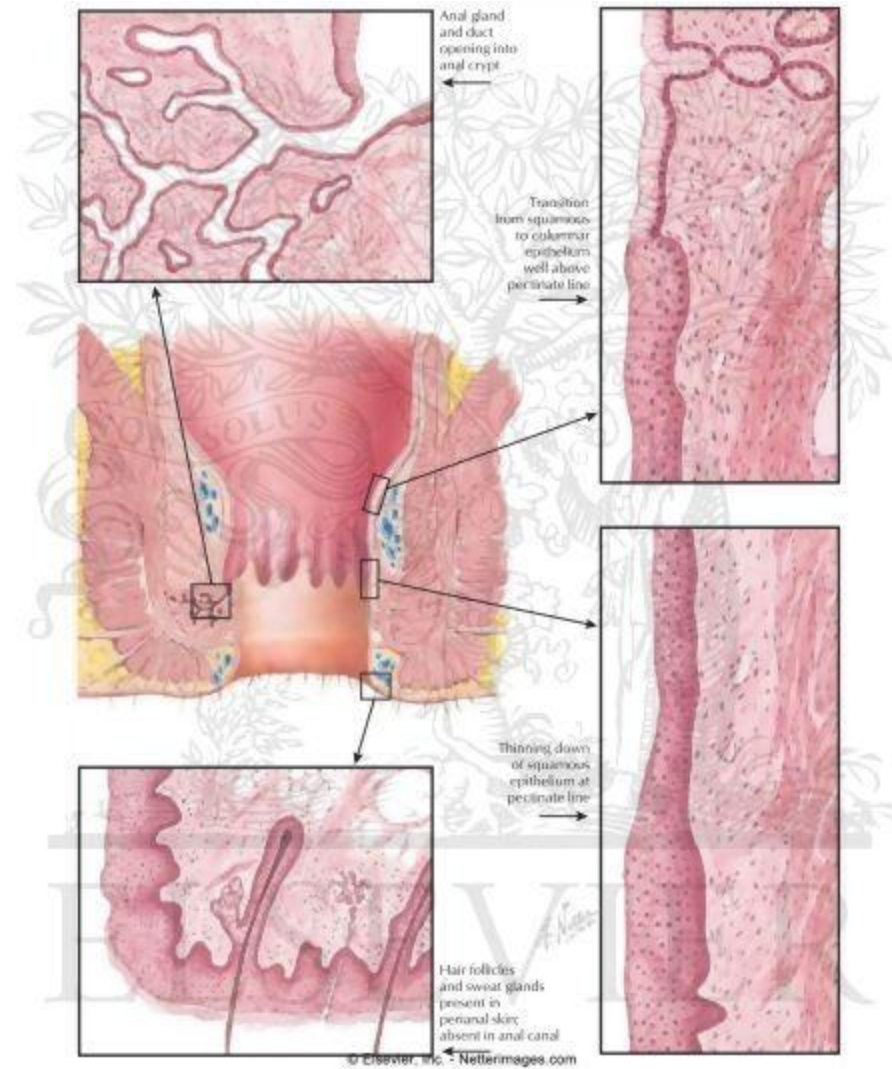
- The lamina propria is rich in lymphoid cells and in nodules that frequently extend into the submucosa
- This richness in lymphoid tissue (GALT) is related to the abundant bacterial population of the large intestine.
- The muscularis comprises longitudinal and circular strands
- This layer differs from that of the small intestine, because fibers of the outer longitudinal layer congregate in three thick longitudinal bands called **teniae coli**.
- In the intraperitoneal portions of the colon, the serous layer is characterized by small, pendulous protuberances composed of adipose tissue—the **appendices epiploicae**.



- So the differences between the small and large intestine are :
- Mucosa is thicker and contains crypts but no Villi
- 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.

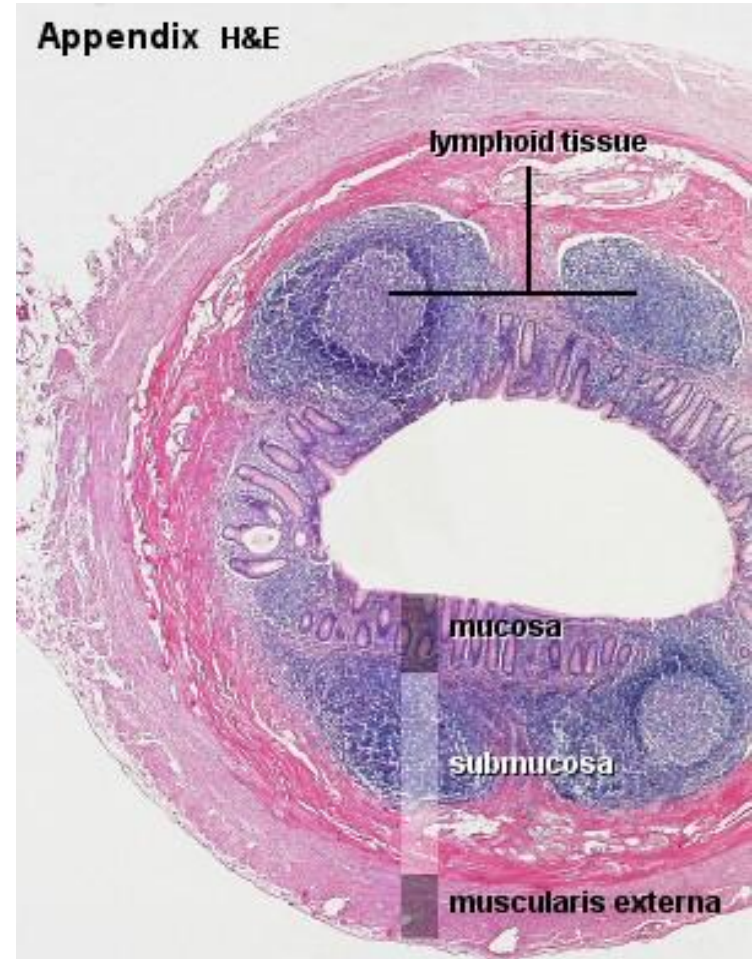


- In the anal region, the mucous membrane forms a series of longitudinal folds, the **rectal columns of Morgagni**
- **These columns connects to the anal orifice to form the anal valves and sinuses.**
- About 2 cm above the anal opening, the intestinal mucosa is replaced by stratified squamous epithelium
- 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.



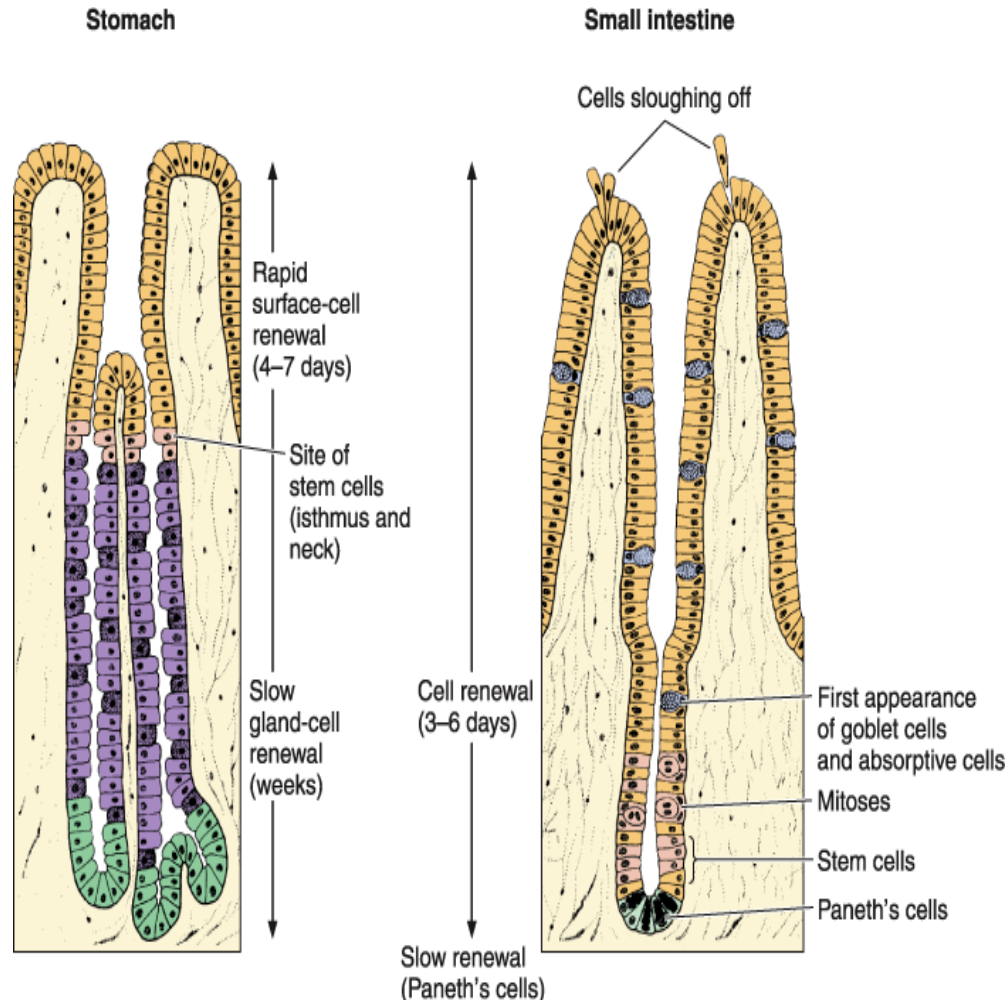
Appendix

- The appendix is an evagination of the cecum
- is characterized by a relatively small, narrow, and irregular lumen
- 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)



Cell Renewal in the Gastrointestinal Tract

- The epithelial cells of the entire gastrointestinal tract are constantly being cast off and replaced with new ones formed through mitosis of stem cells
- 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
- 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
- In the small intestine the cells die by apoptosis in the tip of the villi or are sloughed off by mechanical action during function.



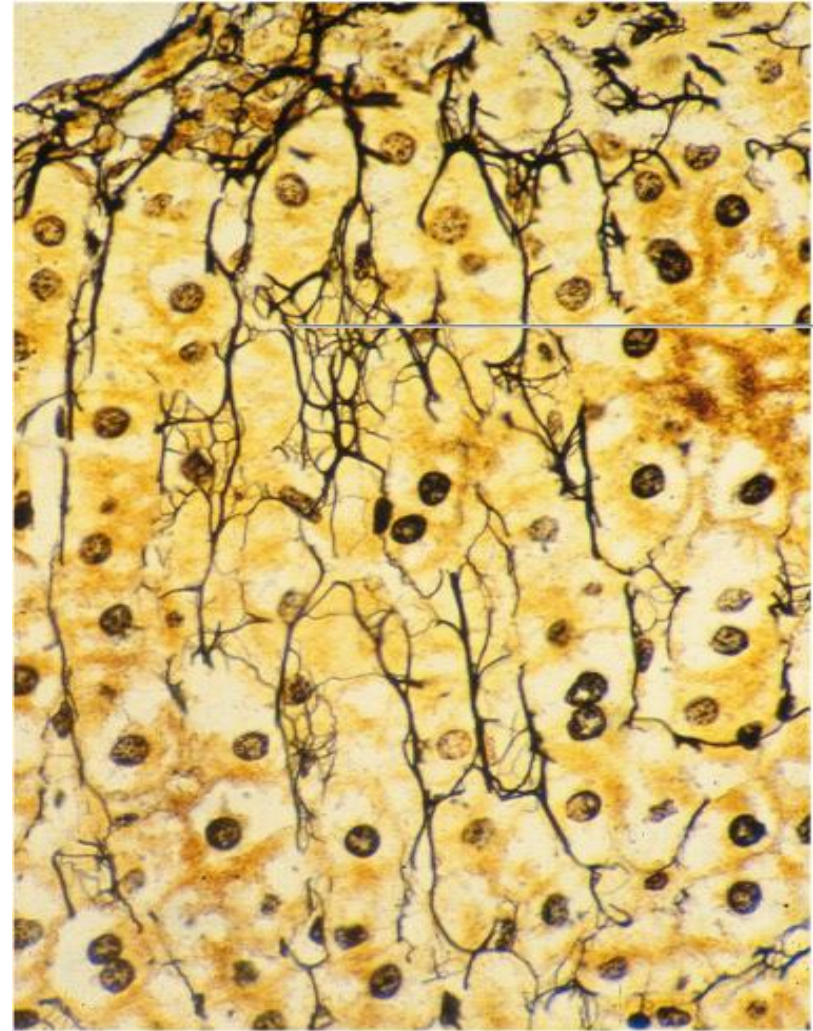
Liver

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

- The position of the liver in 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

- The liver is covered by a thin connective tissue capsule (**Glisson's capsule**)
- 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.

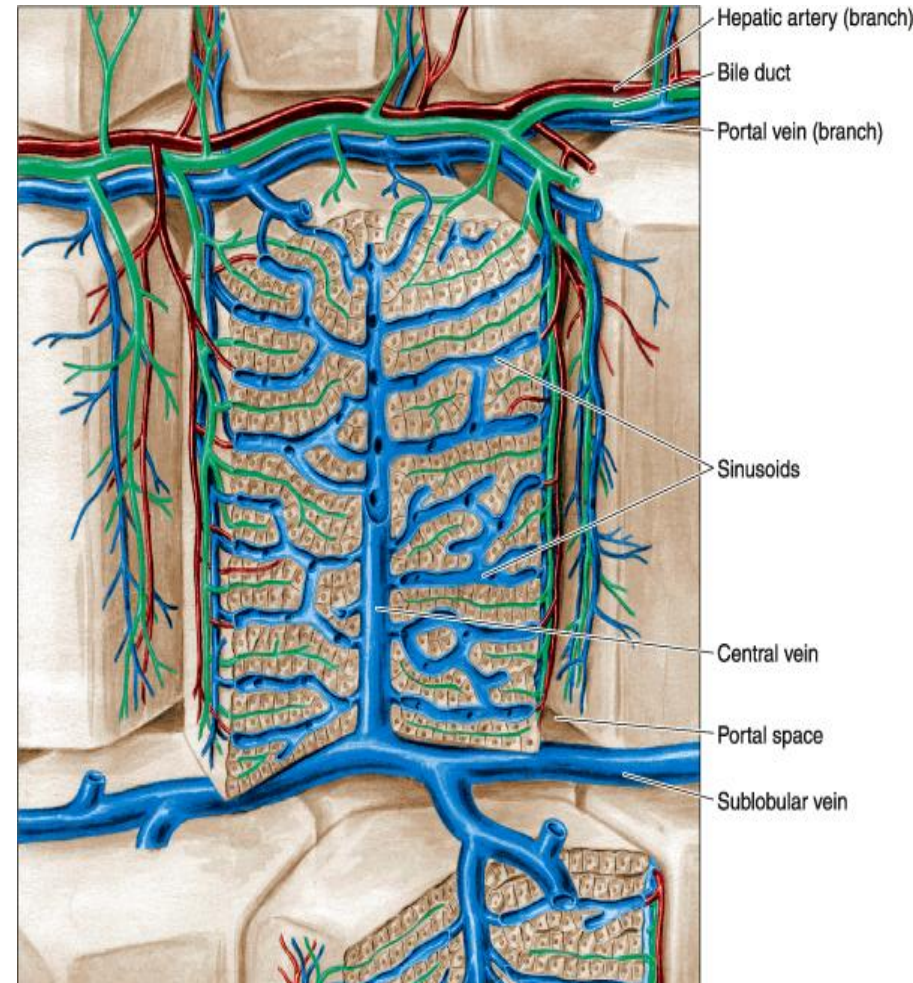


Reticular
fibers

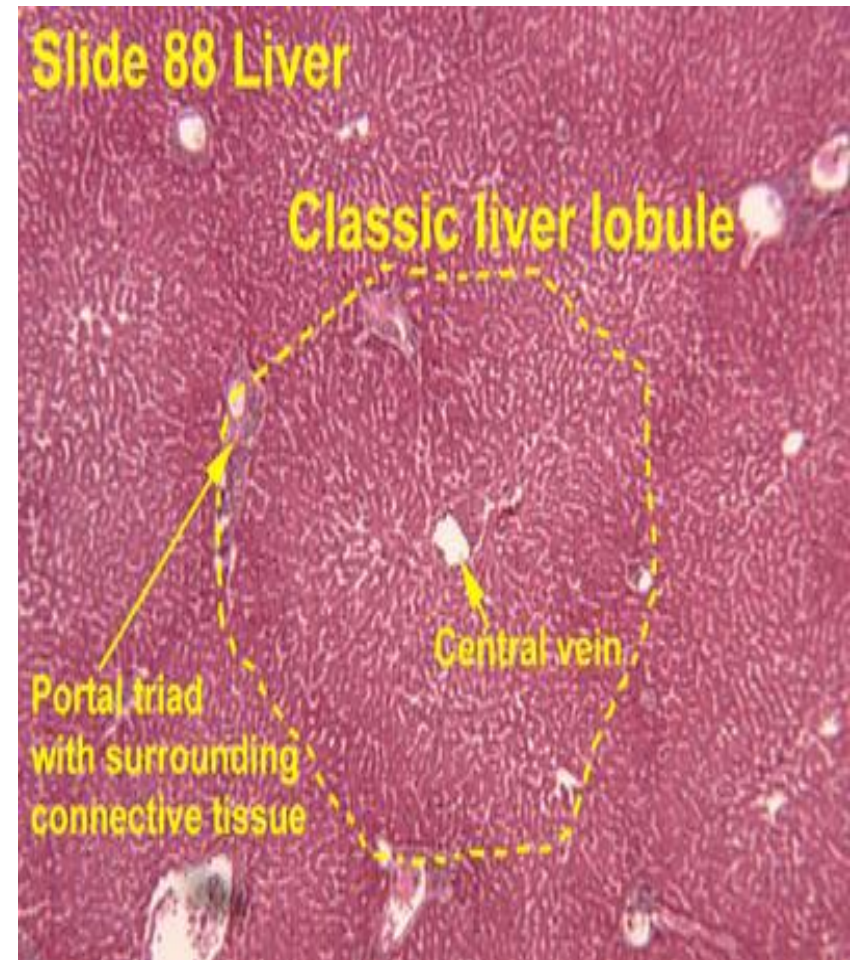
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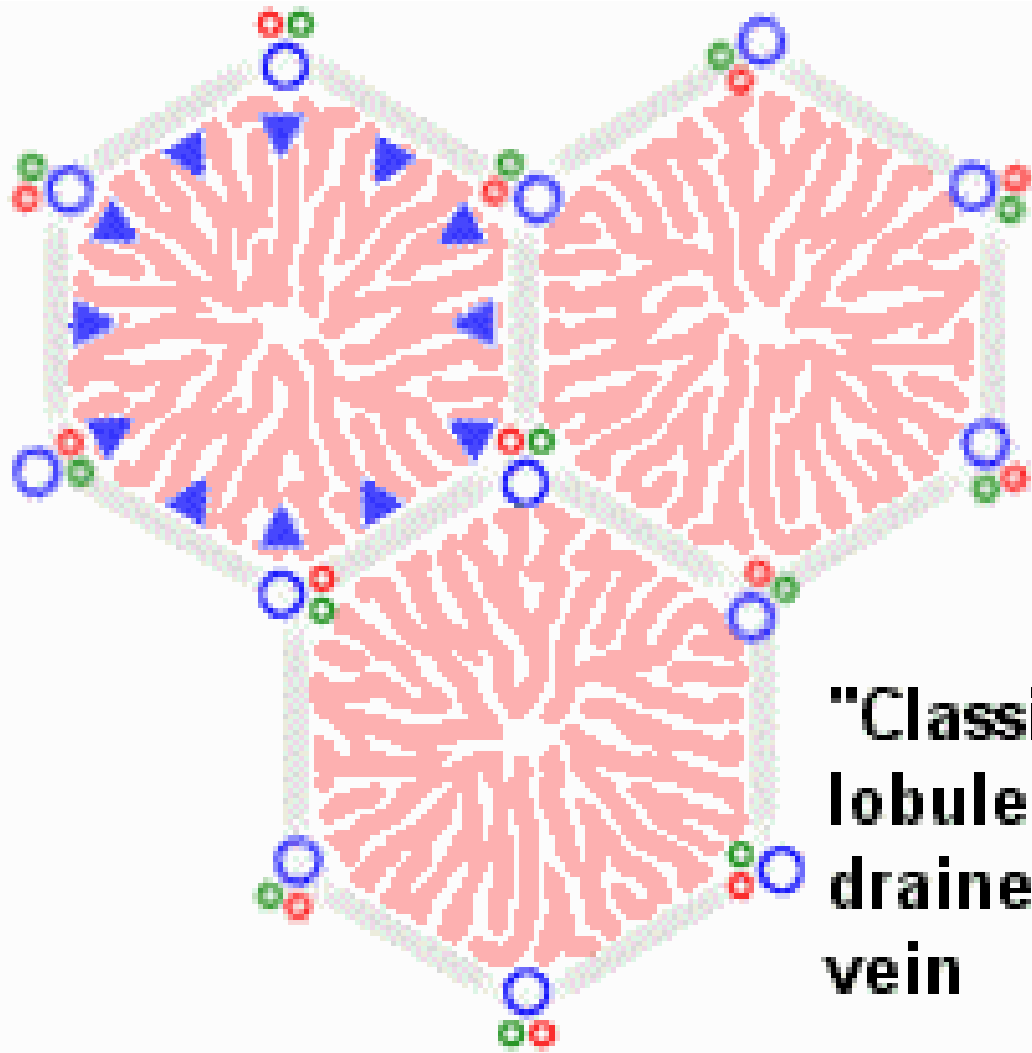
The Liver Lobule

- The basic structural component of the liver is the liver cell, or **hepatocyte**
- These epithelial cells are grouped in interconnected plates and constitute two-thirds of the mass of the liver
- 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



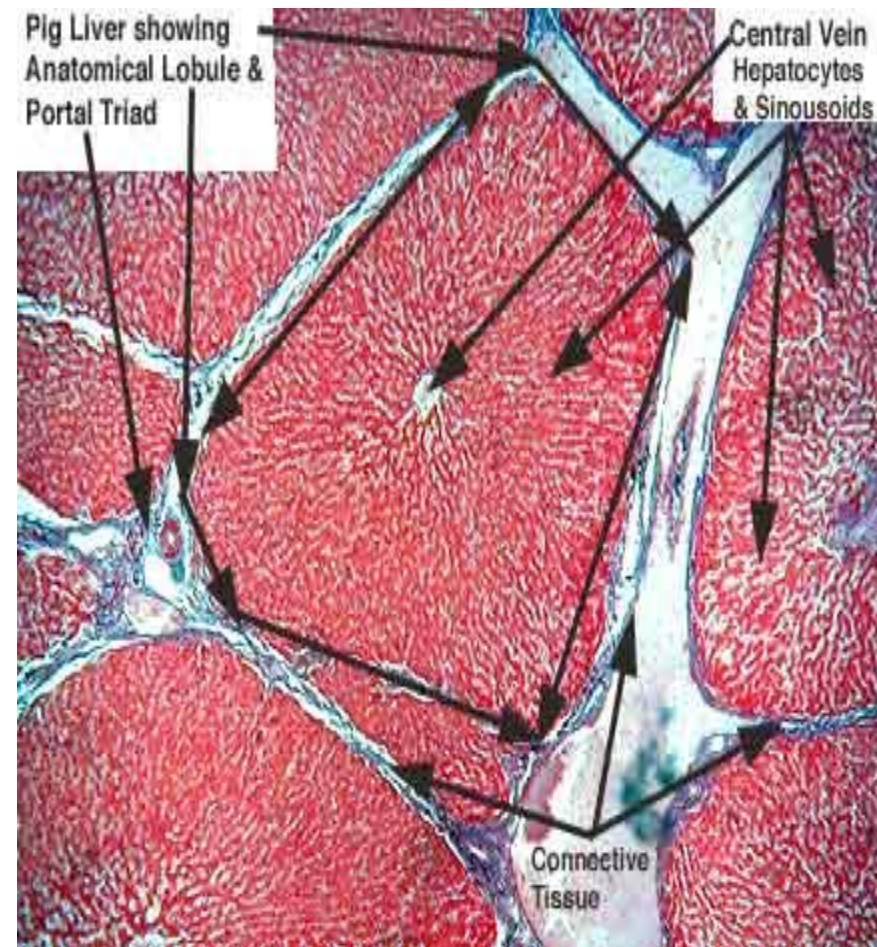
- Portal spaces, regions located in the corners of the lobules, contain connective tissue, bile ducts, lymphatics, nerves, and blood vessels
- The human liver contains three to six portal spaces per lobule, each with a venule (a branch of the portal vein),
 - an arteriole (a branch of the hepatic artery),
 - 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



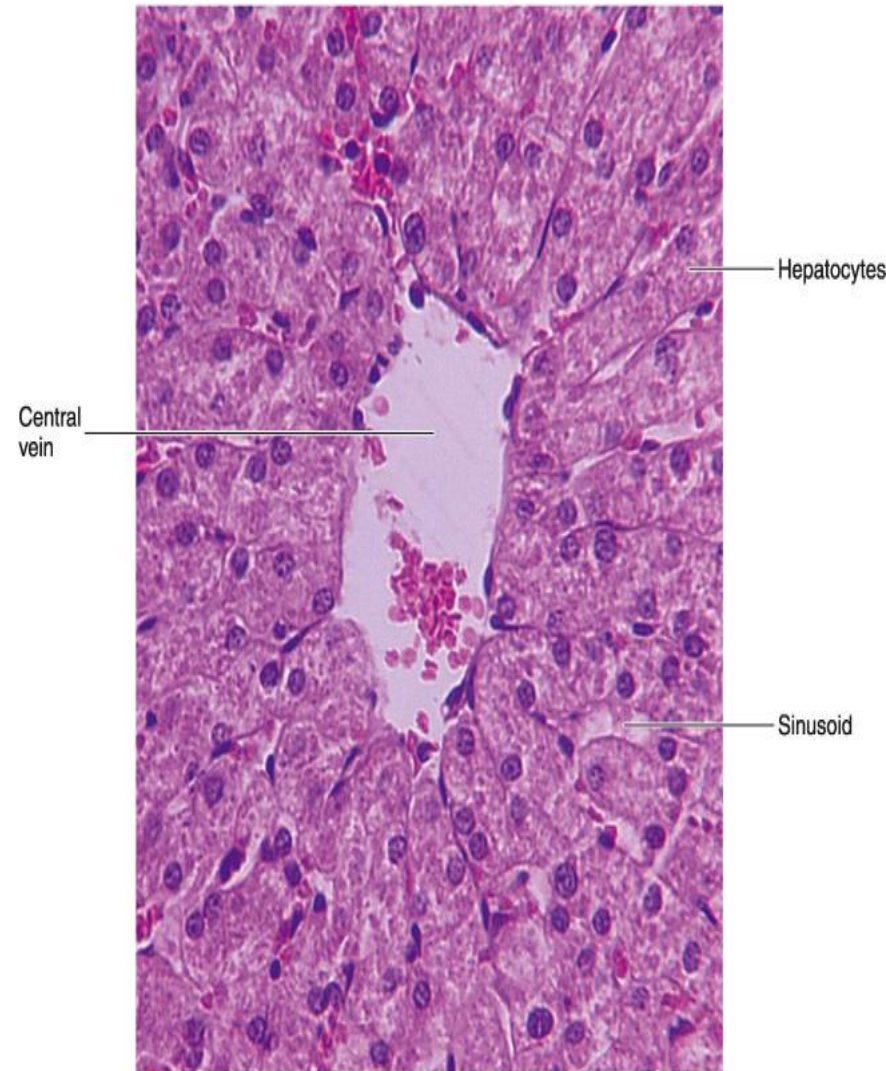


"Classical" liver lobule: the unit drained by a central vein

- In certain animals (eg, pigs), the lobules are separated by a layer of connective tissue
- 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.

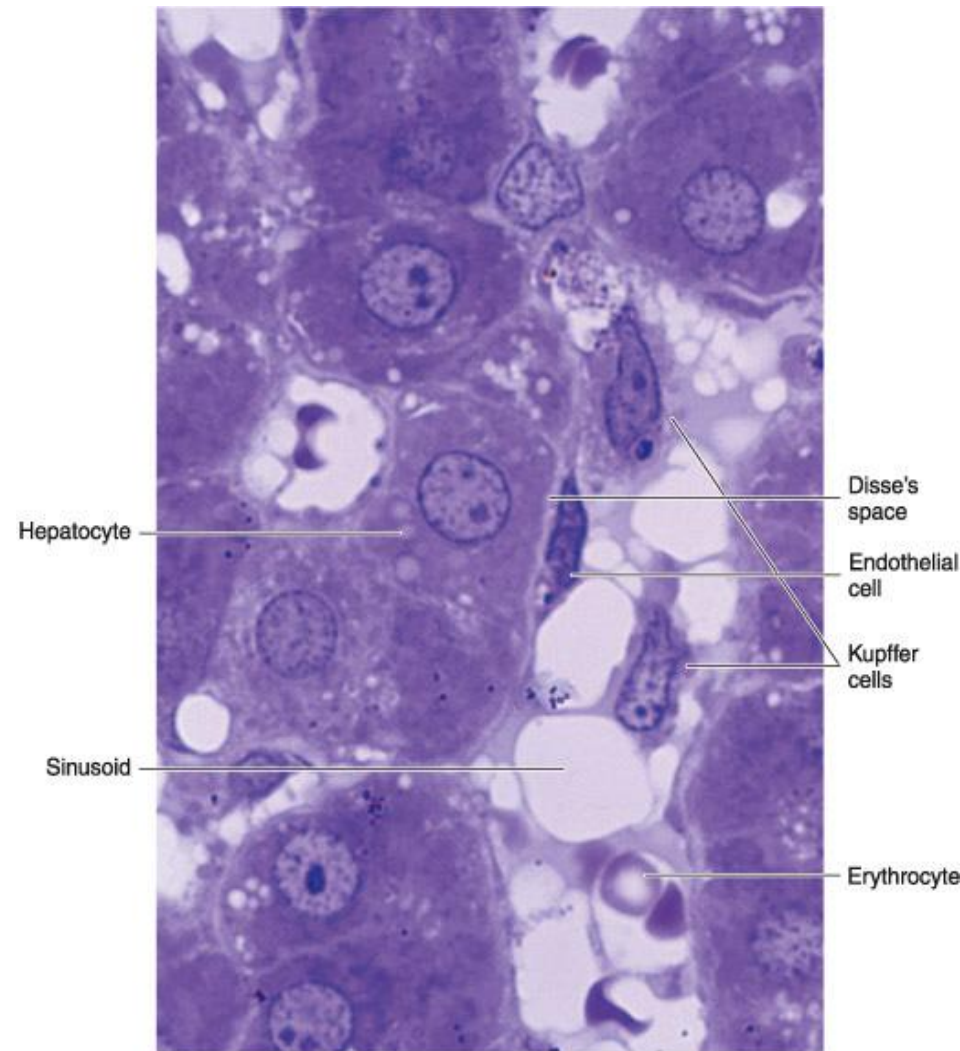


- The hepatocytes in the liver lobule are radially disposed and are arranged like the bricks of a wall
- These cellular plates are directed from the periphery of the lobule to its center and anastomose freely, forming a labyrinthine and spongelike structure
- The space between these plates contains capillaries, the **liver sinusoids**
- sinusoidal capillaries are irregularly dilated vessels composed solely of a discontinuous layer of fenestrated endothelial cells.
- The fenestrae 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.

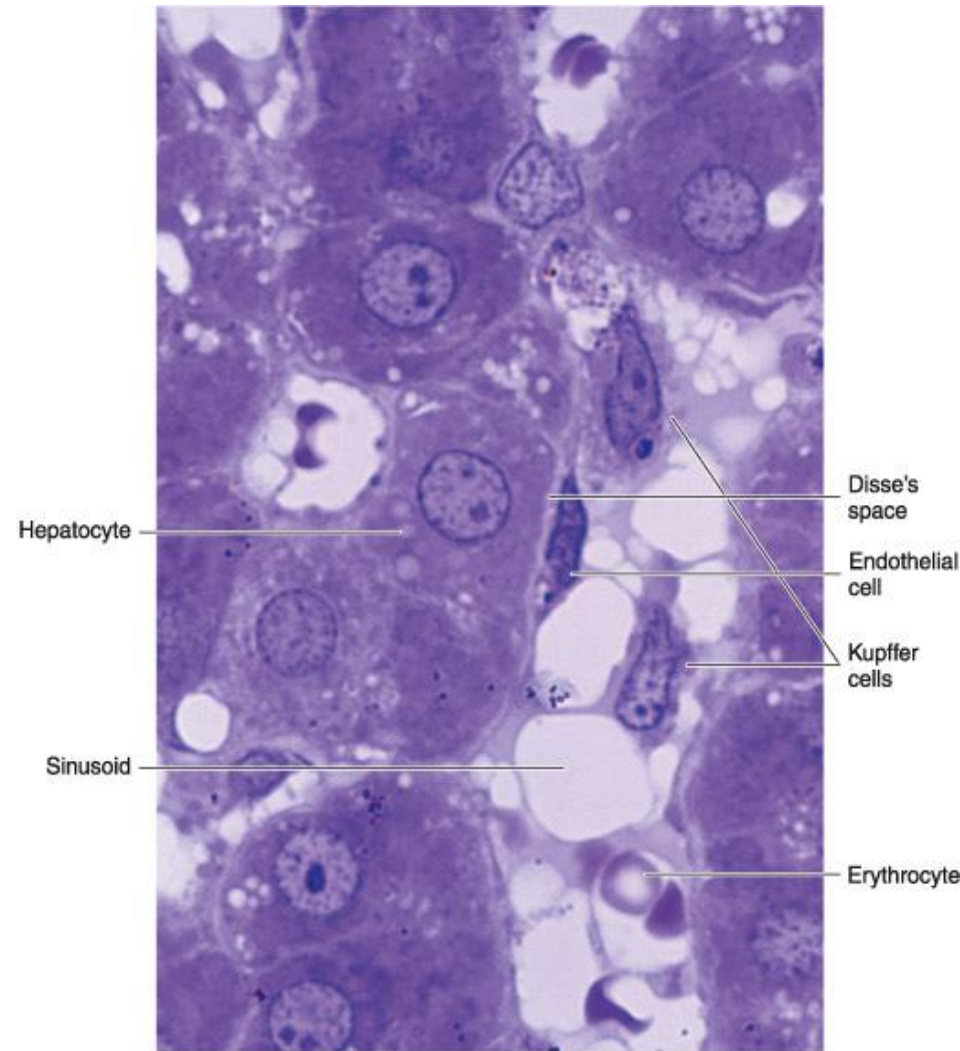


A

- 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 but not of cellular elements into the space of Disse
- 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.



- The sinusoid is surrounded and supported by a delicate sheath of reticular fibers
- In addition to the endothelial cells, the sinusoids contain macrophages known as **Kupffer cells**
- These cells are 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

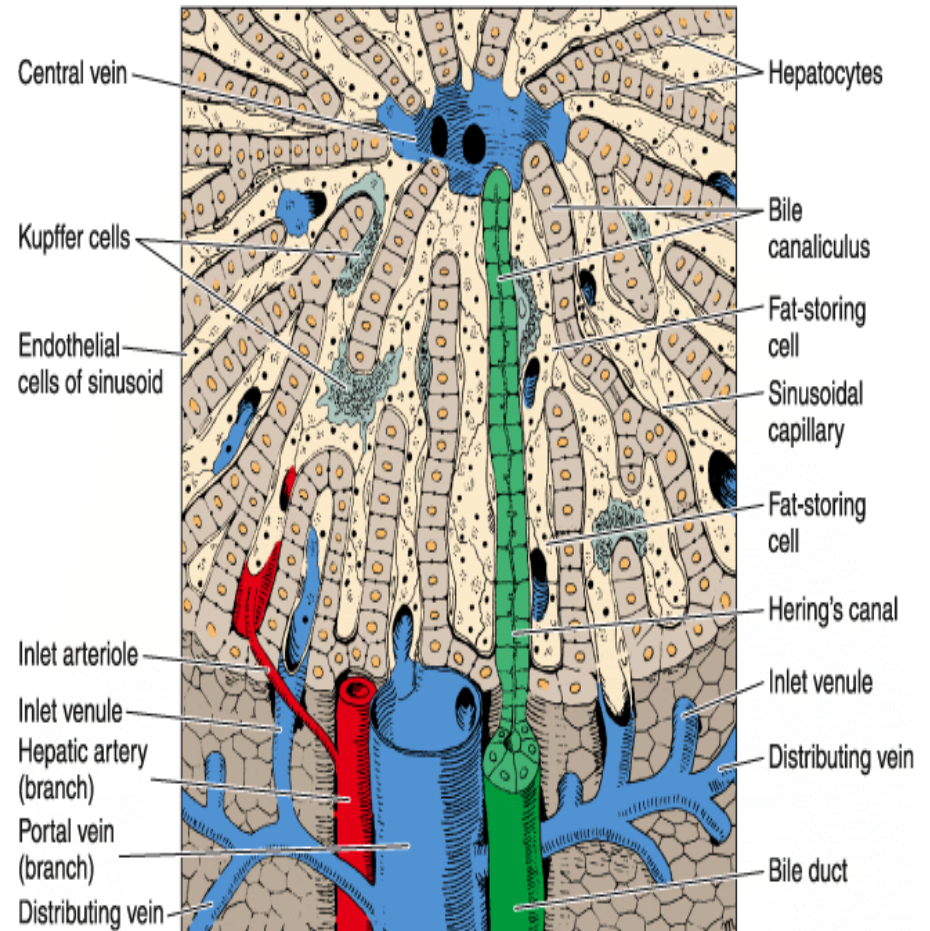


- In the space of Disse (perisinusoidal space), **fat-storing cells**, also called stellate or Ito's cells, contain vitamin A rich lipid inclusions
- In the healthy liver, these cells have several functions, such as
- uptake, storage, and release of retinoids
- synthesis and secretion of several extracellular 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 A₂).

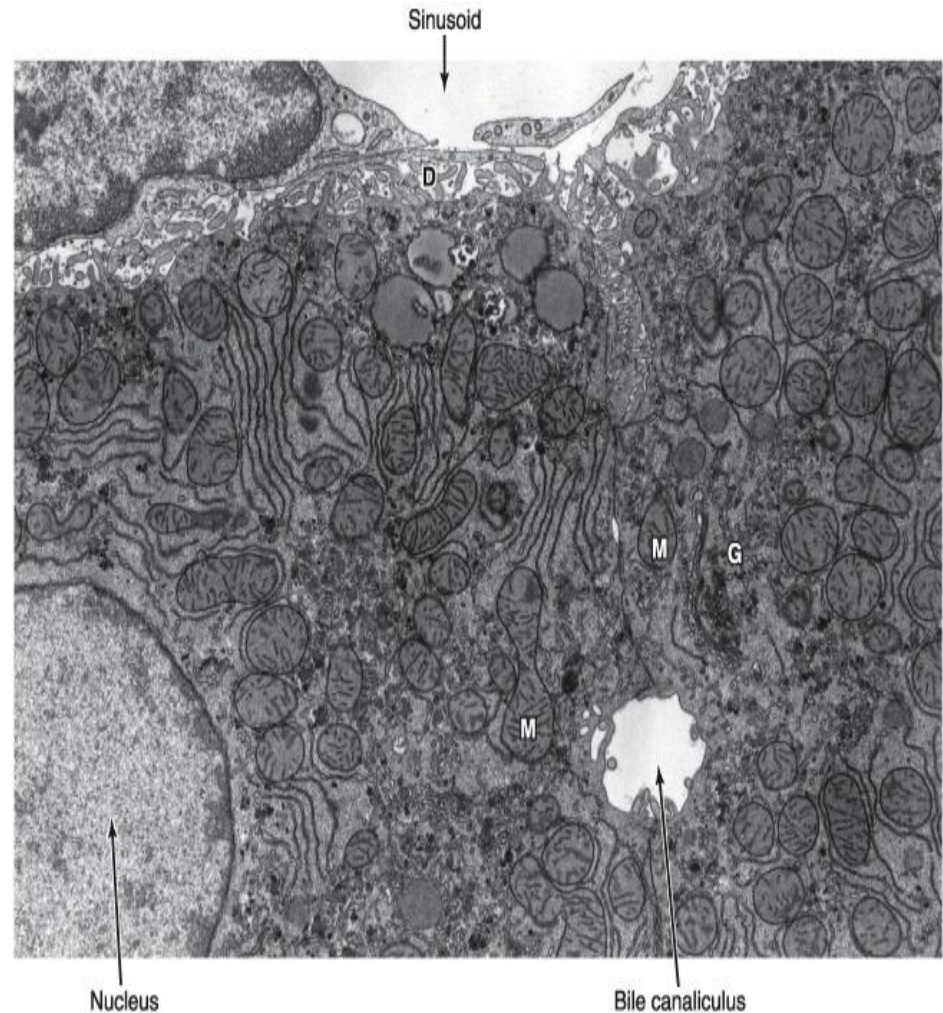


The Hepatocyte

- Hepatocytes are polyhedral, with six or more surfaces, and have a diameter of 20-30 μm
- 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
- Wherever two hepatocytes abut, they delimit a tubular space between them known as the **bile canaliculus**
- At the periphery, bile enters the **bile ductules**, or **Hering's canals** composed of cuboidal cells



- 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.

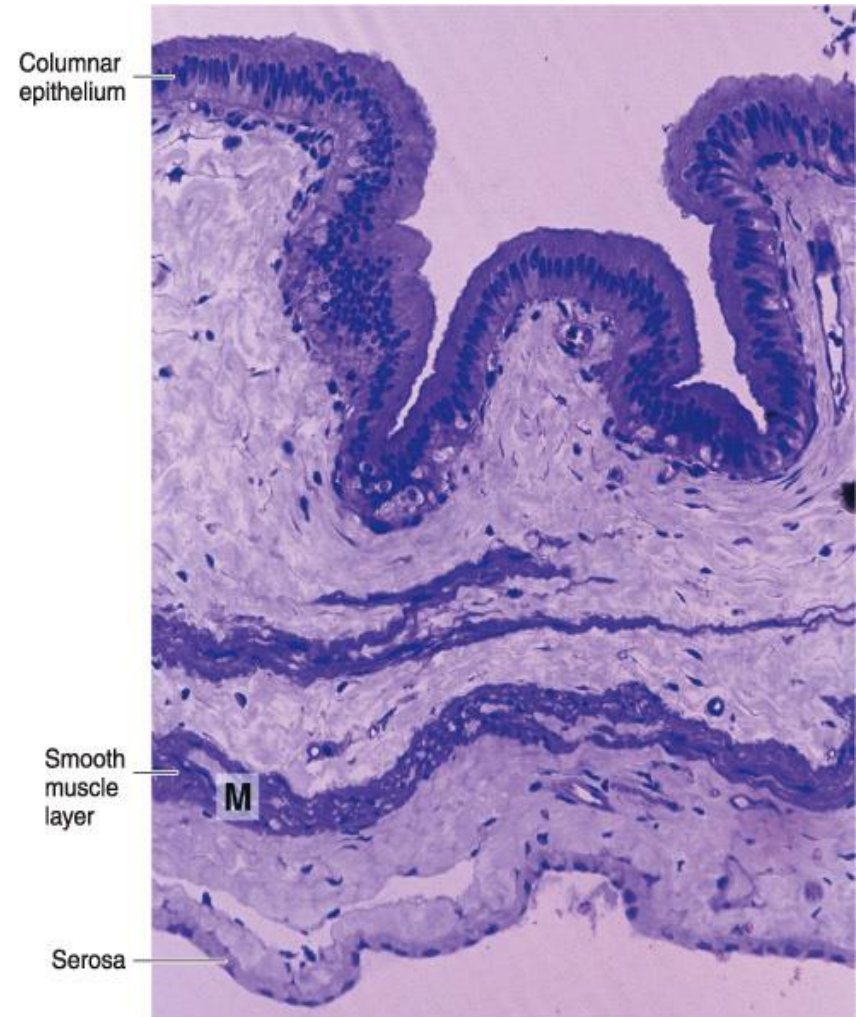


- The surface of the hepatocyte that faces the space of Disse contains many microvilli that protrude into that space, but there is always a space between them and the cells of the sinusoidal wall
- The hepatocyte has one or two rounded nuclei with one or two nucleoli
- Some of the nuclei are polyploid
- In the hepatocyte, the rough endoplasmic reticulum forms aggregates dispersed in the cytoplasm; these are often called **basophilic 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.

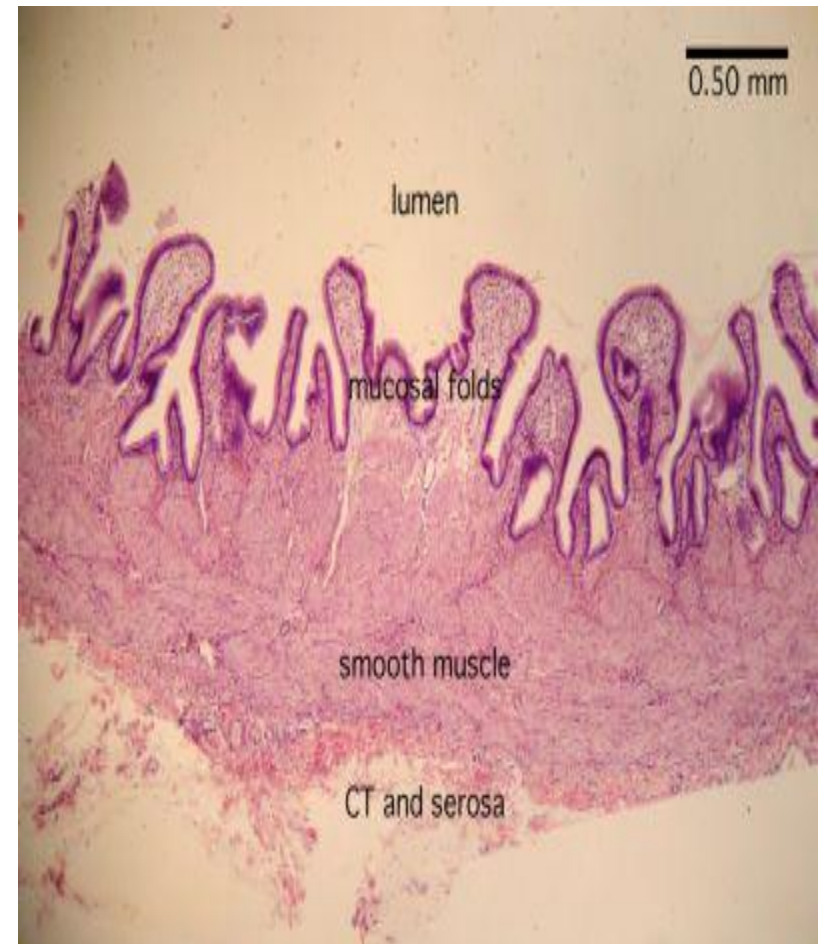


Gallbladder

- The gallbladder is a hollow, pear-shaped organ attached to the lower surface of the liver
- It can store 30-50 mL of bile.
- The wall of the gallbladder consists of a mucosa composed of simple columnar epithelium and lamina propria, a layer of smooth muscle, 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).

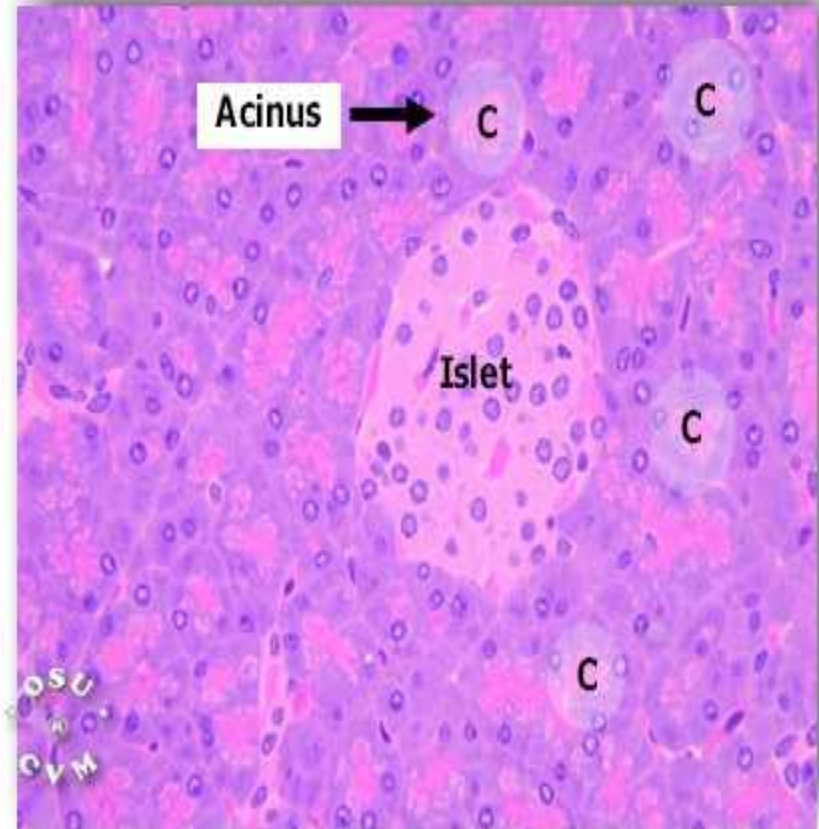


- The main function of the gallbladder is to store bile, concentrate it by absorbing its water, and release it when necessary into the digestive tract
- Contraction of the smooth muscle of the gallbladder is induced by **cholecystokinin**, a hormone produced by enteroendocrine cells located in the epithelial 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.



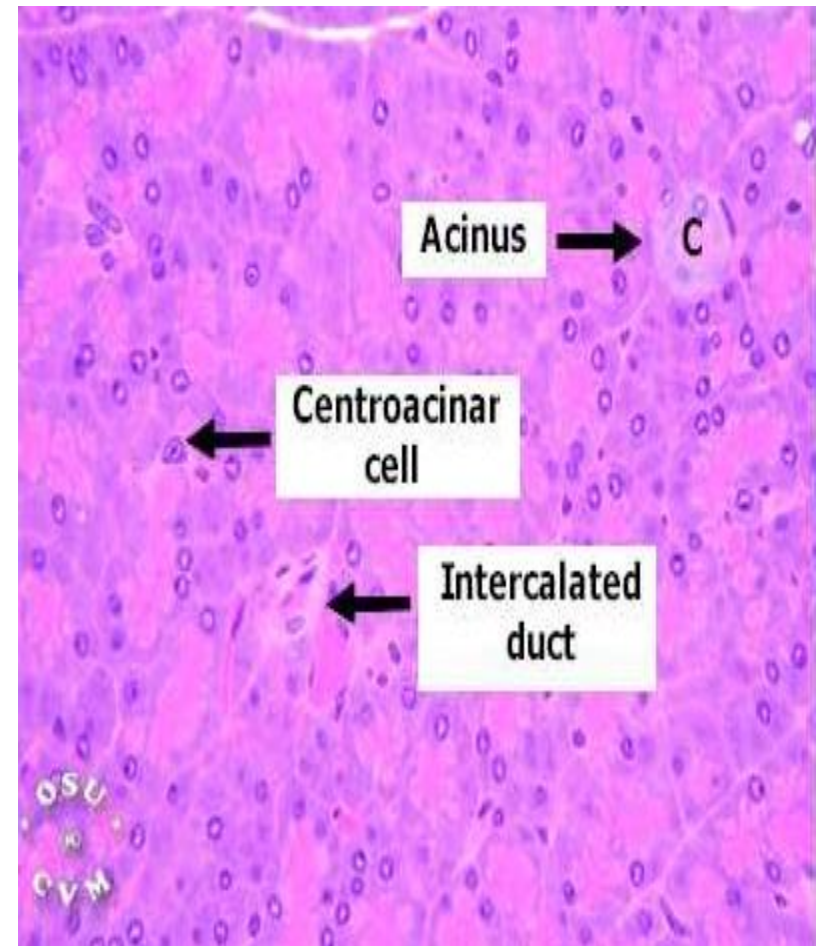
Pancreas

- The pancreas is a mixed exocrine-endocrine gland that produces digestive enzymes and hormones
- 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
- exocrine portion of the pancreas is a compound acinar gland, similar in structure to the parotid gland

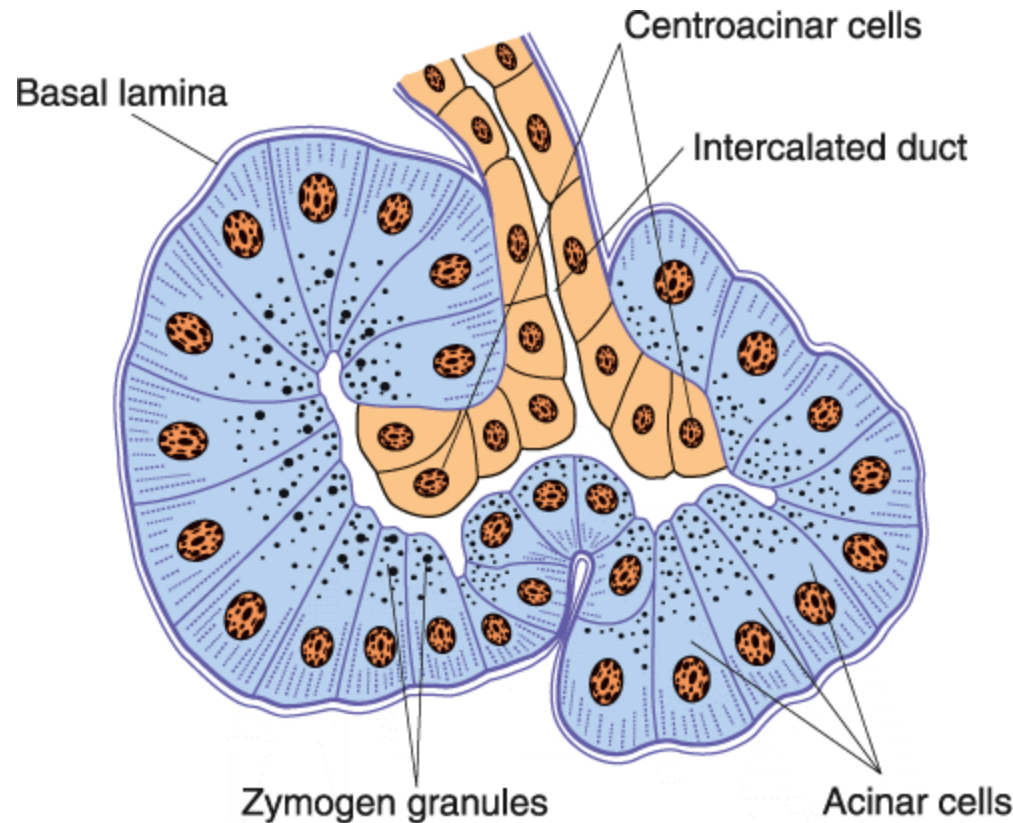


Differences between the parotid and the pancreas

- 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.

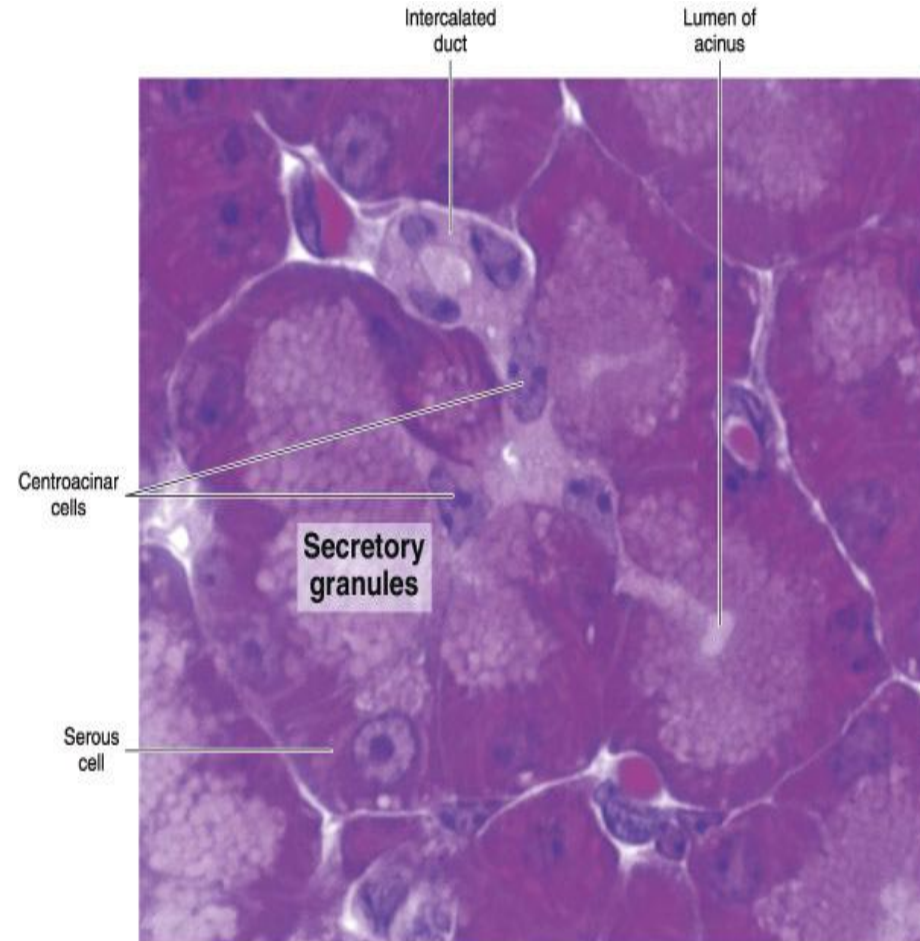


- The exocrine pancreatic acinus is composed of several serous cells surrounding a lumen
- These cells are highly polarized, with a spherical nucleus, and are typical protein-secreting cells.
- The number of zymogen granules present in each cell varies according to the digestive phase and attains its 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 A₂,**
- **and nucleases (deoxyribonuclease and ribonuclease)**
- 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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