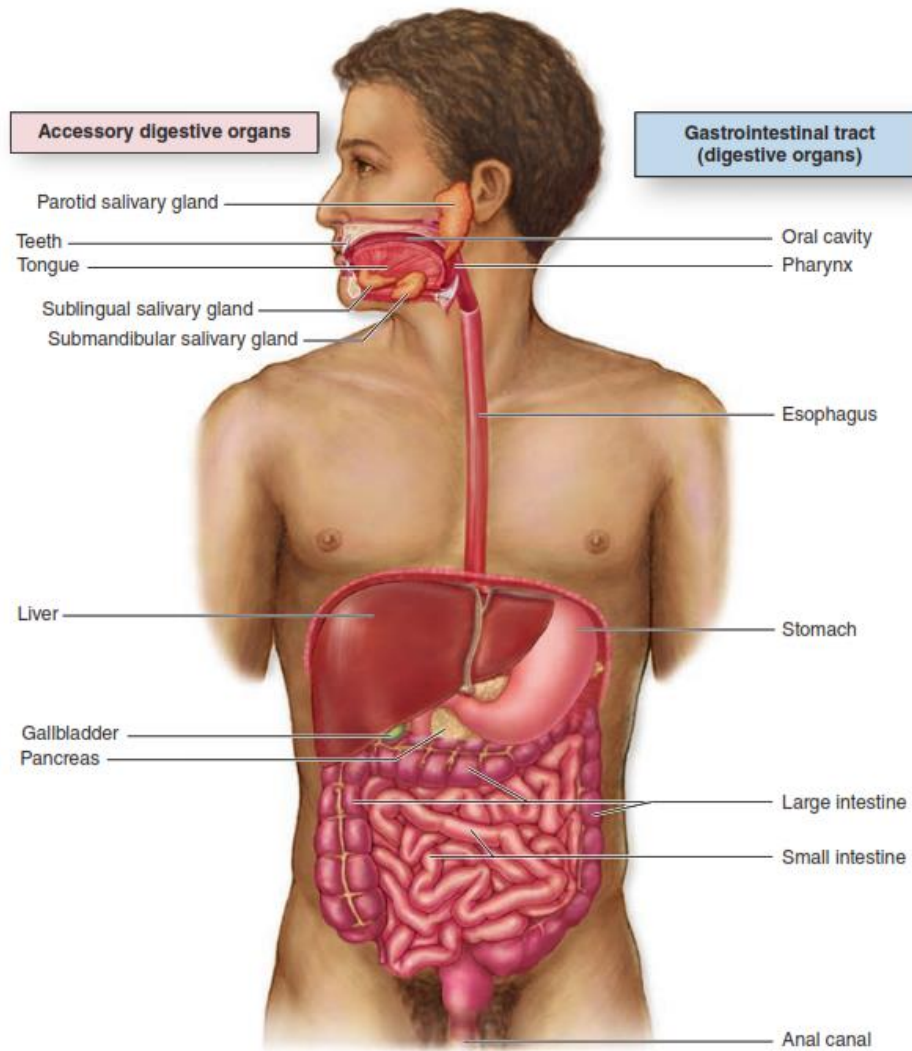


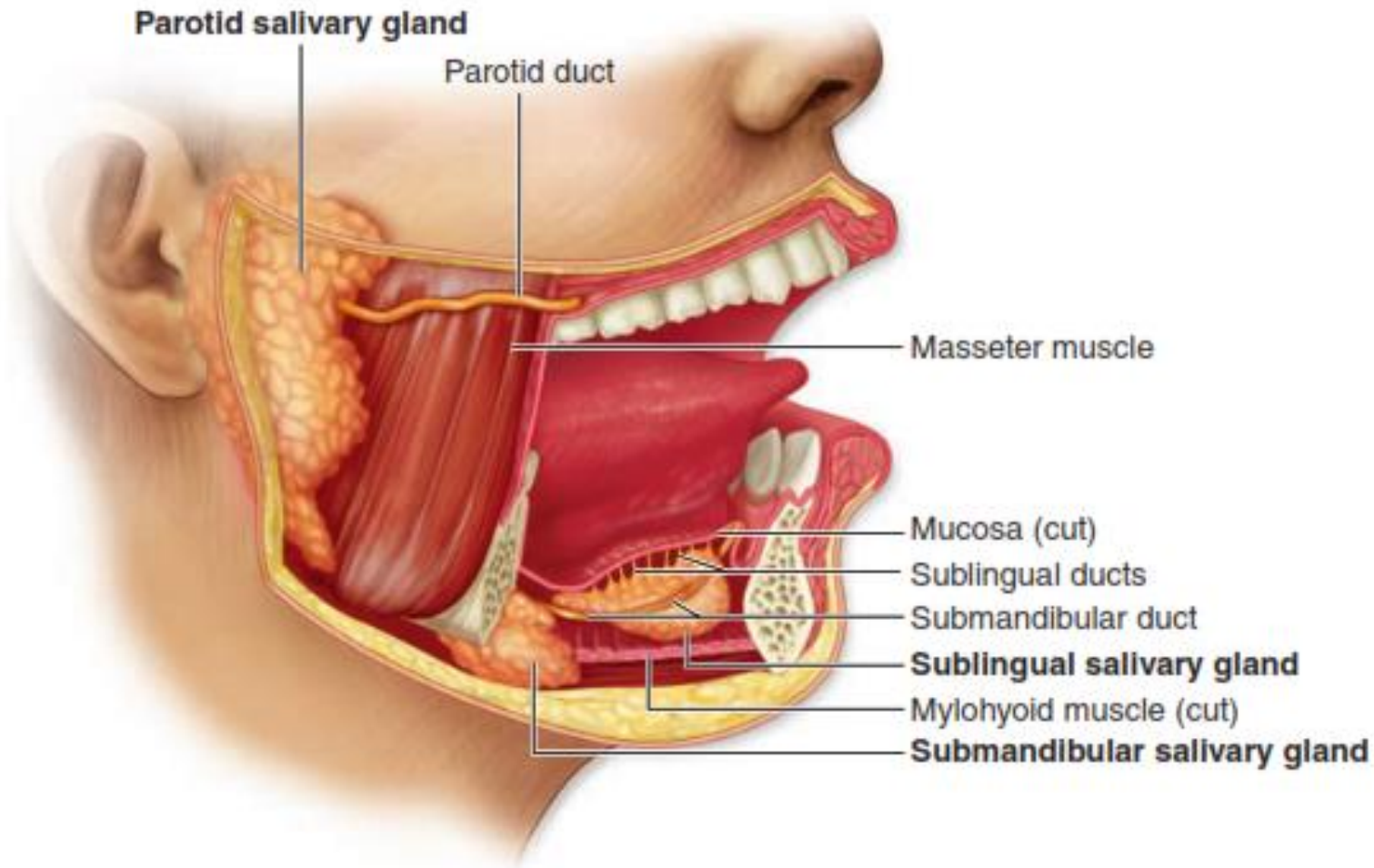


University of Kragujevac  
Faculty of Medical Sciences  
Integrated Academic Studies of Medicine  
Department of Histology and Embryology

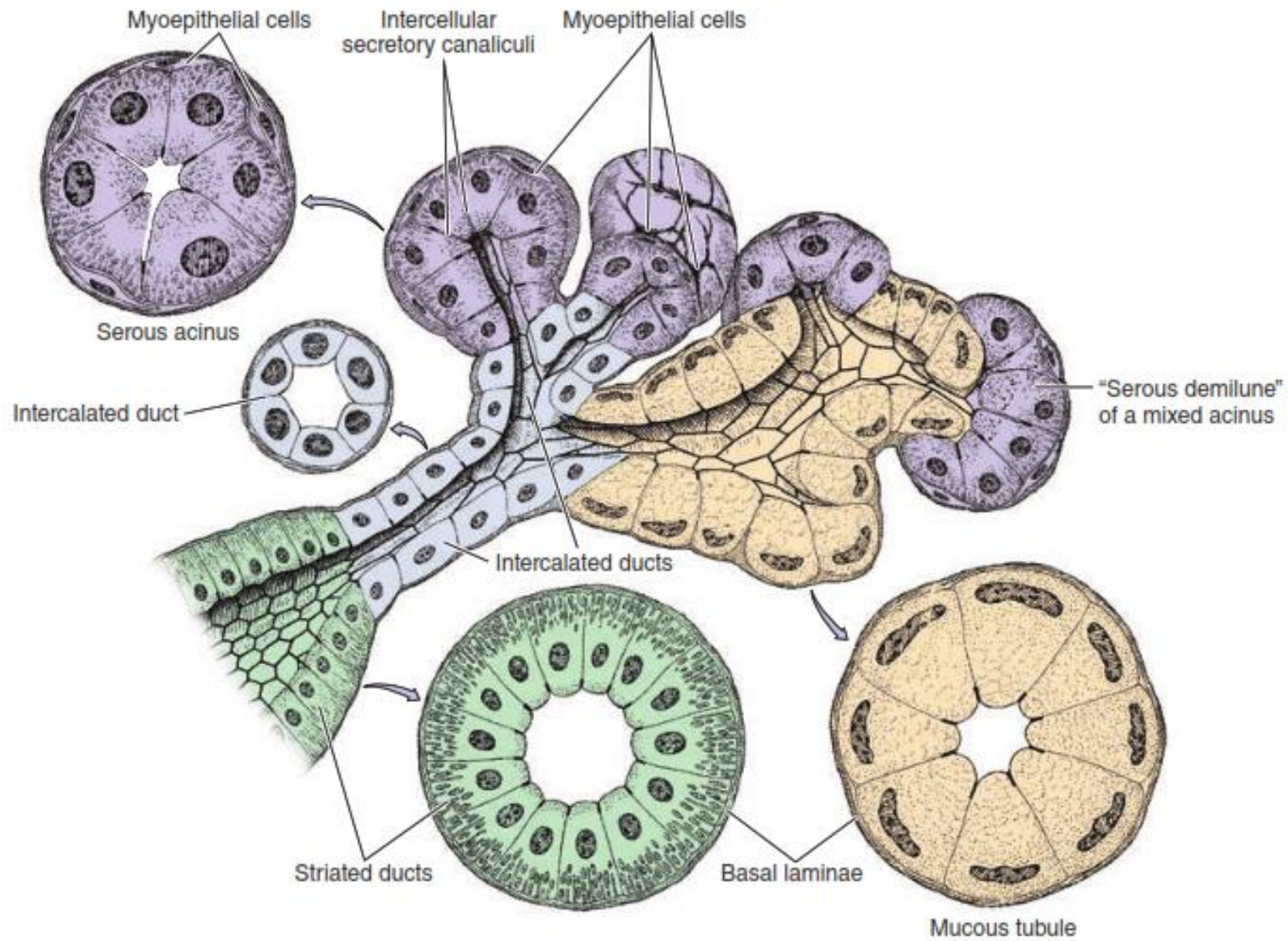
# Organs Associated with the Digestive Tract



- **SALIVARY GLANDS**
- **LIVER**
- **PANCREAS**
- **GALLBLADDER**

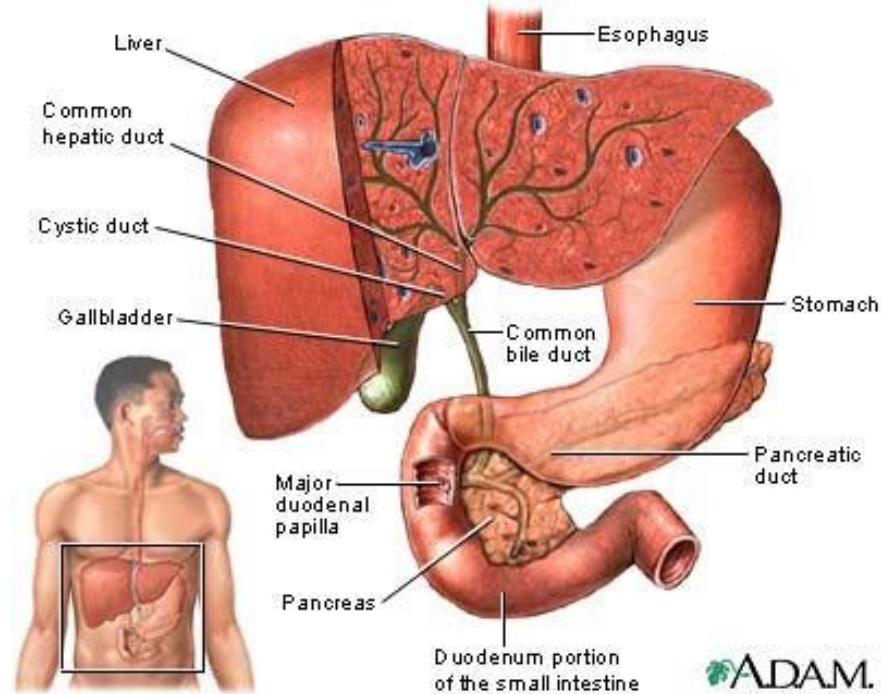


There are three bilateral pairs of major salivary glands, the **parotid**, **submandibular**, and **sublingual glands**, which together produce about 90% of saliva. Their locations, relative sizes, and excretory ducts are shown here. These glands plus microscopic minor salivary glands located throughout the oral mucosa produce 0.75-1.50 L of saliva daily.



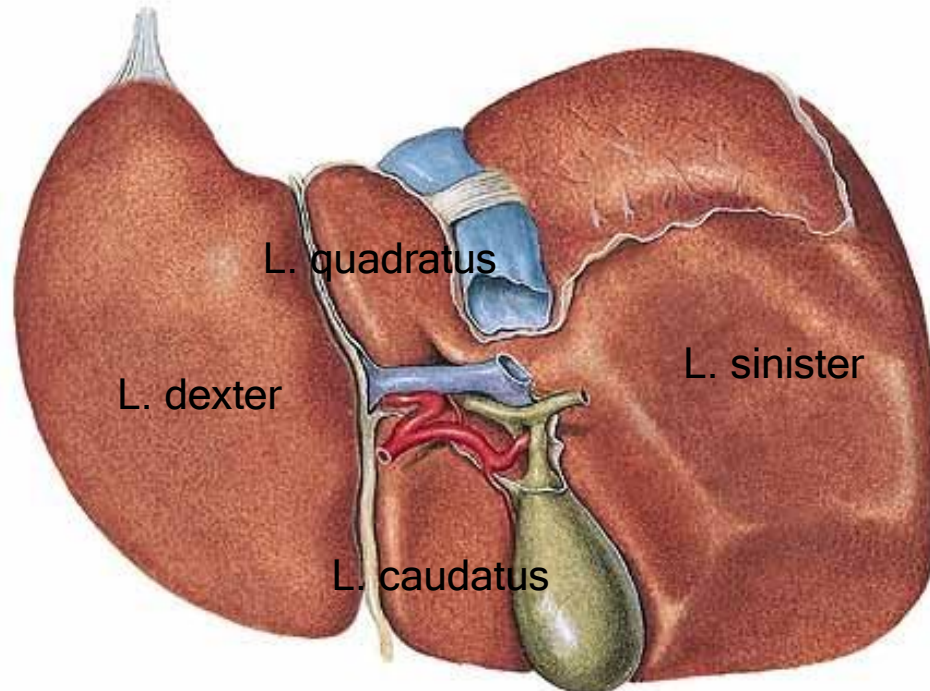
**LIVER**





# LIVER

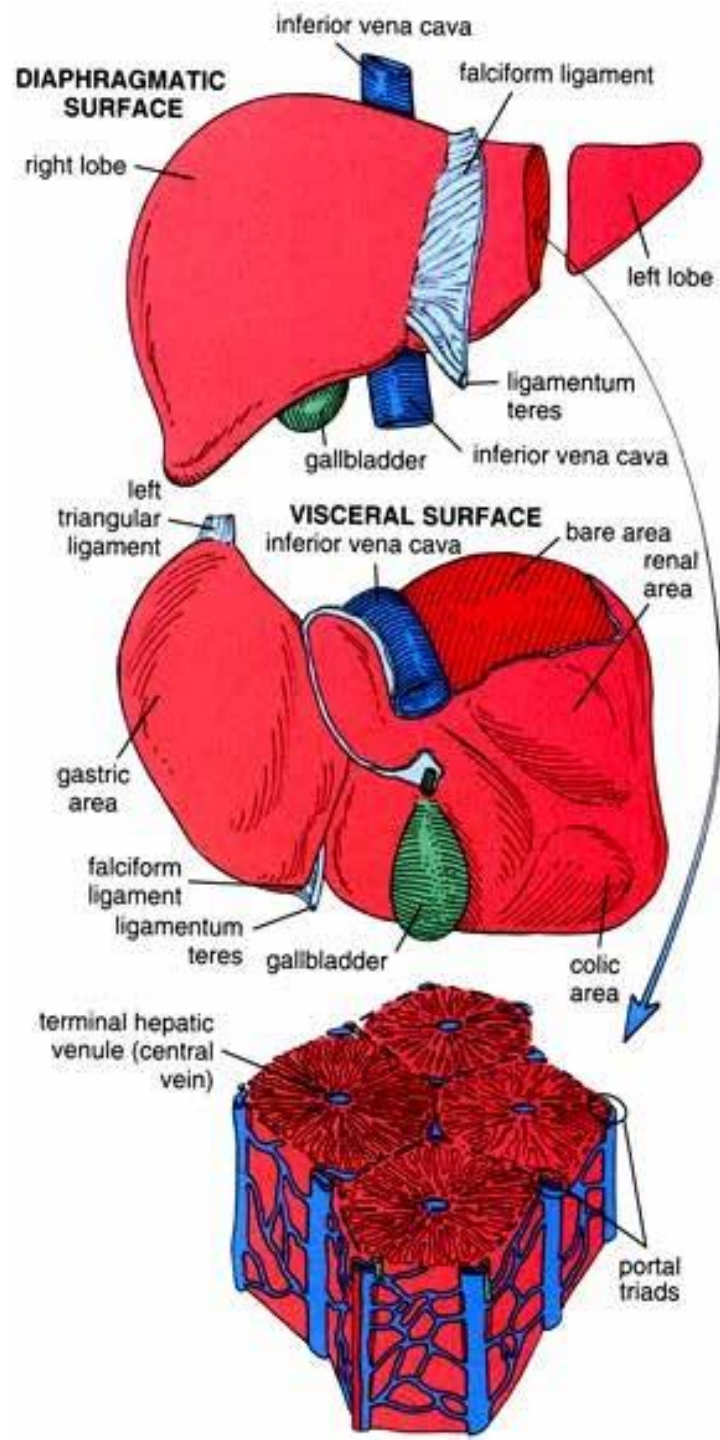
- The largest gland of the human body (1-1.5 kg)
- 2.5% of body weight
- It contains 4 lobes and a large number of lobules
- Gleason's capsule and visceral peritoneum
- In the lower part of the liver there is a hilus
- A specific position in the circulatory system



# LIVER

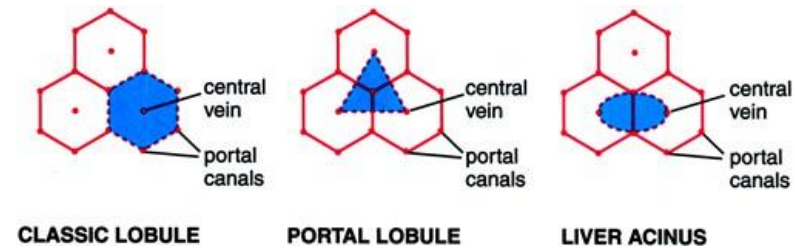
The structural components of the liver are:

- a) hepatocytes - parenchymal cells arranged in the form of hepatic plates (laminae hepatis);
- b) connective tissue stroma permeated with blood vessels, nerves, lymphatic vessels and bile ducts;
- c) sinusoidal capillaries or sinusoids of the liver located between the hepatic plates;
- d) perisinusoidal spaces limited by liver sinusoids and hepatic plates;
- e) Kupffer and perisinusoidal (Ito) cells located in sinusoids and perisinusoidal spaces.



# The structural components of the liver

- The basic morpho functional unit of the liver can be considered the classic liver lobule, portal lobule or liver acinus.





# Classic liver lobule

- A classic liver lobe is a block of liver parenchyma with a prismatic shape, limited by a narrow layer of loose connective tissue.
- The liver contains about a million classical lobules.
- Each lobule consists of a network of parenchymal cells (hepatocytes), a labyrinth system of blood capillaries (sinusoidal capillaries or liver sinusoids) and a network of bile capillaries.
- The lobules have the shape of irregular pentagonal or hexagonal prisms about 2 mm long and about 0.7 mm in diameter.
- In humans, the interlobular connective tissue is scarce.

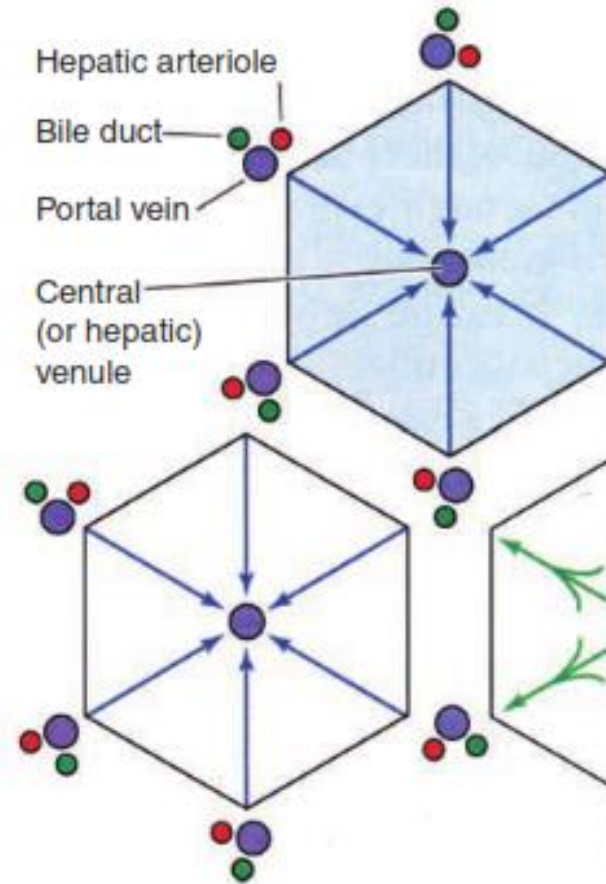
# Classic liver lobule

- In places where the corners of three adjacent lobes meet, the connective tissue is more abundant and that part of the interlobular space is designated as Kiernan's space or portal canal.
- In the connective tissue of the portal canal there is a portal triad consisting of:
  - a) vena interlobularis, branch of the portal vein;
  - b) arteria interlobularis, a branch of the hepatic artery
  - c) ductus billiferus, initial interlobular bile duct.
- In addition to the blood vessels and the bile duct in Kiernan's space, there are one or more lymphatic vessels, as well as nerve fibers that follow the blood vessels and enter the lobulus together with them.

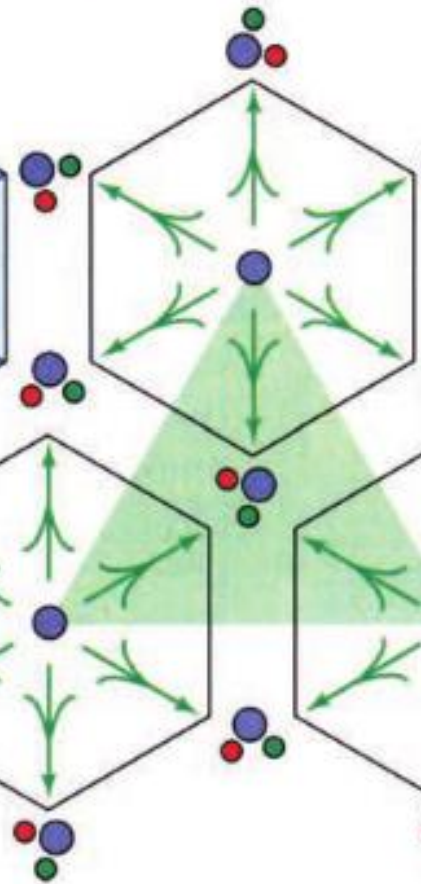
# Classic liver lobule

- In the center of the classic lobule there is a post-capillary venule better known as the vena centralis.
- The skeleton of the lobule is built by hepatocytes arranged in rows that in space form plates called laminae hepatis or Remak's plates. Remak's plates are made of one or two layers of hepatocytes, and extend in the form of rays from the central vein to the periphery of the lobule.
- In the labyrinthine space between the hepatic laminae, there are liver sinusoids.
- Hepatocytes from the periphery of the lobule form a border plate that separates the lobule from the surrounding connective tissue. In the boundary plate there are numerous openings through which blood vessels enter the lobulus, and bile ducts exit it. The classic lobule is a morphological reflection of the vascular network of the liver.

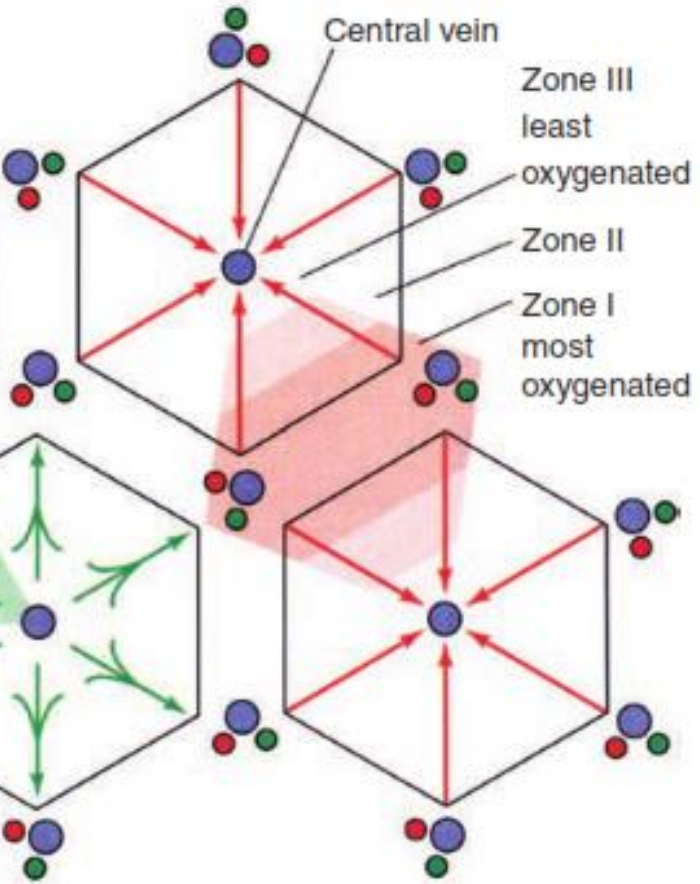
**(a) Classic Hepatic Lobule**  
Drains blood from the portal vein and the hepatic artery to the hepatic or the central vein



**(b) Portal Lobule**  
Drains bile from hepatocytes to the bile duct

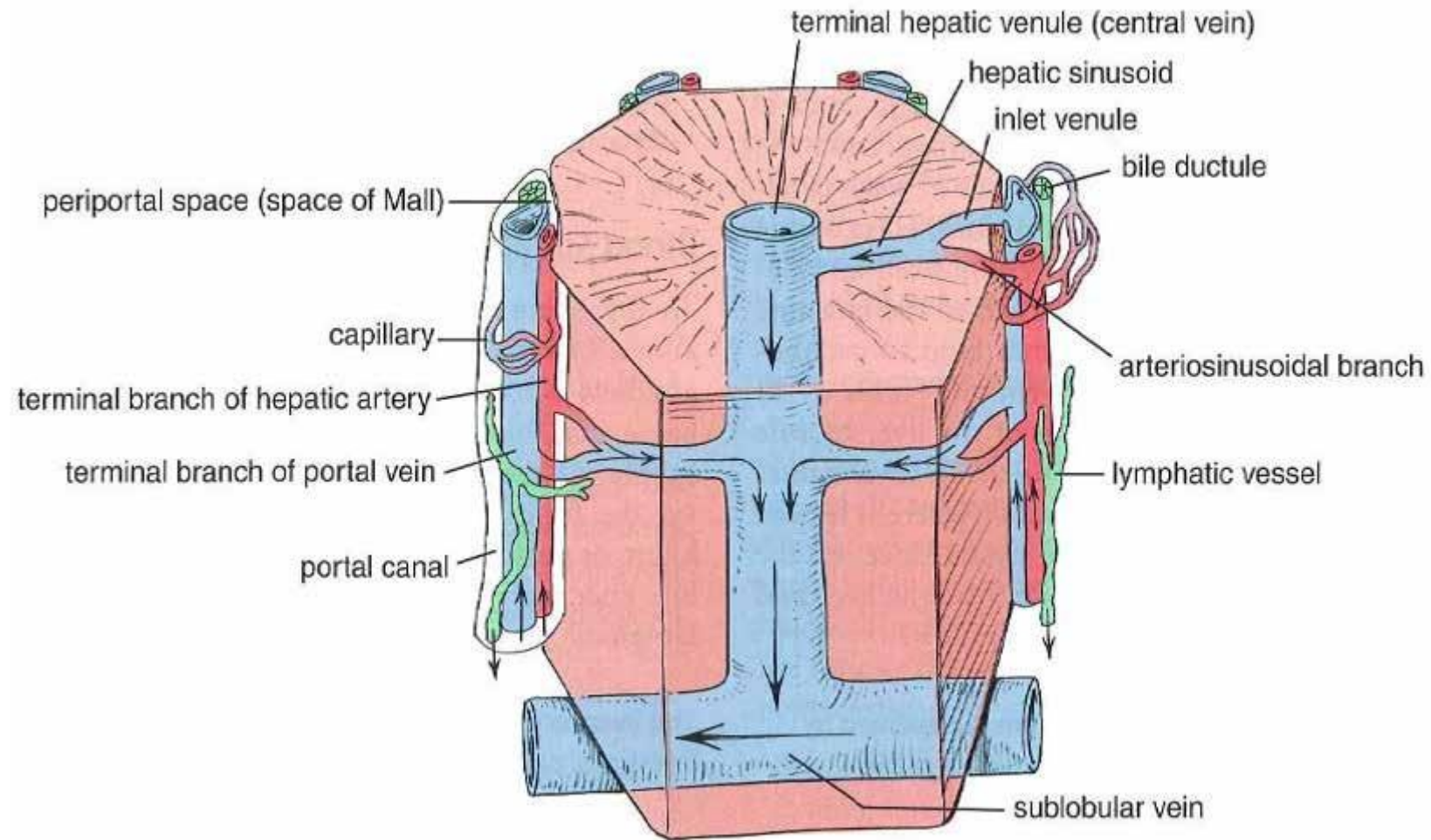


**(c) Hepatic Acinus**  
Supplies oxygenated blood to hepatocytes





# Classic liver lobule

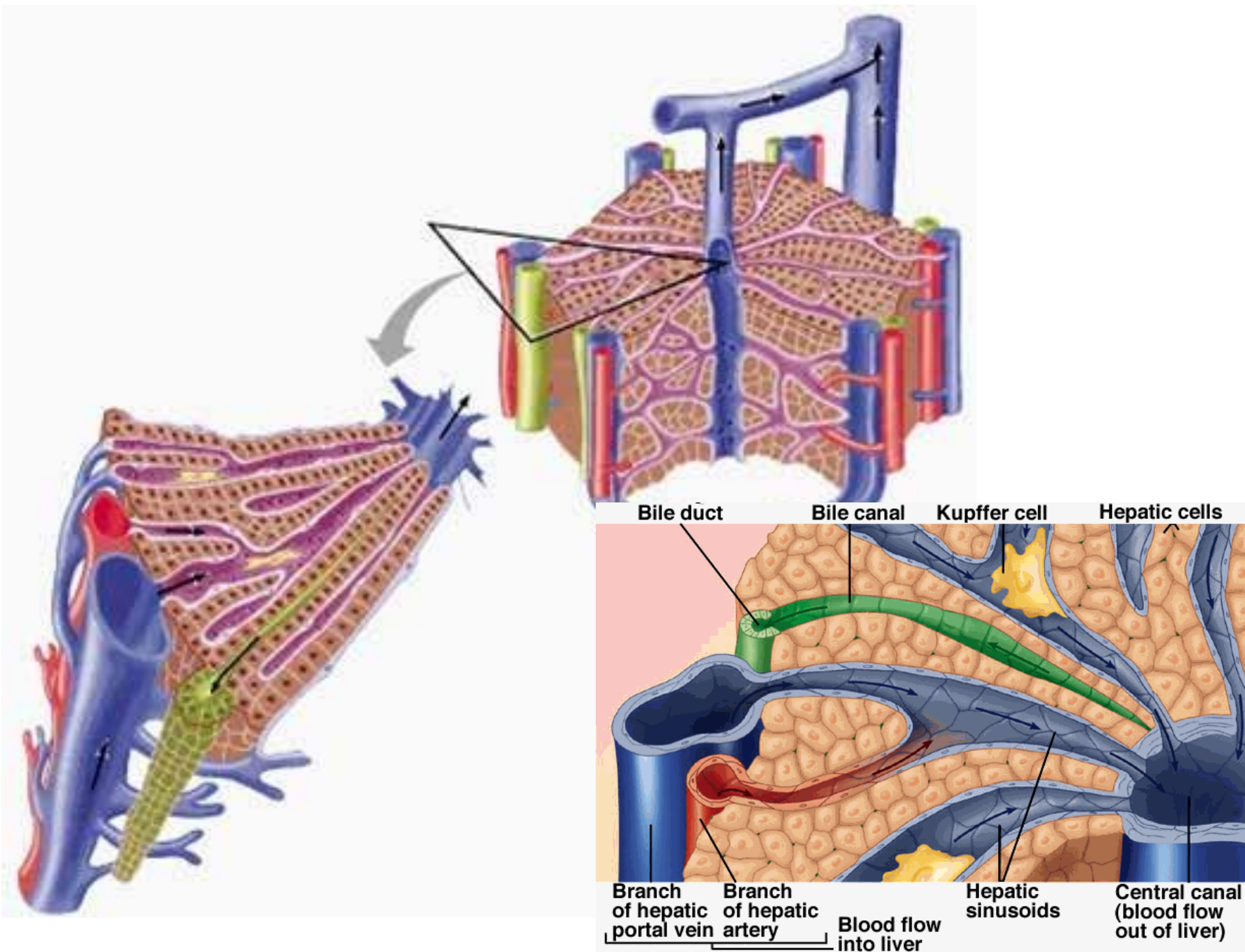


# Liver blood flow

- The liver is a specific organ in that it receives  $\frac{3}{4}$  of venous blood and only  $\frac{1}{4}$  of arterial blood.
- The functional blood vessel is the vena portae, and the nutritional artery is the hepatica propria.
- The portal vein brings blood from the intestines, spleen and pancreas.
- About 75% of the blood destined for the liver reaches the liver through the portal vein.
- After passing through the hilus, the portal vein divides into a larger number of branches that enter Kiernan's spaces - interlobular veins.
- Interlobular veins give branches that wrap around the lobulus - distributing venules.
- Tiny branches called perforating venules separate from the distributing venules, which break through the border plate and flow into the sinusoids of the liver.

# Liver blood flow

- Arteria hepatica propria brings oxygenated blood to the liver.
- It branches in the same way as the portal vein giving interlobular arteries which further branch into distributing arterioles.
- From the distributing arterioles, on the one hand, perforant arterioles arise, which penetrate through the border plate and pour oxygenated blood into the sinusoids of the liver.
- From the distributing arterioles, a capillary network is formed that feeds the interlobular connective tissue.
- The capillary network continues with venules that release deoxygenated blood into the liver sinusoids, which means that part of the blood from the nutritional bloodstream also reaches the lobulus as venous blood.





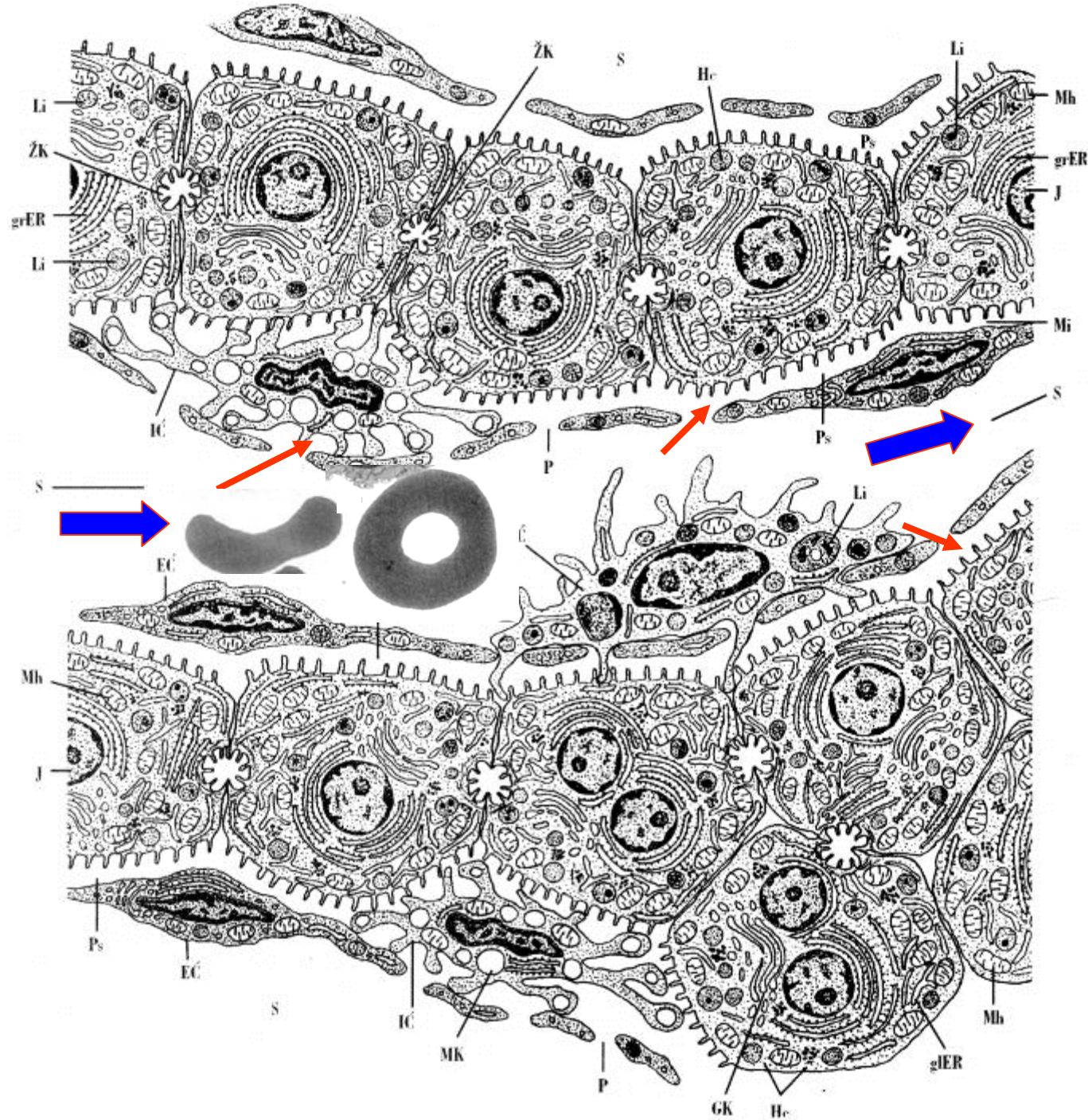
# Sinusoidal capillaries

- Liver sinusoids are wide and winding capillaries of sinusoidal (discontinuous) type.
- Liver sinusoids are made up of endothelial cells and stellate sinusoidal macrophages known as Kupffer cells.
- Endothelial cells:
  - pinocytotic vesicles
  - actin and myosin filaments
  - organelles poorly represented
  - pore diameter up to 3  $\mu\text{m}$

# Sinusoidal capillaries

## Kupffer cells

- liver macrophages
- 15% of liver cells
- deposit iron and Er fragments
- they secrete prostaglandins and cyclins



Sinusoidal  
capillaries

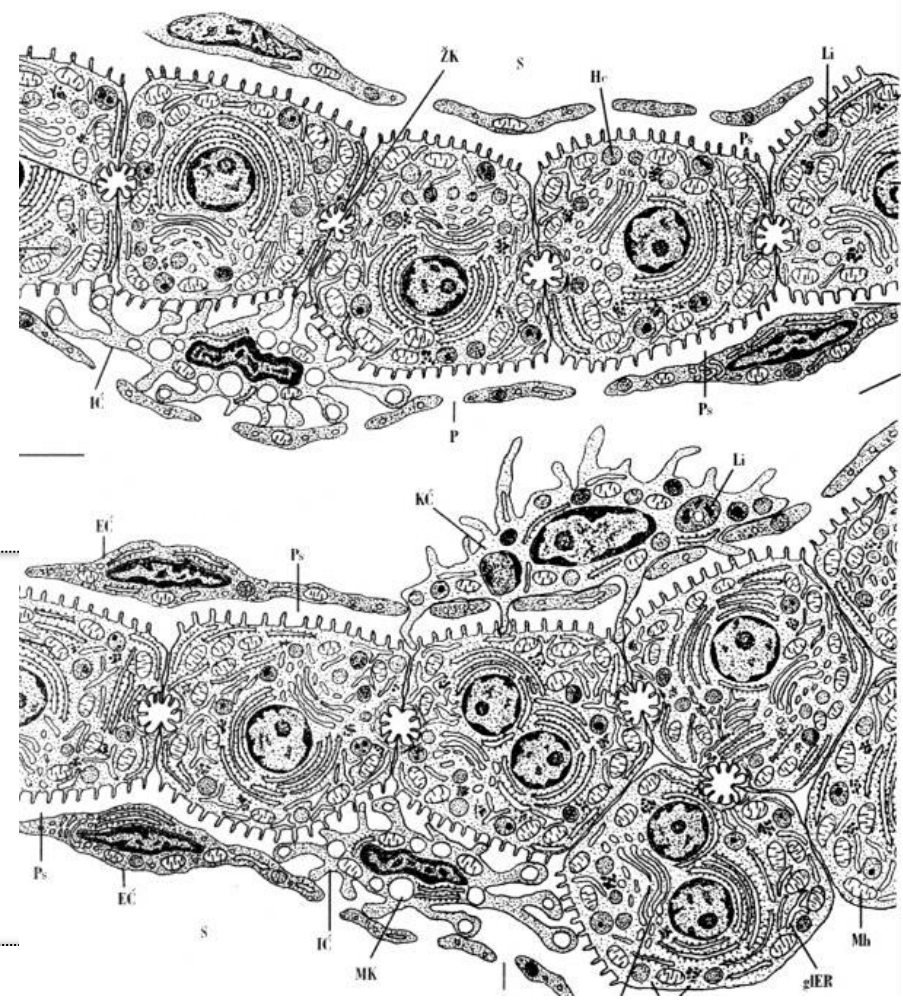
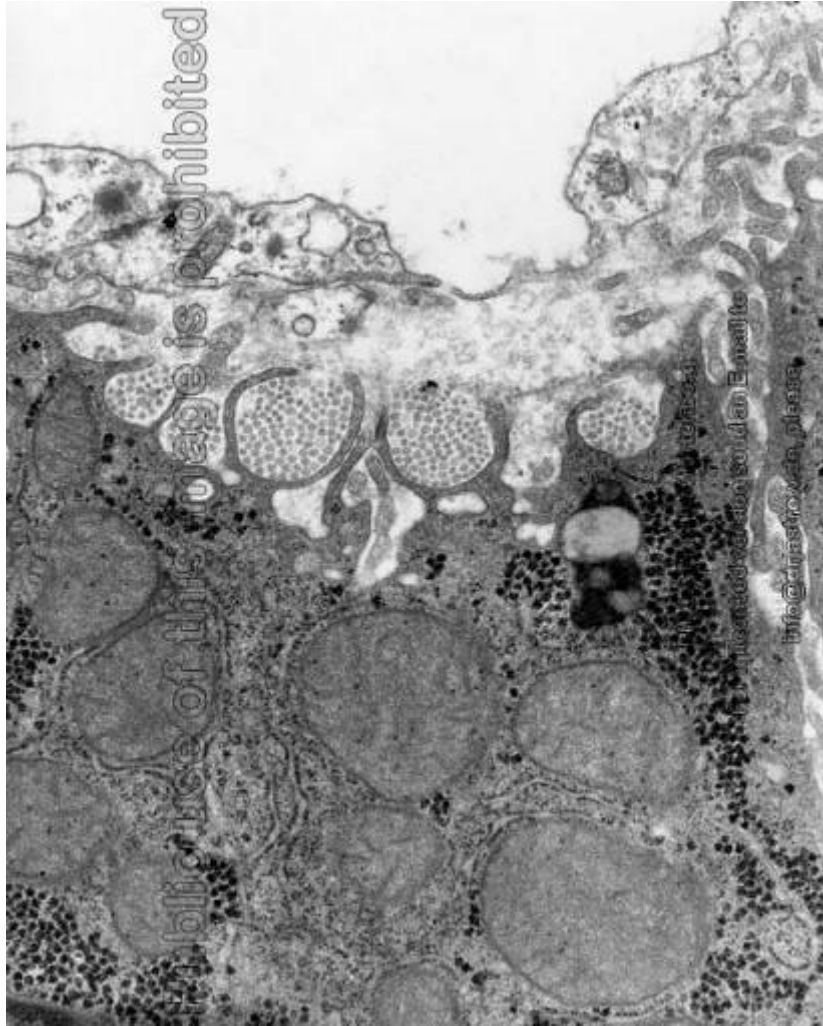
# Perisinusoidal spaces

- Perisinusoidal or Disse spaces are located between sinusoidal capillaries and hepatocytes.
- The inner border of Disse's space is formed by the basal surfaces of sinusoidal endothelial cells, and the outer by the basal surfaces of hepatocytes.
- Blood plasma is filtered through the pores in the wall of the sinusoid, enters the perisinusoidal space and "bathes" the parenchymal cells of the liver.
- Microvilli extend from the basal surface of hepatocytes into the perisinusoidal space, increasing the surface area through which the exchange of matter between liver cells and blood plasma is carried out about 6 times.



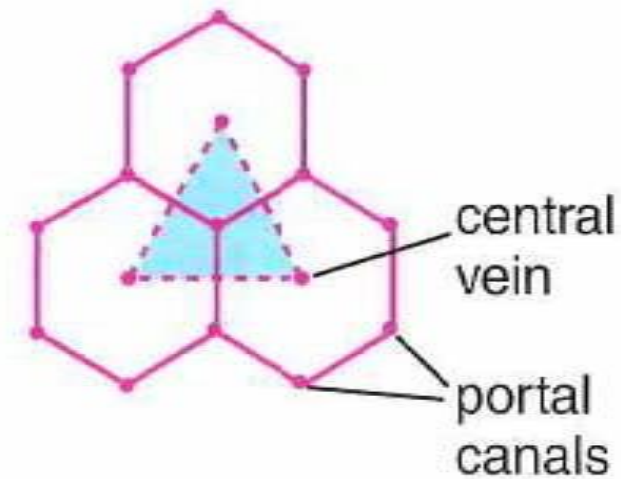
# Perisinusoidal spaces

- In the adult liver, liver stellate cells or perisinusoidal (Ito) cells are present in Disse's spaces.
- Ito cells
- store about 80% of the body's vitamin A
- they synthesize reticular fibers
- Lymph vessels. There are no lymphatic vessels in the classical lobule of the liver. The fluid of the perisinusoidal spaces is the equivalent of lymph and it flows through the boundary plate into Mall's spaces. Mall's spaces are narrow fissures between the border plate and the stroma of the portal canal.



# Portal lobule

- If the initial bile ducts are followed, the basic morphofunctional unit of the liver can be considered the portal lobule.
- It is a segment of liver tissue that has the shape of an equilateral triangle in cross-section.
- In the center of that triangle is the portal canal, i.e. ductus biliferus, and its vertices are formed by the three central veins closest to the given biliferous ductus.
- The portal lobule is a morphological reflection of the network of bile ducts.



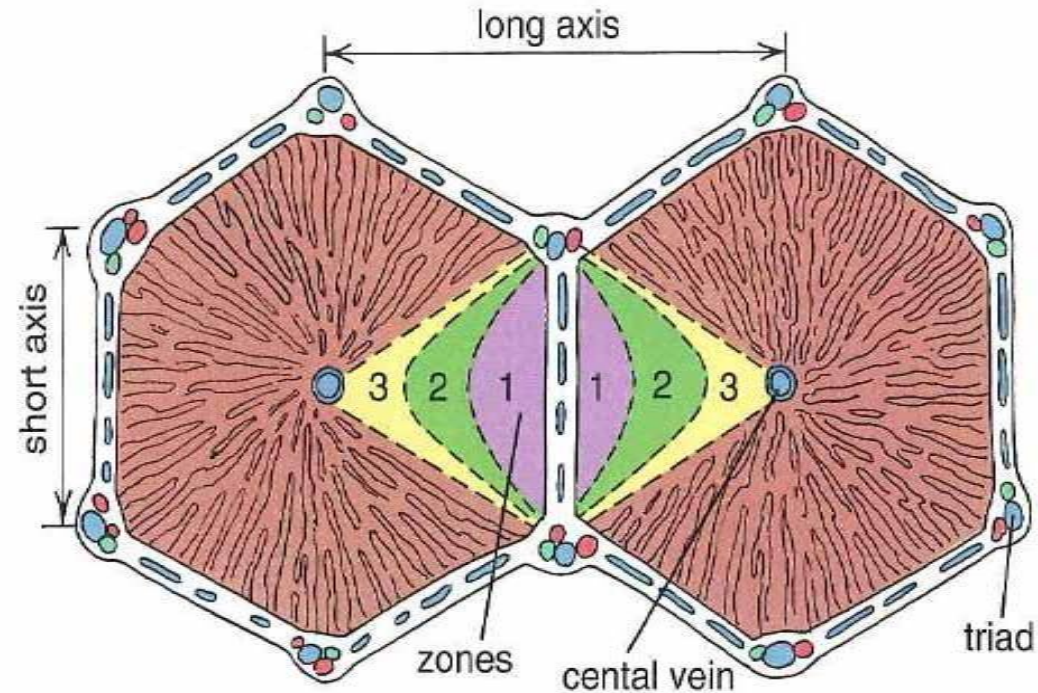
**PORTAL LOBULE**

# Liver acinus

- Hepatic acinus is the smallest structural and functional unit of liver tissue suitable for the interpretation of metabolic activity and pathological processes in the liver, it is also called Rapaport's acinus.
- Liver acinus is a morphological reflection of liver function in physiological and pathological conditions.
- It is a rhombus-shaped segment of liver tissue that covers approximately one-sixth of each of two adjacent classical liver lobules along with the interlobular ligament that separates them.
- The vertices of such an imaginary rhombus are formed by two close portal canals and two central veins of adjacent classical lobules. The shorter axis of the acinus is the line that connects the two portal canals and corresponds to the border between the two classic lobules, while the longer axis connects their central veins.

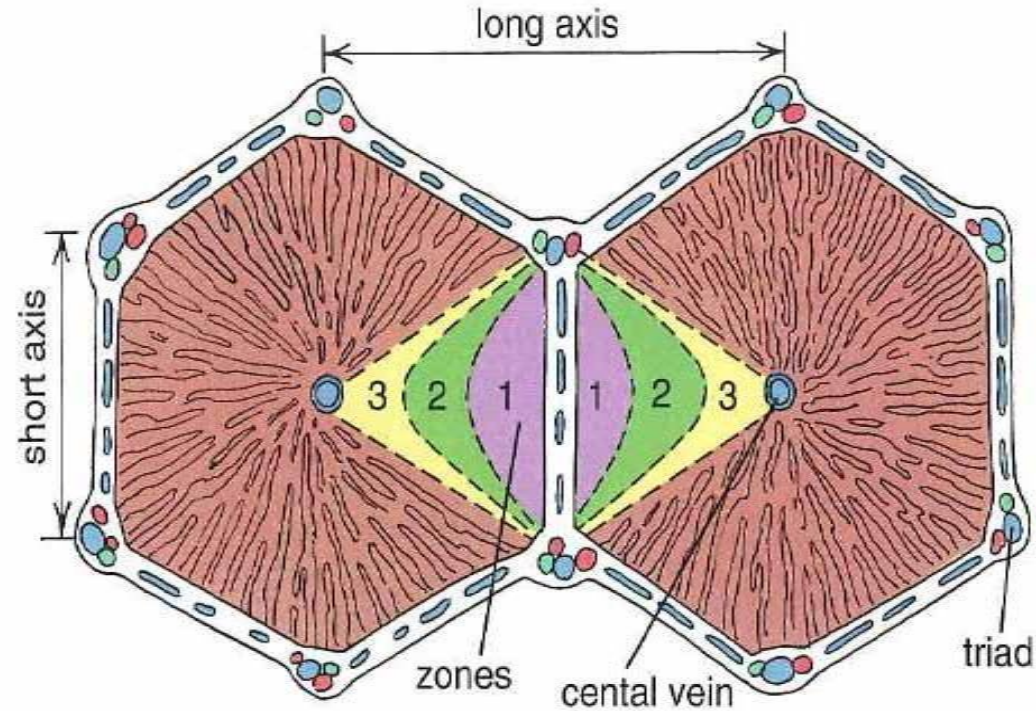


# Liver acinus



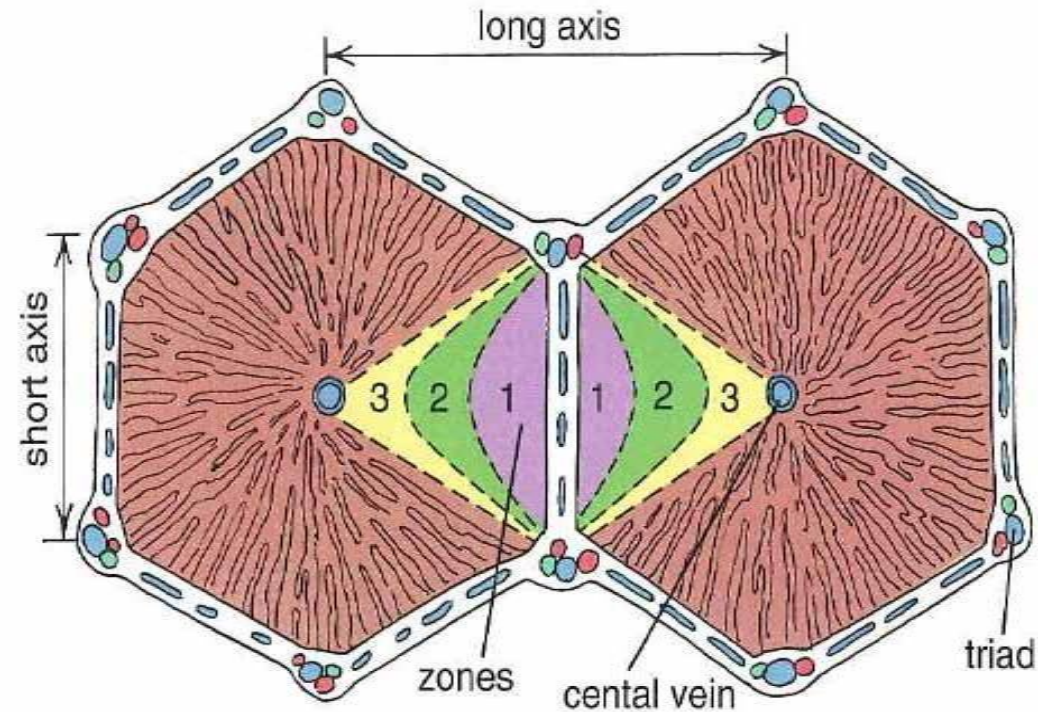
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# Liver acinus

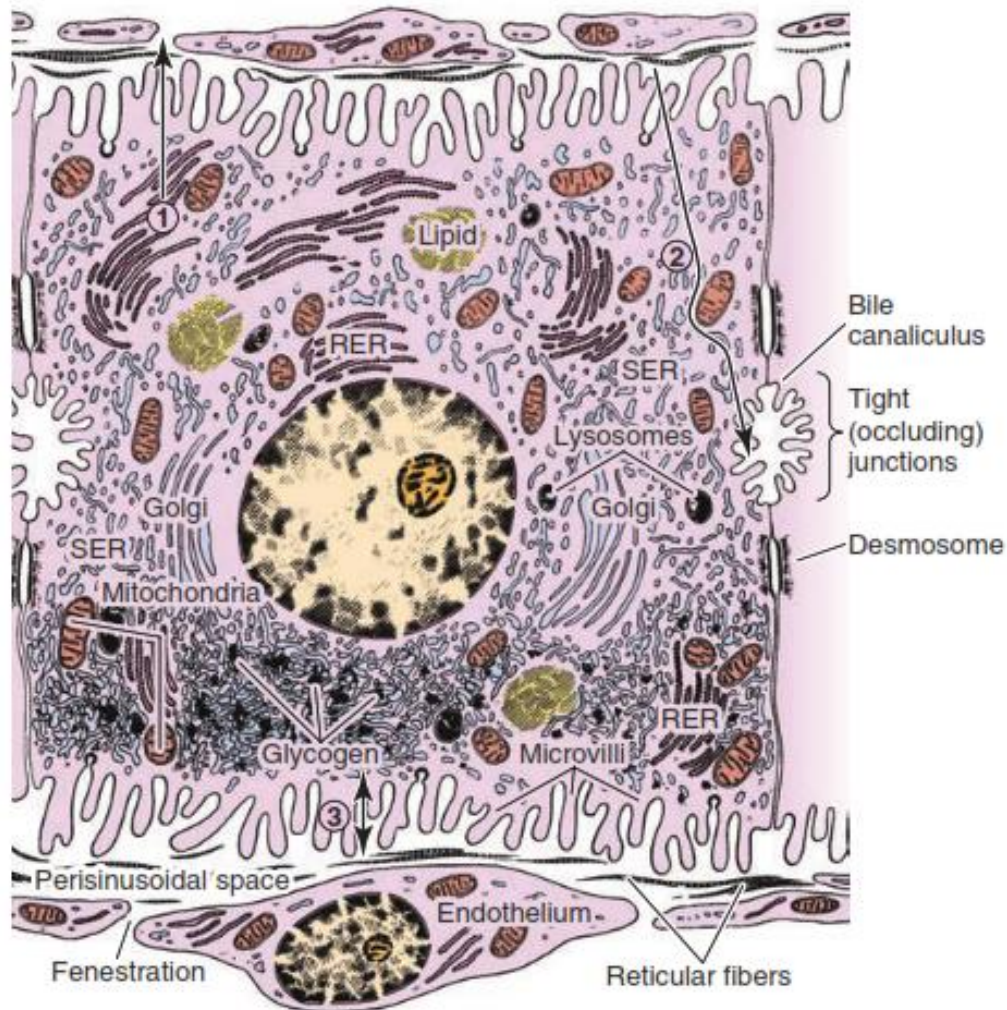
- In the center of the liver acinus there are distributing arterioles and venules, as well as their terminal branches.
- Three zones of hepatocytes:
  - **zone I** hepatocytes are located on the periphery of the classical lobule (most active, most O<sub>2</sub> and food, but also toxins),
  - **zone III** hepatocytes are located around the central vein and are the furthest from the distributing blood vessels (centrilobular necrosis),
  - **zone II** hepatocytes extends between zone I and zone III.

# Hepatocyte

- Hepatocytes are glandular cells that make up about 80% of the liver's cell population. They have a polygonal shape and a size of 20-30  $\mu\text{m}$ .
- 25% of hepatocytes have two nuclei, and the majority of mononuclear hepatocytes are polyploid
- The plasmalemma of hepatocytes shows different specializations depending on the orientation.
- The section of the plasmalemma facing the sinusoids is referred to as the basal or vascular domain. It has numerous microvilli and receptors to control the intake of substances.
- The section of the plasmalemma that rests on neighboring hepatocytes and builds bile capillaries with them is called the lateral or biliary domain.
- The sides of hepatocytes form bile capillaries.

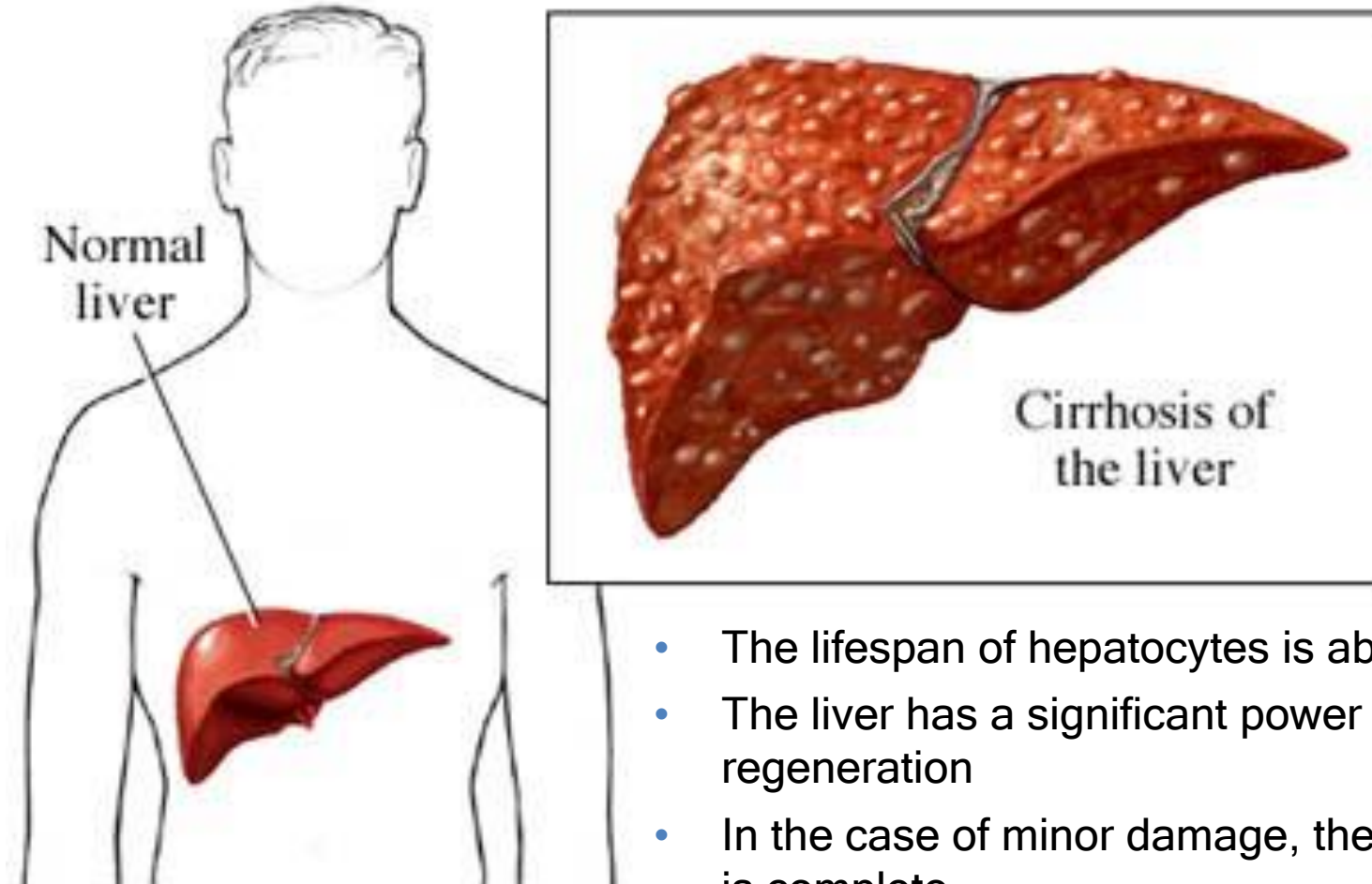


# Hepatocyte



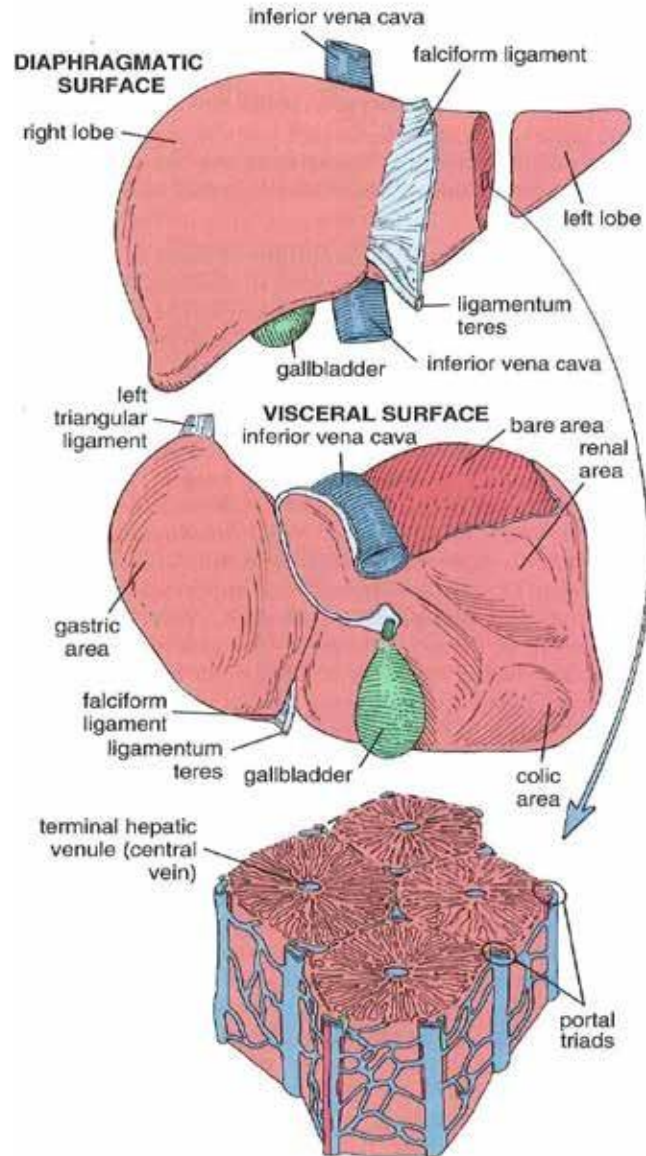
A diagram of hepatocyte cytoplasmic organization, with major functions localized. (1) RER is primarily engaged in synthesis of **plasma proteins** for release into the perisinusoidal space. (2) Potentially toxic compounds, bilirubin (bound to albumin) and bile acids are taken up from the perisinusoidal space, processed by enzymes in the tubulovesicular system of the SER, and secreted into the **bile canaliculi**. (3) Glucose is taken up from the perisinusoidal space and stored in **glycogen granules**, with the process reversed when glucose is needed.

# Liver regeneration



- The lifespan of hepatocytes is about 5 months
- The liver has a significant power of regeneration
- In the case of minor damage, the regeneration is complete
- In case of long-term action of harmful factors, connective tissue is formed, i.e. nodules of different size

# Liver functions



## Production of plasma proteins

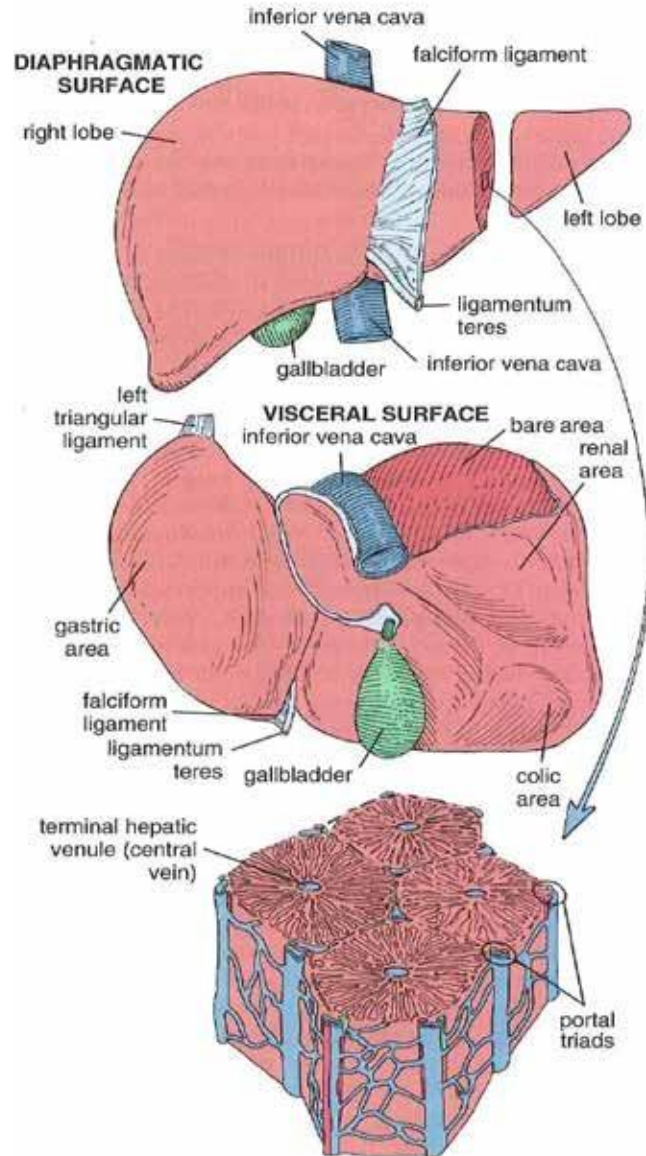
- synthesis of albumin, fibrinogen, prothrombin, lipoproteins (VLDL, LDL and HDL), glycoproteins (haptoglobin, transferrin, hemopexin) and non-immune alpha and beta globulins

## Depot of vitamins and iron

- Vit A (retinol-retinal-rhodopsin)
- Vit D (cholecalciferol) D3 in 25 hydroxycholecalciferol
- Vitamine K
- Fe (ferritin-hemosiderin)



# Liver functions



## Exocrine function

- bile secretion (bile acids, bilirubin, cholesterol, phospholipids)

## Endocrine function

- Vit D, T4 to T3, degradation of insulin and glucagon

## Metabolic functions

- Glucose-glucose 6phosphate-glycogen
- beta Oxidation of fatty acids
- Synthesis of non-essential AKs

## Detoxification and neutralization

- inactivation of non-hydrophilic drugs and toxins
- Phase I by oxidation, hydroxylation (sER and M) cytochrome 450
- Phase II by conjugation with glycine, taurine, etc.

**Bile ducts**

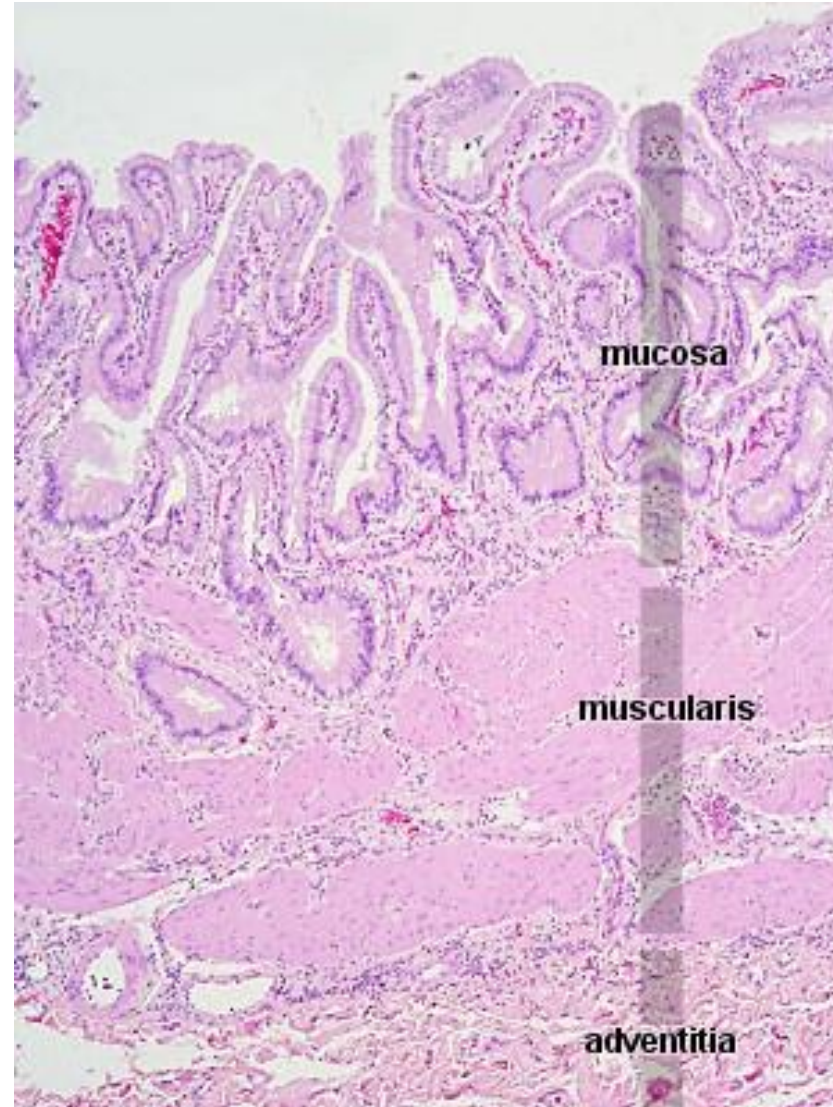


# Bile ducts

- Hepatocytes synthesize bile and secrete it into the system of bile ducts, which further transport it to the gallbladder and duodenum.
- According to the position, the bile ducts are divided into:
- Intrahepatic bile ducts - begin with bile capillaries between hepatocytes, form bile ducts (Hering's ducts, one row of cuboidal cells), then flow into interlobular bile ducts or biliferous ducts (the wall consists of one row of cuboidal cells - they become cylindrical towards the hilus); near the hilus, smooth myocytes appear in the wall.
- Extrahepatic bile ducts - (ductus hepaticus dexter et sinister, ductus hepaticus communis, ductus cysticus, ductus choledochus) consist only of mucosa (simple cylindrical epithelium, lamina propria and lamina muscularis),

# Gall bladder (vesica fellea s. **billiaris**)

- The wall of the gallbladder is made up of:
- **Mucosa** - makes numerous folds that branch and anastomose.
- The epithelium is simple, cylindrical, making openings (Rokitanski-Aschofli crypts, diverticulums)
- Lamina propria - fenestrated capillaries and small venules, no lymphatic vessels
- **Fibromuscular layer** - muscle bundles of a specific arrangement; they contract under the influence of cholecystokinin.
- **Adventitia** - in the part of the gallbladder that rests on the liver; in the rest of the serosa; under the peritoneum there is a subserous body.



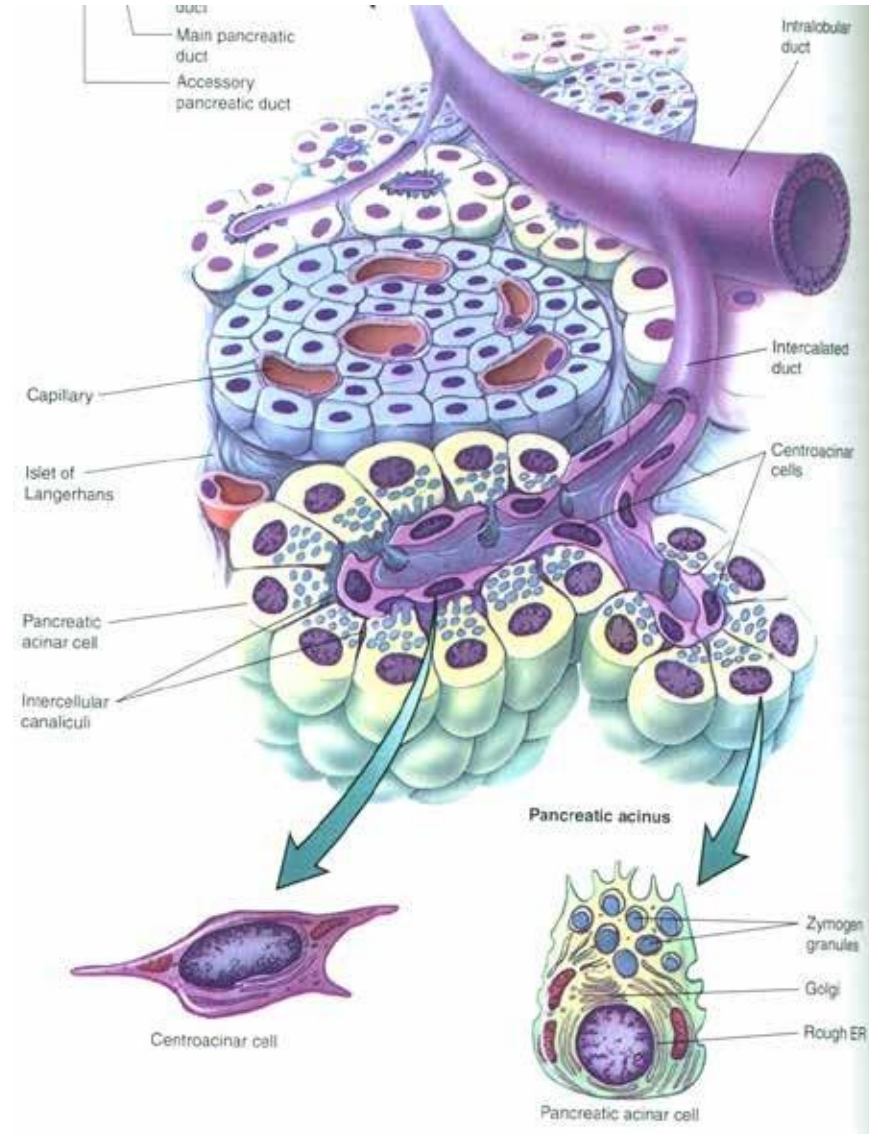
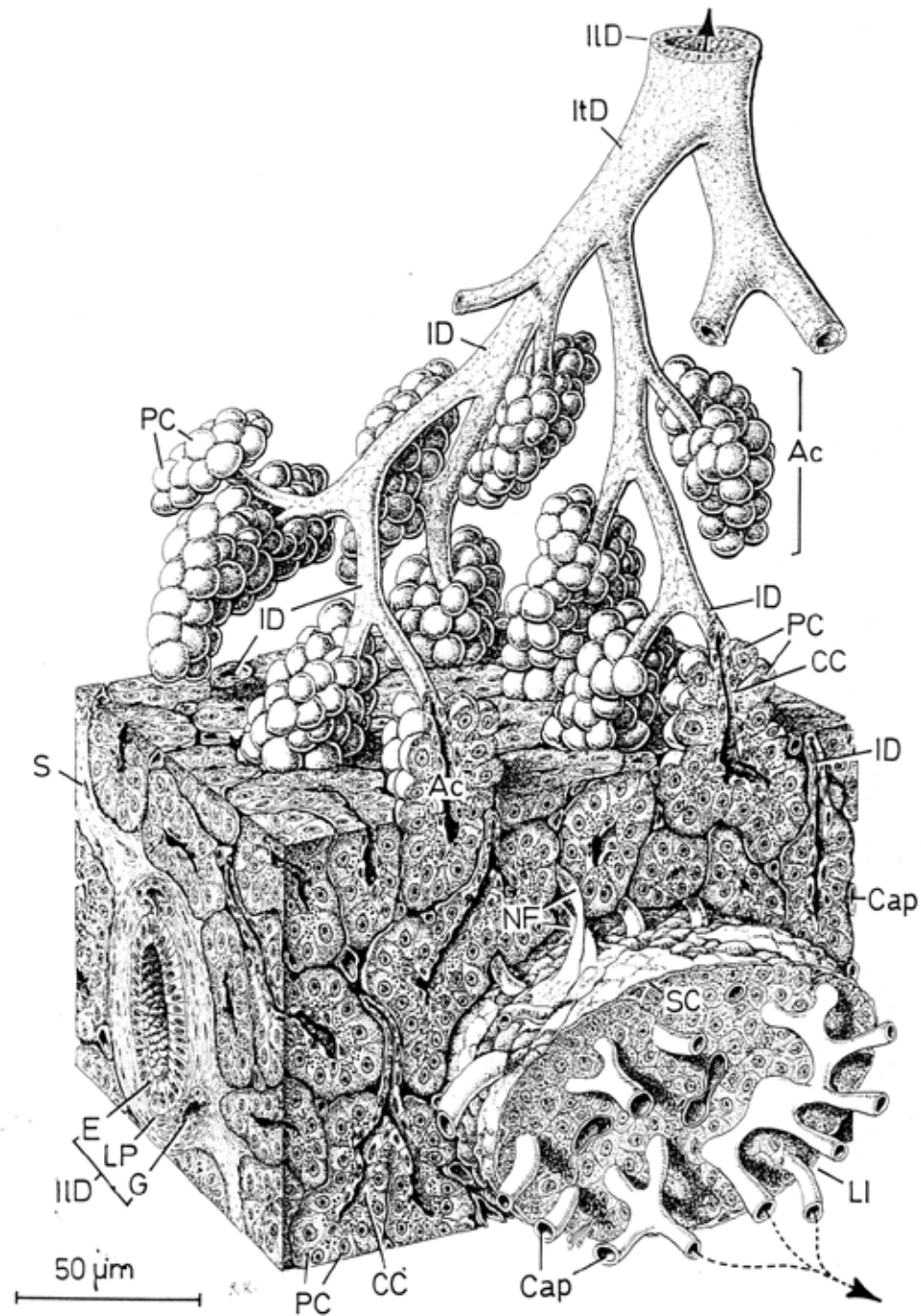
# PANCREAS

# Pancreas

- Pancreas (Greek: pan-all; kreas-meat) is a gland with dual secretion.
- The exocrine part of the pancreas secretes enzymes that are taken to the duodenum and participate in the digestion of all digestible food components.
- The endocrine part of the pancreas secretes hormones that are injected into the blood.
- The pancreas has an elongated shape and consists of a head, body and tail. The main pancreatic duct or Wirsung's duct extends along the entire length of the gland, which flows into the duodenum in the ampulla of Vater, together with the main bile duct.
- Wrapped in a transparent capsule from which the septa are separated.

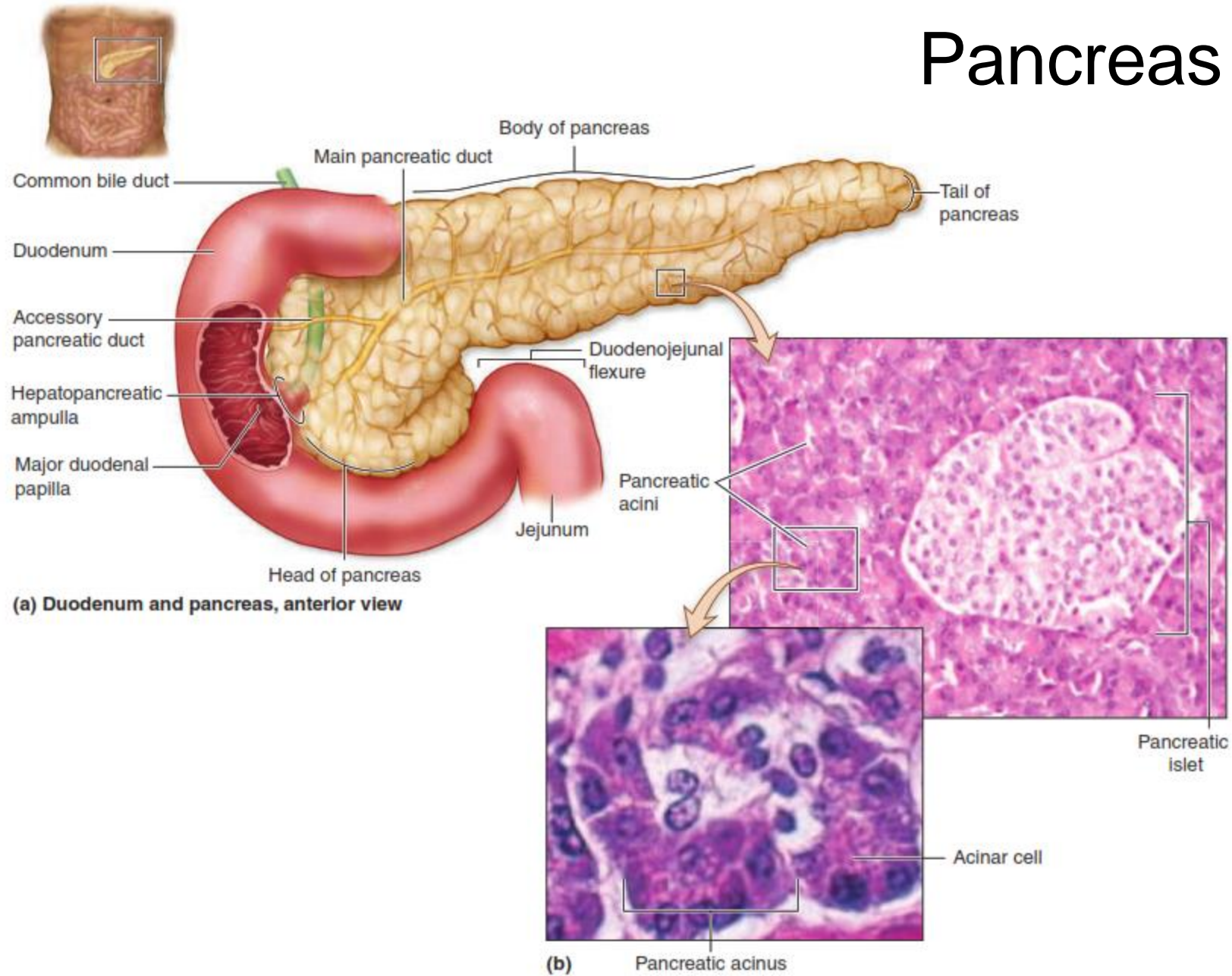


# Pancreas





# Pancreas



# Exocrine pancreas

- **The exocrine pancreas consists of**
  - acinus and
  - output channels.
- 
- **Acinus is made of :**
  - pancreatic acinar cells (pancreocytes)
  - pancreatic centroacinar cells

# Exocrine pancreas

- Pancreatocytes are pyramidal serous cells with a narrow apical surface and a broad base lying on the basal lamina.
- Short microvilli extend from the luminal surface of the cell.
- The basal domain of the plasmalemma contains receptors for cholecystikinin and acetylcholine.
- In the apical parts there are eosinophilic zymogen granules.
- Pancreatocytes contain enzymes for digestion of:
  - protein:
    - a) endopeptidases - trypsinogen, chymotrypsinogen
    - b) exopeptidases - procarboxypeptidases and proaminopeptidases
  - lipid: lipase
  - carbohydrates: amylase
  - of nucleic acids: DNA-ase and RNA-ase.

# Exocrine pancreas

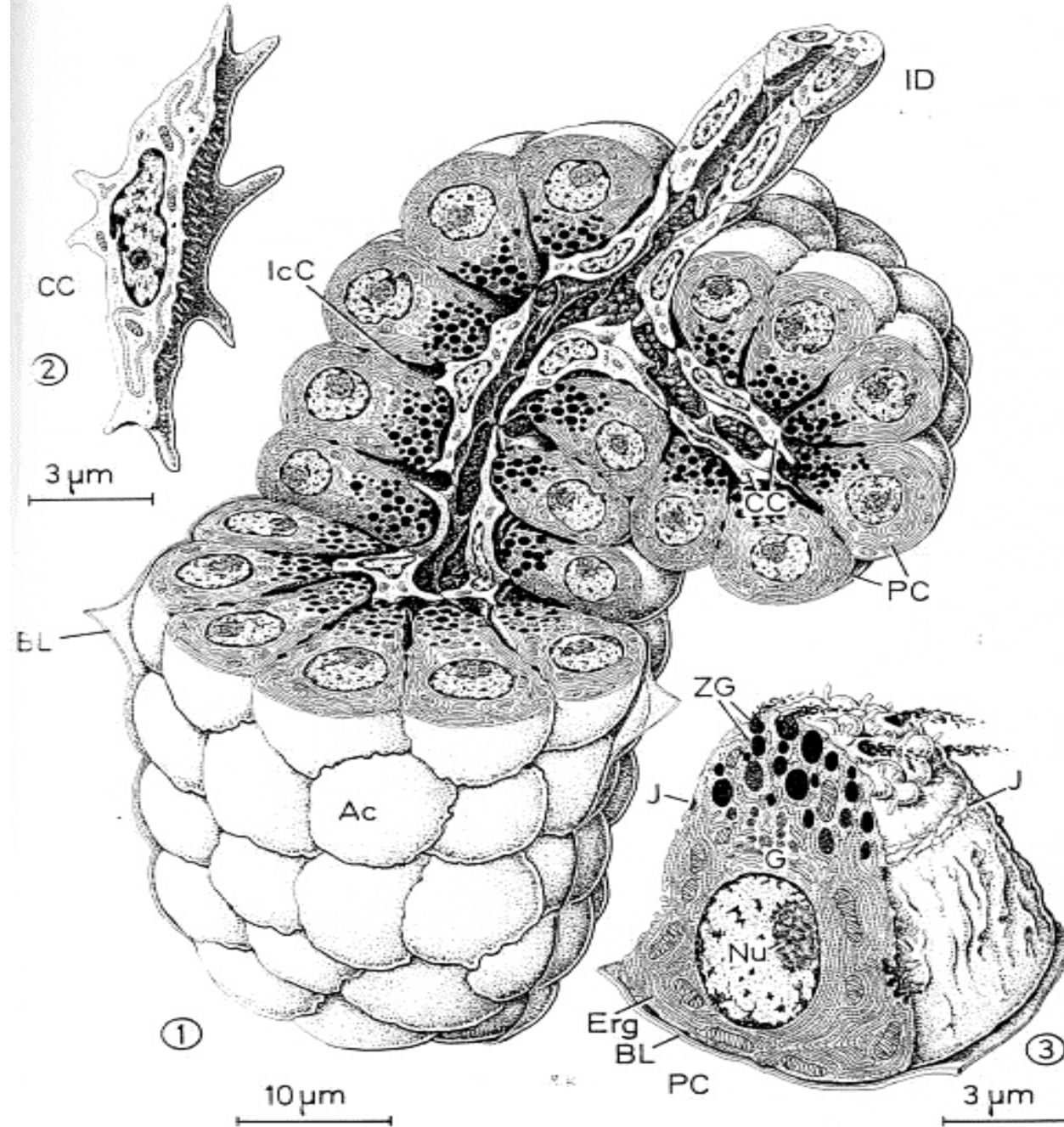
- Pancreatic centroacinar cells are located in the core of the acinus.
- They are flattened stellate cells with bright cytoplasm, with poorly developed organelles, except relatively numerous mitochondria.
- They are separated from the apical parts of pancreocytes by narrow fissures. These cells form an incomplete barrier between the pancreocytes and the lumen of the acinus, leaving intercellular clefts through which the secretion of acinus cells passes.
- They have receptors for secretin on the plasmalemma.
- They regulate the activity of pancreocytes.

# Exocrine pancreas

- Pancreatic centroacinar cells form the beginning of excretory ducts of the exocrine pancreas.
- Outside the acinus, the centroacinar cells continue to the flat and then the cuboidal cells of the ductus intercalatus.
- Several intercalate ducts join to form the ductus interlobularis.
- There are no pars striata ducts in the pancreas.
- The intralobular ducts leave the lobules and continue with the interlobular ducts.
- These ducts drain directly into the main pancreatic duct.
- 1-3 liters of alkaline secretion is secreted daily



# Exocrine pancreas

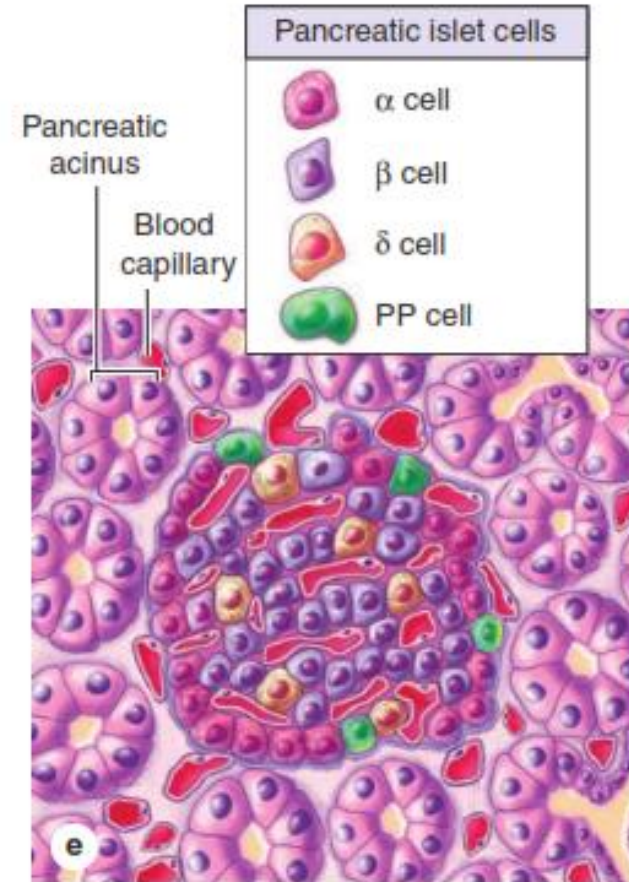


# Endocrine pancreas

- Endocrine cells of the pancreas are called insulocytes and are found in smaller or larger groups between the acini of the exocrine pancreas.
- Groups of endocrine cells are called insulae or islets of Langerhans.
- The pancreas contains about a million islets and they are the most numerous in the tail of the organ. The islets of Langerhans make up about 1-2% of the volume of the pancreas.
- Around them is a thin layer of reticular fibers that extend into the insula following the fenestrated capillaries.
- An incomplete layer of Schwann cells, which follow the fibers of the autonomic nervous system, separates the endocrine from the exocrine pancreas.

# Endocrine pancreas

- Insulocytes form irregular rows or groups that are in close contact with capillaries and nerve terminals.
- Different types of insulocytes are recognized by the shape, size and electron density of secretory granules.
- The main cell types of the islets of Langerhans, which make up about 95% of the total glandular population, are:
  - $\alpha$ -cells
  - $\beta$ -cells
  - $\delta$ -cells. which make up about 95% of the total glandular population.
- The remaining 5% of insulocytes are PP-, D1-, EC- and G-cells.



# Endocrine pancreas

- $\beta$  -cells are the most numerous cells of the islets of Langerhans. They account for about 70% of insulocytes.
- In the cytoplasm, they contain numerous secretory granules in which an electron-dense core can be seen, surrounded by a wide electroluminescent band (halo).
- The core of the granule contains crystallized insulin.
- Other biologically active substances (amylin, cholecystokinin 8 and insulin-like growth factor 2) are also present in  $\beta$ -cell granules, which is referred to as colocalization.
- $\alpha$ -cells make up about 15-20% of the endocrine cells of Langerhans tracts. They are located on the periphery of the islets and are significantly larger than  $\beta$  -cells. The granules contain an osmiophilic core, surrounded by an electroluminescent halo.  $\alpha$ -cells secrete the peptide hormone glucagon, which has the opposite effects of insulin.

# Endocrine pancreas

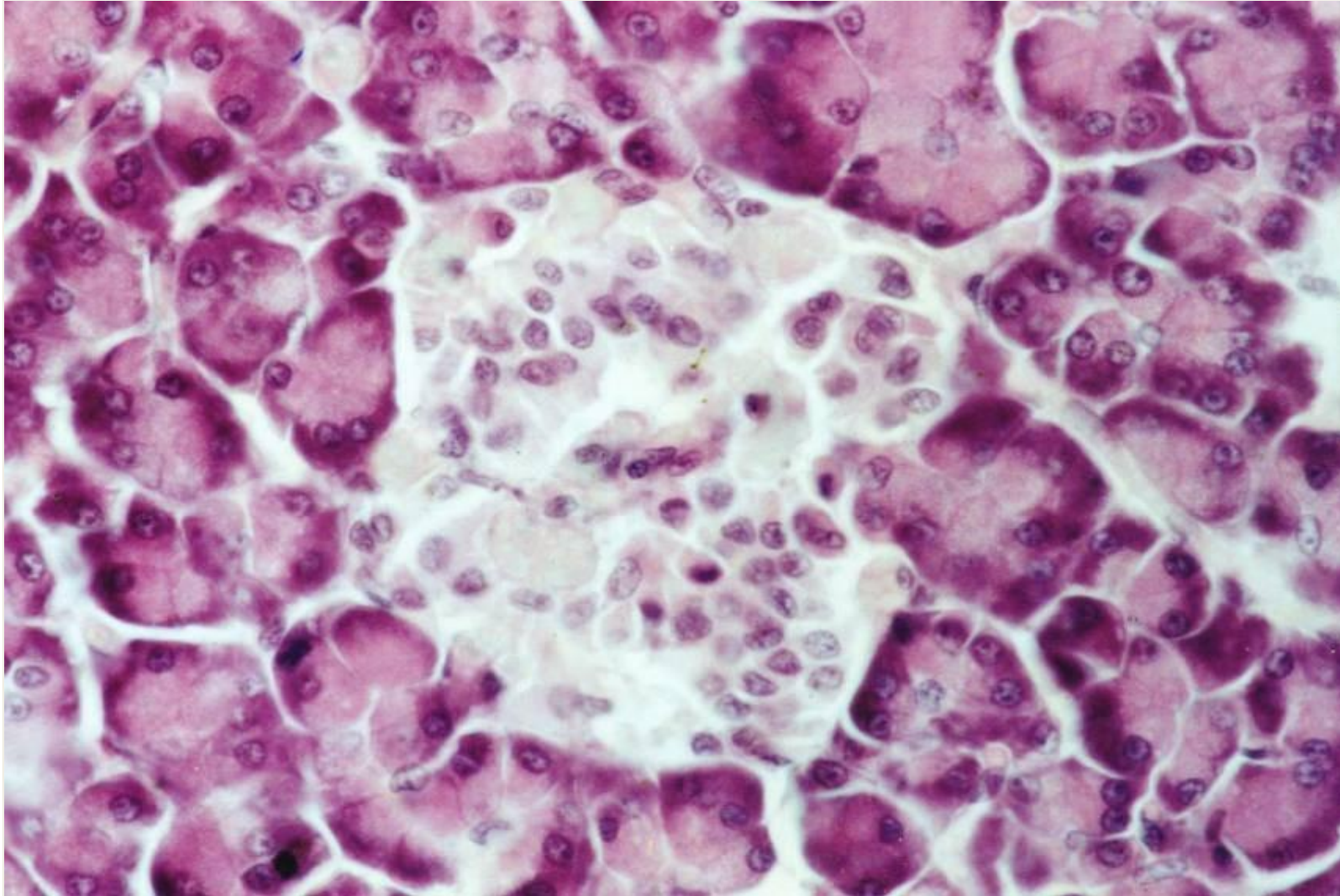
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- The granules contain an osmiophilic core, surrounded by an electroluminescent halo.
- $\alpha$ -cells secrete the peptide hormone glucagon, which has the opposite effects of insulin.
- $\delta$ -cells make up about 5-10% of the cellular content of the endocrine pancreas. They are larger than  $\alpha$ - and  $\beta$ -cells.
- $\delta$ -cells secrete the hormone somatostatin.



# Endocrine pancreas

- PP (F)-cells make up only about 1% of endocrine cells.
- PP-cells secrete pancreatic polypeptide.
- D1-cells secrete VIP (vasoactive intestinal peptide) which has an effect similar to glucagon.
- EC-cells secrete the hormone serotonin, which enhances intestinal peristalsis.
- G-cells are present only in the fetus and in that period they secrete the hormone gastrin.

# Endocrine pancreas



# Major cell types and hormones of pancreatic islets

Cell Type	Quantity (%)	Hormone Produced	Hormone Structure and Size	Hormone Function
$\alpha$	~30	Glucagon	Polypeptide; 3500 Da	Acts on several tissues to make energy stored in glycogen and fat available through glycogenolysis and lipolysis; increases blood glucose content
$\beta$	~60	Insulin	Dimer of $\alpha$ and $\beta$ chains with S-S bridges; 5700-6000 Da	Acts on several tissues to cause entry of glucose into cells and promotes decrease of blood glucose content
$\delta$ or D	5-10	Somatostatin	Polypeptide; 1650 Da	Inhibits release of other islet cell hormones through local paracrine action; inhibits release of GH and TSH in anterior pituitary and HCl secretion by gastric parietal cells
PP	Rare	Pancreatic polypeptide	Polypeptide; 4200 Da	Stimulates activity of gastric chief cells; inhibits bile secretion, pancreatic enzyme and bicarbonate secretion, and intestinal motility