



University of Kragujevac, Faculty of
Medical Sciences

Integrated academic studies of
Pharmacy

Department of Histology and
Embryology

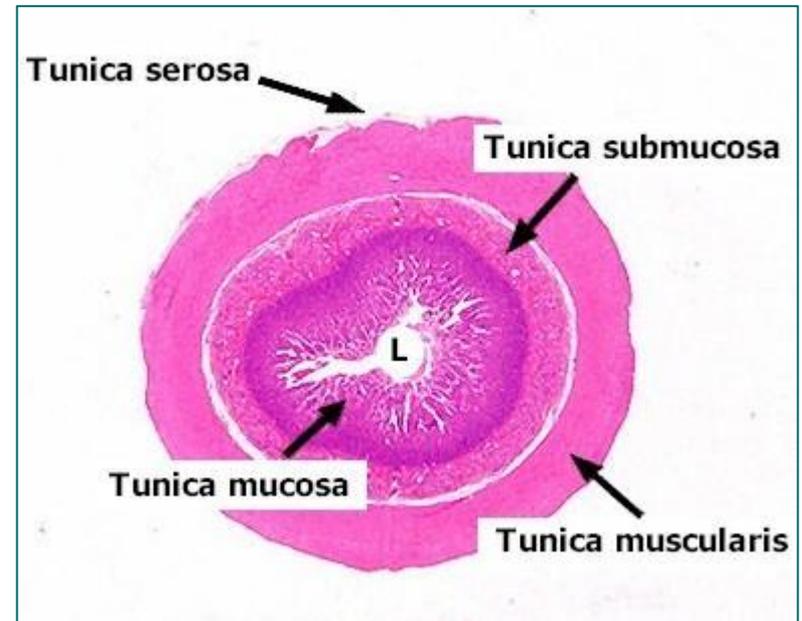
DIGESTIVE SYSTEM, LIVER, PANCREAS AND GALLBLADDER

DIGESTIVE SYSTEM

- The digestive system consists of:
 - oral cavity
 - pharynx
 - esophagus
 - stomach
 - small intestine
 - colon
 - glands associated with the digestive system (salivary glands, liver, gall bladder and pancreas)

Digestive tract

- **Tunica mucosa**
 - lamina epithelialis
 - lamina propria
 - lamina muscularis mucosae
- **Tunica submucosa**
- **Tunica muscularis**
 - stratum circulare
 - stratum longitudinale
- **Tunica serosa/adventitia**



Mucosa

Epithelium

Lamina propria

Muscularis
mucosae

Submucosa

Submucosal gland

Blood vessel

Submucosal nerve plexus

Muscularis

Inner circular layer

Myenteric nerve plexus

Outer longitudinal layer

Serosa

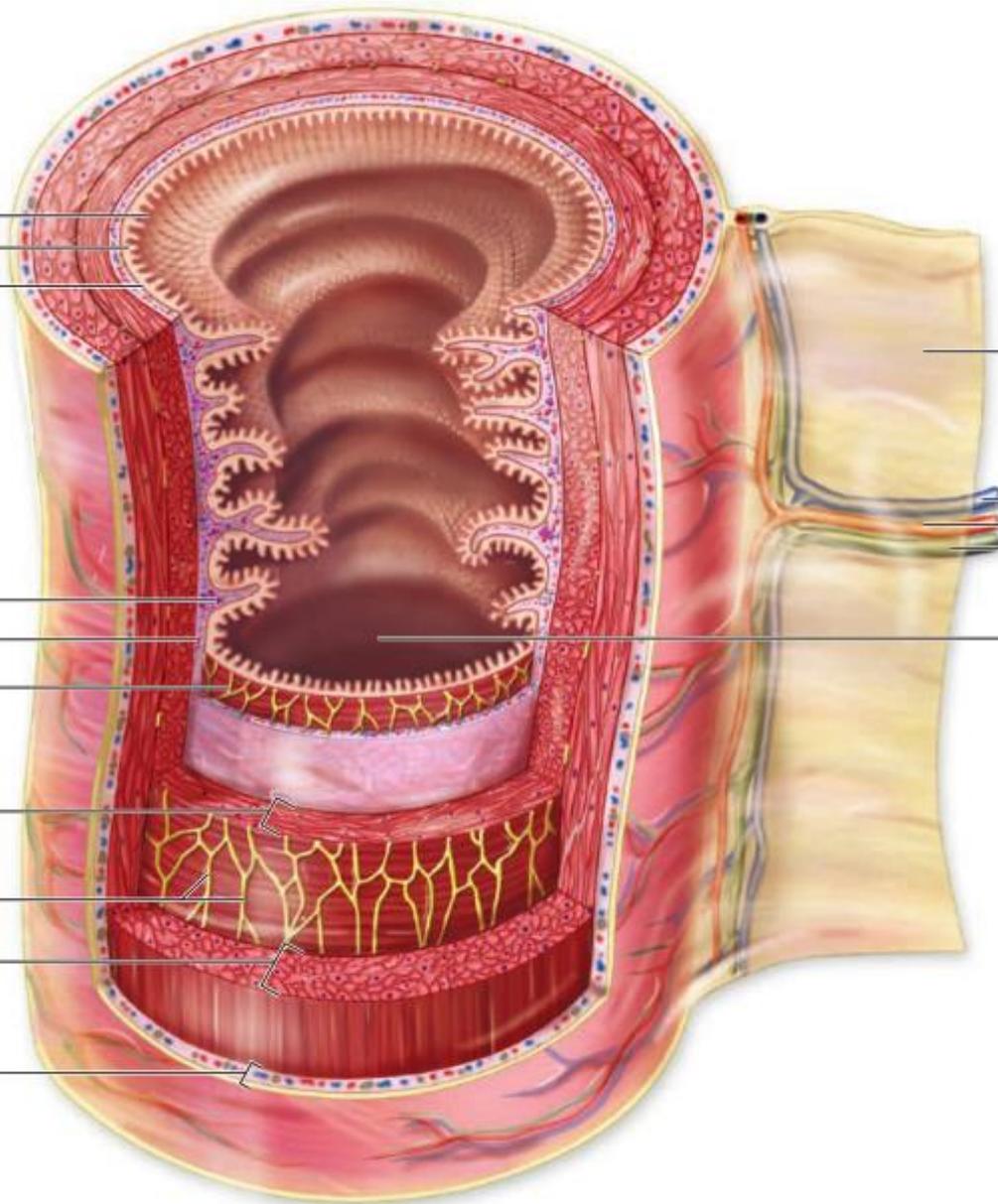
Mesentery

Vein

Artery

Lymph vessel

Lumen



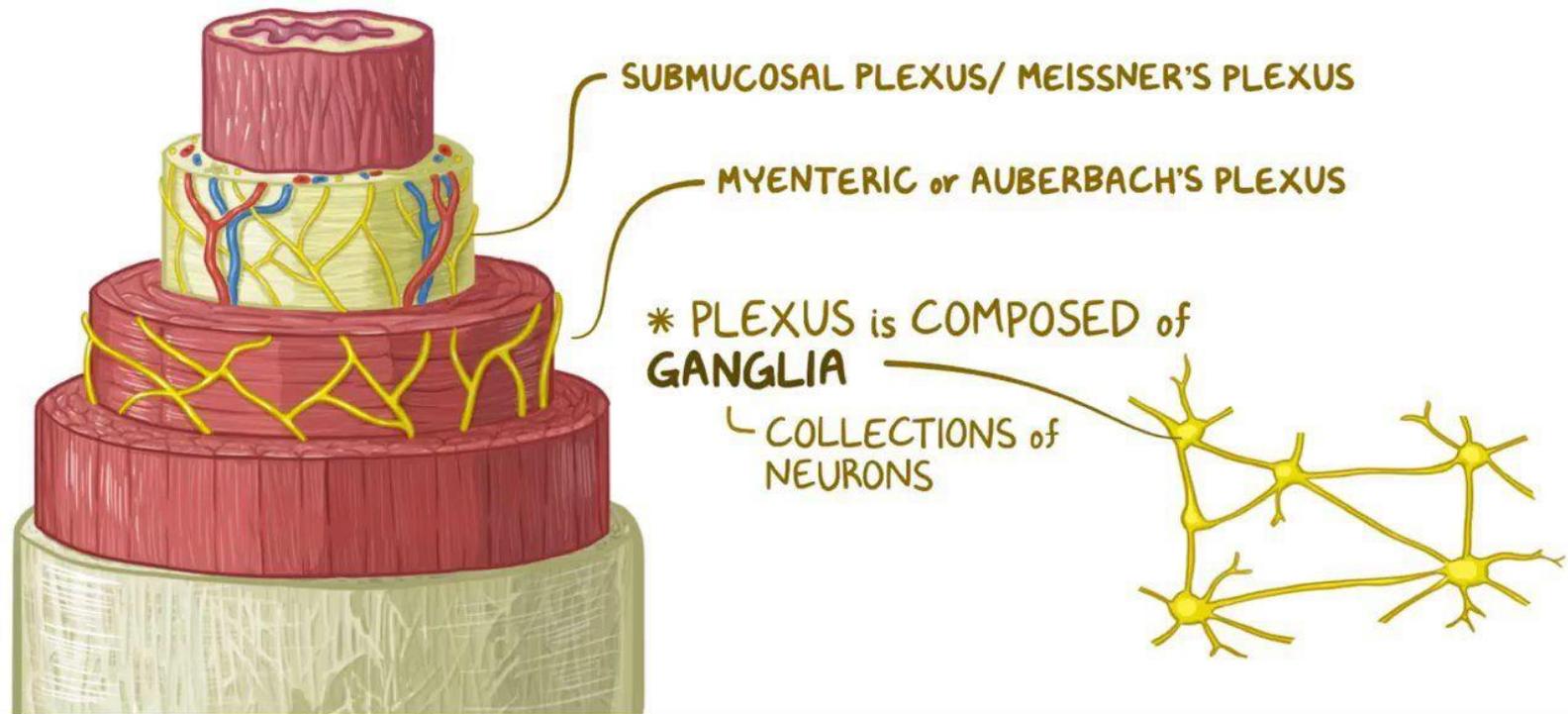
Innervation of the digestive tube

- The digestive tract is innervated by internal (own) enteric neurons and external sympathetic and parasympathetic neurons.
- Enteric neurons form the enteric nervous system (ENS).
- The ENS is a part of the autonomic nervous system that functions in conjunction with the sympathetic and parasympathetic, but can also act independently of them (classifying it as a separate component).
- The ENS includes about 100 million neurons located in the wall of the digestive tube from the proximal part of the esophagus to the anus.
- Neurons of the ENS build two tangles: Meissner's submucosal tangle and Auerbach's myenteric plexus.
- In both bundles, neurons form groups that are connected to each other by myelinated nerve fibers.

Meissner's submucosal plexus

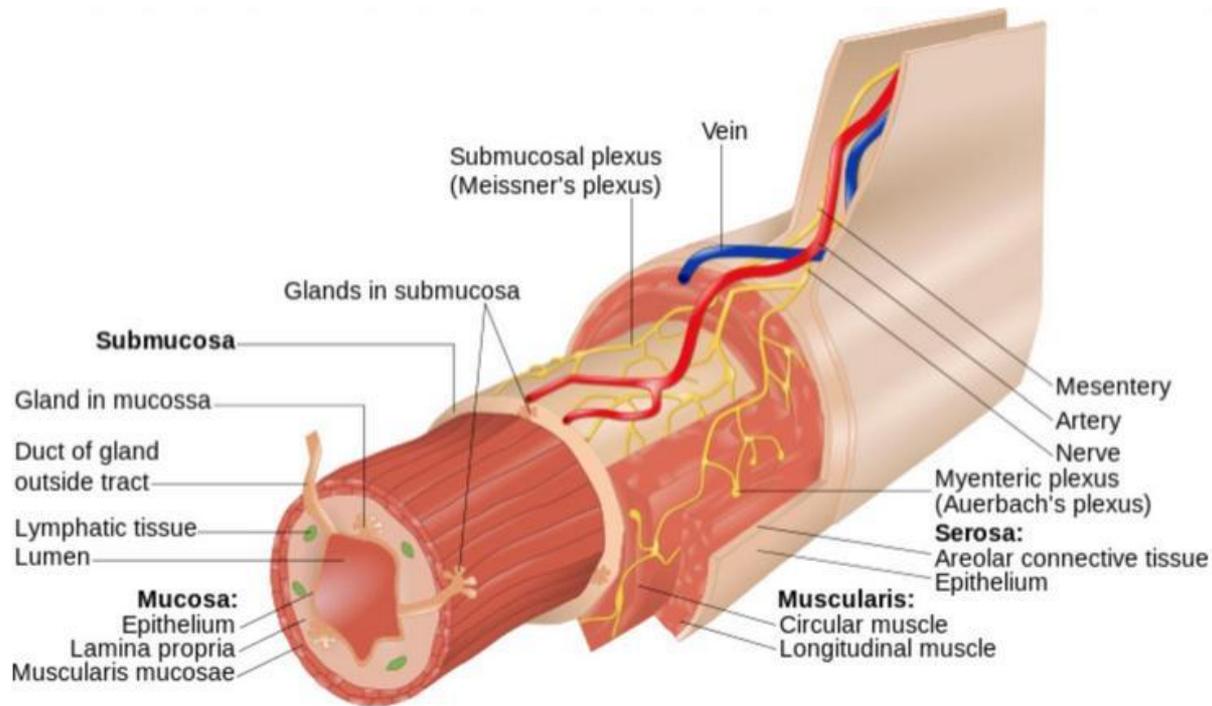
ENTERIC NERVOUS SYSTEM

* FOUND WITHIN WALLS of ENTIRE GI TRACT



- It controls endocrine and exocrine secretion, mucosal mobility, microcirculation, and inflammatory and immune reactions in the digestive tract.

Auerbach's myenteric plexus



- The myenteric nerve plexus controls peristaltic movements.

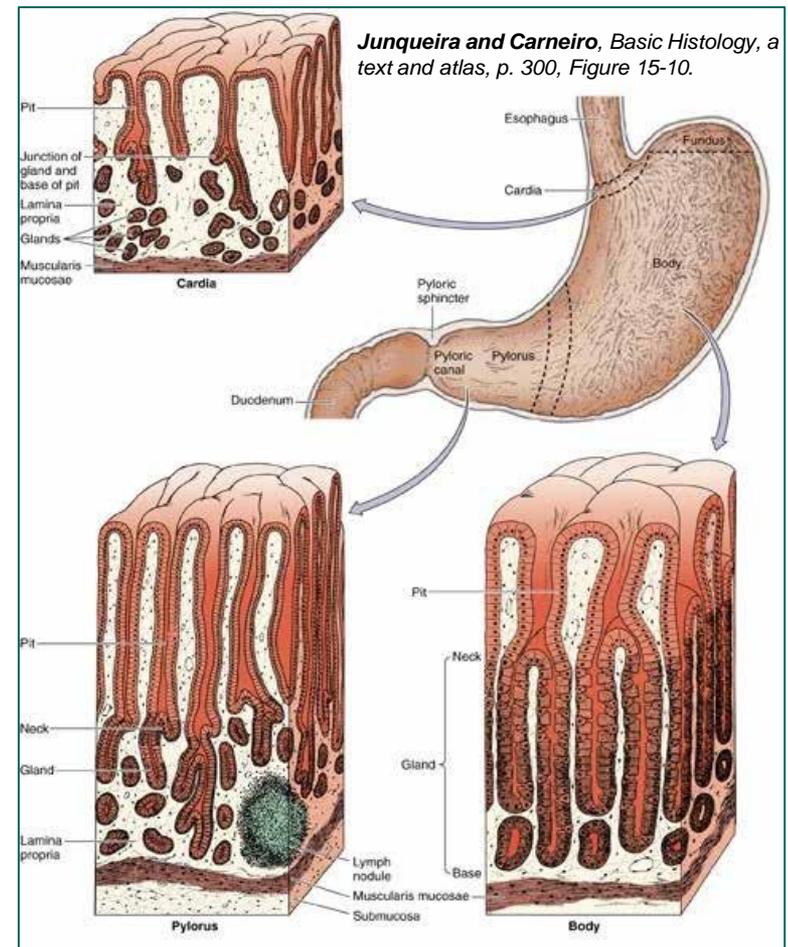
Esophagus (oesophagus)

- **Tunica mucosa**
 - lamina epithelialis
 - nonkeratinized stratified squamous epithelium
 - lamina propria
 - esophageal glands
 - lamina muscularis
 - A relatively thick layer of muscle cells
- **Tunica submucosa**
 - gll. oesophageae
- **Tunica muscularis**
 - stratum circulare
 - stratum longitudinale
- **Tunica adventitia**



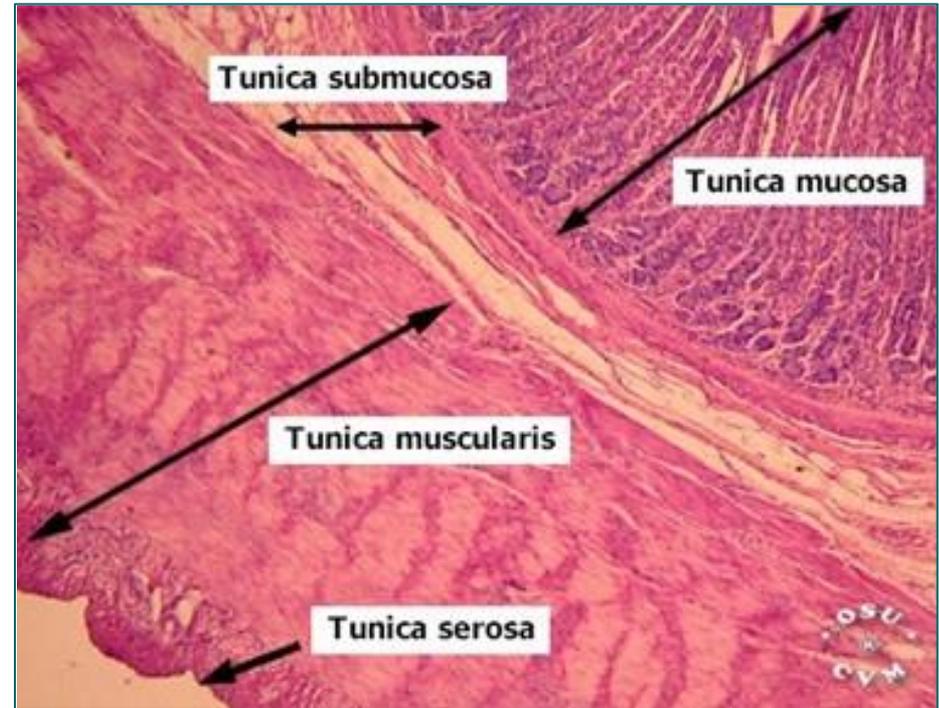
Stomach (ventriculus, gaster)

- Four anatomical regions:
 - **Pars cardiaca**
 - **Fundus ventriculi**
 - **Corpus ventriculi**
 - **Pars pylorica**
- The body and the fundus have an identical structure.
- The mucosa and submucosa of the stomach form long folds - **rugae**.
- The mucosa forms protrusions of the **areae gastricae**, separated by shallow furrows.
- **Foveolae gastricae** pits are visible on their surface, at the bottom of which the gastric glands open.



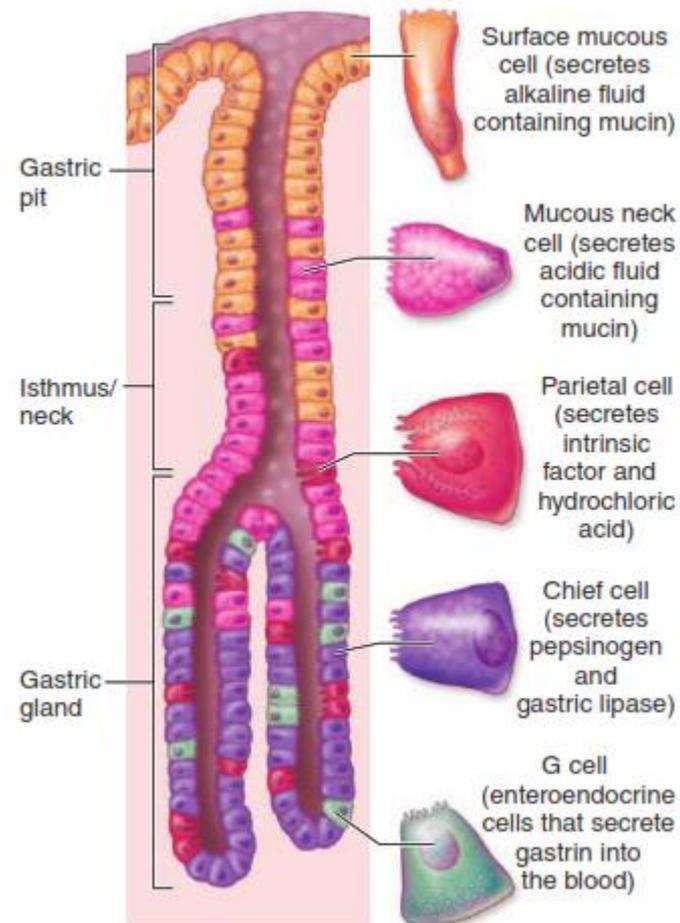
Body and bottom of the stomach (corpus et fundus ventriculi)

- **Tunica mucosa**
 - lamina epithelialis
 - **Simple columnar epithelium**
 - lamina propria
 - **foveolae gastricae** (1/4)
3-7 glands open at the bottom
gll. gastricae propriae /
(gastric glands) - base, body and neck of the gland
 - lamina muscularis
 - double-layered, thinner than the esophageal one
- **Tunica submucosa**
 - Connective tissue, blood vessels, Meissner's plexus
- **Tunica muscularis**
 - stratum obliquum (cardia)
 - stratum circulare (the whole stomach, in the pylorus - **m. sphincter pylori**)
 - stratum longitudinale (curves)
- **Tunica serosa**



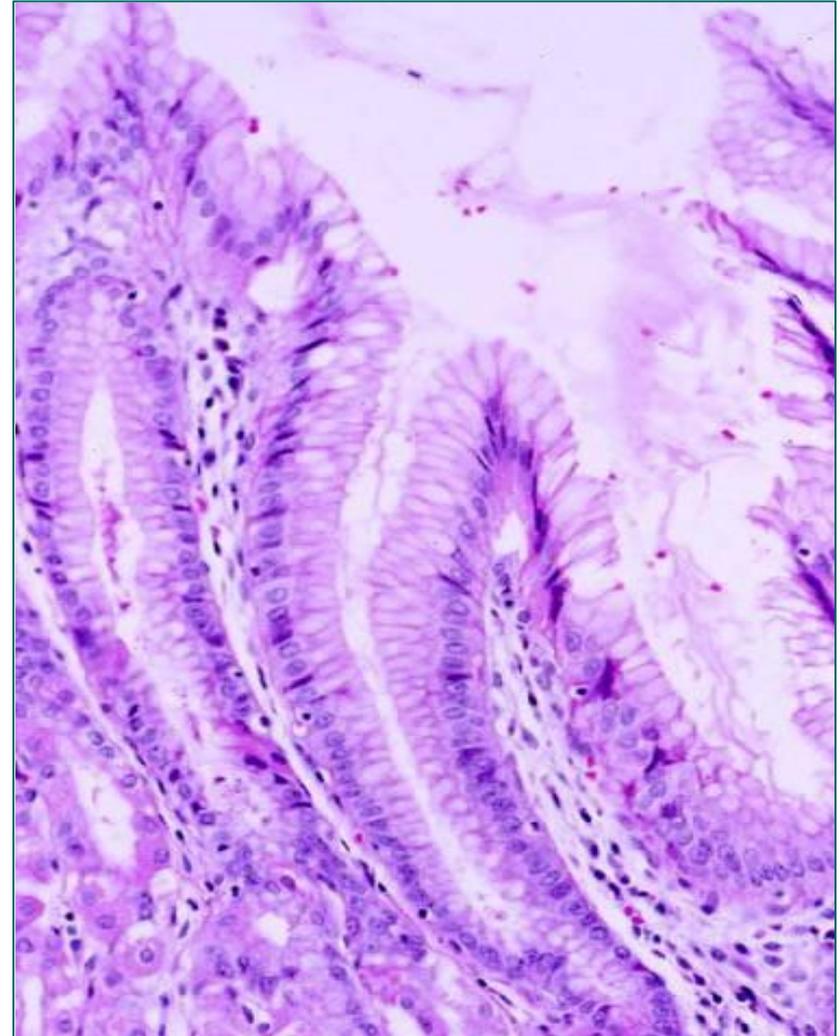
Epithelium of gastric pits and specific gastric glands

- The surface of the stomach and the pit of the stomach is covered by a simple cylindrical epithelium, which they make up exclusively superficial mucus cells.
- At the bottom of each pit, 3-7 simple tubular, specific gastric glands open.
- The epithelium of specific gastric glands continues on the epithelium of the gastric pits.
- It consists of five cell types:
 - **Mucous neck cells**
 - **Stem cells**
 - **Chief (pepsinogenic) cells**
 - **Parietal (oxyntic) cells**
 - **Endocrine (enteroendocrine) cells**



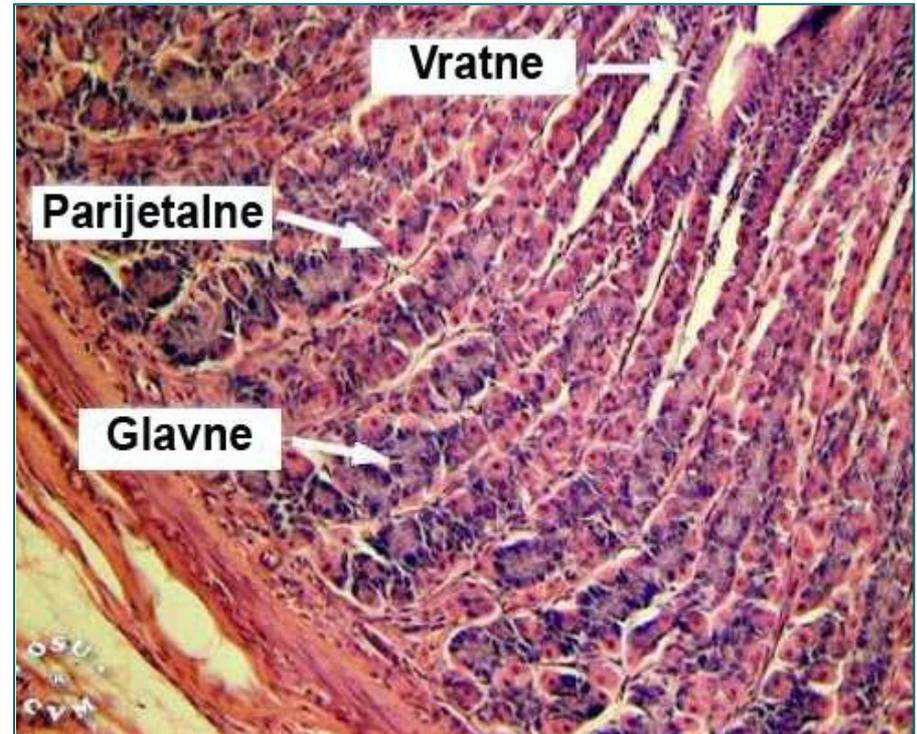
Superficial mucus cells

- On the apical surface, rare and thin microvilli and glycocalyx.
- Basal - oval, heterochromatic nucleus, grER, and Golgi (supranucleus).
- Apically - mucigenic granules - are released by exocytosis at the apical pole.
- They contain glycosaminoglycans that bind bicarbonate ions.
- In the stomach, mucin is converted into mucus - it forms a thick gelatinous layer resistant to HCl.
- Protective role, but suitable medium for *H. pylori*.



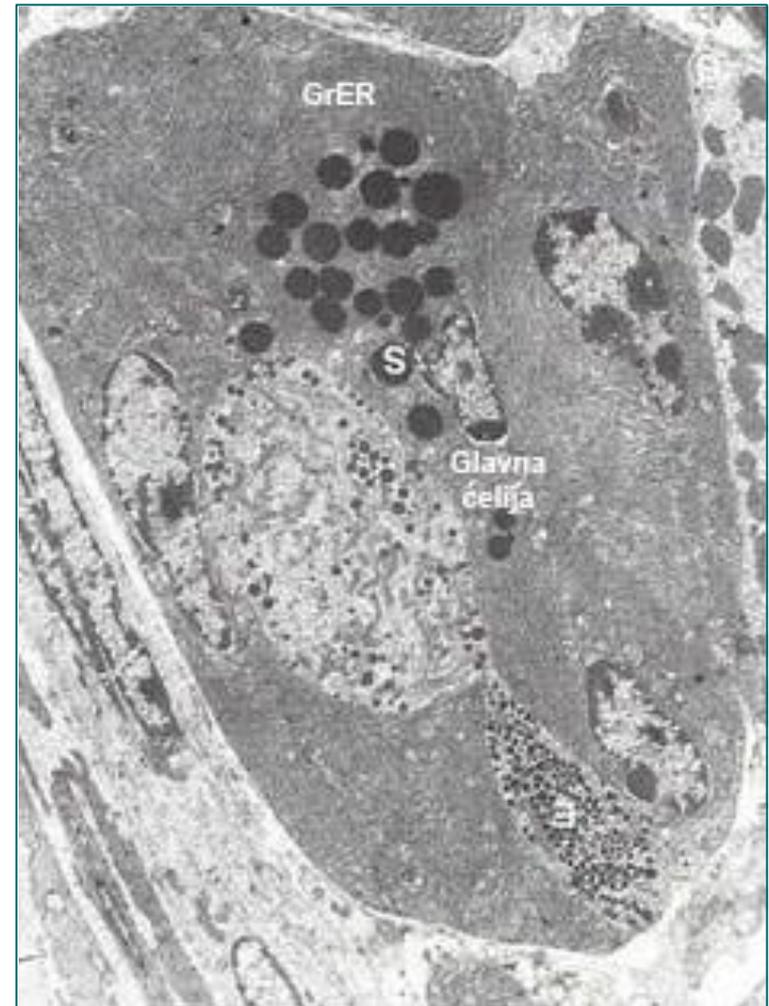
Neck mucus and stem cells

- Neck mucus cells are located in the neck, and partially in the body of the gastric glands.
- Similar in ultrastructure to superficial mucus, the secretion "lubricates" the chyme.
- Stem cells are few in number, located exclusively in the neck of the gastric glands.
- Euchromatic nucleus, expressed nucleolus, ribosomes.
- Their proliferation and differentiation renews the entire epithelium.
- Superficial, cervical mucous and endocrine 4-7 days, main and marginal - 1-3 years.



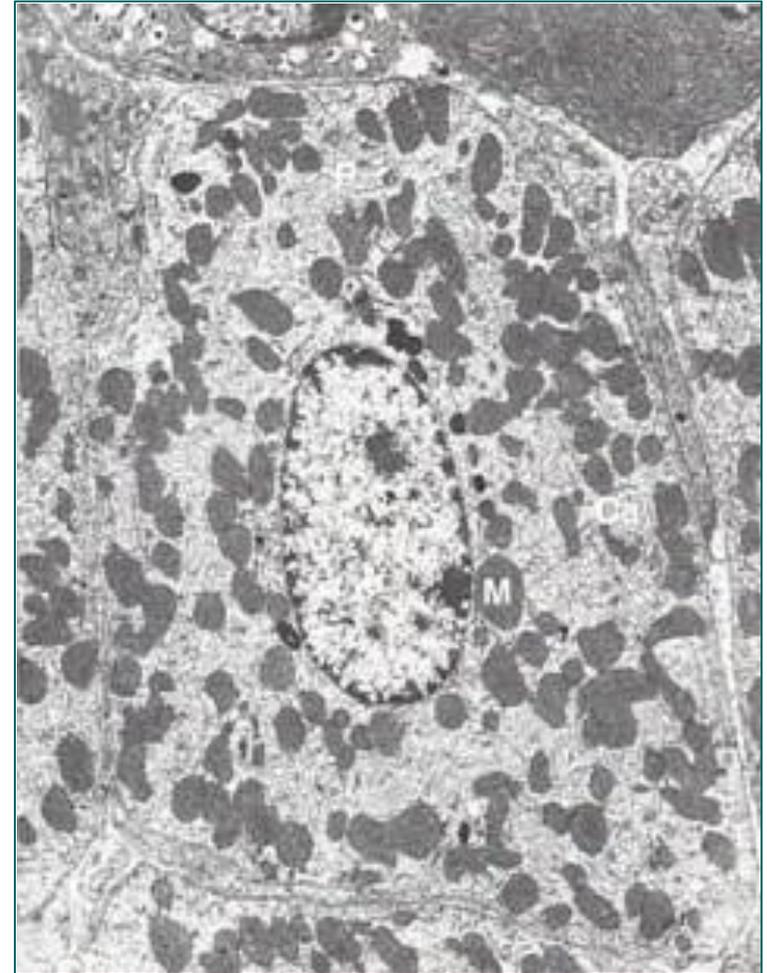
Chief (pepsinogenic) cells

- Basophilic, low-cylindrical or cuboidal cells.
- They are located in the lower half of specific gastric glands (there are none in the cardia, rare in the pylorus).
- The most numerous among the glandular cells of the stomach.
- Nucleus round, basal, nucleoli prominent, developed grER, Golgi complex - supranuclear - zymogen granules are separated and released by exocytosis at the apical pole.
- In the composition of the granules - pepsinogen - in an acidic environment it is converted into a proteolytic enzyme - pepsin.
- A small amount of gastric lipase.
- In the basal domain, receptors for the secretin hormone.



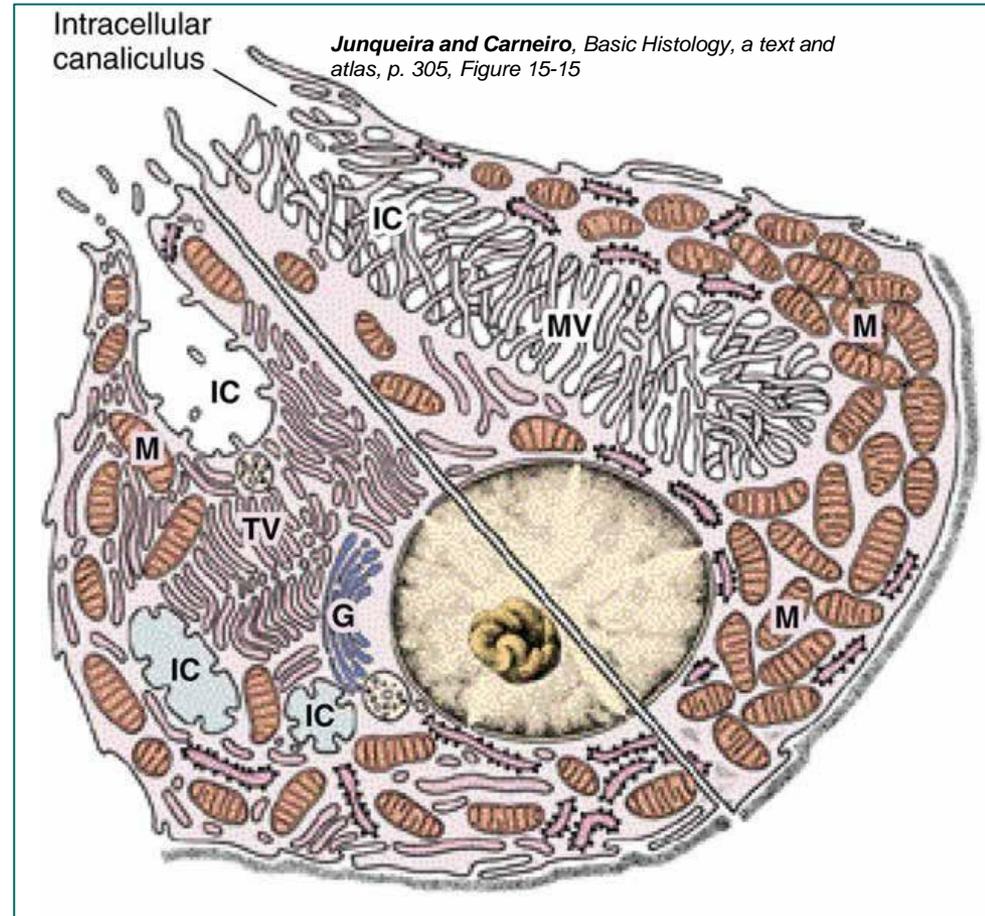
Ивичне (паријеталне) ћелије

- Крупне, **округле** или **пирамидне ћелије** смештене у горњој половини специфичних желудачних жлезда.
- Базе - ламина проприја; врх између апикалних делова суседних ћелија.
- Једно до два централно постављена једра, доста митохондрија, **систем разгранатих интрацелуларних каналића** (инвагинације апикалне плазмалеме), тубуловезикуларни систем грЕР.
- У базалном домену ћелије - рецептори за гастрин, хистамин и ацетил холин (промовише секрецију HCl)



Parietal (oxyntic) cells

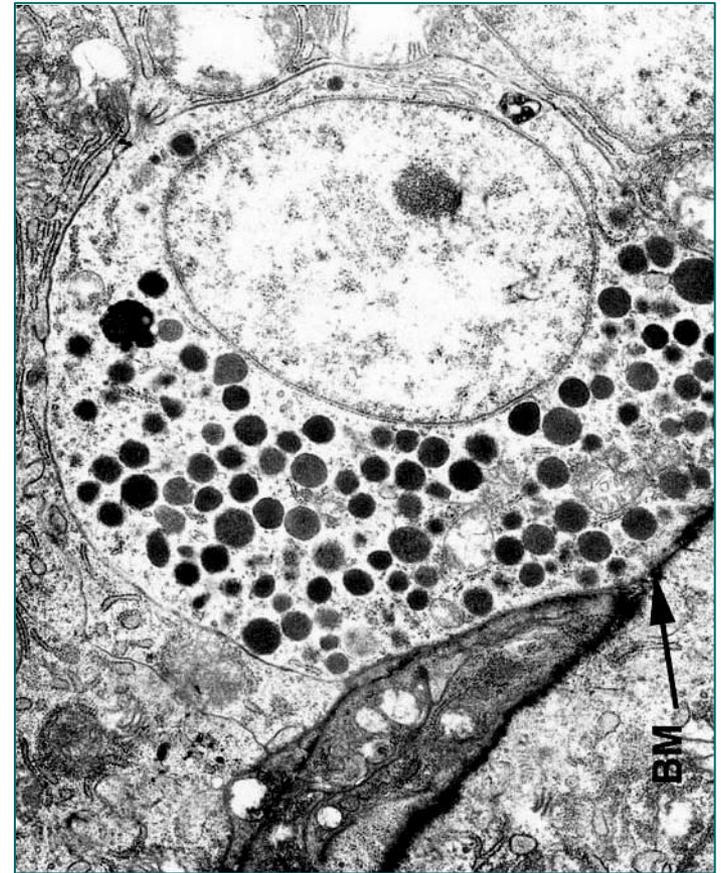
- Hydrogen ions are pumped from the cytoplasm into the tubule by the hydrogen pump on the membrane of the intracellular tubule and exchanged for a potassium ion that is expelled into the cytoplasm.
- Chlorine ions are introduced into the tubule through the chlorine channels.
- Chlorine and hydrogen ions are bound in the intracellular channel.
- From the intracellular channels, HCl reaches the lumen of the gastric gland - sterilization of the gastric contents.
- In addition to HCl, parietal cells also synthesize internal (intrinsic or Castle) factor - a glycoprotein necessary for the absorption of vitamin B12.
- The intrinsic factor-vitamin B12 complex is created in the stomach and absorbed in the ileum.
- Deficiency - pernicious anemia



Шема паријеталне ћелије која показује ултраструктурне разлике између мирујуће и активне ћелије. IC = интрацелуларни каналикули, G = Голџи, M = Митохондрије, TV = тубуловезикуле

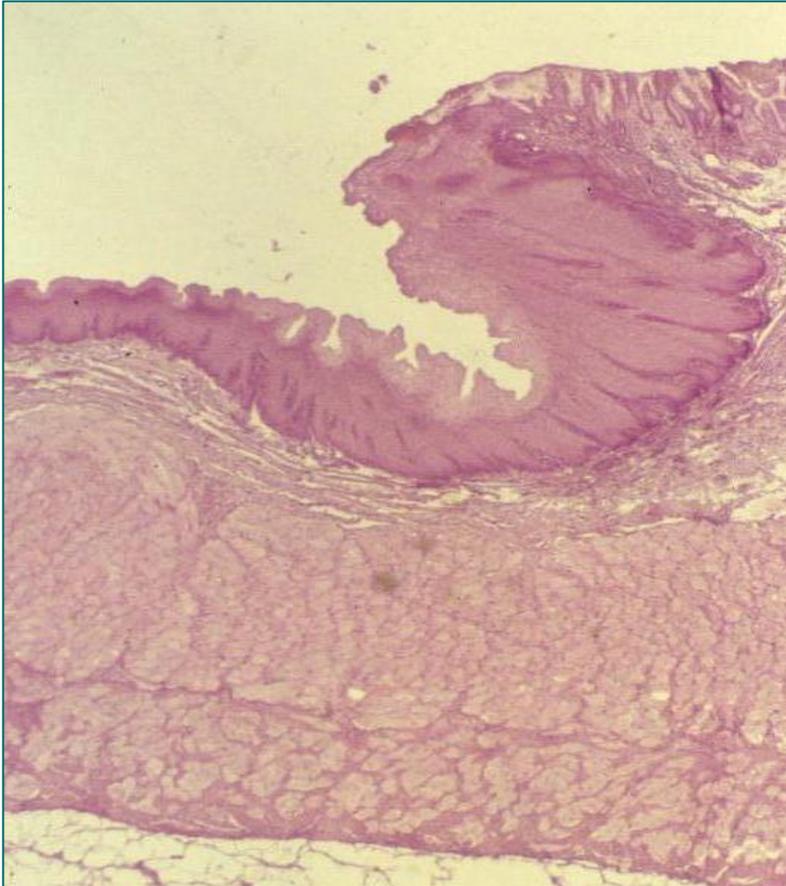
Endocrine (enteroendocrine) cells

- Heterogeneous population belonging to DNES.
- Argyrophilic cells are present in all parts of the gastric glands, mostly in the base.
- Core - apical, basal pole of granules with peptides and biogenic amines.
- The contents are released by exocytosis at the basal pole and diffuse to the capillaries of the lamina propria.
- Open type cells receive information from the lumen via microvilli.
- Cells of the closed type over the receptors at the basal pole.



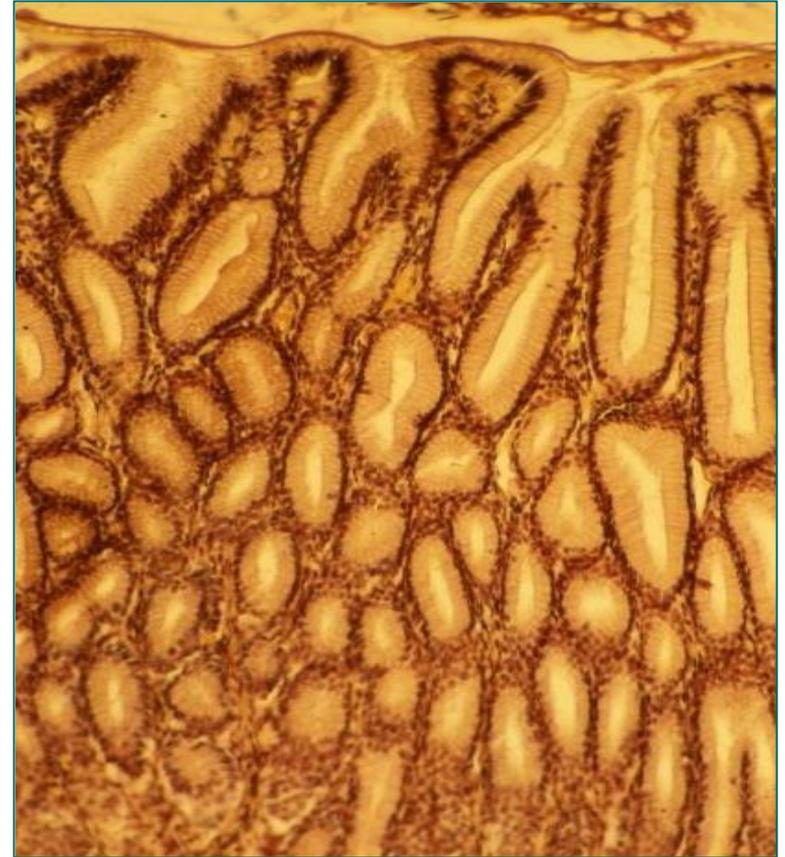
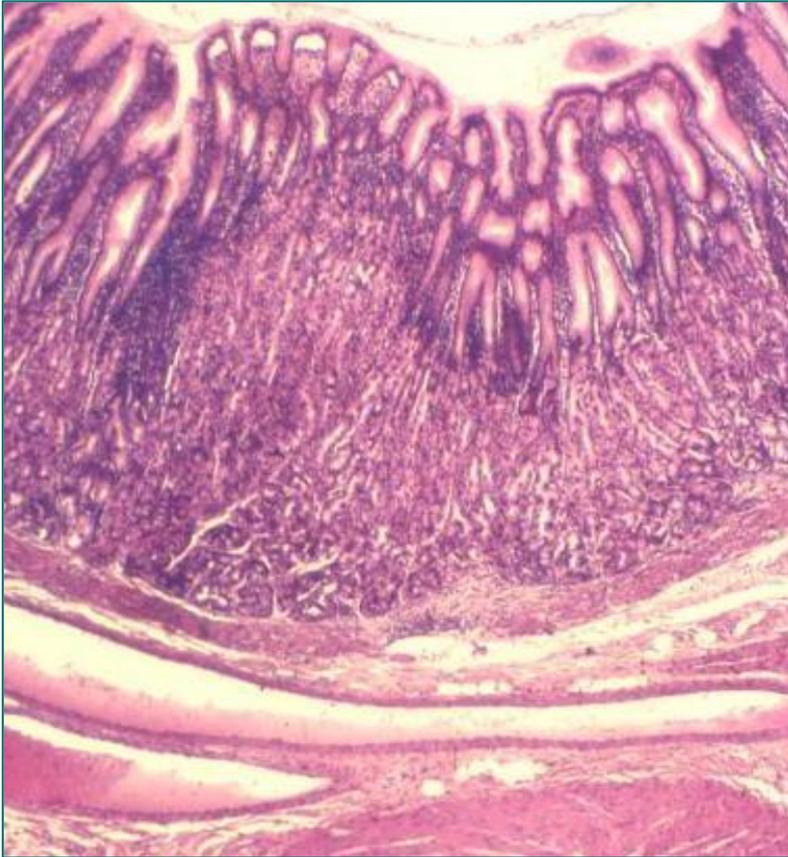
Dr Ihab El-Zhogby of the Faculty of Veterinary Medicine at Zagazig University in Egypt

Cardia (pars cardiaca)



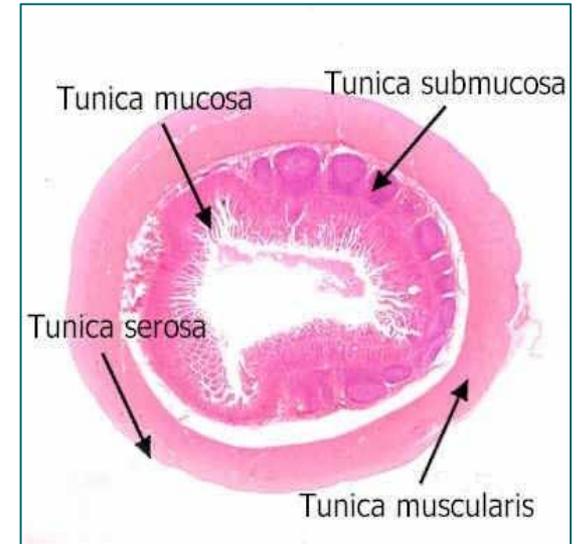
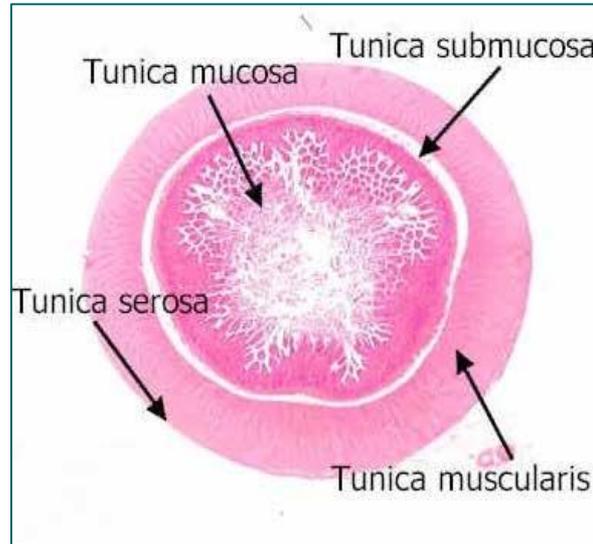
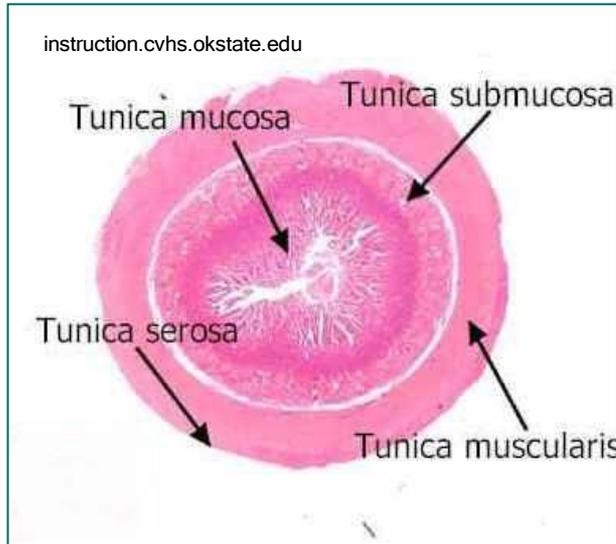
- **Ora serrata** - change of the squamous non keratinised epithelium of the esophagus into a single-row cylindrical epithelium of the stomach.
- In lamina propria gll. cardiaca.

Pylorus (pars pylorica)



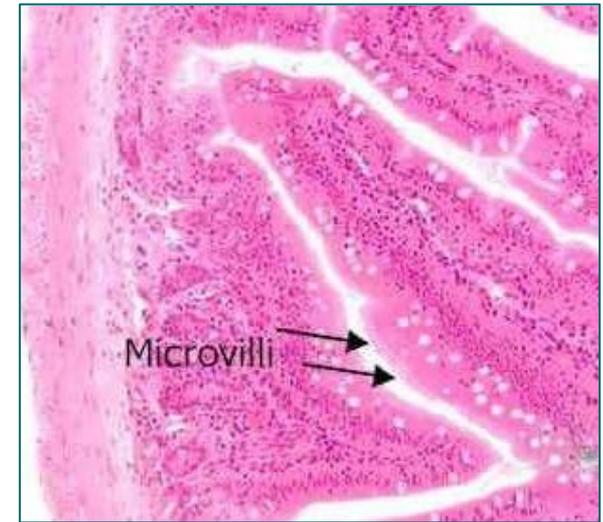
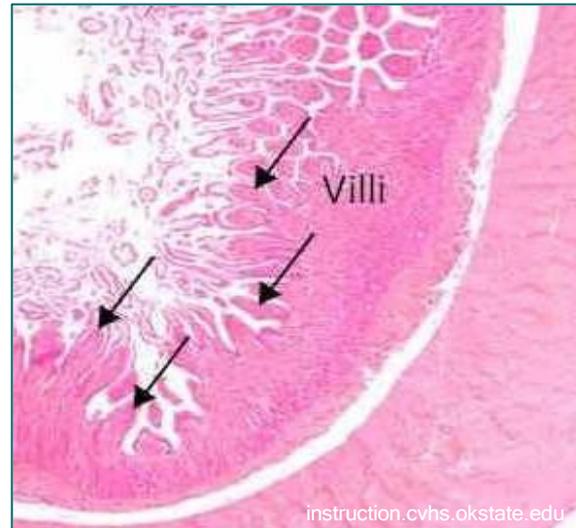
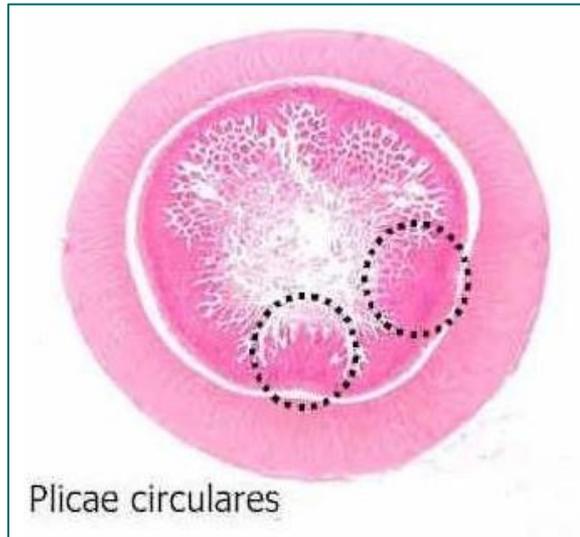
- Deep gastric pits and short pyloric glands (gll. pyloricae) in the lamina propria (strongly branched).
- Tunica muscularis - m. sphincter pylori (middle sublayer)

Small intestine (intestinum tenue)



- The small intestine extends from the pylorus to the ileocecal valve.
- It is about 6m long and has three segments:
 - duodenum - (25 cm)
 - jejunum (2.5 m)
 - ileum (3.5 m)

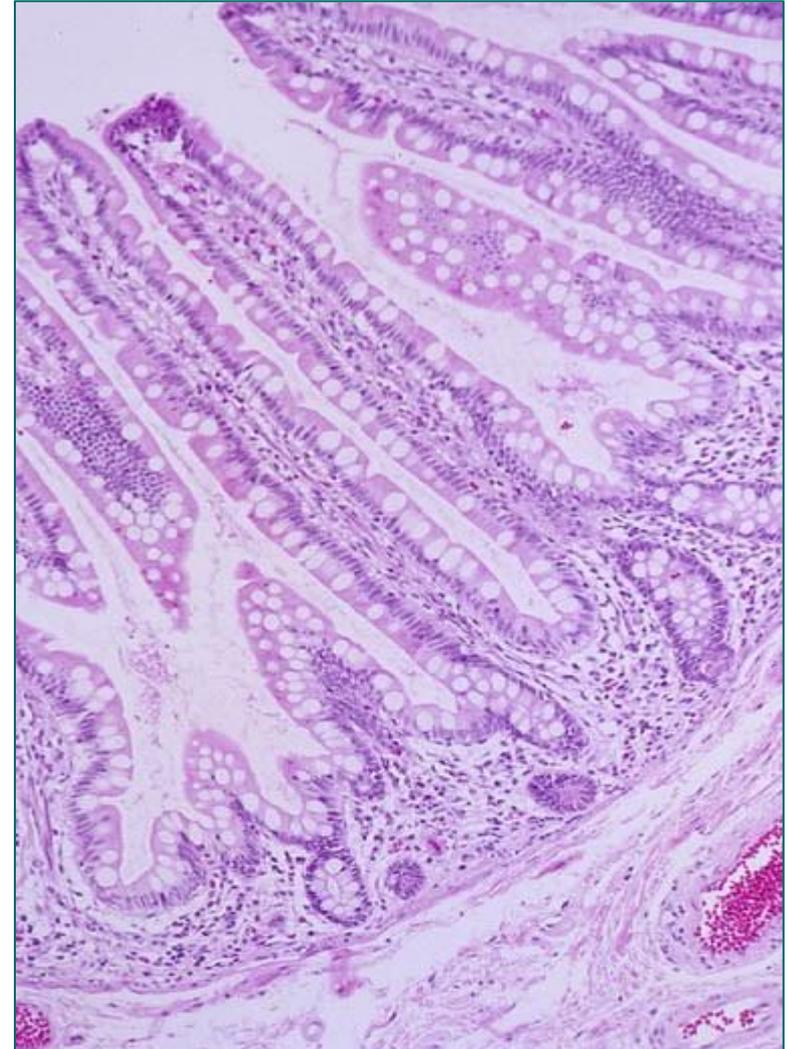
Specializations that increase the absorptive surface of the small intestine



- Circular folds (plicae circulares, Kerkring's folds) - folds of the mucosa and part of the submucosa (1-1.5 cm). They appear 5 cm from the pylorus, they are most numerous in the distal parts of the duodenum and the initial parts of the jejunum (least in the ileum).
- Intestinal villi (villi intestinales) – mucosal protrusions that protrude into the intestinal lumen (0.5-1.5mm). In the duodenum - leaf-shaped, in the jejunum and ileum finger-shaped.
- Microvilli (microvilli) - cytoplasmic extensions of enterocytes (1 μ m). Each enterocyte has several thousand microvilli - a brushy (striated) covering.
- Specializations increase the surface area of the small intestine from 1m² to 900m².

The tunica mucosa of the small intestine

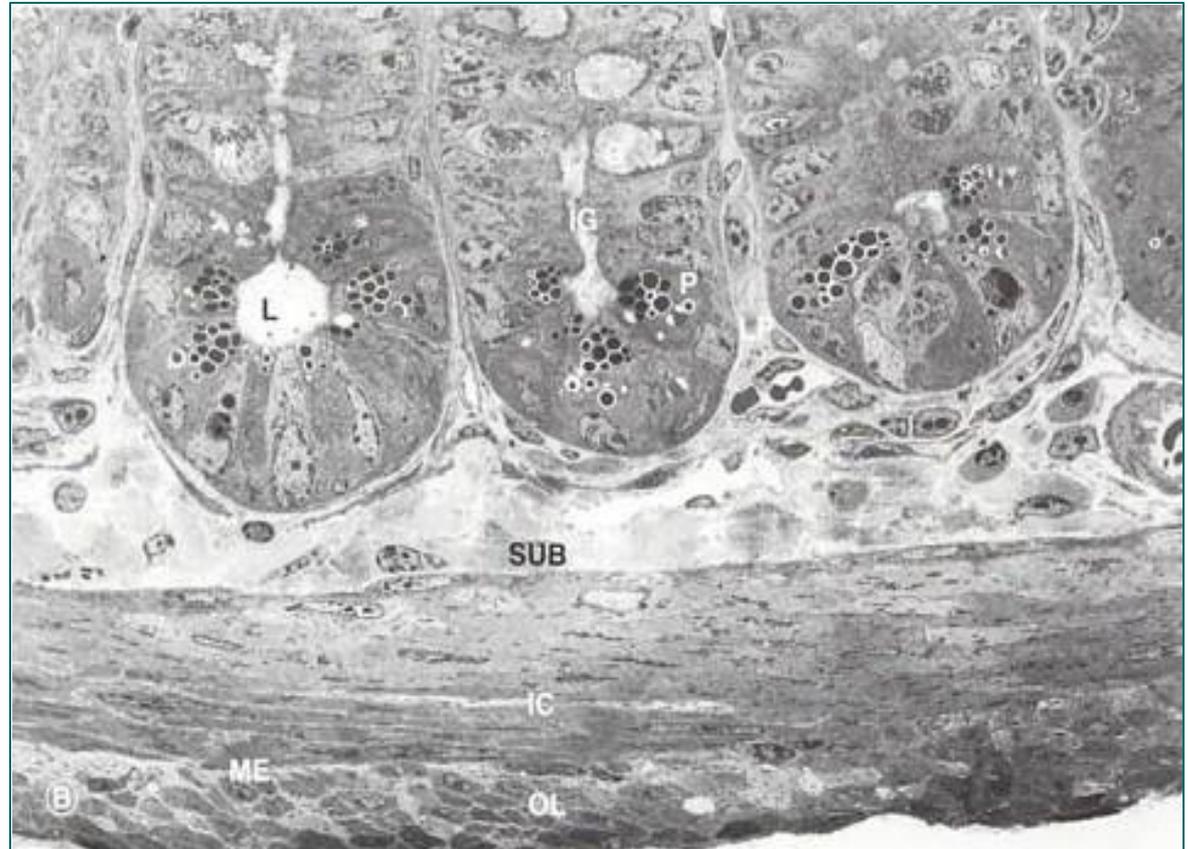
- The tunica mucosa is made up of the epithelium, lamina propria and lamina muscularis of the mucosa.
- Intestinal villi and Lieberkin's crypts (intestinal glands)
- Single-row cylindrical epithelium of villi (surface epithelium) and Lieberkin's crypts (glandular epithelium) differ in their cell composition.
- The villi are in charge of absorbing food, and the Lieberkin crypts (intestinal glands) are responsible for secretion, regulating the normal bacterial flora and restoring the entire intestinal epithelium.



Epithelium of Liberkin's crypt

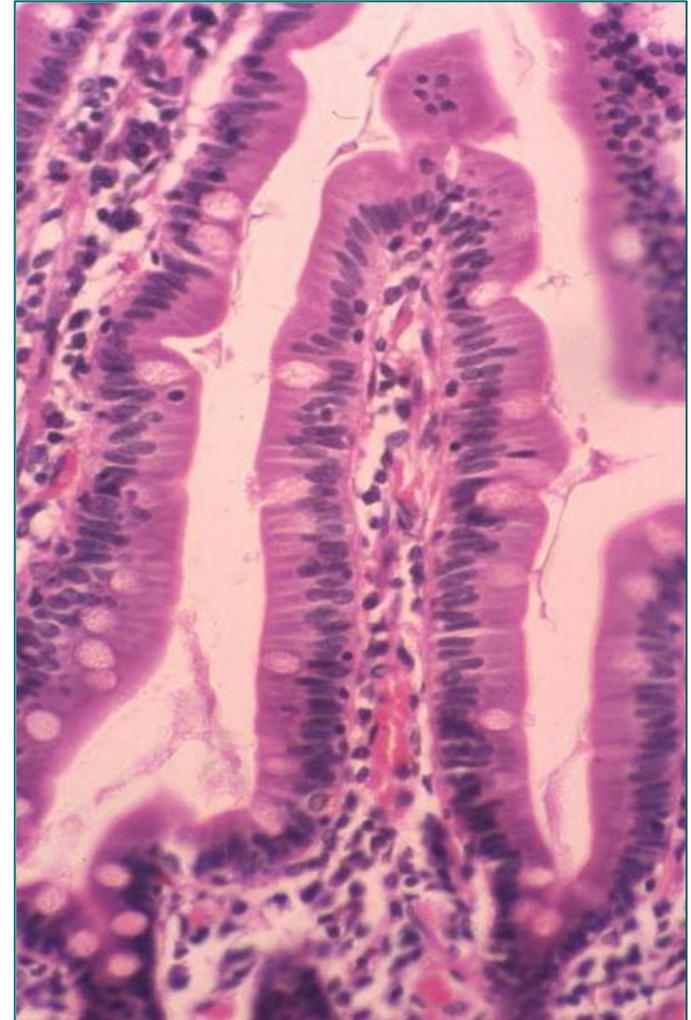
The epithelium of Liberkin's crypts (intestinal glands) is made up of:

- enterocytes
- goblet cells
- enteroendocrine cells
- Paneth cells
- M cells
- stem cells (undifferentiated)



Enterocytes

- Enterocytes are absorptive cells.
- The most numerous cells in the epithelium of the small intestine.
- Specialized for the transport of substances from the lumen to the vascular system of the lamina propria.
- Cylindrical cells connected by occlusive and adherent connections.
- Mitochondria, Golgi, smooth and grER.
- On the apical surface - microvilli - brushy (striped) cover.
- The glycocalyx protects them from autodigestion.
- The glycocalyx contains digestive enzymes incorporated into the apical plasmalemma - terminal digestion of peptides and carbon hydrates.
- At the basal pole – receptor for IgA.
- The lifespan of enterocytes is 1.5 to 3 days.



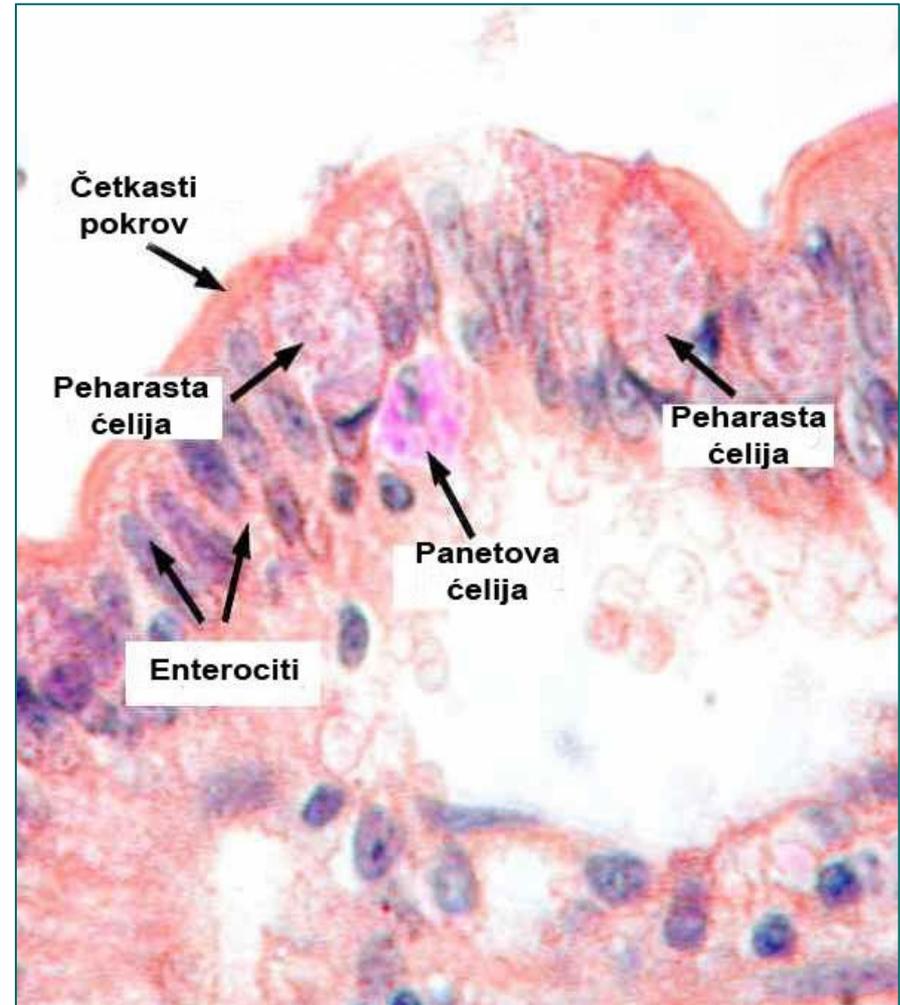
Goblet cells



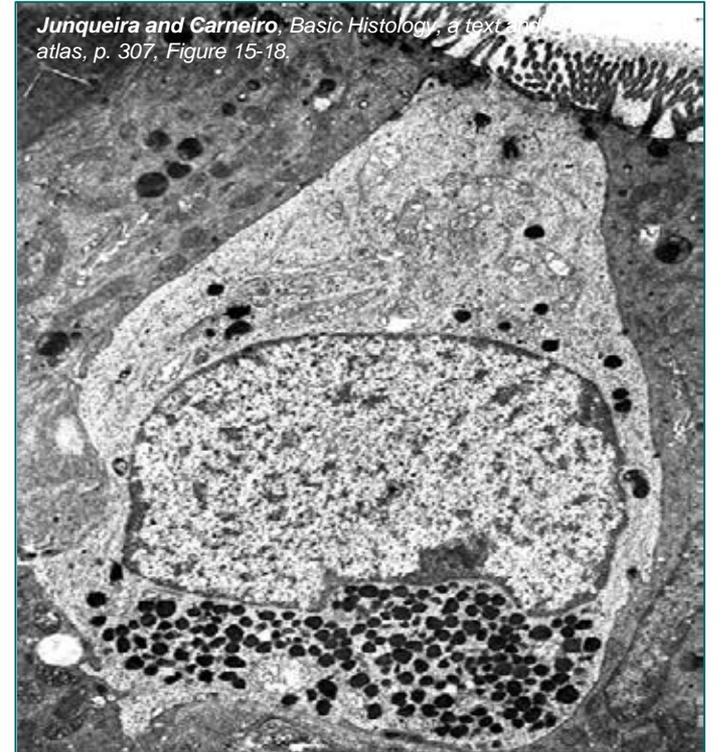
- Their number increases in the proximal-distal direction. Nucleus basal, perinucleus mitochondria, grER and ribosomes; supranuclear - extensive Golgi - mucigenic granules. They synthesize mucin (protective function). They have short and rare microvilli.

Paneth cells

- They are located at the bottom of Lieberkühn's crypts.
- Cylindrical or pyramidal in shape, nucleus and grER localized basally.
- In the supranuclear space - numerous primary and secondary lysosomes and large secretory granules.
- The secretion from the granules is released by exocytosis at the apical pole.
- It contains the enzymes lysozyme (destroys the bacterial wall) and defensin.
- They can phagocytose some strains of bacteria and protozoa.
- Longest lifespan among intestinal cells.



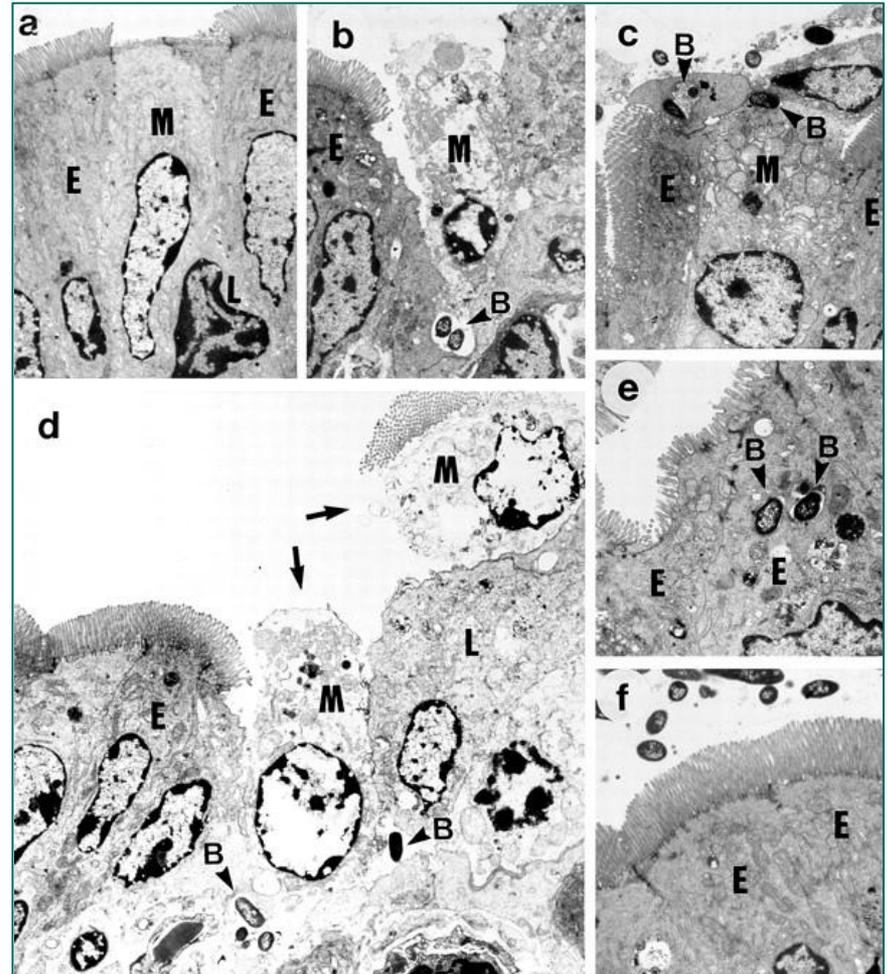
Enteroendocrine cells



- They belong to DNES.
- Subtypes characteristic of the small intestine: I-cells (cholecystokinin); S-cells (secretin); G-cells (gastrin); Mo cells (motilin); K-cells (gastric inhibitory peptide - GIP)

M cells

- They are found in the mucosa covering Peyer's plates and individual lymph follicles along the small intestine and appendix.
- Antigen-transporting cells.
- They have microfolds on the apical plasmalemma - microfold cells.
- Between the basolateral compartments of M cells are intraepithelial T lymphocytes.
- M cells accept antigens from the lumen by endocytosis and transport them to the basolateral compartment (bring them into contact with lymphocytes).
- More recent research has shown that M cells phagocytose bacteria and viruses.
- They can also transport antigens into the lamina propria (discontinuous BM below the M-cells)



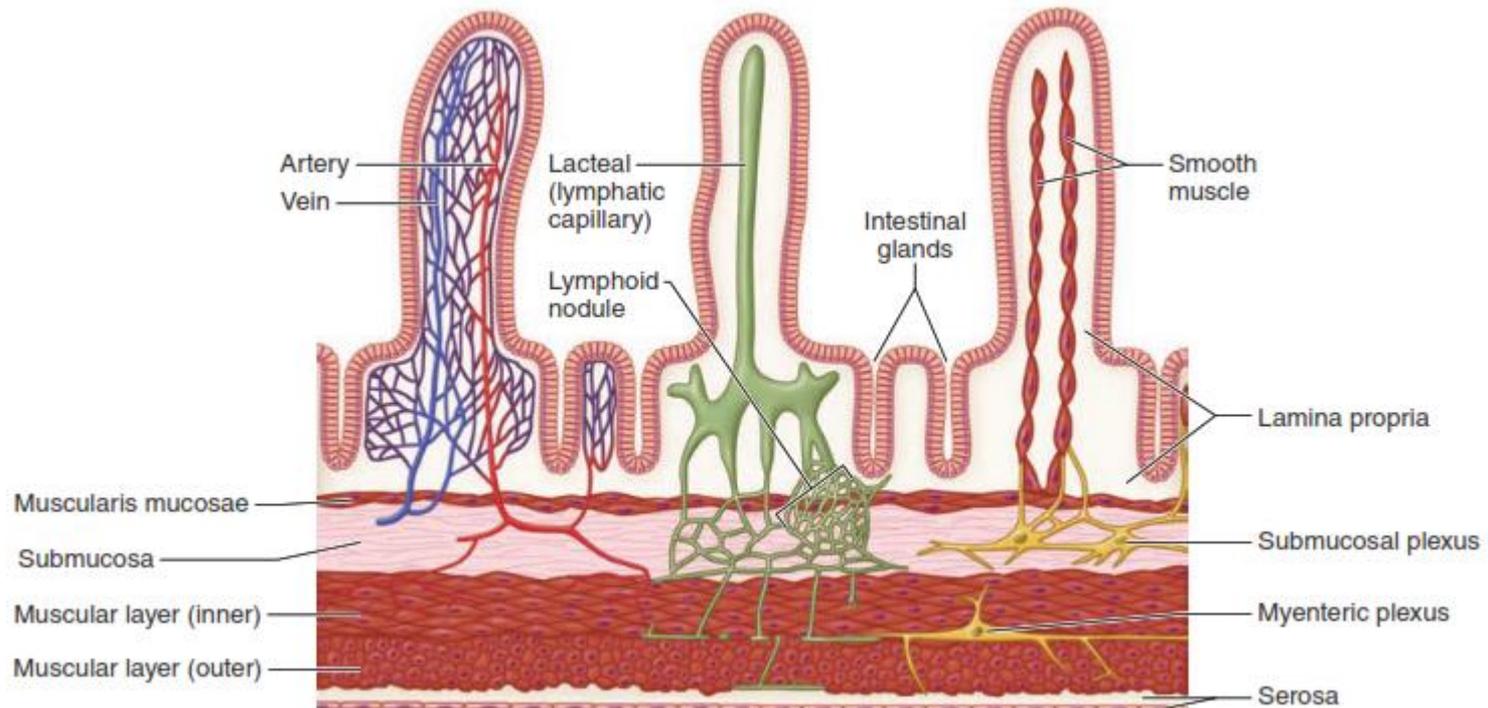
Stem cells

- Located in the lower half of Liberklin's crypts, just above the Paneth cells (cell replication zone).
- They have short microvilli, round bright nucleus, scarce organelles.
- They are connected by adhesive bonds.
- Life cycle 24 hours.
- Their division gives rise to other cells of the intestinal epithelium.
- Panet cells live about 20 days, others 2-6 days.



Intestinal villi (TEM)

- In the lamina propria of the intestinal villi, there is loose connective tissue with blood capillaries (immediately below the basal lamina of the epithelium).
- Lymphatic capillaries (lacteal) pass through the middle intestinal villi.
- The smooth muscle cells of the lamina muscularis separate and extend along the entire length of the villi - Birke's muscle.

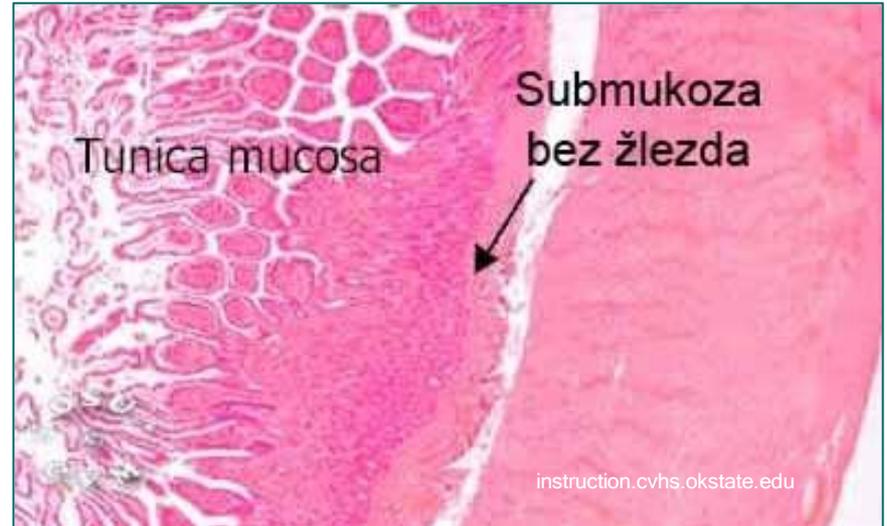


Duodenum

- The main characteristic of the duodenum is the presence of Brunner's glands
- (gll. duodenales) in the submucosa.
- Brunner's glands extend from the pylorus to the duodenojejunal flexure.
- Secretory parts - convoluted tubules.
- Excretory ducts - open in Lieberkühn's crypts or between the villi.
- The glandular epithelium is cuboidal.
- Brunner's glands secrete an alkaline secretion - it neutralizes the HCl of the stomach and corrects the pH of the intestinal contents for the action of pancreatic enzymes.
- They secrete urogastron - inhibits HCl secretion, stimulates cell renewal in the crypts.



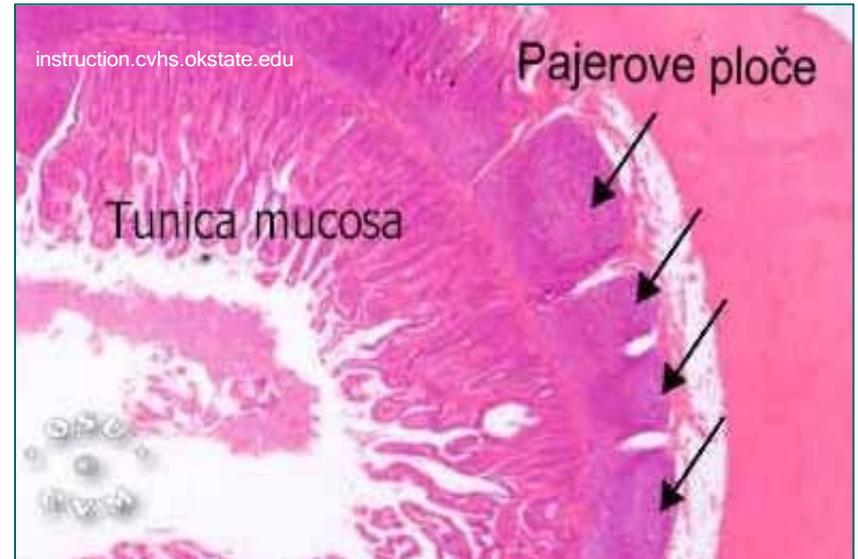
Jejunum



- There are no structural specifics.
- Kerkring's folds are very elongated.
- The villi are long and finger-like.

Ileum

- The lamina propria and submucosa of the ileum contain aggregates (10-400) of lymphatic follicles - Peyer patches.
- Peyer patches are placed in a row along the ileum.
- The intestinal villi above Peyer patches are reduced.
- M-cells are present in the epithelium.
- In the lymph follicles, naive B lymphocytes differentiate into plasma cells and memory B cells.

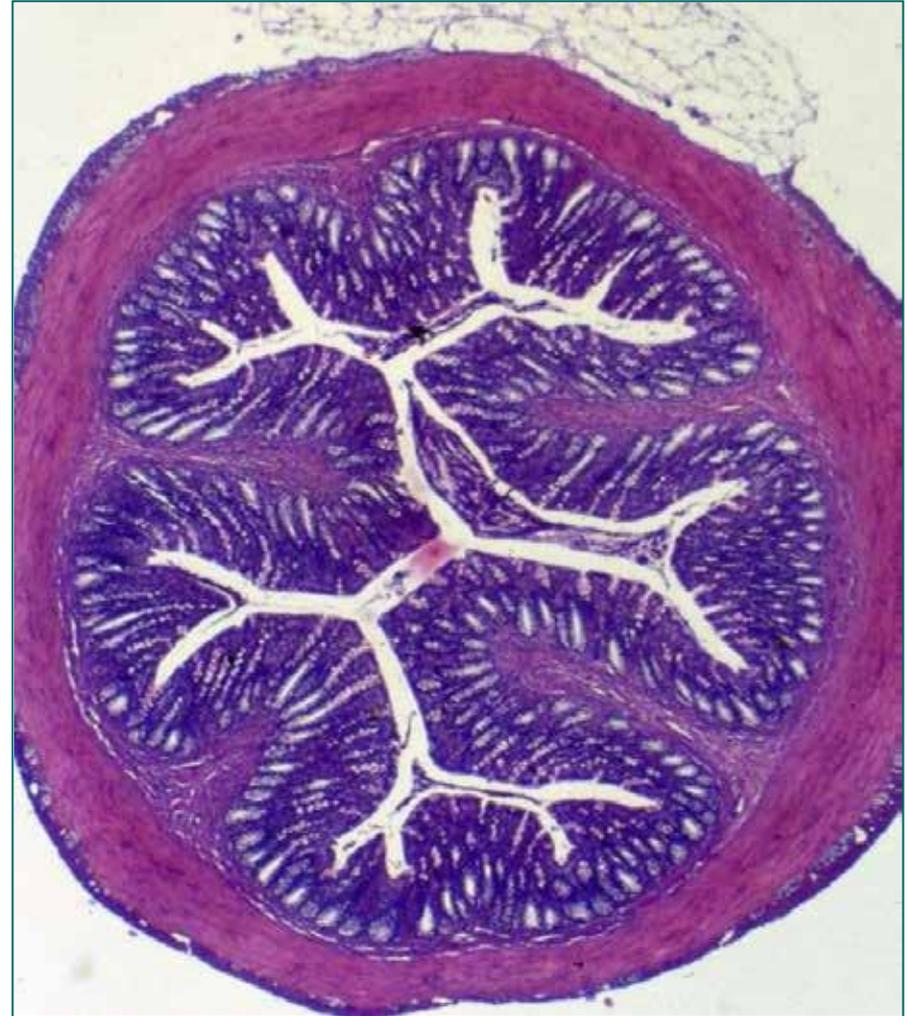


Colon(intestinum crassum)

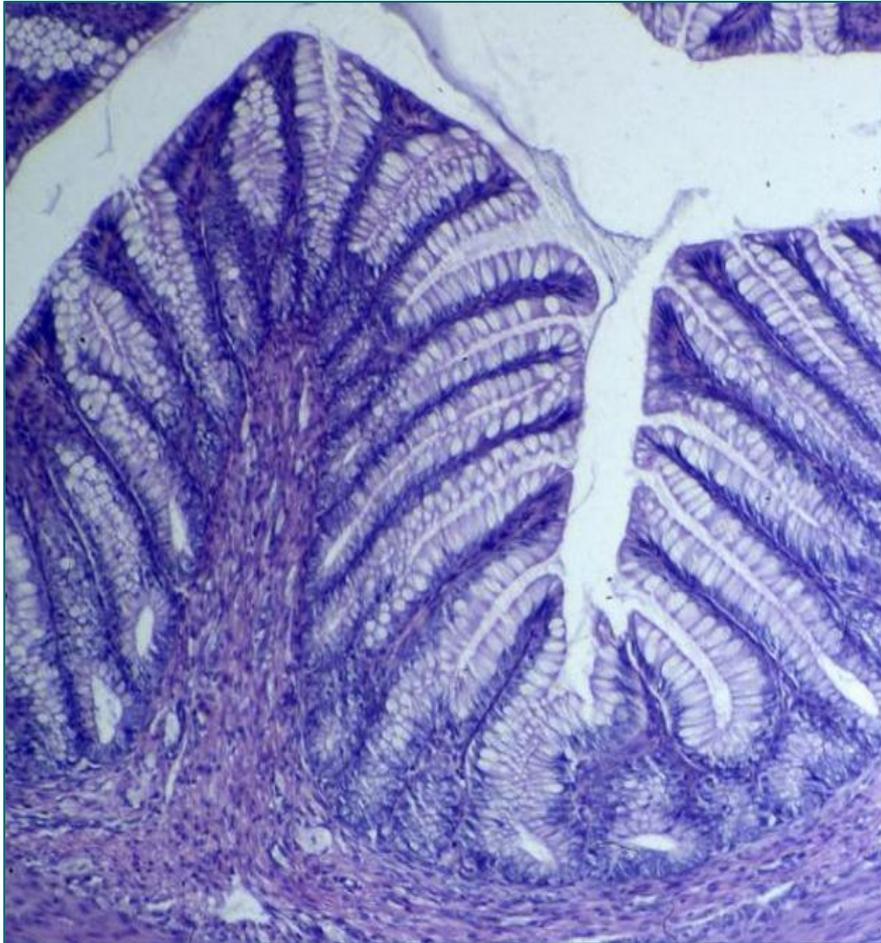
- From the ileocecal valve to the anal canal (1.5m).
- Includes:
 - caecum
 - Appendix vermiformis
 - colon
 - rectum
- More uniformly built than small intestine.
- The differences are in the mucosa and tunica muscularis.
- There are no intestinal villi or circular folds, since only water and electrolyte absorption takes place in it.

Cecum and colon (caecum et colon)

- The mucosa is "smooth" (there are no intestinal villi or circular folds).
- Properly distributed Lieberkühn's crypts (simple, tubular, intestinal glands) in large numbers.
- Submucosa - dense connective tissue, blood and lymphatic vessels, submucosal plexus, fat cells.
- Tunica muscularis - inner circular (even layer) and outer longitudinal - forms three thickened longitudinal bands - taeniae coli (t. mesocolica, t. omentalis, t. libera).
- Their contractions create haustra and plicae semilunares.
- Serosa, retroperitoneal - adventitia.

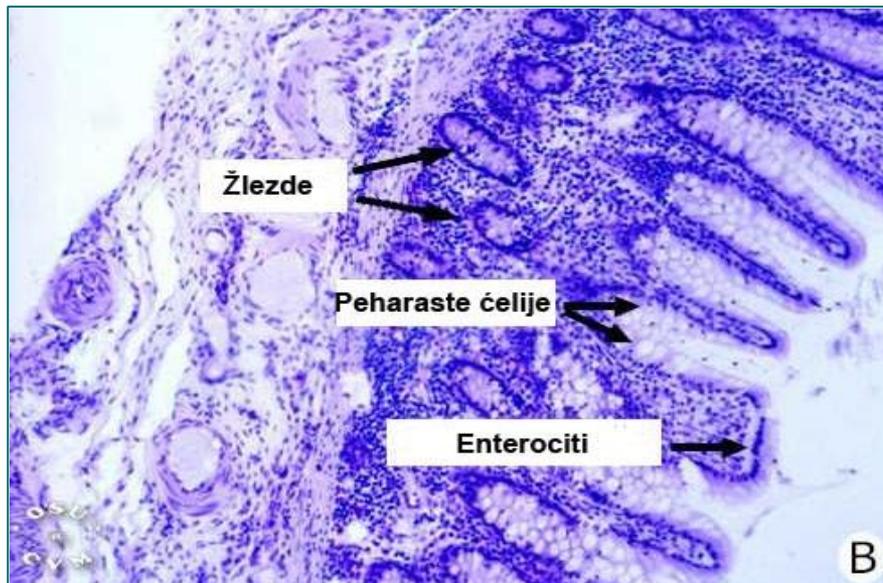
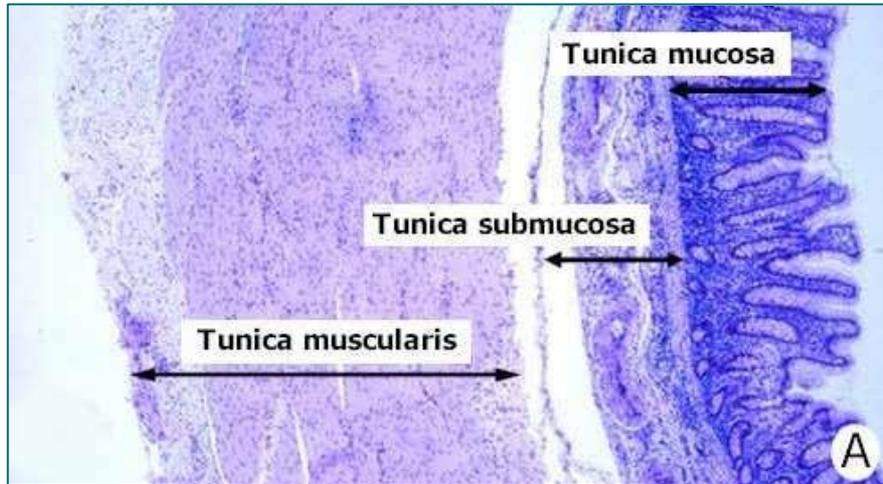


Cecum and colon (caecum et colon)



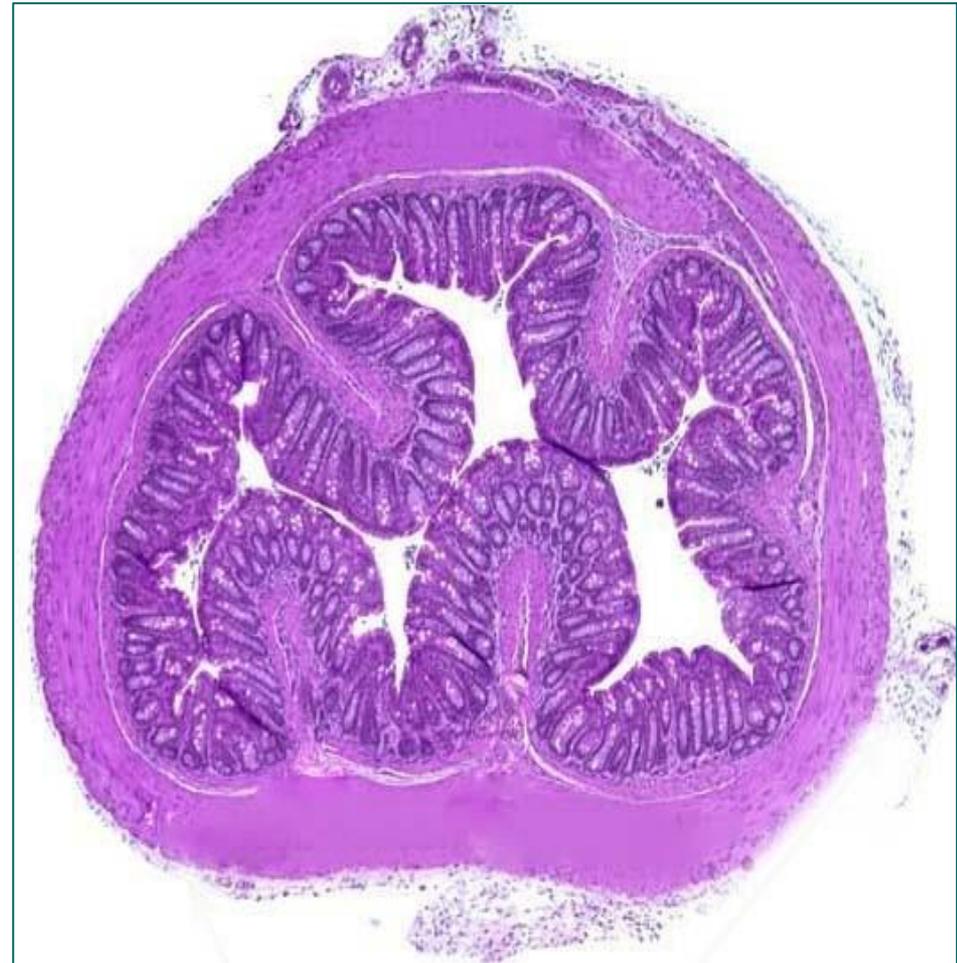
- The crypts extend through the entire thickness of the mucosa, reaching the lamina muscularis).
- Same cell types as in the small intestine, Paneth cells are missing.
- The epithelium is dominated by goblet cells, enterocytes and enteroendocrine cells in smaller numbers, stem cells are present.
- The lamina propria contains blood but not lymphatic vessels (there are no metastases until infiltration into the submucosa).
- Directly below the basal lamina is a collagen plate (5 μ m) - it is created by fibroblasts.
- It regulates the flow of water and electrolytes from the intestinal lumen into the bloodstream

Colon

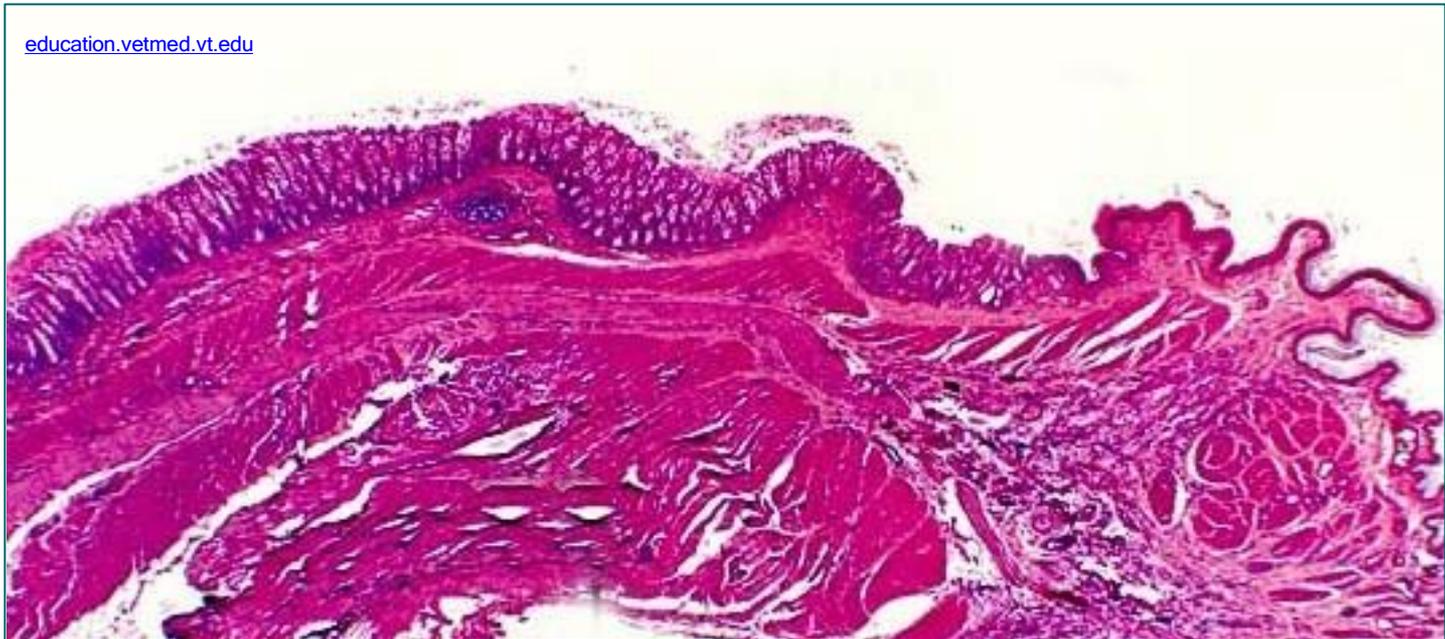


Large intestine (rectum)

- It consists of an upper part (rectum in the narrower sense) and a lower part (anal canal).
- The upper part of the rectum is similar to the colon (deeper crypts of Lieberkühn).
- In the initial part of the rectum, taenia coli disappear, and their bundles merge into one longitudinal sublayer of the tunica muscularis.
- This sublayer is more strongly developed on front and back of the rectum.
- As it is longer than the rectum, it causes its lengthwise folding - plicae transversales.
- The composition of the transverse folds includes the submucosa and the circular sublayer of the tunica muscularis.

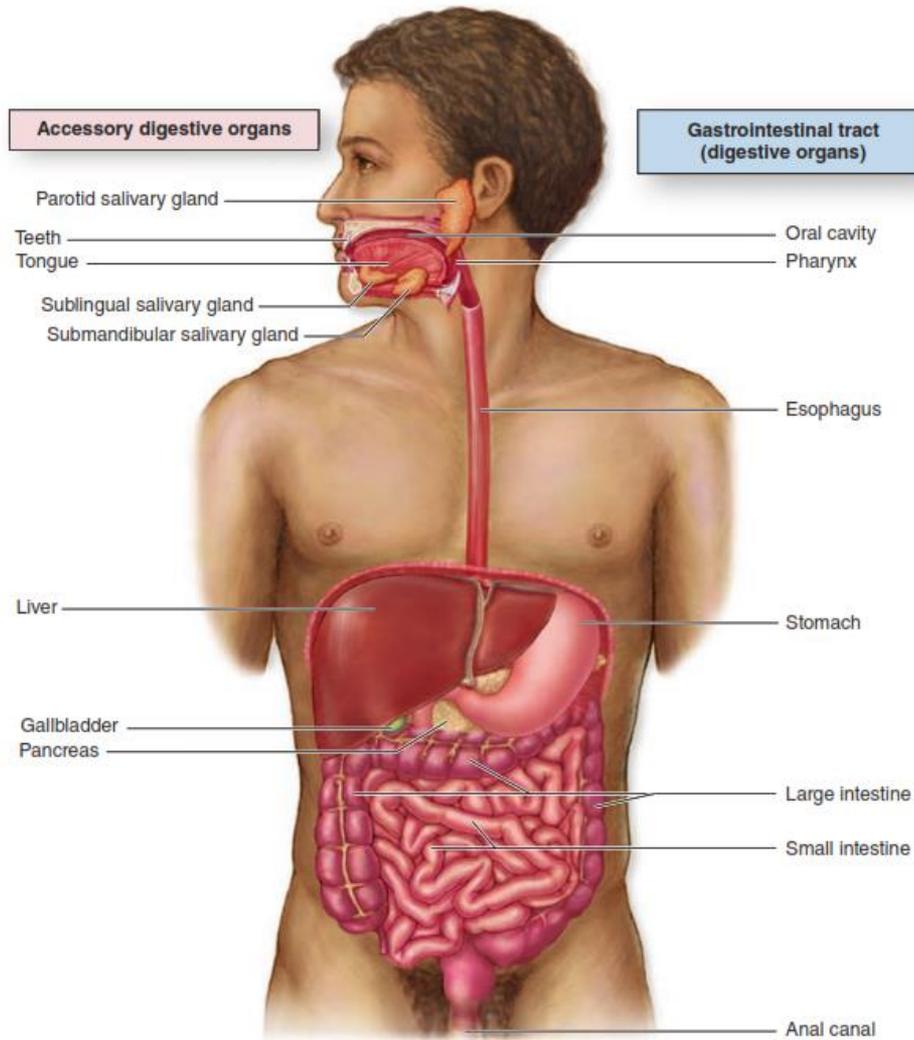


Anal canal



- The anal canal (the final part of the rectum) is 2-3 cm long.
- Three zones in it:
 - Zona columnaris (haemorrhoidalis)
 - Zona intermedia
 - Zona cutanea

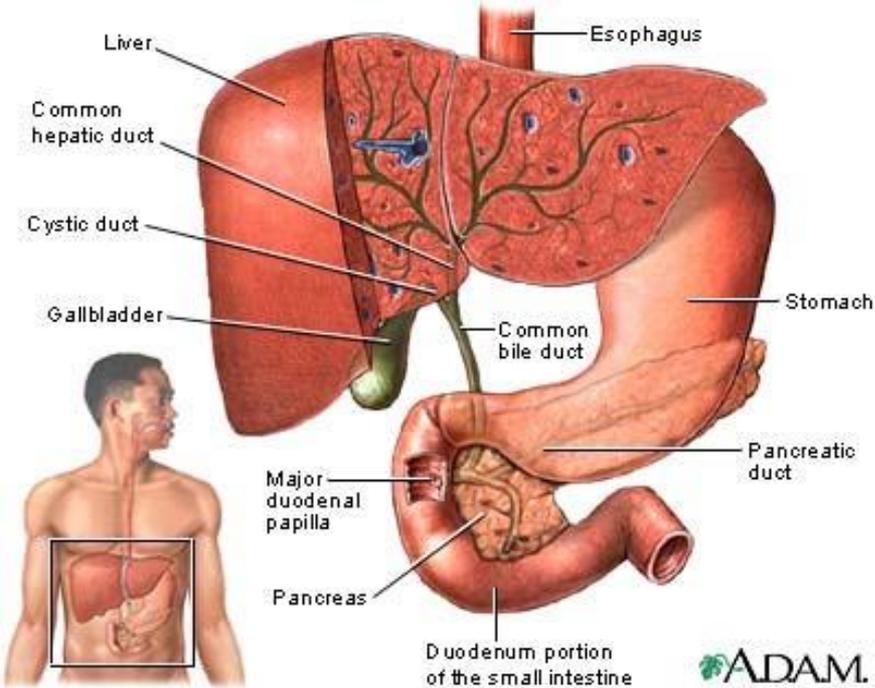
**Organs Associated
with the Digestive Tract**



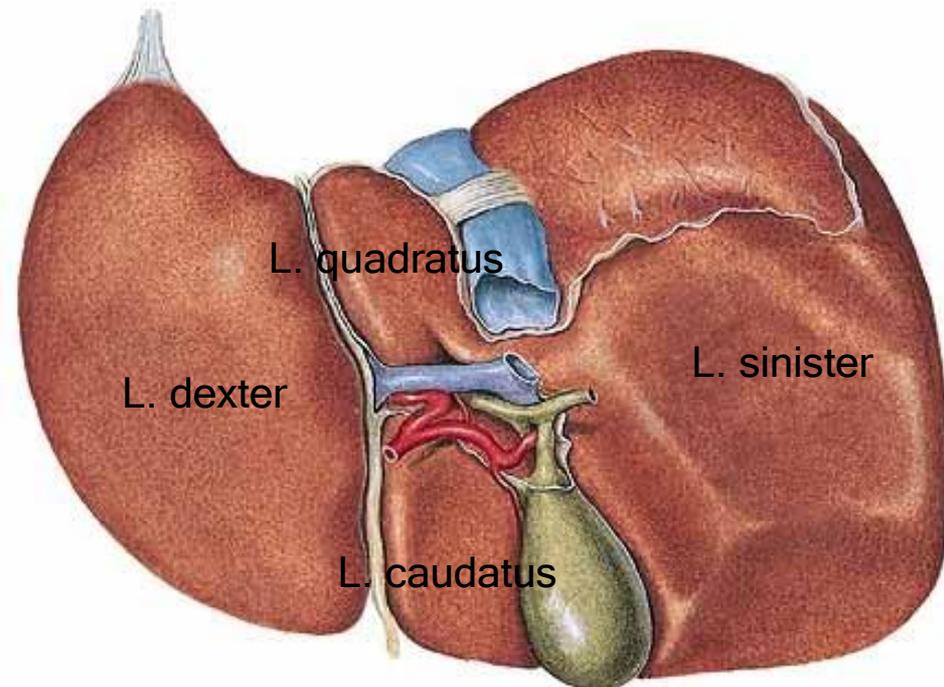
- SALIVARY GLANDS
- LIVER
- PANCREAS
- GALLBLADDER

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



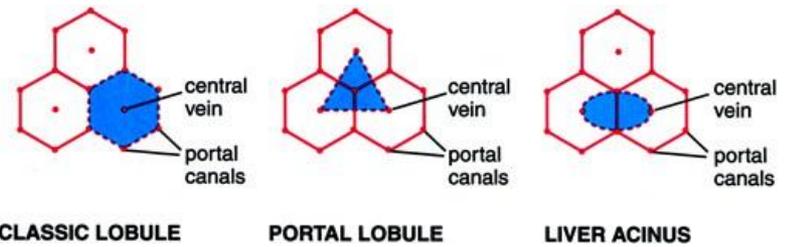
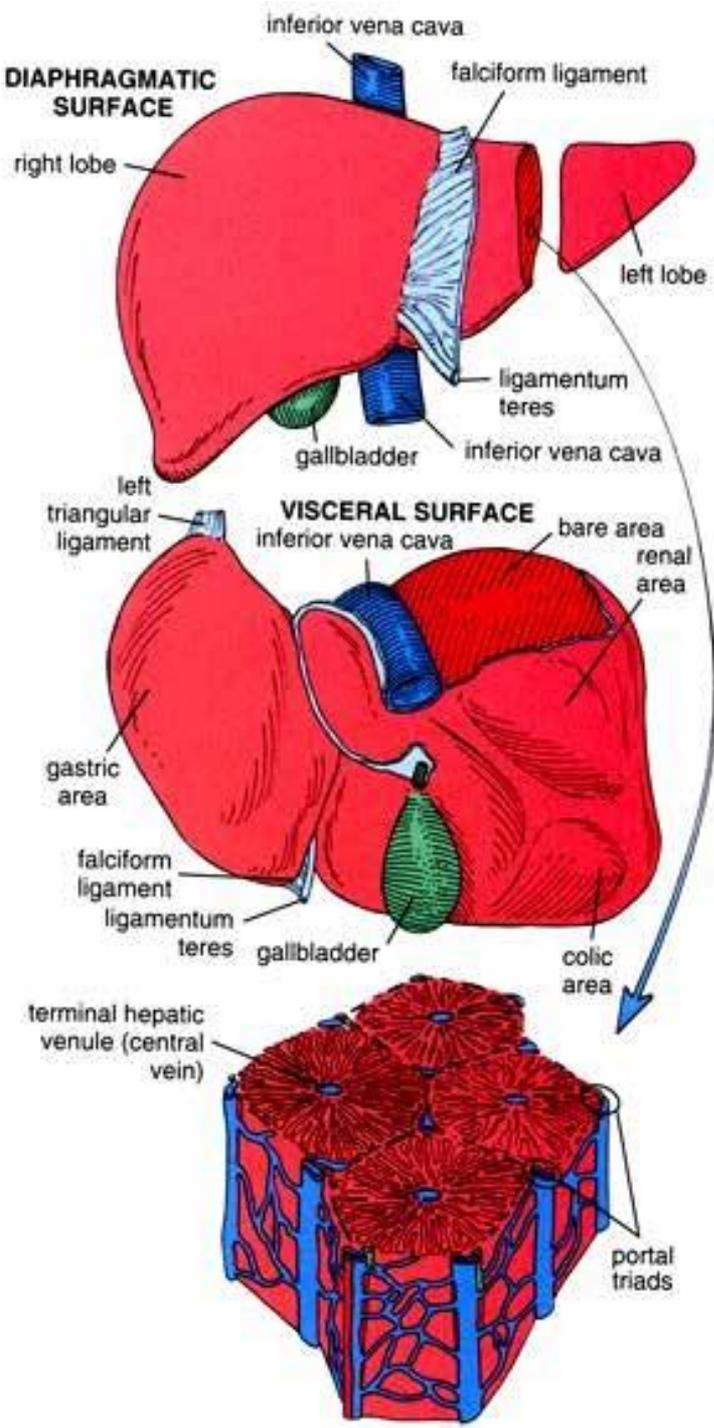
LIVER

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.

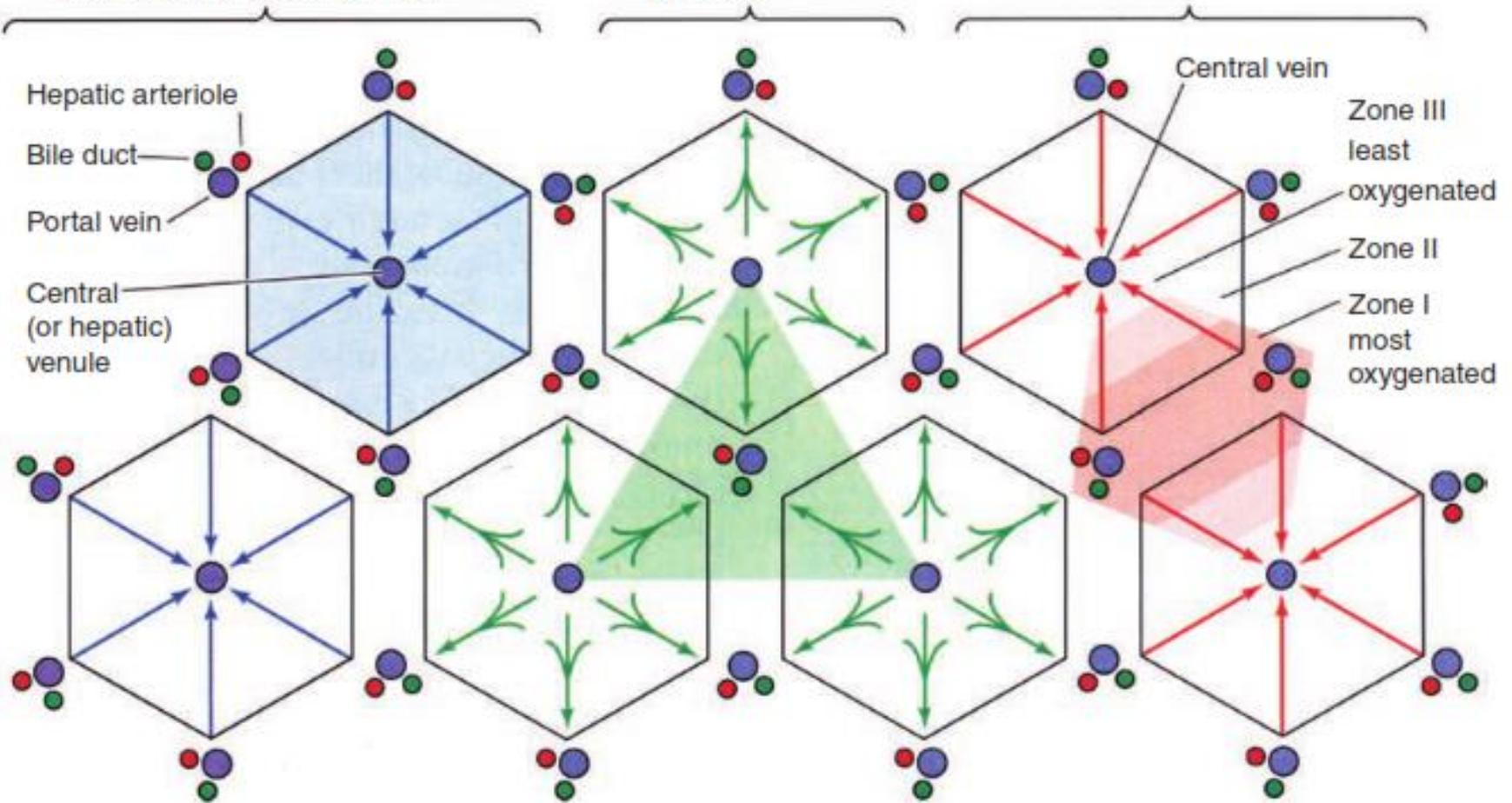
Classic liver lobule

- 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.

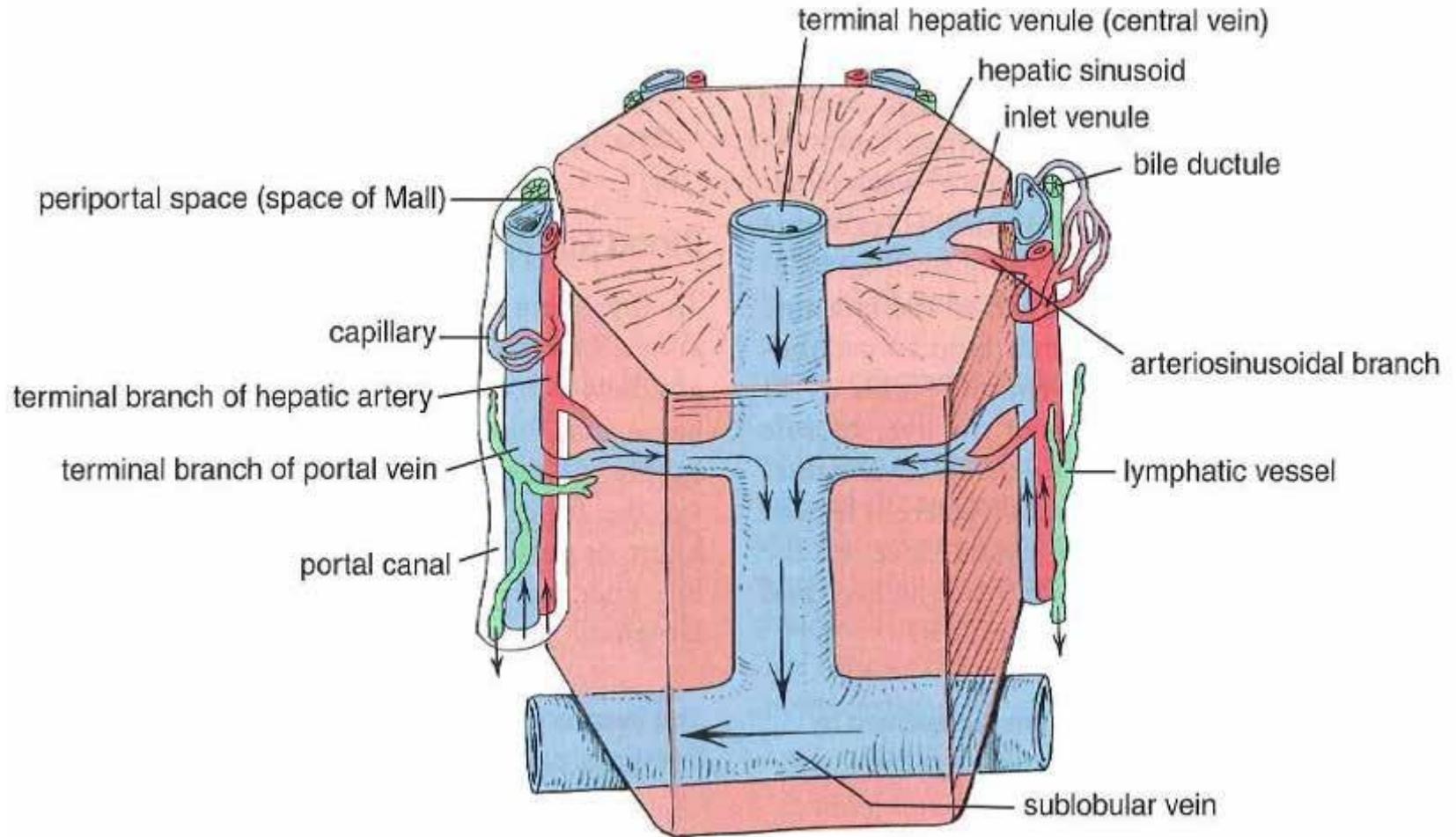
(a) Classic Hepatic Lobule
Drains blood from the portal vein and the hepatic artery to the hepatic or the central vein

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

(c) Hepatic Acinus
Supplies oxygenated blood to hepatocytes



Classic liver lobule

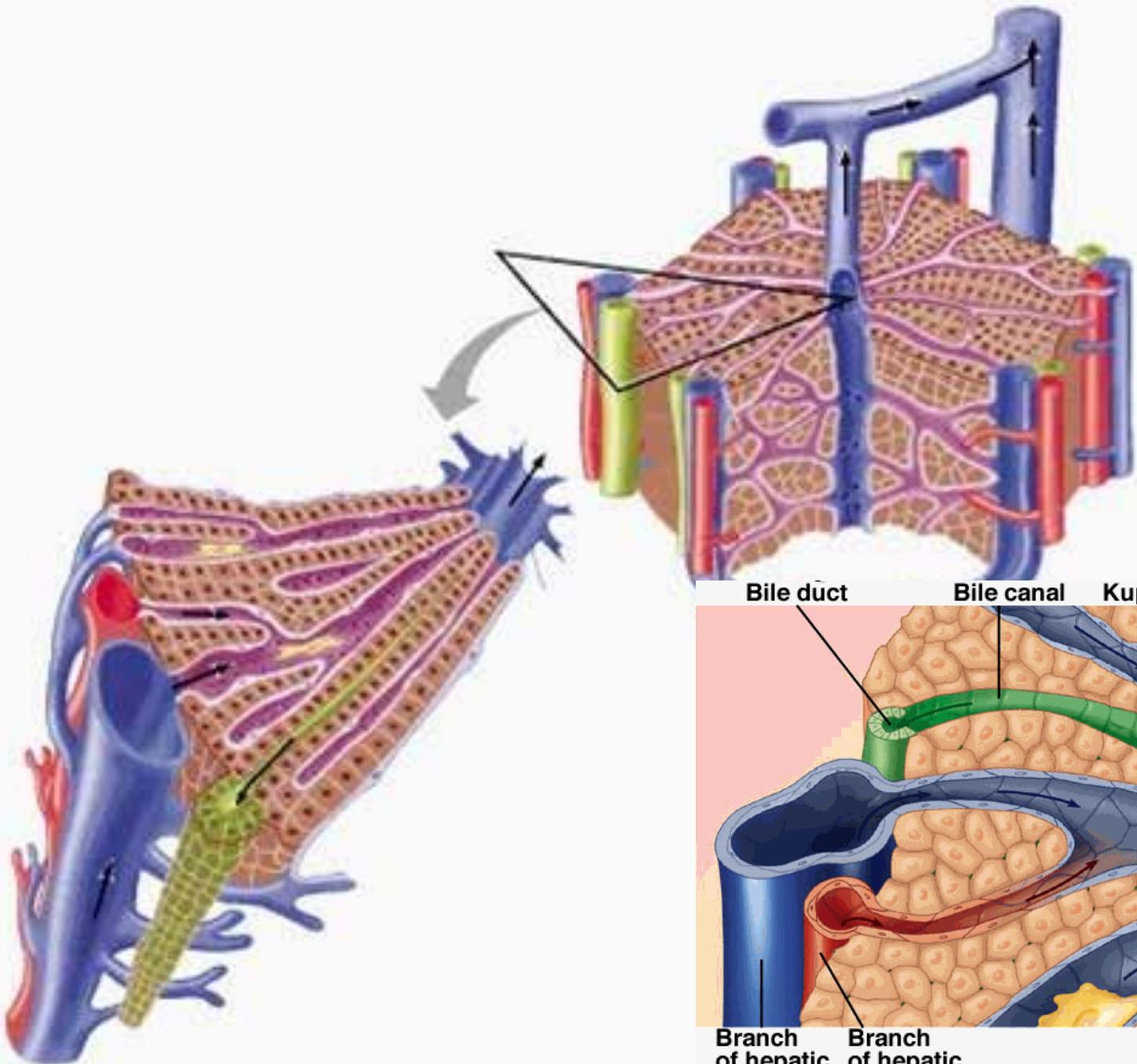


Liver blood flow

- 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.



Bile duct **Bile canal** **Kupffer cell** **Hepatic cells**
Branch of hepatic portal vein **Branch of hepatic artery** **Blood flow into liver** **Hepatic sinusoids** **Central canal (blood flow out of liver)**

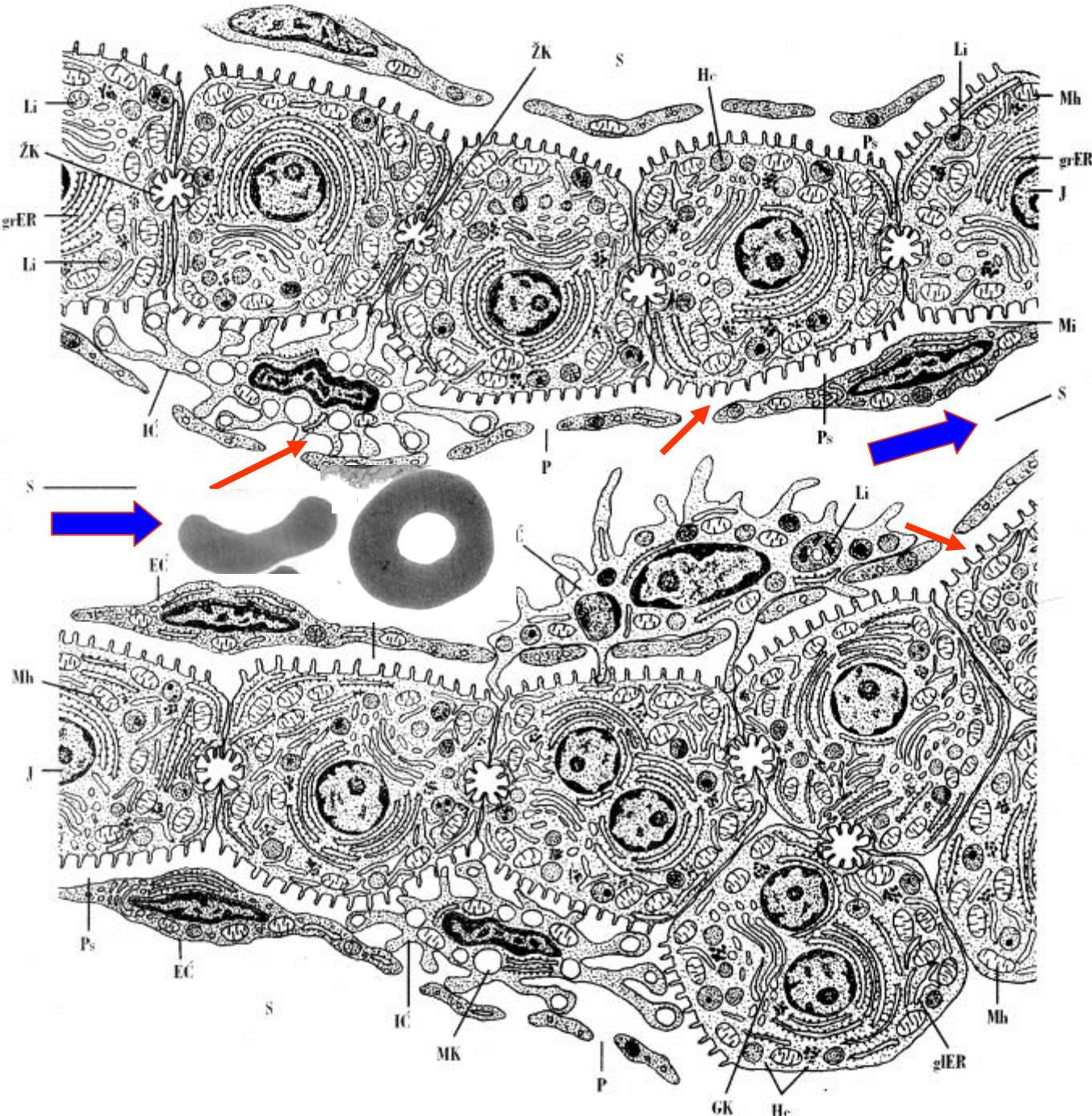
Sinusoidal capillaries

- 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 μm

Sinusoidal capillaries

Kupffer cells

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



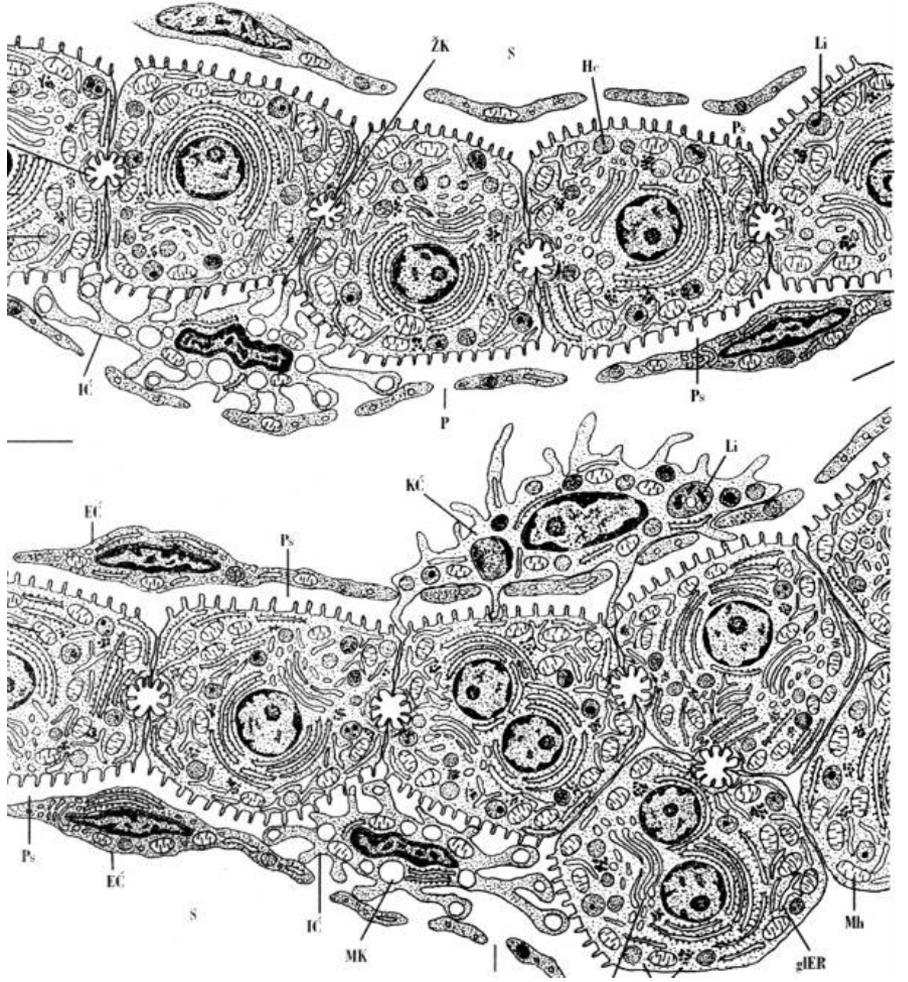
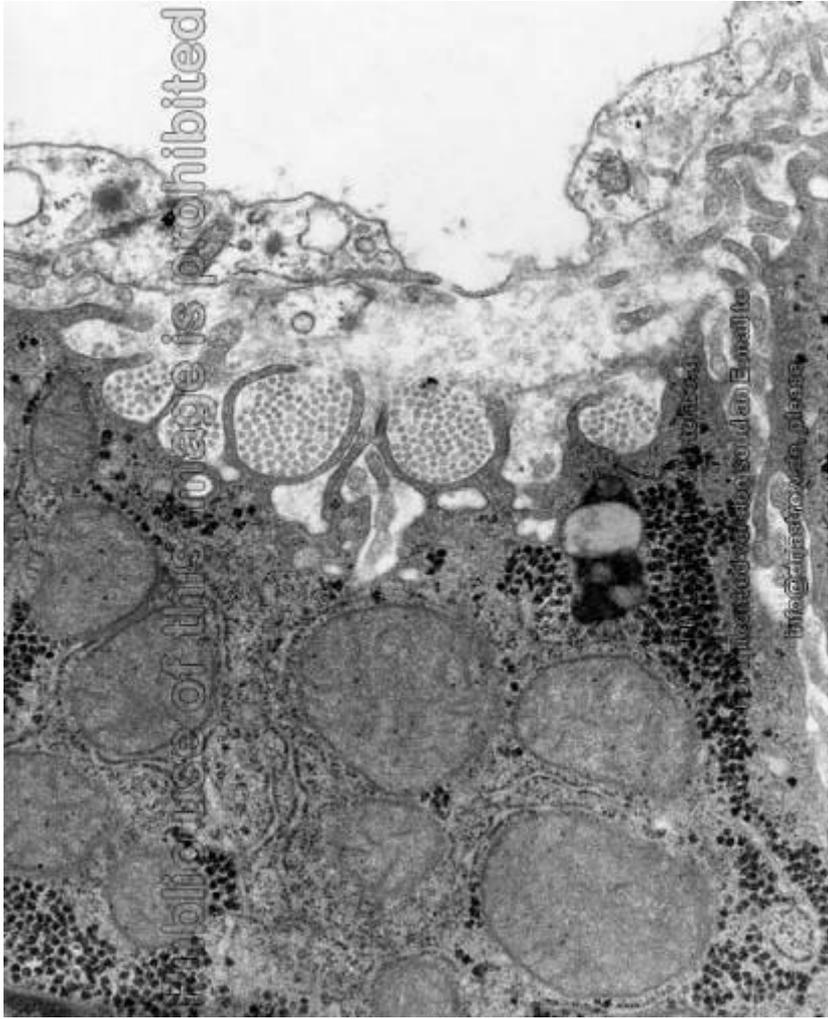
Sinusoidal capillaries

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.

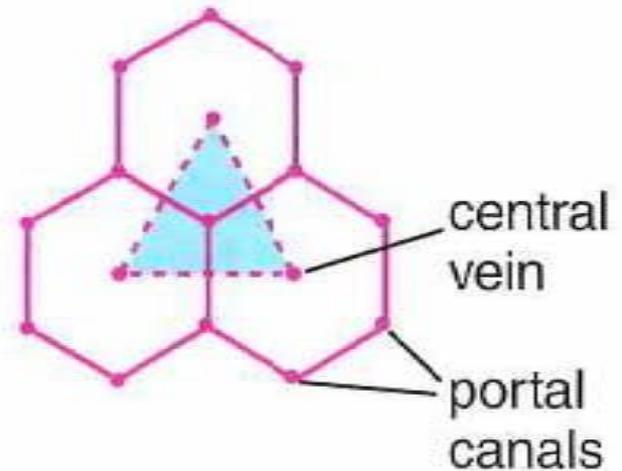
Perisinusoidal spaces

- 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.

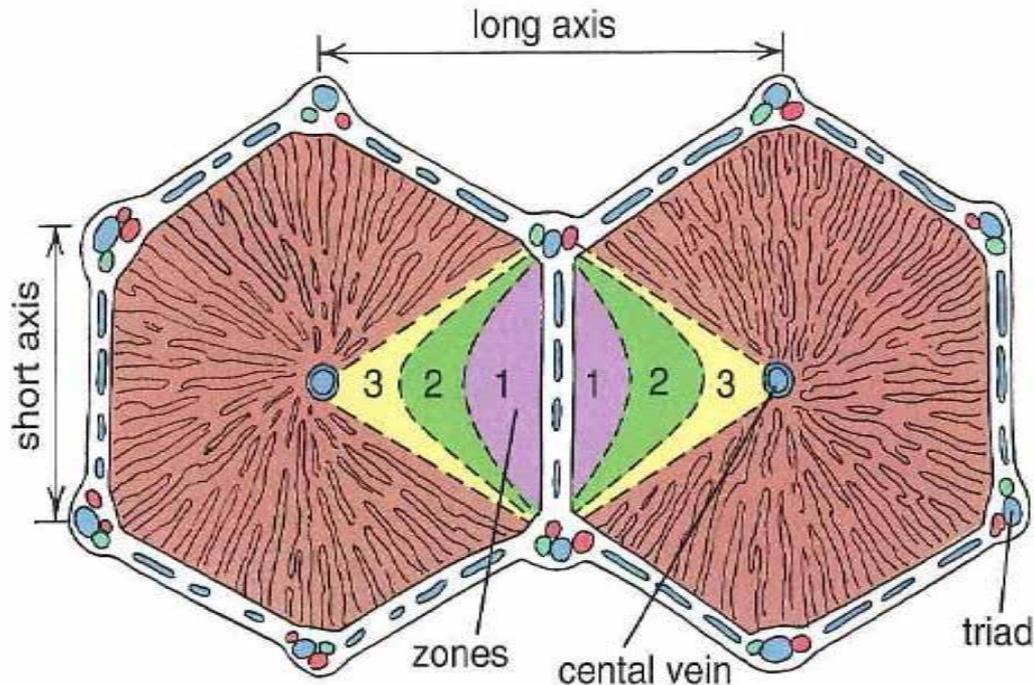


PORTAL LOBULE

Liver acinus

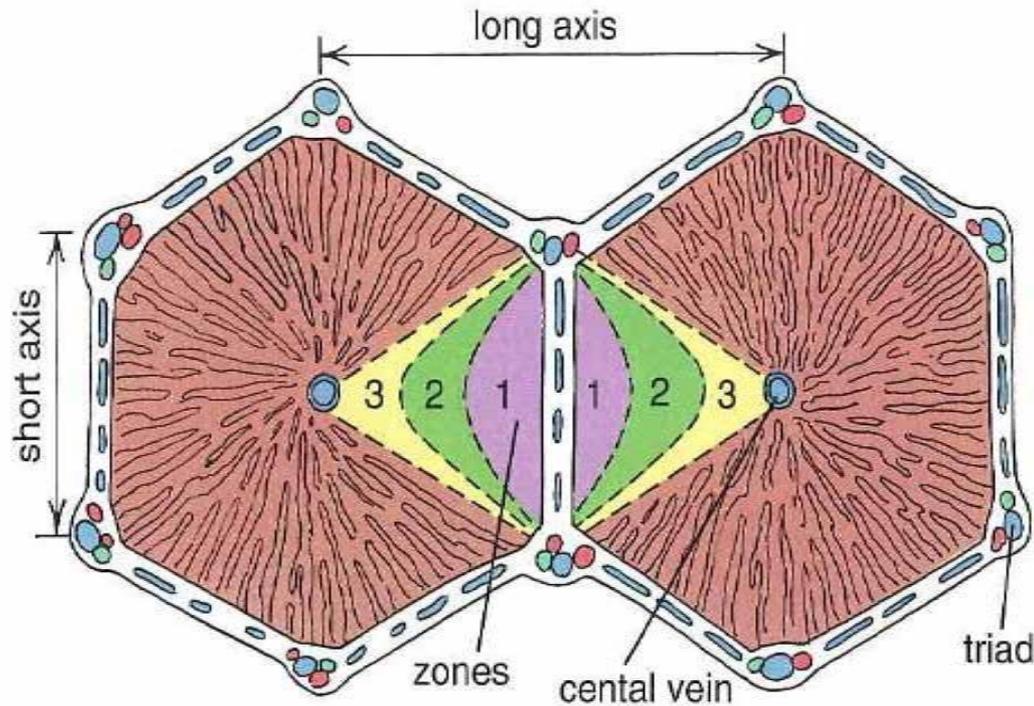
- Hepatic acinus is the smallest structural and functional unit of liver tissue suitable for the interpretation of metabolic activity and pathological processes in the liver, it is also called Rapaport's acinus.
- Liver acinus is a morphological reflection of liver function in physiological and pathological 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



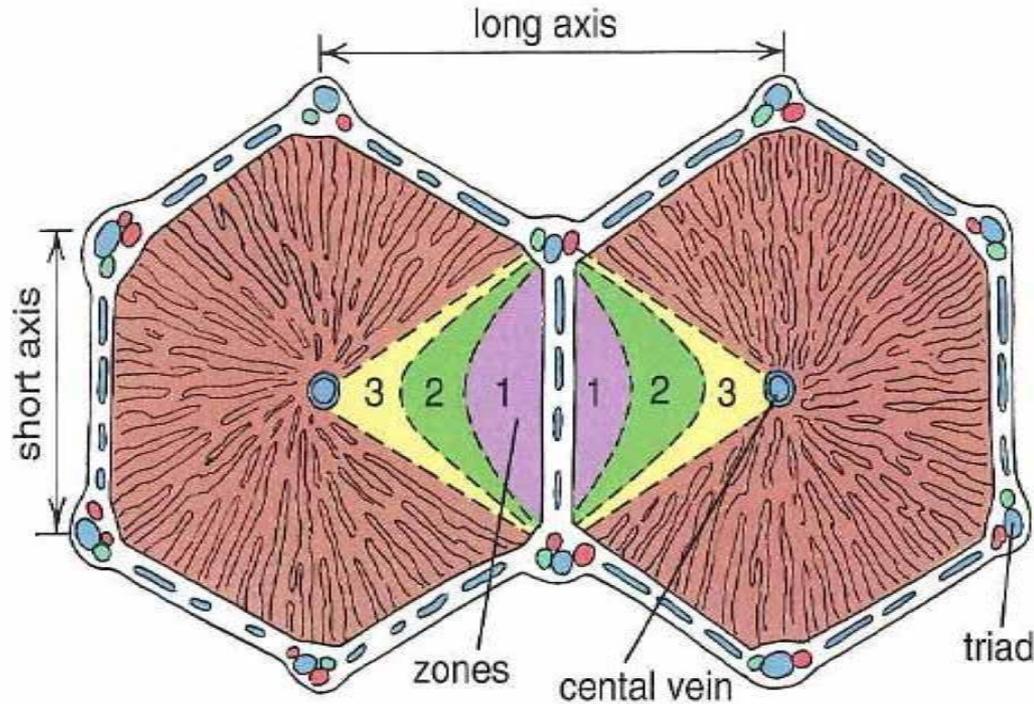
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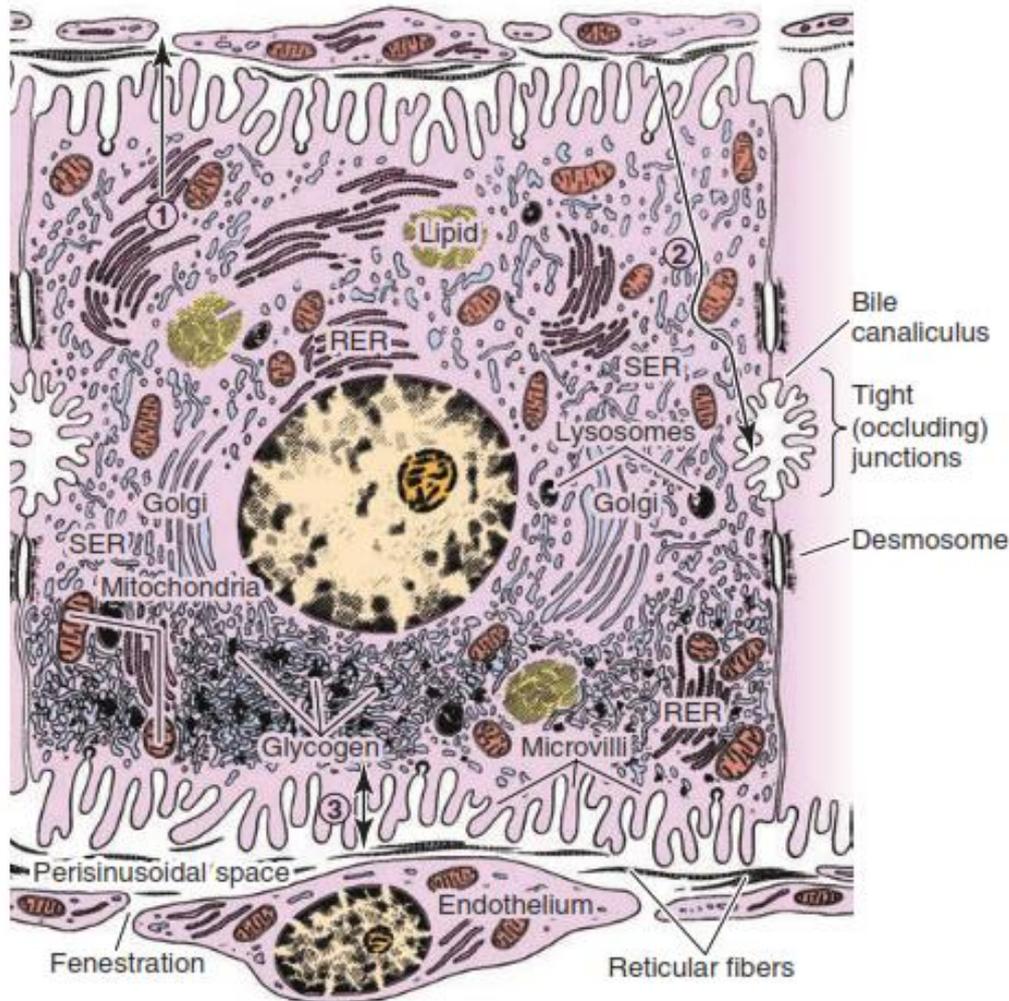
Liver acinus

- 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 O₂ 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

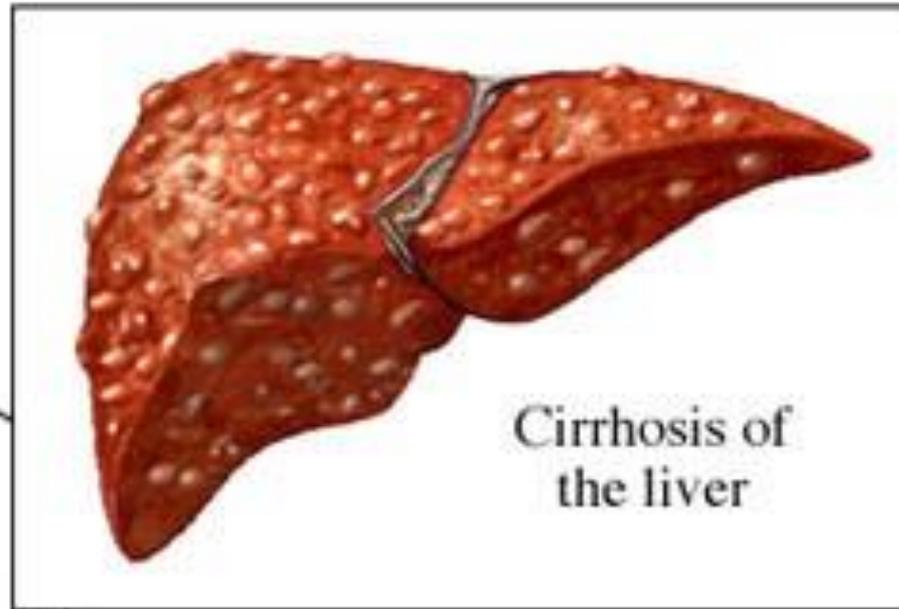
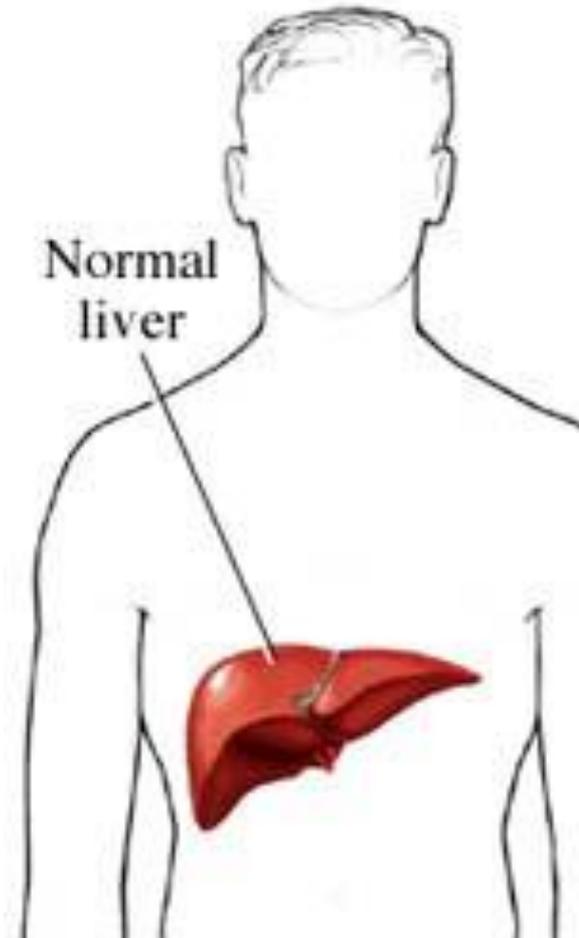
- Hepatocytes are glandular cells that make up about 80% of the liver's cell population. They have a polygonal shape and a size of 20-30 μm .
- 25% of hepatocytes have two nuclei, and the majority of mononuclear hepatocytes are polyploid
- The plasmalemma of hepatocytes shows different specializations 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



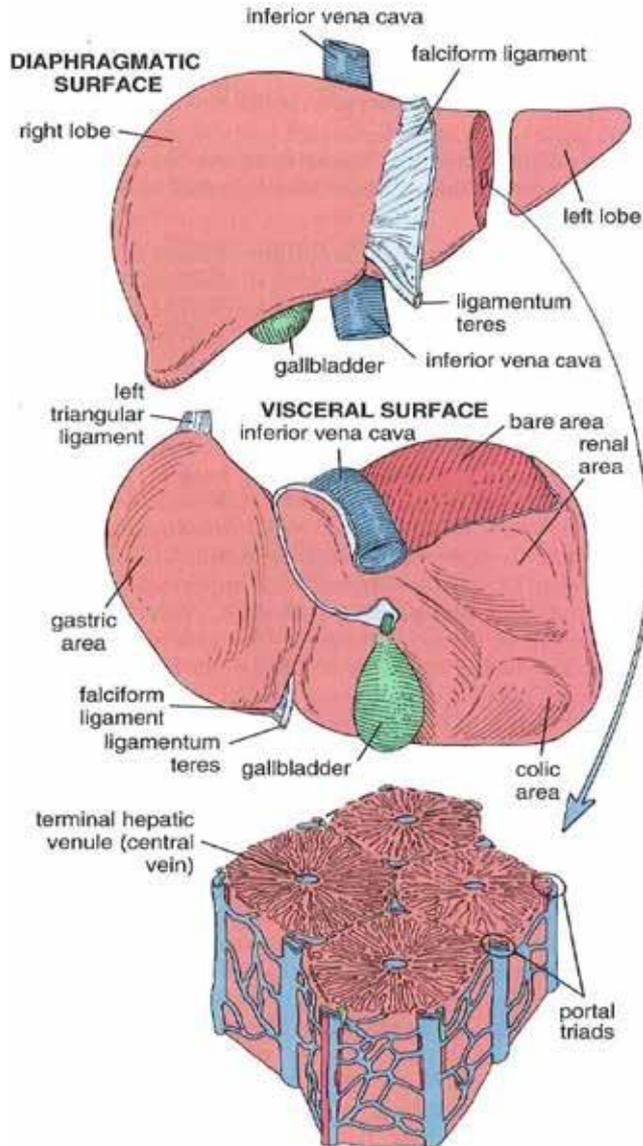
A diagram of hepatocyte cytoplasmic organization, with major functions localized. (1) RER is primarily engaged in synthesis of **plasma proteins** for release into the perisinusoidal space. (2) Potentially toxic compounds, bilirubin (bound to albumin) and bile acids are taken up from the perisinusoidal 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



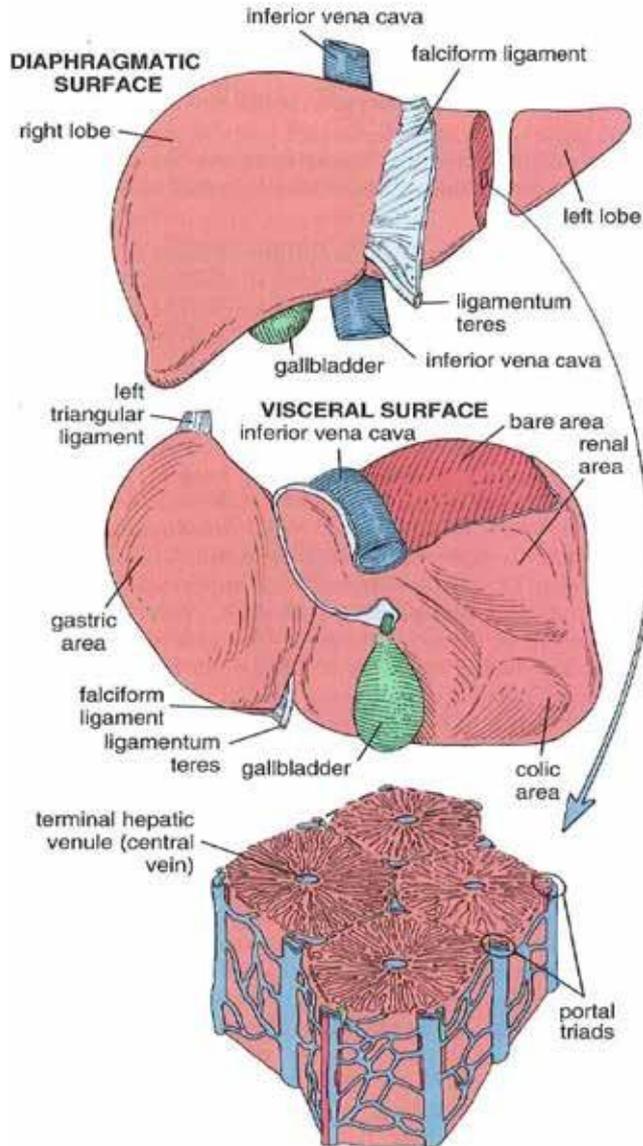
Production of plasma proteins

- 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.

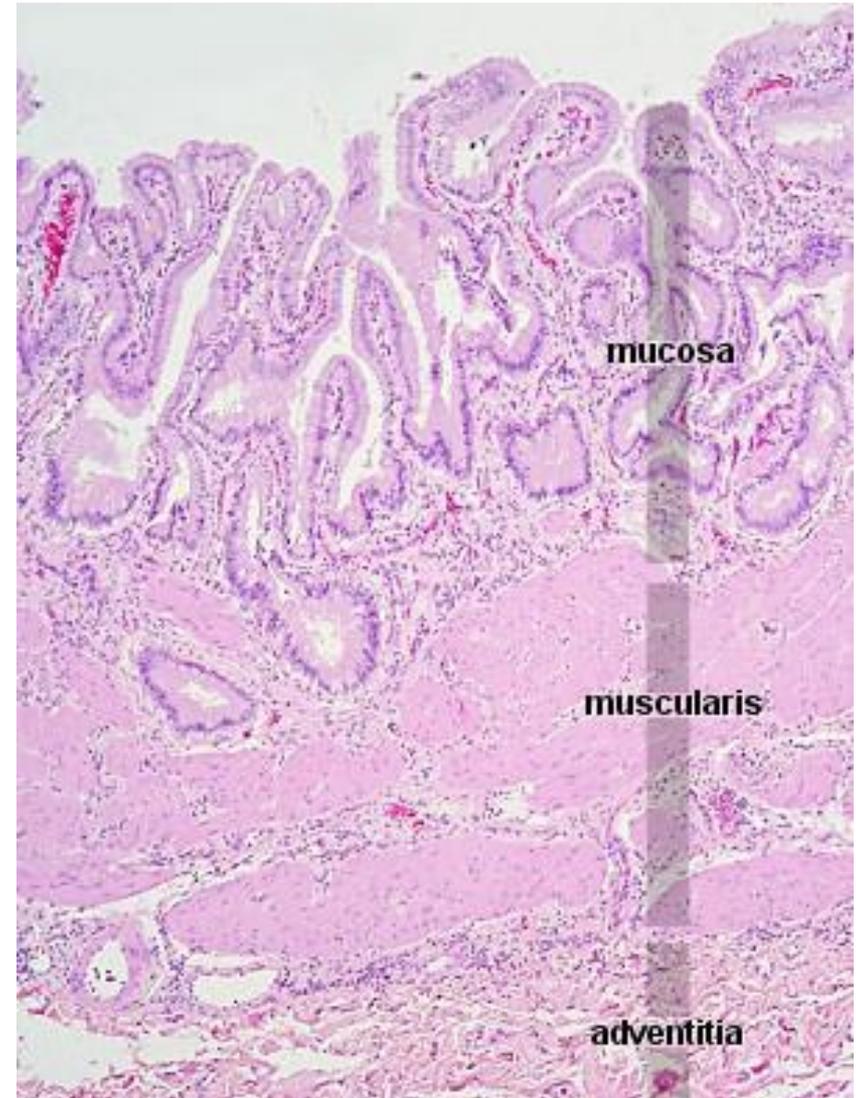
Bile ducts

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.

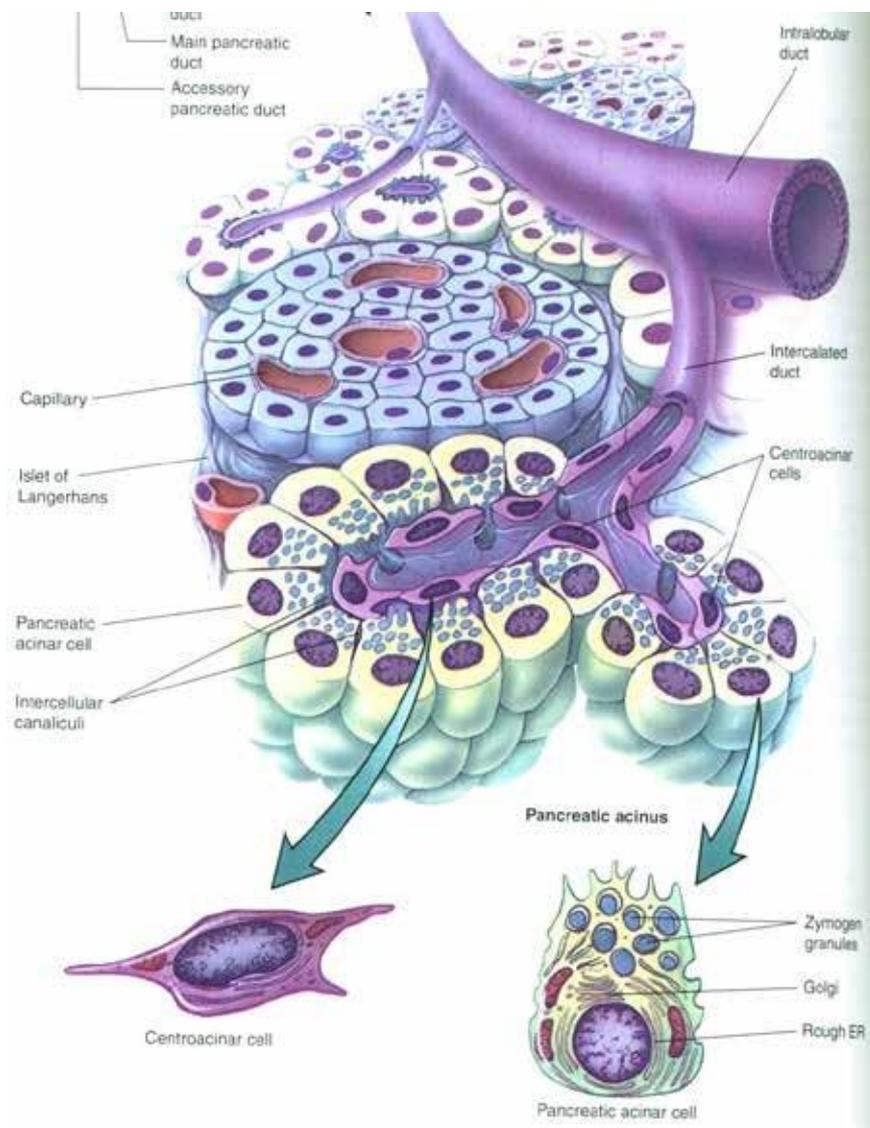
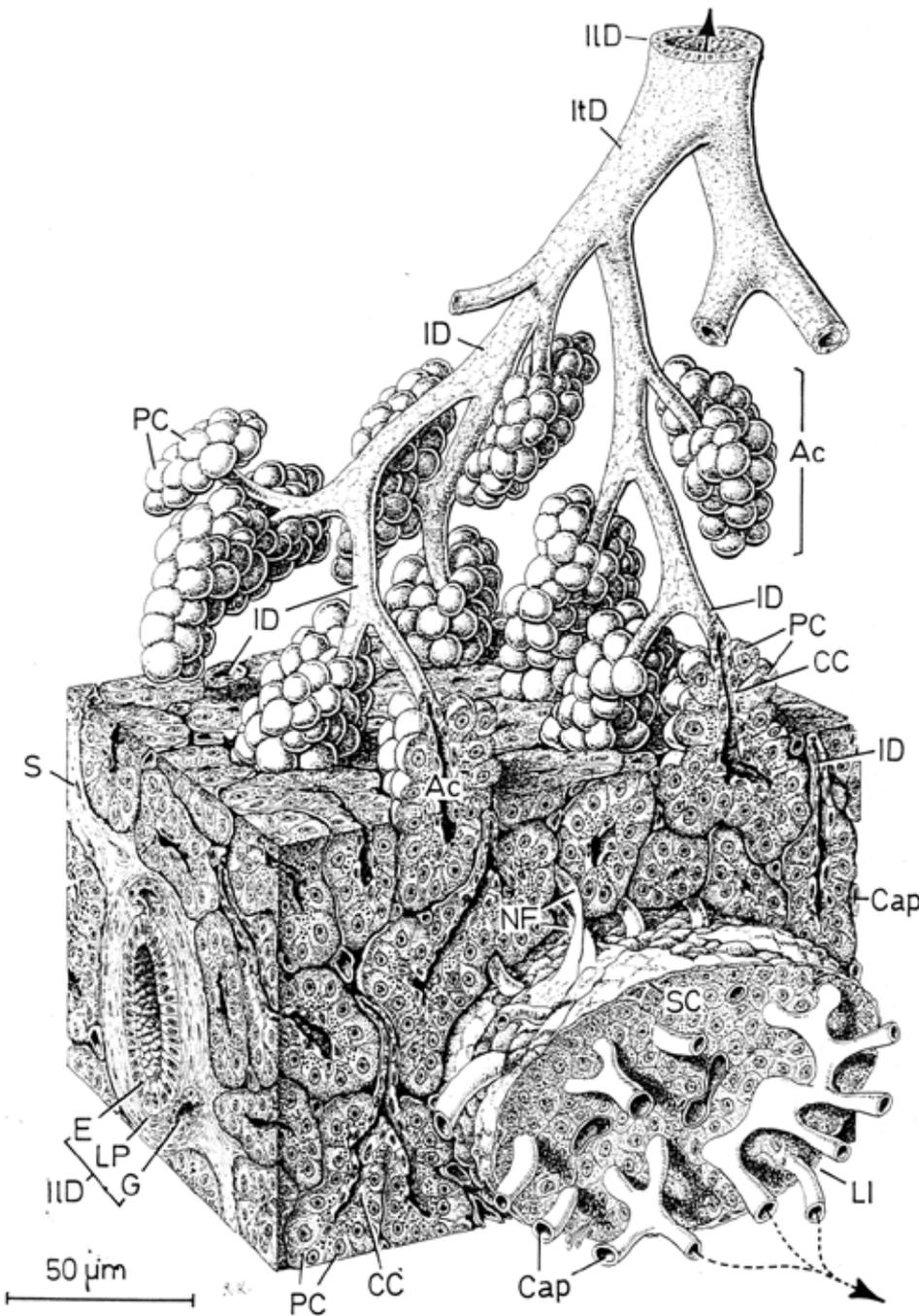


PANCREAS

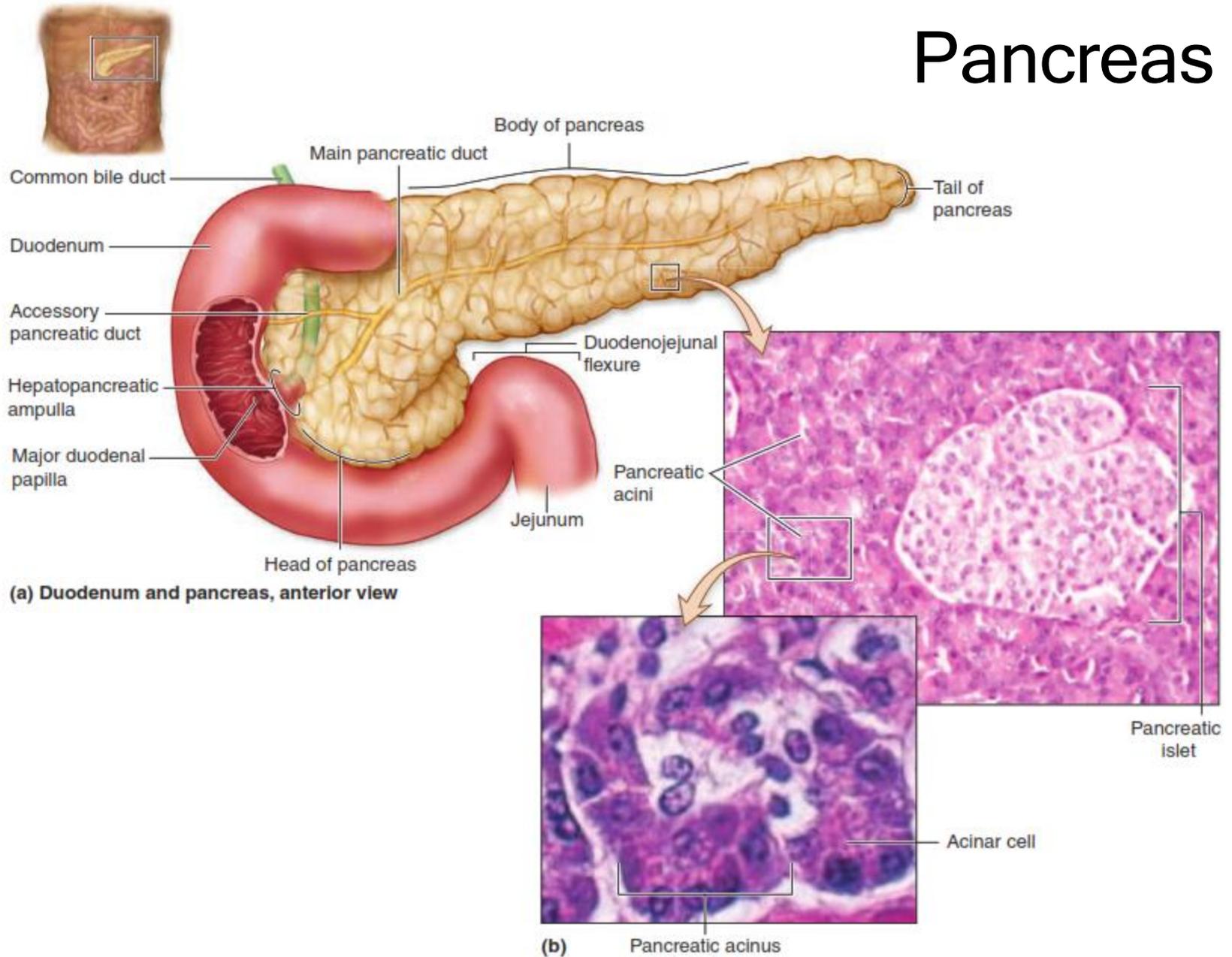
Pancreas

- 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.

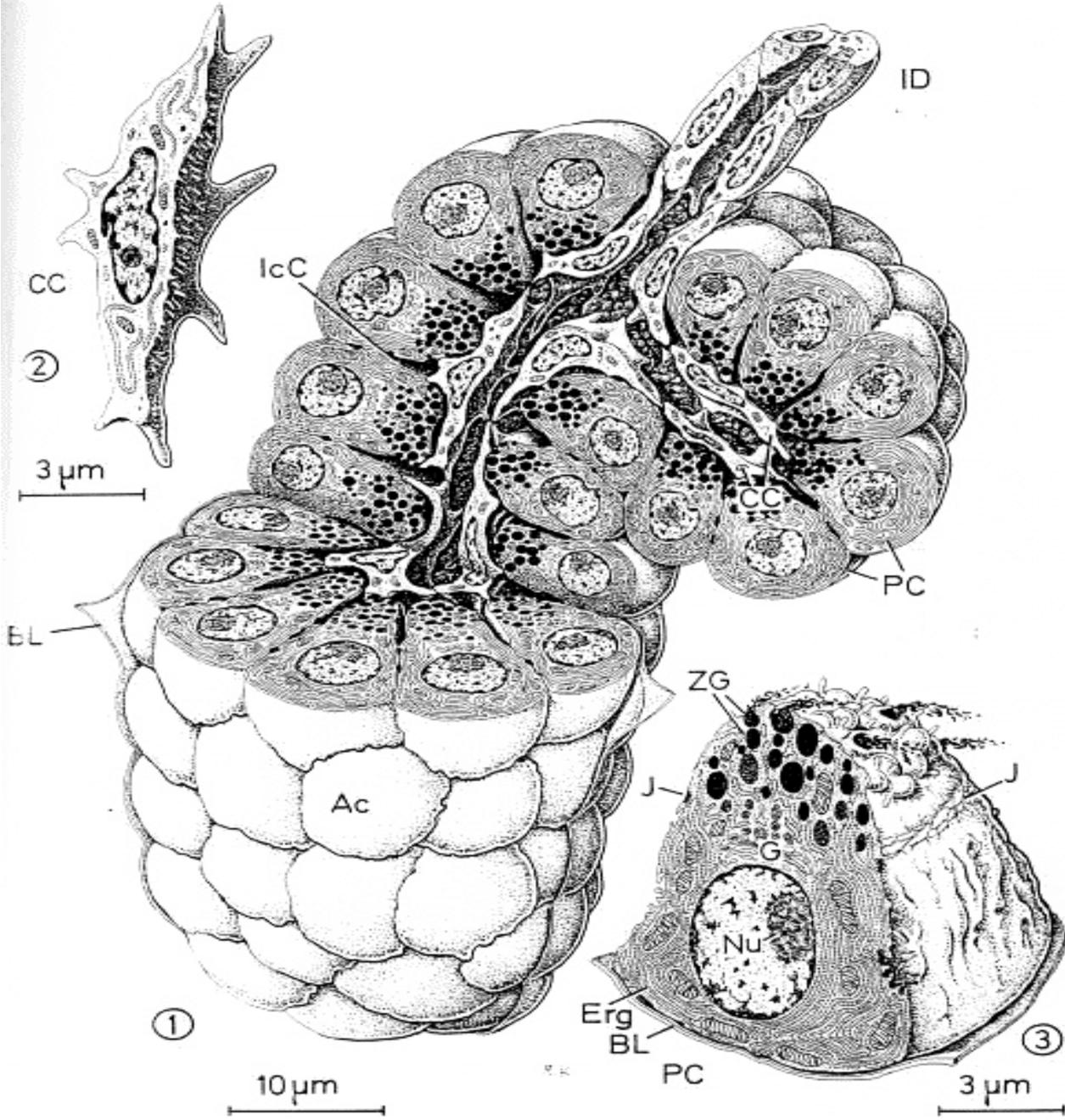
Exocrine pancreas

- 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 pancreatocytes.

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

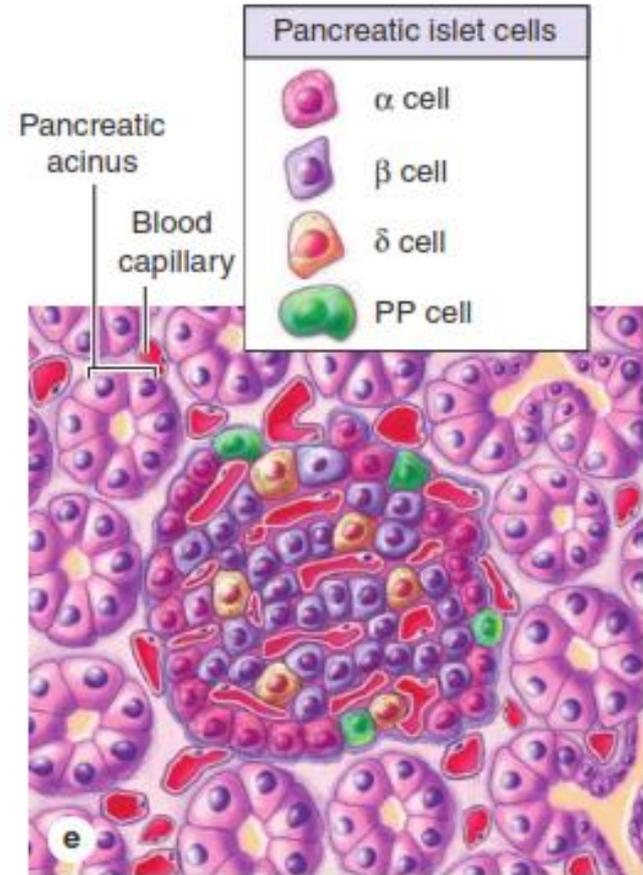


Endocrine pancreas

- 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:
 - α -cells
 - β -cells
 - δ -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

- β -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 β -cell granules, which is referred to as colocalization.
- α -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 β -cells. The granules contain an osmiophilic core, surrounded by an electroluminescent halo. α -cells secrete the peptide hormone glucagon, which has the opposite effects of insulin.

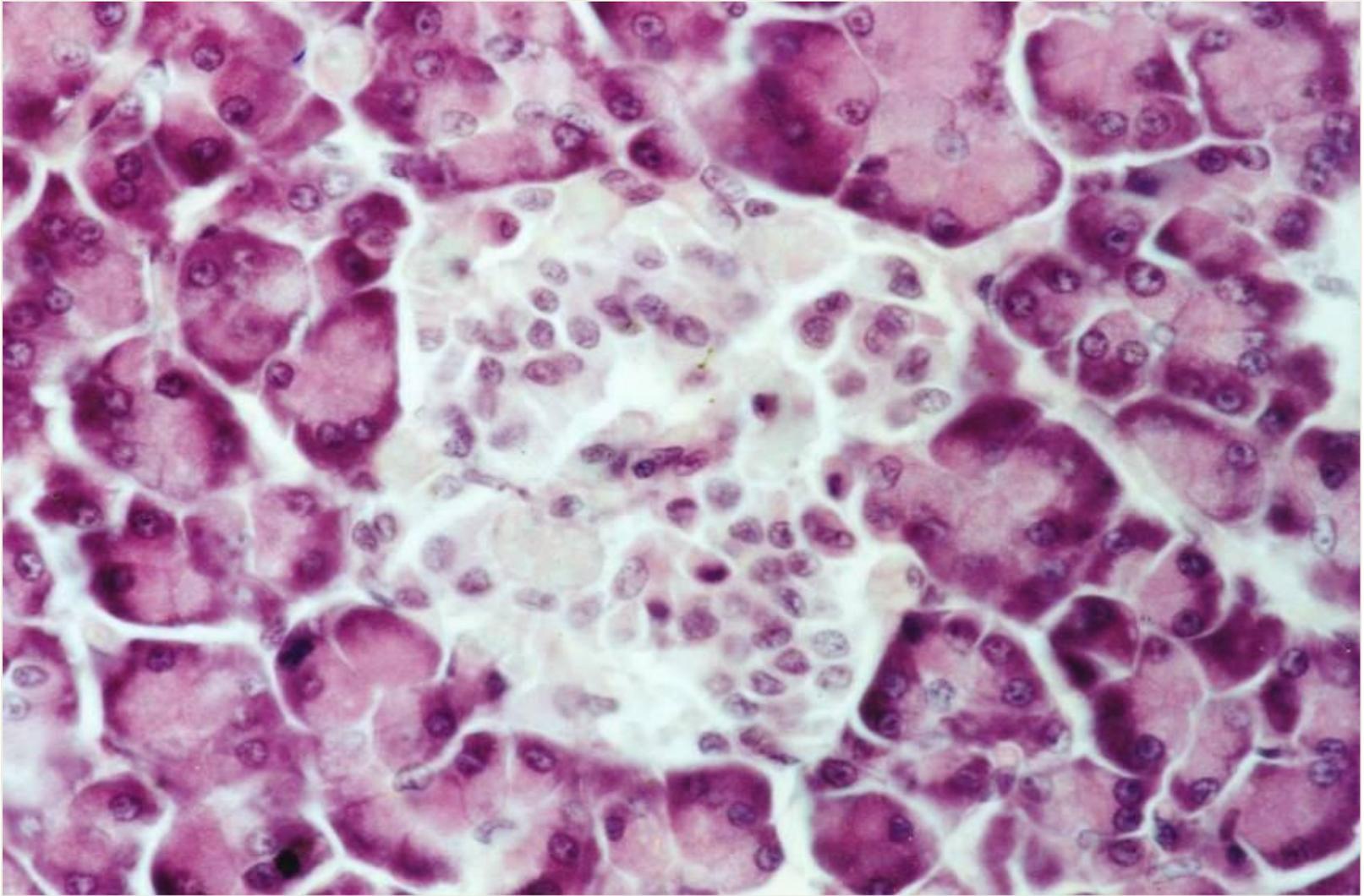
Endocrine pancreas

- α -cells make up about 15-20% of the endocrine cells of Langerhans tracts. They are significantly larger than β -cells.
- The granules contain an osmiophilic core, surrounded by an electroluminescent halo.
- α -cells secrete the peptide hormone glucagon, which has the opposite effects of insulin.
- δ -cells make up about 5-10% of the cellular content of the endocrine pancreas. They are larger than α - and β -cells.
- δ -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
α	~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
β	~60	Insulin	Dimer of α and β 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
δ 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