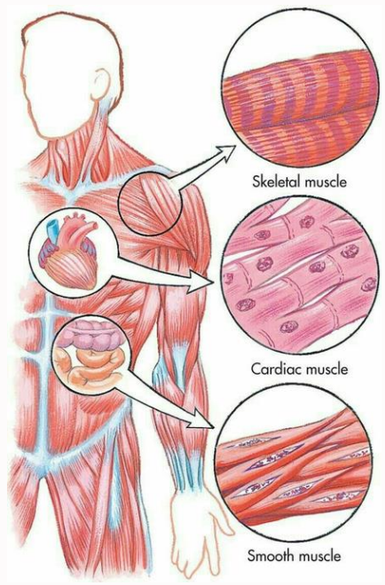
بسـم الله الرحمـٰن الرحيـم

(وَفَوْقَ كُلِّ ذِي عِلْمٍ عَلِيمٌ)

GIS Histology | FINAL 2

Histology of liver , Pancreas & Gallbladder

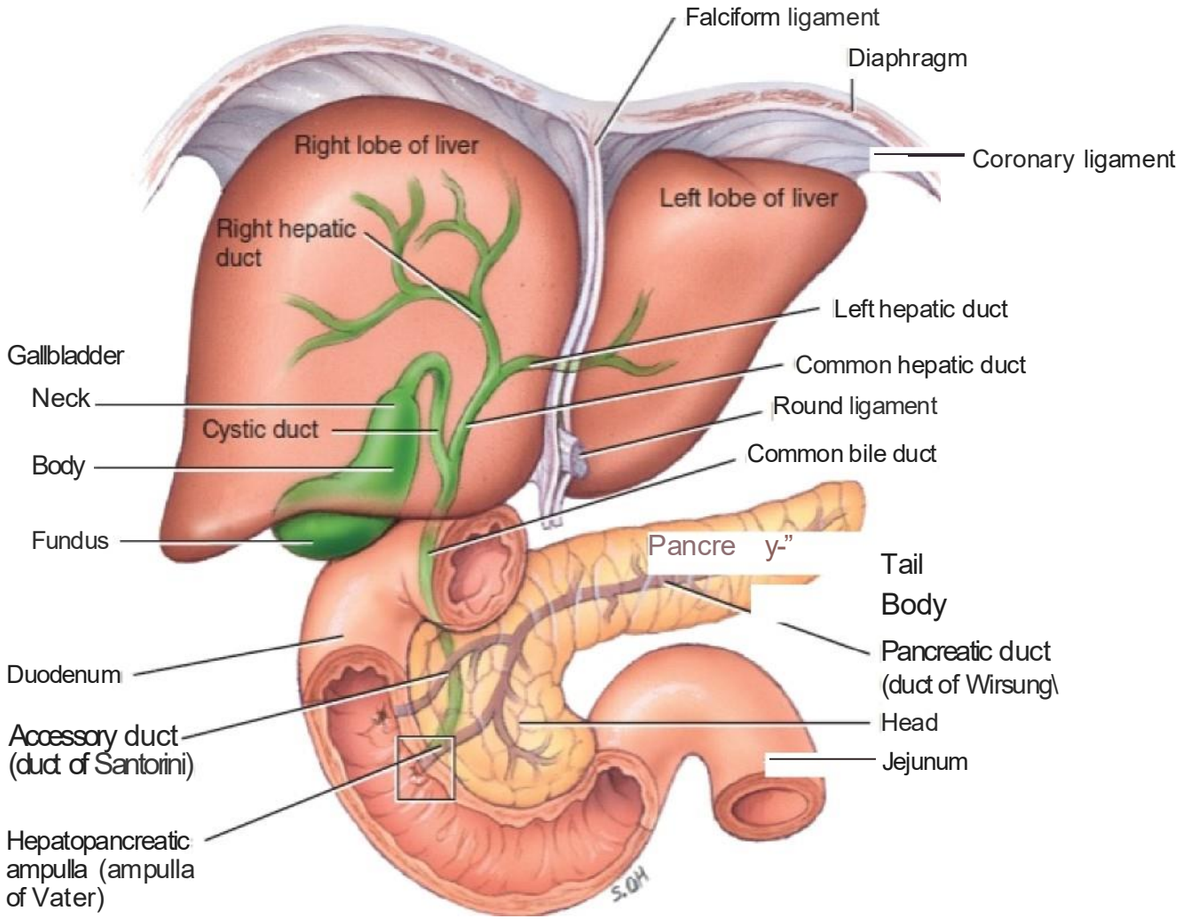


Written by : Sarah Al-bakkar

Reviewed by : Tuqa Al-Soud

Gastrointestinal Tract (GIT)

LIVER, PANCREAS, AND GALLBLADDDER



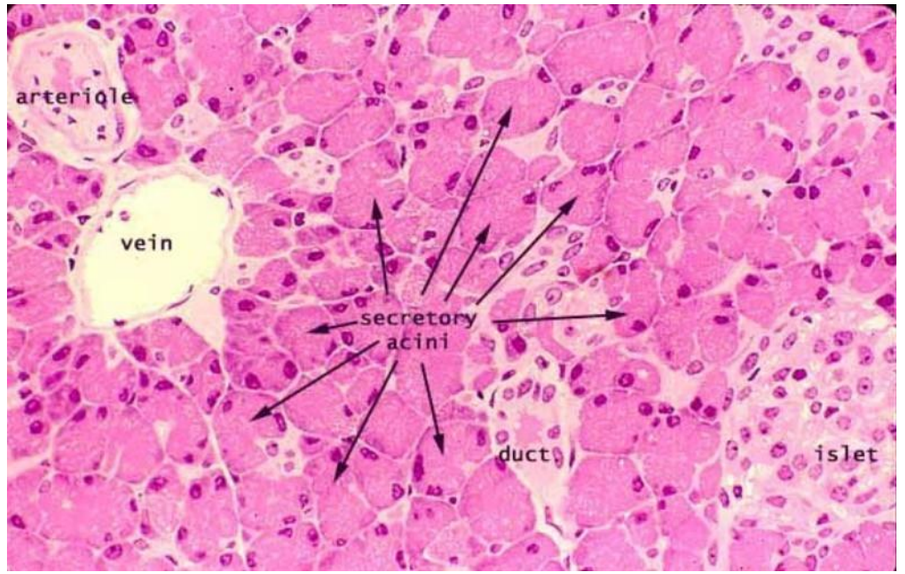
{a) Anterior view

❑ *Explanation of the image above:*

The pancreas is an extremely unique organ in the body because it is a hybrid gland, meaning that it has both: endocrine and exocrine functions at the same time.
And the liver, which you have already studied in the anatomy, is considered one of the most versatile organs in the body. Eventually, the liver releases bile, which reaches the second part of the duodenum through the common bile duct, and this duct joins the main pancreatic duct. One unique feature of the pancreas is that the main pancreatic duct drains almost the entire gland as it passes through the tail, then the body, neck, and head of the pancreas before opening into the duodenum. This arrangement is different from what we saw in the salivary glands, where we had major glands surrounded by a capsule and divided into lobes, and the lobes were further subdivided into smaller compartments called lobules.

Histology Of The Pancreas

- Made up of small clusters of glandular epithelial cells.
- 99% of the clusters, called **acini** constitute the *exocrine* portion of the organ. (Darkly stained zones)
- Cells within acini secrete a mixture of fluid and digestive enzymes.
- 1% of the clusters, called **pancreatic islets** (*islets of langerhans*) form the *endocrine* portion of the pancreas.(lightly stained zones)
- These cells secrete the hormones glucagon, insulin, somatostatin, and pancreatic polypeptide.



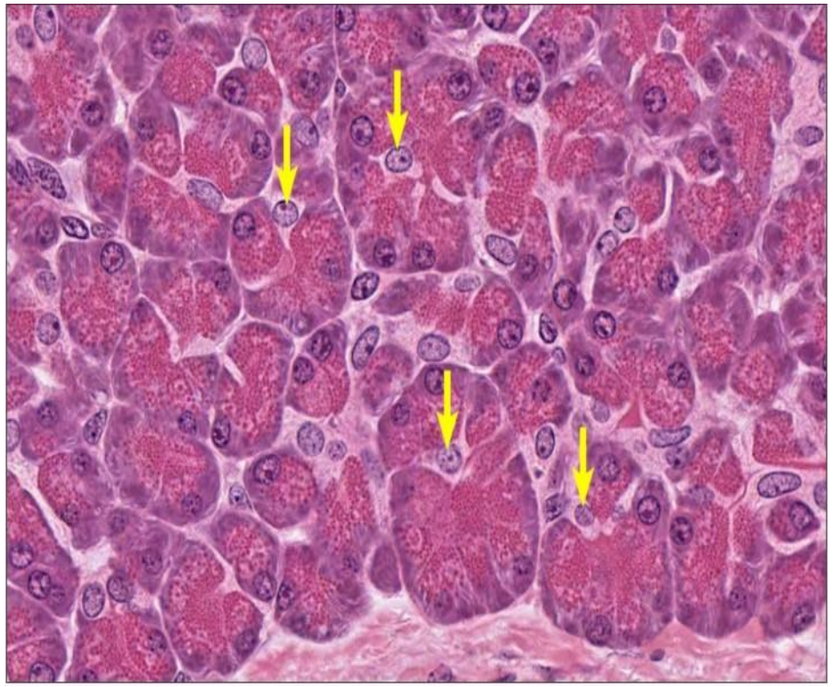
- Has a thin capsule of connective tissue, from which septa extend to separate the parenchyma into lobules

❑ *Histology of the Pancreas*

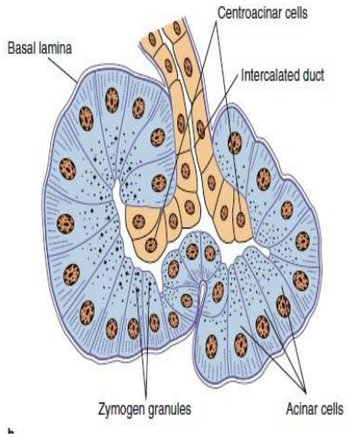
The pancreas, as we said, is a hybrid organ composed of two parts: an **exocrine part**, which means it has ducts that transfer its secretions, and an **endocrine part**, which uses the blood to transport its hormones. Therefore, you should expect a very rich blood supply, especially around the endocrine portion, where we find **sinusoidal capillaries**. These capillaries are leaky, allowing blood to pass freely between the cells and facilitating rapid hormone exchange.

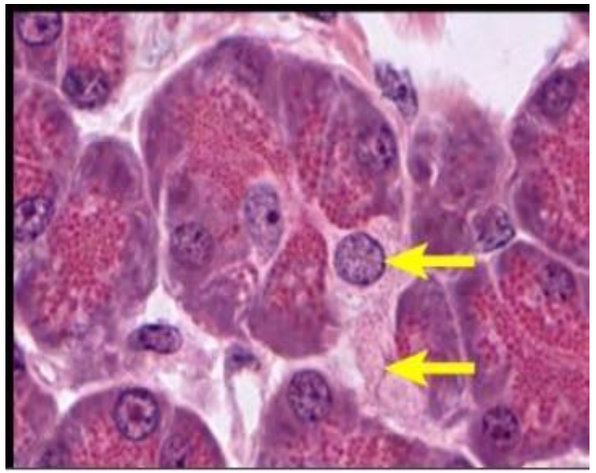
About 99% of the pancreas is exocrine tissue, while only about 1% is endocrine tissue. Despite this very small percentage, this tiny endocrine portion is responsible for controlling blood sugar levels, which shows how important the pancreas is even though it is a relatively small organ.

- The enzymes are produced by cells of serous acini
- Lacks striated ducts
- Pancreatic acinus consists of several **serous cells** surrounding a very small lumen, without myoepithelial cells
- The acinar cells: with round basal nuclei, and numerous zymogen granules apically.
- Each acinus is drained by a short intercalated duct of simple squamous or low cuboidal epithelium.

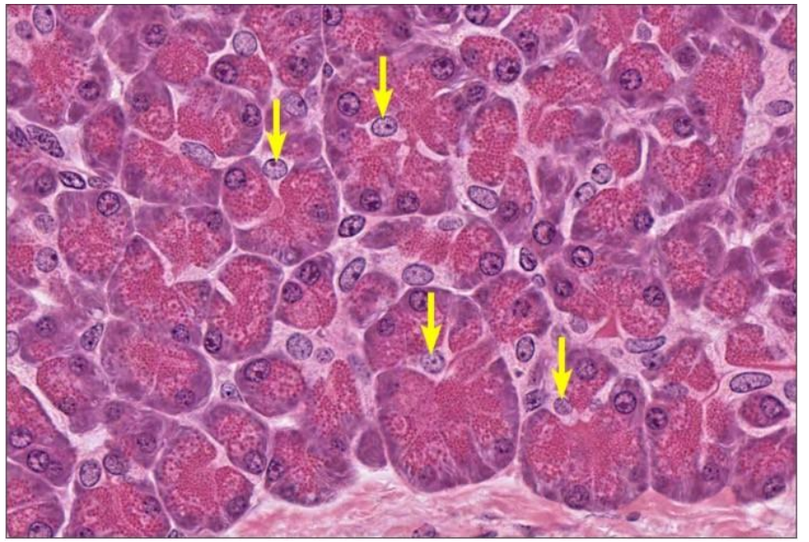


- Centroacinar cells: small pale-staining extend into the lumen of the acinus.
- Cells of the intercalated ducts secrete a large volume of fluid, rich in hco3; alkalinizes and transports hydrolytic enzymes.
- The intercalated ducts merge with intralobular ducts and interlobular ducts (increasingly columnar epithelia) before joining the main pancreatic duct.

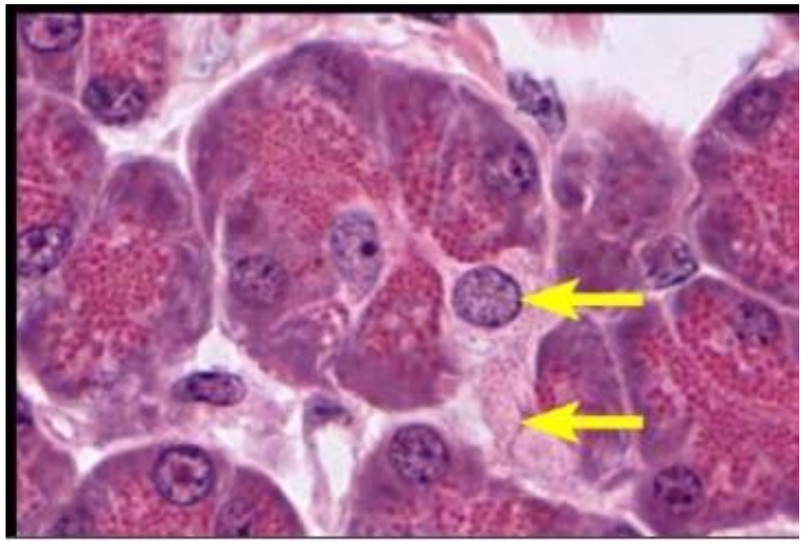




- These cells **(acinar cells)** are typical polarized epithelial cells, just like many other secretory epithelial cells. They have a basally located large nucleus and a relatively **basophilic** basal cytoplasm because the rough endoplasmic reticulum **(RER) is concentrated in the basal part of the cell**. This abundance of RER is responsible for the basophilic staining of the basal cytoplasm.

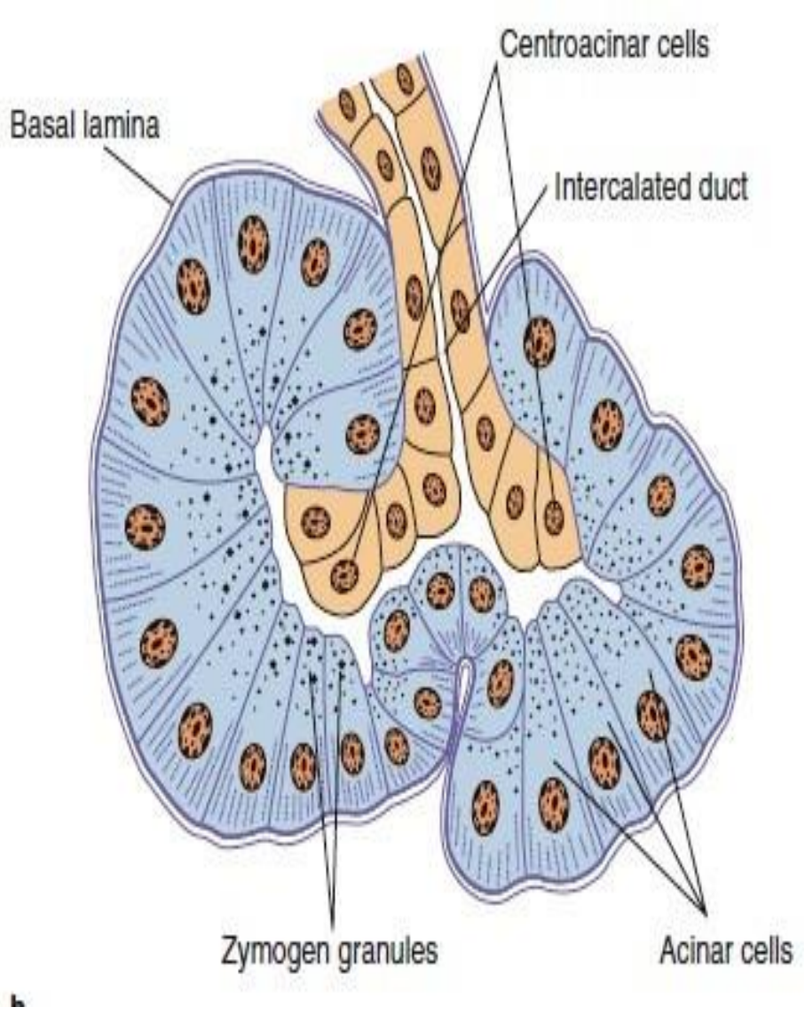


- In this picture, we can see **apical secretory granule**, because the substances synthesized by these cells are packaged into granules and stored in the apical part of the cell until they are released into the lumen.
- **We do not have striated ducts in the pancreas**, so they cannot be identified in this section. **Instead, we mainly see the smaller intercalated ducts.**



- These intercalated ducts open directly into the intralobular ducts, which then drain into the larger excretory ducts that run throughout the pancreas. This arrangement allows the secretions to flow relatively rapidly through the duct system toward the main pancreatic ducts.

- Unlike other glands, the intercalated ducts in the pancreas do not simply begin at the periphery of the acinus. Instead, **they extend into the center of the acinar lumen as centroacinar cells**. These cells are very important because they **secrete bicarbonate and increase the fluid content of the secretion**. This **helps flush the enzymatic contents** through the duct system and carry them through the remaining intercalated ducts, then into the larger intralobular and interlobular ducts.



- The two excretory units empty into the intercalated ducts, which are tiny ducts located within the lobules. The intercalated ducts are lined by low cuboidal epithelial cells and carry the secretion from the acini toward the larger ducts.

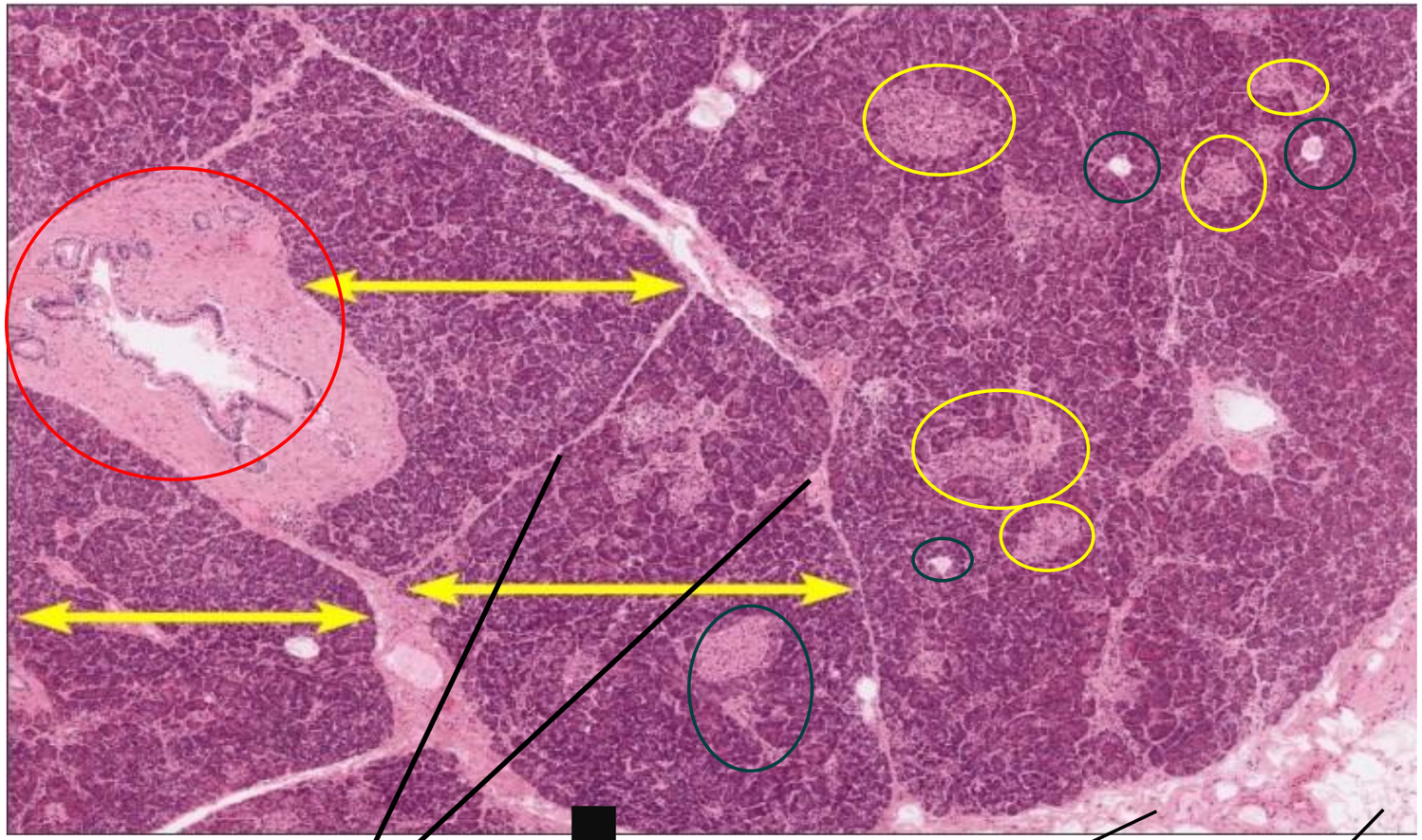
  The intercalated ducts then drain into larger ducts called striated ducts, and after that into the interlobular ducts, so the drainage pathway continues from smaller ducts to larger ducts.

- Here in the pancreas, the situation is completely different because **we do not have striated ducts.** Part of the reason for this difference is related to the way the main pancreatic duct is arranged and how it passes through almost the entire length of the organ.

  In the pancreas, some intercalated duct cells extend into the lumen ; these cells are called centroacinar cells. They appear in the middle of the pancreatic acini and are unique to the pancreas, so they are not seen in salivary glands.

  The centroacinar cells continue into the intercalated ducts, which merge to form intralobular ducts, and then interlobular ducts. These ducts eventually drain into the main excretory pancreatic duct, which finally opens into the second part of the duodenum.

This is a low-magnification H&E-stained image of the pancreas. At this magnification, it is difficult to clearly identify the nuclei and distinguish the individual cell details

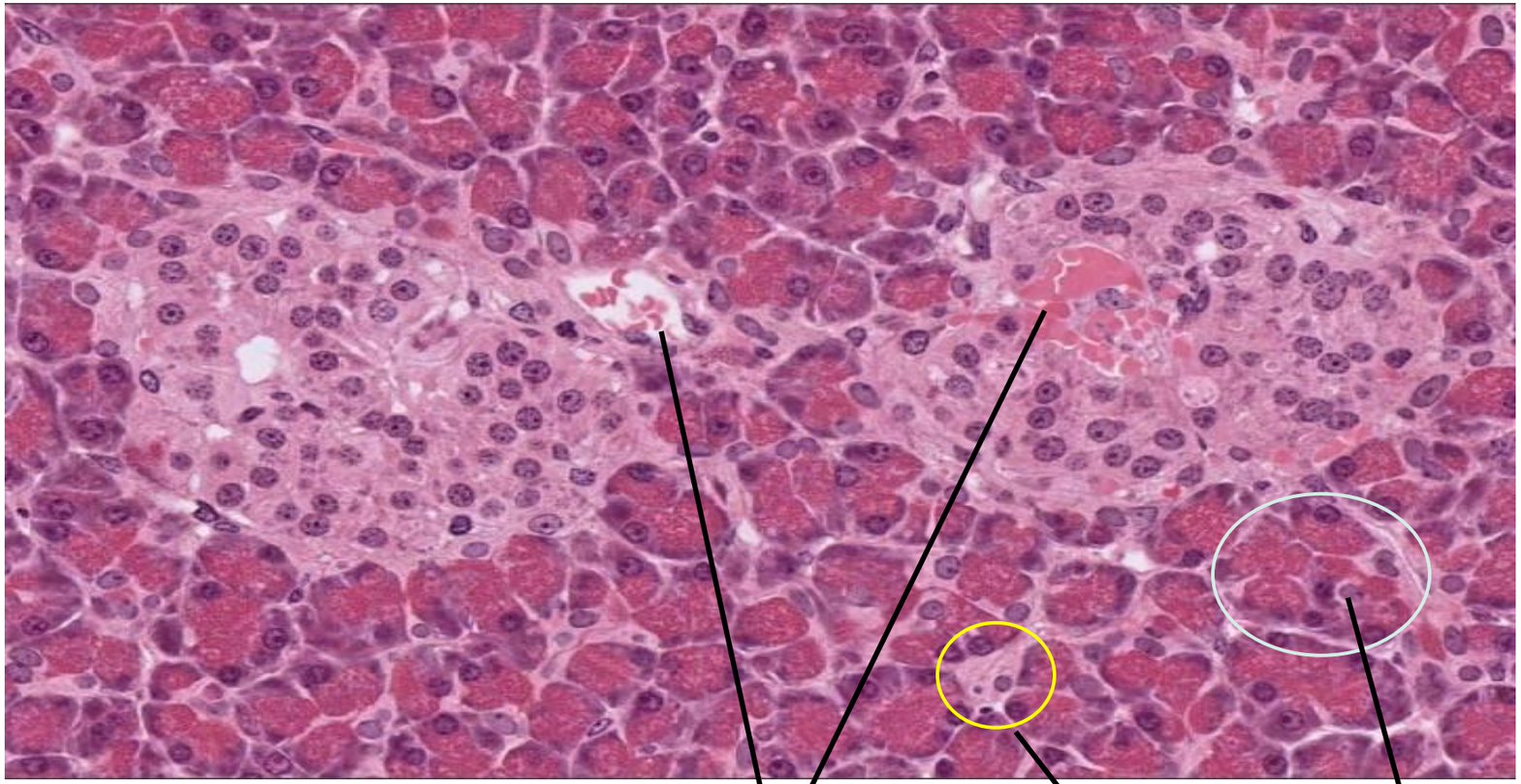


Interlobular duct

Islets of Langerhans

Intralobular duct

The outer surface is covered by a capsule, and the white areas represent fat tissue. The capsule sends septa into the pancreas to divide it into lobules. In this magnification, we can recognize dark-staining areas and lighter areas; the dark areas represent the exocrine portion, while the lighter areas represent the endocrine portion.

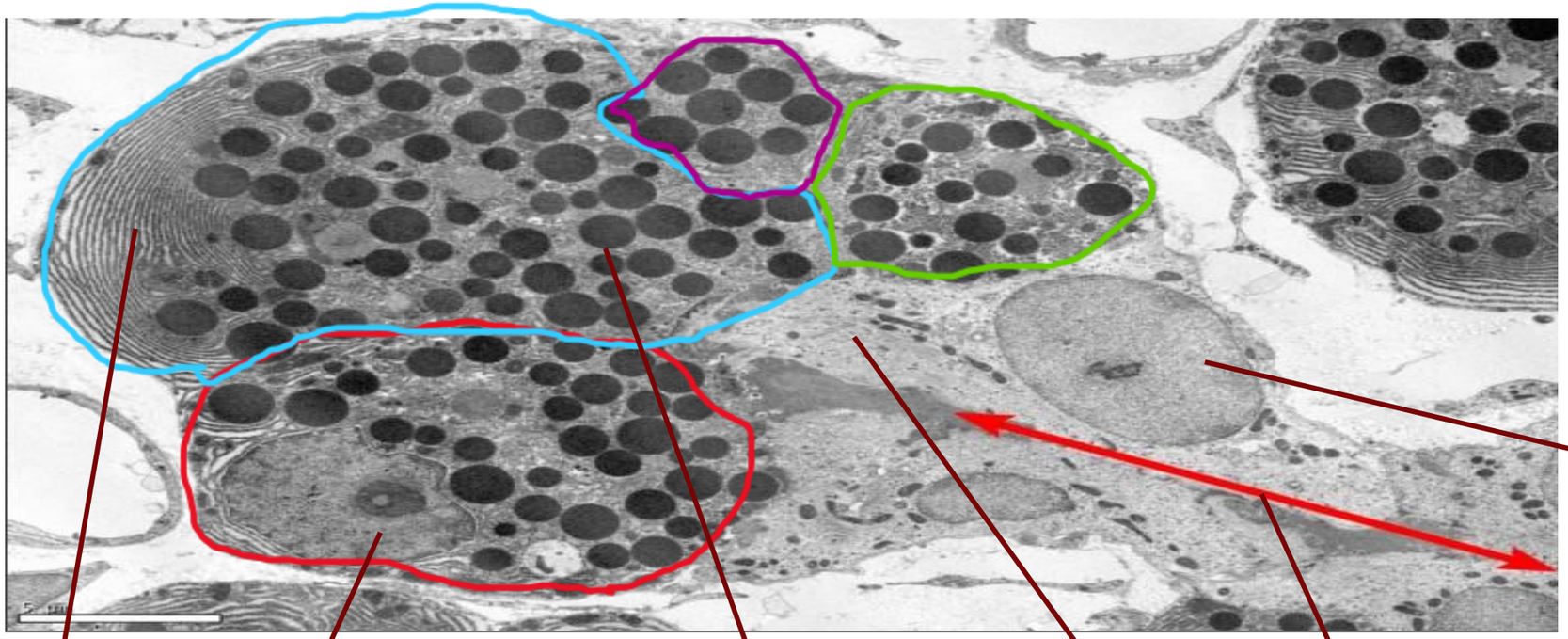


Thy darkly stained areas represent the exocrine portion of the pancreas , while the lighter-stained areas represent the endocrine portion , mainly the islets of Langerhans

These are sinusoids that carry the secretions produced by the endocrine cells into the bloodstream

Intercalated duct

Lightly stained cells within a darkly stained acinus represent centroacinar cells



RER

Nucleus

Granules that contain secretios

Lumen

Intercalated duct

Nucleus

Liver And Gallbladder

READ ONLY

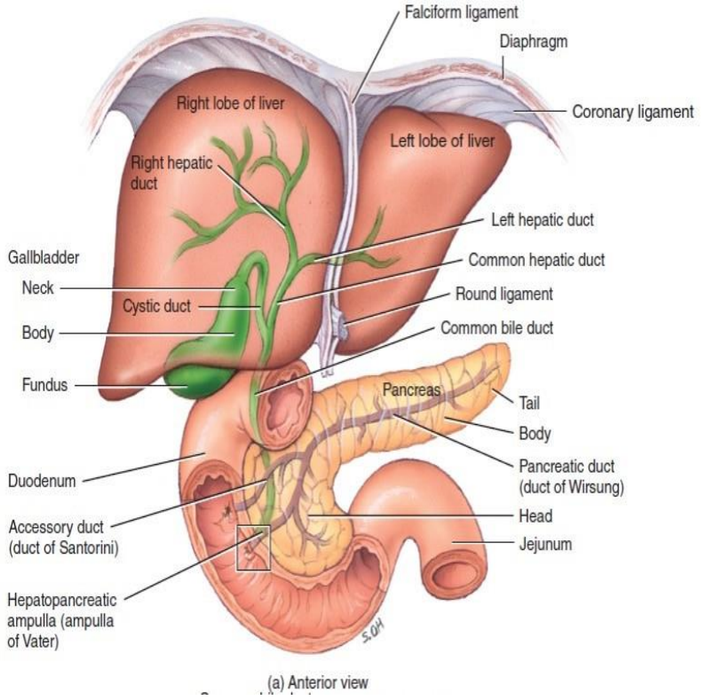
- Liver is the heaviest gland of the body; 1.4 kg in an average adult.

➢Second only to the skin in size.

➢Liver is inferior to the diaphragm and occupies most of the right hypochondriac and part of the epigastric regions of the abdominopelvic cavity.

- The **gallbladder** is a pear-shaped sac located in a depression of the posterior surface of the liver.

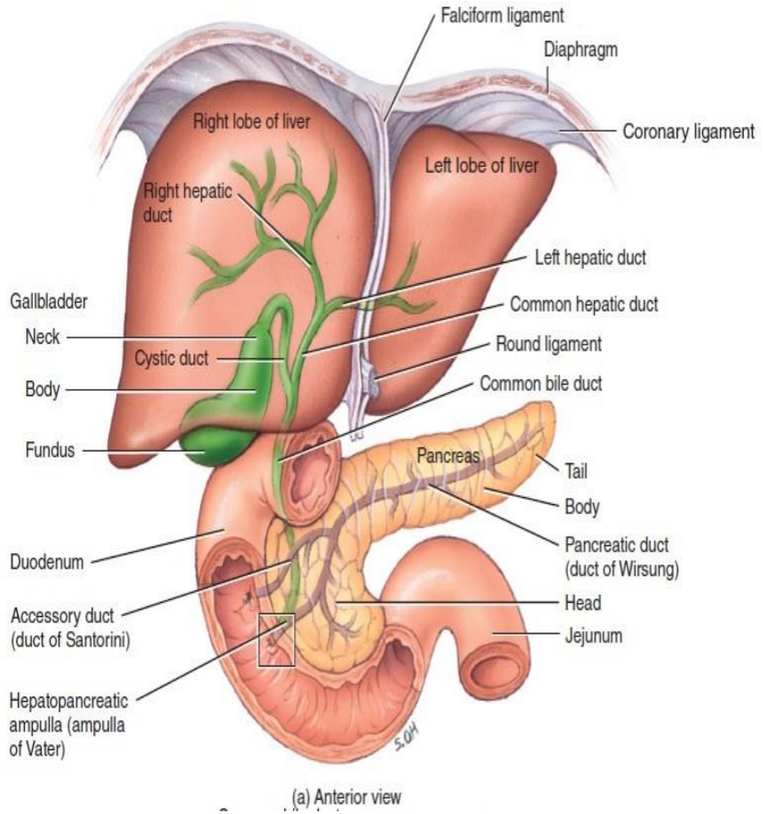
➢ It is 7–10 cm long and typically hangs from the anterior inferior margin of the liver.



Anatomy Of The Liver And Gallbladder

READ ONLY

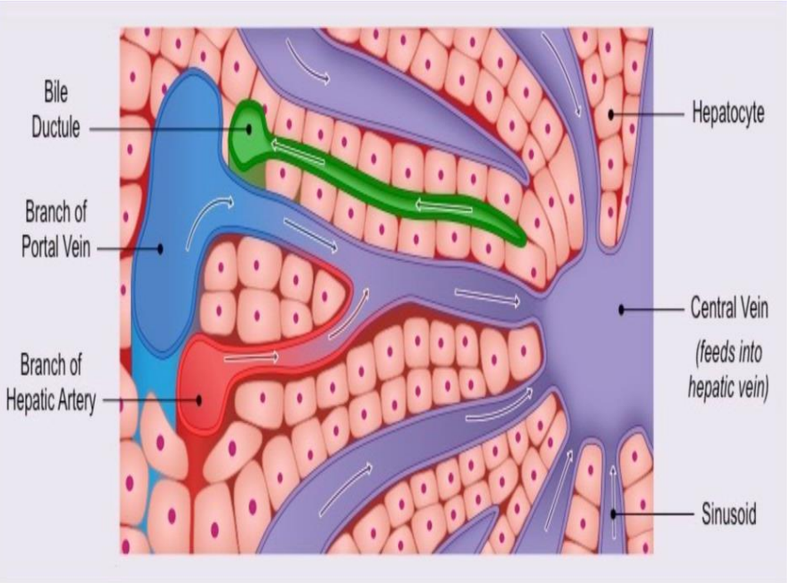
- The liver is almost completely covered by visceral peritoneum and is completely covered by a dense irregular connective tissue layer that lies deep to the peritoneum.
- The liver is divided into two principal lobes—a large **right lobe** and a smaller **left lobe**—by the falciform ligament, and smaller lobes: **quadrate lobe** and **caudate lobe.**
- The parts of the gallbladder include: the broad **fundus (**projects beyond the inferior border of the liver), the **body (**central portion) and the **neck (**tapered portion).



Histology Of The Liver

1. Hepatocytes: are the major functional cells of the liver and perform: metabolic, secretory, and endocrine functions.

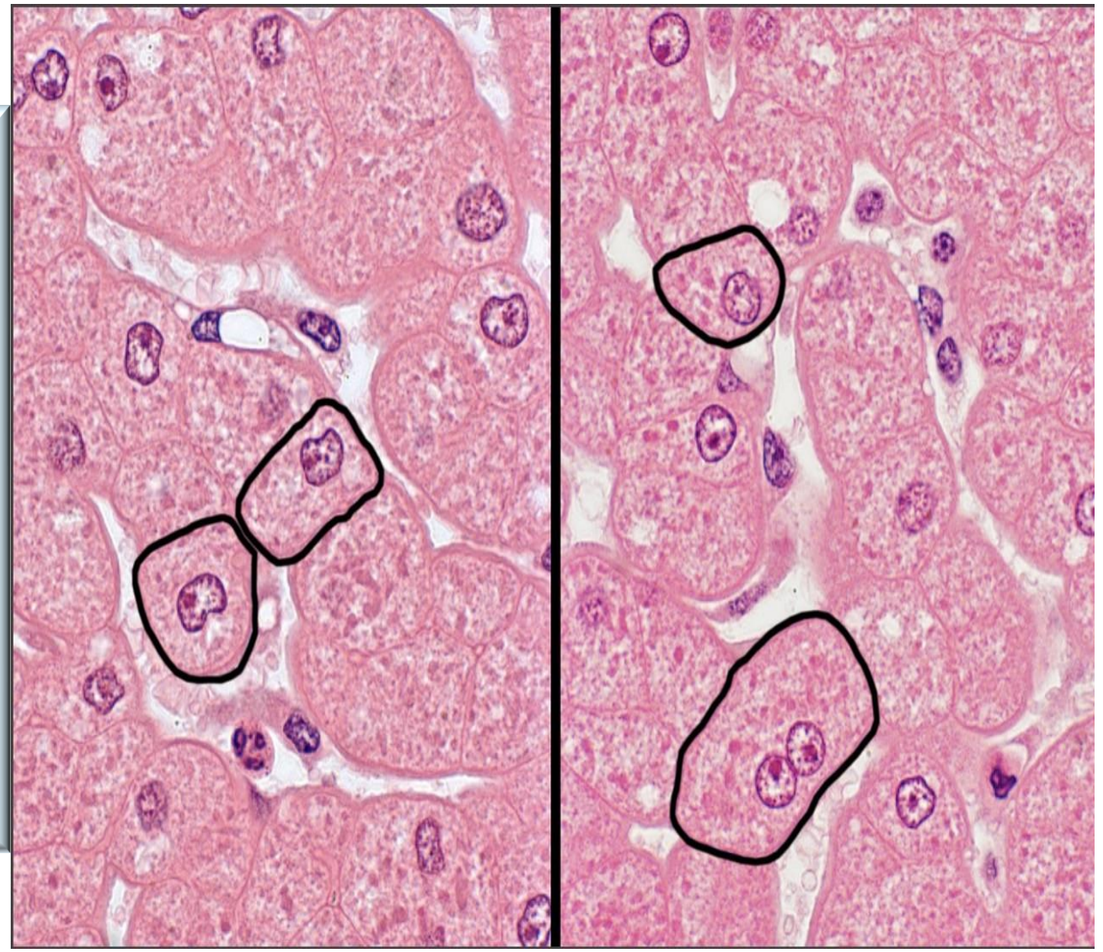
- Specialized epithelial cells with 5 to 12 sides that make up about 80% of the volume of the liver.
- Hepatocytes form complex three-dimensional arrangements called **hepatic laminae.**



- The hepatic laminae are plates of hepatocytes one cell thick bordered on either side by the endothelial-lined vascular spaces called hepatic sinusoids (are blood-filled spaces lined by discontinuous endothelium that allow the exchange of substances between the blood and hepatocytes)
- Grooves in the cell membranes between neighboring hepatocytes provide spaces for canaliculi (hepatocytes secrete bile in).

Hepatocytes

- Most functionally diverse cells of the body---- various functions and secretes several molecules.
- Large cuboidal or polyhedral epithelial cells, with large, round central nuclei.
- Eosinophilic cytoplasm rich in mitochondria.
- Cells are frequently **binucleated**.
- 50% of them are polyploid--- 2-8 times the normal chromosome number.



❑ Histology of the Liver

About 80% of the liver is composed of hepatocytes. These are very important cells because they have both endocrine and exocrine functions.

Endocrine function: some substances produced by hepatocytes are secreted directly into the blood.

Exocrine function: hepatocytes also produce bile, which is collected through tiny bile canaliculi and ducts that gradually become larger, forming the bile ducts.

The liver receives the venous drainage from the gastrointestinal tract (GIT) and the spleen through the portal circulation. This blood does not enter the systemic venous circulation directly; it must first pass through the liver so that hepatocytes can process, store, detoxify, or metabolize the absorbed substances before they reach the rest of the body.

In order for the liver to process the absorbed substances, the blood is brought to it through large veins. These veins must branch again into another set of capillaries inside the liver. This arrangement is called the portal circulation.

Normally, the classical circulation pathway is :
artery → capillary bed → vein

However, in the portal circulation, the pathway is different:
artery → capillary bed → vein → second capillary bed → vein

Blood first passes through the capillaries of the GIT, where absorption occurs. The venous blood carrying the absorbed substances is then collected into veins of the portal system.

Instead of going directly into the systemic circulation, these veins branch again into a second capillary network inside the liver called the hepatic sinusoids

So, in portal circulation there are two capillary beds connected by veins:
1- Capillaries of the GIT
2-Hepatic sinusoids in the liver

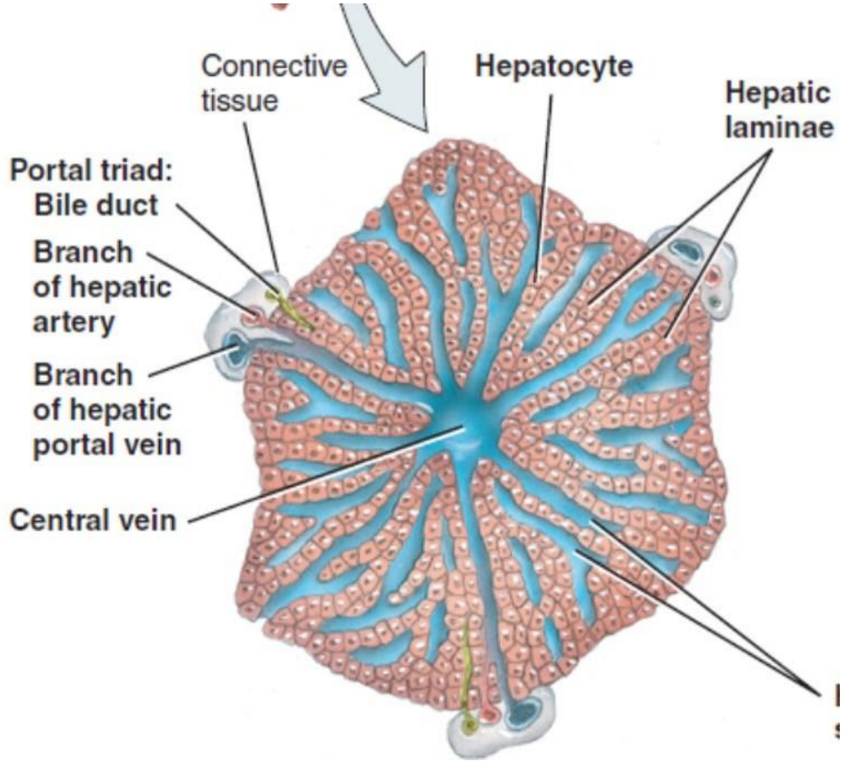
This arrangement allows hepatocytes to process absorbed substances before the blood enters the systemic circulation.

After passing through the hepatic sinusoids, the blood is collected into the hepatic veins, which leave the liver and drain into the systemic circulation.

Portal circulation is therefore characterized by the presence of two capillary beds connected by veins. The liver is one of the main sites in the body where this type of circulation is present, and another example will be seen later in the endocrine system.

Hepatic lobules

- Hepatocytes form hundreds of irregular plates (reticulin support) arranged radially around a small central vein--- lobules (*thousands)*
- Peripherally each lobule has 3-6 portal areas -------- contains three interlobular structures (portal triad):
- A **venule** branch of the portal vein, with blood rich in nutrients but low in O_2,
- An **arteriole** branch of the hepatic artery that supplies O_2,
- One or two small bile **ductules**.
- Lymphatics and nerves.



- Because the liver performs many important functions, it is divided into functional units called hepatic lobules.

- The hepatic lobule is the structural and functional unit of the liver. It consists of a polygonal arrangement of hepatocytes with a central vein located in the center.

- At the corners of the hepatic lobule, there are usually 3–6 portal triads. Each portal triad contains three structures:

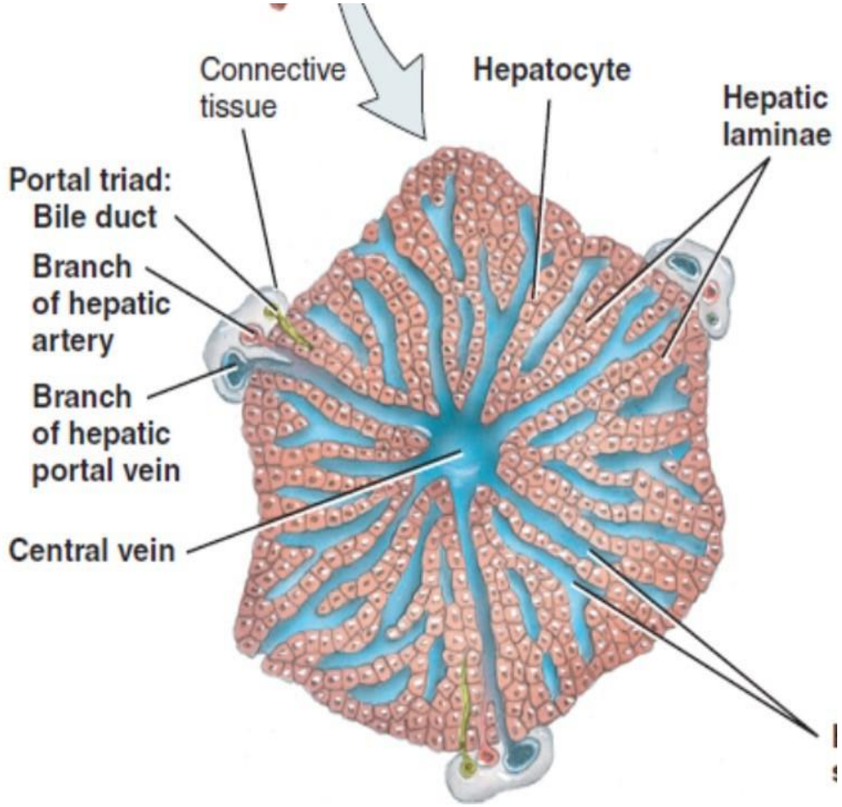
1. A branch of the hepatic artery → supplies oxygenated blood
2. A branch of the portal vein → brings nutrient-rich blood from the GIT for processing by hepatocytes
3. A bile ductule → carries bile produced by hepatocytes

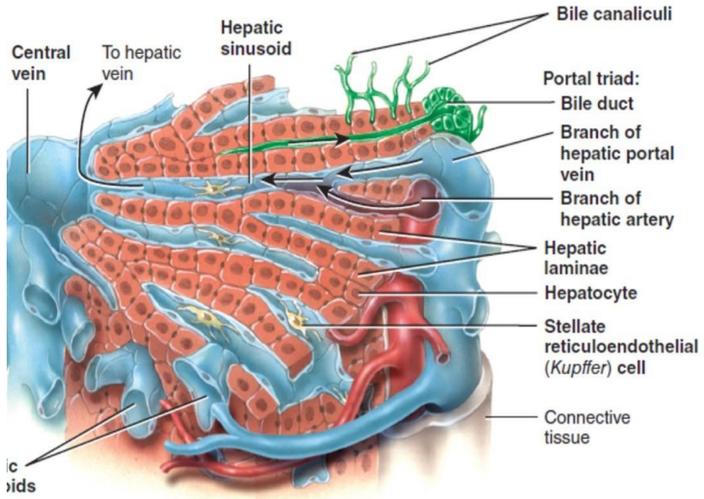
- **So:**
  .One vessel brings substances for the liver to process
  .One vessel supplies oxygen
  .The bile ductule carries bile produced by hepatocytes

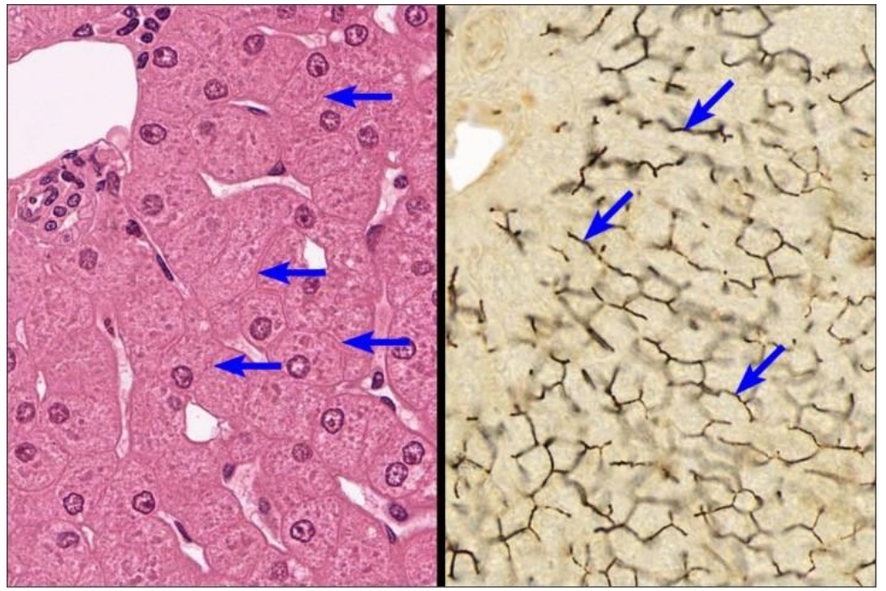
- Within the hepatic lobule, blood flows toward the central vein, while bile flows in the opposite direction toward the bile ductules.

- The hepatic lobule is bordered at its periphery by **portal triads**. Each portal triad contains a **branch of hepatic portal vein**, a **branch of hepatic artery**, and a **bile ductule** . Blood coming from the GIT and spleen reaches the liver through the portal vein. It cannot enter the systemic circulation directly because it must first pass through the liver, so hepatocytes can process, store, detoxify, and metabolize the absorbed substances.

- Inside the hepatic lobule, **blood from the portal vein mixes with oxygenated blood from the hepatic artery in the sinusoids**. This mixed blood flows from the periphery of the lobule toward the central vein. Because **hepatocytes near the periphery** receive the blood first, **they get the highest oxygen supply**. As blood **moves toward the center, oxygen gradually decreases**. Therefore, hepatocytes near the central vein receive the least oxygen. At the same time, hepatocytes produce bile on the opposite side of the cell. **Bile flows in the opposite direction to blood**: from the hepatocytes through the bile canaliculi toward the bile ductules in the portal triads.







- The common hepatic duct joins the **cystic duct** from the gallbladder to form the **common bile duct---**bile enters the duodenum of the small intestine.

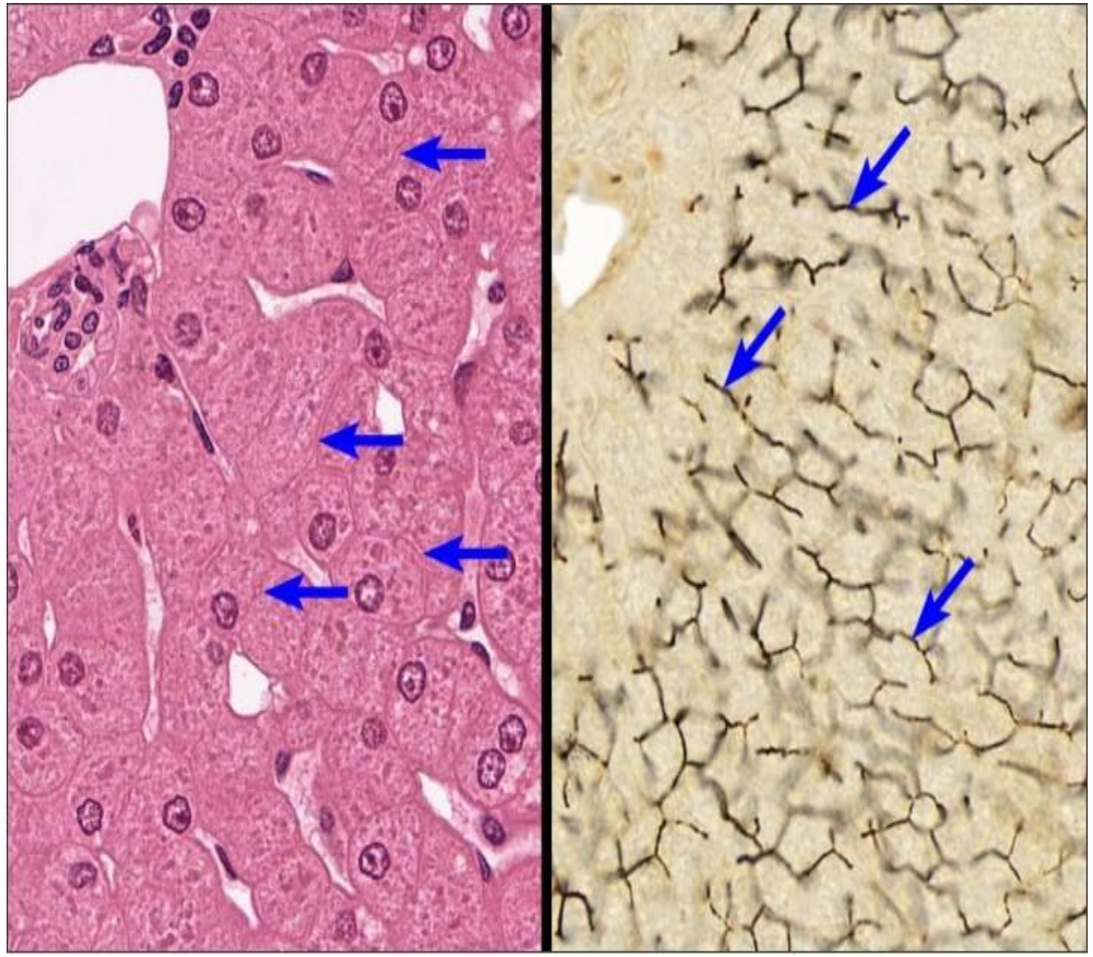
Bile canaliculi: small ducts between hepatocytes that collect bile produced by the hepatocytes.

- From bile canaliculi, bile passes into **bile ductules** and then **bile ducts**.
- The bile ducts merge and eventually form the larger **right** and **left hepatic ducts---**unite---**common hepatic duct**

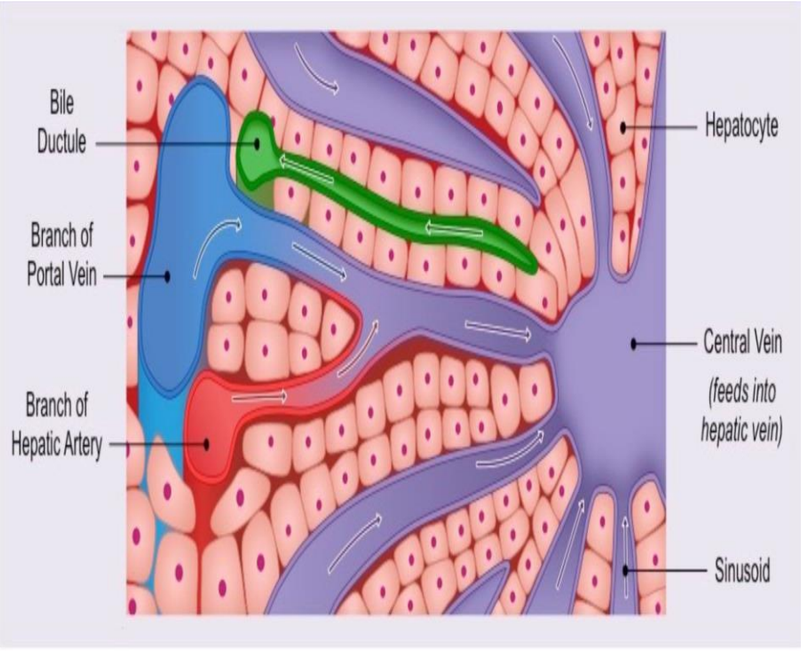
- This image is H&E stained. Here we can see the hepatic laminae (plates of hepatocytes) with the sinusoids located between them.
  The elongated nuclei seen between the hepatocytes belong to the endothelial cells lining the sinusoids.

- At the sites indicated by the arrows, we can see small streak-like spaces representing the bile canaliculi. These tiny channels are formed between adjacent hepatocytes and are responsible for collecting the bile produced by the hepatocytes.

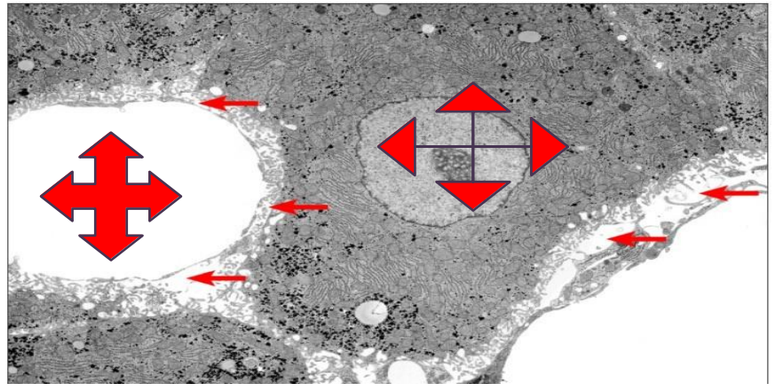
- In the second image, ink was injected into the bile canaliculi, making the bile drainage pathway visible. This demonstrates the complex branching network of the biliary drainage system within the liver.



- **Hepatic sinusoids:** highly permeable blood capillaries(discontinuous+ fenestrated endothelium) between rows of hepatocytes that receive oxygenated blood from branches of the hepatic artery and nutrient-rich deoxygenated blood from branches of the hepatic portal vein.
- Hepatic sinusoids converge and deliver blood into a **central vein--- to hepatic veins----to** inferior vena cava
- **Portal triad:** a bile duct, branch of the hepatic artery, and branch of the hepatic vein.

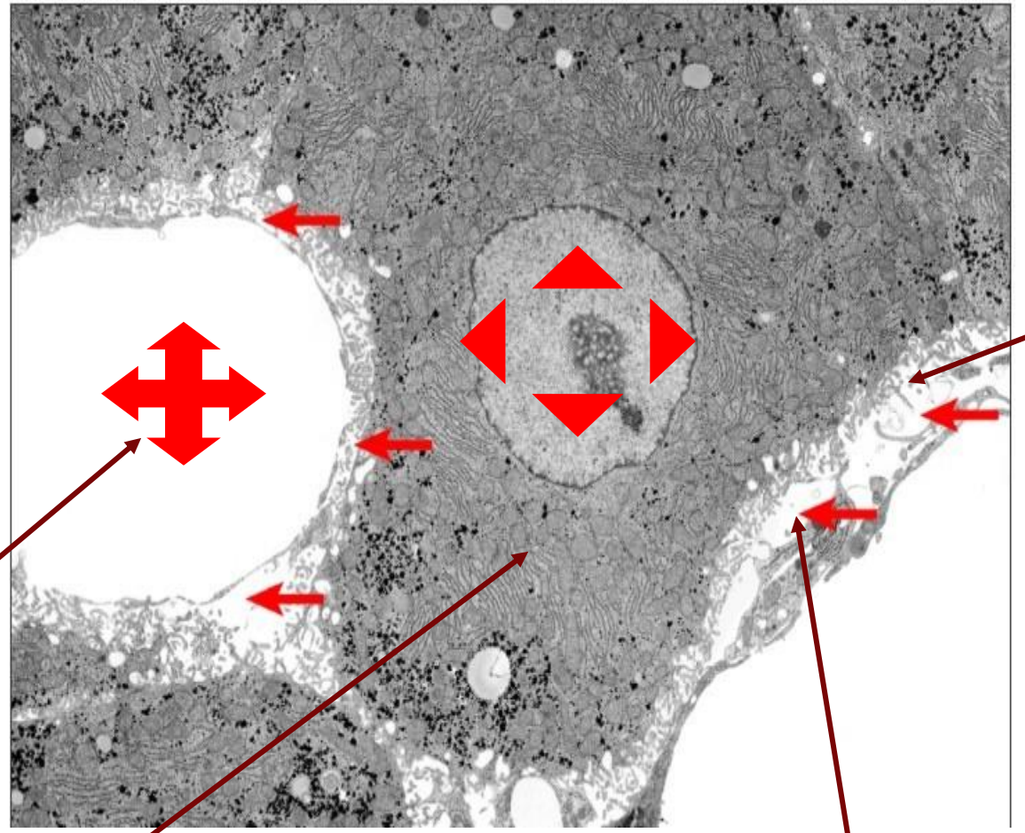


The discontinuities and fenestrations allow plasma to fill a narrow perisinusoidal space (or space of Disse) and directly bathe the many irregular microvilli projecting from the hepatocytes into this space



- **Stellate reticuloendothelial cells (Kupffer) (they line the hepatic sinusoids) :** (*hepatic macrophages)* fixed phagocytes, destroy worn-out WBCs/RBCs, bacteria, and foreign matter in the venous blood draining from the gastrointestinal tract.

This is a transmission electron microscope (TEM) image showing the central vein surrounded by hepatocytes



These extensions are irregular microvilli to create extra surface area so they can process the blood more efficiently.

Central vein

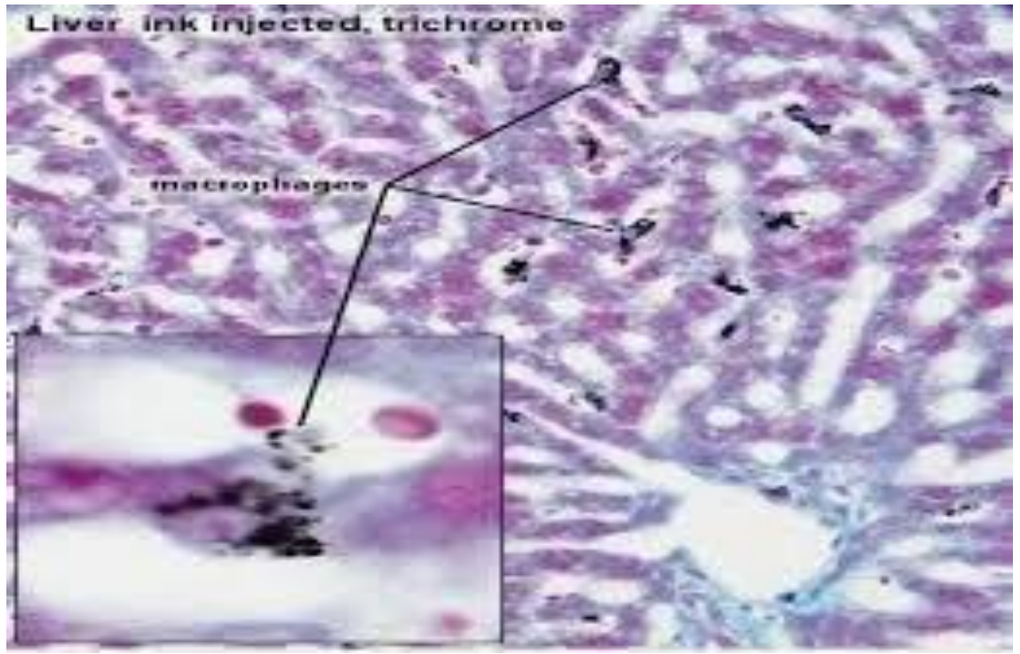
Hepatocytes

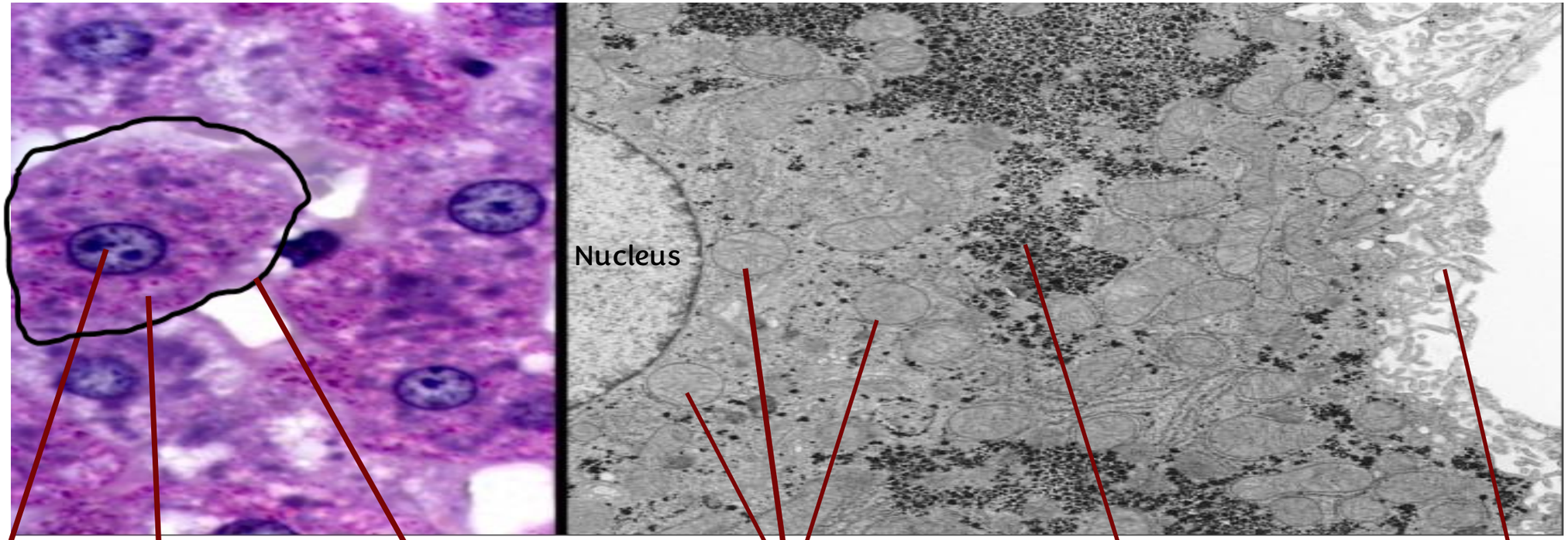
Space of Disse

The presence of this duct system reflects the exocrine function of the liver, because hepatocytes produce bile and secrete it into the bile canaliculi and bile ducts. On the other hand, the presence of sinusoids closely related to the hepatocytes reflects their endocrine function, since many substances produced or processed by hepatocytes are released directly into the blood through these sinusoids.

Kupffer cells are macrophages located inside the liver sinusoids. They perform phagocytosis and contain lysosomal enzymes like other macrophages. However, the injected ink is not easily degraded, so it remains visible within the bile canaliculi and biliary drainage pathways, allowing the complex bile drainage system to be demonstrated clearly.

This image was taken from the first year lab





Nucleus

The hepatocytes appear this way because they store glycogen, which is demonstrated by PAS stain (Periodic acid–Schiff stain).

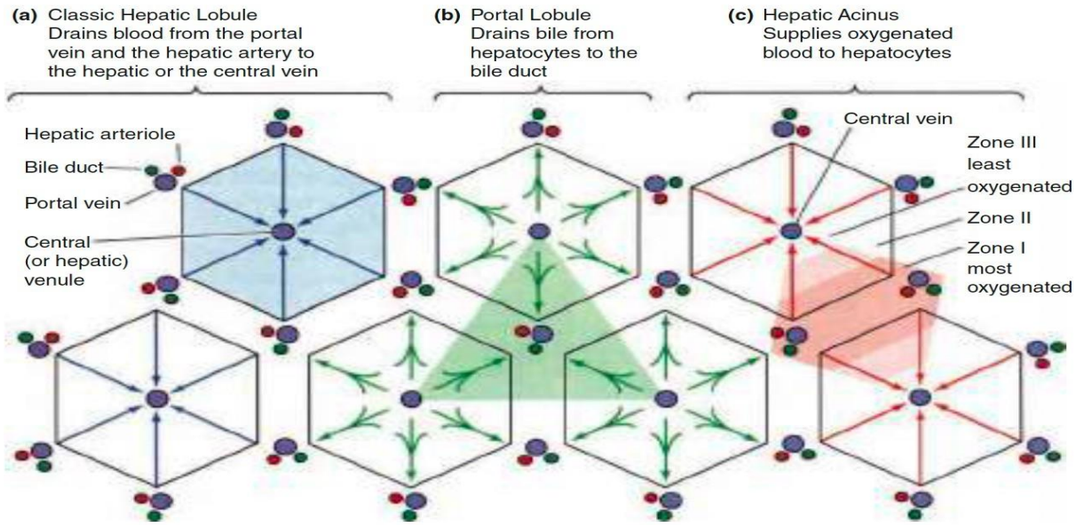
Hepatocyte

Mitochondria

Glycogen

These irregular projections on the surface are microvilli, which increase the surface area of the hepatocyte

- (A) C**lassic lobule** concept offers a basic understanding of the structure-function relationship in liver organization and emphasizes the endocrine function of hepatocytes as blood flows past them toward the central vein.



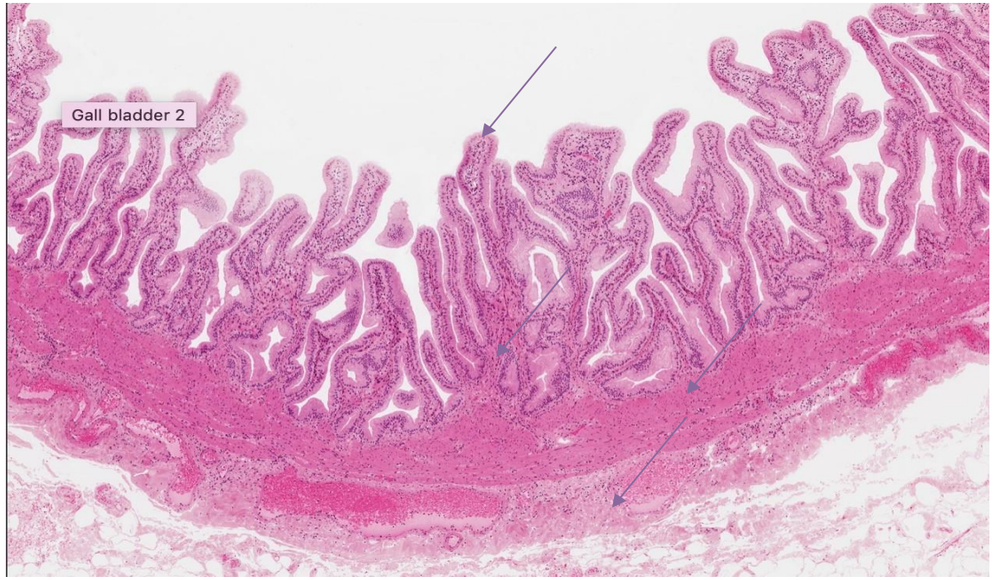
- (B) P**ortal lobule** emphasizes the hepatocytes' exocrine Function and the flow of bile from regions of three classic lobules Toward the bile duct in the portal triad at the center here. The area Drained by each bile duct is roughly triangular.

- (C) H**epatic acinus** concept emphasizes the different oxygen and nutrient contents of blood at different distances along the sinusoids, with blood from each portal area supplying cells in two or more classic lobules. Major activity of each hepatocyte is determined by its location along the oxygen/nutrient gradient:

Periportal cells of zone I get the most oxygen and nutrients and show metabolic activity generally different from the pericentral hepatocytes of zone III, exposed to the lowest oxygen and nutrient concentrations.

Histology Of The Gallbladder

- Mucosa consists of simple columnar epithelium arranged in rugae.
- The wall lacks a submucosa.
- The middle, muscular coat consists of smooth muscle fibers.
- Contraction of the smooth muscle fibers ejects the contents of the gallbladder into the **cystic duct**.



- The gallbladder's outer coat is the visceral peritoneum.
- **The functions of the gallbladder** are to store and concentrate the bile produced by the liver (up to tenfold) until it is needed in the duodenum.
- In the concentration process, water and ions are absorbed by the gallbladder mucosa.
- The lining epithelial cells of the gallbladder have prominent mitochondria, microvilli, and large intercellular spaces

❑ Histology of the Gallbladder

The gallbladder functions to concentrate the bile up to 10-folds, so instead of having about 1 liter of dilute bile, the bile becomes much more concentrated after water and electrolytes are absorbed by the gallbladder.

The gallbladder is lined by simple columnar epithelium, and underneath it we have the lamina propria. In the wall of the gallbladder, there is no submucosa, instead, we only have a thin lamina propria followed directly by the muscular layer.

The muscular layer is relatively thin because the gallbladder is a small sac, so it does not need a thick muscle wall. These smooth muscles contract to empty the gallbladder and release the concentrated bile. The mucosa is thrown into folds (rugae) to increase the surface area for absorption .

رسالة من الفريق العلمي:

إذا كلّف المُعين أعــان

فلا يُلقي الله في طريقك أمراً إلا و قد أعدّ لك عونه ،

قد تشعر بثقل الطَّريق ، لكنك تمضي ...لا بقوّتك ، بل بلطفٍ خفيّ يسوقك .

فاطمئن ، ما دام الله هو الذي كلّفك ، فهو الذي سيُعينك.

For any feedback, scan the code or click on it.

Corrections from previous versions:

Versions	Slide # and Place of Error	Before Correction	After Correction
V0 → V1			
V1 → V2			