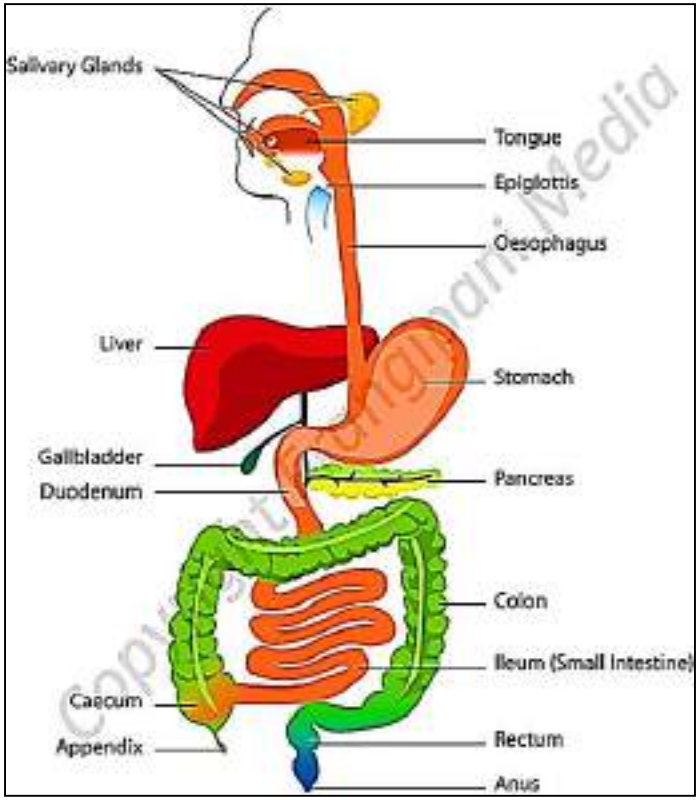
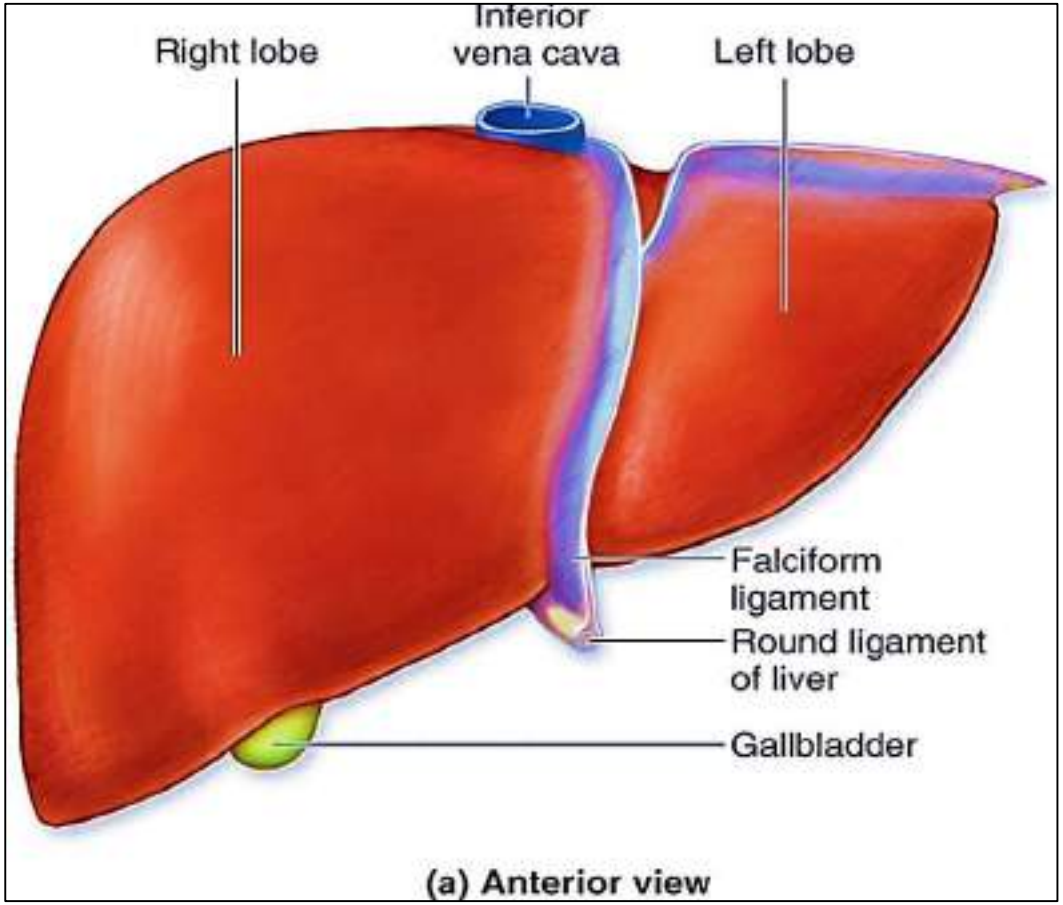
The digestive system IV

Organs associated with digestive tract

- Liver
- Pancreas
- Gall bladder



Liver


Right lobe
Inferior vena cava
Left lobe
Falciform ligament
Round ligament of liver
Gallbladder
(a) Anterior view

Liver

The Liver is the largest gland in the body (1.5 Kg)

Mixed endocrine & exocrine gland

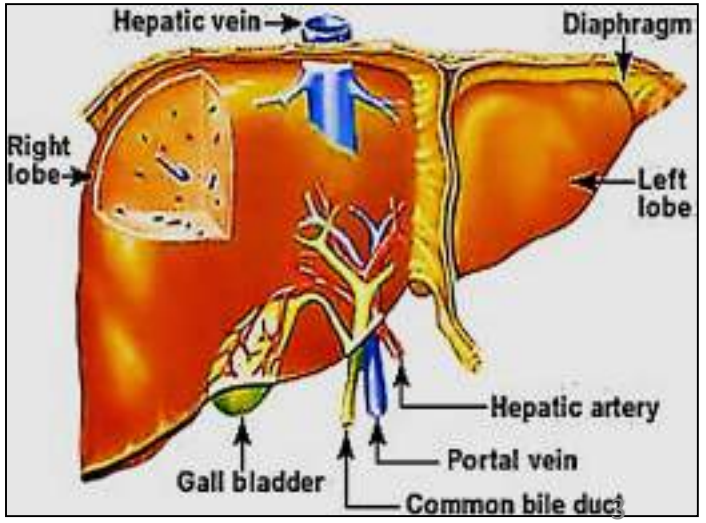
1. Processing & metabolism of nutrients

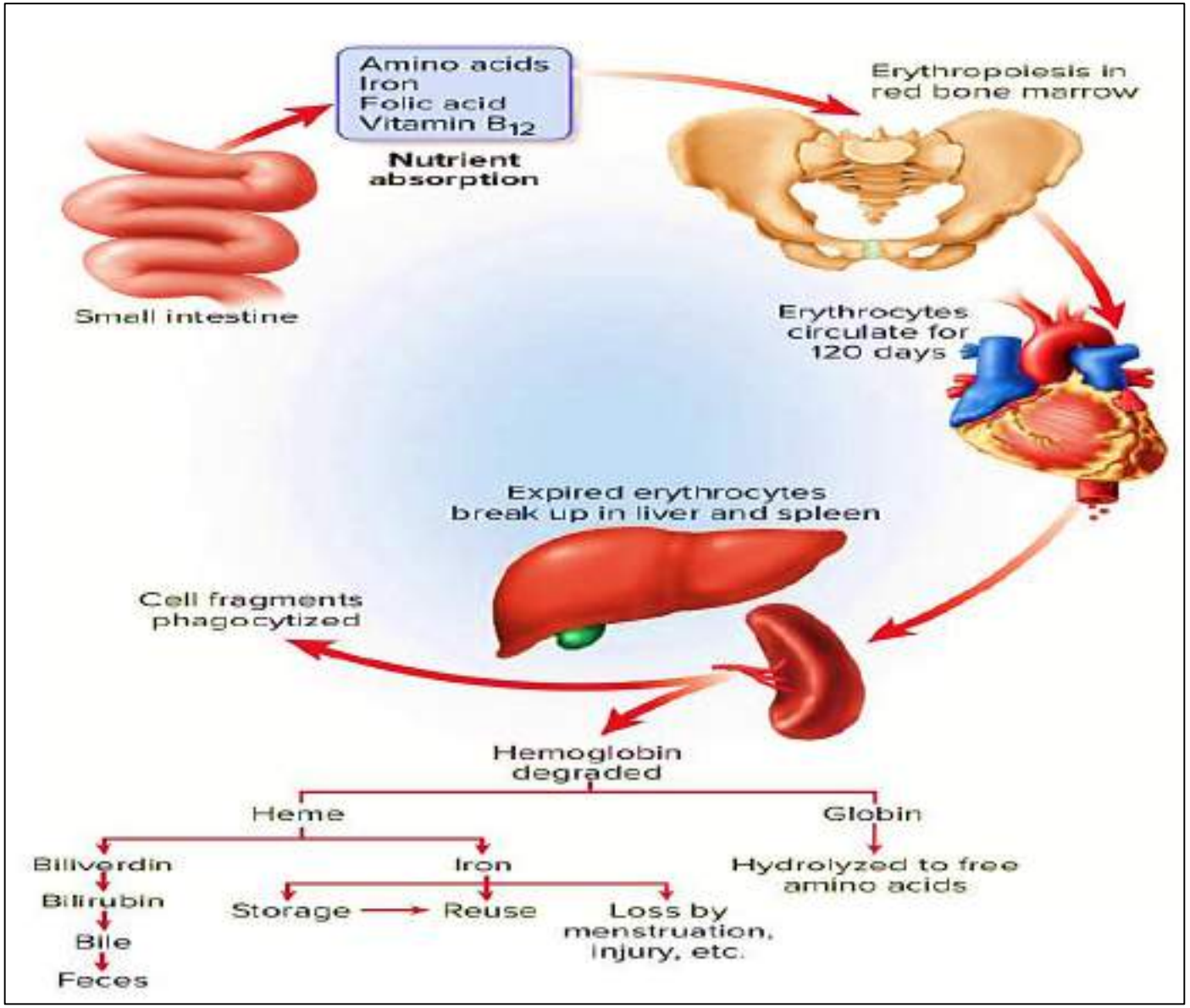
2. Detoxification: modifying potentially dangerous chemicals & removal of old RBCs

3. Endocrine : synthesize and secrete plasma proteins (albumin, prothrombin, fibrinogen), glucose &lipids into blood via blood sinusoids

4. Exocrine: synthesize and secretion of **bile**

5- Storage of: glucose, fat , vit. A, B, D, K




Amino acids
Iron
Folic acid
Vitamin B_{12}
Nutrient absorption
Small intestine
Erythropoiesis in red bone marrow
Erythrocytes circulate for 120 days
Expired erythrocytes break up in liver and spleen
Cell fragments phagocytized
Hemoglobin degraded
Heme
Globin
Biliverdin
Bilirubin
Bile
Feces
Iron
Storage
Reuse
Loss by menstruation, injury, etc.
Hydrolyzed to free amino acids

Blood supply of liver

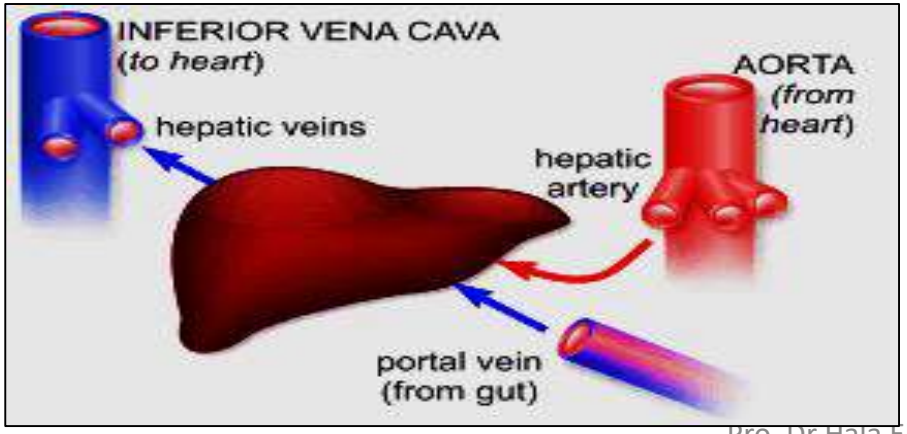
1- Portal vein: 70 - 80%

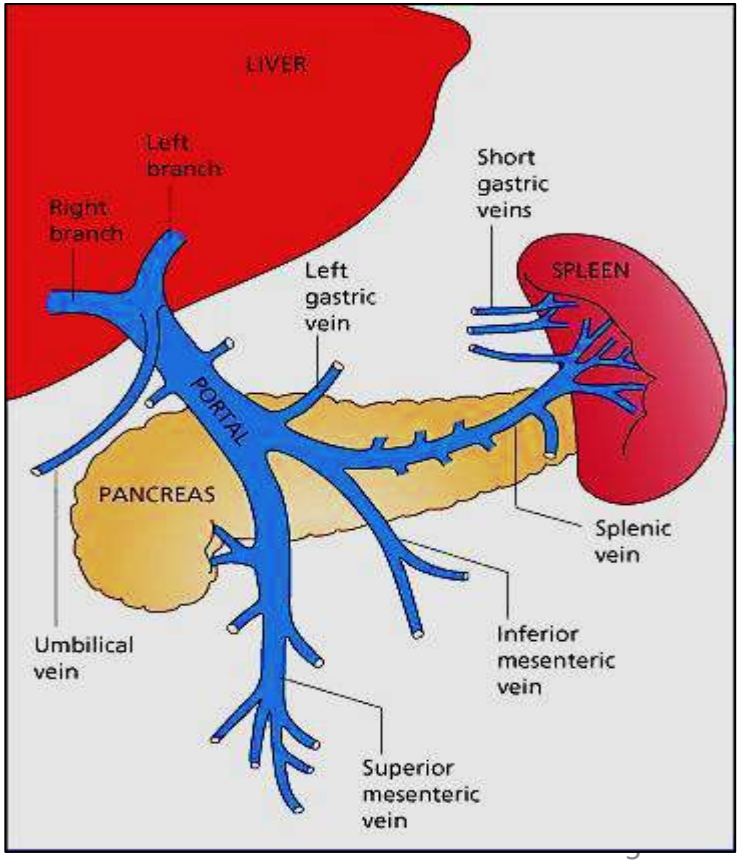
- Main drainage of blood from GIT, spleen, pancreas
- Brings **nutrient rich**, **toxin loaded**, **oxygen poor** blood

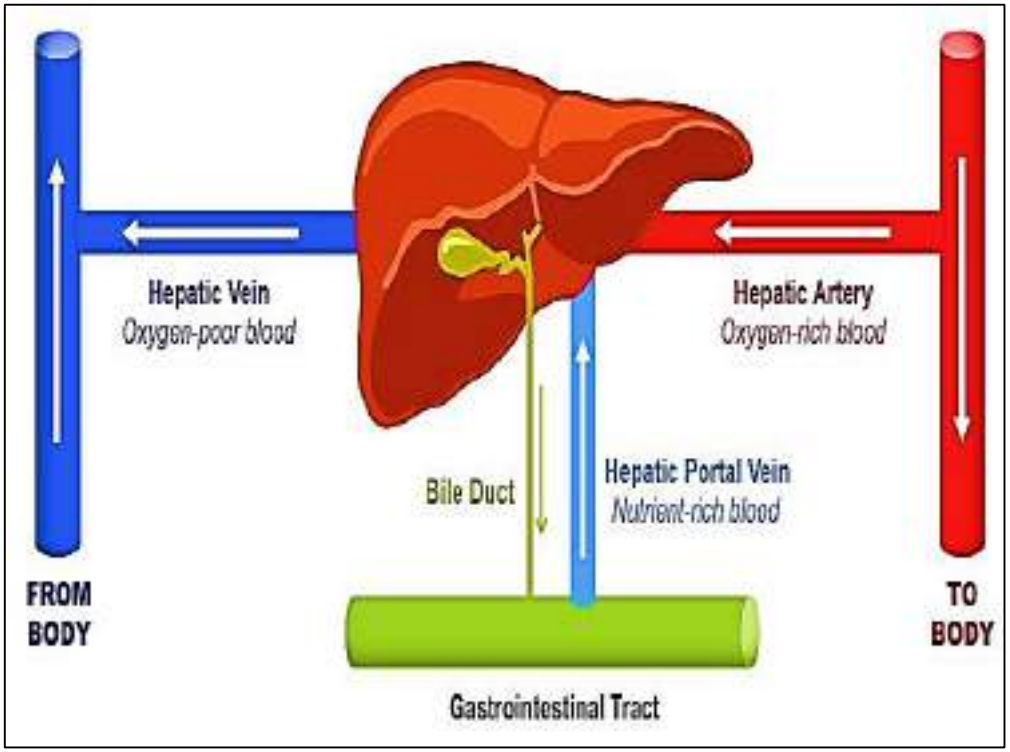
2- Hepatic artery: 30 – 20%

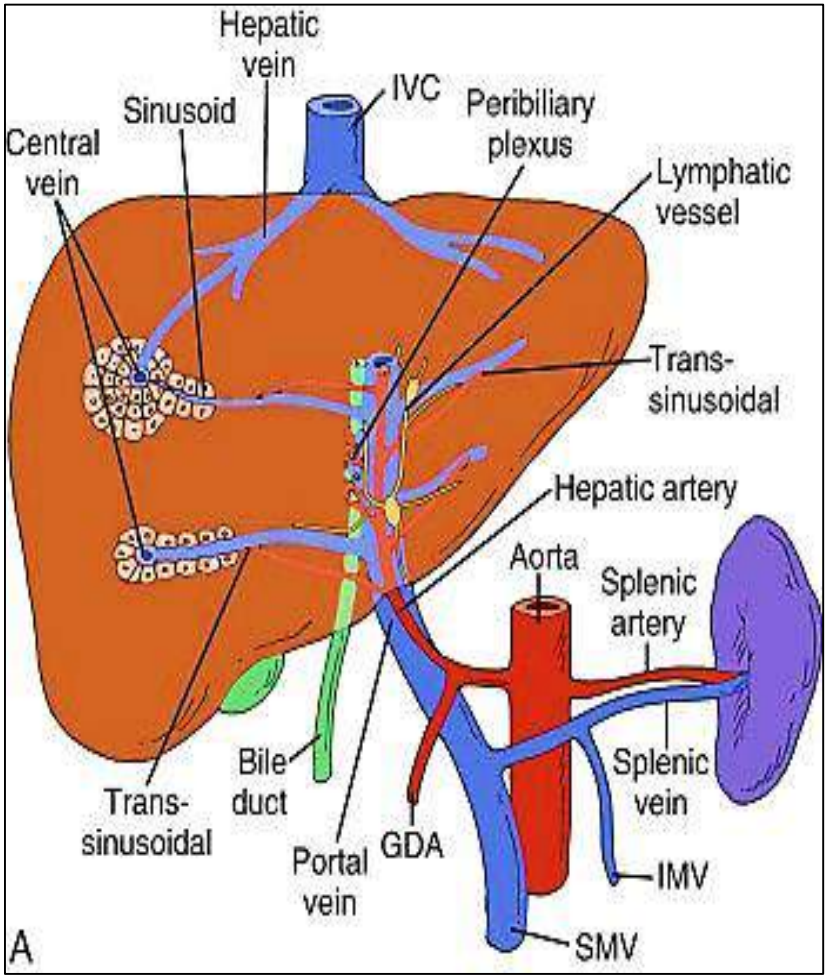
Aorta→ hepatic artery

- Brings **oxygen rich** blood to liver





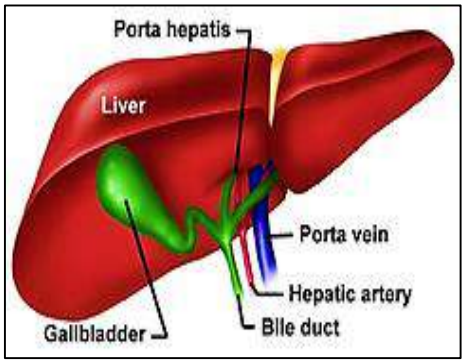




Blood supply of the liver

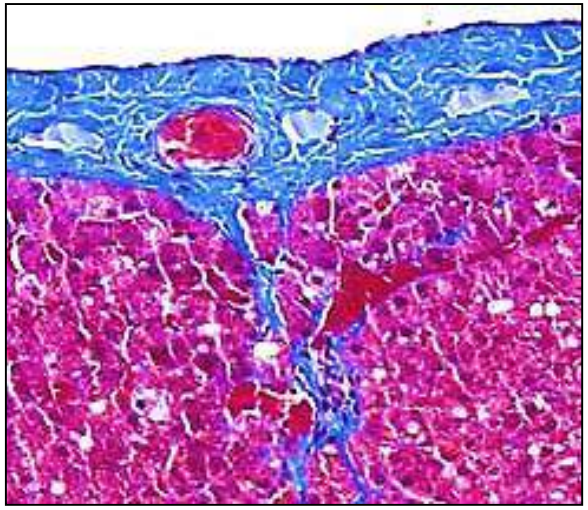
Structure of liver

Stroma & parenchyma

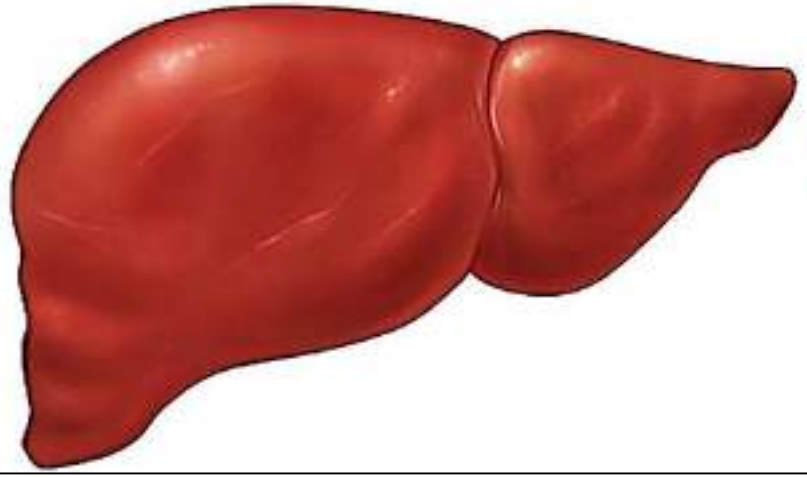


A) Stroma: capsule → septa → reticular fibers

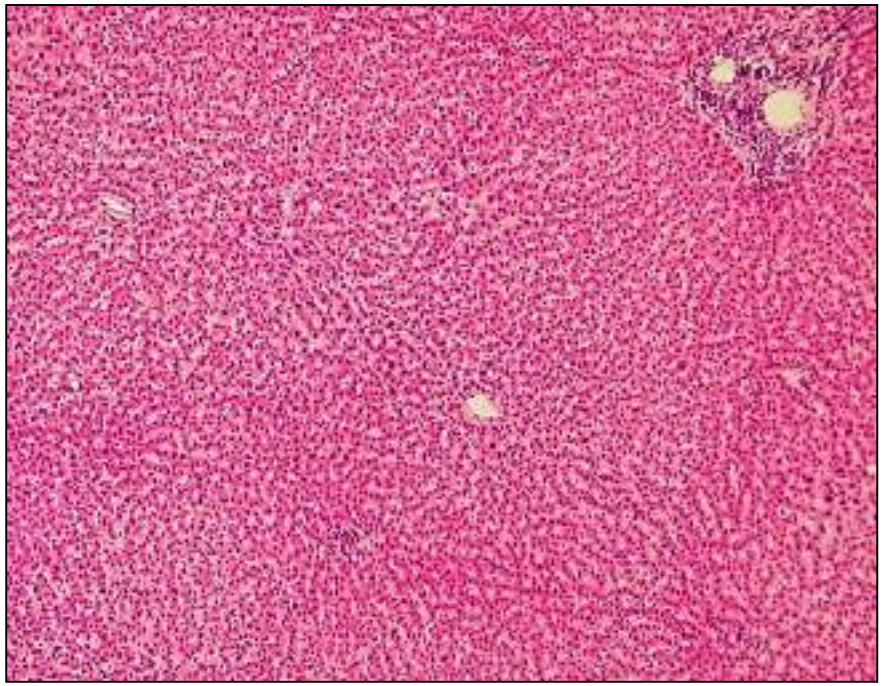
- **Capsule of Glisson:** thin fibrous C.T. sheet, covers the liver. Thick at hilum to form **prota hepatis** which gives rise to C.T. septa divide the liver into lobes and lobules
- **septa**: surround lobules. **Thick and easy to identify in pig's liver.. Lobulation are not clear in humans unless??**
- **Portal tracts**: triangular masses of C.T. at angles between hepatic lobules
- **Reticular fibers**: delicate network surround and support liver cells

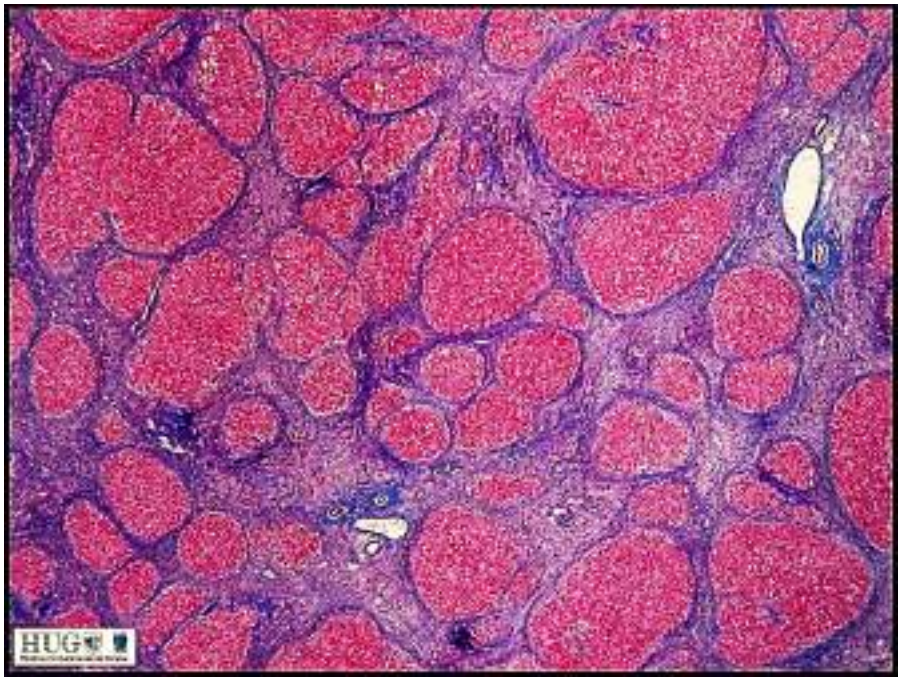


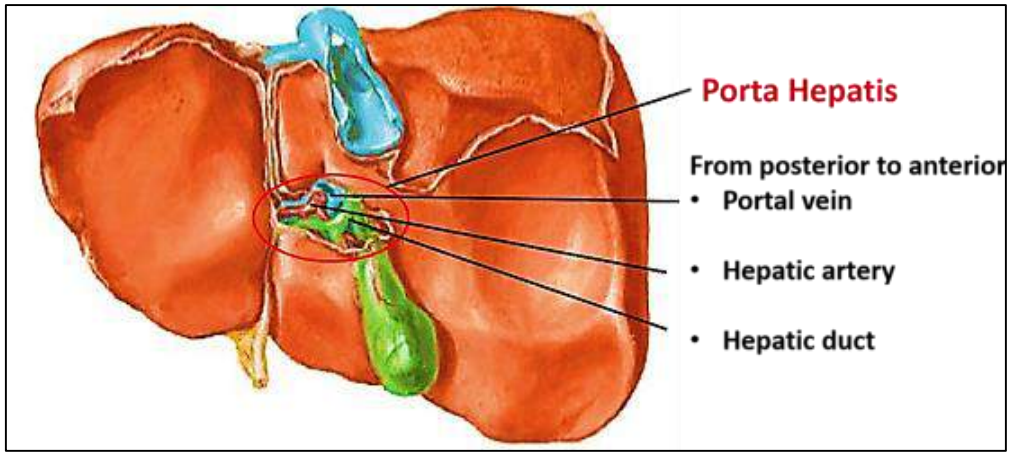
Normal Liver

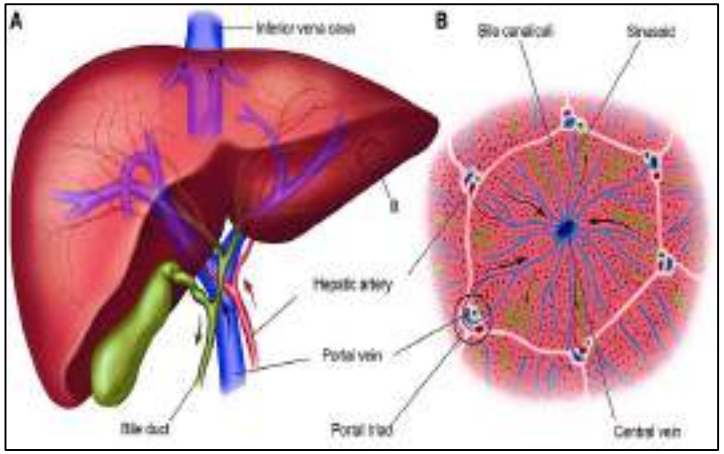


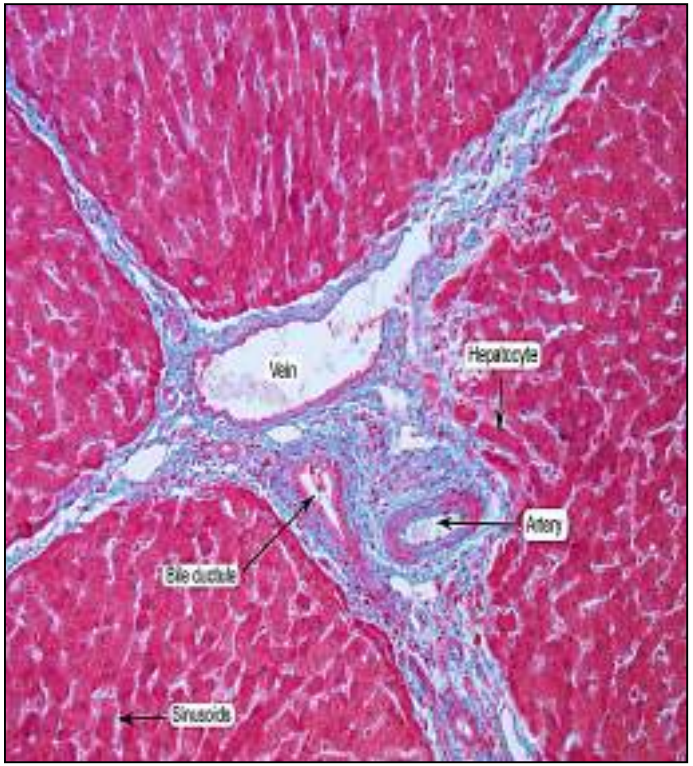
Liver with Cirrhosis





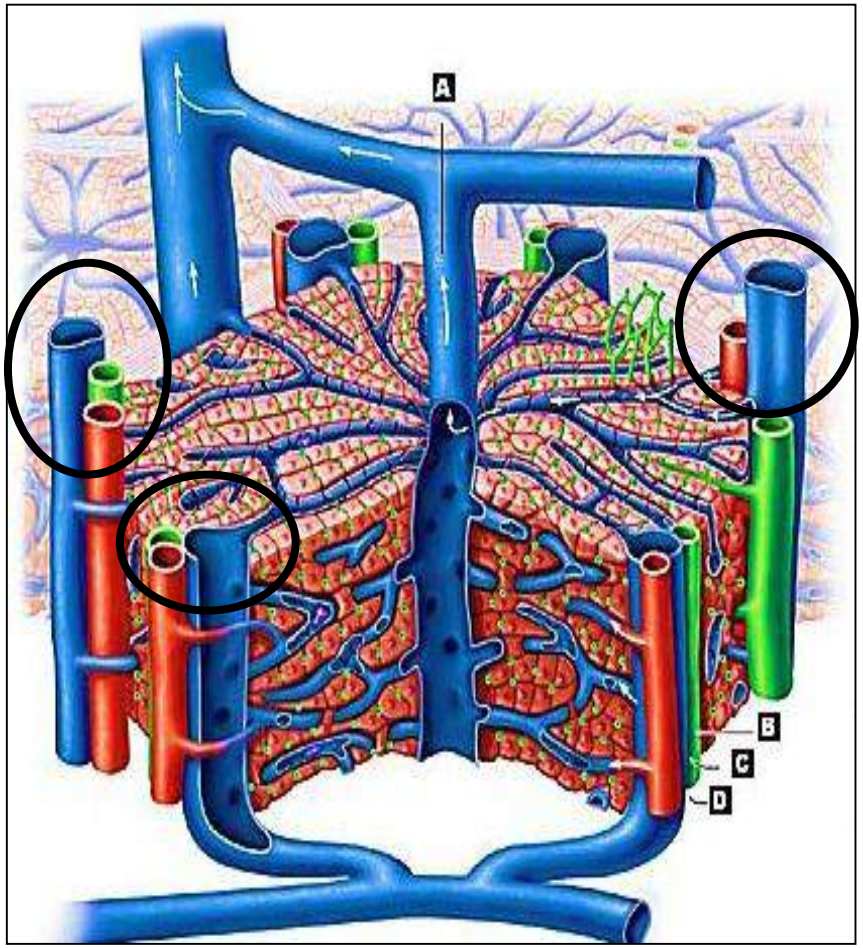


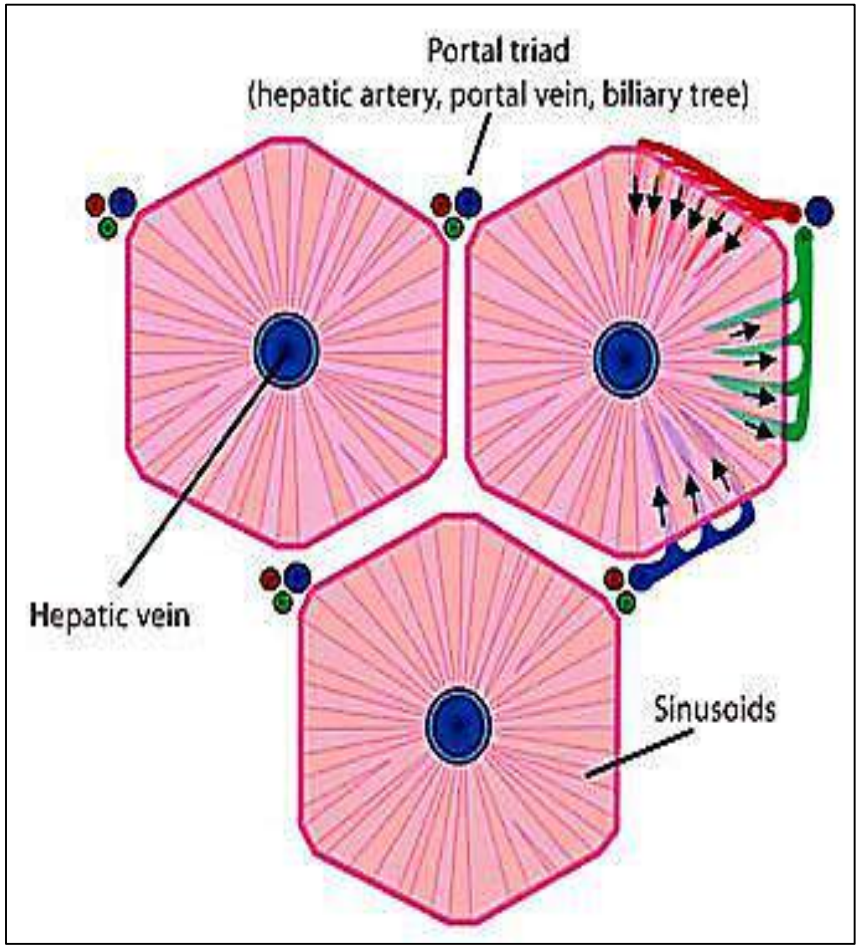




Septa are thick & the lobulation is clear in pig's liver (similar lobulation only seen in human's in liver cirrhosis)

Portal tracts of the liver

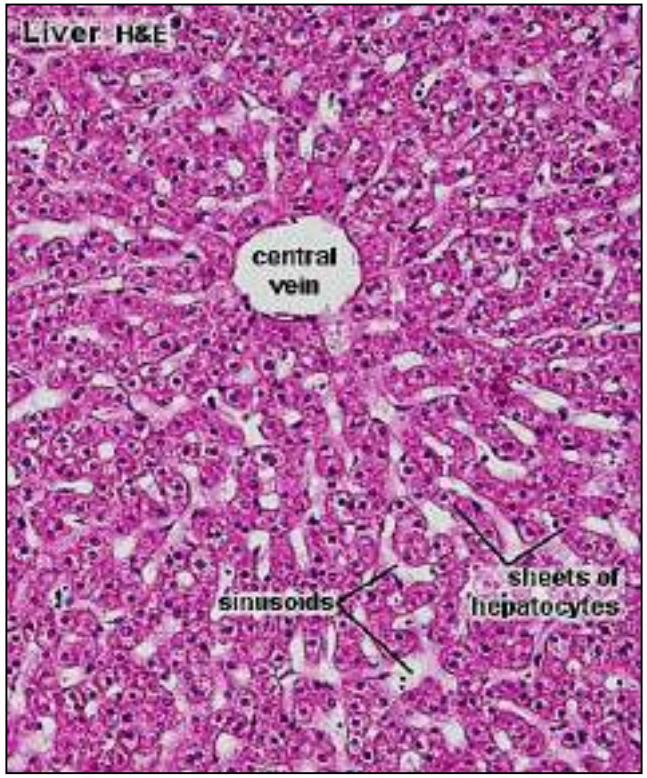


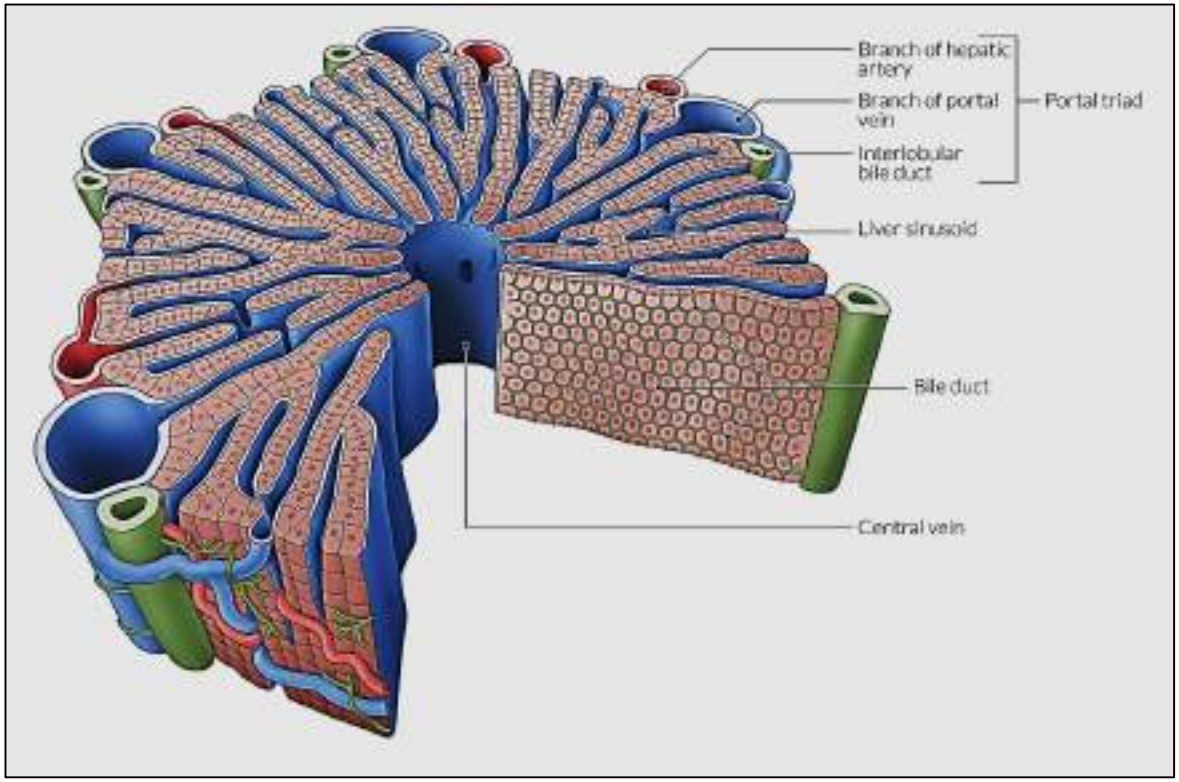


B) Parenchyma : Within each lobule the liver cells arranged in **interconnected plates** (cords) around the central vein

- The plates are two or more rows of cells width

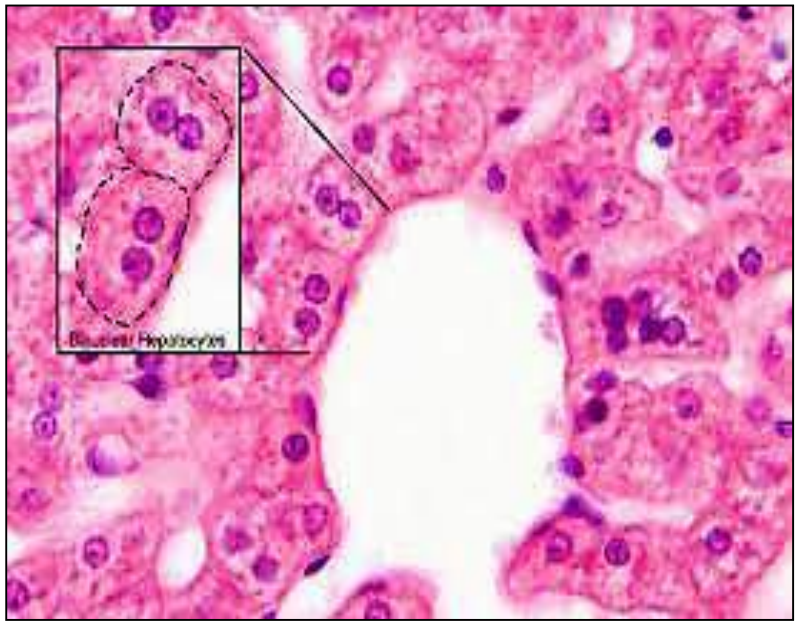
- The spaces between the plates called **liver sinusoids**. They drain **blood** into central vein

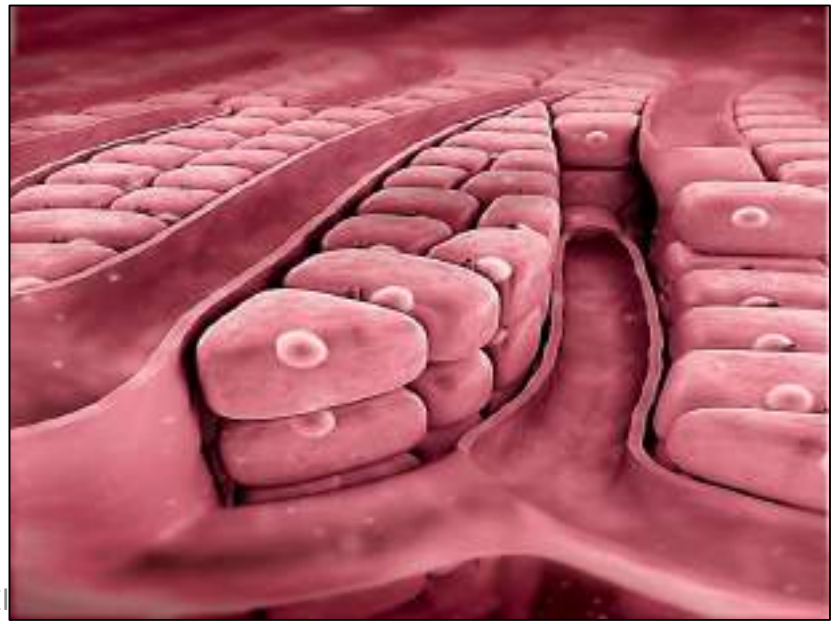




Hepatocytes

- **LM:** large polygonal cells with 1 or 2 nuclei (bi-nucleated) so that they can more efficiently do all the required jobs. (The muscle cells have multiple nuclei)
- Nuclei: central, rounded, e prominent nucleoli
- Acidophilic cytoplasm (↑↑in mitochondria & SER), it also appear vacuolated due to dissolved glycogen and fat





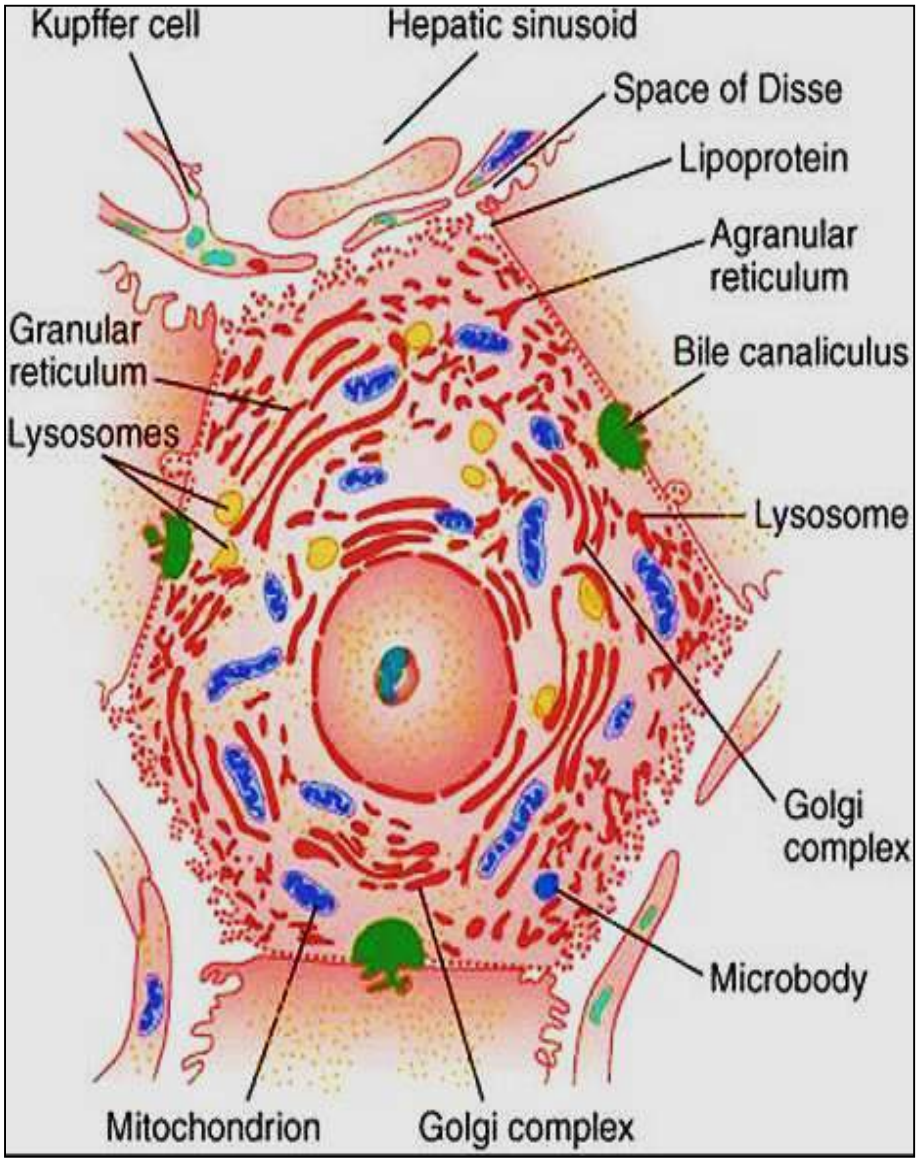
E/M:

Cytoplasm is very rich in organelles & inclusions

- Organelles:
  mitochondria, rER, ribosome, sER (detoxification, bile, glycogen), Golgi complex, lysosomes & peroxisomes.

- Inclusions:
  glycogen granules & fat droplets

- Lipofuscin pigment (aged cells e.g cardiac ms. cells & nerve cells)



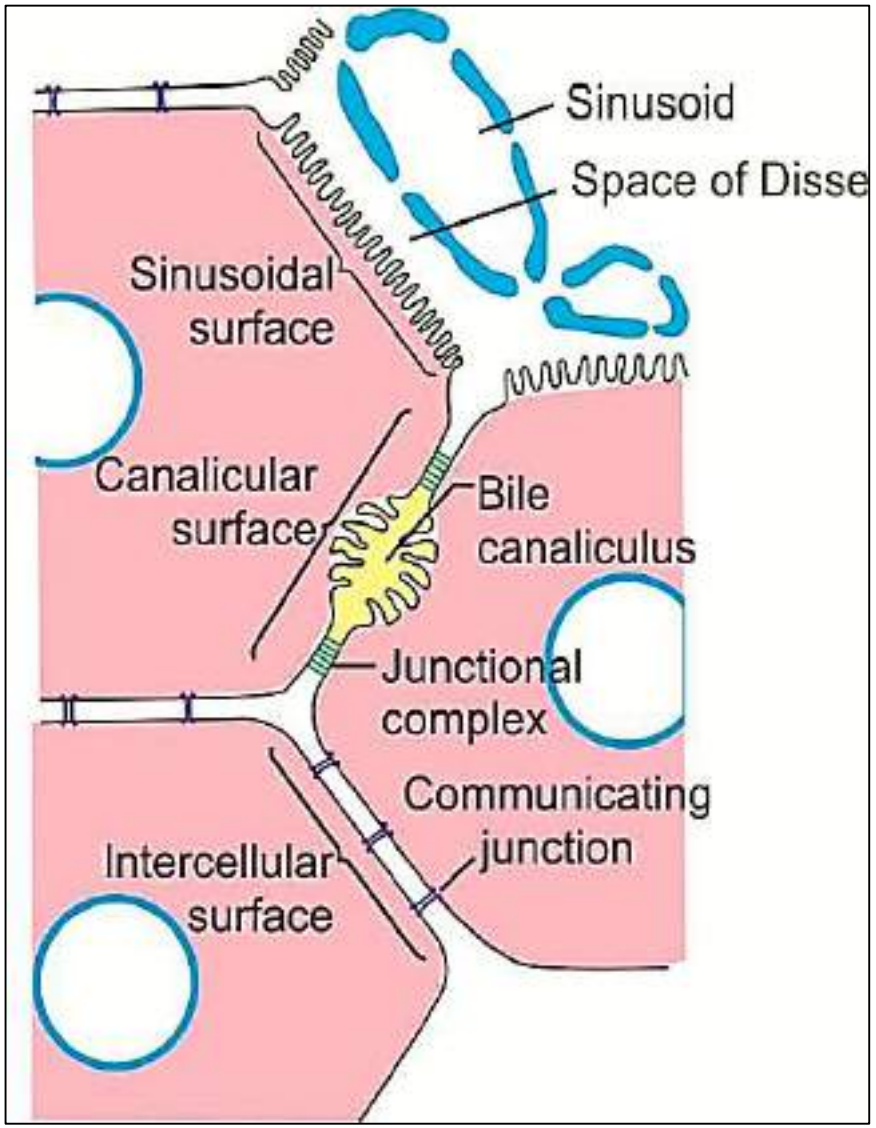
The hepatocytes has two functional surfaces:

1- the vascular side:

Has long microvilli and faces the perisinusoidal space (space of Disse)

2- The intercellular side:

Has short microvilli projecting into the bile canaliculi and is bounded by tight junctions and desmosomes

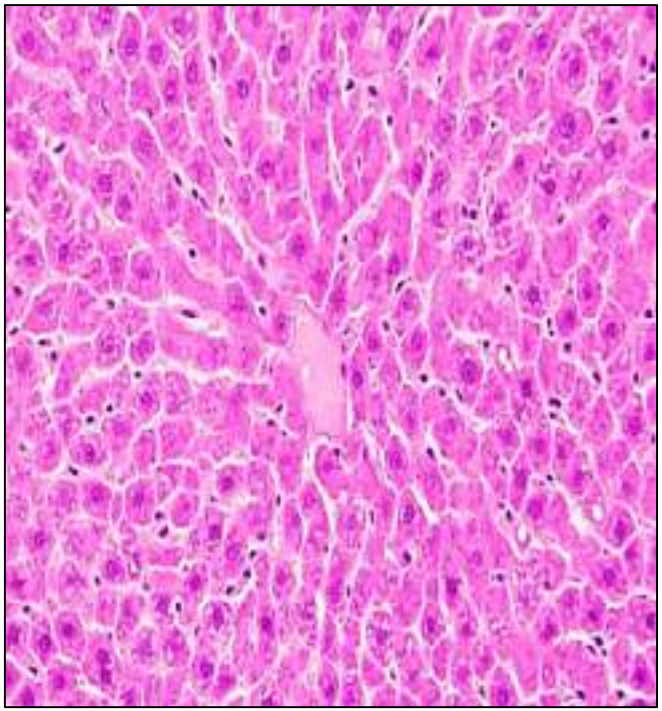


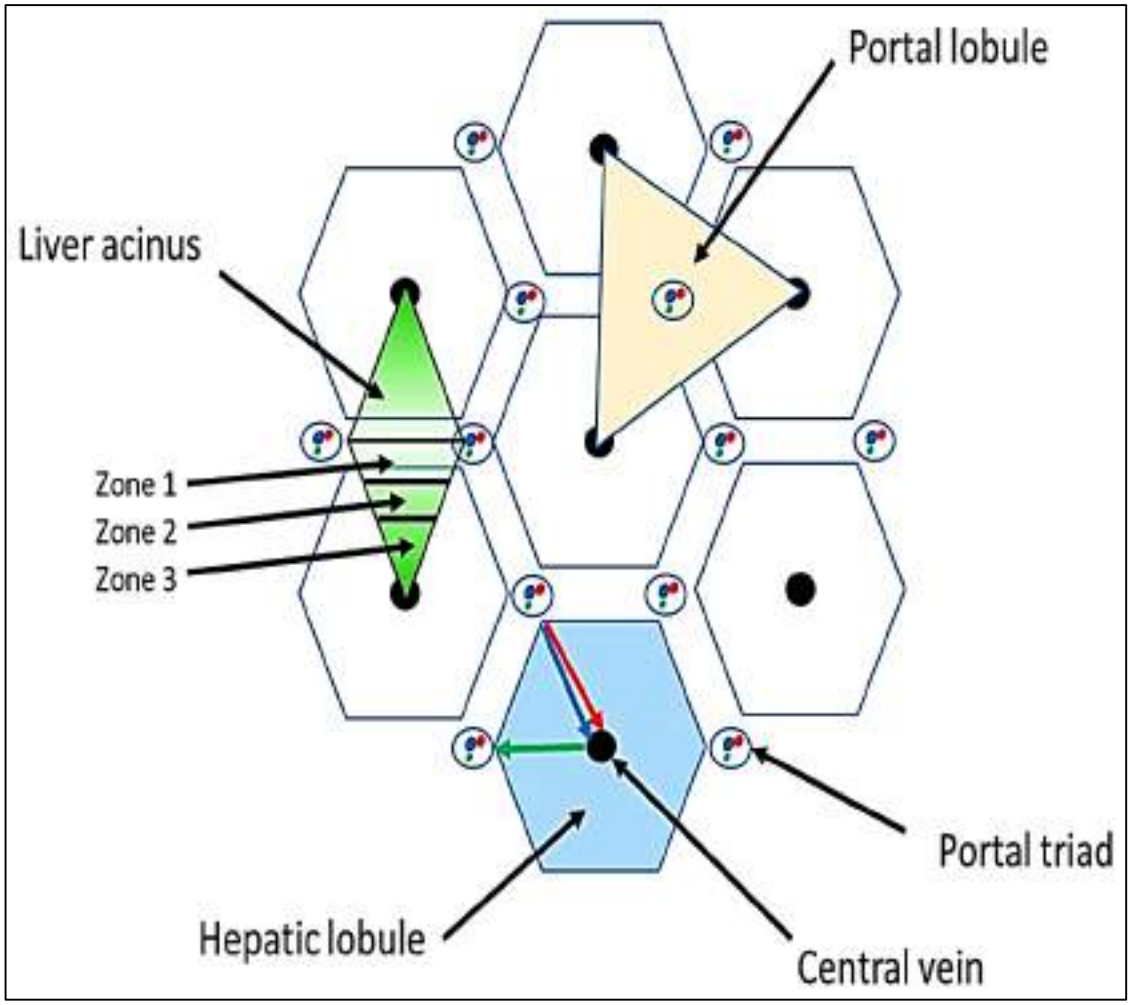
Liver cells (hepatocytes) up to the Function they perform are arranged into either :

1- Classic hepatic lobule

2- Portal lobule

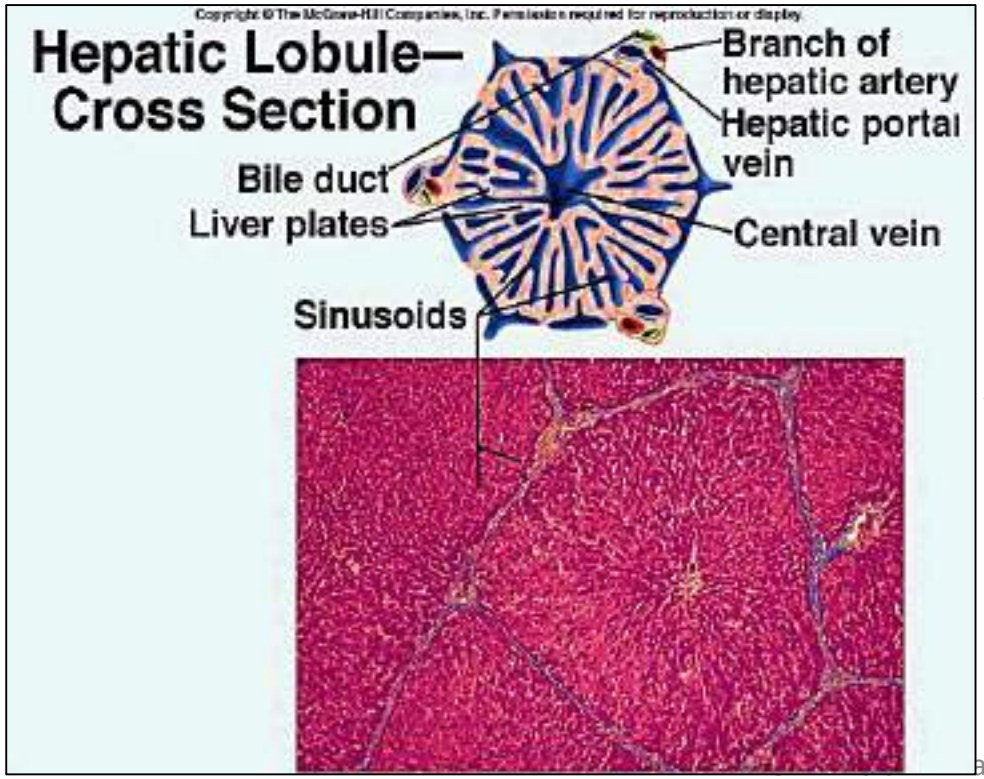
3- Liver acinus

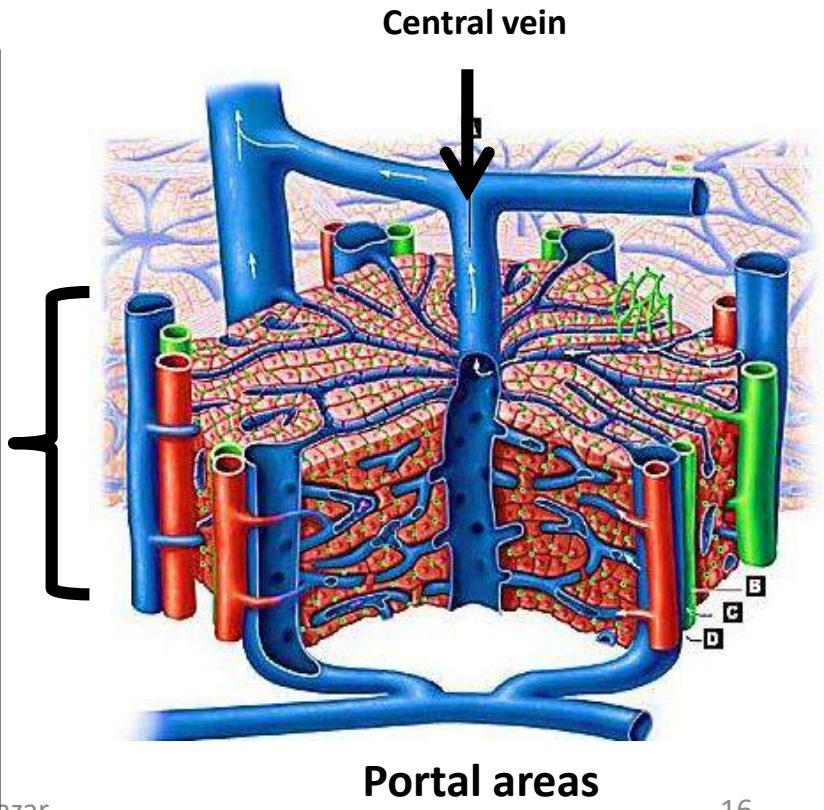




1- Classic hepatic lobule

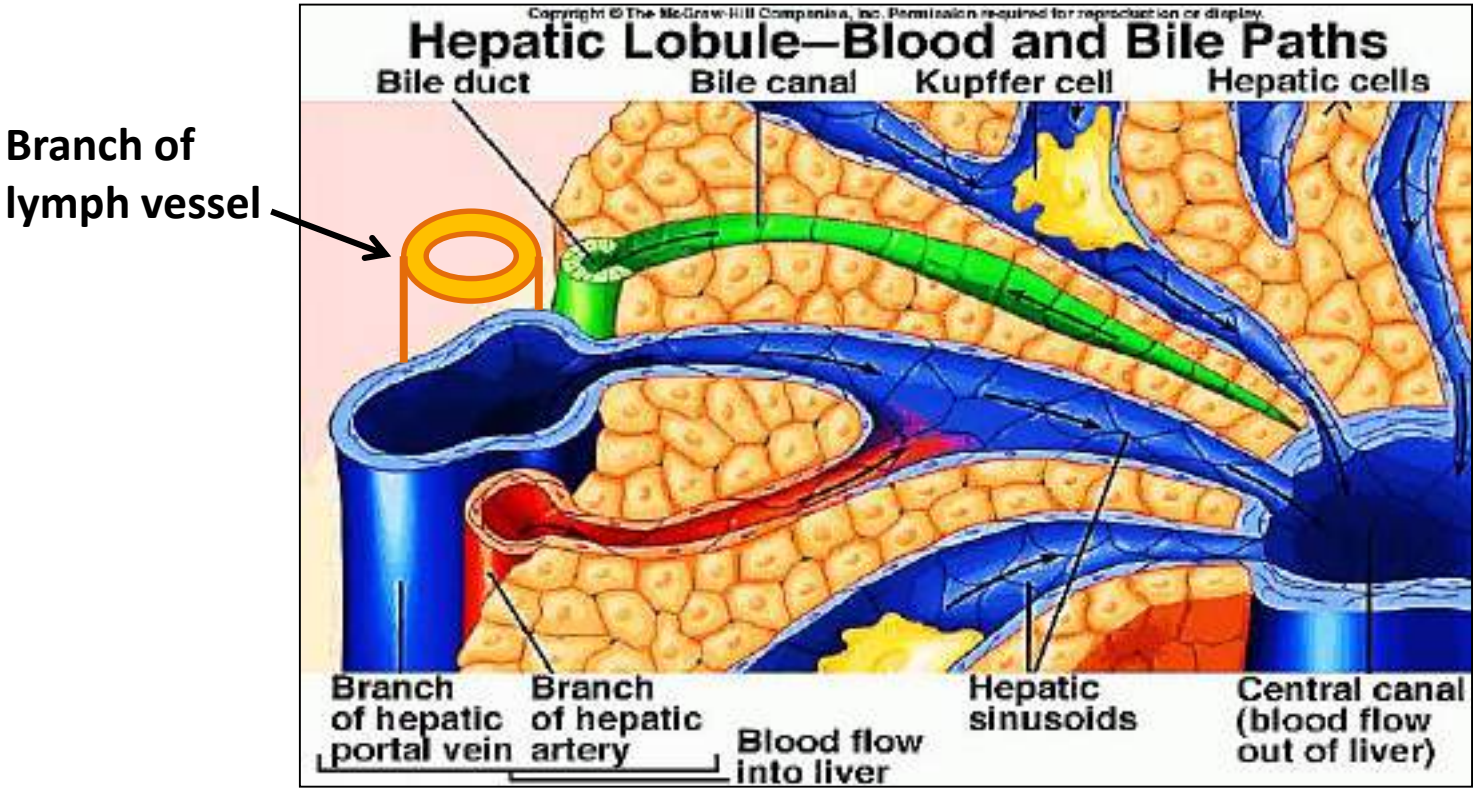
- Hexagonal or polygonal in shape (cross section)
- Surrounded with thick C.T. septa in pig's liver
- Each lobule has 3-6 portal areas (**portal triads**) at its periphery, and **central vein** (CV) at its center



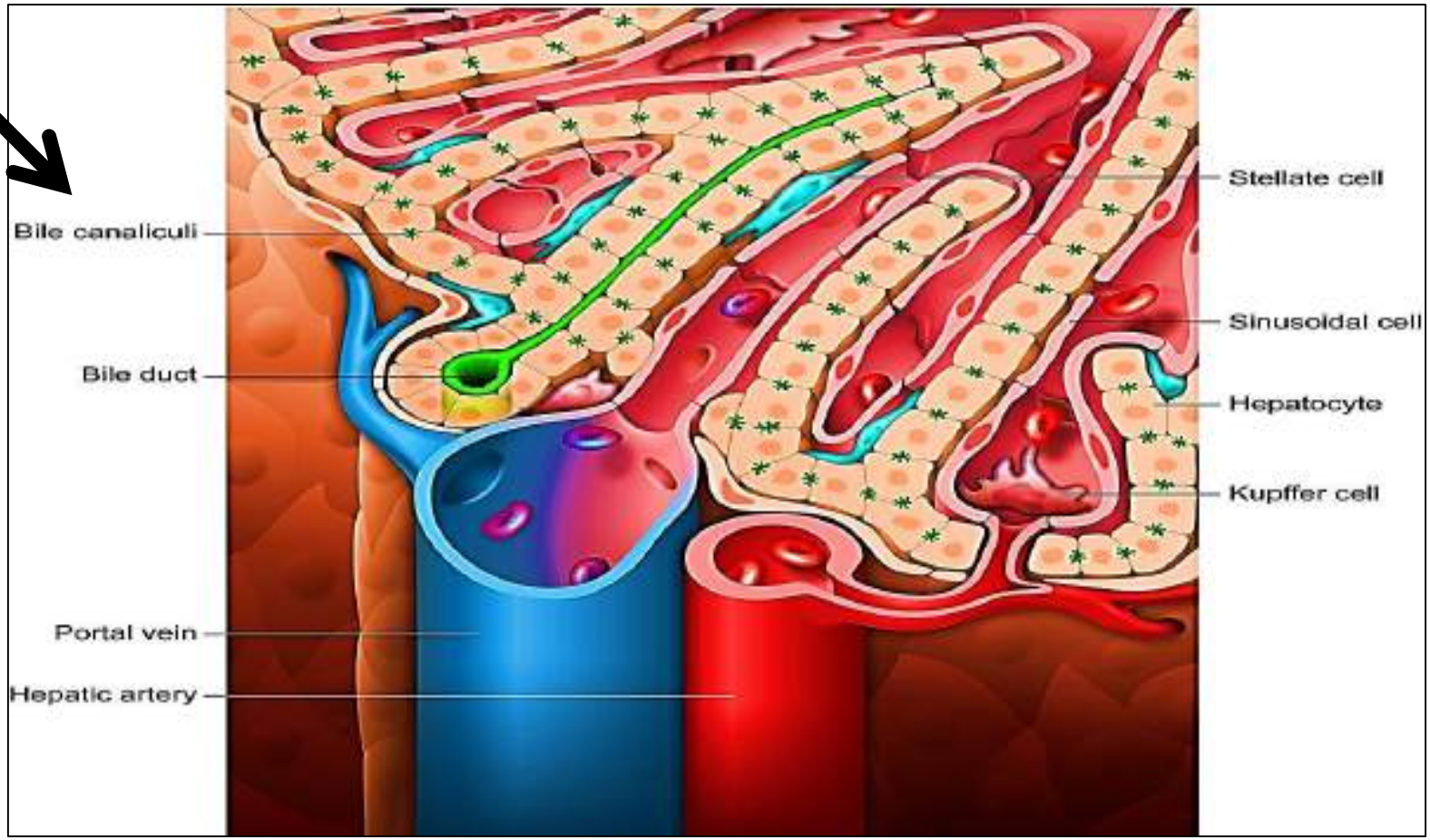


Portal areas (tracts): Each contains :

1. A branch of portal vein: widest with thin wall
2. A branch of hepatic artery: rounded with narrow lumen
3. A branch of bile duct: lined with cubical epithelium
4. Lymph vessel



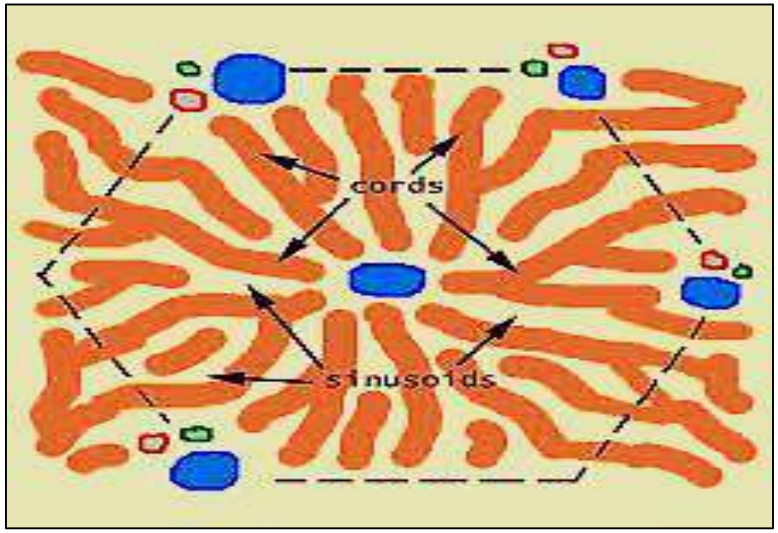
- **Bile canaliculi** present within the plates in-between adjacent hepatocytes, they drain **bile** into the bile ducts in portal areas

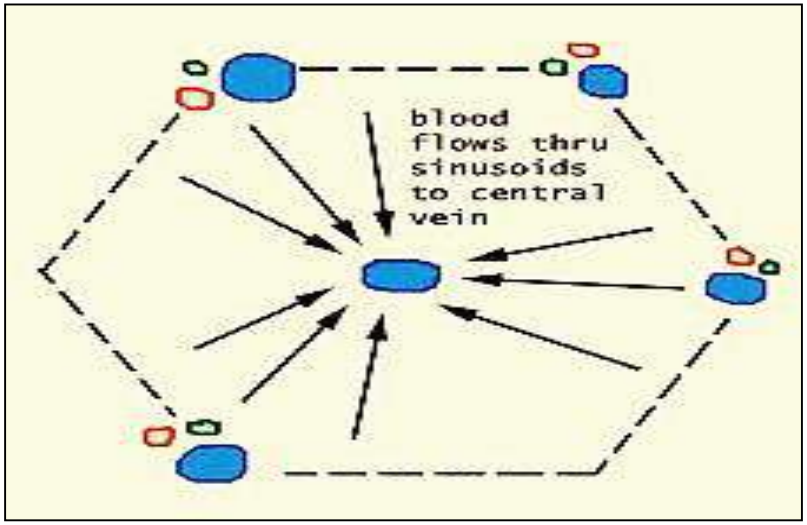


Liver sinusoids and space of Disse

A- Liver sinusoids

- Minute blood channels present **between** plates /cords of liver cells (hepatocytes never exposed to fully oxygenated blood)
- Transport blood from branches of portal vein & hepatic artery in portal area toward central veins (mixed blood)





The flow of blood is centripetal

Drainage of liver sinusoids

- Liver sinusoids

↓

- Central vein

↓

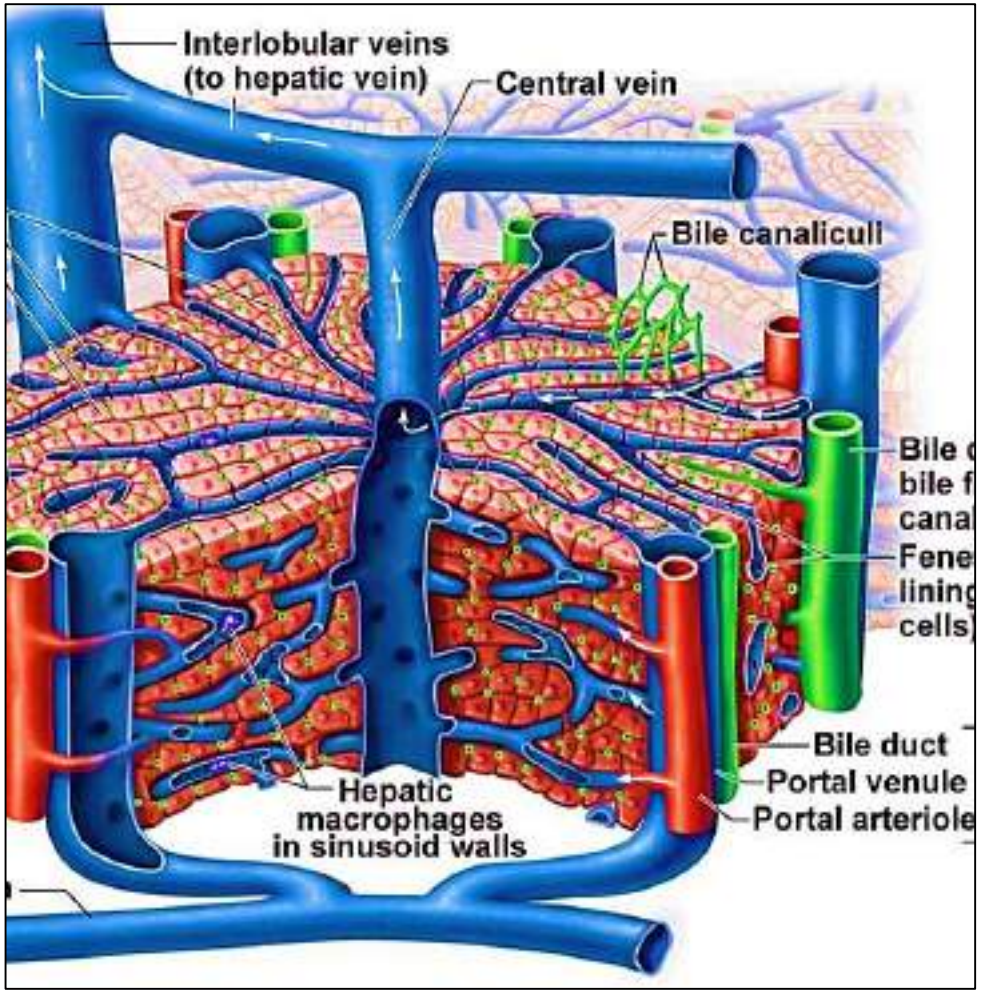
- Hepatic vein

↓

- Inferior vena cava

↓

- Right atrium of heart



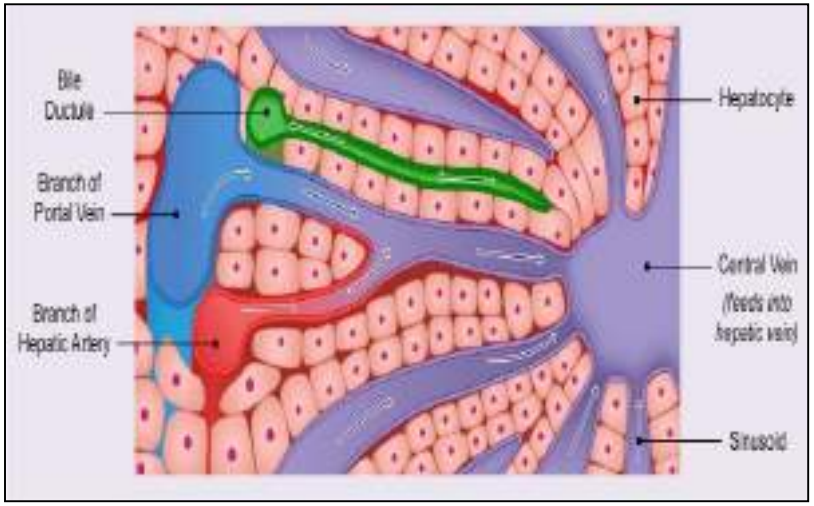
- <u>Lining of blood sinusoids consists of:</u>

✓ fenestrated endothelial cells has no diaphragm

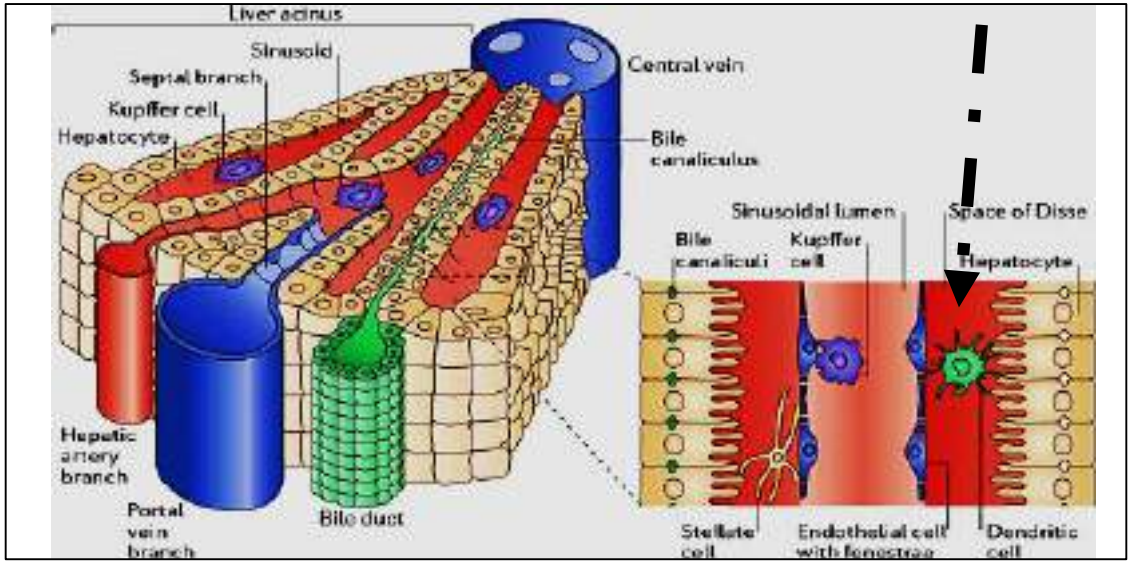
✓ Discontinuous basal lamina

✓ Kupffer cells

✓ Pit cells

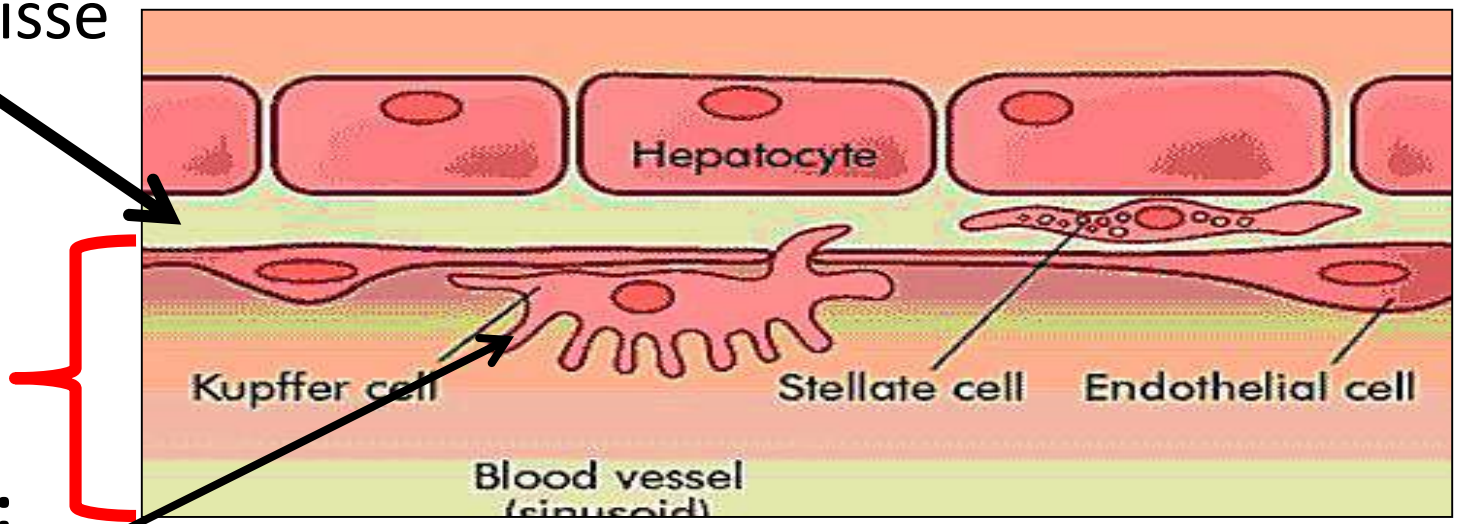


- The wall of the sinusoids is separated from the hepatocytes by a space called **space of Disse**



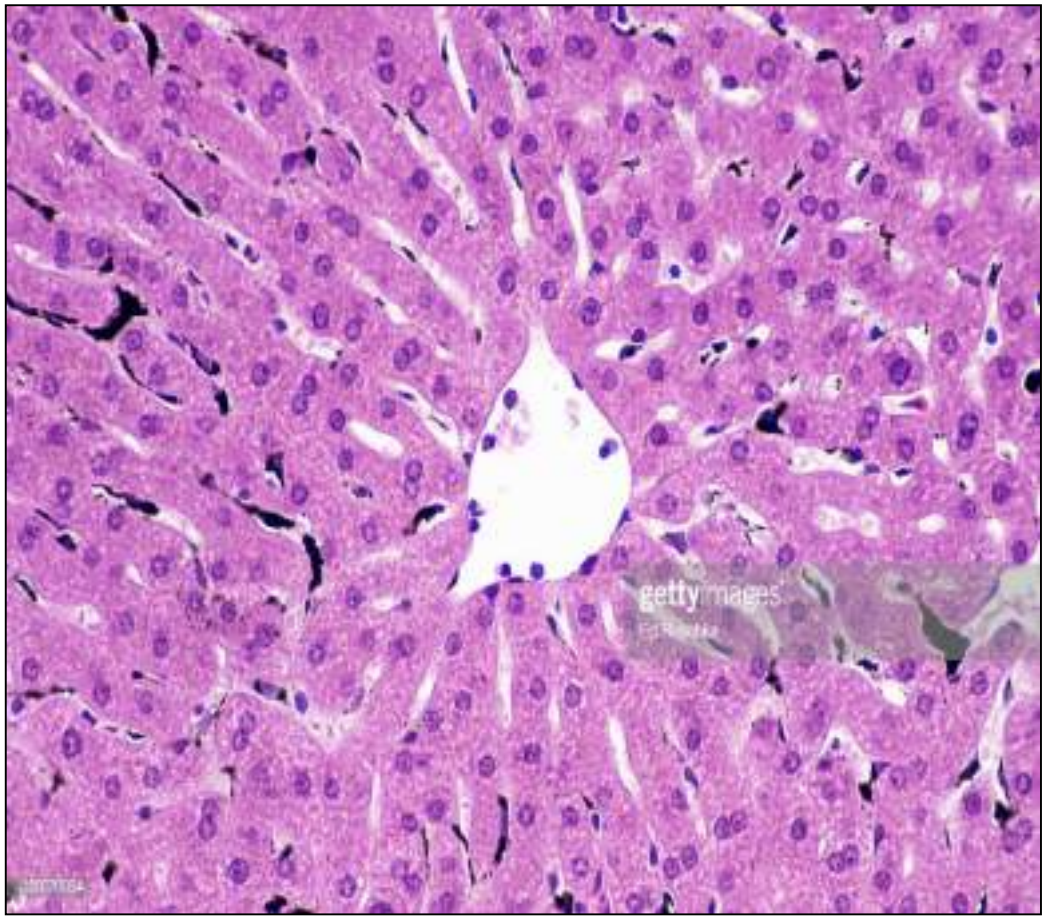
Endothelial cells lining of liver sinusoids:

- Flat cells, contain many holes (fenestrae) to allow free passage of molecules between blood and peri-sinusoidal space of Disse



Kupffer cells:

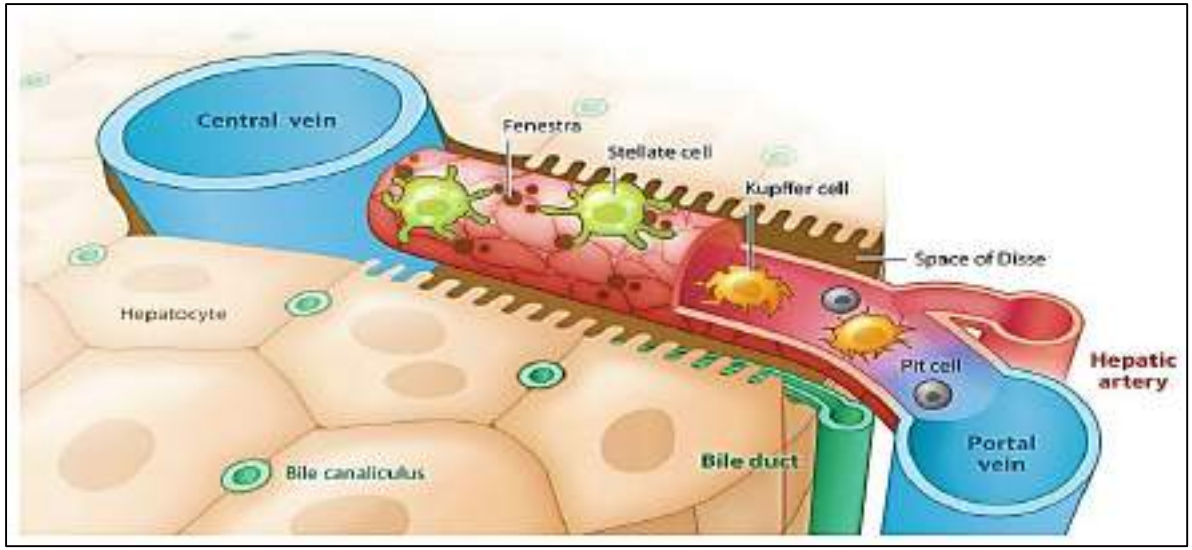
- Macrophages (Fixed) , large cells with large oval nucleus and numerous cytoplasmic processes. Seen in **the blood sinusoids** and in between endothelial cells. Their cytoplasm contain lysosomes, pinocytotic and phagocytic vesicles.



Kupffer cells seen in liver lobules as black cells with special stains (India ink). Found more near <u>portal areas</u>

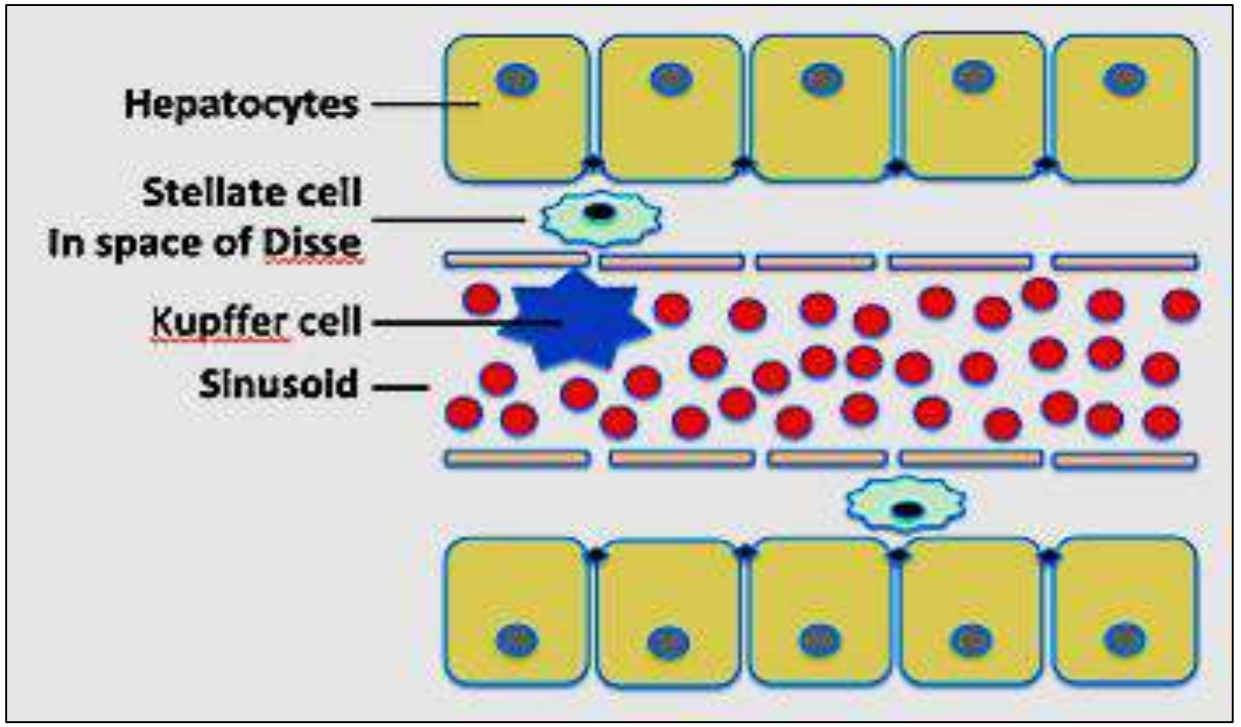
- **<u>Pit cells:</u>** are liver-specific, short lived natural killer (NK) cells also called large granular lymphocytes (LGL). localized inside the lumen of the sinusoid, closely adhering to the endothelial cells and Kupffer cells, and often extending well-developed pseudopodia suggestive of migration along the sinusoidal wall. Multivesicular dense granules are frequently found in the cytoplasm of pit cells which exert antitumor functions by exocytosis of perforin/granzyme-containing granules, which cause death of target cells through receptor-mediated apoptosis , and production of various cytokines that augment the activities of other immune cells.

Safeguard liver cells against hepatitis virus infection or malignancy transformation



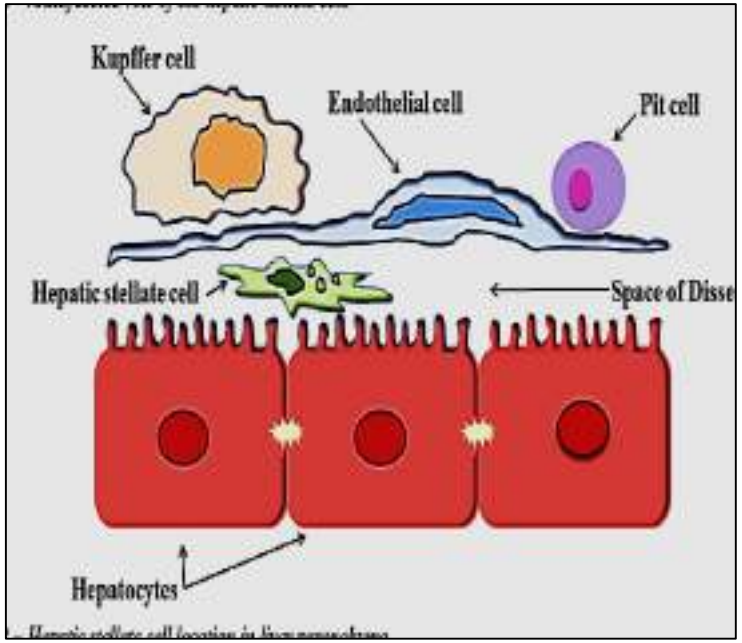
Space of Disse

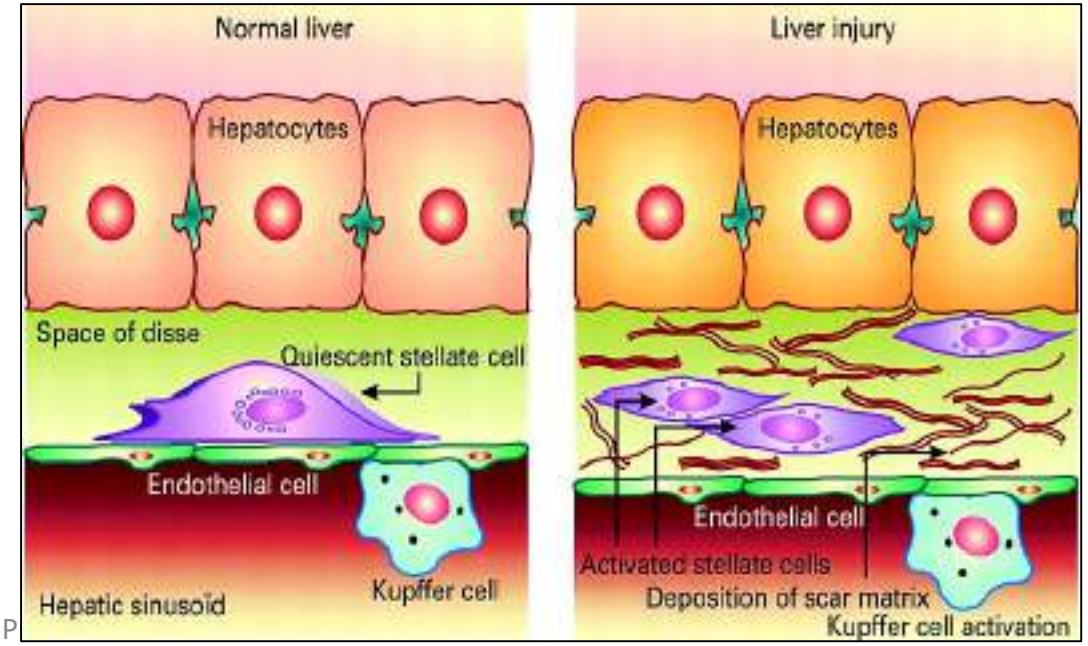
- **EM**: Narrow space separate between the endothelial cells lining of the sinusoids and hepatocytes
- Through out the space exchange of metabolites between blood and hepatocytes takes place



Space of Disse contains:

- Fat storing cells **(Ito cells, stellate cells).** They store Vit. A in small lipid droplets in their cytoplasm, and maintain the extracellular matrix of the space
- Long microvilli of hepatocytes project in the space (↑)
- Blood plasma
- Reticular fibers that support the wall of the sinusoids





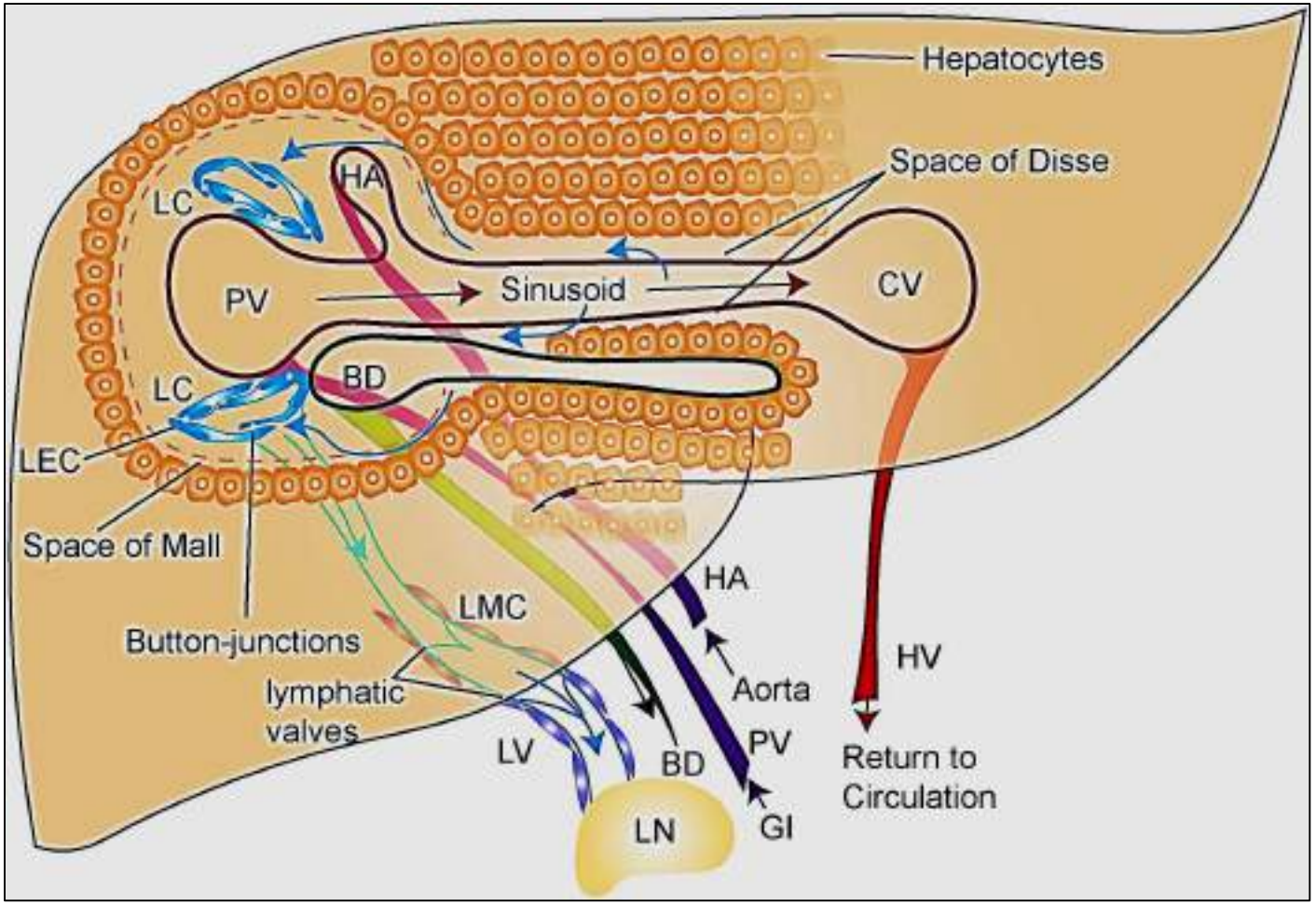
Ito cells:

- Ito cells (peri-sinusoidal fat-storing cells, stellate cells, lipocytes) of the liver are located in the space of Disse.

- They are the main place of vitamin A storage in characteristic lipid droplets.

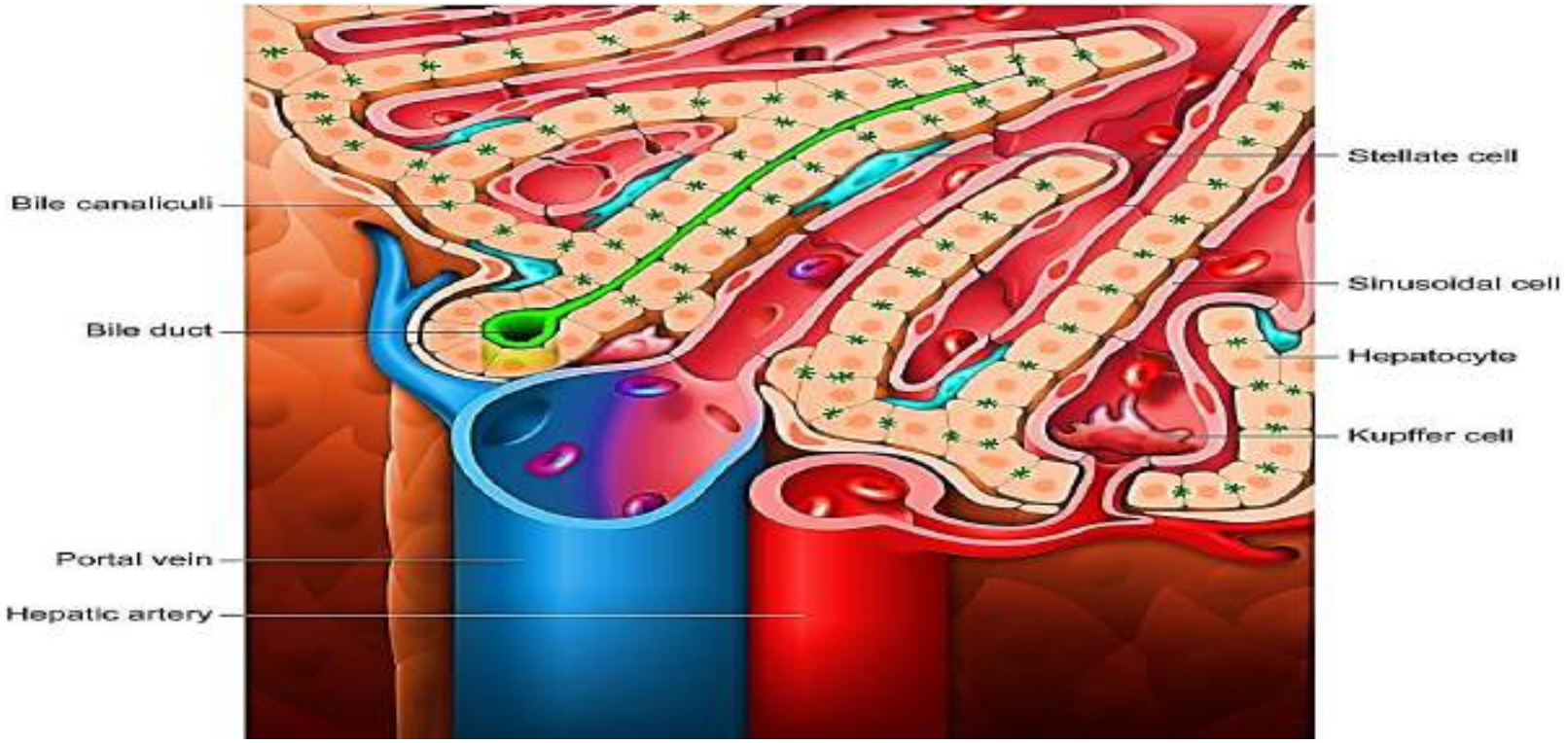
- In chronic inflammation of the liver on (e.g. viral hepatitis & Bilharziasis) they differentiates into myofibroblasts and deposit large amounts of collagen in the space of Disse causing liver fibrosis → ↑ portal hypertension → esophageal varices (famous singer death)

- The peri-sinusoidal spaces of Disse is the beginning of the lymphatic system of the liver

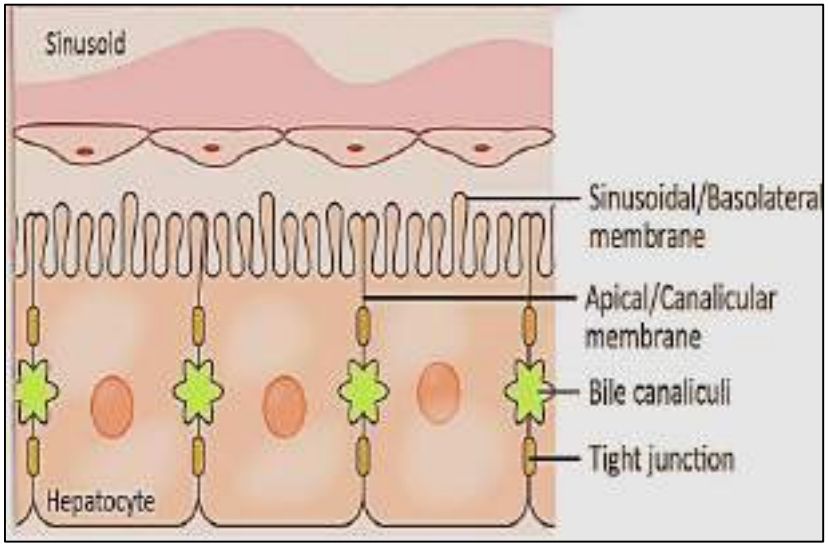


Bile canaliculi and bile ducts

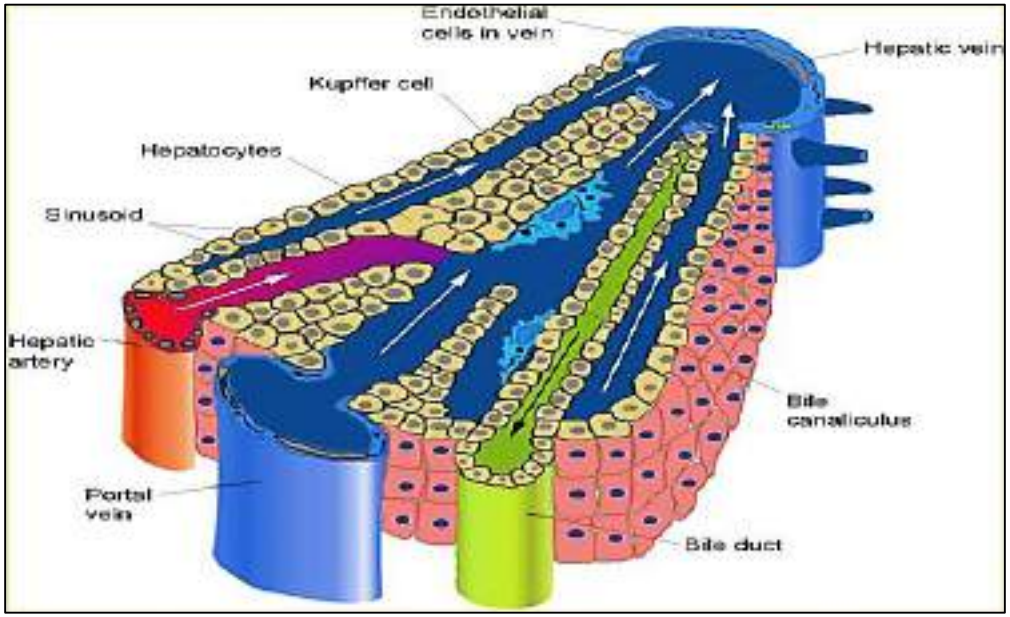
- Minute canals present **within** hepatic plates, in-between adjacent hepatocytes.
- They are bounded by the cell membrane of adjacent hepatocytes



- Small microvilli project from hepatocytes into the canaliculi and tight junctions hold the cell membranes of hepatocytes around the lumen of the canaliculus (hepatocyte polarization)

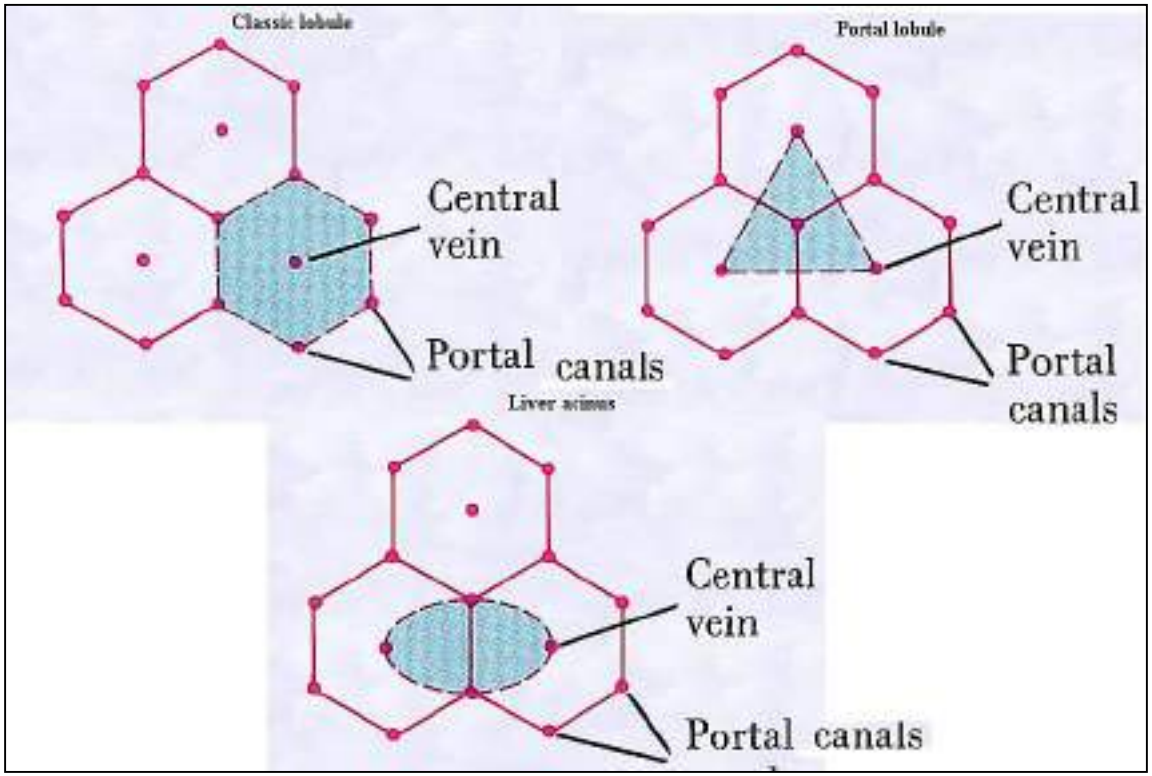


- Bile secreted by hepatocytes drains **out** of the lobule.



Organization of liver parenchyma/function:

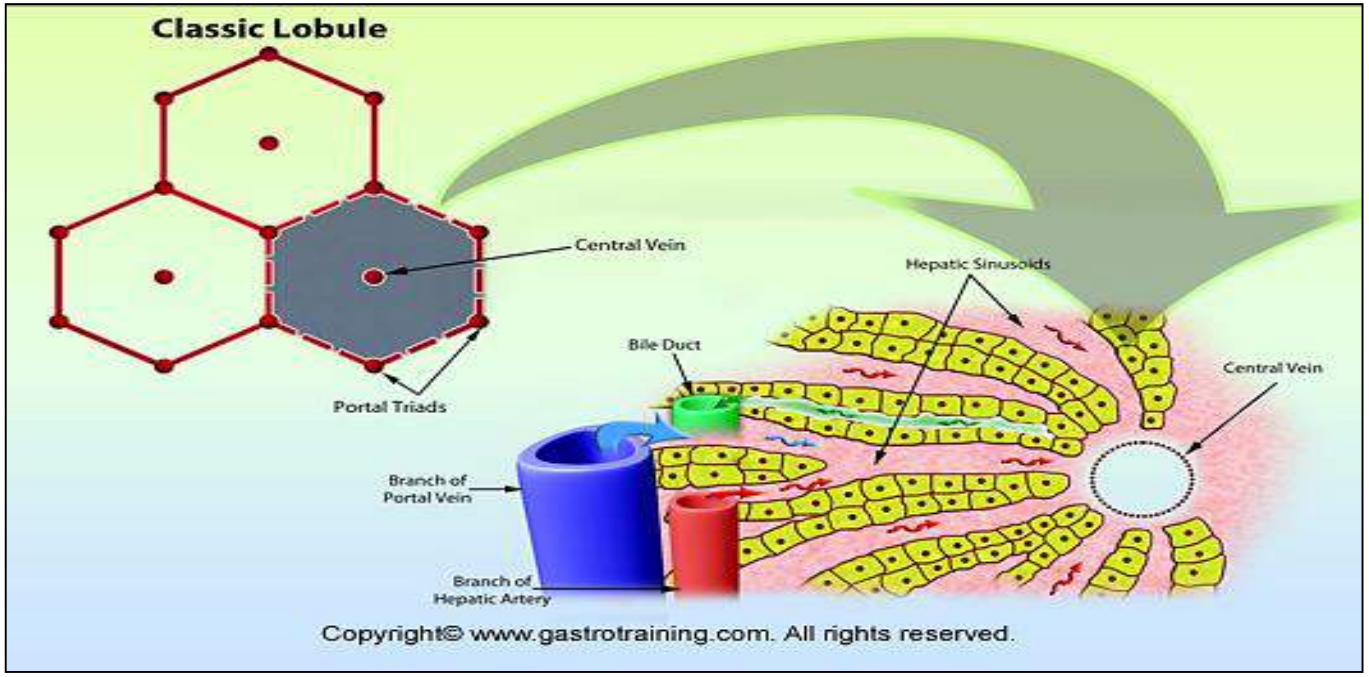
- Classic hepatic lobule → endocrine function
- Portal lobule → exocrine function
- Liver acinus → oxygen/ nutrients supply



Classic hepatic lobule:

Hexagonal in shape with **central vein** in the center, surrounded with 3 – 6 portal tracts at the its corners

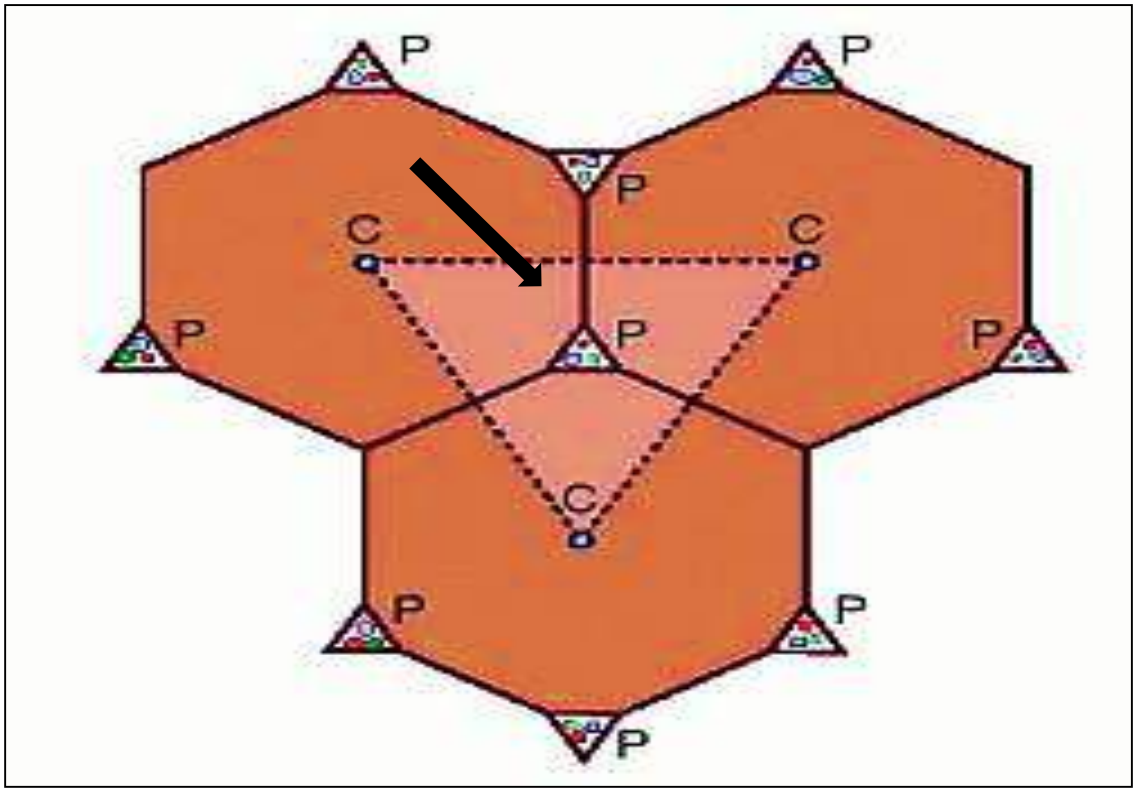
Proteins, glucose secreted by liver cells released directedly into blood sinusoids



Portal lobule:

- Triangular in shape, centered on **portal area (tract**) apices of the triangle are formed by 3 central veins.

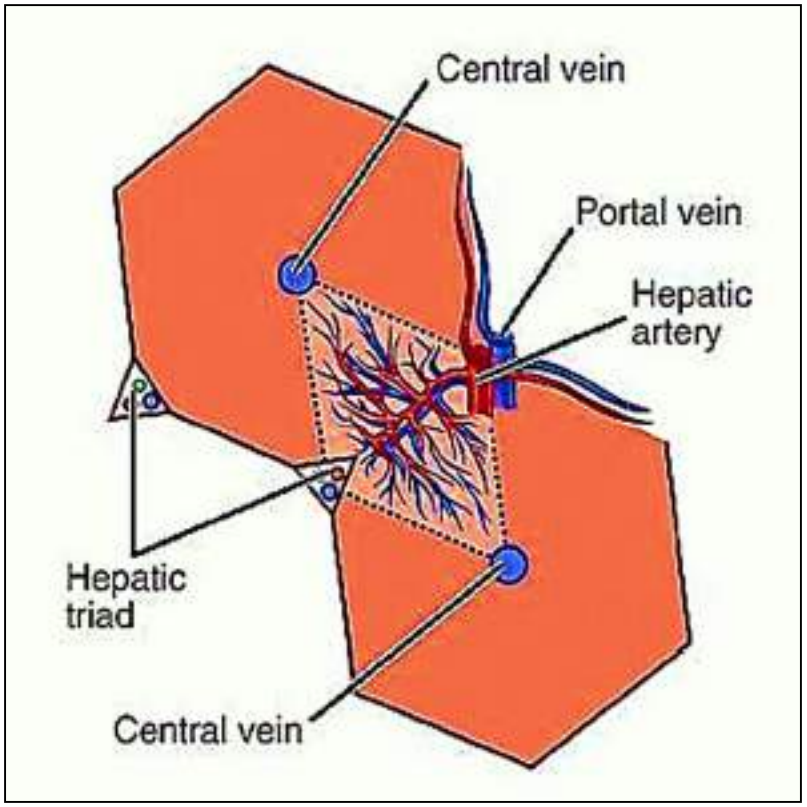
- Hepatocytes of this lobule drain their bile to a bile duct in the center of the triangle



<u>Liver acinus</u>: is the most **important classification**

Diamond shaped mass of liver cells surrounding a central vascular core

It is divided into 3 zones:



Zone 1:

- Close to the vascular core
- Get the most oxygen and nutrients

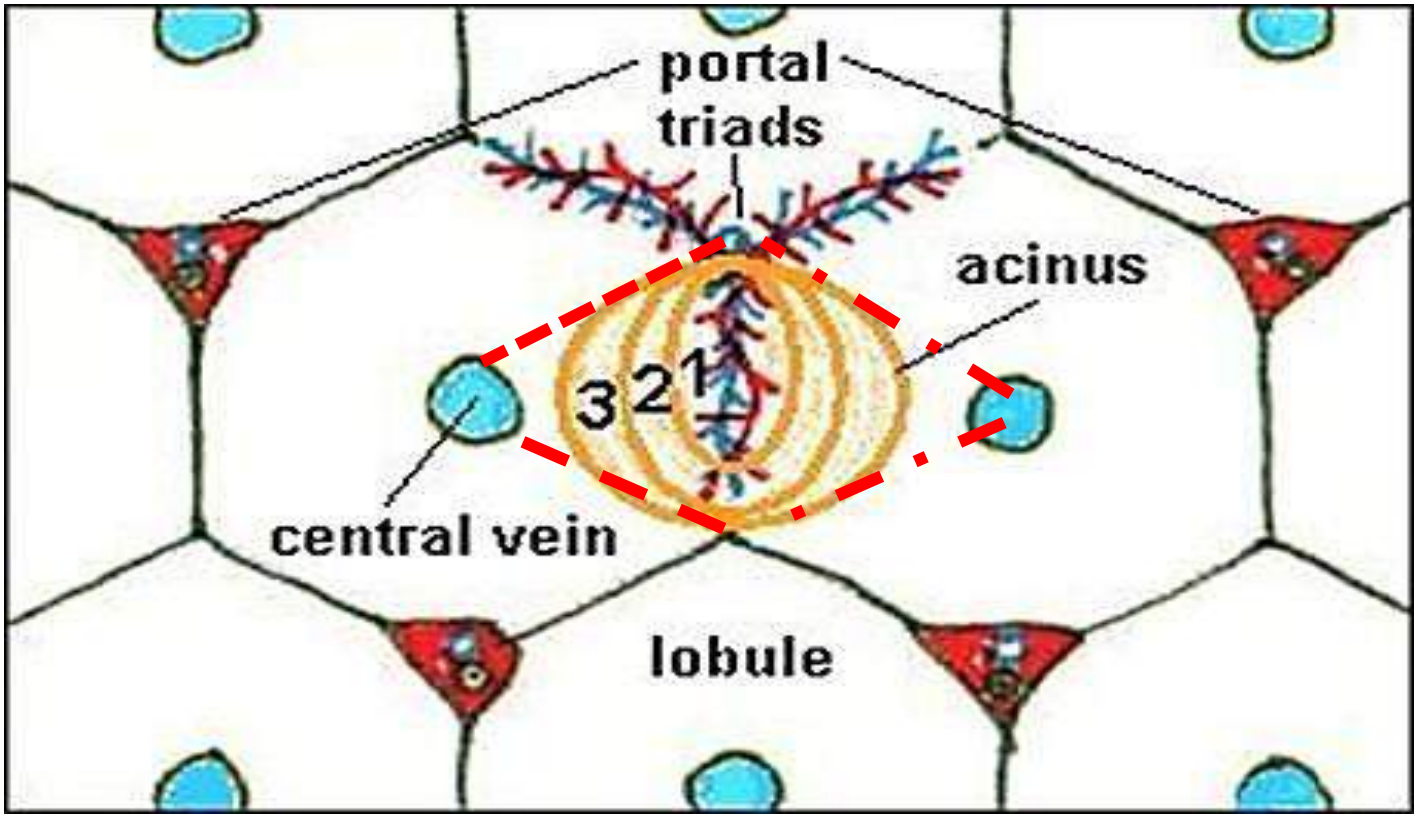
Zone 2:

- Surrounds zone 1
- Get intermediate oxygen /nutrients

Zone 3:

- At the periphery near the central vein
- Get the least oxygen/ nutrient supply

Liver acinus



Arrangement of liver acinus explains the variation in liver cells damage in response to hypoxia & toxins.

zone 1

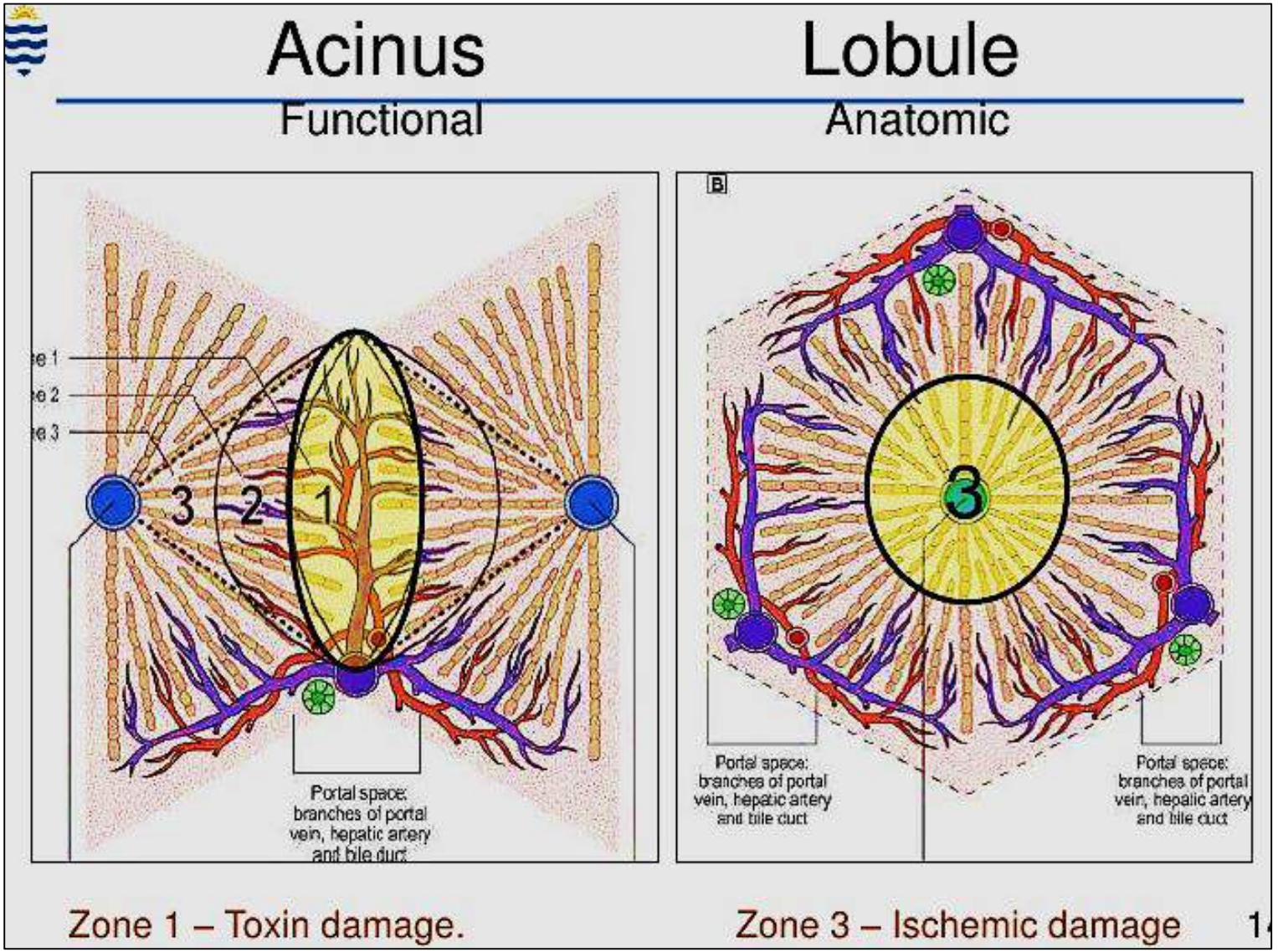
Cells close to the distributing vessels

- **higher** in : oxygen, nutrient & toxin levels
- Least susceptible to ischemia
- **first** to show changes following bile duct occlusion
- **last** to **die** due to circulatory impairment
- **first** to **regenerate**

zone 3

Cells far from the distributing vessels

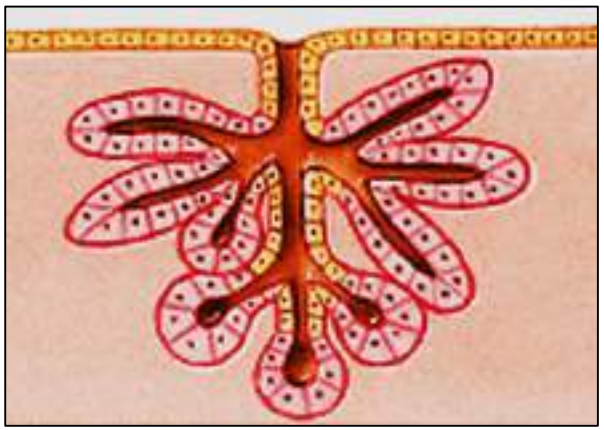
- **first to show ischemic necrosis** (death due to reduced circulation (centri-lobular necrosis)
- **first cells to show fatty accumulation** (alcoholic liver disease) because these cells important for glycolysis
- **last to respond to toxins**

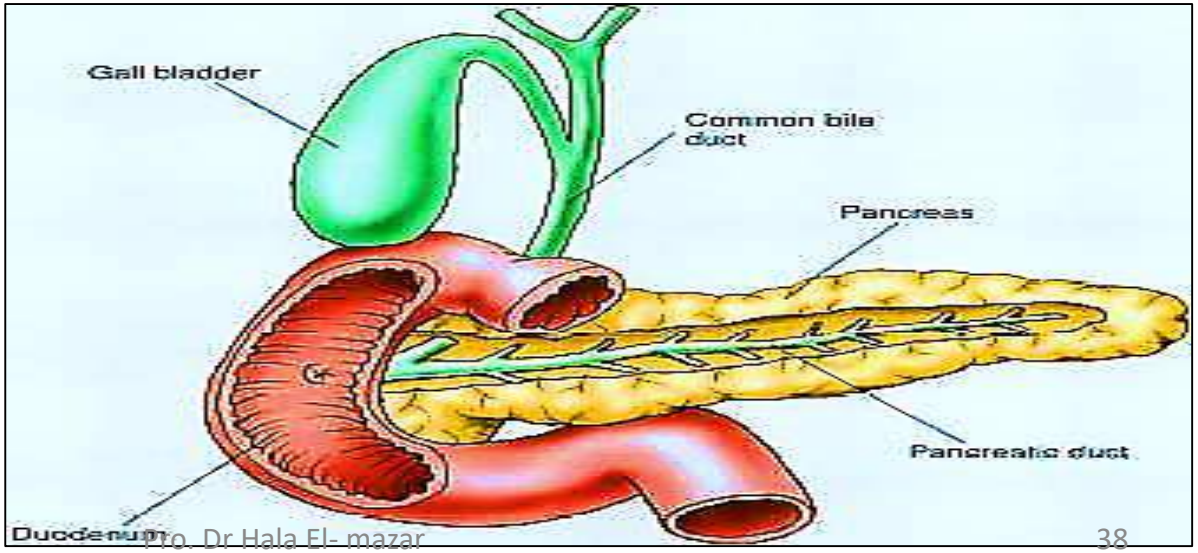

Acinus
Functional
Lobule
Anatomic
3
2
1
Portal space:
branches of portal
vein, hepatic artery
and bile duct
B
3
Portal space:
branches of portal
vein, hepatic artery
and bile duct
Portal space:
branches of portal
vein, hepatic artery
and bile duct
Zone 1 – Toxin damage.
Zone 3 – Ischemic damage

Pancreas

- Mixed exocrine + endocrine gland produce both digestive enzymes and hormones
- **The exocrine part**: compound tubulo-alveolar gland secretes pancreatic enzymes & bicarbonate
- **The endocrine part**: Islets of Langerhans secrete hormones: insulin, glucagon, somatostatin..etc

Tubulo-alveolar gland





Structure of Pancreas

Stroma & Parenchyma

Stroma:

- **Capsule**: thin C.T sheath covers the Pancreas

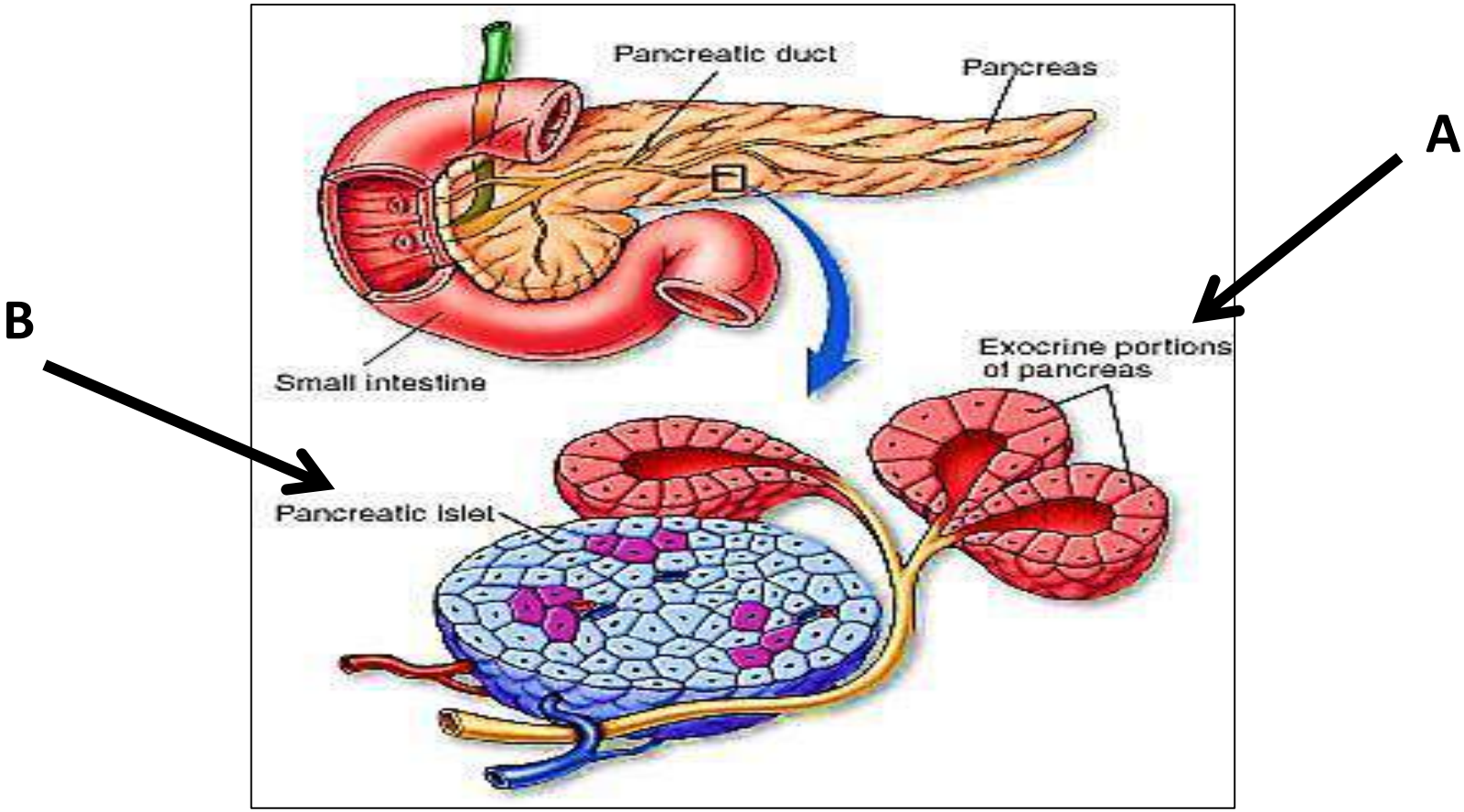
- **Septa** (trabeculae): arise from the capsule, divide the organ into lobes and lobules

- **Reticular fibers**: delicate network of fibers support the parenchyma, rich with blood supply. Stained e sliver

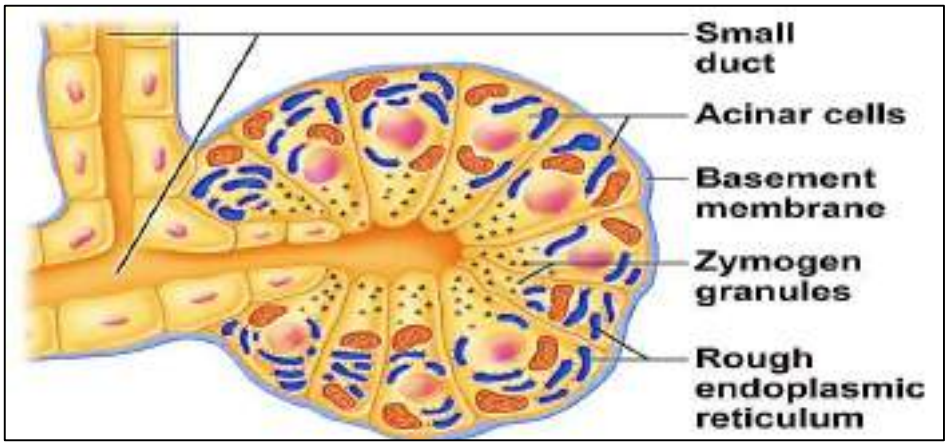
Parenchyma:

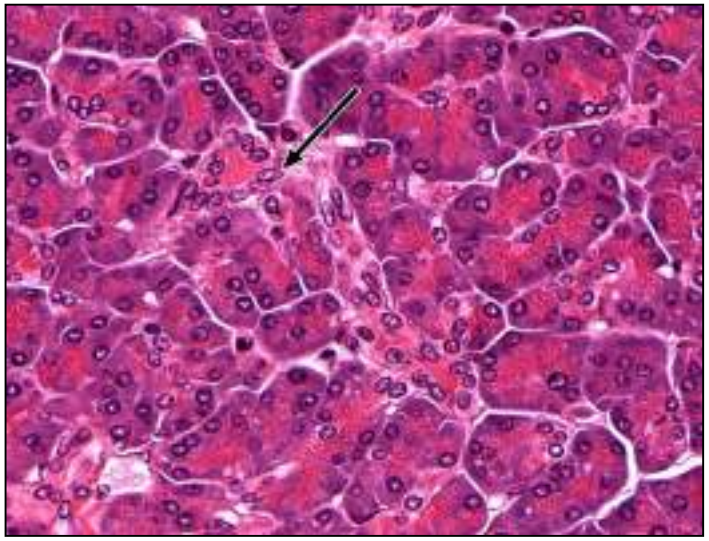
A- Exocrine part (acini & ducts)

B- Endocrine part (islets of Langerhans)



A- Exocrine part: formed of acini & duct system





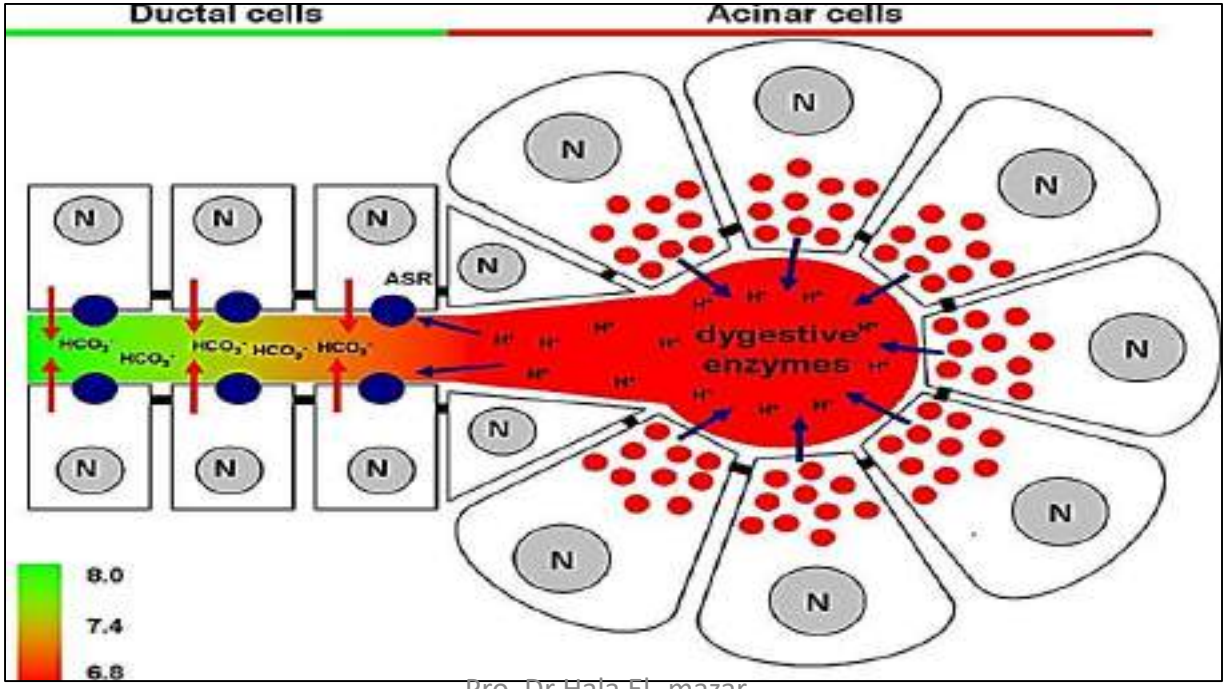
Acini: L/M

- Composed of serous producing cells (enzymes)
- The pancreatic acini has very small lumen
- Cells are pyramidal with rounded basal nuclei
- Cells are protein secreting cells → (exocytosis)
- Cytoplasm shows basal basophilia (rER) & apical acidophilia (zymogen granules)

Pancreatic exocrine secretion is controlled by hormones from the endocrine cells of GIT (stomach & duodenum) :

Cholecytokinin: ++ acinar cells to secrete **pancreatic enzymes.**

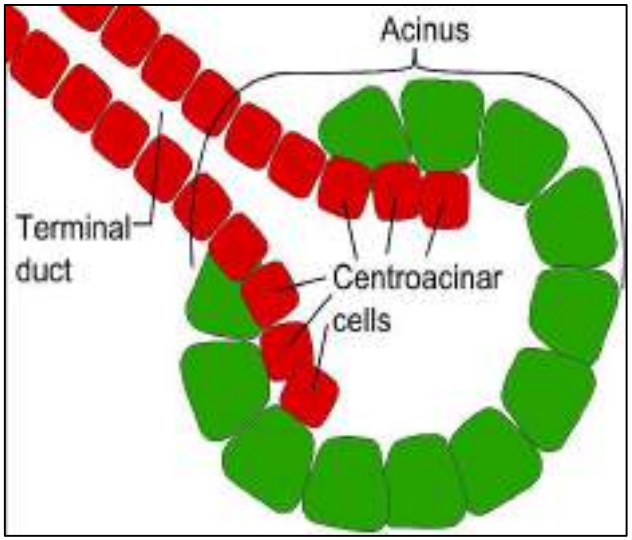
Secretin: ++ **intercalated duct cells** to secrete **alkaline fluid** to neutralize acidic chyme in duodenum.

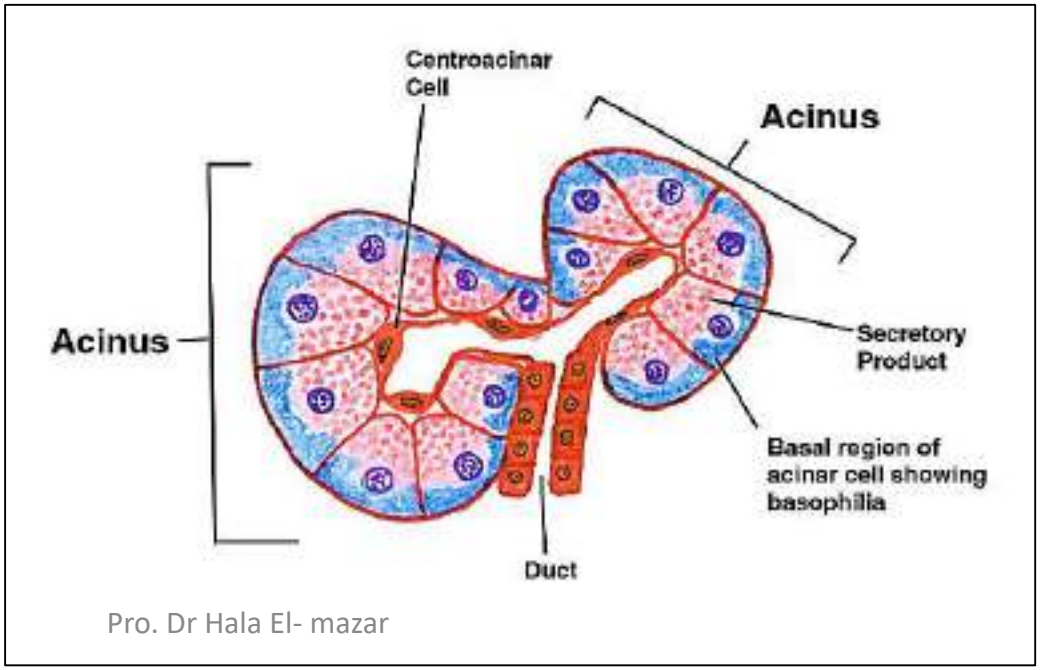


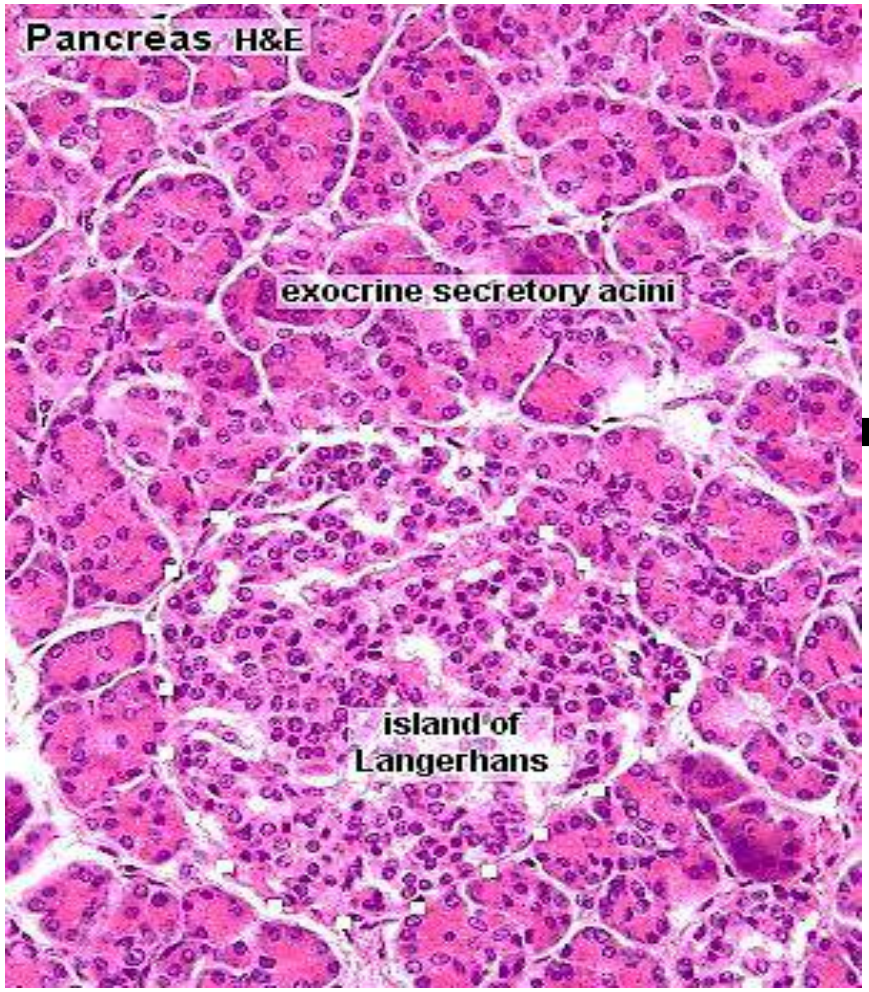
Centroacinar cells:

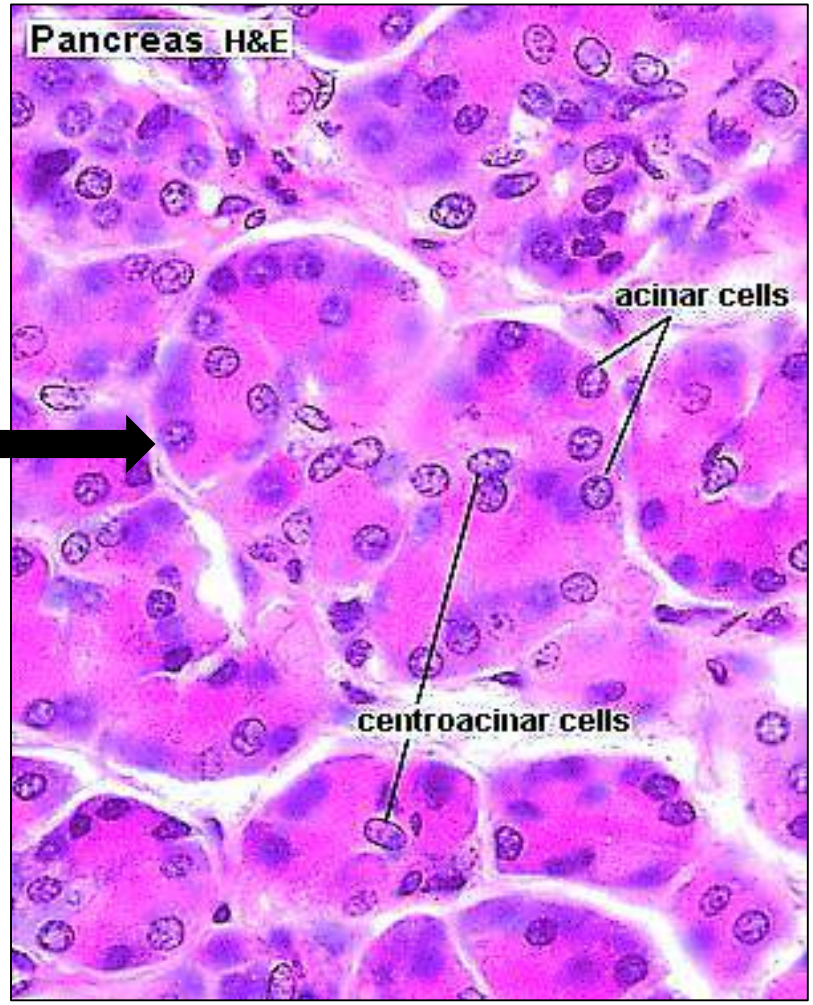
- Flat squamous cells found lining the lumen of the acini

- They represent the beginning of the cells o intercalated duct into
- They secrete **bicarbonate rich fluid** in response to secretin









Section in the pancreas showing the exocrine acini & the endocrine islets of Langerhans

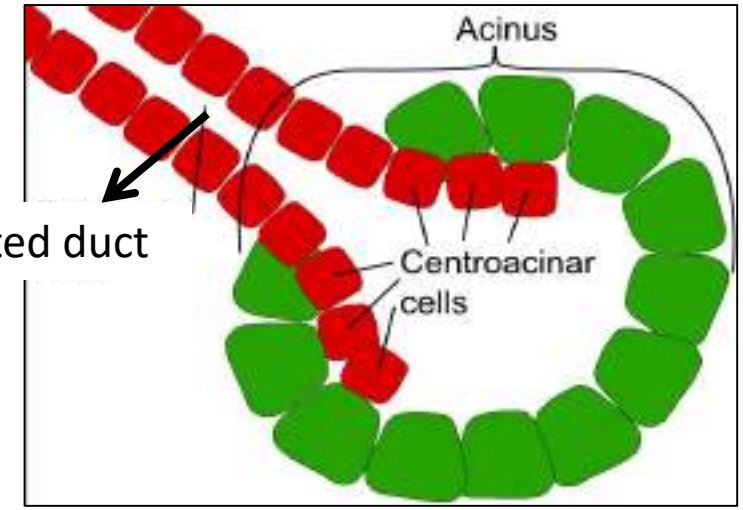
Section in pancreas showing centroacinar cells

Duct system

Intercalated ducts:

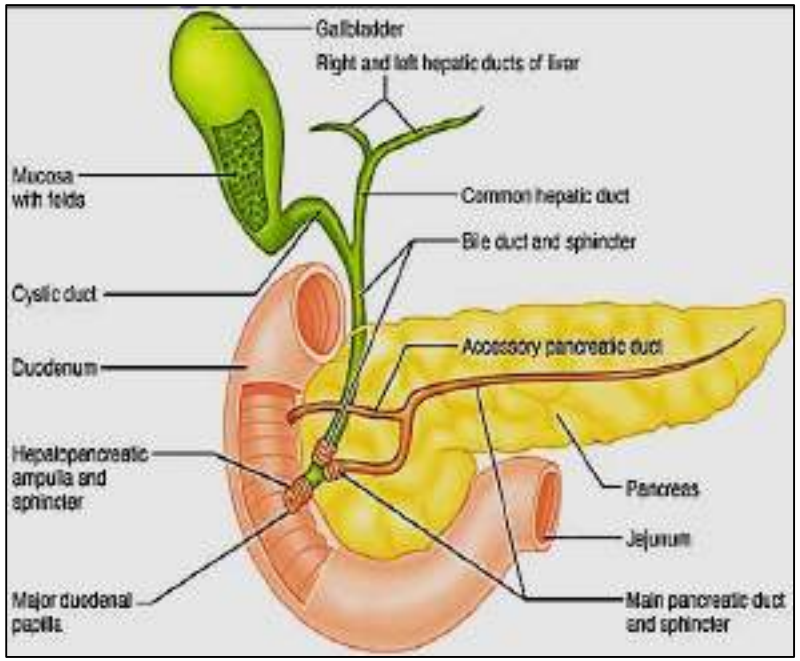
- Thin ducts arise from within the acini
- Lined with simple squamous cells.
- The initial cells called centroacinar cells (secrete HCO3 rich fluid which hydrate and alkalinizes the enzymatic secretion of acinar cells)

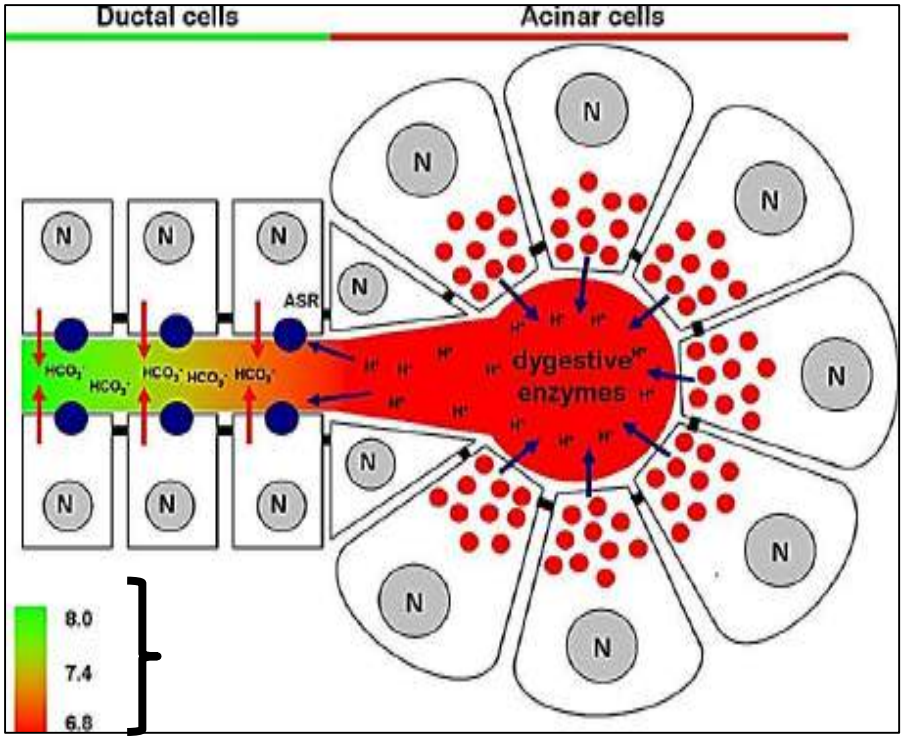
No striated ducts in the pancreas



There are interlobular & interlobar ducts

Main duct: lined with columnar epithelium+ goblet cells + enteroendocrine cells





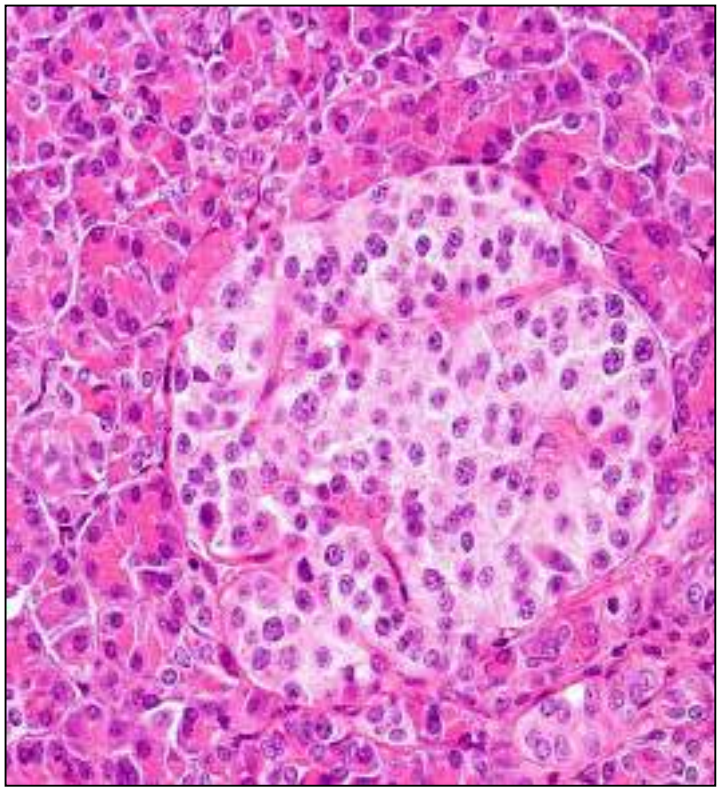
Function of exocrine pancreas:

1- It secretes pancreatic juice rich in **bicarbonate & digestive enzymes** (protease, amylase, lipase, nucleases,…)

B- Endocrine part:

Islets of Langerhans

- Masses of pale staining cells scattered between the pancreatic acini
- They are more in the tail than head of pancreas
- The cells are separated by fenestrated capillaries (highly vascularized)
- Nerve supply autonomic nerve fibers
- Cells of islets of Langerhans are Alpha, Beta, Delta, Ganglion, PPcells

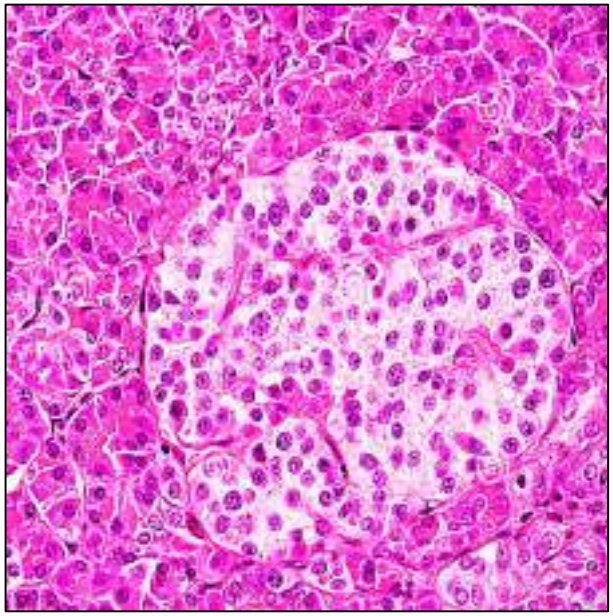


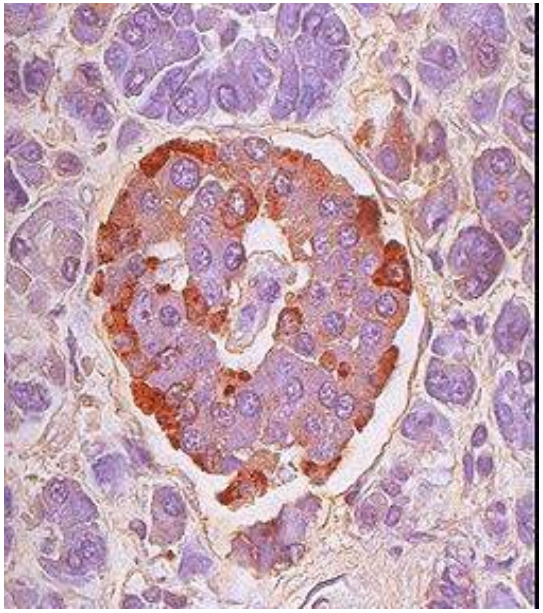
- Histological techniques to differentiate between the different types of pancreatic islets cells are:

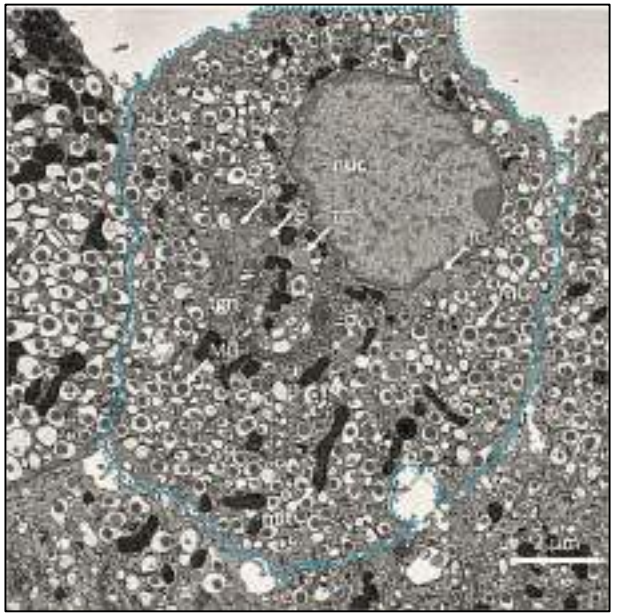
1- Histochemistry

2- Immunohistochemistry

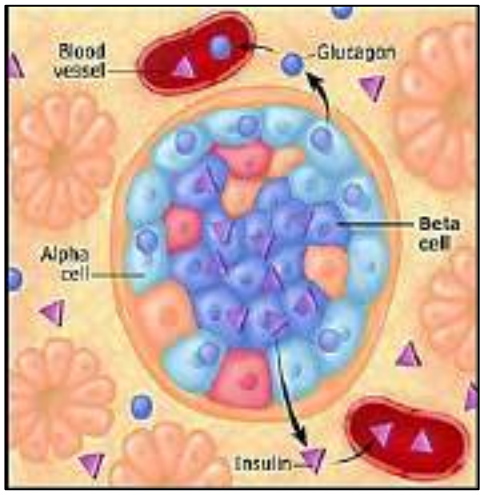
3- Electron microscope (secretory granules)







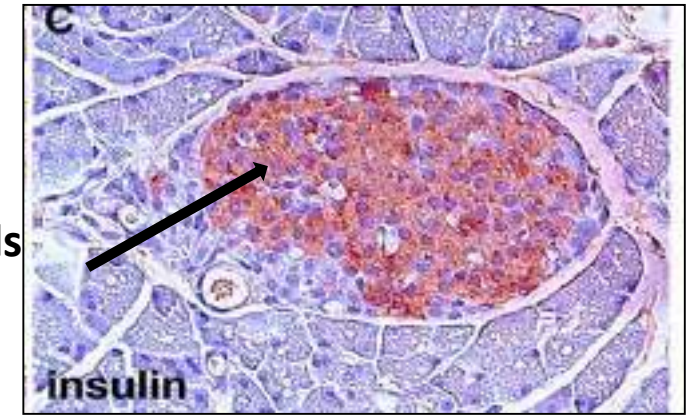
Beta (B) cells (70%):



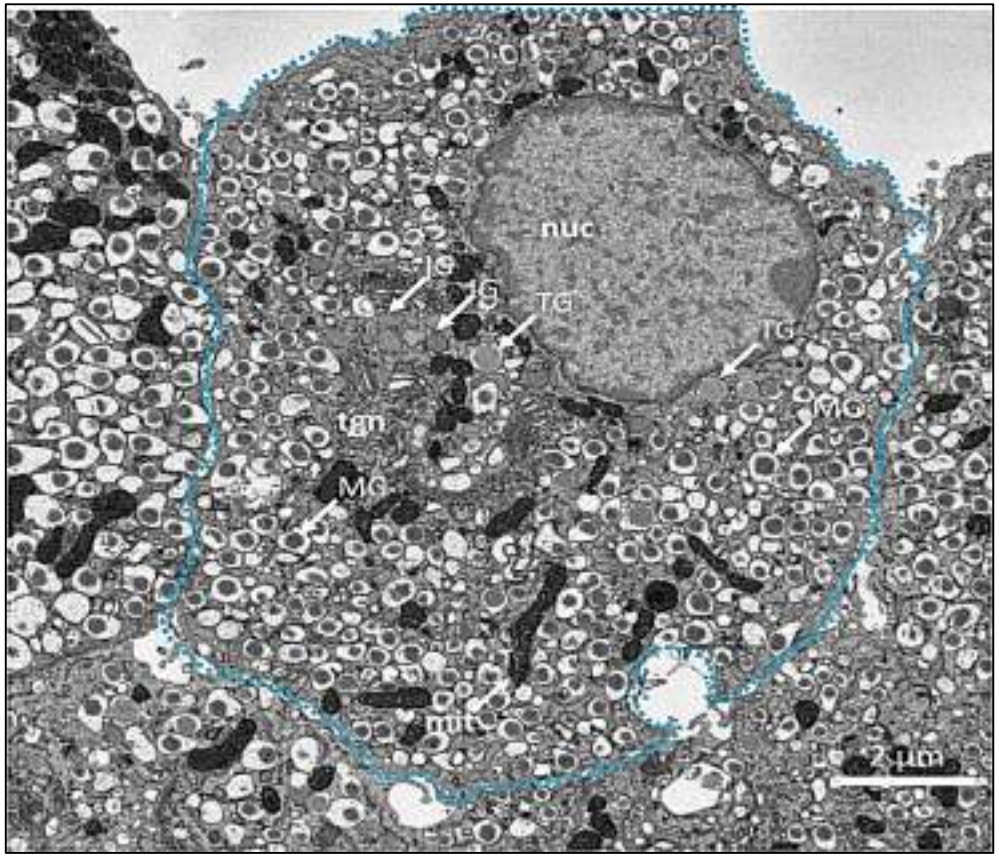
- Produce **insulin h** that **lower** blood sugar
- Cells are small in size, most numerous cell type, central in location in the islets
- Cells divide at very slow rate
- Beta cells secret C- peptide at the same time they sec. insulin.
- C- peptide is a sign that your body is producing insulin

  It prevents neuropathy and vascular problems.

  C- peptide is used as a marker in diabetic patients to evaluate the amount of functional B cells
- B cells secretes GABA which
- suppress glucagon secretion



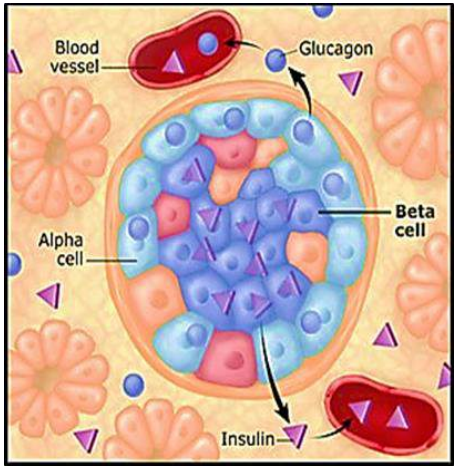
Beta cells

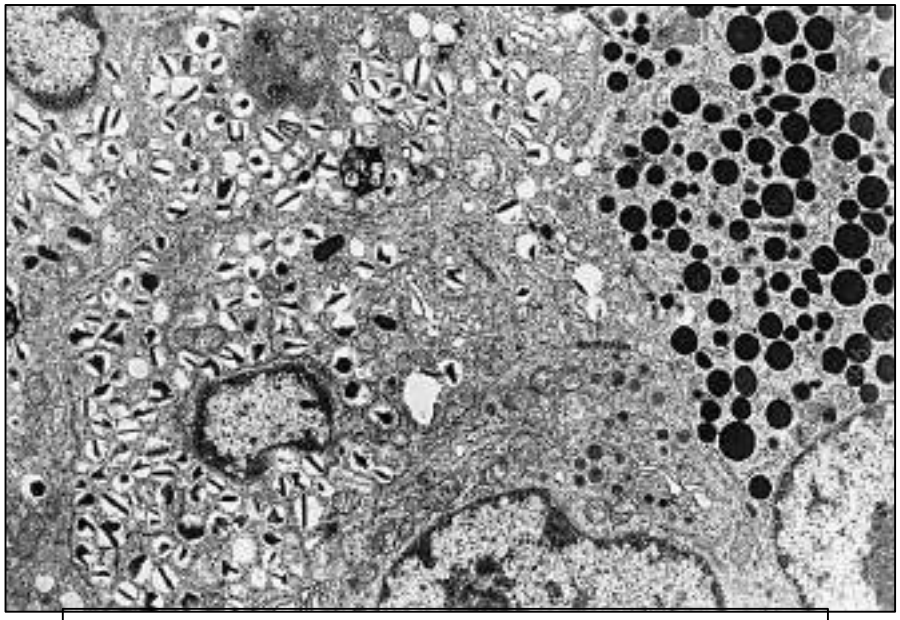


With EM the secretory granules that contain insulin inside B cells have a unique appearance have a rectangular crystalline dense core surrounded by an electro lucent halo

Alpha (A) cells (15%):

- Produce **glucagon H** that **increases** blood sugar
- Cells larger in size, fewer in number, peripheral location in Islets
- EM the secretory granules are numerous with homogenous dense core





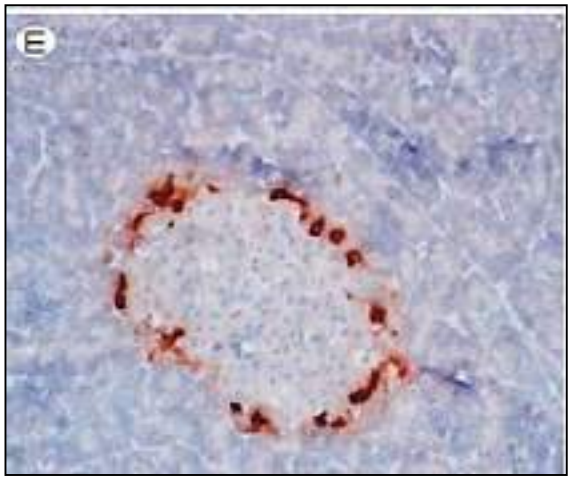
Insulin granules vs glucagon granules

Alpha cells

Delta cells:

- Secret somatostatin (growth inhibiting factor) ↓ other hormones (insulin & glucagon)
- Cells scattered at periphery and less abundant

Delta cells

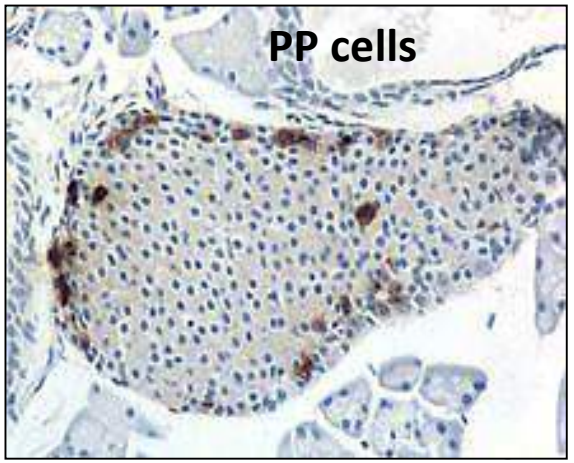


Ganglion cells:

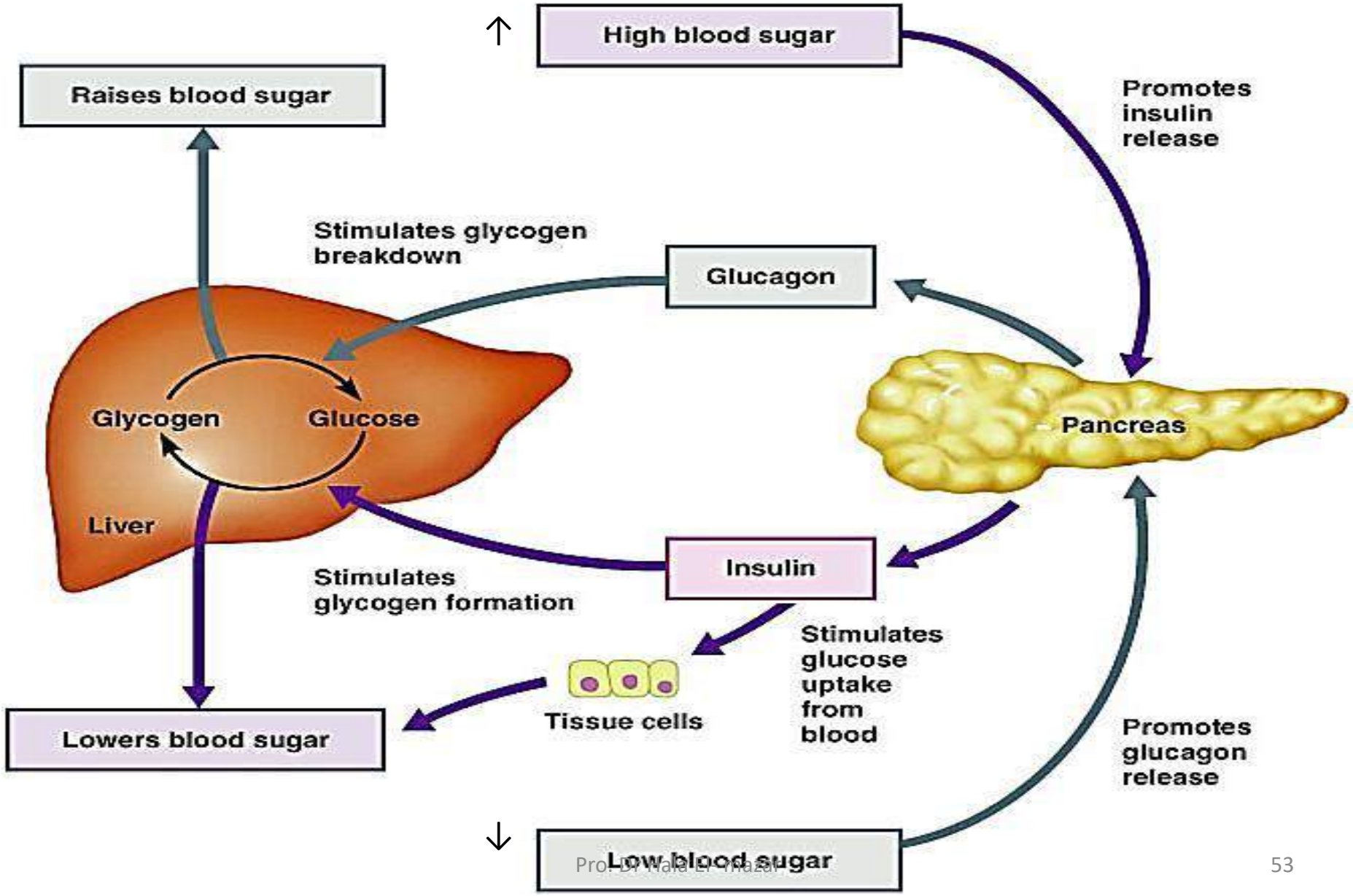
- Aggregation of nerve cells for autonomic nervous control of islets secretion

F (PP) cells (most peripheral)

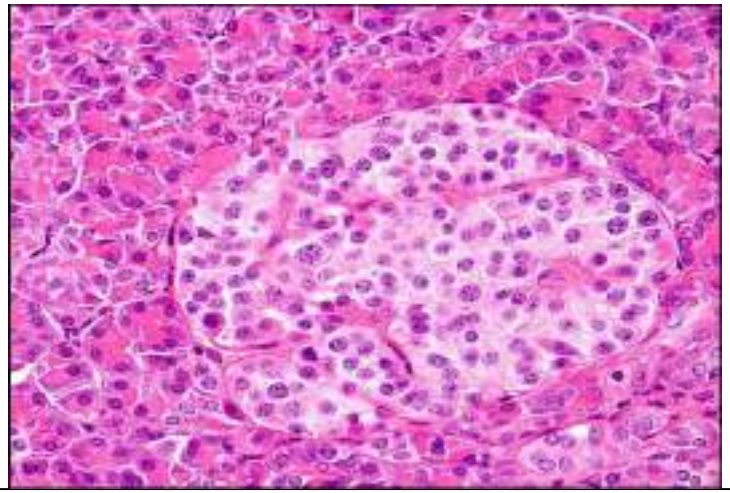
- Very few
- Secrete pancreatic polypeptide h.
- Regulate exocrine pancreas secretions

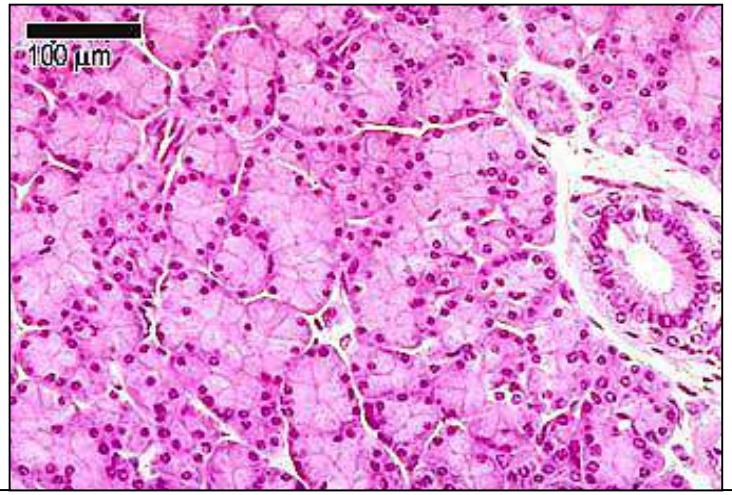


Regulation of blood glucose level



Pancreas vs. Parotid





Pancreas

- **Capsule: thin**
- **Trabeculae: thin, loose**
- **Ducts: few, NO striated secretory ducts inside the lobules**
- **Acini: larger**
  Centroacinar cells in lumen
- **Islets of Langerhans: present**

Parotid

- **Thick**
- **Thick**
- **Abundant, striated secretory ducts are prominent inside the lobules**

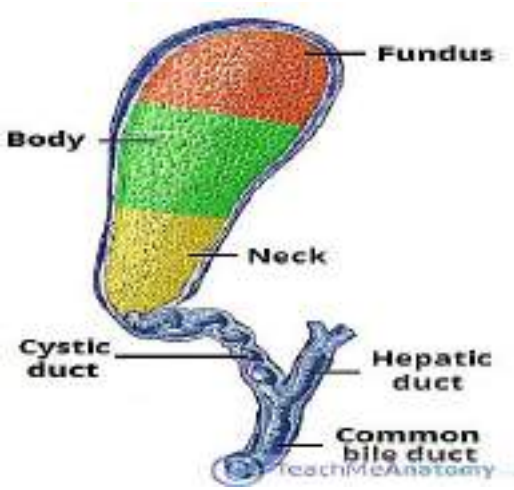
Smaller

No centroacinar cells

- **Abscent**

Gall bladder & biliary tract

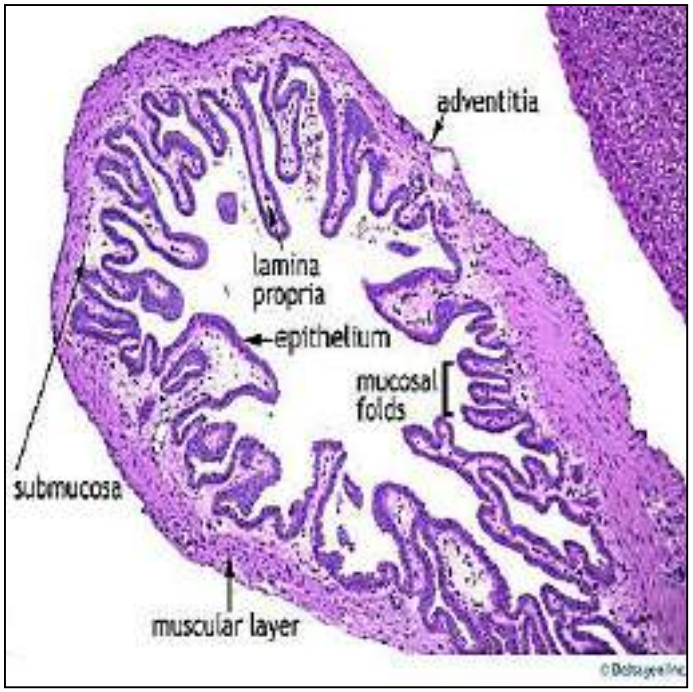
- Hollow pear shaped organ
- Attach to the lower surface of liver
- It stores and concentrate bile secreted by liver
- Wall of gall bladder consists of:



Mucosa: (highly folded)

epithelium: simple columnar with microvilli

No muscularis mucosa



Musculosa

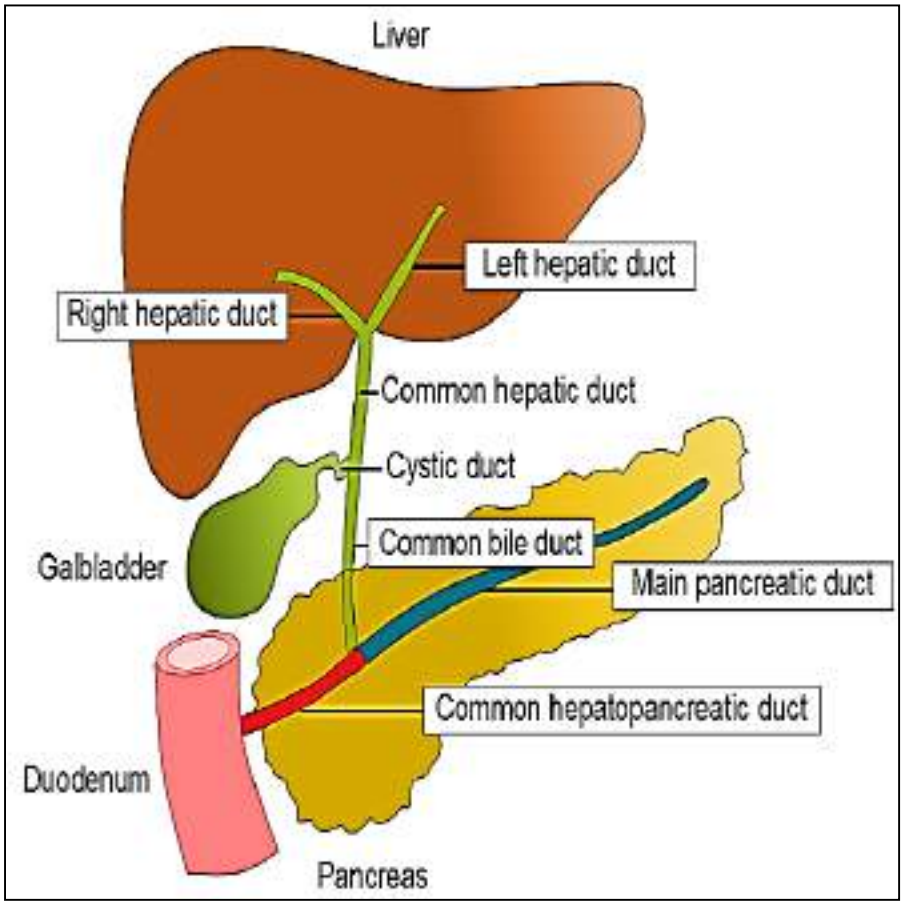
Bundles of irregularly arranged smooth m.

Fibers , elastic & collagenous fibers

Serosa

Biliary tract:

Bile canaliculi → bile ductules (canals of Hering)
→ bile ducts → hepatic ducts (RT & LF hepatic ducts)
→ common hepatic duct → merge with cystic duct
→ common bile duct
→ merge with pancreatic duct → ampulla of Vater
→ open in duodenum



Liver regeneration:

Liver cells have high regeneration capacity

Thank you