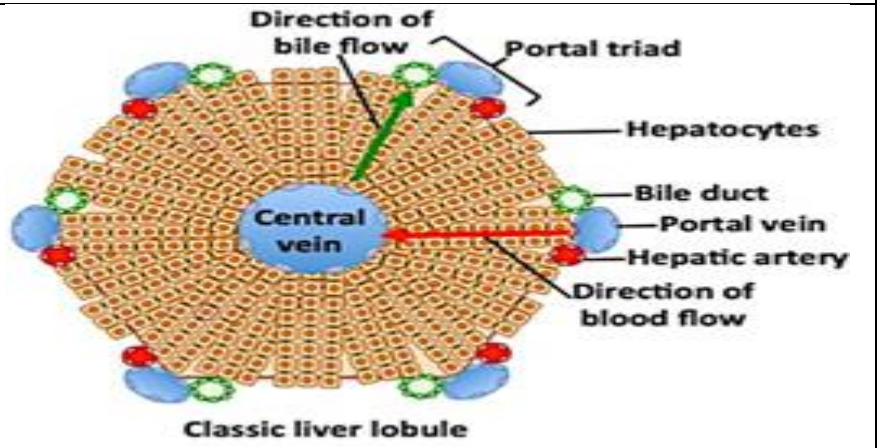
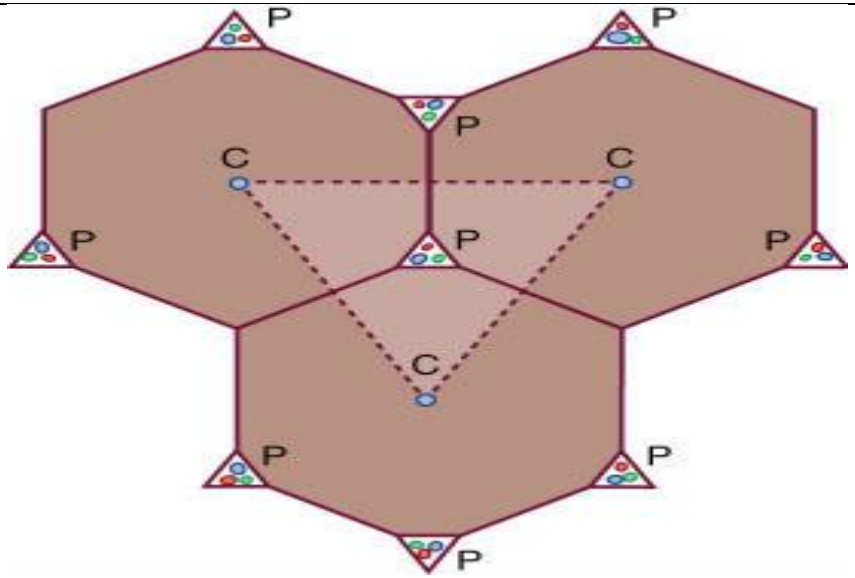
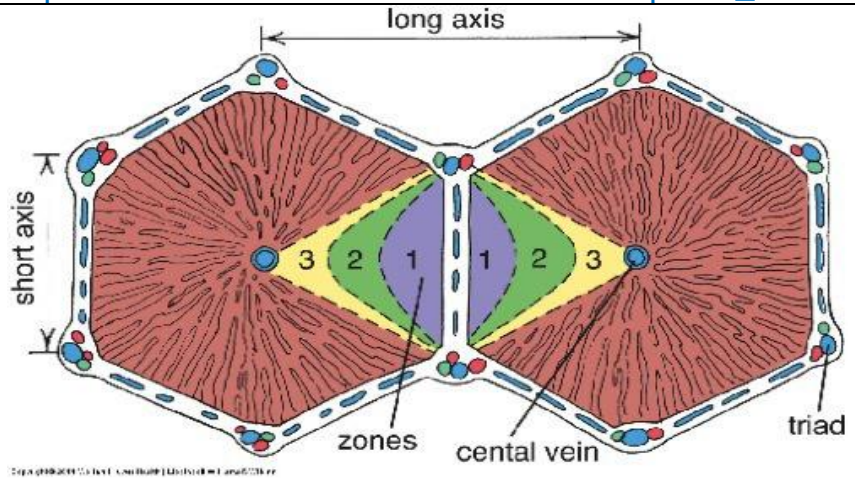
Topic 11. Liver and pancreas.

General structure of LIVER	
Basic structures	**Functions**
Classic lobules **Portal lobules** **Liver acinus**	1) synthesizing and releasing plasma proteins (**fibrinogen, prothrombin, lipoproteins, and albumins**) – **endocrine function.** 2) production of bile **(water, bile salts, bilirubin, cholesterol, fatty acids, lecithin, and electrolytes)** – **exocrine function.** 3) **detoxification**. 4) it is involved in **lipid, carbohydrate, and protein metabolism**. 5) transport wastes (such as **bilirubin**) into the bile.

Blood supply, ducts and spaces of liver		
Sources		**Functions**
1.	**Portal veins**	carry nutrient-rich blood from the small intestine to the hepatic sinusoids through their branches (portal venules)
2.	**Hepatic arteries**	carry oxygen-rich blood to the hepatic sinusoids through their branches (hepatic arterioles).
3.	**Hepatic sinusoids**	carry mixed blood from the hepatic arterioles and portal venules of portal triad to the central veins of classical hepatic lobules.
4.	**Sublobular vein**	collect venous blood from the central veins of the classic liver lobes.
5.	**Large hepatic veins**	collect venous blood from the sublobular veins into the inferior vena cava.
6.	**Perisinusoidal space (spaces of Disse)**	is situated between the sinusoidal endothelium and the hepatocytes. is also the main extracellular compartment from which liver lymph is derived.
7.	**Bile canaliculi**	carry bile to the bile ductules of portal triad of classical hepatic lobules. are enlarged intercellular spaces, located between two adjacent hepatocytes. Tight junctions seal each side of the bile canaliculus, preventing initial bile from leaking out of the canaliculus.

8.	**Hepatic ductules**	collect bile and carry it into the hepatic ducts, which then join the cystic duct from the gallbladder.
9.	**Right and left hepatic ducts**	carry bile into the **common hepatic duct**, which connects to the cystic duct.
10.	**Common hepatic duct**	formed by merging of **right and left hepatic ducts.**
11.	**Common bile duct**	carries bile from the **common hepatic duct and cystic duct, and** joins the pancreatic duct at the hepatopancreatic ampulla and bile enters the duodenum through the major duodenal papilla.
12.	**Lymphatic vessels**	carry lymph from the **liver drains** into the **hepatic lymph vessels** and passes through the **lymph nodes** (near the liver) to then drain into the **thoracic duct**.

General histological structure of LIVER		
Basic structures and features of classification	**Features**	
Classic lobule (is based on the direction of the blood flow)	1. **hexagon** shape. 2. contains **six portal triads** and **one central vein.** 3. blood flows from portal triads into a central vein.	 Classic liver lobule https://vmicro.iusm.iu.edu/hs_vm/docs/lab12_12b.htm

Portal lobule (is based on the direction of the bile flow)	1. **triangular** shape. 2. contains **one portal triad in the center** and three **central veins** in the angles**.** 3. Hepatocytes produce bile and bile enters the bile canaliculi to then drain into the bile ductule of portal triad.	 https://medicine.en-academic.com/137819/portal_lobule
Liver acinus (is on the blood oxygen level, nutrient supply, and metabolic activity)	1. **diamond** shape. 2. contains two **portal triad** and two **central veins** in the angles. 3. subdivides into three zones: zone 1, zone 2, and zone 4. cells of **zone 1** receives the most blood flow and blood toxins first are more likely to be damaged (are situated closer to the portal veins and hepatic arteries of portal triads). 5. cells of **zone 2** have an intermediate response to oxygen and toxins. 6. cells of **zone 3** have a poor oxygen and nutrient supply, but is also less exposed to blood toxins (are situated far from the portal triads and close to the central veins).	 https://quizlet.com/595782776/liver-and-biliary-tract-pathology-flash-cards/

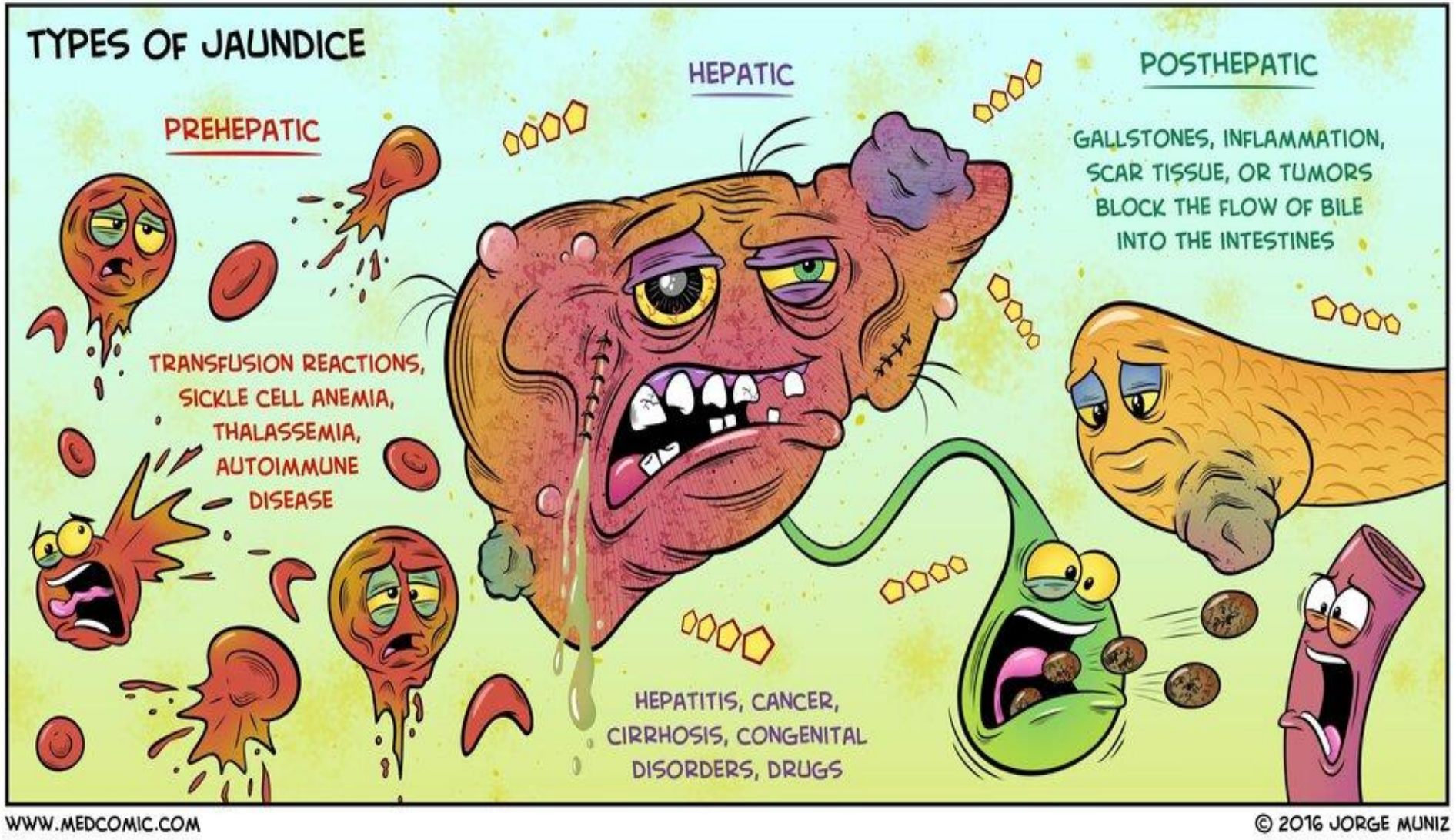
General structures and features of liver parenchyma and stroma	
Basic structures	**Functions**
Capsule	fibrous connective tissue that becomes thicker at the hilum.
Loose connective tissue	surrounds and supports the liver cells and the sinusoidal endothelial cells of the liver lobules, vessels and ducts all the way to their termination (or origin) in the portal spaces between the liver lobules.
Hepatocytes	1. large polygonal cells 2. have round two or more nuclei and about 50% of them are polyploid (4n, 8n or more times the normal diploid chromosome number) 3. they are arranged in plates that are one or two cells thick. 4. between the plates of hepatocytes there are hepatic sinusoids. 5. have many mitochondria, smooth endoplasmic reticulum, rough endoplasmic reticulum and inclusions. 6. Short microvilli of the hepatocytes extend into the space of Disse.
Hepatic sinusoids	1. are discontinuous capillaries 2. **Kupffer cells** (irregular shape cell with ovoid nuclei) are phagocytes that purify luminal surface of the hepatic sinusoids. 3. **Ito cells (fat-storing cells)** or hepatic stellate cells are located in the space of Disse and contain many lipid droplets (store vitamin A) or vacuoles in their cytoplasm.
Portal triad	1. is composed of a **portal vein**, a **hepatic artery**, and a **bile ductile.** 2. vessels and bile duct are surrounded by connective tissues, which usually contains a lymphatic vessel. 3. **portal vein** (large lumen, thin vessel wall) gives branches (**portal venules**) which feed the hepatic sinusoids. 4. **hepatic artery** (small lumen, wall with 2 to 3 cell layers thick of smooth muscle that) gives branches (**hepatic arterioles**), which feed hepatic sinusoids.

General structure of GALLBLADDER				
Structure			**Functions**	
It stores, concentrates, and releases bile.				
1.	**Mucosa** has many branching folds	Simple columnar epithelium	columnar epitheliocytes with many microvilli on the apical surfaces.	absorb water from bile in the lumen and transport it into the interstitial tissue
			some columnar epitheliocytes have interdigitating lateral membranes and many mitochondria in the cytoplasm	transport water
		Lamina propria	loose connective tissue	
2.	**Muscularis**		1) consists of interlacing longitudinal and obliquely oriented bundles of smooth muscle fibers. 2) forms at neck of the gallbladder **spiral valve of Heister**	1) helps empty bile through the cystic duct into the bile duct 2) controls the opening or closing of the gallbladder
3.	**Serosa/adventitia**		**serosa** consists of connective tissue and mesothelium	covers most of the gallbladder
			adventitia consists of only connective tissue	attaches the gallbladder to the liver
4.	**Cystic duct**		1) mucous membrane is lined by simple columnar epithelium (cholangiocytes). 2) lamina propria and submucosa are relatively thin, with mucous glands. 3) has thin muscularis layer.	carry bile to the gallbladder and from the gallbladder to the common bile duct

Jaundice

Symptom - skin and sclera become markedly yellow.
Reason - high level of common bilirubin (due to either direct or indirect bilirubinb type, or both at the same time) in the bloodstream.

	Type	**Pathology** in which this type of jaundice is observed
1.	Prehepatic	1) transfusion reaction 2) sickle cell anemia 3) thalassemia 4) autoimmune disease
2.	Hepatic	1) hepatitis 2) cancer 3) cirrhosis 4) congenital disorders 5) drugs
3.	Posthepatic	1) gallstones 2) inflammation 3) scar tissue or tumors which block the flow of bile to the intestines



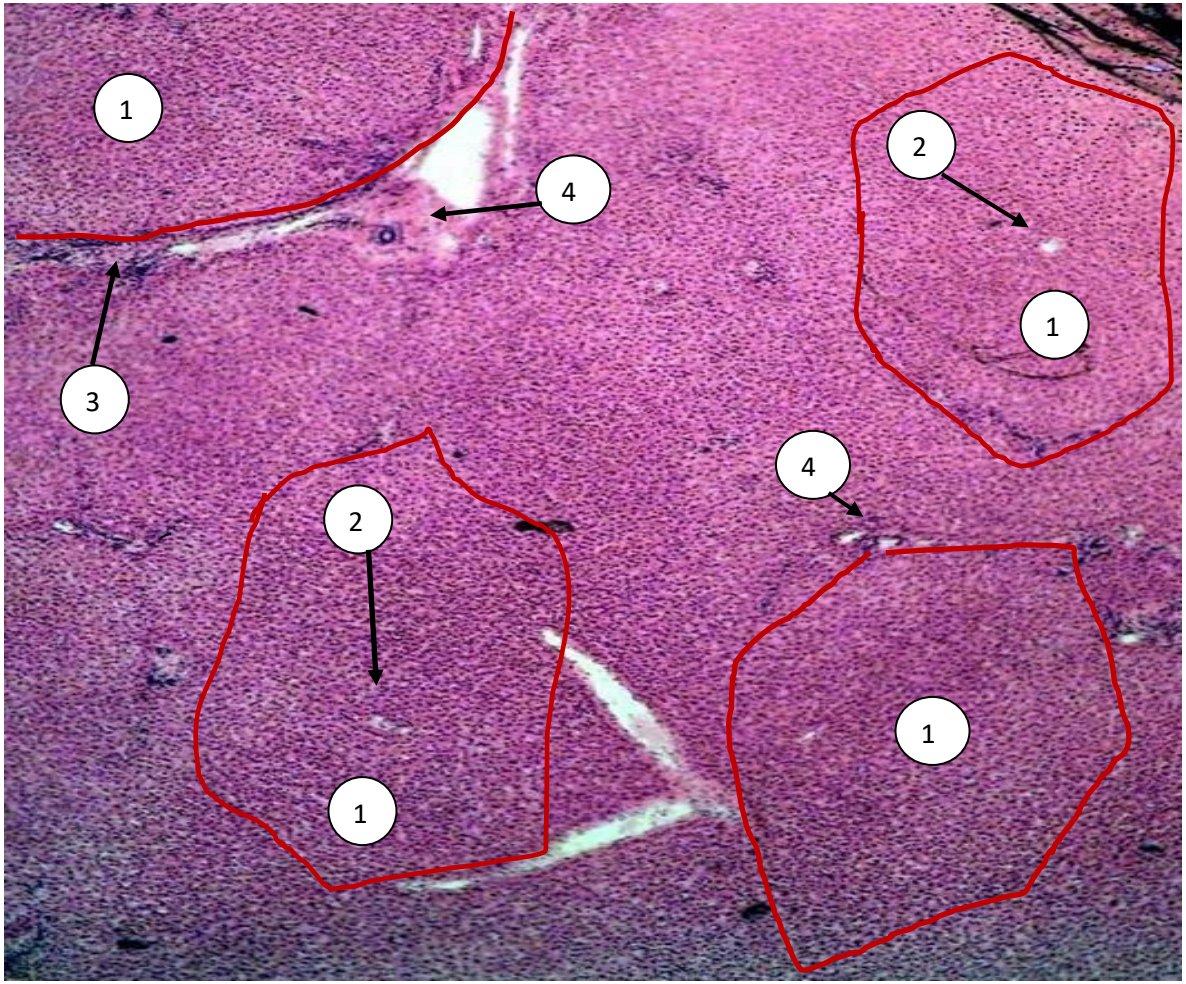
https://www.medcomic.com/medcomic/types-of-jaundice

General structure of PANCREAS				
1.	Anatomical structure	Has three parts (**head, body and tail**).		
2.	Histological structure	**Stroma**	**Parenchyma**	
		1) thin capsule (dense connective tissue) covers the pancreas sends septums into parenchyma. 2) septums separate the pancreatic lobules.	**Exocrine portions** Pancreatic acini	**Endocrine portions** islets of Langerhans
3.	System of ducts	1) begins from **intercalated ducts** (formed by centroacinar cells) and then drained into the **intralobular ducts**, the **interlobular ducts**, and finally into the **main duct**. 2) **Endocrine portions don't have system of ducts.**		

General structure of pancreas EXOCRINE PORTION			
Parts			**Features and functions**
1.	**Pancreatic acini**	Pancreatic acinar cells	1) have a round nucleus 2) cytoplasm contains many zymogen granules in the apical region, RER in the basal region, Golgi complex near the nucleus. 3) **Function:** secrete enzymes which help in the digestion of proteins, lipids, and carbohydrates. 4) **Enzymes**: a) proteases - **trypsinogens, chymotrypsinogen, proelastases, protease e, kallikreinogen, procarboxipeptidases** b) α -amylase c) lipases d) nucleaseS (**DNAase and RNAase**).

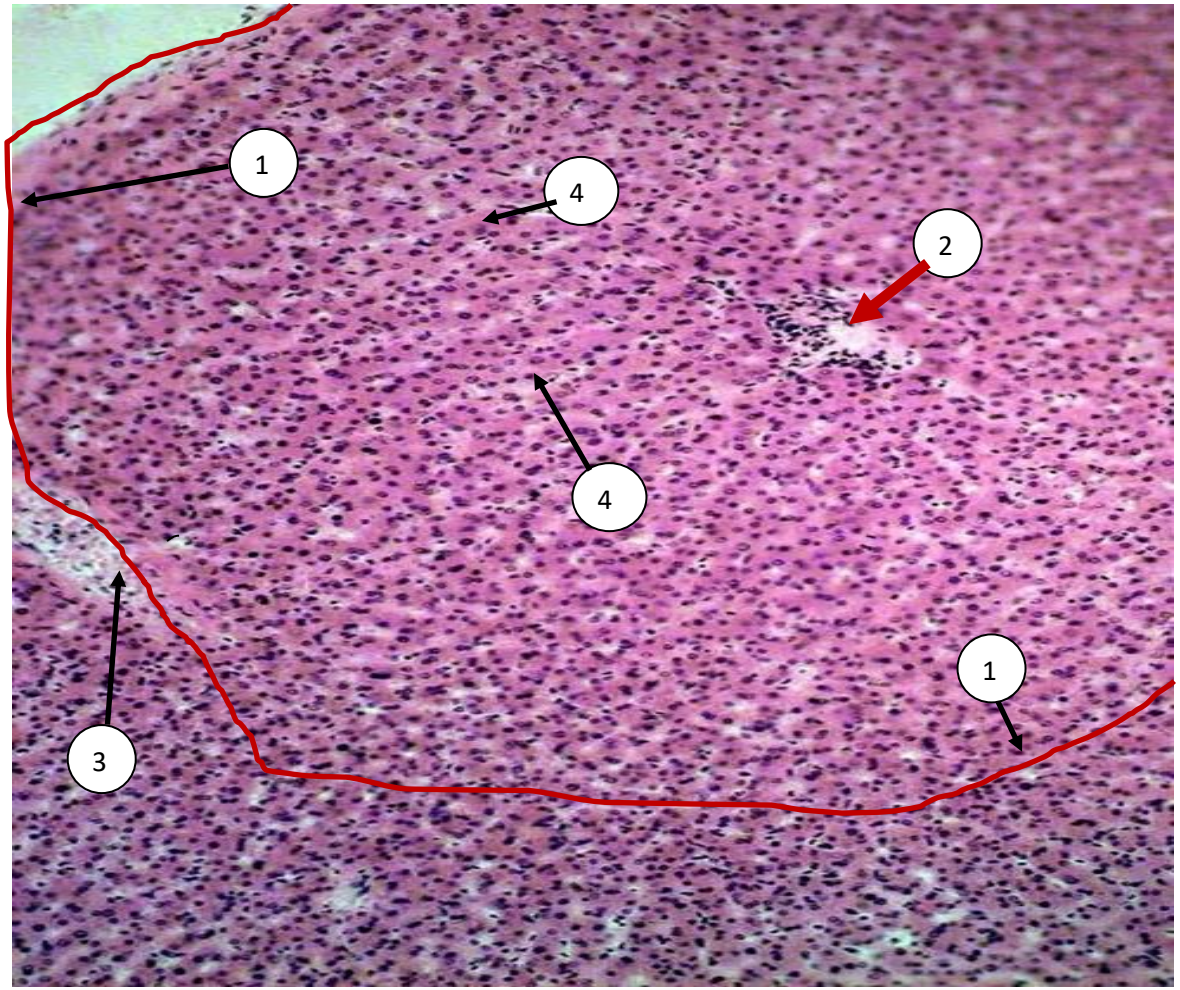
		Centroacinar cells	1) have many mitochondria but less RER. 2) are located at the center of each acinus and form initial parts of the intercalated ducts. 3) **Function:** secrete fluid (with **sodium** and **bicarbonate**) which helps neutralize acidic food contents entering the duodenum from the stomach.
2.	**Septum**	Loose connective tissue	1) includes blood vessels, nerves and ducts 2) separate lobules into secretory acinuses
3.	**System of ducts**	intercalated ducts	1) formed by centroacinar cells 2) transport primary pancreatic secretion 3) are lined by simple squamose or cuboidal epithelium
		intralobular ducts	1) formed by merging of intercalated ducts 2) are lined by simple cuboidal epithelium
		interlobular ducts	1) are lined by simple columnar epithelium with goblet and endocrine cells.
		main duct	1) opens at the hepatopancreatic ampulla of duodenum through the major duodenal papilla 2) are lined by simple columnar epithelium with goblet and endocrine cells. 3) smooth muscle cells form a sphincter at the exit of duct.

General structure of pancreas ENDOCRINE PORTION				
Strucure			**Hormone and functions**	
	islets of Langerhans	alpha cells	glucagon	1) cells include small and medium granules which have an electron-dense core with a very narrow electron-lucent surround. 2) stimulates the synthesis and release of glucose from the liver into the blood (increasing blood glucose levels).
		beta cells	insulin	1) cells include larger granules, a less dense core, and a wide lucent area surrounding the core. 2) stimulates glucose entry in many cells, in this way regulating carbohydrate metabolism and lowering blood glucose levels.
		delta cells	somatostatin	inhibit glucagon and insulin secretion
			gastrin	stimulate gastric gland secretion
		PP cells	pancreatic polypeptide	inhibit exocrine pancreatic secretion
		capillaries	fenestrated or sinusoidal capillaries	



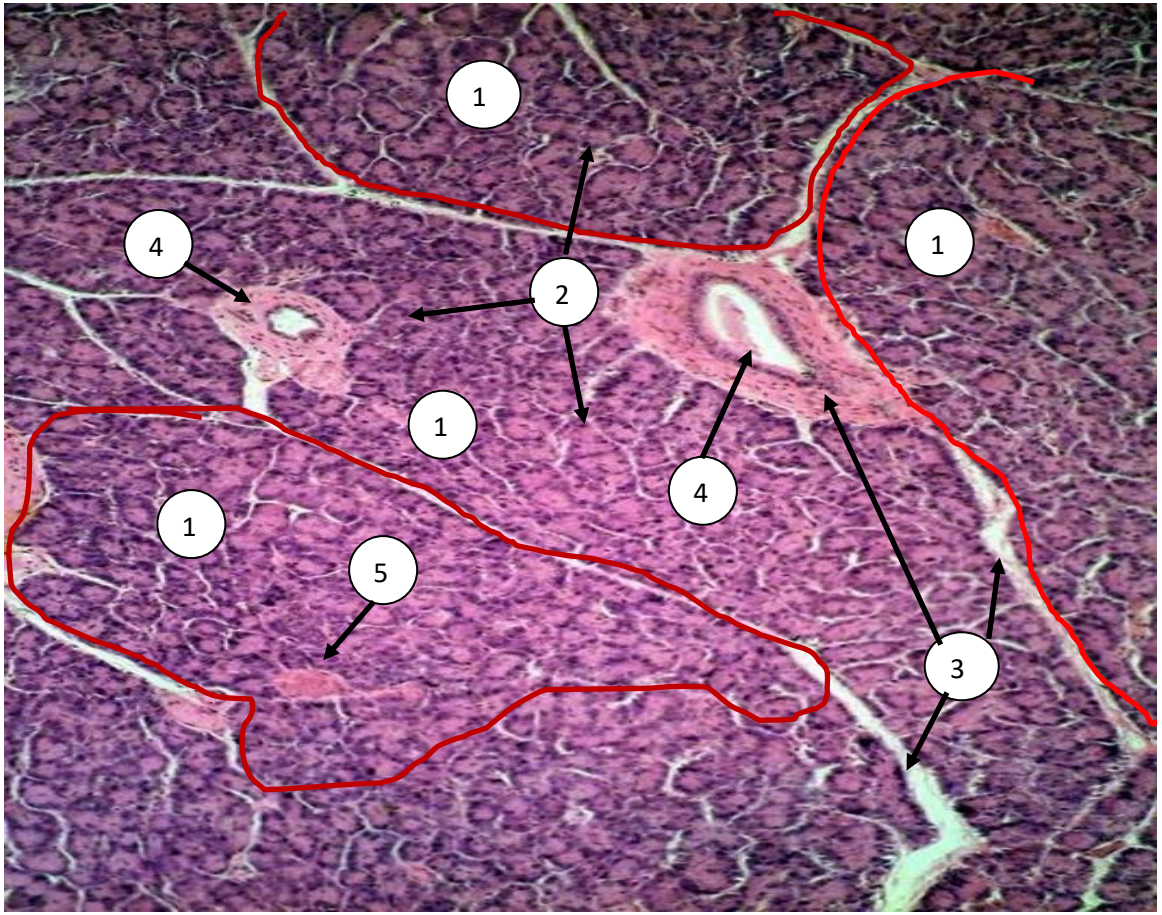
Liver
Magnification X 100.

On the preparation of the liver there are classic lobules (1). Inside the classic lobule there is the central vein (2). Between the classic lobules there is a loose connective tissue (3). In the corners of the classic lobule there are portal triads (4).



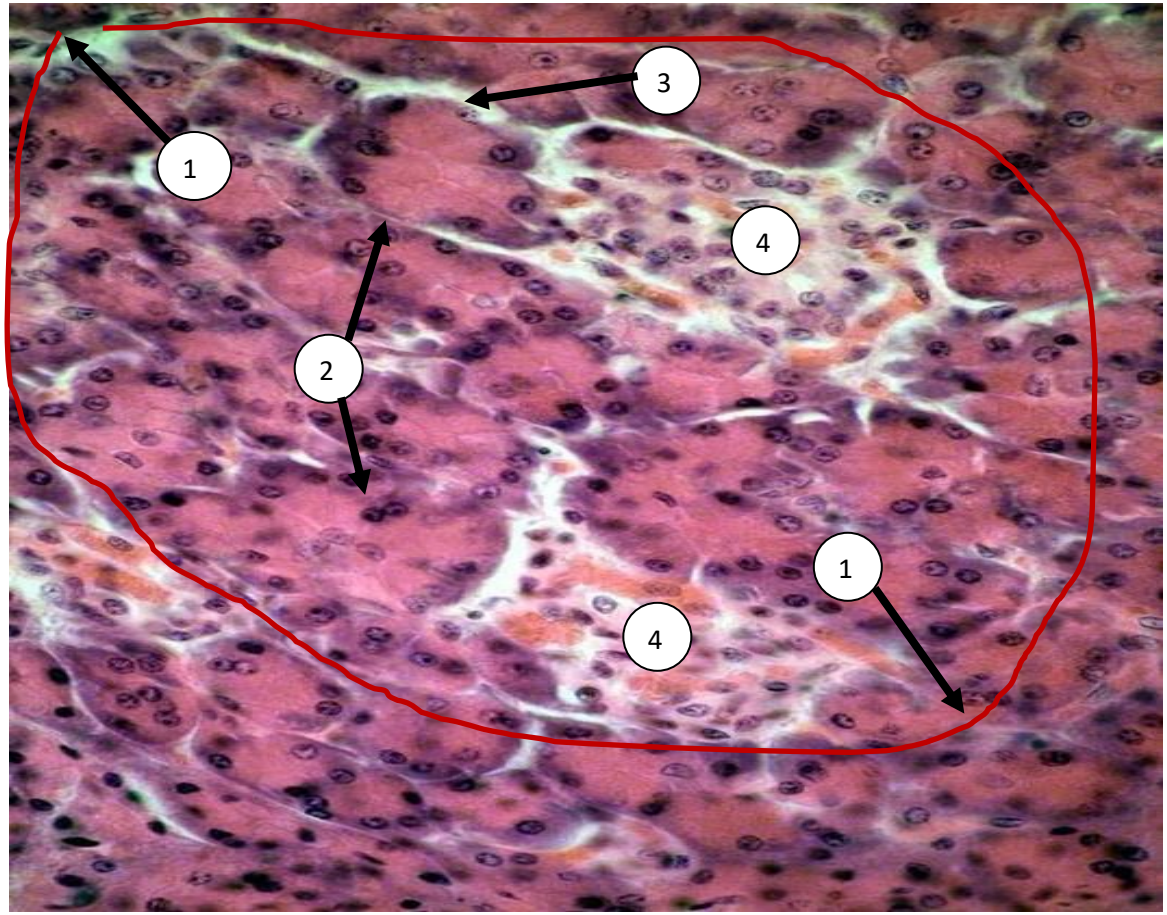
Liver
Magnification X 100.

On the preparation of the liver there is classic lobule (1). Inside the classic lobule there is the central vein (2). Between the classic lobules there is a loose connective tissue (3). Classic lobule consists of hepatocytes which form liner cords (4).



Pancreas
Magnification X 100.

On the preparation of the pancreas there are lobules (1). Parenchyma of pancreas (pancreatic lobules) consists of pancreatic acini (2). Between the lobules there is a loose connective tissue (3) with interlobular ducts (4). In the lobules there are islets of Langerhans (5).



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On the preparation of the pancreas there are lobules (1). Parenchyma of pancreas (pancreatic lobules) consists of pancreatic acini (2). Between the acini there is a loose connective tissue (3). In the lobules there are islets of Langerhans (4).

VOCABULARY

Hepatocytes are the main functional cells of the liver. They are large and polygonal epithelial cells that constitute roughly up to 80% of the liver mass. The hepatocytes have one (sometimes two) round central-placed nuclei surrounded by cytoplasm rich with organelles that facilitate protein and lipid synthesis and secretion (rough and smooth endoplasmic reticulum, Golgi apparatus and mitochondria).

Portal triad. The liver, as an organ, is supplied with blood from two separate systems. Mostly - through the portal hepatic vein (75%), which transports venous blood from the intestines, spleen and pancreas. In spite of the low oxygen content, this blood carries a large amount of nutrients, endocrine products, destroyed red blood cells and toxins that have entered the body. Another main source is the hepatic artery (25%), which delivers blood saturated with oxygen to the liver. The hepatic portal vein and hepatic artery together with the bile duct form the portal triad. These structures provide blood to the hepatocytes and sinusoids, after which it is drained into the central vein. The second way of outflow is through the hepatic veins, which flow into the inferior vena cava.

Kupffer cells. Sinusoids include a specific type of cells called Kupffer cells, which have ovoid nuclei. These monocytic derivatives of the mononuclear phagocytic system are located in the wall of the sinusoid, from which they project processes into its lumen. Hence, Kupffer cells constantly monitor the blood flowing through the sinusoids, thus phagocytising destroyed red blood cells, antigens and microorganisms.

Ito cells. In the perisinusoidal space is a certain type of cells called Ito cells, or stellate hepatic cells. Their role is to store hepatic vitamin A in lipid droplets, which is further released as retinol. Meanwhile, Ito cells are also considered to be responsible for liver fibrosis, as they produce large collagen amounts in case of liver damage.

Classic lobule is formed of hexagonal layers of hepatocytes overlapping each other. Inside each plate, hepatocytes diverge from the central vein outward. As they approach the periphery, the hepatocytes are organized in rows similar to the spokes of wheels. Between the bands of hepatocytes are hepatic sinusoids, which flow into the central vein.

Portal lobule. While the appearance of the classical lobule reflects the blood distribution and arrangement of the liver

tissue, the shape of the portal lobule reflects the exocrine liver function, i.e. biliary secretion. Each functional unit in this case is a triangle whose central axis passes through the portal field and the imaginary vertices pass through the three different but nearest portal channels enclosing it. The area occupied by the triangle displays the parts of the liver that excrete bile into the exact same bile duct.

Pancreatic islets (islets of Langerhans) are irregularly shaped clusters of endocrine tissue found in the pancreas of most vertebrates. They are named after the German physician Paul Langerhans, who first identified them in 1869. Human islets consist of circa 30% glucagon-producing α-cells, circa 60% insulin producing β-cells, with the remainder circa 10% made up of δ-cells (somatostatin-producing), γ- or PP cells (pancreatic polypeptide-producing), and ε-cells (ghrelin-producing), with these endocrine cells randomly distributed throughout the islet.

Acinar cell are in the shape of a pyramid, arranged in a radial pattern around a small central lumen and have intracellular, zymogen granules bound to the membrane in the apical region. A perinuclear region that is more basophilic, with a rough endoplasmic reticulum, provides the acinar cell a bicolor, apical-basal polarized view. Inactive precursor proteins (trypsinogen, procarboxypeptidase, chymotrypsinogen, proelastase and kallikreinogen) are synthesized and retained in zymogen granules, prepared for discharge by fusion of the granules with the apical membrane upon cell activation by acetylcholine and cholecystokinin.

Intercalated ducts. The thin ducts running from the acini to the wider excretory ducts lying outside the lobule are known as intercalated ducts and can be revealed by small aggregations of 3-5 mildly elongate nuclei that lie among the acini; the ductal cell cytoplasm is extremely pale. Similar to the salivary glands, intercalated pancreatic duct cells provide bicarbonate ions (sodium and water are passively taken up) to the secreted exocrine juice. But unlike the salivary glands, the pancreas does not have striated ducts for sodium reuptake, so the end product is saturated with both sodium and bicarbonate.

Centroacinar cells. The primary, intraacinar part of the intercalating duct is covered with simple squamous epithelial cells, the so-called centroacinar cells, which indicate the beginning of the ductal system of the pancreas exocrine part. Centroacinar cells are small, pale-staining cells with microvilli on their apical surfaces. The pale-staining character reflects the sparse cytoplasm, small amount of rER, small size of the Golgi apparatus, and the lack of zymogen granules within the cell. Unlike acinar cells, centroacinar cells contain carbonic anhydrase, which catalyzes the generation of HCO_3- from CO2.

Links:
https://www.kenhub.com/en/library/anatomy/hepatocytes
https://www.kenhub.com/en/library/anatomy/liver-histology
https://www.britannica.com/science/islets-of-Langerhans
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5867580/
https://www.sciencedirect.com/topics/medicine-and-dentistry/centroacinar-cell
https://histology.medicine.umich.edu/resources/pancreas

TESTS

1. On histological preparation **parenchyma of organ it is submitted by lobes which have the 6-angular prisms shape** and consist from trabeculas between sinusoidal capillaries which radiality converge to the central vein. What anatomic organ has the given morphological structure?
Liver
Thymus
Pancreas
Spleen
Lymph node

2. There is **large number of carbohydrates in the human diet**. What structures are detected while **in the cytoplasm of hepatocytes**?
Glycogen granules
Droplets of fat.
One big fat drop.
Increase the number of free ribosomes
The inclusion of lipofuscin.

3. A viral infection has damaged **cells that form walls of bile capillaries**. This stimulated conditions for inflow of **bile into the blood of sinusoidal capillaries**. What cells are damaged?
Hepatocytes

Kupffer's cells
Ito cells
Pit-cells
Endotheliocytes

4. During proliferation of connective tissue **in parenchyma of the liver** (fibrosis) due to chronic diseases there **is disruption of blood circulation in classic liver lobule.** What is the direction of blood flow in these structures?
From the periphery to the center
From the center to the periphery
Around lobule
From the top to the bottom
From the bottom to the top

5. Examination of 28-year-old patient with **hepatocerebral degeneration revealed an impairment of ceruloplasmin synthesis.** This defect is associated with the following organelles:
Granular endoplasmic reticulum
Smooth endoplasmic reticulum
Mitochondria
Lysosomes
Golgi complex

6. An electron micrograph of internally **lobed liver sinusoid represented cells, which can be seen in the cytoplasm granules with a seal like fruit pit.** We know that this is a natural killer cell. Which cell is represented.
Pit-cell
Hepatocytes
Endothelial cells of sinusoid
Kupfer cells
Fat-storing cell

7. In the patient from therapeutic department with severe **liver pathology revealed violations of coagulation. What is the function of the liver can be affected in this case**?
Protein synthesis
Detoxication
Endocrine
Protective
Bile formation

8. An examination of the patient revealed **abnormalities of the liver**. Which **embryonic germ layers have been damaged**?
Endoderm middle sections of primary colon
Endoderm posterior wall
Foregut endoderm
Mesonephritic duct
Hindgut endoderm

9. As a result of stab wounds in the **liver was damaged the hepatic artery, but the liver lobule blood continued to flow.** Which vessel provided blood flow in lobules?
Interlobular vein
Interlobular artery
Portal vein
Sublobular vein
Hepatic vein

10. In histological slide of **parenchyma of the organ slices is presented, the shape is hexagonal prisms** and consist of **anastomosing plates between which are sinusoidal capillaries that converge radially to the central vein**. What is the anatomical organ has given morphological structure?
Liver
Pancreas
Thymus

Spleen
Lymph node

11. During carbohydrate over-feeding of the animals **in the cells of the liver we can find histologically a large amount of glycogen granules.** What group of cell structures includes glycogen?
Trophic inclusion
Secretory inclusion
Excretory inclusion
Pigment inclusion
Organelles with special functions

12. As a result of **hepatotrophic poisons in hepatocytes was destroyed granular EPR**. Synthesis of which components will be change in the epithelium of the liver?
Albumin and fibrinogen
Phospholipids
Glycogen
Cholesterol
Vitamins

13. Damage of junctions between **liver hepatocytes which causes pathological processes as a result of it bile gets into bloodstream, causes jaundice.** Disorder of what type of intercellular junction may explain this appearance?
Tight (zonular occludentes)
Simple contact
Zonular adherents
Desmosomes
Gap junctions

14. A **large number of glycogen is detected in the cytoplasm of a hepatocyte in a specimen**. What process in the body causes this appearance?

Increased blood sugar
Reduced blood sugar
Increased absorption of lipids in the intestine
Reduced absorption of lipids in the intestine
Increased absorption of proteins in the intestine

15. A patient with signs of **jaundice** is admitted into the surgery department. **Bile from the bile capillary does not enter the bloodstream in normal circumstances.** What ultrastructural feature of hepatocyte structure contributes to this?
Presence of zonula occludentes between hepatocytes
Their polygonal shape
Presence of hepatocyte biliary surface
The absence of bile capillary wall
Presence of microvilli on the surface of the capillary

16. A **polygonal cell with a bright big nucleus and big nucleolus is found in microscopic research of a liver lobe**. It has many well developed organelles and inclusions in it's cytoplasm. What are these cells?
Hepatocytes
Endothelial cells
Stellate macrophage
Pit-cell
Ito-cell

17. In a specimen of parenchymal organ we can make out unclearly distinct **hexagonal shaped segments, in the centre of which lies a vein and in interlobular tissue are the triads (artery, vein, and excretory ducts).** What organ is this?
Liver
Pancreas
Thymus
Spleen
Thyroid gland

18. The walls of **bile capillaries are damaged as a result of a viral infection. This created conditions for flow of bile into the blood of the sinusoidal capillaries.** What cells were damaged?
Hepatocytes
Fat-storing cells
Ito-cells
Pit-cells
Endothelial cells of sinusoid

19. The patient since **14 years old has diabetes**. What endocrine cells of **pancreatic islands** don't function?
B – cells
D - cells
A - cells
D1-cells
PP - cells

20. In patients after **acute pancreatitis** is determined massive damage of **acinar cells**. By which **cells will go their recovery**?
Intercalated duct cells
Cells of islets of Langerhans
Cells of interlobular duct
Cells of gland's stroma
Endothelium of blood vessels

21. Endocrinologist diagnosed in patient disorders of the **endocrine function of the pancreas, resulting descending of the hormone glucagon in the blood.** The function of this gland cells broken in this case?
A-cells of the islets of Langerhans
B-cells in the islets of Langerhans
D-cells of islets of Langerhans

D1-cells of islets of Langerhans
PP-cells of islets Lanhenhans

22. A ptient has **disturbed digestion of proteins, fats and carbohydrates**. It is most licely to be caused by reduced secretion of the following digestive juice:
Pancreatic
Saliva
Gastric
Bile
Intestinal

23. A 50 years old patient complains with **increased appetite, thirst, decreased body weight, weakness and fatigue.** During laboratory examination revealed **increase the amount of sugar in the blood**. Which cells dysfunctions are associated with the development of this disease?
B cells
A -cell
Thyrocytes
Pankreatocytes
Lipotropocytes

24. In histological slide were studied **exocrine portion of the pancreas**. In the cells of **the exocrine parenchyma contained secretory granules with enzymes.** How do they come (these enzymes) to the digestive tract?
Through duct system
Through the bloodstream
Fall into the lymph
Axonic transport
Dendritic transport

25. During the study of **pancreatic cells plasmolemma** after exposure to drugs offenses were discovered in the structure of the **glycocalyx**. What are the chemical components of the glycocalyx is composed of cells of the pancreas?
Oligosaccharides
Proteins
Lipids
Mineral salts
Water

26. In the histological slide of the **pancreas** we can find a **group of cells**. Some of them are **centrally located and has basophilic secretory granules.** Their **secret regulates carbohydrate metabolism**. What kind of cells they are?
B cells
PP cells
A cells
Adipocytes
D cells

27. A high concentration of **insulin is revealed** in the blood of a 48-year old woman. The activity of which **pancreatic cells causes this?**
B-cells
A-cells
D
D1
PP

28. In a preparation of **a gland** we distinguish **acini, which consist of 8-12 secretory cells with a cranial shape, has a light nucleus and 1-2 nucleoli**.The basal part of the cell is stained basophysically and the apical part contains oxyphyllic granules, **myoepitheliocytes are absent**. What is this gland?
Pancreas
Parotid glands

Submandibular salivary gland
Breast
Oil bag

29. **Crypts of the small intestine** are composed of all the following **except**:
Kupfer's cells
Goblet cells
Panet's cells
Intestinal epithelial cells
Columnar epithelial cells

30. A 55-year old patient visits an endcrinologist about the violation of **endocrine pancreatic function**, manifested by a **decrease of glucagon hormone in the blood**. The function of which cells is damaged?
A-cells
B-cells
D-cells
D1-cells
PP

Links:
https://www.testcentr.org.ua/en/exams/all-about-the-exams/about-medical-licensing-exams
https://www.testcentr.org.ua/banks/stomat/k1-stom-f-eng.pdf
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