CARDIOVASCULAR SYSTEM

The cardiovascular system includes the heart, arteries, vessels of microvascular bed, veins and lymphatic vessels. The heart and the system of blood vessels provide the circulation of blood through the all parts of the body. The activity of the cardiovascular system is aimed at the maintenance of metabolism and constancy of internal environment of the organism. Oxygen, nutrients and biologically active substances are carried with blood to the tissues and cells. The waste products of the cells are also removed with blood and lymph.

Arteries (arteriae) deliver blood to the organs and regulate their blood supply. The hemodynamic conditions of arteries are characterized by the high speed of blood flow and high blood pressure.

Arteries are classified into three types on the basis of their structure:

1. Muscular arteries (arteries of extremities and inner organs);
2. Mixed or musculo-elastic arteries (carotid artery, subclavian artery);
3. Elastic arteries (aorta and pulmonary arteries).

Elastic arteries are large arteries such as aorta and pulmonary artery, blood passes through this type of arteries with high pressure and high speed.

Tunica interna (intima) consists of endothelium, subendothelial layer and twist of elastic fibers (internal elastic membrane). Endothelium consists of large flat elongated cells with their long axes oriented parallel to the direction of blood flow in the artery, which lie on the basal lamina.

Subendothelial layer is formed by loose connective tissue. This layer is characterized by the presence of a lot of star-shaped cells and the smooth muscle cells.

The internal elastic membrane in elastic arteries consists of the twist of elastic fibers. It is **not conspicuous** because it is one of many elastic layers in the wall of the vessel.

The tunica media consists mostly of elastic elements, which form about 40-50 elastic fenestrated lamellae. These lamellae are connected together by elastic fibers and together with elastic elements of other tunics form the one common elastic framework. Between lamellae the smooth muscle cells are found. All these structures are drowned in the ground substance, which is rich in glycosaminoglycans.

Tunica externa (adventitia) is formed by loose connective tissue with big amount of longitudinally oriented elastic and collagen fibers. Vasa vasorum (blood vessels) and nervi vascularis are present in the tunica adventitia and may partially enter the outer part of tunica media. Tunica adventitia helps prevent the expansion of the arterial wall beyond physiologic limits during systole of the cardiac cycle.

Mixed arteries. The wall of mixed arteries consists of three layers:

- tunica interna (intima)
- tunica media
- tunica externa (adventitia)

Tunica intima consists of three layers:

- endothelium with the basal lamina
- subendothelial layer
- internal elastic membrane

Subendothelial layer is formed by loose connective tissue with longitudinally oriented collagen and elastic fibers. Between these fibers the low-differentiated star-shaped cells of connective tissue are located. The ground substance is rich in sulphated glycosaminoglycans.

Internal elastic membrane lies on the border with tunica media. In histologic sections it appears as prominent, **well-defined**, undulating structure.

Tunica media contains smooth muscle cells, which are arranged in a spiral fashion in the arterial wall. Elastic fibers can be oriented radially, spirally or bowingly. A small amount of collagen fibers and fibrocytes is present in tunica media too. The ratio of smooth muscle cells and elastic fibers in mixed arteries is 1:1. The tunica adventitia of muscular arteries is separated from the tunica media by a recognizable external elastic membrane. The external elastic membrane is thinner than the internal one, but structurally they are the same.

Tunica externa (adventitia) consists of two layers:

- external – is formed by loose connective tissue
- internal - contains separated bundles of the smooth muscle cells

Nerves and small vessels travel in the adventitia and give off branches that penetrate into the tunica media as the vasa vasorum.

Muscular arteries consist of three layers:

- tunica interna
- tunica media
- tunica externa (adventitia)

The structure of the wall of muscular arteries is almost the same as the one of mixed arteries. The differences are in structure of tunica media and tunica externa. In tunica media the number of elastic fibers decreases, but the number of the smooth muscle cells increases. The contraction of the smooth muscle cells maintains blood pressure thereby providing blood supply to organs, which are located far from heart. All the tunics of the muscular arteries are significantly thinner than the ones of the mixed arteries. External elastic membrane consists of thick longitudinally arranged elastic fibers, which densely interlace and sometimes could have the appearance of solid elastic lamella. Tunica adventitia is formed only by loose connective tissue.

The vessels of microvascular bed

As the diameter of arteries decreases, all the tunics of their wall become thinner. Arteries gradually turn into arterioles, which the microvascular bed starts with. The exchange of water, ions, micro- and macromolecules between blood and tissues occurs through the wall of the vessels of microvascular bed. This process of

exchange between blood, lymph and tissues is called **microcirculation**. The interstitial and intraorganic homeostases depend on the process of microcirculation. Microvascular bed consists of arterioles, associated capillary network, and postcapillary venules.

Arterioles are small blood vessels, 50-100 mcm in diameter, which gradually turn into capillaries. Arterioles control the flow of blood to the capillary network by contraction of the smooth muscle cells. The wall of arterioles contains all three layers, which are inherent in the large blood vessels, but they become much thinner. The wall of arterioles is lined with endothelium, underlying solitary cells of subendothelial layer and thin internal elastic membrane. In the tunica media spirally arranged smooth muscle cells form only 1-2 layers. The smooth muscle cells of the tunica media directly contact with endothelial cells because of presence of perforations in the internal elastic membrane and in the basal lamina of endothelium.

Endothelial cells have receptors to biologically active substances, which regulate the tone of arterioles and due to the endothelio-myocytic gap junctions they transmit received signals to the smooth muscle cells. Except endothelio-myocytic junctions in arterioles are present myo-myocytic junctions, due to that arterioles provide the function of ‘taps of cardiovascular system’. The tunica adventitia is a thin, ill-defined sheath of connective tissue that blends with the connective tissue in which these vessels travel.

Capillaries provide the main functions of cardiovascular system – exchange of fluids containing gases, metabolites, and waste products between blood and tissues, formation of histohematogenous barriers, microcirculation. Hemodynamic conditions in capillaries are characterized by low blood pressure and low speed of blood flow. Capillaries – are the thinnest vessels. The lumen of many capillaries is narrower than the diameter of erythrocyte. Some capillaries could have the wide and irregular lumen, which changes over the vessel. Such type of capillaries is called sinusoidal.

In most cases capillaries form networks, but sometimes they can form loops (in papillae of the skin) and glomerullae (in kidneys).

The wall of capillaries consists of three layers:

- internal layer consists of endothelial cells, which lie on the basal lamina
- middle layer consists of pericytes connected by the basal lamina
- external layer consists of adventitial cells and thin collagen fibers drowned in ground substance

Endothelium of capillaries is formed by a continuous layer of flattened, elongated, and polygonally shaped **endothelial cells**, which lie on the basal lamina. These cells are well-defined by the impregnation of silver. Endothelial cells are characterized by winding borders and flattened oval nuclei. The cytoplasm is not rich in organelles, contains pinocytotic vesicles (transendothelial transport) and microfilaments, which form the cytoskeleton. The cells are joined by tight junctions (zonulae occludentes) and gap junctions. The luminal surface of endothelial cells is covered with glycoproteins and contains solitary microvilli.

Basal lamina of capillaries has a fine-fibered structure, contains collagen, glycosaminoglycans and lipids. Between endothelial cells and pericytes basal lamina becomes thinner and interrupts, while the cells here are joined by tight junctions.

Pericytes are the cells of connective tissue. The pericyte, when present, intimately surrounds the capillary, with branching cytoplasmic processes, and is enclosed by a basal lamina that is continuous with that of the endothelium. Pericytes were revealed to contain afferent nerve endings, which is probably connected with their function – regulation of size of capillary lumen.

Adventitial cells are low-differentiated cells, which are located outwardly from pericytes. They are surrounded by ground substance and collagen fibers.

Classification of capillaries

- capillaries with continuous endothelial layer – **somatic type**, are located in muscle, skin, CNS
- fenestrated capillaries – **visceral type**, characterizedby fenestrations, that provide channels across the capillary wall (typically found in endocrine glands and sites of fluid and metabolite absorption such as the gallbladder, kidney, and intestinal tract)
- **discontinuous capillaries** (also called **sinusoidal capillaries** or **sinusoids**) are typically found in the liver, spleen, and bone marrow. They are larger in diameter and more irregularly shaped than other capillaries, have slit-like holes in endothelium and basal lamina.

Arterio-venous anastomoses (AVA). This part of microvascular bed allow arterial blood to bypass capillaries by providing direct routes between arteries and veins. AVA are located in almost all organs.

Two types of AVA are distinguished:

- **true AVA (shunts)**, through which arterial blood flows. They are divided into two types:

a) simple AVA – the border of transition of arteriole to venule is located at the area, where the tunica media ends. The regulation of blood flow is provided by smooth muscle cells of tunica media of arteriole, without special contractile elements.

b) AVA with special contractile elements such as bolsters or pads, which are located in subepithelial layer and are formed by longitudinally arranged smooth muscle cells. The contraction of the muscular pads, which project on the lumen of anastomosis, leads to the ceasing of blood flowing. Epithelioid type of AVA (simple and complex) are also applied to this subtype.

In simple epithelioid AVA the smooth muscle cells gradually change to the short light oval cells (E-cells), which resemble epithelial cells.

In complex AVA (glomerular) afferent arteriole is divided into three-four branches, which turn into venous segment.

- **atypical AVA (semi-shunts)** are connections between arterioles and venules through short vessel of capillary type. That's why blood that flows into venous bed is not completely arterial.

AVA serves for the regulation of blood pressure, blood supply of organs, arterialization of venous blood, and mobilization of deposited blood, passage of interstitial fluid to the venous bed.

Venules. Three types of venules are distinguished:

- postcapillary
- colligens
- muscular

The structure of postcapillary venules resembles the one of venous part of capillary, but in their wall are found more pericytes.

In venulae colligens are found the smooth muscle cells and the tunica externa becomes more conspicuous.

Muscular venules are characterized by the presence one-two layers of smooth muscle cells in tunica media and by well-defined tunica externa.

The venous part of microcirculatory bed together with lymphatic capillaries provides the drainage function by the regulation of hemo-lymphatic balance between blood and interstitial fluid and removing waste products. Through the wall of venules, as through the capillaries, is realized the migration of leukocytes. Low speed of blood flow, low blood pressure and elasticity of venules provide the blood deposition in these vessels.

Veins provide the return of blood to the heart and deposition of blood.

The general plan of vein structure is the same as in the arteries, but some differences are present:

1. The wall of the vein is thinner than the one of the accompanying artery
2. In veins collagen fibers prevail over elastic ones. Elastic fibers are less developed.
3. External elastic membrane is absent, internal elastic membrane is underdeveloped.
4. In histological specimen the lumen of vein are irregular in shape, while in arteries it is round.
5. In veins tunica externa is the thickest one, while in arteries – tunica media
6. In some types of veins valves are present.

The classification of veins is based on the degree of development of muscular elements in their wall:

1) Amuscular veins
2) Muscular veins

a) veins with low development of muscular elemnts
b) veins with medium development of muscular elements
c) veins with high development of muscular elements

Amascular veins. This type of veins includes veins of dura mater and pia mater, veins of retina, spleen, bones and placenta. The wall of these veins is lined with endothelium with basal lamina. Tunica media is absent. Tunica externa is formed by thin layer of loose connective tissue, which is inosculated with surrounding tissues, due to that veins do not collapse and provide blood outflow.

Veins with low development of muscular elements. The structure of the wall of this type of veins is connected with the hemodynamic conditions. Blood moves through these veins under the force of gravity. Subendothelial layer is low-developed, in tunica media are present a lot of smooth muscle cells. In tunica externa occasional smooth muscle cells occur. Veins of upper part of the body, neck, face and *v.cava superior* are in this category.

Veins with medium development of muscular elements. The example of such type of veins is *v.brachialis*. The tunica interna forms valves and contains longitudinally oriented smooth muscle cells. Internal elastic membrane is almost not defined. Tunica media is thin with circularly arranged smooth muscle cells. External elastic membrane is absent, that's why loose connective tissue of tunica media directly join loose connective tissue of tunica externa.

Veins with high development of muscular elements. These veins are characterized by high development of muscle cells in all three tunics. In tunica interna and externa they are longitudinally arranged, in tunica media – circularly.
The characteristic feature of these veins is the presence of valves. This category includes veins of lower part of the body and lower limbs.

Valves – are pocket-like folds of tunica interna opened towards the heart. They prevent retrograde movement of blood because of gravity. The valve is formed by loose connective tissue and in some cases small amount of smooth muscle cells.
Great saphenous vein (v. cava inferior) is structurally different from other veins. Tunica interna and media are low-developed. Tunica externa is 6-7 times thicker than tunica externa and media together and contains a lot of longitudinally arranged bundles of smooth muscle cells. The valves are absent in great saphenous vein, their function is provided by the folds of tunica externa.
According to the size veins are classified into small, medium and large.

Lymphatic vessels

Lymphatic system conveys fluids from the tissues to the venous bed. Lymphatic vessels are functionally connected with blood vessels, especially in the microcirculatory bed. Exactly in the microcirculatory bed the formation of tissue fluid occurs.

Classification. Lymphatic vessels include:

- lymphatic capillaries
- intraorganic and extraorganic lymphatic vessels
- thoracic duct and right lymphatic duct

The structure of the wall of lymphatic vessels has a lot of in common with the structure of the wall of veins that could be explained by the same conditions of hemo- and lymphodynamics (low pressure, low speed of blood flow, direction of flow from the tissues to the heart)

Two types of lymphatic vessels are distinguished: muscular and amascular. Medium and big lymphatic vessels contain three well-developed layers (tunica interna, media and externa). Tunica interna forms numerous folds – the valves. The dilatated areas between adjacent valves are called lymphangions. Tunica media is more conspicuous in the vessels of lower limbs. Before lymph is returned to the blood, it passes through lymph nodes, where it is exposed to the cells of the immune system. The characteristic feature of the wall of large lymphatic vessels (thoracic duct and right lymphatic duct) is high-developed tunica externa, which is 3-4 times thicker than tunica interna and media together. In tunica externa are located longitudinally arranged bundles of the smooth muscle cells. It is located up to nine semilunar valves in thoracic duct.

Lymphatic capillaries – are flattened "blind-ended" vessels, through which tissue fluid and waste products enter. The wall of lymphatic capillaries is formed by endothelium lying on discontinuous basal lamina; pericytes do not occur. Anchoring filaments extend between the incomplete basal lamina and the perivascular collagen. These filaments may help maintain the patency of the vessels during times of increased tissue pressure. The diameter of lymphatic capillaries could be changed depending on the blood volume. Lymphatic capillaries provide drainage function, taking part in the processes of removing of blood plasma filtrate from the connective tissue.

The Heart (cor) – is muscular pump, which maintains unidirectional flow of blood. The wall of the heart consists of three layers:

- endocardium
- myocardium
- epicardium

Endocardium consists of four layers:

- endothelium on the basal lamina;
- subendothelial layer – loose connective tissue, which is rich in low-differentiated cells;
- musculo-elastic layer – formed by the smooth muscle cells and elastic fibers;
- external layer of connective tissue – formed by loose connective tissue, which contains elastic, collagen and reticular fibers.

Myocardium consists of the **cardiac muscle tissue** and layers of loose connective tissue with nerves and blood vessels. Two types of cardiac muscle cells are distinguished:

- **typical or contractive**
- **atypical or conductive** which form the conducting system of the heart

Contractive cardiac muscle cells – are rectangular-shaped cells with centrally located nucleus. Myofibrils in their cytoplasm are longitudinally arranged. Basal lamina takes part in the formation of 'T-tubules'.

The conducting system of the heart includes sinoatrial node, atrioventricular node, atrioventricular bundle of His. All this structures are formed by conductive cardiac muscle cells, which generate and conduct nerve impulses to the contractive cardiac muscle cells. There are distinguished three types of conductive muscle cells:

1. The first type – pacemaker cells, they can generate and rhythmically send impulses without any stimulation from the nervous system. They are small, polygonal cells, containing small amount of randomly arranged myofibrils. T-systems are absent.
2. The second type – transitional. The cells are thin and elongated. Myofibrils are usually better developed and laid parallel to one another.
3. The third type – the cells of bundle of His. These cells are big in size with eccentrically located nucleus. Myofibrils are thin and randomly arranged, located at the peripheral part of the cell. T-systems are not present.

Epicardium and pericardium. The outer covering of the heart or epicardium is also known as the visceral layer of serous pericardium. Epicardium consists of the thin layer of connective tissue covered with mesothelium.
There is a space between the epicardium and pericardium containing a minimal amount of serous fluid, which act as a lubricant.

THE ORGANS OF HEMATOPOIESIS AND IMMUNE DEFENSE

There are distinguished central and peripheral organs of hematopoiesis and immune defense.
The central organs are:

- red bone marrow;
- thymus.

The functions of the central organs of hematopoiesis are:

- the formation of all types of the blood cells;
- providing conditions for the antigen-independent activation of lymphocytes.

The peripheral organs are:

- lymph nodes;
- spleen;
- lymph nodules of the digestive tract and the respiratory system.

The functions of the peripheral organs of hematopoiesis are:

1. Providing the division of T- and B-lymphocytes, which come here from the central organs of hematopoiesis.
2. Antigen-dependent activation of T- and B-lymphocytes
3. Elimination of the blood cells that have finished their life cycle.

Red bone marrow. In adults bone marrow lies entirely within the flat bones and the epiphyseal ends of long bones.

The functions of red bone marrow are the formation of erythrocytes, platelets (trombocytes), granulocytes, monocytes, B-lymphocytes and precursors of T-lymphocytes.
There are distinguished the following parts in red bone marrow:

- rough stroma (bone);
- gentle stroma (reticular tissue);
- parenchyma.

Rough stroma is formed by the endosteum of spongy bone trabeculae and supports the gentle stroma.
Gentle stroma – is the reticular connective tissue that serve as a framework for the developing blood cells.
Parenchyma consists of the blood cells on the different stages of development (hematopoietic stem cells, progenitor stem cells, lineage-restricted progenitor cells of erythrocytes, trombocytes, granulocytes, monocytes and lymphocytes).

The most intensive division and maturation of the blood cells occurs near the endosteum. The red bone marrow is highly vascularized and contains numerous fenestrated (sinusoidal) capillaries, which provide the passage of the mature blood cells into the bloodstream.
Hematopoietic cells are arranged in nests or "islands". Each island contains the cells of the one blood cell lineage. Each island in which erythrocytes develop contains a macrophage. Since the developing erythrocytes need the iron ions for the formation of hemoglobin molecule, they surround the macrophage, which stores the iron. The macrophages serve as "breadwinners" for the erythroblasts, enriching them in iron. Immature erythroid cells are surrounded by the glycoproteins. As the erythroid cells mature, the amount of glycoproteins decreases. At the same time the mobility of the cells increases and they pass into the bloodstream.

Granulopoietic cells form the islands too. Developing cells of granulocyte lineage are surrounded by proteoglycans. In the process of maturation granulocytes are stored in the red bone marrow.

Megakaryoblasts and megakaryocytes are in close contact with hemocapillaries thereby the peripheral part of their cytoplasm through the pores enters the capillary lumen. The separation of the cytoplasm compartments occurs directly in the bloodstream.

In normal physiological conditions only mature blood cells could pass through capillary wall. Myelocytes and erythroblasts could pass into the bloodstream only in pathological conditions. Entering the bloodstream, the blood cells provide their function in the vessels of microcirculatory bed or in the connective tissue or lymphoid organs.

In the age of 12-18 years, the red bone marrow of the long bones diaphyses is substituted to the inactive **yellow bone marrow**. Yellow bone marrow consists of adipocytes, which contain the pigment lipochrome. Although normally yellow bone marrow doesn't provide hematopoietic function, in case of severe loss of

blood or some pathologic states it can revert to the red bone marrow by repopulation the yellow bone marrow by circulating stem cells.

In senile age red and yellow bone marrows acquire gelatinous consistence and transforms into the **gelatinous bone marrow**.

Thymus – is the central organ of lymphocytopoiesis and immunogenesis.

The functions of thymus are:

1. reproduction of T-lymphocytes;
2. antigen-independent activation of T-lymphocytes;
3. production of thymosin, thymuline, thymopoetin that regulate the reproduction and maturation of T-lymphocytes in the central and peripheral hematopoietic organs.
4. secretion of biologically active substances:

a) insulin-like factor (decreases the glucose level in blood);
b) calcitonin-like factor (decreases the calcium serum level);
c) growth factor (stimulates the body growth).

Thymus is surrounded by the connective tissue capsule, from which trabeculae extend into the parenchyma of the organ and divide it into lobules. Basal lamina, containing pores lies between the capsule and parenchyma. Thymus is formed by the **epithelial tissue**. The epithelial cells (epithelioreticular cells) have processes.

Thymic lobule is the structural and functional unit of the organ. Each lobule consists of the framework, which is formed by the contacting processes of epithelioreticulocytes.

The spaces within the extensive meshwork of epithelioreticulocytes are occupied by T-lymphocytes and macrophages.

There are distinguished two portions in the thymus parenchyma:

- thymic cortex (dark-stained)
- thymic medulla (light-stained)

In the **thymic cortex** the following cells are located:

- small and medium lymphocytes;
- macrophages and their subtype – dendritic cells;
- epithelioreticulocytes;
- T-lymphoblasts.

Epithelioreticulocytes, macrophages and dendritic cells of the subcapsular zone of the thymus provide the microenvironment and essential conditions for the maturation of T-lymphocytes (thymocytes). That's why such cells are called the "nanny-cells".

The precursors of T-lymphocytes are delivered to thymus from the red bone marrow. Here under the action of thymosin, which is produced by the epithelioreticulocytes, T-lymphocytes undergo cell division and some of them are phagocyted by the macrophages. It is considered that T-lymphocytes of thymic cortex migrate into the bloodstream, without getting to the thymic medulla. With the bloodstream T-lymphocytes are delivered to the peripheral

organs of lymphopoiesis – lymph nodes and spleen, where they are differentiated into subpopulations. However not all the lymphocytes formed in thymus pass into the bloodstream, but only those that have passed the **T- cell education"** and obtained the receptors to the specific antigens. T-lymphocytes, which have the receptors to their own antigen as a rule die in thymus.

The cells of thymic cortex are separated from the blood by the **blood-thymus barrier** which prevents the differentiating lymphocytes from the contact with antigens.

The following components constitute the blood-thymus barrier:

- endothelium of hemocapillaries with underlying basal lamina;
- surrounding perivascular connective tissue with residing macrophages;
- epithelioreticular cells with their basal lamina.

The thymic medulla is formed by:

- small, medium and large T-lymphocytes;
- T-lymphoblasts;
- epithelioreticulocytes;
- macrophages.

The lymphocytes of thymic medulla are the recirculating pool of T-lymphocytes, they can pass into the bloodstream and back through the postcapillary venules and lymphatic vessels. The characteristic feature of the thymic medulla is the presence of the **thymic (Hassall's) corpuscles**. They are formed by closely packed concentrically arranged epithelioreticulocytes that exhibit large vacuoles, keratin granules and dense fiber bundles.

During the human life thymus undergoes the several changes that are called the **age involution.** The thymic parenchyma is gradually substituted by the adipose or loose connective tissue, the amount of Hassall's bodies increases.

There four phases in the age involution of thymus:

1. rapid phase (until 10 years);
2. slow phase (from 10 to 25 years);
3. accelerated phase (from 25 to 40 years);
4. delayed phase (after 40 years).

The absence of thymic involution is the sign of serious pathology, which is called **status thymicolymphaticus.** This state is accompanied by the glucocorticoid insufficiency of adrenal cortex and overgrowth of lymphoid tissue in organs. The resistance of the body to the infections, intoxications and cancer development is significantly reduced.

In case of the action of unfavorable factors, like trauma, starvation, infection or intoxication, the **accidental involution** of thymus occurs. Accidental involution is the manifestation of the defense reactions of the body. It is characterized by the mass death of lymphocytes, their migration to the peripheral hematopoietic organs, the division and enlargement of epithelioreticular cells.

Lymphatic nodules of the alimentary canal and respiratory passages are considered to be the dissociated analog of the Bursa Fabricii of the birds, i.e.

the central organ of lymphopoiesis. Here the antigen-dependent activation of B-lymphocytes occurs. Lymphatic nodules are the discrete concentration of T- and B-lymphocytes. They are commonly found in the lamina propria of the mucous and in the submucosa of the alimentary canal and respiratory passages respectively. T-lymphocytes in lymphatic nodules just play an auxiliary role in the maturation of B-lymphocytes. Upon obtaining the immune competence, B-lymphocytes pass into the bloodstream. The part of them returns to the nodule and transforms into the plasma cells that produce antibodies – immunoglobulin A.

Lymph nodes are small bean-shaped encapsulated organs located along the pathway of lymphatic vessels. The antigen-dependent activation of T-and B-lymphocytes occurs in the lymph nodes. Lymph nodes serve as filters through which lymph percolates on its way to the blood vascular system.

The lymph nodes include:

- rough stroma (capsule and trabeculae);
- gentle stroma (reticular connective tissue);
- parenchyma (T- and B-lymphocytes, macrophages, dendritic cells).

The connective tissue capsule of the lymph nodes contains the smooth muscle cells.

In the lymph node the following portions are distinguished:

- cortex;
- paracortex (deep cortex);
- medulla.

The cortex is formed by lymphatic nodules (follicles) – concentrations of B-lymphoblasts, macrophages and dendritic cells. They have an ability to fix the antigen-antibody complexes on their surfaces. The contact with the dendritic cells stimulates the B-lymphocytes to produce antibodies. The framework of the nodule is formed by the reticular connective tissue. The follicles are surrounded by the reticuloendothelial cells. Structurally reticuloendothelial cells are the reticular cells, but they provide the function of endothelial cells as they line the sinuses of the lymph nodes. Among reticuloendotheliocytes the numerous fixed macrophages (the coastal cells) are revealed.

Each follicle has the germinal center located in the central region and peripheral mantle zone (or corona). The germinal center appears lightly stained in histologic sections. Here the reproduction and proliferation of predominantly B-lymphocytes occurs. Mantle zone represents an outer ring of small and medium lymphocytes that encircles the germinal center. In histologic sections it appears dark.

Dendritic cells of germinal centers are the subtype of macrophages; they have an ability to fix the antigen-antibody complexes by means of the antibody's receptors and retain antigen on its surface.

The paracortex is located between the cortex and medulla of the lymph node. This region contains numerous T-lymphocytes and macrophages and is called **thymusdependent.** Macrophages in the paracortex are represented as

interdigitative cells, which have lost their ability to phagocytosis. These cells secrete the biologically active substances, which stimulate the proliferation of T-lymphocytes. In the paracortex the proliferation of T-lymphocytes, their blast transformation and differentiation into the effector cells (T-killers, helpers etc) occurs.

The **medulla** of the lymph node is formed by the medullary cords, which contain B-lymphocytes, plasma cells, macrophages. Medullary cords extend from the cortex to the hilum. In the medulla the proliferation and maturation of plasma cells occur. The medullary cords are surrounded by the reticuloendothelial cells, which lie on the bundles of reticular tissue and form the walls of sinuses.

The cortex and the medulla of the lymph nodes are Burso-dependent zones, while the patacortex is thymusdependent zone.

The sinuses of lymph nodes – are the slit-like spaces between the layers of reticuloendotheliocytes, which surround the the lymphatic follicles and medullary cords on the one side and connective tissue stroma on another side.

There four types of lymphatic sinuses:

1. marginal or subcapsular sinuses (between the capsule and the follicles);
2. parafollicular sinuses (between the follicles and trabeculae);
3. medullary sinuses (between the medullary cords and traeculae);
4. portal sinus (in the area of hilum).

The system of sinuses provides the lymph circulation from the portal sinus, into which the afferent lymphatic vessels drain, to the marginal sinus, from which blood drains to the system of efferent lymphatic vessels. At the same time lymph is filtered due to phagocytic activity of the macrophages and is enriched in T- and B-lymphocytes, memory cells and immunoglobulins.

Spleen is the unpaired organ, located in the upper left quadrant of the abdominal cavity, has rich blood supply.

The functions of the spleen:

1. proliferation and antigen-dependent activation of lymphocytes;
2. elimination of the erythrocytes and platelets that have finished their life cycle;
3. storage of blood and calcium ions
4. production of the biologically active substances (splenin, the factor of erythropoiesis inhibition);
5. in fetus – the universal organ of hematopoiesis.

There are distinguished the following portions in the spleen:

- rough stroma (connective tissue capsule and trabeculae);
- gentle stroma (reticular tissue);
- parenchyma (lymphocytes, plasma cells, macrophages, erythrocytes, dendritic and interdigitative cells, destroyed erythrocytes and platelets).

The rough stroma of the spleen – the connective tissue capsule, from which the trabeculae extend into the parenchyma. Together with the collagen and elastic fibers in the stroma of the spleen the smooth muscle cells and blood vessels are present.

The gentle stroma of the spleen is formed by the reticular cells and reticular fibers, which form the meshwork. In the spaces of this meshwork the parenchymal cells are located.

In the spleen parenchyma are distinguished:

- the white pulp;
- the red pulp.

The white pulp is formed by lymphocytes, plasma cells, macrophages, dendritic and interdigitative cells and the cells that are located within the reticular tissue meshwork. These cells are arranged in circular cell clusters, which are called lymphatic follicles (nodules) or splenic corpuscles. The follicles are surrounded by the capsule, which is formed by the reticuloendothelial cells.

In the lymphatic follicle the four zones are distinguished:

1. periarterial zone;
2. mantle zone;
3. marginal zone;
4. light germinal center.

The light germinal center of lymphatic follicles contains:

- B-lymphocytes;
- typical macrophages;
- dendritic cells;
- reticular cells.

Periarterial zone contains:

- T-lymphocytes, which form the clusters near the central artery of the spleen;
- interdigitative cells (macrophages).

The dark mantle zone is formed by densely packed:

- small B-lymphocytes;
- T-lymphocytes;
- plasma cell;
- macrophages.

Marginal zone is located near the red pulp and is formed by:

- B-lymphocytes
- T-lymphocytes
- macrophages

Marginal zone is surrounded by the fenestrated capillaries. After the maturation lymphocytes pass from the germinal center and periarterial zone into mantle and marginal zones with the following passage into the bloodstream.

Periarterial lymphatic sheaths – are the elongated clusters of B-lymphocytes located along the pulp artery of the spleen. At the periphery of the lymphatic sheath small T-lymphocytes are revealed.

The red pulp consists of the clusters of the blood cells, which are surrounded by reticular cells or are located in the system of **splenic sinuses**. The areas of the red pulp located between splenic sinuses are called the **splenic pulp cords.** The transformation of B-lymphocytes to plasma cells and transformation of monocytes to macrophages take place in the splenic cords.

The macrophages of the spleen recognize and destroy old or damaged erythrocytes and platelets. The hemoglobin of eliminated erythrocytes is used for the synthesis of bilirubin and transferrin. The molecules of transferrin are phagocyted by the macrophages of the red bone marrow and are used for the formation of new erythrocytes.

Blood supply of the spleen

Branches of the splenic artery enter the white pulp from the trabeculae. The central artery sends branches to the white pulp itself and to the sinuses at the perimeter of the white pulp called marginal sinuses. The central artery continues into the red pulp, where it branches into several relatively straight arterioles called penicillar arterioles. The penicillar arterioles then continue as arterial capillaries. Some arterial capillaries are surrounded by aggregations of macrophages and are thus called sheathed capillaries. Sheathed capillaries then empty directly into the reticular meshwork of the splenic cords rather than connecting to the endothelium-lined splenic sinuses. Blood entering the red pulp in this manner percolates through the cords and is exposed to the macrophages of the cords before returning to the circulation by squeezing through the walls of the splenic sinuses. This type of circulation is referred to as open circulation, and it is the only route by which blood returns to the venous circulation in humans. Open circulation exposes the blood more efficiently to the macrophages of the red pulp. Both transmission and scanning lectron micrographs often show blood cells in transit across the endothelium of the sinus, presumably reentering the vascular system from the red pulp cords. The blood collected in the sinuses drains to tributaries of the trabecular veins that converge into larger veins and eventually leaves the spleen by the splenic vein. The splenic vein in turn joins the drainage from the intestine in the hepatic portal vein.

ENDOCRINE SYSTEM

The endocrine system together with the nervous system provides the regulation and coordination of all functions of the body. Endocrine system includes endocrine glands and solitary endocrine cells that are scattered all over the body. Although endocrine glands don't have excretory ducts, they are highly vascularized, so their secretory products pass directly into the bloodstream. Both the endocrine glands and the solitary endocrine cells produce hormones and release them into the blood and lymph. Hormones – are biologically active substances, which stimulate or inhibit the main functions of the body: metabolic processes, somatic growth and reproductive functions.

Hormones are chemically divided into three classes:

- **Peptides** (oligopeptides, polypeptides, glycopeptides);
- **Derivatives of amino acids** (neuroamins);
- **Steroids** (sex hormones, corticosteroids).

All of these biologically active substances are produced in very small amounts. When released into the blood or lymph, hormones interact with the specific receptors on the surface of the target cells.

Mechanism of action. The hormone molecule, circulating through the bloodstream, 'recognizes' its specific receptor on the surface of the target cell according to the principle of complementarity of 'key' (hormone) to 'keyhole' (receptor of plasmolemme). Regulation of hormonal function is controlled by **feedback mechanisms**. Hormonal production is often controlled through feedback mechanisms from the target organ. In general, feedback occurs when the response to a stimulus (action of a hormone) has an effect on the original stimulus (hormone-secreting cell).The nature of this response determines the type of feedback. Two types of feedback are recognized; a negative feedback occurs when the response diminishes the original stimulus. It is much more common than a positive feedback, which occurs when the response enhances the original stimulus.

There are distinguished four groups of elements of the endocrine system.

The first group – central endocrine organs: hypothalamus, pituitary gland (hypophysis) and pineal gland (epiphysis). These organs are anatomically and functionally connected with the central nervous system and provide the coordination of all other links of the endocrine system.

The second group – **peripheral endocrine organs**: thyroid gland, parathyroid glands and adrenal glands. These endocrine glands affect target cells all over the body, stimulating or inhibiting their metabolic activity.

Розрізняють чотири групи елементів ендокринної системи.

The third group – organs that provide both endocrine and non-endocrine functions. This group includes pancreas, ovaries, testes, kidneys, placenta etc.

The fourth group – the cells of the **diffuse neuroendocrine system**, which are scattered all over the all organs and systems of the body.

Central endocrine organs

Hypothalamus – the central endocrine organ that combines nervous and humoral (hormonal) regulation of the body. Hypothalamus includes about 30 pairs of nuclei (a cluster of neurosecretory cells) that are located in the area of the floor of the third ventricle.

For convenience hypothalamus is divided into three parts:

- anterior hypothalamus
- middle hypothalamus
- posterior hypothalamus

The endocrine function of hypothalamus is associated with the activity of special neurosecretory cells of anterior and middle hypothalamus.

Two pairs of nuclei are located in the anterior hypothalamus:

- supraoptic nucleus
- paraventricular nucleus

The neurosecretory cells of supraoptic nucleus produce hormone **Vasopressin**. Biological action of Vasopressin results to the increasing of blood pressure by promoting the contraction of the smooth muscle in small arteries and arterioles. Another biological effect of Vasopressin is reduction of urine excretion by the facilitation of resorption of water from the distal tubules and collecting ducts of

the kidney. That's why the second name of this hormone is **antidiuretic hormone (ADH)**. Supraoptic nuclei are formed by the large cholinergic neurosecretory cells that contain secretory granules in perikaryones and cell processes. Axons of these cells pass through the median eminence and pituitary stalk to the posterior pituitary, where they end near the blood capillaries, forming dilatations called **Herring bodies**.

The cells of paraventricular nuclei produce **oxytocin** that causes the contraction of smooth muscles of the uterus and myoepithelial cells of the breast.

Hormones through the axons of neurosecretory cells enter the posterior pituitary, where they pass into the bloodstream through the axovasal synapses. The central part of these nuclei is formed by large cholinergic neurosecretory cells, while the peripheral part consists of small adrenergic neurosecretory cells. Axons of these cells enter posterior pituitary (neurohypophysis). The nuclei of hypothalamus are formed by the large or small multipolar neurons that contain well-developed granular EPR, Golgi apparatus. These organelles provide synthesis and secretion of hormones. Specific granules, containing biologically active substances are revealed in the cytoplasm of all neurosecretory cells.

Middle hypothalamus contains arcuate, dorsomedial, ventromedial, suprachiasmatic nuclei and preoptic area. Small adrenocholinergic cells of these nuclei produce two groups of biologically active substances – **liberins and statins** that affect on the cells of anterior lobe of hypophysis.

Liberins and statins are also named "releasing-factors". Liberins and statins are physiological antagonists. Liberins promote the production and secretion of hormones from the anterior lobe of the pituitary gland, while statins inhibit it. Liberins and statins are discharged into the blood and reach the pituitary gland due to the hypothalamohypophyseal portal system.

The hypothalamohypophyseal portal system provides the crucial link between the hypothalamus and the pituitary gland. The arteries that supply the pars tuberalis, median eminence, and infundibulum give rise to fenestrated capillaries (the primary capillary plexus). These capillaries drain into portal veins, called the hypophyseal portal veins, which run along the pars tuberalis and give rise to a second fenestrated sinusoidal capillary network (the secondary capillary plexus).

This system of vessels carries the neuroendocrine secretions of hypothalamic nerves from their sites of release in the median eminence and infundibulum directly to the cells of the pars distalis. Most of the blood from the pituitary gland drains into the cavernous sinus at the base of the diencephalon and then into the systemic circulation.

Hypophysis – the central endocrine organ, which provides the regulation of the activity of the peripheral endocrine glands (hypophysis-dependent organs) and also affects directly on some non-endocrine cells.

Hypophysis-dependent endocrine organs are:

- thyroid gland;
- adrenal cortex;
- endocrine part of gonads.

Non-endocrine cells regulated by hypophysis are:

- lactocytes of mammary gland;
- melanocytes;
- adipocytes;
- chondrocytes;
- spermatogoniums of testis etc.

The pituitary gland has two functional components:

• Anterior lobe **(adenohypophysis)**, the glandular epithelial tissue
• Posterior lobe **(neurohypophysis),** the neural secretory tissue.

The anterior lobe of the pituitary gland consists of three parts:

• Pars distalis
• Pars intermedia
• Pars tuberalis

In the posterior lobe of pituitary gland (neurohypophysis) Herring bodies are located, where hormones of suprapotic and paraventricular nuclei of hypothalamus (oxytocin and vasopressin) are stored and released into the capillary bed.

The anterior lobe (adenohypophysis) has a typical organization of endocrine tissue. The cells of adenohypophysis produce hormones.

Pars distalis is formed by the cells arranged in cords and nests with interweaving capillaries.

Two groups of cells are distinguished among endocrinocytes of pars distalis:

- chromophilic
- chromofobe

Chromophilic endocrinocytes contain secretory vesicles, which are intensively stained with histological dyes. In chromofobe cells such vesicles are absent that's why their cytoplasm is achromatous on histological specimens.

Among chromophilic endocrinocytes three types of cells are distinguished:

- basophilic
- acidophilic
- corticotropes (intermediate cells).

Basophilic endocrinocytes of pituitary gland contain granules, which are stained with basic dyes. Among basophilic endocrinocytes the following cells are distinguished:

- **gonadotropes**, these cells produce **follicle-stimulating hormone (FSH)**, which stimulates spermatogenesis in testis in males and follicular cells of ovaries in females and **luteinizing hormone (LH)**, whose function is the stimulation of development of corpus luteum in females and stimulation of Leydig cell production of testosterone in males. Gonadotropes are characterized by peripherically located nucleus and centrally located macula (well-developed Golgi complex). The cytoplasm contains a lot of secretory vesicles, which are 200-250 nm in diameter, a lot of mitochondria and well-developed rough EPR. In case of the lack of sex hormones in the body the cells of anterior lobe of pituitary gland increase the production of

gonadotrophic hormones acoording to the principle of negative feedback. Due to this gonadotropes undergo hypertrophy; the cytoplasm of some cells becomes occupied by a large vacuole (in the area of macula) that displaces the nucleus to the periphery. Such transformed gonadotropes are called castration cells.

- **thyrotropes** produce **thyroid-stimulating hormone (TSH)** that regulates the activity of thyroid gland. These large polygonal cells contain very small secretory vesicles (80-150 nm).

Acidophilic endocrinocytes of pituitary gland contain in their cytoplasm the large dense secretory vesicles, which are stained with acid dyes. There are distinguished the following types of cells among acidophilic endocrinocytes:

- **mammotropes** (PRL-cells, lactotropes) produce **prolactin (PRL)**. Prolactin is responsible for maturation of lactocytes of mammary gland and initiation of secretion of components of milk. It also maintains the functioning of corpus luteum. The size of granules in mammotropes is about 500-600 nm.
- **somatotropes (GH cells)** produce **somatotropin (growth hormone)** that affects the protein metabolism thereby providing the growth of the body. The size of granules is about 400 nm.

Acidophilic edocrinocytes are smaller than the basophilic ones, they are round or oval in shape, contain centrally located nuclei. Mitochondria are quite big but not numerous. Rough EPR is highly developed. Golgi complex is moderately developed and is attached to the nucleus.

Corticotrpes –is the third group of chromophilic cells that doesn't refer to the basophilic nor acidophilic. Corticotropes produce **adrenocorticotropic hormone (ACTH)** that stimulates the endocrine function of the cells of adrenal cortex. Corticotropes are irregular in shape, contain well-developed mitochondria and rough EPR. Nuclei consist of separated particles. The diameter of secretory vesicles is 100-200 nm.

All of the hormones of anterior pituitary are proteins. Highly developed rough EPR and Golgi complex are responsible for their synthesis and secretion.

Chromofobe endocrinocytes constitute approximately 60% of the cells of anterior pituitary and include different types of cells. They are low-differentiated cambial cells, which form the reserve for substitution of the endocrinocytes that have finished their live cycle.

Pars intermedia is represented as a thin strip of epithelium, which is separated from the posterior lobe of pituitary gland by a thin layer of loose connective tissue. Pars intermedia is formed by two types of cells:

- **melanotropes** that produce **melanocytes-stimulating hormone (MSH)**, which stimulates the production and release of melanin by melanocytes of skin and hair.
- **lipotropes** that produce **lipotropin**, which stimulates the metabolism of lipids.

Pars tuberalis is an extension of the anterior lobe along the stalklike infundibulum. It is formed by the cords of cuboidal epithelial cells with basophilic

cytoplasm. Some cells of tuberal cords contain basophilic granules in their cytoplasm. The function of the cells of pars tuberalis is still unclear.

Posterior lobe (neurohypophysis) contains Herring bodies – the dilatations of axons of neurosecretory cells of hypothalamus, where secretory vesicles with oxytocin and vasopressin are stored. The supporting and trophic functions are provided by glial cells called **pituicytes**. These cells are irregular in shape, with many branches, and resemble astroglial cells.

Epiphysis (pineal gland, pineal body) – is the central endocrine organ, which provides the regulation of the photoperiodicity of the functioning of organs and systems of the body, especially its circadian rhythm (day/night cycle). Besides this, epiphysis takes part in regulation of reproductive system functioning. The pineal gland is photosensitive organ; it obtains information about light and dark cycles from the retina via the retinohypothlamic tract. It is located at the posterior wall of third ventricle near the center of the brain. The pineal gland is a flattened, pine cone–shaped structure, hence its name. It measures 5 to 8 mm high and 3 to 5 mm in diameter and weighs between 100 and 200 mg. It is covered with connective tissue capsule, from which septa extend into the gland and divide it into lobules. Each lobule of pineal gland consists of two types of cells:

- neurosecretory (pinealocytes)
- gliocytes (astroglial cells)

Pinealocytes are the chief cells of pineal gland located mostly in the center of the lobules. They are large polygonal cells with branched processes. The expanded, clublike endings of the processes are associated with the blood capillaries. The cytoplasm contains well-developed smooth and rough EPR, Golgi complex, mitochondria and lysosomes.

According to the functional activity there are distinguished two types of pinealocytes:

- light cells that are poor in secretory inclusions;
- dark cells containing acidophilic and basophilic granules.

Pinealocytes are considered to be the heterogenous cell population, since they produce about 40 types of regulatory peptides and biologically active amines – **serotonin and melatonin**.

Melatonin inhibits the secretion of gonadoliberine by hypothalamus thereby slowing down the sexual maturation. In adults melatonin controls pigment metabolism, sexual functions, daily and seasonal rhythms, processes of cell division and differentiation, reveals anticancer activity.

The lack of serotonin in CNS is the pathogenic factor of depression.

The regulatory peptides of pineal gland are luliberin, thyreotropic hormone (analog of pituitary TRH), and hormones-regulators of mineral exchange (Sodium exchange).

In humans pineal gland reaches the maximal development to the age of 5-6 years, after this, in spite of continuing functioning, it undergoes age involution. A part of pinealocytes undergo atrophy, while the stroma expands. Derived from the

precipitation of salts, the calcified concretions appear in the stoma of pineal gland. These concretions are called brain sand.

Peripheral endocrine organs

Thyroid gland – is the peripheral endocrine organ that regulates the basal metabolism and takes part in the maintenance of level of Calcium in the blood.

Thyroid gland is covered with connective tissue capsule, which sends trabeculae into the parenchyma that partially outline irregular lobes and lobules. Thyroid follicles constitute the structural and functional units of the gland. A thyroid follicle is a roughly spherical cystlike compartment with a wall formed by a simple cuboidal or low columnar epithelium, the follicular epithelium. The cells of follicular epithelium are called **thyrocytes**. The follicles contain a gel-like mass called colloid. Colloid consists of the protein – thyreoglobulin. The molecule of thyreoglobulin consists of thyroxin (the hormone of thyroid gland), which is bound to polypeptide chain (globulin). The apical surfaces of the follicular cells are in contact with the colloid, and the basal surfaces rest on a typical basal lamina.

Follicles are separated by the layers of loose connective tissue, through which numerous nerve fibers, blood and lymphatic capillaries pass. The clusters of thyroid epithelial cells, lymphocytes, tissue basophiles and mast cells are also revealed in these connective tissue layers.

Follicular thyrocytes – are the main component of thyroid gland. Their shape depends on their functional activity. Normally they are cuboidal in shape, in case of thyroid hyperfunction and in children they are prismatic, and in case of thyroid hypofunction and in aged people thyrocytes become flattened. The short microvilli located on the apical surface of the follicular cells take part in the secretion of thyreoglobulin into the lumen of the follicle. The increase of functional activity of thyrocytes is accompanied by the increasing of the number and high of microvilli. The cytoplasm of thyrocytes contains well-developed rough EPR and Golgi complex.

Synthesis of thyroid hormones involves two phases:

Production phase. Thyrocytes absorb Iodine ions and aminoacid tyrosine from blood that flows into the gland. In rough EPR the formation of thyreoglobulin molecule occurs. Then in Golgi complex thyreoglobulin is packaged into vesicles. After this, thyreoglobulin is secreted by exocytosis into the lumen of the follicle. The process of iodination of thyreoglobulin occurs at the microvillar surface of the thyrocytes**. Thyroxin and tetraiodothyronine** are formed.

Secretion phase starts with the reabsorption of colloid. In response to the TSH (thyroid-stimulating hormone), thyrocytes take thyreoglobulin from colloid and the reverse process starts: polypeptide chain is hydrolyzed by lysosomal enzymes of thyrocyte. Released tyrosine is excreted through the basal lamina to the capillary network, which surrounds the follicle.

Thyroxin and tetraiodothyronine regulate the oxygen consumption and the general level of metabolic processes of body thereby affecting the basal metabolism.

Another type of cells of thyroid gland is **parafollicular cells (C-cells)**. They are located in the periphery of the follicular epithelium and lie within the follicle basal lamina. These cells have no exposure to the follicle lumen. Parafollicular cells are

large irregular in shape with numerous secretory vesicles in the cytoplasm. The characteristic feature of parafollicular cells is their ability to reduce the heavy metal oxides that's why they are argyrophilic. The cytoplasm contains well-developed rough EPR and Golgi apparatus.

There are distinguished two types of parafollicular cells: cells of the first type produce the hormone **calcitonin**, cells of the second type – **somatostatin**. Calcitonin decreases the serum calcium level by depositing it in the bone tissue. Somatostatin, being the antagonist of somatotropin, inhibits the protein synthesis.

Parafollicular cells can provide both synthesis of regulatory peptides and neuroamines - serotonin and noradrenalin.

The thyroid hypofunction in early childhood can lead to the development of cretinism (physical and mental retardation). In adults thyroid hypofuntion causes myxedema. The symptoms of myxedema are: increase in body weight, body temperature decrease, hair loss, signs of central nervous system depression, apathy, bradycardia.

In case of thyroid hypofunction Grave's disease develops. The symptoms of Grave's disease are opposite to the symptoms of myxedema.

Parathyroid gland. There are four parathyroid glands in human body. They are located on the posterior surface of thyroid gland. Each parathyroid gland is surrounded by a thin connective tissue capsule. Parenchyma is formed by epithelial trabeculae and cords of glandular cells (**parathyrocytes**). The cords of cells are separated by the connective tissue septa that extend from the capsule. These connective tissue septa contain blood and lymphatic capillaries. Parathyrocytes are connected together by desmosomes, interdigitations and zonulae occludens.

Parathyrocytes have well-developed rough EPR, Golgi apparatus, mitochondria, their cytoplasm contains secretory vesicles. Depending on the functional state of parathyrocytes, their cytoplasm could be stained basophilic (chief cells) or acidophilic. Among chief parathyroctes light and dark cells are distinguished. In the cytoplasm of light cells the inclusions of glycogen are revealed. Parathyrocytes produce the **parathyroid hormone (PTH).** Parathyroid hormone acts as antagonist of calcitonin, providing the level of calcium in the blood to increase by causing the demineralization of bones (stimulates the activity of osteoclasts). PTH and calcitonin have reciprocal effects in the regulation of blood calcium levels. The activation of parathyrocytes occurs according to the principle of negative feedback due to the presence of calcium-sensing receptors on their surface.

If the parathyroid glands are totally removed, death will ensue because muscles, including the laryngeal and other respiratory muscles, go into tetanic contraction as the blood calcium level falls.

Adrenal (suprarenal) glands – are twin endocrine glands, which are embedded in perirenal fat at the superior poles of the kidney. The adrenal glands are covered with connective tissue capsule, in which two layers are distinguished: external (dense) and internal (loose). Parenchyma is organized into two distinct regions: the cortex and the medulla. Cortical endocrinocytes form cords, which are oriented

perpendicularly to the surface of the gland. The spaces between cords are filled with loose connective tissue.
Adrenal cortex is divided into three zones on the basis of morphological and functional features:

- zona glomerulosa
- zona fasciculata
- zona reticularis

The cells of the **zona glomerulosa** are arranged in closely packed ovoid clusters – "glomerules". These cells contain a small amount of the lipid inclusions. The mitochondria are characterized by the **shelf-like cristae**. The endocrine cells of zona glomerulosa produce the hormone **aldosterone.** Aldosterone regulates the sodium and potassium homeostasis and water balance. It also hastens the inflammatory reactions and promotes collagen synthesis.

Between zona glomerulosa and zona fasciculate a thin layer of low-specialized cells is located. This layer is called **sudanophobe zone**. The division of the cells of sudanophobe zone provides the replacement and regeneration of the cells of zona glomerularis and zona fasciculata.

Zona fasciculata. The cells of zona fasciculata are large and arranged in long straight parallel cords – in "fascicles". Depending on their functional state these cells could have dark or light cytoplasm, be cuboidal or prismatic in shape. The microvilli are revealed on the cell surface reversed to the capillaries. The cytoplasm of endocrinocytes of the zona fasciculata is rich in lipid inclusions. The mitochondria are characterized by the **lamellar cristae**. The zona fasciculata secretes **glucocorticoids (cortisol, hydrocortisol, corticosterone),** which regulate the metabolism of carbohydrates, proteins, lipids, stimulate energy metabolism and depress the immune and inflammatory responses.

Zona reticularis. The cells of the zona reticularis are noticeably smaller than those of the zona fasciculata. These polygonal cells are arranged in anastomosing cords, which under the microscope remain reticulum. The cells of the zona reticularis decrease in size and become cuboidal, rounded or irregular in shape. The cells have relatively few lipid inclusions. The mitochondria are characterized by the **tubular cristae**. Endocrinocytes of the zona reticularis secrete **weak sex steroid hormones** – dehydroepiandrosterone (hormone, similar to testosterone), and small amounts of female sex hormones (estrogen and progesterone).
Between the three main zones of adrenal cortex the clusters of low-differentiated cells are revealed. These cells are the source of physiological regeneration of adrenal cortex. The first layer of such cells is located between the connective tissue capsule and the zona glomerulosa. The second germinative layer, called sudanophobe zone, is located between the zona glomerulosa and the zona fasciculata. Between the zona reticularis and adrenal medulla the **X-zone** is located. X-zone consists of the rests of embryonic adrenal cortex.

Adrenal medulla is separated from the adrenal cortex by the discontinuous layer of loose connective tissue. The adrenal medulla is formed by the large rounded or

polygonal cells. The cells of adrenal medulla are divided into two groups on the basis of their products of secretion:

- epinephrocytes
- norepinephrocytes

Epinephrocytes have light cytoplasm that is rich in secretory granules containing **adrenalin**. The cytoplasm of norepinephrocytes contains the granules filled with **noradrenalin**. Under the microscope the cytoplasm of norepinephrocytes appears dark. The release of adrenalin and noradrenalin occurs as a response to the stress-factors of external environment that could be life-threatening. The sudden release of adrenalin and noradrenalin (**catecholamines**) establishes conditions for maximum use of energy and thus maximum physical effort.

Diffuse neuroendocrine system (DNES) consists of endocrine cells scattered almost all over the organs and systems of the body. There are distinguished two types of cells of DNES: the cells of neural origin, which are developed from neuroblasts of neural crest, and cell of non-neural origin.

Endocrinocytes of the first group are united in the APUD-system. They are able to store and decarboxylate the precursors of biologically active amines (serotonin, noradrenalin, adrenalin). In these cells the production of neuroamines is combined with the synthesis of biologically active regulative peptides. Nowadays about 50 types of apudocytes and their hormones are discovered.

APUD- system includes the enteroendocrine cells of the digestive tract, the neurosecretory cells of CNS, the melatonin-synthesizing cells of the pineal gland, the parafollicular cells of the thyroid gland and the cells of the adrenal medulla. Their function doesn't depend on the pituitary gland, but it is closely related with nerve impulses, which pass along the sympathetic and parasympathetic nerve fibers.

Diffuse endocrine cells of non-neural origin are not able to store and decarboxylate the precursors of biologically active amines. This group includes endocrine cells of testes and ovaries. They produce steroid hormones and their activity is under control of the pituitary gland.

OVERVIEW OF THE DIGESTIVE SYSTEM

The main function of the digestive system is to provide the nutrition of all organs, tissues and cells of the body. In the alimentary canal the food is grinded, macerated, chemically treated and absorbed into the blood and lymph. The digestive system consists of the alimentary canal and digestive glands. The digestive glands are classified into the big digestive glands located outside the alimentary canal (big salivary glands, liver, pancreas) and the numerous small digestive glands located inside the alimentary canal. In the wall of alimentary canal (predominantly in mucosa) a lot of lymphatic tissue is found. The lymphatic tissue of the digestive tract is represented by diffuse lymphatic tissue, lymphatic nodules and aggregates of nodules.

Morphologically the parts of digestive system are:

- oral cavity
- pharynx
- esophagus
- stomach
- intestine (small and large)

The general structure. All portions of alimentary canal are lined with mucosa (tunica mucosa). Normally it is always wet and covered with mucous.

Mucosa consists of three (in some cases two) main components:

- lining epithelium
- lamina propria
- muscularis mucosae (is absent in some portions)

Under the mucosa **submucosa** is located. Submucosa is formed by dense irregular connective tissue. It is absent in gingiva and hard palate.

The underlying layer is called **tunica muscularis (muscularis externa).** In the wall of oral cavity, pharynx and the upper third of esophagus it is formed by the striated muscle; in the middle third of esophagus – by both smooth and striated muscle; in the lower third of esophagus, stomach and intestine – by the smooth muscle.

Up to the stomach the tunica muscularis is covered by **the adventitia** consisting of loose connective tissue. The intraperitoneal organs of alimentary canal (stomach, the part of intestine) are covered with the tunica **serosa** (a serous membrane consisting of mesothelium and small amount of underlying connective tissue).

Pay attention that there are differences in the structure and relief of mucosa in the different portions of alimentary canal. The mucosa could form invaginations (gastric pits, intestinal crypts), plicae and villi (in the small intestine).

THE ORAL CAVITY AND ASSOCIATED STRUCTURES

The oral cavity is the first portion of the alimentary canal. The functions of the oral cavity are the mechanically breaking down and tasting of the food, the initial digestion of the food by hydrolytic enzymes. It also takes part in the process of speech articulation (phonation).

The oral cavity is divided into the vestibule and the oral cavity proper. The oral cavity vestibule is the space between lips, cheeks and teeth. The oral cavity proper is bounded by the teeth and gums anteriorly, the tongue and the floor of the mouth inferiorly, the hard and soft palate superiorly and the entrance to the oropharynx posteriorly. The vestibule of the oral cavity is lined with stratified squamos non-keratinized epithelium.

The mucosa lining the oral cavity has the following features:

- lined with stratified squamos epithelium

- the absence or poor development of muscularis mucosae
- the absence of submucosa in some areas
- high vascularization

The lips. The lips with the cheeks form the anterior wall of the oral cavity. The core of the lips is formed by the striated muscle (m.orbicularis oris). There are distinguished three parts of the lips:

- the cutaneous part (pars cutanea);
- the transitional part (pars intermedia);
- the mucous part (pars mucosa).

The cutaneous part of the lip is covered with the skin, which have a typical structure (stratified squamos keratinized epithelium; the presence of sweat and sebaceous glands and hair follicles).

The transitional part (red border or vermillion) is characterized by a thicker but mildly keratinized epithelium and numerous, densely arranged, long papillae of the lamina propria, reaching deep into the epithelium and carrying large capillary loops close to the surface. Thus blood is visible through the thin parts of the translucent epithelium and gives the red color to the lips. The sebaceous glands are found in the connective tissue, the sweat glands and hair follicles are absent in this part.

The mucous part of the lip is lined with mucosa. The epithelium of the mucosa is stratified squamos non-keratinized. The lamina propria is formed by dense connective tissue, has short irregular papillae and contains blood vessels and excretory ducts of the lip salivary glands. The submucosa is formed by loose connective tissue, which consists of strands of densely grouped collagen fibers and contains fat and small mixed salivary glands between these strands. According to their structure the minor salivary glands of the lip are the compound tubulo-alveolar ones. The muscularis mucosae is absent that's why the submucosa connects the lamina propria directly to the thin fascia of the muscles.

The cheek (bucca) – is the muscular structure covered with the skin externally and with the mucosa internally. There are distinguished three zones in the mucosa of the cheek:

- maxillary
- intermediate
- mandibular

The muscularis mucosae is absent in the buccal mucosa.

Maxillary and mandibular zones have the same structure as the mucous part of the lip. These zoned are lined with stratified squamos keratinized epithelium. The well-defined submucosa contains numerous buccal salivary glands.

The intermediate zone of the cheek extends from the angle of mouth to the ramus of mandible. It is lined with stratified squamos non-keratinized epithelium. The lamina propria forms large papillae. The salivary glands are not found, but sometimes occasional reduced sebaceous glands occur.

The gum (gingival) is covered with the mucosa, which is firmly attached to the periosteum of alveolar processes. The mucosa is lined with stratified squamos epithelium, which may be keratinized or non-keratinized, but most often is parakeratinized. The lamina propria forms the long papillae. The muscularis mucosae is absent. The gingival mucosa is rich in nerve endings.

The hard palate. The mucosa of the hard palate is tightly fixed to the underlying periosteum and therefore immovable. Like the gingival it is pink. The epithelium is uniform in form with a rather well-keratinized surface. The lamina propria, a layer of dense connective tissue, is thicker in the anterior than in the posterior parts of the palate and has numerous long papillae.

Palatine rugae (transverse palatine ridges)

The palatine rugae,irregular and often asymmetric in humans, are ridges of mucosa extending laterally from the incisive papilla and the anterior part of the raphe. Their core is made of a dense connective tissue layer with fine interwoven fibers. The posterolateral zone of the hard palate called glandular zone contains compound tubulo-alveolar salivary glands.

The soft palate and uvula consist of the musculo-tendinous core covered with mucosa. There are distinguished two surfaces: anterior (oropharyngeal) and posterior (nasopharyngeal).

The mucosa of the oropharyngeal surface is lined with stratified squamos non-keratinized epithelium. The lamina propria contains a lot of thick elastic fibers. The muscularis mucosae is absent. The submucosa is well-defined and contains salivary glands. In the uvula the aggregations of the salivary glands are revealed even in the tunica muscularis.

The mucosa of the nasopharyngeal surface is covered with pseudostratified ciliated epithelium containing the goblet cells. The lamina propria doesn't contain papillae and is separated from the epithelium by well-defined basal lamina. Under the lamina propria the layer of elastic fibers lies. The muscularis mucosae and the submucosa are absent.

The tongue (lingua) is the essential organ for human speech, taste sensation and swallowing. The tongue is the muscular organ formed by the striated muscle.

The striated muscle of the tongue is arranged in bundles that generally run in three planes, with each arranged at right angles to the other two.

The muscle fibers are bounded to each other by endomysium. The bundles of muscle fibers are surrounded by perimysium, where the blood vessels and nerves pass.

The tongue is lined with mucosa. The dorsal, lateral and inferior surfaces of the tongue are characterized by the different relief of mucosa.

The simplest structure of mucosa is found on the inferior surface of the tongue. Here it is lined with stratified squamos non-keratinized epithelium. The lamina propria forms short papillae. Underlying submucosa is directly attached to the muscles. Due to the presence of the submucosa the mucosa could be easily moved.

The mucosa of the lateral and dorsal surfaces of the tongue is firmly attached to the muscle. This type of mucosa is called **specialized mucosa** due to the presence of

numerous **lingual papillae** associated with **taste buds** on its surface. Four types of lingual papillae are described: filiform, fungiform, circumvallate and foliate. All of the papillae are the derivates of tongue mucosa and have the similar structure.

Filiform papillae are the smallest and the most numerous. They are distributed all over the dorsal surface of the tongue. The filiform papillae are covered with highly keratinized stratified squamos epithelium, which lies on the basal lamina. The core of the papilla (the primary papilla) is formed by connective of the **lamina propria**. From the tips of primary papilla the secondary papillae protrude toward the epithelium. The filiform papillae do not contain taste buds; they serve only a mechanical role.

Fungiform papillae are scattered among the filiform papillae. As the name implies they are mushroom-shaped projections of the lamina propria of mucosa. These papillae are visible to the unaided eye as round reddish prominences. Their color is derived from a rich capillary network visible through the relatively thin epithelium. They are covered with stratified squamos non-keratinized epithelium and contain taste buds on their dorsal surface.

Circumvallate papillae are found in the mucosa just anterior to the V-shaped sulcus terminalis. The human tongue has only 8-12 of these large papillae. Each papilla is surrounded by a moatlike invagination lined with stratified squamous epithelium that contains numerous taste buds. Ducts of lingual salivary (von Ebner's) glands empty their serous secretion into the base of the moats. It may serve to wash out the soluble elements of food. The core of the circumvallate papillae (primary papillae) is formed by connective tissue. Their free surface shows numerous secondary papillae that are covered by a thin, smooth epithelium.

Foliate papillae are located at the lateral surfaces of the tongue. As the other papillae they are the projections of lamina propria of the tongue mucosa and are covered with the stratified squamos non-keratinized epithelium. The lamina propria of these papillae forms three deep secondary papillae. Each foliate papilla is separated from others by the deep mucosal cleft. Foliate papillae contain taste buds. In adults the foliate papillae may not be revealed.

THE TEETH AND SUPPORTING STRUCTURES

Anatomically every tooth consists of the crown, neck (cervix) and root. Crown is the part of the tooth located above the gum line is the tooth crown. The tooth neck is surrounded by the gum; the root is embedded into the alveolar process of maxilla or mandible. The tooth consists of several hard and soft tissues.

The hard tissues of the tooth are:

- enamel
- dentin
- cementum

The soft tissues are:

- pulp

- periodontium (surrounds the tooth)

Enamel covers the anatomical crown of the tooth. Enamel is the hardest substance of the body. It consists of 96-98% of inorganic components and 3-4% of organic (proteins, lipids, carbohydrates). The inorganic component is represented predominantly by hydroxyapatite crystals and small amonts of calcium fluoride and calcium carbonate.

The organic component consists of some unique proteins and lipids. Enamel rod is the structural and functional unit of the enamel. Each enamel rod spans the full thickness of the enamel from dentinoenamel junction to the outer enamel surface. Enamel rod is formed by the bundle of hydroxyapatite crystals. The thickness of enamel rod is about 3-5 mcm. On the cross-section the rods reveal a key-hole shape. The ballooned part, or "head:, is oriented superiorly, and the "tail" is directed inferiorly toward the root of the tooth. The interrod substace is not revealed in human enamel. The role of interrod substance is performed by the "tails" of enamel rods.

Because of the S-like shape of enamel rods on the longitudinal section of the tooth some prisms are sectioned longitudinally, when another are cross-sectioned. Their alteration causes different light refraction that appears as the alterating light and dark bands called Hunter-Schreger bands. Besides this, on the longitudinal section of the tooth the contour lines of Retzius are observed. The lines of Retzius represent evidence of rhythmic growth of the enamel in the developing tooth.

In tooth enamel the areas with high organic content are revealed. Such areas are called enamel lamellae and enamel tufts. Enamel lamellae are thin, leaf-like structures that extend from the enamel surface toward the dentinoenamel junction. Enamel tufts arise at the dentinoenamel junction and reach into the enamel to about one fifth to one third of its thickness. They were so termed because they resemble tufts of grass when viewed in ground sections. Enamel lamellae and enamel tufts are considered to be the initial points in caries development.

The enamel surface is covered with the cuticle (Nasmyth's membrane), which consists of the rests of ameloblasts. Erupted enamel is normally covered with a pellicle, which is apparently a precipitate of salivary proteins.

Dentin – is the calcified living material that forms the crown, the neck and the root of the tooth. Dentin consists of 70-72% of inorganic material (predominantly hydroxyapatite and small amounts of calcium fluoride, calcium hydrocarbonate, magnesium and sodium). The organic material constitutes about 28-30% of dentin mass and is represented mostly by the I type of collagen, mucopolysaccharides and lipids. Dentin consists of dentinal tubules grounded into the calcified amorphous substance. Within the dentinal tubules the processes of specialized cells - odontoblasts (Tom's fibers) are situated. The Tom's fibers provide the nutrition of the hard tissues of the tooth and supply it with mineral salts. Dentinal tubules extend from the pulp cavity and end perpendicular to dentinoenamel or dentinocementum junction. Dentinal tubules are grounded into

the amorphous substance, which consists of the collagen fibers and cementing material. On the basis of the collagen fibers arrangement there are distinguished two layers of dentin: mantle dentin and circumpulpal dentin. **Mantle** dentin is the outermost layer of dentin characterized by the **radial** direction of collagen fibers (von Korff's fibers). **Circumpulpal** dentin is charactezied by the **tangential** direction of collagen fibers (von Ebner's fibers).

The **predentin** is located always adjacent to the pulp tissue and is 2 to 6 mm wide, depending on the extent of activity of the odontoblast. It is not mineralized. The dentinal tubules and Tom's processes pass through the predentin before they enter the calcified dentin. The areas of hypomineralized dentin are revelaed at the peripheral layers of dentin too. Such areas are termed interglobular spaces or **interglobular dentin**. The areas of interglobular are the largest near the dentinocementum junction, where they are termed **Toms' granular layer**.

In case of dentine damage odontoblasts start to produce reparative (tertiary dentin). It is characterized as having fewer and more twisted tubules than normal dentin.

Cementum is the hard tissue that covers the root of the tooth from the neck to the apex. The thickest layer of cementum is revealed near the root apex. Structurally cementum reminds the bone tissue. It consists of 68% of inorganic (calcium salts) and 30% of organic component. The calcified ground substance of cementum contains collagen fibers. There are distinguished two types of cementum: **cellular and acellular.** Acellular (primary) cementum covers the whole surface of the root. Cellular (secondary) cementum covers only the root apex and the bifurcations of multirooted teeth.

The cells of cementum, like the cells of bone tissue), lie in small cavities (lacunae) and connect to the source of nutrition by their processes. But, unlike the bone tissue, cementum doesn't contain blood vessels. The nutrition of cementum is provided by diffusion through the periodontal vessels. Acellular cementum doesn't contain cells and cell processes. It consists only of collagen embedded in ground substance.

Dental pulp –is the soft tissue of the tooth. It provides nutrition, regeneration, innervation and defense of the tooth. The pulp is formed by loose connective tissue, which is rich in cells, blood vessels and nerves.

The pulp contains three layers:

- peripheral (layer of odontoblasts)
- intermediate (subodontoblastic)
- central

The peripheral layer of dental pulp consists immature collagen fibers (pre-collagen) and specialized cells – odontoblasts.

Odontoblats – are the pear-shaped cells, located in the peripheral (odontogenic) layer of the pulp. The narrow apical domain of odontoblast gives a rise to the long branched process, which pass into the entire thickness of dentine through the dentinal tubule. Some of these processes even reach the enamel. Nucleus is located at the basal domain of odontoblast. Odontoblasts are characterized by basophilic cytoplasm, well-developed rough EPR, mitochondria and Golgi complex. Odontoblasts produce collagen, by which the collagen fibers of

dentine are formed and alkaline phosphatase, which regulates the process of dentin calcification. In erupted tooth dentinoblasts supply dentine and enamel with nutrients and mineral salts and provide the regeneration of dentin.

The intermediate layer (zone of Weill) is poor in cells and contains not numerous immature odontoblasts. It contains pre-collagen and argyrophylic fibers and low-differentiated connective tissue cells.

The central layer contains blood vessels, nerves, collagen and reticular fibers and connective tissue cells: fibroblasts, macrophages, adventitial cells etc.

Periodontium is the fibrous connective tissue joining the tooth to its surrounding bone. Collagen fibers that project out of the matrix of the cementum and embed in the bony matrix of the socket wall form the bulk of the periodontal ligament. These fibers are called **Sharpey's fibers.** Between the fibers the typical connective tissue cells are located. Periodontal ligaments form complicated architechtonics of periodontium that provides the physiological movement of the tooth. Periodontium is highly vascularized and innervated.

TOOTH DEVELOPMENT

The process of tooth development is the continuous and complicated one. It begins in the embryonic period and stops at the age of 18-21 years. Teeth are the derivates of oral epithelium. All the tissues of tooth have mesenchymal origin, except enamel, which is developed from the ectodermal epithelium.

The process of tooth development consists of three stages:

1. The formation of tooth germs
2. The differentiation of tooth germs
3. The histogenesis of the tooth tissues

The formation of the tooth germs occurs in the 6^{th} week of intrauterine life with the formatiom of primary epithelial band. At about 7th week the primary epithelial band divides into an inner (lingual) process called **dental lamina** and an outer (buccal) process called vestibular lamina. The dental laminae serve as the primordium for the ectodermal portion of the deciduous teeth. The epithelium of dental lamina invades the underlying ectomesenchyme thereby forming the **tooth buds**. This is the initial stage of tooth formation, where enamel organ starts development. The surrounding mesenchymal cells proliferate that results in their condensation in two areas. The area of condensation below the enamel organ is called **dental papilla.** The ectomesenchymal condensation that surrounds the enamel organ is **dental sac**. The dental papilla and dental sac are not well-defined during bud stage; they become more defined during the subsequent **cup and bell stages.** There are distinguished three layers in the enamel organ:

1. inner enamel epithelium attached to the dental papilla – simple columnar epithelium formed by ameloblasts. Ameloblasts are the enamel-secreting cells;
2. outer enamel epithelium separates enamel organ from dental sac. The cells of this layer don't leave any derivates.

3. pulp of enamel organ or stellate reticulum is located between the outer and inner enamel epithelium. It is formed by the star-shaped cells that obtain their shape due to the water being drawn into the enamel organ from dental papilla. The pulp of enamel organ takes part in formation of the pellicula of enamel.

The cells of dental papilla give a rise to dental pulp and dentine. The cells of the internal layer of dental sac differentiate into cementoblasts, the cells of external layer – into periodontium.

The histogenesis of the tooth tissue begins in the 4^{th} month of intrauterine development with the formation of dentin. The dentin matrix is secreted by the cells of dental papilla - odontoblasts. Odontoblasts produce organic matrix and collagen, from which the dentine fibers are built, thereby forming predentin. After this the calcification of predentine occurs and it transforms into dentin.

The cells of inner enamel epithelium transform into ameloblasts. Ameloblasts produce glycoproteins. After being secreted, these glycoproteins are arranged in thin filaments. The calcified bundles of filaments form enamel rods. Cementum and periodontium are formed by the cells of dental sac. Cementum formation occurs in postembryonic period just before the tooth eruption.

SALIVARY GLANDS

The excretory ducts of three pairs of major salivary glands empty into the oral cavity.

The major salivary glands are parotid, submandibular and sublingual glands. The major salivary glands are situated outside the oral mucosa. The minor salivary glands are located in the submucosa of different parts of the oral cavity. They include labial, buccal, lingual and palatine glands. According to their structure salivary glands are compound alveolar or tubulo-alveolar. Each salivary gland consists of the secretory acinus and salivary ducts.

All salivary glands are characterized by the merocrine type of secretion (without destruction of secretory cells). On the basis of the nature of secretory products salivary glands are divided into serous, mucous and mixed (seromucous). The secretory cells of serous salivary glands (serous cells) produce proteins (predominantly enzymes). The mucous cells secrete mucin and proteglycans. Mixed salivary glands contain both serous and mucous cells. The secretory products of all salivary glands together compose saliva. Saliva contains inorganic (sodium, potassium, calcium) and organic (enzymes – amylase, maltase, hyaluronidase, pepsine-and tripsine-like enzymes, acid phosphatase, alkaline phosphatase, lysozyme; mucous: glycoproteins, proteoglycans, mucin) components. It also may contain leukocytes, desquamated epithelial cells and a number of products of excretion (like uric acid, kreatin and iodine). Saliva provides the significant role in the maintenance of water-salt homeostasis.

Saliva moistens the food, prepares it for swallowing, and helps in speech articulation. Due to the presence of enzymes saliva provides the initial digestion of

the food. Saliva has an antibacterial effect due to the presence of leukocytes and lysozyme.
Besides the exocrine function salivary glands provide the endocrine function too. Hormones secreted by salivary glands include parotin, insulin-like factor, nerve growth factor, epithelial growth factor, lethal factor etc.

Parotid gland – is compound branched tubulo-alveolar gland, which produces serous secretion and biologically active substances. The gland is surrounded by the dense connective tissue capsule, from which septa divide the secretory portion of the gland into lobes and lobules. The septa contain blood vessels and interlobular excretory ducts.

Secretory acini of parotid gland produce only serous secretion. They consist of conical serous cells (serocytes) and myoepithelial cells. Serous cells have small apical portion facing the lumen of acinus, where acidophilic secretory vesicles are revealed. The wide basal portion contains nucleus. In the spaces between serous cells the intercellular secretory canaliculi are located. At first the secretion of serous cells enters the intercellular canaliculi and after that passes into the lumen of acinus. The lumen of intercellular canaliculi is about 1 mcm in diameter.
Myoepithelial cells form the second layer of cells of secretory acinus. They are also called stellate cells, because of their star-like shape. They embrace the acinar secretory cells like a basket. Myoepithelial cells are always located between basal lamina and the basal plasma membrane of epithelial cell. The contraction of myoepithelial cells causes the moving of secretory products towards the excretory ducts.

Salivary ducts

Intercalated ducts begin from the acinus; are lined with simple cuboidal or squamos epithelium. The second layer of cells is formed by myoepithelial cells.

Striated ducts are the prolongation of intercalated ducts. Striated ducts are located within the lobule of acinus. The diameter of striated ducts is significantly larger than that of the intercalated ducts. They are lined with simple low columnar epithelium. The epithelial cells are characterized by acidophilic cytoplasm. The apical portion of epithelial cells contains microvilli, secretory vesicles and Golgi complex. The infoldings of the basal plasma membrane are seen in histologic sections as “striations.” Longitudinally oriented, elongated mitochondria are enclosed in the infoldings. Basal infoldings associated with elongated mitochondria are a morphologic specialization associated with reabsorption of fluid and electrolytes. The second layer of cells is formed by myoepithelial cells.

Interlobular ducts are lined with two-layer epithelium which gradually transforms into the stratified one. Interlobular ducts are surrounded by small amounts of connective tissue.
Excretory ducts of the parotid gland are lined with stratified cuboidal epithelium. As the ducts approach the oral epithelium, stratified squamous epithelium may be

present. The excretory duct of parotid gland enters the oral cavity opposite the second upper molar tooth.

Submandibular gland is compound branched alveolar, in some areas tubulo-alveolar salivary gland. According to the nature of secretory products it is mixed gland (seromucous). The gland is surrounded by the connective tissue capsule.

Secretory acini. There are two types of secretory acini of submandibular gland : serous and mixed (seromucous). In submandibular gland serous acini prevail under the mixed.

The structure of serous acini is similar to that of parotid gland. Mixed acini are larger than the serous ones and consist of two types of cells – serous and mucous. Mucous cells are larger than the serous ones and occupy the central portion of the acinus. Flattened dense nucleus is located at the basal portion of mucous cells. Mucous cells synthesize and store mucous within the cytoplasm as mucinogen granules. Mucinogen granules are not stained with routine H&E- staining, that's why the cytoplasm of mucous cells appears empty. Mucous acini have a cap of serous cells that are thought to secrete into the highly convoluted intercellular space between the mucous cells. Because of their appearance in histologic sections, such caps are called serous demilunes (Giannuzzi). The demilunes are surrounded by myoepithelial cells.

Intercalated ducts of submandibular gland are less branched and shorter than those of parotid gland.

Striated ducts are well-developed long and branched. They are lined with columnar epithelium with defined basal striation.

Interlobular ducts are lined with two-layer epithelium which gradually changes into the stratified one.

Excretory duct. A duct from each of the two submandibular glands runs forward and medially to a papilla located on the floor of the mouth just lateral to the frenulum of the tongue.

As the duct approaches the oral epithelium, stratified squamous epithelium may line its lumen.

Sublingual gland is the compound branched tubulo-alveolar gland. According to the nature of secretory products it is mixed (seromucous). It contains three types of secretory acini: serous, mucous and mixed (seromucous).

Serous acini are not numerous. Their structure is the same as that of parotid and submandibular glands.

Mixed acini are the most numerous. They consist of mucous cells and seromucous demilunes. The cells of demilunes are significantly different from that of submandibular gland. Their secretory vesicles contain mucin. These cells produce serous and mucous secretion at the same time, that's why they are called "seromucous". Seromucous cells contain well-developed rough EPR. In the spaces between seromucous cells the intercellular secretory canaliculi are located.

Mucous acini are formed by typical mucous cells.

Myoepithelial cells surround all types of secretory acini.

Intercalated ducts are almost not defined in sublingual gland.
Striated ducts are poorly developed and very short. They are lined with columnar or cuboidal epithelium with basal striation.
Iterlobullar and excretory ducts have the same structure as that in submandibular gland. Excretory duct of submandibular gland empties into the submandibular duct as well as directly onto the floor of the mouth. As the duct approaches the oral epithelium, stratified squamous epithelium may line its lumen.

ESOPHAGUS

Esophagus is the portion of alimentary canal that delivers food and liquid from the pharynx to the stomach. The length of esophagus is about 30 cm. The wall of esophagus is formed by four layers: mucosa, submucosa, tunica muscularis externa and adventitia.

The mucosa consists of three layers: epithelium, lamina propria and muscularis mucosae. The epithelium of esophagus is stratified squamos non-keratinized. The lamina propria is formed by loose connective tissue. At the level of cricoid cartilage and in the terminal portion of esophagus the **lamina propria** contains secretory acini of **esophageal cardiac glands**. These simple branched glands produce mucous. Their acini are formed by cuboidal and columnar mucous cells. Besides mucous cells the acini of esophageal cardiac glands contain endocrine cells and solitary parietal cells, which produce H+ ions. The ducts of these glands are lined with columnar epithelium.

There are distinguished three types of endocrine cells on the basis of their cytochemical properties. The first type cells are enterochromaffine cells producing serotonin. The second type cells remind the enterochromaffine-like cells of stomach. The nature of third type cells is uncertain.

Muscularis mucosae is composed of longitudinally organized smooth muscle, between which the elastic fibers are revealed. Muscularis mucosae plays a significant role in the food passage and protects the mucosa from damage by the foreign objects in case of swallowing them.

The submucosa is formed by dense irregular connective tissue that contains the acini of esophageal glands proper. Esophageal glands proper are compound branched tubulo-alveolar glands, which produce mucous. The small ducts of these glands are covered with simple low columnar epithelium, the large ducts – by stratified squamos epithelium, in which ciliated cells sometimes occur. The esophageal glands proper are the most concentrated in the upper half of esophagus. Mucous secreted by cardiac glands of esophagus and esophageal glands proper lubricates the lumen and facilitates the passage of the food. On cross section of esophagus, the lumen in its is normally collapsed state has a branched appearance because of longitudinal folds. When a bolus of food passes through the esophagus, the lumen expands without mucosal injury.

Muscularis externa consists of two muscle layers: inner circular layer and outer longitudinal layer. Between these layers the loose connective tissue is located. In the upper one third of esophagus it is formed by striated muscle. Striated muscle and smooth muscle bundles are mixed and interwoven in the muscularis externa of the middle third of the esophagus. The muscularis externa of the distal third consists only of smooth muscle. At the level of cricoid cartilage the thickening of internal circular layer forms the upper sphincter of esophagus; the thickening of circular layer at the terminal part of esophagus forms the lower sphincter. The contraction of muscularis externa provides the moving of food bolus towards the stomach. From one side adventitia is connected to the loose connective of muscularis externa, from another side – to the connective tissue of mediastinum. The abdominal portion of esophagus is covered with serosa, which is formed by mesothelium and underlying connective tissue.

STOMACH

Stomach provides the several important functions in human body. The main function of stomach is providing conditions for breaking down of food bolus by its gastric secretions. The enzymes of gastric juice – pepsin and chemosin break down the proteins and lipids. These enzymes are active only in acidic environment. Besides the activation of gastric enzymes, the acidic environment causes the death of pathogenic microorganisms, which can enter the gastrointestinal tract with food.
The absorption of water, salts, monosaccharides and alcohols occurs through the wall of stomach. Through the wall of stomach to the lumen of gastrointestinal tract the excretion of ammonium, urea and alcohol occurs. The endocrine function of stomach is represented by the production of biologically active substances – gastrin, serotonin, motilin, enteroglycon, which regulate the secretion of gastric glands, motility of stomach and intestine. The mucosa of stomach produces the internal antianemic factor, which is necessary for absorption of vitamin B12. The mechanical function of stomach is performed by mixing of the food with gastric juice.
The wall of stomach consists of four layers: mucosa, submucosa, muscularis externa and serosa.
Mucosa of stomach forms rugae, mammilated areas and gastric pits (foveolae).
Gastric **rugae** are the folds formed by mucosa and submucosa.
Mammilated areas are the bulging irregular areas of the stomach surface, which are bounded by grooves of the mucosa. The origin of mammilated areas is explained by that the gastric glands form aggregations, which are separated from each other by connective tissue. The superficial veins of connective tissue are visible through the mucous as reddish lines. These reddish lines are the boundaries of mammilated areas.
Gastric pits – are the invaginations of epithelium into the lamina propria. They are revealed all over the surface of stomach.
The mucosa of stomach consists of three layers: epithelium, lamina propria and muscularis mucosae. Epithelium lining mucosa is simple columnar glandular

epithelium. On the apical surface of epithelial cells microvilli are revealed. The apical domain of epithelial cells contains granules filled with mucous secretion. The secreted mucous covers the surface of mucosa and protects it from self-digestion by gastric juice. The basal domain contains nucleus and Golgi apparatus.
The epithelium near the gastric pits contains low-differentiated epithelial cells, which undergo division and substitute old and dead epithelial cells of mucosa.
The lamina propria is formed by loose connective tissue, containing gastric glands. **Lamina propria** also contains the aggregations of lymphocytes arranged in lymphatic nodules or diffuse lymphatic tissue.
The gastric glands (fundic glands) are simple, branched, tubular glands. Each fundic gland is composed of five types of cells:

- chief cells;
- parietal cells;
- mucous neck cells;
- undifferentiated adult stem cells (accessory mucous cells);
- enteroendocrine cells.

The muscularis mucosae is composed of two relatively thin layers, usually arranged as an inner circular and outer longitudinal layer. In some regions, a third layer may be present; its orientation tends to be in a circular pattern.

The glands of stomach have different structure in the different parts of stomach. There are distinguished three types of glands in stomach: fundal (gastric), pyloric and cardiac glands. The gastric (fundal) glands are the most numerous and present throughout the entire gastric mucosa except for the relatively small regions occupied by cardiac and pyloric glands.
The gastric (fundal) glands contain five main types of cells:
Chief cells are located predominantly in the deeper part of the fundic glands. The apical portion of cytoplasm owns secretory vesicles, containing digestive enzyme precursors. The apical surface of chief cells is covered with microvilli. The basal portion contains nucleus, rough endoplasmic reticulum and Golgi complex. In H&E sections the cytoplasm of chief cells appears basophilic. The secretions of chief cell are **pepsinogen and chemosin**. Pepsinogen is an inactive proenzyme. On contact with the acid gastric juice, pepsinogen is converted to pepsin, a proteolytic enzyme. Chemosin breaks down the proteins of milk; it is produced predominantly in children.
Parietal cells produce **H+ and Cl- ions**, from which hydrochloric acid is formed. Hydrochloric acid provides the acidic environment in stomach. Parietal cells are found in the neck of the fundic glands, among the mucous neck cells, and in the deeper part of the gland. They are large, irregular- shaped cells, sometimes binucleate. When examined with the electron microscope, parietal cells are seen to have an extensive intracellular canalicular system that communicates with the lumen of the gland. Numerous mitochondria supply the high levels of energy necessary for acid secretion. Parietal cells take part in the production of inner antianemic factor.

Mucous neck cells are localized at the neck region of the gland and line its excretory ducts. They are cuboidal or columnar in shape. The basal portion of cytoplasm contains nucleus, the apical – mucinogen granules.
Undifferentiated adult stem cells (accessory mucous cells) are the source of regeneration of all cells of gastric glands.
Enteroendocrine cells are found between the chief cells at every level of the fundic gland. They are the constituting part of diffuse neuroendocrine system (DNES) or APUD-system.
On the basis of type of produced biologically active substances there distinguished several types of enteroendocrine cells of stomach: EC-, ECL-, G-, P-, D-, A- and X-cells. These cells regulate synthesis and secretion of gastric juice, motility and blood supply of stomach and other organs of digestive system.
EC (enterochromaffine)-cells – produce **serotonin and melatonin**, which stimulate the secretion of digestive enzymes, mucous secretion and motility of stomach. Melatonin regulates the fotoperiodicity of digestive system functioning.
ECL (enterochromaffine-like)-cells – produce **histamine**, which regulates the activity of parietal cells.
G-cells – produce **gastrin**, which stimulates the secretion of pepsinogen by chief cells and the secretion of hydrochloric acid by parietal cells.
P-cells – produce **bombesin**, which stimulates the secretion of hydrochloric acid and pancreatic juice, and stimulates contraction of the smooth muscle of gallbladder.
D-cells – produce **somatostatin**, which acts directly on the acid-producing parietal cells to reduce acid secretion. Somatostatin can also indirectly decrease stomach acid production by preventing the release of gastrin, secretin and histamine.
D1-cells – produce **vasoactive interstitial peptide** (VIP), which induces the relaxation of smooth muscle of arteries, decreases blood pressure and stimulates the secretion of pancreatic enzymes.
A-cells – produce **glucagon**, which causes the liver cells to convert glycogen into glucose.
Submucosa is formed by dense irregular connective tissue containing numerous elastic fibers.
Muscularis externa consists of three layers of smooth muscle: an outer longitudinal layer, a middle circular layer, and an inner oblique layer. Between the muscle layers myenteric (Auerbach's) nerve plexus is located.
Serosa is formed by connective tissue lined with mesothelium.
Cardiac and pyloric glands are simple, branched, tubular glands.
Pyloric glands are located in the pyloric antrum (the part of the stomach between the fundus and the pylorus). They differ from the fundic glands in that they are much more branched, their lumen is relatively wide, they almost don't contain parietal cells.
Cardiac glands are limited to a narrow region of the stomach (the cardia) that surrounds the esophageal orifice. They are composed mainly of mucus-secreting cells, with occasional interspersed enteroendocrine cells. The short excretory ducts of cardiac glands are lined with columnar epithelium, containing cells with

elongated nuclei. The duct segment is the site at which the surface mucous cells and the gland cells are produced.

INTESTINE

The intestine is divided into the large intestine and small intestine on the basis of their structural and functional properties.

The small intestine is the longest component of digestive system, extending from stomach to cecum. It measures over 6 m and is divided into three anatomic portions:

- duodenum;
- jejunum
- ileum.

The small intestine is the principal site for the breakdown of proteins, lipids and carbohydrates.

The several enzymes take part in the digestion of proteins: enterokinase, kinasogen and tripsin break down the simple proteins; erepsin breaks down peptides to amino acids; nuclease breaks down complex nucleopoteins. Amylase, maltase, invertase, lactase and phosphatase break down carbohydrates. Lipase breaks down lipids. The small intestine is the site of absorption of digested products into the blood and lymphatic vessels. The small intestine performs mechanical function – by peristaltic contractions it pushes the chymus towards the large intestine. Besides this, the small intestine performs endocrine function. The enteroendocrine cells of the intestine secrete the several biologically active substances: serotonin, histamine, motilin, secretin, enteroglucone, cholecystokinin, pancreozymin, gastrin.

The wall of the small intestine consists of four layers:

- mucosa;
- submucosa;
- muscularis externa
- serosa.

Mucosa consists of epithelium (simple columnar epithelium with brushed border), lamina propria (loose connective tissue) and muscularis mucosae. The characteristic feature of the small intestine relief is the presence of **plicae circularis**, **villi** and **crypts**.

Plicae circularis (circular folds) are permanent transverse folds, formed by mucosa and underlying submucosa.

Villi – are fingerlike projections of mucosa, that extend from the mucosal surface for 0,5-1,5 mm into the lumen of intestine. The core of villi is formed by loose connective tissue of the lamina propria containing occasional smooth muscle cells. The surface of villi is covered with simple columnar epithelium, which includes three types of cells:

- columnar epithelial cells (enterocytes);
- goblet cells;
- enteroendocrine cells.

Enterocytes are the most numerous cells of the epithelium of villi. They are the tall columnar cells, measuring about 25 mcm. Each enterocyte possesses several thousands closely packed microvilli, located on its apical surface. Microvilli increase the apical surface area as much as 600 times. Microvilli are recognized in the light microscope as forming a **striated border** on the luminal surface. They are about 1 mcm high and 0,1 mcm in diameter.

The basal cytoplasm of enterocytes contains oval nucleus, developed rough endoplasmic reticulum and lysosomes.

The most apical cytoplasm contains a network of contractile microfilaments – terminal web, which take part in the formation of tight junctions and zonulae occludens between enterocytes, thereby providing the impermeability of intestinal epithelium.

Enterocytes of villi are the main absorptive cells specialized for the transport of substances from the lumen of the intestine to the circulatory system. The microvilli of enterocytes absorb the digestive enzymes on their surface and use them to break down the nutrients. This process is termed **parietal digestion**. The products of digestion of proteins and carbohydrates (amino acids and monosaccharides) are transported from the apical portion of enterocyte to basal portion, where they pass through the basal lamina into the blood vessels. Water, mineral salts and vitamins are absorbed in the same way. The absorption of lipids occurs by phagocytosis of emulsified fat drops or by absorption of glycerin and fatty acids with following resynthesis of neutral fat inside the cell cytoplasm. Lipids pass into lymphatic capillaries through the basal lamina of enterocytes.

Goblet cells – are unicellular glands, which produce mucous secretion. The characteristic shape, with the apical accumulation of granules and the narrow basal stem, is responsible for the name of the cell, as in a glass “goblet”. Goblet cells are interspersed among the other cells of the intestinal epithelium. The mucus produced by goblet cells serves for lubrication of intestinal mucosa and facilitates the passage of chymus.

Endocrine cells are scattered among the eneterocytes. The endocrine cells of small intestine include EC-, A-, S-, I-, G-, D-cells. They secrete biologically active substances, which regulate secretion, absorption and motility of small intestine.

Intestinal crypts – are the tubular invaginations of epithelium into the lamina propria. Crypts are found between two adjacent villi. The small intestine contains about 150 millions crypts. Crypts, like villi, increase the surface area of small intestine.

Besides enterocytes, goblet cells and endocrine cells, the epithelium of crypts contains **enterocytes without striated border** and **Paneth cells**.

Paneth cells are found in the bases of intestinal crypts. These cells are columnar in shape. They have a basophilic basal cytoplasm, a supranuclear Golgi apparatus, and large, intensely acidophilic, apical secretory vesicles. Paneth cells produce ezymes, which neutralize hydrochloric acid entered to the intestine with food particles and dipeptidase (erepsin), which breaks down dipeptides to amino acids.

Enterocytes without striated border are undifferentiated cells, which are the source of regeneration of intestinal epithelium. These cells remind enterocytes, but do not contain microvilli.

Lamina propria is formed by loose connective tissue; sometimes the elements of reticular tissue are found. Lamina propria contains aggregations of lymphocytes, which form solitary and aggregated lymphatic nodules.

Muscularis mucosae consists of two layers of the smooth muscle – inner circular and outer longitudinal.

Submucosa consists of dense connective tissue, containing numerous nerves plexus, blood and lymphatic vessels. The submucosa of duodenum contains the acini of duodenal (Brunner's glands). Duodenal glands are compound, branched, tubular glands producing seromucous secretion. Their acini consist of mucous cells, Paneth cells and endocrine cells (S-cells). The excretory ducts of Brunner's glands empty at the bases of intestinal crypts. The ducts are formed by mucous cells; as the duct approaches the intestinal mucosa, mucous cells are replaced by enterocytes. The secretion of Brunner's glands protects duodenal mucosa from the damaging effect of gastric juice.

Muscularis externa is formed by two layers of the smooth muscle: inner circular and outer longitudinal. The myenteric plexus (Auerbach's plexus) is located between these two muscle layers. The muscular contraction moves chymus towards the large intestine.

Serosa is formed by loose connective tissue covered with mesothelium. It covers all the portion of the small intestine except duodenum. Only anterior surface of duodenum is covered with serosa, the rest parts are surrounded by loose connective tissue (adventitia).

Large intestine – is the part of alimentary canal that provides the formation and movement of fecal masses. In the lumen of large intestine the metabolic products, heavy metal salts and other substances are excreted. The bacterial flora of large intestine produces vitamins A, D, and facilitates the digestion of cellulose. Anatomically the large intestine consists of the **cecum** with its projecting **vermiform appendix**, the **colon**, the **rectum**, and the **anal canal**. The colon is further subdivided on the basis of its anatomic location into **ascending colon, transverse colon, descending colon**, and **sigmoid colon**. The large intestine measures 1,5 m in length and 10 mm in diameter.

The wall of large intestine consists of four layers: mucosa, submucosa, muscularis externa and serosa or adventitia.

The mucosa of large intestine consists of epithelium (simple columnar), lamina propria and muscularis mucosae. The inner relief of the large intestine is characterized by the numerous intestinal crypts; neither plicae circulares nor villi are present. The mucosal epithelium of the large intestine contains the same cell types as the small intestine except Paneth cells, which are normally absent in humans. The goblet cells are the most common in the epithelium of large intestine.

Mucus, covering the epithelium, facilitates the passage of fecal masses.

The lamina propria contains numerous lymphatic follicles, which can form solitary lymphatic follicles or distort the regular spacing of the intestinal glands and extend into the submucosa. The aggregations of diffuse leukocytes and lymphatic follicles in the alimentary canal are considered to be the analog of the Bursa Fabricii of birds, which provides the maturation and immune activation of B-lymphocytes.
The most numerous lymphatic follicles are revealed in the wall of vermiform appendix. The wall of the appendix is covered with simple columnar epithelium, which is not rich in goblet cells. Paneth cells and enteroendocrine cells are revealed in the epithelium of the appendix. The great bulk of serotonin and melatonin is secreted by the enteroendocrine cells of the appendix.
Because of the poor development of the muscularis mucosae, the lamina propria merges with submucosa. The lamina propria contains and the submucosa numerous large lymphatic follicles, which merge together. The vermiform appendix performs the function of immune defense.
The muscularis mucosae consists of two layers: the inner circular layer and the outer longitudinal.
The submucosa is formed by dense irregular connective tissue, containing aggregations of adipocytes and numerous lymphatic follicles.
The muscularis externa contains two layers: inner circular and outer longitudinal. Between them the layer of loose connective tissue is located.
The muscular layer of colon is not continuous and forms teniae coli. **Teniae coli** represent three narrowed, thickened,equally spaced bands of the outer longitudinal layer of the muscularis externa.
The most portion of the large intestine is covered with serosa, except the caudal part covered with adventitia.
Rectum and anal canal. The rectum is divided into two parts: the upper pelvic part and the lower anal part. The upper part is distinguished from the rest of the large intestine by the presence of folds called **transverse rectal folds**.
The mucosa of the pelvic part is lined with simple cuboidal epithelium forming deep crypts.
The anal part is divided into three
zones according to the character of the epithelial lining:
- columnar zone is covered with stratified columnar epithelium;
- transitional zone is covered with stratified squamous non-keratinized epithelium -
- cutaneous zone, which is found in the lower third of the anal canal. This zone is lined with stratified squamous epithelium that is continuous with that of the perianal skin.

The lamina propria forms 10-12 longitudinal folds, contains blood vessels, solitary lymphatic follicles, rudimental anal glands. The lamina propria of transitional zone is rich in elastic fibers, sebaceous glands and lymphocytes.

The lamina propria of cutaneous zone contains acini of the apocrine sweat and sebaceous glands.

The muscularis mucosae is formed by the inner circular and the outer longitudinal layers of the smooth muscle.

The submucosa is formed by loose connective tissue containing vascular and nerve plexus.

The muscularis consists of two layers: the inner circular and the outer longitudinal. It forms two sphincters, which play an important role in act of defecation. The inner anal sphincter if formed by the inner layer of the muscularis externa; the outer anal sphincter is formed by the striated muscle. The upper part of rectum is covered with serosa; the anal part – with adventitia.

LIVER

The liver – is the largest gland of digestive system. It carries out the various functions:

- detoxication of waste products (formation of urea from the toxic nitrous products of protein metabolism);
- inactivation of hormones, biogenic amines and a number of drug substances;
- taking part in defense reactions;
- synthesis of glycogen, which is the source of maintenance of constant glucose level in blood;
- synthesis of blood plasma proteins: albumins, fibrinogen, prothrombin etc;
- production of bile, which is necessary for emulsification of lipids;
- playing a significant role in metabolism of cholesterol and iron;
- storage of fat-soluble vitamins (A,D,E etc.);
- hemopoietic function in embryonic period.

Structure. The liver is surrounded by a connective tissue capsule, which is firmly inosculated with visceral peritoneum. According to the classic conception the hepatic (classic) lobule is a structural and functional unit of liver. The classic hepatic lobule is a roughly hexagonal mass of tissue with flat basis and prominent apex. Each lobule measures about 2.0 - 0.7 mm. The number of hepatic lobules is approximately 500 thousands. The interlobular connective tissue forms the stroma of the liver. The blood vessels and bile ducts pass through the connective tissue stroma. In humans there is normally very little interlobular connective tissue, so the classic lobule is difficult to recognize.

Blood supply. According to the classic conception of hepatic lobules, the system of blood circulation in liver can be imaginably divided into three parts: the system of blood inflow to the lobules, the system of blood circulation within the lobules, and the system of blood outflow from the lobules. The liver has a dual blood supply consisting of a venous (portal) supply via the hepatic portal vein and an arterial supply via the hepatic artery. By these two vessels the system of blood inflow is represented.

The portal vein collects blood from all unpaired organs of abdominal cavity and carries it to the liver. The portal blood carried to the liver is largely depleted of oxygen and contains nutrients and toxic material adsorbed in the intestine, blood cells and breakdown products of cells from the spleen, endocrine secretions of pancreas. The hepatic artery carries oxygenated arterial blood to the liver. These two large blood vessels branch into the smaller ones: lobular (vv. seu aa. lobulares), segmental (vv. seu aa. segmentales), interlobular (vv. seu aa.

interlobulares), perilobular (vv. seu aa. perilobulares) veins and arteries. They are accompanied by bile ducts and together constitute the portal triad. The lymphatic vessels are located near the portal triad. The interlobular arteries and veins travel along the lateral faces of the lobule; the perilobular arteries and veins branch off from the interlobular and encircle the lobules at different levels. The interlobular and perilobular veins have poorly developed muscular layer, but in the areas of furcation the aggregations of muscular elements, which form sphincters are found. The corresponding interlobular and perilobular arteries are referred to muscular type of arteries. From the perilobular arteries and veins the blood capillaries arise. At the periphery of the lobule the arterial and venous capillaries fuse together and form the sinusoid capillaries, through which blood flows in direction from the periphery to the center of hepatic lobule. The sinusoid capillaries are approximately 30 mcm in diameter and characterized by discontinuous basal lamina. They travel in radial direction between the plates of liver cells – hepatic laminae, and drain into the central vein located in the center of hepatic lobule.

With the central vein the system of blood outflow from hepatic lobules begins. Blood leaves the lobule and flow into the collecting or sublobular veins. The sublobular veins, like the interlobular ones, are located between the lobules, but they are not accompanied by arteries and bile ducts. The sublobular veins fuse into three or four hepatic veins, which then drain into the vena cava inferior. The central and sublobular veins are referred to amascular type of veins.

The hepatic lobules consist of hepatic laminae and sinusoid blood capillaries. The hepatic laminae, as well as sinusoid capillaries, radiate from the periphery towards the center of hepatic lobule, where the central vein is located. The wall of capillaries is lined with endothelium. The small pores are revealed at the areas of cell junctions. Between the endothelial cells the numerous macrophages (Kupffer's cells), which do not form the solid layer, are found. These cells are the part of macrophagic system. The Kupffer's cells provide the destruction of microorganisms; at that they loose a connection with capillary wall and become the free macrophages.

The basal lamina is absent at the most part of the capillary wall, it is found only at its central and peripheral parts. Between the capillary and hepatic lamina the perisinusoidal space of Disse is found. The perisinusoidal space is the site of exchange of materials between blood and liver cells. Small, irregular microvilli extended from the basal surface of the hepatocytes (liver cells) and the processes of macrophages project into this space. The other cell type found in the perisinusoidal space is the hepatic stellate cell (commonly called an Ito cell).

The Ito cells are small cells (5-10 mcm), which are located between hepatocytes and contact with the space of Disse. Their cytoplasm contains numerous small lipid droplets, which usually surround the nucleus. The Ito cells are considered to be the primary storage site for hepatic vitamin A. In certain pathologic condition these cells differentiate into cells with characteristics of myofibroblasts and start to synthesize collagen fibers. The perisinusoidal space contains reticular fibers, which are the main supporting structures for soft tissue of the hepatic lobule.

According to the classic conception, the hepatic lobules are formed by hepatic laminae and intralobular sinusoid capillaries. The hepatic laminae consist of two rows of hepatocytes – epithelial cells of liver, which are arranged in radial direction. Between the hepatocytes the blood and bile capillaries run in the same direction, from periphery to center. The bile capillaries do not posses their proper wall. The wall of bile capillaries is formed by the plasmolemme, so-called biliary surface, of two adjacent hepatocytes. The lumen of bile capillary is separated from the intercellular space due to the presence of tight junctions (zonulae occludens) between the hepatocytes. That's why in normal conditions the bile does not enter the intercellular space and further into the blood. The biliary surface of hepatocytes contains microvili projecting into the lumen of bile capillaries.

The bile capillaries begin blindly at the central end of hepatic lamina and run along it, slightly curving and giving a rise to blind-ended branches, and, finally, at the periphery of hepatic lobule they pass into the cholangioles – short tubules with narrow lumen bonded by 2-3 cells. The cholangioles drain into interlobular bile ducts.

So, the bile capillaries are located within the hepatic lamina, while the blood capillaries run between the laminae. Thereby, each hepatocyte has two portions – the first one is biliary portion facing the lumen of bile capillary, into which the cell secretes bile; and the second one is vascular portion facing the interlobular blood capillary, into which it discharges glucose, urea, proteins and other substances. The blood flow in the classic lobule is directed from periphery to center; the bile flows in opposite direction – from center to periphery.

Recently another conceptions of the structural and functional unit of the liver was suggested. These new units are called portal lobule and liver acinus.

Portal lobule. The morphologic axis of the portal lobule is the interlobular bile duct of the portal triad of the classic lobule. Its outer margins are imaginary lines drawn between the three central veins that are closest to that portal triad. These lines define a triangular block of tissue that includes those portions of three classic lobules that secrete the bile that drains into its axial bile duct. This concept allows a description of hepatic parenchymal structure comparable to that of other exocrine glands.

The liver acinus. The liver acinus is the structural unit that provides the best correlation between blood perfusion, metabolic activity, and liver pathology. The liver acinus is lozenge shaped and represents the smallest functional unit of the hepatic parenchyma. The short axis of the acinus is defined by the terminal branches of the portal triad that lie along the border between two classic lobules.
The long axis of the acinus is a line drawn between the two central veins closest to the short axis. Therefore, in a two-dimensional view the liver acinus occupies parts of adjacent classic lobules. This concept allows a description of the exocrine secretory function of the liver comparable to that of the portal lobule.

The liver cells or h**epatocytes**. Hepatocytes are polyhedral cells, about 20-25mcm in diameter. These cells usually posses two or more round nuclei, which contain small amounts of heterochromatin; sometimes large polyploidic nuclei occur. The cytoplasm remains basophilic and acidophilic, contains all types of

general organelles and various inclusions. The rough ER synthesizes blood plasma proteins and enzymes for inactivation of harmful substances, drugs and hormones. The smooth ER is involved in glycogen synthesis, the Golgi apparatus – in bile secretion, the peroxysomes – in metabolism of fatty acids. Hepatocytes posses numerous mitochondria and are lack of lysosomes. The main inclusions of hepatocytes are glycogen, lipids, iron and vitamins.

Bile-excreting ducts include the following: interlobular bile ducts, right and left hepatic ducts, common hepatic duct, cystic duct, and common bile duct. The wall of interlobular ducts consist simple cuboidal epithelium, which gradually becomes columnar as the lumen of duct expands, and a thin layer of underlying connective tissue. The rest of excretory ducts have roughly common structure. They are the tubes, about 3,5 – 5mm in diameter, whose wall consists of three layers: mucosa, muscularis and adventitia.

The mucosa consists of simple columnar epithelium and lamina propria containing numerous elastic fibers and occasional mucous glands.

The muscularis is thin, consists of spirally arranged bundles of the smooth muscle, between which the layers of connective tissue are found. The muscular layer is highly developed only in the wall of cystic duct at the area of its transition into the gallbladder and in the wall of common bile duct at the area, where it drains into the duodenum. At these areas the bundles of the smooth muscle are arranged circularly and form the sphincters, which regulate the passage of bile into the duodenum.

The adventitia is formed by loose connective tissue.

The gallbladder is a thin-walled hollow organ. Its wall consists of three layers: mucosa, muscularis and adventitia. The gallbladder is covered with peritoneum.

The mucosa forms numerous folds. It is lined with simple columnar epithelium with the striated border. The lamina propria containing numerous elastic fibers underlies the epithelium. At the neck of gallbladder it contains mucus-secreting tubo-alveolar glands.

The muscularis consists of bundles of the smooth musce, arranged in a network, mainly with a circular orientation. At the area of the neck the muscle elements form sphincter.

The adventitia is formed by dense connective tissue, containing a network of numerous thick elastic fibers.

PANCREAS

Pancreas is a mixed gland, which performs both the endocrine and the exocrine function.

The exocrine pancreas produces the pancreatic juice, which is rich in digestive enzymes – tripsin, lipase, amylase etc. The pancreatic juice is delivered by excretory duct into the lumen of duodenum, where its enzymes break down proteins, lipids and carbohydrates. The endocrine pancreas synthesize a number of

hormones – insulin, glucagon, somatostatin, bombesin, pancreatic polypeptide, which take part in regulation of metabolism of carbohydrates, lipids, and proteins.

Structure. The pancreas is covered by a connective tissue capsule, which continues with the visceral peritoneum. The connective tissue septa extend from the capsule to parenchyma of pancreas and divide it into lobules. These connective tissue septa contain blood vessels, nerves, nerve endings, and excretory ducts. The lobules include the endocrine and exocrine portions of the gland.

The exocrine portion is represented by pancreatic acini, intercalated and interlobular ducts, and common pancreatic duct, which empties into the duodenum.

The pancreatic acinus is a structural and functional unit of the exocrine pancreas. Each acinus includes secretory portion and intercalated duct. With the intercalated ducts the system of excretory ducts begins. Then they in turn drain into the intralobular ducts, interlobular ducts, and eventually into the common pancreatic duct, which empties into the duodenum.

The pancreatic acinus is sac-like structure of about 100-150 mcm in size. The acini consist of 8-12 large secretory cells, the acinocytes, and a number of duct cells called centroacinar cells.

The acinocytes (exocrine pancreocytes) a conical-shaped cells with narrowed apex and wide base, which rest on the basal lamina of acinus. The basal plasmolemme forms internal folds, while the apical plasmolemme forms microvilli. The neighboring acinocytes are attached to each other by desmosomes or zonulae occludens. Their nuclei are located in the basal portions and contain 1-2 nucleoli. The basal cytoplasm contains well-developed rough ER, where the synthesis of pancreatic enzymes takes place; a big amount of ribosomes explains the basophilic staining of this portion of cytoplasm. Because of the absence of granules, the basal cytoplasm was named the homogenous zone. The apical cytoplasm contains numerous acidophilic granules, which contain inactive pancreatic enzymes and it is called zymogen zone. The perinuclear cytoplasm contains well-developed Golgi complex; the mitochondria are distributed through a whole cytoplasm.

The secretory activity of acinocytes is cyclic. The secretory cycle consist of the phase of absorption of primary substance, phase of synthesis, phase of cumulation, and the discharge of secretion. The full secretory cycle lasts in average 1,5-2 hours.

The discharged secretion enters the intercalated duct, whose wall consists of small cells. In some cases the duct cells laterally attach to the acinocytes, lying with them on the common basal lamina; in other cases they migrate to the center of acinus, locating on the apical surface of acinocytes. In last case, the duct cells are called centroacinar cells. The centroacinar cells are flattened elongate cells; their nucleus is surrounded by a thin layer of light cytoplasm.

The intercalated ducts continue with the interacinous ducts, whose wall is lined with simple cuboidal epithelium. The plasmolemme of epithelial cells forms internal folds and microvilli. Their cytoplasm contains numerous mitochondria and well-developed Golgi apparatus. The epithelial cells of ducts are suggested to produce the fluid component of pancreatic juice.

The interacinous ducts drain into larger intralobular ducts, whose wall is lined with simple cuboidal epithelium. The epithelial cells contain large nuclei, numerous mitochondria, low-developed Golgi apparatus, free ribosomes and rough ER. The intralobular ducts are surrounded by loose connective tissue containing blood capillaries and nerve fibers. The interlobular ducts continue with the interlobular ducts.

The interlobular ducts lie in the connective tissue septa between the lobules. They drain into the common pancreatic duct, which runs within the thickness of gland, from the tail to head, where it opens into the lumen of duodenum. All these ducts are lined with mucosa, which consists of columnar epithelium and the lamina propria. In the ostium of common duct the smooth muscle, which form the sphincter, are found. The epithelium of ducts contains goblet cells and endocrine cells producing hormones (pancreozymin, cholecystokinin). These hormones stimulate the activity of pancreatic acinocytes and the bile secretion by hepatocytes. The lamina propria contains small glands too.

Endocrine pancreas is represented by islets of Langerhans, which are found between the pancreatic acini. They are the most numerous in the caudal part of the gland. Each islet is covered with connective tissue covering, which may be discontinuous.

The islets consist of the endocrine cells – insulocytes, among which the fenestrated capillaries surrounded by a pericapillary space are located. The discharged hormones first enter the pericapillary space, and then they pass through the capillary wall into the bloodstream.

The insulocytes are smaller than the acinocytes. By the routine staining their cytoplasm is poorly stained; and they appear pale against the dark exocrine parenchyma. Their cytoplasm contains secretory granules, which differs by their morphological and chemical properties in different cells of islets. On the basis of granule contents, the five types of cells were defined among the insulocytes:

1. B-cells (basophilic);
2. A-cells (acidophilic);
3. D-cells (dendritic);
4. D1-cells (argirophilic);
5. PP-cells

B-cells are the most numerous (70-75%). The main part of these cells lies in the center of islet. Their granules are water-insoluble, but completely soluble in alcohol. They are stained by aldehydefuchsine, gentian violet in blue color. The size of granules is about 275nm. These granules contain insulin. The principal biological effect of insulin is decreasing of glucose level in blood. It facilitates assimilation of glucose by cells of the body.

A-cells constitute approximately 20-25% of the whole mass of insulocytes. They occupy predominantly peripheral parts of the islets. A-granules are resistant to alcohol, but are soluble in water. By an acidic fuchsine they are stained in bright-red color. The size of granules is about 230nm. The granules of A-cells contain

glucagon. Glucagon is an indirect antagonist of insuline. It stimulates the breakdown of glycogen to glucose, thereby increasing the glucose level in blood.

D-cells – constitute only 5% of insulocytes, are located peripherally. They are pear-shaped or star-shaped cells, which contain granules filled with somatostatin. It inhibits the secretion of insulin and glucagon by A- and B-cells; and inhibits the synthesis of pancreatic enzymes by exocrine cells of the pancreas.

D1-cells contain small (160nm) argirophilic granules. These cells secrete vasoactive interstitial peptide (VIP), which decreases arterial pressure and stimulates the activity of exocrine and endocrine portions of the pancreas.

PP-cells are polygonal cells containing small granules (140nm). They constitute 2-5% of insulocytes. PP-cells produce pancreatic polypeptide, which stimulates secretion of gastric and pancreatic juice.

Besides the exocrine and endocrine cells, one more type of cells was described – intermediate or acino-insular cells. They are arranged in groups around the islets. They contain both the large zymogen and the small insular. It was suggested that such cells produce tripsin-like enzymes, which release the active insulin from proinsulin.

RESPIRATORY SYSTEM

The functions of the respiratory are air conduction, air filtration, respiration and several non-respiratory functions. The principal function of this system is gas exchange (respiration). The other functions include the thermoregulation and humidification of inspired air, its filtration from dust and microorganisms (conditioning function), deposition of blood in well-developed vascular system, taking part regulation of blood clotting by synthesis of thromboplastin and heparin, synthesis of some hormones, maintenance of water-salt and lipid metabolism, phonation, smell sensation and immune defense.

The air passages of the respiratory system consist of conducting portion and respiratory portion (alveoli). The conducting portion of the respiratory system consists of those air passages that lead to the sites of respiration within the lung where gas exchange takes place. The conducting passages include those located outside as well as within the lungs. The passages external to the lungs consist of nasal cavities, nasopharynx, larynx, trachea and bronchial tree including terminal bronchioles.

The respiratory portion is that part of the respiratory tract in which gas exchange occurs. Sequentially, it includes respiratory bronchioles, alveolar ducts, alveolar sacs and alveoli.

The nasal cavities consist of the nasal vestibule and the nasal cavity proper. The nasal cavity is divided into two regions: respiratory region and olfactory region.

The nasal vestibule is a cavity bounded by cartilaginous part of nose. It is lined with stratified squamos epithelium, a continuation of the skin of the face. In the connective tissue layer underlying the epithelium the sebaceous glands and hair follicles are found.

The respiratory portion of nasal cavity is lined by the respiratory mucosa, which contains ciliated, pseudostratified columnar epithelium and underlying lamina propria. The ciliated, pseudostratified columnar epithelium of the respiratory mucosa is composed of five cell types: ciliated cells, goblet cells, brush cells, small granule cells (Kulchitsky). Ciliated cells possess cilia that projects into the mucus covering the surface of the epithelium. Goblet cells are interspersed among the ciliated cells; they synthesize and secrete mucus. Brush cells bear short, blunt microvili on their apical surface. Basal cells are the stem cells, from which the other cell types arise. Small granule cells resemble basal cells, but contain secretory granules. They are referred to as the enteroendocrine cells of the APUD system.

The lamina propria of respiratory mucosa is formed by loose connective tissue containing numerous elastic fibers and acini of mucus-secreting glands, whose excretory ducts empty at the epithelial surface. The secretion of these glands together with the secretion of goblet cells moistens the mucosa and retains the particles of dust and microorganisms, which are then removed by sweeping motion of the cilia.

The lamina propria also contains lymphatic nodules. The aggregations of lymphatic nodules near the pharyngeal openings of auditory tubes form tubal tonsils; on the posterior wall of nasopharynx – pharyngeal tonsil. The mucosa of the nasal cavity has a rich vascular network that includes a complex set of capillary loops, which are located immediately under the epithelium. The arrangement of blood vessels allows the inhaled air to be warmed by blood flowing through the loop closest to the surface; however it also increases the risk of nasal bleeding.

Larynx – is the passageway of air between the oropharynx and trachea. In addition to serving as a conduit for air, the larynx serves as the organ for producing sounds. The wall of larynx consists of three layers: mucosa, fibrocartilaginous layer, and adventitia.

The mucosa of larynx, except the vocal folds, is lined with ciliated, pseudostratified columnar epithelium containing numerous goblet cells. The lamina propria is formed by loose connective tissue, which continues with loose connective tissue of the submucosa. The lamina propria, as well as submucosa, contains numerous elastic fibers, which are located among the striated muscles of vocal folds, and immediately continue with the perichondrium of laryngeal cartilages. At the anterior surface of larynx the lamina propria contains secretory acini of compound sero-mucous glands and an aggregation of lymphatic nodules, which form the laryngeal tonsil.

In the middle portion of larynx the mucosal folds, which form true and false vocal cords, are located. Theese folds are covered with stratified squamos epithelium. The contraction of vocalis muscles contained within each true vocal fold changes the degree of glottal opening, thereby changing the pitch of sounds produced by the air expelled from lungs and passing through the larynx.

The fibrocartilaginous layer consists of hyaline and elastic cartilages, surrounded by dense connective tissue. It performs the function of supportive and protective framework of the larynx.

The adventitia of larynx is formed by loose connective tissue.

The larynx is separated from the trachea by epiglottis, which is formed by elastic cartilage. At the level of epiglottis the laryngeal mucosa transits into mucosa of the trachea. The epiglottis is lined with simple squamos non-keratinized epithelium. The lamina propria forms papillae, which project into the epithelium.

Trachea is a hollow tubular organ, whose wall consists of four layers: mucosa, submucosa, fibrocartilaginous layer, and adventitia.

The mucosa consists of epithelium and lamina propria. The ciliated, pseudostratified columnar epithelium of trachea is composed of ciliated, goblet, endocrine (granule), basal and brush cells.

Ciliated cells are columnar-shaped cells containing hair-like cilia projecting from their apical surface. The cilia provide a coordinated sweeping motion of the mucous coat in the direction opposite to the inspired air.

Goblet cells – are unicellular endoepithelial glands producing mucous secretion, which is rich in hyaluronic and sialic acid. Their secretion supplemented by that of the mucous glands of lamina proria moistens the epithelium and retains the dust particles.

The endocrine cells are pyramidal-shaped cells containing secretory granules. These cells produce peptide hormones and biogenic amines. They are referred to as enteroendocrine cells of APUD system. The principal function of endocrine cells of the trachea is regulation of contraction of the smooth muscle of air passages.

The lamina propria underlying the epithelium is formed by loose connective tissue, which is rich in elastic fibers, blood vessels and capillaries. The elastic fibers are arranged mainly in longitudinal direction. The lamina propria also contains lymphatic nodules and bundles of the smooth muscle cells.

The submucosa is formed by loose connective tissue, which is the continuation of those of the lamina propria. The submucosa contains acini of mixed sero-mucous glands, whose excretory ducts open at the mucosal surface.

The fibrocartilaginous layer consists of C-shaped hyaline cartilaginous rings unclosed at their posterior wall. In humans tracheal cartilages number about 16 to 20. Between the cartilaginous rings a dense regular connective tissue attached to the perichondrium is located. The free ends of cartilaginous rings are connected by the smoth muscles. Such arrangement provides flexibility to the posterior surface of trachea and also maintains patency of the lumen, which is important during swallowing.

The adventitia is formed by loose connective tissue, which continues with a loose connective tissue of adjacent parts of the mediastinum.

The lungs occupy the principal part of chest and constantly change their shape depending on the respiratory phase. They are surrounded by the serous tunic – visceral pleura.

Structure. The lung consists of conducting air passages – the bronchial tree, and a system of alveoli, which are the sites of gas exchange.

The bronchial tree. At the level of T5 (fifth thoracic vertebra) the trachea divides into two main bronchi (right and left), which extend to the right and left lung respectively. On entering the hilum of the lung, each main bronchus divides

into the lobar bronchi. The lobar bronchi are in turn divided into segmental bronchi, subsegmental bronchi, small bronchi, and terminal bronchioles. According to their diameter and structure, all named bronchi are classified into main, large, medium, small bronchi and terminal bronchioles.

All bronchi have the similar general structure: their wall consists of four layers – mucosa, submucosa, fibrocartilaginous layer, and adventitia. The structural features of these layers depend on the caliber of bronchus. Further only the characteristic features of one or another layer are described.

The main bronci are about 15mm in diameter. The mucosa, as in the trachea, is lined with ciliated, pseudostratified epithelium; and contains the muscularis mucosae, which separates it from the submucosa. The muscularis mucosae consists of two layers of the smooth muscle – the inner circular and the outer longitudinal. The characteristic feature of the main bronchi is the presence of fibrocartilaginous layer formed by closed hyaline cartilaginous rings.

The large bronchi have a diameter of 15 to 5mm. The well-developed muscularis mucosae consists of one layer of the smooth muscles arranged in oblique-longitudinal direction. Due to their contraction the mucosa of large bronchi forms the movable folds.

The lamina propria is rich in elastic fibers, which are longitudinally arranged and provide stretching of the bronchial wall and its return to initial condition during breathing. Besides this, the lymphatic nodules are often revealed within the lamina propria. The mucosa contains numerous glands.

The fibrocartilaginous layer contains separated, irregular-shaped hyaline cartilage plates, which are connected together by loose connective tissue continuing with the perichondrium.

The adventitia is formed by loose connective tissue.

The medium bronchi are from 2 to 5mm in diameter. Compared with the large bronchi, the epithelium of medium bronchi consists of less tall epithelial cells; but it still remains ciliated, pseudostratified columnar epithelium containing goblet cells. The lamina propria contains more elastic fibers. Within the submucosa the mixed sero-mucous glands are found. In the fibrocartilaginous layer the hyaline cartilage is represented as small “islands”. As the cartilaginous islands become smaller, the hyaline cartilage is substituted into the elastic one.

The small bronchi are from 2 to 1mm in diameter. The epithelium gradually undergoes transition into the double-layer one, but it remains ciliated and contains goblet cells. The muscularis mucosae becomes more developed. The glands and cartilaginous islands gradually disappear. The absence of cartilage and presence of highly developed muscularis mucosae result in formation of the high longitudinally oriented folds. That’s why on a cross-section the lumen of small bronchi has a star-like shape. The small bronchioles regulate the passage of air into the respiratory portions of the lungs.

The terminal bronchioles are approximately 0,5mm in diameter. The mucosa is lined with ciliated, simple cuboidal epithelium containing brushed, secretory and brushless cells.

The secretory cells (Clara) are nonciliated cells that have a characteristic rounded or dome-shaped apical surface projection. They have a well-developed basal rER, a supranuclear Golgi apparatus, secretory granules and numerous cisternae of smooth ER in the apical cytoplasm. These cells secrete lipo- and glucoproteins, enzymes, which are used for synthesis of surface-active agent similar to surfactant.

The brush cells are characterized by an ovoid shape and a presence of short microvili on the apical surface. These cells are considered to perform the function of chemoreceptors.

The brushless cells are prismatic in shape; their apical cytoplasm contains glycogen granules, mitochondria and secretory granules. Their function is unrevealed.

The lamina propria contains longitudinally oriented elastic fibers. The muscularis mucosae is performed by small bundles of the smooth muscle. That's why the bronchioles are easily extensible during inspiration and return to initial condition during exhalation.

The pulmonary acinus is a structural and functional unit of the respiratory portion of the lung. The acinus consists of respiratory bronchioles ofI, II, III-rd order, alveolar ducts and alveolar sacs.

The respiratory portions of the lung are the sites of gas exchange between blood and alveolar air. The pulmonary acinus begins with the respiratory bronchiole, which arises immediately from the terminal bronchiole. The respiratory bronchioles are lined with simple cuboidal epithelium, within which the ciliated cells occasionally occur. The muscularis mucosae wears and breaks up into separated, circularly arranged bundles of the smooth muscle. The loose connective tissue of adventitia continues with the interstitial connective tissue.

The respiratory bronchiole is in turn divided into respiratory bronchioles of the II-nd, and then the III-rd order. The respiratory bronchiole of the III-rd order gives a rise to two alveolar ducts. The alveolar ducts divide into two blind-ended alveolar sacs.

The acini are separated from each other by thin connective tissue septa; 12-18 acini compose the pulmonary lobule. The characteristic feature of acini is the presence of alveoli. The wall of respiratory bronchioles contains only singular alveoli. The wall of alveolar ducts and alveolar sacs contains numerous alveoli.

The alveolus has a shape of open vesicle about 0,25mcm in diameter. At the bottom of alveoli the discrete holes, called pores of Kohn, are found; they are about 9-19mcm in diameter and connect the adjacent alveoli. The average number of pores per one alveolus is from 13 to 21 pairs. The inner surface of alveolus is lined with one layer of cells lying on the basal lamina. The alveolar epithelium is composed of two principal types of cells:

- respiratory alveolar cells (type I pneumocytes);
- secretory alveolar cells (type II pneumocytes).

The respiratory alveolar cells are extremely thin squamos cells, which lie most of the surface of the alveoli. They contain short cytoplasmic projections on their apical surface, which increases the contact area between alveolar epithelium and air. The cytoplasm of the respiratory alveolar cells contains pynocytic vesicles and

small mitochondria. The nuclear-free portions of respiratory alveolar cells adjoin the nuclear-free portions of endothelial cells of capillaries. In such areas the basal lamina of capillary endothelium is closely attached to the basal lamina of respiratory alveolar cells. A thin layer of surfactant, a type I epithelial cell and its basal lamina, and a capillary endothelial cell and its basal lamina are the components of the thinnest air-blood barrier. Often, these two basal laminae are fused. Connective tissue cells and fibers that may be present between the two basal laminae widen the air–blood barrier.

The secretory alveolar cells lie on the common basal lamina with the respiratory alveolar cells. These cells are cuboidal in shape; their cytoplasm contains well-developed Golgi apparatus, ER. Their apical cytoplasm is filled with granules that are resolved with the TEM as stacks of parallel membrane lamellae, the lamellar bodies. They are rich in a mixture of phospholipids, neutral lipids, and proteins, that is secreted by exocytosis to form an alveolar lining, surface-active agent called surfactant.

The surfactant consists of three phases:

- membranous component;
- aqueous component (hypophase);
- reserve surfactant – the myelin-like structures.

The outer membranous component consists of phospholipids and proteins. The underlying hypophase is composed of proteins dissolved in water. Surfactant prevents collapse of the alveoli during exhalation, participates in the clearance of foreign materials and prevents transudation of fluid from the capillaries of interalveolar septa.

Besides the above-listed cells, the alveolar epithelium contains alveolar macrophages. These cells are derived from blood monocytes and belong to the mononuclear phagocytotic system. In air spaces, they scavenge the surface to remove inhaled particulate matter (e.g., dust and pollen), thus giving them one of their alternative names, dust cells. They can also phagocytize microorganisms, red blood cells, and components of surfactant.

Externally the alveolus is surrounded by blood capillaries and network of elastic fibers. The alveolus is encircled by a network of thin collagen fibers, fibroblasts and mast cells. Because of the alveoli are closely attached to one another, each capillary contact with several alveoli at the same time. It provides optimal conditions for gas exchange between blood and alveolar air.

Pleura. The visceral pleura is firmly attached to the lungs, its elastic and collagen fibers continue with the interstitium of the lungs. The visceral pleura is covered with mesothelium, and contains smooth muscle cells.

URINARY SYSTEM

The urinary system consists of paired kidneys, paired ureters, which lead from the kidney to the urinary bladder and the urethra, which leads from the bladder to the exterior of the body.

The kidney is an organ, which continuously produce the urine. It is the main organ, which remove certain waste products of metabolism from the body. The main, vital function of the kidney is an excretory one. Besides this, the kidneys take part in regulation of blood osmotic pressure, maintain the acid-base balance and carry out an endocrine function. The kidneys are paired bean-shaped parenchymatous organs surrounded by a fibrous capsule; the anterior surfaces of kidneys are covered by the serous coat (peritoneum).

Examination with the necked eye of the cut face of hemisected kidney reveals that its substance can be divided into two distinct regions:

- cortex, the outer reddish brown part, located immediately below the capsule;
- medulla, the much lighter-colored inner part.

The caps of cortical tissue extend into the medulla, forming so-called renal columns. The renal columns divide the medulla into 8-12 conical portions called renal pyramids. The bases of pyramids face the cortex and the apices face the renal sinus. The apical portions of pyramids form the renal papillae, which project into a minor calyx. Each medullary pyramid and the associated cortical tissue at its base and sides (one half of each adjacent renal column) constitute a lobe of the kidney.

A series of vertical striations emanate from the medulla into the cortex. These striations are called medullary rays.

The stroma of kidneys is formed by loose connective tissue, which is rich in reticular cells and reticular fibers.

The parenchyma of kidneys consists of epithelial renal tubules, which along with blood capillaries form the nephrons.

Nephron is the fundamental structural and functional unit of the kidney. It consists of a system of straight and convoluted epithelial tubules, which arise from each renal corpuscle. The length of nephron varies from 13 to 50mm; the total length of all neurons is approximately 100km.

Nephron consists of the following parts:

- glomerulus surrounded by a Bowman’s capsule;
- the proximal thick segment, which consists of the proximal convoluted and straight tubules;
- the thin segment, which consists of the thin descending limb and thin ascending limb;
- the distal thick segment, which consists of the distal straight and convoluted tubules.

The proximal straight tubule, the thin segment and the distal straight tubule constitute the loop of Henle.

The capillary glomerulus and its surrounding capsule form the renal (Malpighian) corpuscle.

On the basis of their localization and structure the nephrons are divided into the cortical and juxtamedullar.

Among cortical nephrons there are distinguished two types: the short ones and the intermediate ones. The short cortical nephrons have their renal corpuscles located in the outer part of the cortex; they have short loops of Henle located within the cortex. The intermediate nephrons have their loops of Henle extending

in the outer part of the cortex (80%).

The juxtamedullar nephrons (20%) have extremely long loops of Henle, which extend well into the inner region of the medulla; their renal corpuscles, proximal and distal regions are located at the border with the renal medulla.

The nephrons open into the collecting renal tubules. The collecting tubules begin in the cortex and together with the straight ducts of cortical nephrons constitute the medullary rays. Then the collecting tubules reach the medulla and travel to the apex of the pyramids, where they merge into the papillary ducts.

The renal corpuscle consists of the capillary glomerulus and the surrounding capsule (Bowman's). The Bowman's capsule is a double-layered epithelial cup, that consist of the inner (visceral) and outer (parietal) layers, between which the slit-like "capsule space" is found. The glomerulus consists of from 50 to 100 capillary loops, which are the branches of the afferent glomerular arteriole. These capillaries merge and form the efferent glomerular arteriole. The efferent arteriole has a smaller diameter than the afferent one, creating the higher pressure (50mmHg) in capillaries of the glomerulus. This is the necessary condition for realization of the first phase of urine formation, the phase of **filtration**.

The filatration apparatus of the kidney, also called glomerular filtration barrier, consists of three different components:

- endothelium of the glomerular capillaries, which posseses numerous fenestrations of about 70 to 90 nm in diameter, and lies on the inner surface of the basement membrane;
- the glomerular basement membrane is the joint product of the endothelium and cells of the visceral layer of Bowman's capsule. It consists of three layers: two of them (the lamina rara externa and the lamina rara interna) are electron-lucent layers; the middle layer is the electron-dense one (lamina densa) containing a microfibrillar meshwork with a mesh diameter of about 7nm;
- visceral layer of Bowman's capsule is formed by large (about 30mcm) polygonal epithelial cells called **podocytes**. The basal portions of podocytes extend processes, cytotrabeculae, around the capillaries and develop numerous secondary processes called foot pedicles or cytopodia. The expanded bases of the foot pedicles contact with the basement membrane.

The foot processes interdigitate with foot processes of neighboring podocytes. The elonagated spaces between the interdigitating foot processes are called filtration slits and covered by an ultrathin filtration slit diaphragm that spans the filtration slit slightly above the basement membrane.

These three components form the glomerular filtration barrier, through which the blood is filtered, resulting in the formation of primary urine, which is collected in the capsule space.

The glomerular filter has a selective permeability; it restricts the movement of particles, which have a larger diameter than the mesh diameter of middle layer of the basement membrane. Normally, the blood cells, plasma proteins and large molecules, like antibodies, can not pass through the glomerular filter. If the barrier is injured, these components of blood can be revealed in patients' urine.

The renal corpuscles contain an additional group of cells called mesangial cells. The mesangial cells are positioned much the same as podocytes, in that they are enclosed by the basement membrane. These cells and their extracellular matrix constitute mesangium of the renal corpuscle. A part of the mesangial cells are macrophages carrying an Ia-antigen, which enables the immune inflammatory reactions in the glomeruli.

The outer (parietal layer) of Bowman's capsule consists of one layer of squamos or cuboidal cells lying on the basal lamina. Epithelium of the outer layer of capsule continues with epithelium of the proximal segment of nephron.

The proximal segment of nephron consists of two parts: the long proximal convoluted tubules and the short proximal straight tubules. The diameter of proximal tubules is approximately 50-60mcm. The proximal convoluted tubule begins with the urinary pole of renal corpuscle; then it coils and returns back to its renal corpuscle. The proximal straight tubule continues with the thin segment of nephron. The wall of proximal convoluted tubule is lined with cuboidal cells, which lie on basal lamina. The apical portion of these cells contains a brush border, composed of relatively long, closely packed and straight microvilli. Their basal portion reveals basal striations, consisting of elongate mitochondria, which are concentrated between the invaginations of basal cytolemme and oriented vertically to the basal lamina. The cytoplasm of cells of the proximal convoluted tubule is acidophilic and heterogeneous due to the presence of various inclusions (urates, lipids, pigments etc), pinocytotic vesicles and lysosomes.

The proximal convoluted tubule is the initial and main site of reabsorption, the back absorption of glucose, electrolytes, proteins and water from the primary urine into the blood. The mechanism of this process is associated with surface specializations of cells engaged in absorption and fluid transport. The microvilli of proximal convoluted tubule cells are covered with a well-developed glycocalyx that contains high concentrations of alkaline phosphatase, which provides the entire reabsorption of glucose. By pinocytosis the proximal convoluted tubule cells take up proteins and small peptides, break them down to aminoacids and disharge into the blood through the basal lamina. The mitochondria take part in reabsorption of some electrolytes due to the content of succinate dehydrogenase and other enzymes; the folds of cytolemme play a significant role in passive reabsorption of water. The cells of the proximal straight tubule (i.e., the thick descending limb of the loop of Henle) are not as specialized for absorption as are those of the proximal convoluted tubule. They are shorter, with a less well-developed brush border. The mitochondria are smaller than those of the cells of the convoluted segment and are randomly distributed in the cytoplasm. There are fewer cytolemme invaginations and endocytotic vesicles, as well as fewer lysosomes.

The thin segment of nephron has a diameter of 12-15mcm. Its wall is lined with only one layer of squamos epithelial cells, which contain light poor in organelles cytoplasm. The length of the thin segment varies with the location of the nephron in the cortex. Juxtamedullary nephrons have the longest limbs; cortical nephrons have the shortest. The cortical nephrons contain only descending limb of the thin segment.

Flowing through the thin segment, the primary urine losses water, which passes through the wall of tubule due to high concentrations of sodium chloride in the interstitium. The cells of the straight and adjacent part of distal convoluted tubules actively transport the sodium ions from the primary urine to the interstitium, thereby providing the necessary concentration gradient between the urine and the interstitial fluid. As a result, the ultrafiltrate that enters the thin descending limp is isosmotic, whereas the ultrafiltrate leaving the thin ascending limb is hyposmotic to plasma; and the osmothic pressure in interstitium increases dramatically. It leads to a passive reabsorption of water in the distal convoluted tubules and collecting tubules.

The distal straight tubule has a diameter of 30 mcm, its epithelium is similar to the epithelium of the distal convoluted tubule. The cuboidal epithelial cells lie on the basal lamina. The distal segment cells do not reveal the brush border. Their basal portions contain deep folds of cytolemme, where the large elongate mitochondria are located.

The collecting tubules are not referred to as a part of nephron; they "serve" for several nephrons. In their upper portion they are lined with simple cuboidal epithelium, in the lower – with the simple columnar one.

Two distinct types of cells are present in the collecting tubules:

- Light cells are pale-staining cells with true basal infoldings. The function of these cells – is reabsorption of water regulated by the antidiuretic hormone;
- Dark cells structurally resemble the parietal cells of stomach glands, which secrete the chloride ions. The secretory function of the dark cells is considered to provide the acidation of urine.

The process of urine formation consists of several phase. The first phase takes occurs in the renal corpuscle: the primary urine is formed by the process of filtration. The second phase occurs in the system of tubules: by the process of reabsorption proteins, glucose, electrolytes, water and essential substances return to the blood. The urine is concentrated, its volume decreases from 100 to 1,5-2 liters per day. The last phase of urine formation is the secretory one: it occurs in the collecting ducts, where the dark cells disharge chloride ions and acidate the urine.

Endocrine system of the kidney. It represented by the juxtaglomerular (renin) and the prostaglandin apparatus.

The juxtaglomerular apparatus consists of the following components:

1. juxtaglomerular cells;
2. cells of macula densa;
3. juxtavascular cells (Gorrmaghtigh's);
4. mesangial cells of renal corpuscles.

The juxtaglomerular cells are located mainly under the endothelial in the wall of the afferent arteriole and least in the efferent arteriole. These cells are oval-shaped; their cytoplasm contains the granules of rennin, which they secrete into the blood. Renin catalyzes the formation of angiotensin, which causes the constriction of

blood vessels, thereby increasing the blood pressure. Besides this, rennin stimulates the production of aldosteron by the adrenal cortex.

The macula densa – is an area of distal segment of nephron located between the afferent and the afferent arteriole. Epithelial cells of macula densa, unlike other epithelial cells of the distal segment, do not have basal folds; but they have a special structure of basal lamina, which is discontinuous here. The EM examination reveals splitting of the basal lamina, and the processes of juxtavascular cells between its layers. The cells of macula densa functionate as the sodium receptor, reacting on the changes in sodium concentration in urine and stimulating the juxtaglomerular cells to renin secretion.

Juxtavascular cells (Gorrmaghtigh's) lie in the triangular space, bounded by the afferent and efferent arteriole and the macula densa. Theses cells are oval or irregular-shaped, posses long processes, which contact with mesangium; their cytoplasm contains fibrillar structures. The juxtavascular cells and mesangial cells are considered to start the renin synthesis in case of exhaustion of the juxtaglomerular cells. Besides renin, the juxtaglomerular apparatus produce erythropoietin – the factor of erythropoiesis stimulation.

Prostaglandin apparatus consists of the interstitial cells and cells of collecting tubules. The interstitial cells are mesenchymal cells located in stroma of medullary pyramids. Their elongated cell bodies give a rise to numerous processes, some of which surround the tubules of loop of Henle, another – the blood capillaries. The cytoplasm of interstitial cells contains developed organelles and lipid inclusions. These cells produce one of the prostaglandin types, which reduces blood pressure. The light cells of the collecting tubules also produce prostaglandin.

That means that endocrine system of the kidneys takes part in regulation of general and renal blood circulation, thereby regulating the process of urine formation.

Blood supply. Each kidney receives a large branch from the abdominal aorta, called the renal artery. The renal artery branches within the renal sinus and sends interlobar arteries into the substance of the kidney. These arteries travel between the pyramids as far as the cortex and then turn to follow an arched course along the base of the pyramid between the medulla and the cortex. Thus, these interlobar arteries are designated arcuate arteries. Interlobular arteries branch from the arcuate arteries and ascend through the cortex toward the capsule. As they traverse the cortex toward the capsule, the interlobular arteries give off branches, the afferent arterioles, one to each glomerulus. Afferent arterioles give rise to the capillaries that form the glomerulus. This capillary network is called primary capillary network or rete mirabile, because here the capillaries are located between two arterioles. These capillaries merge into the efferent arteriole. Leaving the renal corpuscle, the efferent arteriole again branches into the capillary network, which surrounds the renal tubules, called secondary or peritubular capillary network. Its functions – are trophic of nephron and taking part in the reabsorption phase of urine formation. From the peritubular capillary network the venous system of renal circulation begins. Generally, venous flow in the kidney follows a reverse course to arterial flow, with the veins running in parallel with the corresponding arteries.

Peritubular capillaries near the kidney surface and capillaries of the capsule drain into stellate veins, which in turn drain into interlobular veins , interlobar veins, and the renal vein. Such system of blood circulation is true only for cortical nephrons and is called cortical circulation. Its characteristic features are associated with the process of urine formation, in which the cortical nephrons are involved.

In juxtaglomerular system of circulation, the afferent and efferent arteriole have the same diameter or the efferent arterioles are even wider. That's why the blood pressure in these capillaries is significantly lower that those in the capillaries of cortical nephrons.

Another difference of the juxtaglomerular circulation system is that the efferent arterioles descend into the mudulla and break up into bundles of so called vasa recta. In the renal medulla the efferent arterioles and the vasa recta give a rise to branches, which form the medular peritubular capillary network. The vasa recta form loops at the different levels of medulla and turn in the opposite direction, draining into veins. The capillaries of medulla in turn drain into straight veins, arcuate veins, and so forth. The juxtaglomerular nephrons do not actively form the urine. As cortical nephrons, they act as shunts, through which blood can easily pass in conditions of intensive circulation.

The urinary tracts begin in kidney by the renal calyces and renal pelvis, and then continue with the ureter, urinary bladder and urethra. All named organs, except the urether, have the same general organization. They consist of mucosa, submucosa, muscularis and adventitia (in some areas serosa).

The mucosa is covered with the transitional epithelium with underlying lamina propria. The lamina propria is formed by dense connective tissue, which becomes looser in deep layers, where in continues with the submucosa.

Due to the presence of submucosa, the mucosa of ureter and urinary bladder form deep folds, which enable these organs to stretch and expand the lumen of ureter, which is important during the passage of urine calculus. On a cross-section the lumen of ureter reveals star-like shape. The submucosa in lower parts of ureter contains small tuboalveolar glands, structurally resembling glands of the prostatic gland. The muscularis form two layers in the upper parts of ureter and two layers in its lower parts. It consists of the smooth muscle bundles, which spirally encircle the ureter; these bundles are the continuation of the muscularis of renal pelvis and continue with the muscularis of urinary bladder. Only in the area, where the ureter opens into the urinary bladder the smooth muscle bundles have only longitudinal direction, which provides the opening of ureteral ostium independently on the condition of the smooth muscles of urinary bladder.

The urinary bladder contains three openings, two for the ureters (ureteric orifices) and one for the urethra (internal urethral orifice). The triangular region defined by these three openings, the trigone. The urinary trigone does not contain the submucosa; the lamina propria of this region contains tuboalveolar glands resembling the prostatic glands.

The muscularis of renal calyces and renal pelvis consists of two layers of the smooth muscle – the inner longitudinal and the outer circular, however near the pyramidal papillae only the circular layer is found; its contraction compress the

papilla and causes the discharge of urine. The muscularis of urinary bladder consists of three layers: the outer and inner longitudinal and the middle circular layer. In the area of trigone there is only one muscular layer. These muscular layer consists of two parts:

1. Muscles, which combine the muscular structures of both ureters
2. Muscle-sphincter of trigonum, which opens the urethral ostium. It consists of two layer: the outer layer of striated muscle and the inner layer of smooth muscle.

MALE REPRODUCTIVE SYSTEM

The male reproductive system includes testes, genital excurrents ducts, accessory sex glands and penis. The main function of the male reproductive system is the formation of male gametes - spermatozoa. Besides this, it has an endocrine function.

Testis. The functions of the testes are:

1. the formation of spermatozoa
2. the production of the male sex hormone - testosterone

Each testis is surrounded by an unusually thick dense connective tissue capsule called **tunica albuginea**. Along the posterior surface of testis the tunica albuginea thickens and projects inward as the **mediastinum testis**. The connective tissue septa extend from the tunica albuginea and divide the parenchyma of testis into approximately 250 lobules. **The lobule** is the structural and functional unit of the testis. Each lobule consists of one to four densely packed, highly convoluted **seminiferous tubules**. The seminiferous tubule is approximately 50 cm long and 150 to 250mcm in diameter.

Each tubule within the lobule forms a loop and, because of its considerable length, is highly convoluted, actually folding on itself within the lobule. The ends of the loop are located near the mediastinum of the testis, where they assume a short straight course. This part of the seminiferous tubule is called the **straight tubule** (tubulus rectus). It becomes continuous with the **rete testis**, an anastomosing channel system within the mediastinum. Then, the channels of rete testis connect the approximately 20 **eferent ductules**, which empty into the **duct of the epididymis**.

The seminiferous tubule consists of a seminiferous (or germ) epithelium surrounded by a tunica propria. The tunica propria of the seminiferous tubule consists of three layers:

1. basal layer;
2. myoid layer;
3. fibrous layer.

The basal layer is located between the basal lamina of the seminiferous epithelium and the basal lamina of myoid cells. It is formed by a network of collagen fibers.

The myoid layer consists of the contractive, so-called “myoid” cells, containing the

actin filaments. The myoid cells provide the rhythmical contraction of the seminiferous tubule wall.

The fibrous layer consists of two portions:

1. acellular layer – is immediately attached to the myoid layer; consists of the basal lamina of myoid cells and collagen fibers;
2. the layer of fibroblast-like cells attached to the endothelial cells of blood capillaries.

The seminiferous tubules are surrounded by connective tissue, containing numerous blood and lymphatic vessels, which supply the seminiferous epithelium with nutrients.

The basal, myoid and fibrous layers together with the endothelial cells of blood capillaries form the **blood-testis barrier.** The blood-testis barrier prevents the passage of toxic agents into the seminiferous tubules.

The blood capillaries are accompanied by the connective tissue layers, where the endocrine cells of testis (Leydig cells) are located. The function of Leydig cells is production of the male sex hormone – testosterone.

Leydig cells are polygonal in shape, have acidophilic cytoplasm, well-developed smooth endoplasmic reticulum and mitochondria with tubular or vesicular crysts. In their cytoplasm the inclusions of glycogen and glycoproteins are found.

The seminiferous epithelium is composed of two basic cell populations:

1. supporting cells (sustentacular or Sertoli cells);
2. spermatogenic cells.

Sertoli cells are columnar cells with extensive apical and lateral processes that surround the adjacent spermatogenic cells and occupy the spaces between them. The cytoplasm of Sertoli cells contains well-developed smooth endoplasmic reticulum, Golgi apparatus and inclusions of carbohydrates and lipids.

Each Sertoli cell is bound together with the neighboring cell through tight junctions. This divides the seminiferous (germ) epithelium into two compartments:

1. the outer basal
2. the inner adluminal

The basal compartment contains spermatogonia, which take the nutrients immediately from the microcirculatory bed by diffusion.

The adluminal compartment contains spermatocytes, spermatids and spermatozoa, which are supplied with nutrients by Sertoli cells. Sertoli cells form the microenvironment for the developing spermatozoa, protecting them from toxins and antigens. Sertoli cells phagocyte defective germ cells and produce biologically active substances: the androgen-binding protein, which deliver testosterone directly to spermatids). Besides these, the sustentacular cells (light) produce inhibin, which inhibits the secretion of follicle-stimulating hormone by adenohypophysis, and antimullerian hormone (dark cells).

The process by which the male gametes are created is called **spermatogenesis**. Spermatogenesis occurs in the seminiferous tubules in the following sequence of cell forms:

1. spermatogonia

2. primary spermatocytes
3. secondary spermatocytes
4. spermatids
5. spermatozoa

As the precursors of the spermatozoa divide and differentiate, they migrate towards the lumen of the seminiferous tubule.

Spermatogenesis consists of four phases:

1. reproduction
2. growth
3. maturation
4. differentiation

The phase of reproduction (proliferation). In this phase spermatogonial stem cells undergo multiply **mitotic** divisions. Each spermatogonia contains diploid number of chromosomes. The proliferation of spermatogonia is regulated by the follicle-stimulating hormone.

Under the influence of testosterone a part of spermatogonia reach the **phase of growth** and become **primary spermatocytes**. They replicate their DNA shortly after they form and before meiosis begins, so that each primary spermatocyte contains the normal chromosomal number (2*n*) and double the amount of DNA (4*d*).

Prophase of the first meiotic division, during which the chromatin condenses into visible chromosomes, lasts up to 22 days in human primary spermatocytes. At the end of prophase, 44 autosomes and an X and a Y chromosome, each having two chromatin strands (chromatids), can be identified. Homologous chromosomes are paired as they line up on the metaphase plate. The **paired homologous chromosomes**, called **tetrads** because they consist of four chromatids, exchange genetic material in a process called **crossing-over**. During this exchange, the four chromatids rearrange into a tripartite structure called a **synaptonemal complex**. This process ensures genetic diversity.

The phase of maturation begins when the primary spermatocytes enter the metaphase of the first meiotic division. After crossingover is complete, the homologous chromosomes separate and move to the opposite poles of the meiotic spindle. Thus, the tetrads, which have been modified by crossing-over, separate and become dyads again. The two chromatids of each original chromosome (although modified by crossing-over) remain together. The cells derived from the first meiotic division are called **secondary spermatocytes.** These cells immediately enter the prophase of the second meiotic division without synthesizing new DNA. Each secondary spermatocyte has a reduced number of chromosomes to (1n), which is represented by 22 autosomes and an X or a Y chromosome. Each of these chromosomes consists of two sister chromatids.

The secondary spermatocyte has the (2d), diploid amount of DNA. During metaphase of the second meiotic division, the chromosomes line up at the metaphase plate, and the sister chromatids separate and move to opposite poles of the spindle. As the second meiotic division is completed and the nuclear

membranes re-form, two haploid **spermatids**, each containing 23 single-stranded chromosomes (1n) and the (1d) amount of DNA, are formed from each secondary spermatocyte.
This means that as result of meiotic division each spermatogonium gives a rise to four spermatids.
The phase of differentiation. In this phase the spermatids are remodeled and differentiate into the mature sperm. The elements of Golgi apparatus are transformed into acrosome. Acrosome is the special structure, which provides the penetration of spermatozoa into the oocyte. The microtubules and centriole take part in the formation of flagellum. Flagellum – is the special organelle used for locomotion. The proximal part of flagellum is surrounded by mitochondria. The excesses of cytoplasm are phagocyted by Sertoli cells. Sertoli cells secrete the fluid which helps the mature sperm to move towards the distal part of the seminiferous tubule. The process of differentiation of the spermatids into the mature sperm lasts approximately 75 days.
The exccurent ducts system begins with the **straight tubules** of testes, which are the immediate continuation of the seminiferous ducts.
The wall of the straight ducts, as the wall of other portions of the exccurent ducts system, consists of three layers:

1. mucosa
2. muscularis
3. adventitia (tunica albuginea)

The mucosa of the straight tubules is lined with simple columnar epithelium, which can reveal secretory activity.
The straight tubules become continuous with the **rete testis**. The tubules of the rete testis are covered with simple cuboidal or simple squamos epithelium. Epithelial layer of tubules of the rete testis contains macrophages, which phagocyte defective spermatozoa.
The muscularis is formed by the circular layer of the smooth muscle.
The adventitia is formed by loose connective tissue.

Efferent ductules in number of 15-20 empty into the **duct of the epididymis**. The efferent ductules are lined with pseudostratified columnar epithelium, that contains ciliated tall columnar cells and basal cells.
In the lumen of the ducts of the epididymis the differentiation of spermatozoa finishes. Under the influence of androgens this epithelium produces protein substances, which regulate the “packing” of the polysaccharides and enzymes into the acrosome. Besides this, the secretion of epithelial cells rarefies sperm. The lumen of the duct of the epididymis is the reservoir of spermatozoa.
The wall of the duct of the epididymis consists of three layers:

1. mucosa;
2. muscularis;
3. adventitia.

The mucosa is lined with simple or double-layer columnar epithelium, which consists of two types of cells:

1. ciliated cells – the elongated columnar cells, containing stereocilia on the apical surface;
2. basal cells – the cells, lying between the basal portions of the ciliated cells.

The passage of the sperm along the exccurent ducts is provided by contraction of the circular layer of the smooth muscle.

The adventitia is formed by loose connective tissue.

The duct of the epididymis continues with the **ductus deferens.**

The ductus deferens – is paired tube, which is approximately 45cm long and 0,2-0,5mm in diameter. The function of the ductus deferens – is the ejaculation of sperm**.** The wall of the ductus deferens consists of three layers:

1. mucosa;
2. muscularis;
3. adventitia.

The mucosa of the ductus deferens is lined with double-layer columnar epithelium.

The muscularis contains three layers of the smooth muscle: the inner longitudinal, the middle circular and the outer longitudinal.

The adventitia is formed by loose connective tissue. The distal end of the ductus deferens forms the ampulla of the ductus deferens.

The ejaculatory duct – is the portion of the excurrent ducts system, which forms as a result of confluence of the two ductus deferens and the short excretory ducts of seminal vesicles. It passes through the thickness of prostate gland.

The wall of the ejaculatory duct consists of three layers:

1. mucosa;
2. muscularis;
3. adventitia.

The mucosa of the ejaculatory duct forms numerous folds. It is lined with double-layer columnar epithelium, containing ciliated and low basal cells. It is considered that the irritation of stereocilia of the epithelial cells in the ductus deferens and the ejaculatory duct is the reason of the sensation of orgasm in the moment of ejaculation.

The muscularis of the ejaculatory duct is not as defined as that of the ductus deferens.

The adventitia of the ejaculatory duct continues with the stroma of prostate gland.

Urethra. In males, the urethra has three distinct segments – prostatic urethra, membranous urethra and penile (spongy) urethra.

The wall of the urethra consists of three layers:

1. mucosa;
2. submucosa;
3. muscularis.

Epithelium of the mucosa differs in different segments of the urethra: the prostatic urethra is lined with transitional epithelium, the membranous urethra – with pseudostratified columnar epithelium, the spongy urethra – with stratified squamos nonkeratinized epithelium.

The pseudostratified epithelium of the spongy urethra contains numerous goblet cells and occasional endocrine cells. The lamina propria, containing numerous blood vessels and small mucous glands, lies under the epithelium.
The submucosa is formed by loose connective tissue, containing venous plexus.
The muscularis of the urethra is formed by bundles of the smooth muscle; it is the most developed in the prostatic segment and becomes thinner towards the spongy segment.

Accessory sex glands

Seminal vesicles – are paired sex glands, the excretory ducts of which combine with the ampulla of the ductus deferens to form the ejaculatory duct.
The secretion of the seminal vesicles contains fructose – a monosaccharide used by the spermatozoa to maintain their metabolism. Besides this, the products of secretion of the seminal vesicles dilute sperm, thereby providing alkaline environment, which increases motility of the spermatozoa.
The wall of the seminal vesicles consists of three layers:

1. mucosa;
2. muscularis;
3. adventitia.

The mucosa is lined with simple columnar epithelium, forms numerous folds. The lamina propria of mucosa is rich in elastic fibers and contains acini of mucus-secreting alveolar glands.
The muscularis is formed by bundles of the smooth muscle, which are arranged in two layers: the inner circular and the outer longitudinal.
The adventitia of the seminal vesicles is formed by dense connective tissue, containing numerous elastic fibers.

Prostate gland is the large accessory sex gland, which surrounds the upper (prostatic) segment of urethra. The excretory ducts of the prostatic gland empty into the urethra.
The prostate gland provides both the endocrine and the exocrine functions. The endocrine part of the prostate gland secretes biologically active substances, which affect on the production of male sex hormones and the process of spermatogenesis, stimulate the growth of nerves and the smooth muscle contraction etc.
The prostate gland is under the influence of testosterone; in case of castration, it undergoes atrophy.

The exocrine function of the prostate gland is the production of secretion, which dilute the ejaculate and increases the motility of spermatozoa. This secretion contains immunoglobulins, enzymes, vitamins, lactic acid, zinc etc. Contraction of the smooth muscle of the prostate gland facilitates the ejaculation.

The prostate gland – is the lobular gland, covered by a thin connective tissue capsule. The parenchyma of the prostate gland is formed by separate glands located in the mucosal layer of the organ. The excretory ducts of these glands empty into the prostatic segment of urethra. The glands, surrounding the urethra, are divided into three groups: the central, the peripheral and the transitional.

The central group consists of the small glands, located within the mucosa of the prostate gland and surrounding ejaculatory ducts as they pierce the prostate gland.

The transitional group is located within the connective tissue of submucosa. The glands of this group encircle the prostatic urethra.

The peripheral group comprises 70% of the glandular tissue of the prostate. It surrounds the central group and occupies posterior and lateral parts of the gland.

The glands of the peripheral group are called the prostatic glands proprii. The acini of the prostatic glands proprii consist of the two types of epithelial cells:

1. tall columnar mucus-secreting cells;
2. basal cells, located between the mucus-secreting cells.

Before entering the urethra, the excretory ducts dilatate and form the irregular-shaped ampulles, which are covered with pseudostratified columnar epithelium.

The fibromuscular elements of the prostate gland are formed by loose connective tissue and radially arranged bundles of the smooth muscles, which divide the gland into lobules.

At the area entrance of the ejaculatory duct into the prostatic urethra, the wall of the prostatic gland forms convexity – **seminal colliculus**. Erection of the seminal colliculus prevents the passage of sperm into the urine bladder. Behind the seminal colliculus the **prostatic utricle** is located.

Bulbourethral glands – are paired compound tuboalveolar glands, which empty into the proximal segment of the urethra. The secretion of these glands dilutes sperm. Their acini consist of squamos, cuboidal or columnar mucus-secreting cells. The acini are surrounded by loose connective tissue and bundles of the smooth muscle.

Penis – is the intromittent organ, which provides the ejaculation of sperm into the female genital tract and serves to urination. It consists of two dorsal masses of erectile tissue, the corpora cavernosa, and a ventral mass of erectile tissue, the corpus spongiosum. In the corpus spongiosum the spongy part of urethra is embedded. Erection of the penis involves the filling of the vascular spaces of the corpora cavernosa and corpus spongiosum. Penis is covered by the tunica albuginea. The tunica albuginea consists of the connective tissue, containing numerous venous anastomoses. The balanus is covered with skin, containing sebaceous glands. The arteries of penis are called **helicine arteries**. These arteries dilate during erection to increase the blood flow to the penis.

The wall of arteries and veins of penis is rich in muscular elements, which prevent the blood outflow and provide rigidity of the organ.

FEMALE REPRODUCTIVE SYSTEM

The female reproductive system has two interrelated functions: gametogenesis (the production of gametes) and endocrine function (the production of female sex hormones).

The female reproductive system consists of internal reproductive organs and external genitalia. The internal female reproductive organs are the ovaries, uterine tubes, uterus and vagina.

Ovaries are paired almond-shaped organs, which have two functions: oogenesis and endocrine function.

The ovarian structure in adult women

The surface of the ovary is covered by a simple cuboidal epithelium, which continues with the mesothelium that covers the mesovarium. The free surface of epithelium contains microvilli. Under the epithelium a dense connective tissue layer, the tunica albuginea, lies. Under the tunica albuginea the ovarian cortex and ovarian medulla are located.

The medulla is formed by a connective tissue stroma, containing large blood vessels, nerves and nerve endings.

The cortex surrounds the medulla and consists of stroma and parenchyma.

The stroma is formed by connective tissue, containing collagen and a small amount of elastic fibers. This connective tissue contains the interstitial cells, which remind those of testis and can produce steroid hormones.

The parenchyma of ovarian cortex consists of ovarian follicles at the different stages of development:

- primordial follicles,
- primary follicles,
- mature (Graafian) follicles,
- corpus luteum and corpus albicans,
- atretic follicles.

Primordial follicles first appear in the ovaries during the third month of fetal development. Primordial follicles contain **primary oocyte** at diplotene stage of meiosis prophase. The primary oocyte is surrounded by a single layer of **squamos** follicle cells. These follicles are about 50mcm in diameter. They are located in the stroma of the cortex just beneath the tunica albuginea.

Primordial follicles develop into the **primary follicles** at the 19-20th week of fetal development. The several changes occur in oocyte and in the follicle cells. The oocyte enlarges, and the surrounding flattened follicle cells proliferate and become **cuboidal**. The oocyte together with the follicle cells starts to produce mucoproteins and glucosaminoglycans, which form the **zona pellucida**. It appears between the oocyte and adjacent follicle cells.

The primary follicles contain **primary oocyte** arrested in the diplotene stage of prophase I (the prophase of the **first** meiotic division). The meiotic resting phase that then begins is called the **dictyotene** and it lasts till puberty**.**

Secondary follicles are characterized by stratified follicular epithelium, which is now identified as **stratum granulosum**, and fluid-containing antrum. The stratum granulosum has a relatively uniform thickness except for the region associated with the oocyte. Here the granulose cells form a thickened mound, the **cumulus oophorus**, which projects into the antrum. The cells of the cumulus oophorus that immediately surround the oocyte and remain with it at ovulation are referred to as the **corona radiata.** The oocyte and corona radiata are moved to the upper pole of growing follicle.

The fluid secreted by the granulosa cells is called **liquor folliculi** and contains the female sex hormone – estrogen. As the follicle grows, stromal cells surrounding it form a sheath of connective tissue cells, known as the theca folliculi. Futher the numerous blood vessels penetrate the **theca folliculi** and it differentiates into two layers – the theca interna and the theca externa. The theca interna contains interstitial cells surrounded by branched capillaries. The theca externa is the outer layer of dense connective tissue.
The secondary follicles still contain the **primary** oocyte.
Despite enlargement of the follicle due to the cumulation of the liquor folliculi, the oocyte doesn't increase in size. The secondary follicles start their development in puberty.
Mature follicle – is the follicle prepared to ovulation. The corona radiata composed of cumulus cells that send penetrating microvilli throughout the zona pellucida to communicate via gap junctions with microvilli of the oocyte.Through these processes the nutrients come to the oocyte from the follicle cells, which produce lipoproteins of yolk. Graafian follicle, has a diameter of 10 mm or more. Because of its large size, it extends through the full thickness of the ovarian cortex and causes a bulge on the surface of the ovary.
A surge in the release of follicle-stimulating hormone is induced in the adenohypophysis approximately 24 hours before ovulation. Triggered by this surge, the first meiotic division of the primary oocyte resumes, resulting in the formation of the **secondary oocyte** and the first polar body.
The further growth of the Graafian follicle causes the rupture of its wall and release of the oocyte.
The process of transformation of primary follicles into the mature follicles is called the follicle growth. The follicle growth is controlled by the gonadotrope hormones of adenohypophysis – follicle-stimulating hormone and small amounts of luteinizing hormone. The initial stages of the follicle growth do not depend on gonadotropin stimulation.
Normally, only one follicle completes maturation in each cycle and ruptures to release its secondary oocyte.
The optimal conditions of the follicle growth are provided by the blood-follicular barier, which consists of endothelial cells of capillaries of the theca, endothelial basal lamina, interstitial elements of theca, basal lamina of the follicle epithelium, the follicle cells and the zona pellucida.
Ovulation – is the process by which a secondary oocyte, surrounded by the cells of corona radiata is released from the mature follicle. The oocyte firmly adheres to the fimbriae of the utrine tube and is actively transported by ciliated epithelium, preventing its passage into the peritoneal cavity. At this time the oocyte is arrested in the metaphase of the first meiotic division. The ovulation is mediated by the luteinizing hormone of hypophysis.

Thecocytes (interstitial cells) and stratum granulosum produce estrogen hormones (estradiol, estron and estriol). Estrogen provides the development of sexual characteristics (enlargement of pelvis; development of mammary glands, uterus,

epoophorons; woman pattern of hair distribution; beginning of menstruation) and controls the first phase of menstrual cycle (regeneration and proliferation phases).

After the ovulation, the rests of mature follicle (granular cells and thecal cells) are transformed into the temporary endocrine gland – **corpus luteum**.

The development of corpus luteum consists of four stages:

- the first stage – proliferation and vascularization
- the second stage – glandular metamorphosis
- the third stage – blossom
- the fourth stage – regression.

The stage of proliferation and vascularization. After the rupture of mature follicle, bleeding from the capillaries in the theca interna into the follicular lumen leads to formation of the **corpus hemorrhagicum** with a central clot. The clot is rapidly substituted by connective tissue. The granulosa layer is penetrated by several blood capillaries.

The stage of glandular metamorphosis. Cells of the granulosa and theca interna layers differentiate into granulosa luteal and theca luteal cells. The luteal cells are filling with lipid droplets, that gives them a yellow color.

The blossom of corpus luteum. The luteal cells start to produce progesterone. Progesterone controls the phase of secretion of menstrual cycle, prepare the endometrium for the implantation of developing zygote. Progesterone is essential for supporting the pregnancy during first 3-4 month. If fertilization and implantation do not occur, the corpus luteum remains active for 12-14 days. In this case it is called **the corpus luteum of menstruation**.

If fertilization and implantation occurs the functioning of corpus luteum lasts 11-12 weeks. In this case it is called **the corpus luteum of pregnancy**.

The stage of regression. The luteal cells decrease in size and undergo autolysis. The connective tissue of central scar grows, forming the **corpus albicans**. The corpus albicans sinks deeper into the ovarian cortex as it slowly disappears over a period of five months.

Atrretic follicles are formed as a result of that only some of the follicles, which start to growth, complete their maturation. Most of them undergo degeneration – **atresia**. In case of atresia, the oocyte dies and the zona pellucida remains in the center of follicle. The process of atresia is controlled by the hormone donadocrinin (the analog of inhibin of testes).

There is one more hormone produced by the ovaries – relaxin. It is considered to soften pubic symphysis and facilitate cervical dilatation during childbirth.

Oogenesis – is the process of development of the female gonads. Oogenesis consists of three periods:

1. proliferation
2. growth
3. maturation

The period of proliferation lasts from the 2nd to the 5th month of intrauterine development. In this period the primordial germ cells (oogonia) undergo **mitotic** division and reach the number of about 7 millions cells. The primordial germ cells are of extragonadal origin and migrate from the yolk sac into the cortex of embryonic gonad. About two months before the birth the most part of these oogonia die. The remaining surviving oogonia enter meiosis I and become the primary oocytes. But the first meiotic division is not complete, because the process is **arrested at the diplotene stage of meiotic prophase.**

The period of growth starts from the 3rd month of intrauterine development. In this period the primary oocyte of primary follicle grows to the primary oocyte of mature follicle. The oocyte increases in size, becomes surrounded by the follicle cells. The oocyte stays in the meiotic resting phase called the **dictyotene**. Girls are born with the primary oocytes. The primary oocytes remain arrested in dictyotene for 12 to 50 years.
In puberty oocytes undergo the following, so-called "big growth". The oocyte increases in size, cumulates yolk. The zona pellucida and corona radiata are formed and surround the oocyte. The zona pellucida consists of glycoprotein complexes. Microvilli of the follicular cells pass through the zona pellucida and adhere to the oocyte surface. Above the zona pellucida the cells of corona radiata and cumulus oophoron are located.

The period of maturation starts when the oocyte resumes meiosis, starting from the prophase I. The first meiotic division results in the formation of two cells: the first big cell – is the secondary oocyte, containing almost all cytoplasm of maternal cell; the second cell – is the first polar body. Each of these cells contain the diploid number of chromosomes. The second meiotic division starts just after the first one, but it is arrested at the metaphase and resumes only **after fertilization**. The secondary oocyte is released from the follicle in the process of ovulation and enters the uterine tube, where it contacts with spermatozoids.
The meiosis II occurs **only in case of fertilization** and again results in the formation of two cells: the first one – is the mature **haploid** oocyte; the second one – is the second polar body.

The uterine tubes (oviducts) are paired tubes that extend bilaterally from the uterus towards the ovaries. The wall of uterine tube consists of three layers:

1. the mucosa;
2. the muscularis
3. the serosa.

The mucosa consists of the epithelium and the lamina propria. Epithelium of the mucosa (simple columnar ciliated epithelium) contains ciliated cells and mucus-secreting cells. The lamina propria is formed by loose connective tissue.

The muscularis consists of two layers of the smooth muscle: inner circular and outer longitudinal.
The serosa consists of loose connective tissue covered by mesothelium.

Each uterine tube could be divided into four anatomical parts:

- **The infundibulum** is the funnel-shaped segment of the tube adjacent to the ovary. The proximal end communicates with the ampulla. Fringed extensions, or fimbriae, extend from the mouth of the infundibulum toward the ovary. In the moment of ovulation the fimbriae increase in volume and sweep the oocyte. The ciliated cells lining and peristaltic contraction of the uterine tube provide the transport of the oocyte along it.
- **The ampulla** is the longest segment of the tube, constituting about two thirds of the total length, and is the site of fertilization.
- **The isthmus** is the narrow, medial segment of the uterine tube adjacent to the uterus.
- **The uterine or intramural part**, measuring about 1 cm in length, lies within the uterine wall and opens into the cavity of the uterus.

The functions of the uterine tubes are:

- providing conditions for the capacitation of spermatozoids;
- providing the environment, favorable for fertilization;
- in the uterine tubes the initial stages of embryogenesis occur.

Uterus – is the muscular organ which serves for the development of fetus.
The wall of the uterus consists of three layers:

1. the mucosa (endometrium);
2. the muscularis (myometrium);
3. the serosa (perimetrium).

The **endometrium** is the most dynamic layer of the uterus, since it undergoes the hormone-induced changes during the menstrual cycle. The endometrium consists of two layers: **basal layer** (stratum basale) and **functional layer** (stratum functionale). The functional layer proliferates and degenerates during the menstrual cycle. The endometrium is covered by simple columnar epithelium with underlying lamina propria. The lamina propria contains the **uterine glands**. The mouths of the uterine glands are surrounded by ciliated cells.
The uterine glands extend through the whole thickness of the endometrium and even reach the surficial layers of myometrium. They are simple tubular glands.
The lamina propria is formed by loose connective tissue. Some connective tissue cells of the lamina propria diffentiate into the **decidual cells.** The decidual cells are the large rounded cells, containing inclusions of glycogen and lipoproteins in their cytoplasm. The number of decidual cells increases during the placenta formation in pregnancy.
The myomterium is formed by the smooth muscle cells, containing processes. The myometrium consists of three layers:

1. **the outer (submucosal)** layer; the smooth muscle bundles are oriented parallel to the long axes of the uterus;
2. **the middle layer (stratum vasculare)** contains numerous blood and lymphatic vessels; the smooth muscle bundles are oriented in a circular or spiral pattern;
3. **the inner (supravascular) layer**; the smooth muscle bundles, like in the outer layer, are oriented parallel to the long axis of the uterus.

   Loose connective is located between the muscular layers of the myometrium.

   Because of the absence of submucosa, the myometrium is immediately attached to the basal layer of the endometrium.

The perimetrium – is the serous covering of the uterus. The perimetrium consists of mesothelium and underlying thin layer of loose connective tissue. The perimetrium covers the entire posterior surface of the uterus but only part of the anterior surface. The remaining part of the anterior surface consists of connective tissue or adventitia.

The mucosa of the cervix uteri differs dramatically from the rest of the uterus. The portion of the cervix that projects into the vagina, the **vaginal part** or **ectocervix**, is covered with a stratified squamous epithelium. The cervical canal is covered by mucus-secreting columnar epithelium. The mucosa of the cervical canal forms folds and two longitudinal crests. Besides this, it contains several branched mucus-secreting glands. The muscular layer of the cervix is formed by well-developed circular layer of the smooth muscle, which forms the **sphincter uteri**.

The vagina – is a fibromuscular tube, which joints the internal reproductive organs to the external environment.

The vaginal wall consists of the three layers:

1. the mucosal layer;
2. the muscular layer;
3. the adventitial layer.

The mucosa is lined with stratified squamos non-keratinized epithelium, consisting of three layers:

1. the basal layer
2. the transitional layer
3. the functional (outer) layer

The outer layer is called the functional layer, because it undergoes the rhythmical changes during the menstrual cycle. Cells of the functional layer contain keratohyaline granules, which store glycogen. The breakdown of glycogen leads to the formation of lactic acid, that’s why vaginal mucus has acidic pH and bactericidical action. The vaginal wall doesn’t contain glands. Numerous elastic fibers are present immediately below the epithelium, and some of the fibers extend into the muscular layer. The lamina propria is infiltrated by lymphocytes.

The muscular layer is formed mainy by the longitudinally arranged smooth muscle bundles, but in the middle portion a small amount of the circularly arranged smooth muscle bundles can be found.

The adventitia is formed by loose connective tissue.

The external genitalia (vulva) unclude:

1. the vestibule;
2. the labia minora and the labia majora;
3. clitoris.

The vestibule is lined with stratified squamos nonkeratinized epithelium. The large paired vestibular glands (Bartholin's glands) are present in the lateral wall of the vestibule. These tubuloalveolar glands secrete lubricating mucus.

The labia minora – are paired hairless folds of the skin. The core of connective tissue within each fold contains numerous elastic fibers, blood vessels and sebaceous glands.

The labia majora are two large longitudinal folds of the skin, covered with pubic hair. They contain a large amount of subcutaneous adipose tissue. Sebaceous and sweat glands are present in the labia majora.

The clitoris is an erectile structure that is homologous to the penis. Its body is composed of two small erectile bodies, the corpora cavernosa; the glans clitoris is a small, rounded tubercle of erectile tissue. The skin over the glans is very thin.

The ovarian-menstrual cycle. The cyclic changes of the functional layer of endometrium are called menstrual cycle. The ovarian cycle is the cyclic changes in secretion of estrogen and progesterone by ovaries.

The duration of the menstrual cycle is counted from the first day of previous menstruation to the first day of the next one. In most women the cycle normally repeats every 28 days and consists of the several phases:

1. desquamative phase (menstrual)
2. regenerative phase
3. proliferative phase
4. relative rest phase
5. secretory phase

The menstrual period. At the **menstrual (desquamative)** phase (1-3rd days of the cycle) desquamation of the functional layer of endometrium occurs. It continuous until only the basal layer remains. The blood vessles of the endometrium have an unusual structure: there are distinguished the spiral arteries and the straight arteries. The spiral arteries supply the functional layer of endometrium, the straight arteries – the basal layer. Before the menstruation, the periodic contraction of the wall of the spiral artery causes the ischemia and the following necrosis of the functional layer. When the necrotizing endometrium undergoes desquamation, the blood vessels start bleeding. These changes are caused by the decline of sex hormone levels: the corpus luteum has already stopped to produce progesterone; the follicle growth hasn't started yet so estrogen is not produced too.

The postmenstrual period. The regenerative phase (3-5th days of cycle) starts with the growth of follicles and production of estrogen by them. Estrogen provides the regeneration of the functional layer of the endometrium. At the end of the menstrual phase, the endometrium consists of a thin band of connective tissue, about 1 mm thick, containing the basal portions of the uterine glands and the lower portions of the spiral arteries. This layer is the basal layer. The epithelial cells of basal portions of the uterine glands migrate to cover the denuded endometrial surface.

The proliferative phase (5-11th days of cycle). The epithelial cells proliferate rapidly, which results in that the endometrium becomes 2-3 times thicker (3mm). Stromal cells proliferate and secrete collagen and ground substance. Spiral arteries lengthen and the endometrium is reestablished. This phase, like a previous one, is controlled by estrogen.

The relative rest phase (11-14th days of cycle). At this phase the endometrium is completely reestablished. The ovaries continue to produce estrogen. In the end of this phase the ovulation occurs.

During the whole postmenstrual phase the ovaries produce estrogen, while the pituitary gland actively secretes the follicle-stimulating hormone.

The premenstrual period. The secretory phase (15-28th days of cycle). These phase starts after the ovulation and is regulated by progesterone. The endometrium becomes two times thicker than in the previous phase (5-6mm). The growth seen at this stage results from hypertrophy of the epithelial cells, an increase in vascularity, and edema of the endometrium.

Under the influence of progesterone, the uterine glands enlarge and and their lumina become sacculated as they fill with secretory products. The gland epithelium produce mucoid liquid, which is rich in glycogen. The stromal cell are transformed into the decidual cells. Decidual cells are the large light cells, which are rich in glycogen and lipids.

At the secretory phase there are distinguished two zones in the functional layer of endometrium:

1. the outer compact zone, containing decidual cells;
2. the inner spongy zone, containing enlarged glands.

All the changes, occurring at the secretory phase prepare the endometrium for the implantation of the fertilized oocyte. This phase is regulated by progesterone. Progesterone is produced by the corpus luteum, which develops from the rests of an ovulated follicle under the influence of pituitary luteinizing hormone. Progesterone maintains the edematous endometrium and prevents it from desquamation. If pregnancy doesn't occur, the corpus luteum dies. The decline of the progesterone level causes the start of the menstrual period. With the absence of progesterone, the follicle growth and production of estrogen starts. Estrogen stimulates the regeneration and proliferation of the functional layer and the cycle repeats.

CENTRAL NERVOUS SYSTEM

The central nervous system provides the communication of the body with external environment, the regulation and coordination of functioning of all its organs and systems.

There are two classifications of organs of the nervous system:

1. anatomic; according to this classification the nervous system is divided into the central and the peripheral. The central nervous system includes brain and spinal cord; the peripheral – nerve ganglions, nerve trunks and nerve endings.
2. physiological; according to which the nerve system is divided into the somatic and the autonomic (vegetative). The somatic nervous system provides innervation of the skeletal muscle; the autonomic nervous system innervates inner organs, vessels and glands.

Cerebral cortex contains nerve cell bodies, axons, dendrites, and central glial cells, and it is the site of synapses. In a freshly dissected brains, the cerebral cortex has a gray color, hence the name **gray matter**. In addition to the cortex, islands of gray matter called **nuclei** are found in the deep portions of the cerebrum and cerebellum. The **white matter** contains only axons of nerve cells plus the associated glial cells and blood vessels. These axons travel from one part of the nervous system to another. Whereas many of the axons going to, or coming from, a specific location are grouped into functionally related bundles called **tracts**.

The cerebral cortex is the outer covering of brain, which is formed by the gray matter. The thickness of cerebral cortex is approximately 3mm. It reaches the maximal development in precental gyrus, where its thickness is 5mm.

The cerebral cortex consists of more than 50 millions of nerve cells.

According to morphological features, the neurons of the cerebral cortex are divided into the pyramidal and the extrapyramidal.

The pyramidal neurons have the characteristic pyramidal shape; they are from 10 to 120 mcm high.

There are distinguished the following types of extrapyramidal neurons:

1. basket neurons;
2. spiny stellate neurons;
3. arachnoid neurons;
4. neurons with the axonal brush;
5. axo-axonal neurons;
6. neurons with the double bouquet of dendrites;
7. fusiform neurons with long horizontal axons.

This classification was based on the number, morphology and the type of branching of nerve cell processes.

In cerebral cortex neurons and their processes are arranged in layers. Each layer is characterized by the prevalence of one cell type. The parcellation of the nerve cells into layers is called *cytoarchitectonics.*

There are distinguished six layers of the cerebral cortex:
1. molecular layer;
2. outer granular layer;
3. outer pyramidal layer;
4. inner granular layer;
5. ganglionic (inner pyramidal) layer;
6. multiform layer.

The molecular layer consists predominantly of the fusiform cells with long horizontal dendrites and descending axons, which form horizontal collaterals.

The outer granular layer is formed by small (about 10mcm) cells, which can be round, polygonal, stellate or pyramidal in shape.

The outer pyramidal layer is thin. It is formed by pyramidal cells, which are from 10 to 40mcm in size. The apex of pyramidal cell is always directed towards the surface of the cerebral cortex, the basis – towards the white matter. The dendrites extend from apex and lateral surfaces of the pyramidal neuron, while the axon extends from its basis. The axons of pyramidal neurons form myelinated nerve fibers, which enter the white matter.

The inner granular layer is formed by small stellate neurons.

The ganglionic layer contains the giant pyramidal neurons, which are 120mcm high and 80mcm wide. These cells were discovered by Ukrainian scientist V.O. Bets in 1874. The axons of the Bets cells go to the motor nuclei of the brain and the spinal cord.

The multiform layer contains neurons of various shapes, predominantly fusiform cells.

The molecular and the multiform layers predominantly perform associative function. The granular layers are formed mostly by sensory neurons, the pyramidal and ganglionic layer – by motor neurons.

In the area of precentral gyrus, which is the **primary motor cortex**, the pyramidal, the ganglionic and the multiform layers reach the maximal development. Such type of cortex is called **agranular cortex**.

The sensory areas of cortex, where the afferent conduction pathways of sensory organs end, are characterized by the maximal development of the granular layers. Such type of cortex is called **granular cortex**.

The cortical module is the structural and functional unit of neocortex. The cortical module can be imagined as a vertical column, about 300mcm in diameter. The cortico-cortical fiber, associated with the complex of excitatory and inhibitory neurons, is located in the center of each column. The cortico-cortical fiber is the axon of the Bets cell of the same (associative fiber) or the opposite (commissural fiber) hemisphere. The cortico-cortical fibers form synaptic endings in all layers of the cortex. Besides cortico-cortical fiber, the module contains two afferent thalamo-cortical fibers, which form synapses with spiny stellate neurons of the IV layer of the cortex and with the basal dendrites of pyramidal cells.

The excitatory elements of the module include the spiny stellate neurons of focal and diffuse types.

The inhibitory neurons of the module are the neurons with axonal brush, axo-axonal neurons, basket neurons and neurons with double bouquet of dendrites.
The axons of pyramidal cells contact with three modules within the same hemisphere and two modules of the opposite hemisphere.
The cerebral cortex contains about 3 millions modules.
Among the nerve fibers of the cerebral cortex the following types are distinguished:

- associative fibers, which connect the areas of cortex within the same hemisphere;
- commissural fibers, which connect the areas of cortex of opposite hemispheres;
- projection fibers, which connect the cortex with the lower parts of brain and with the spinal cord.

Within the cerebral cortex the nerve cell processes are arranged in tangential bundles, so-called stripes, located between the layers of nerve cell bodies. The arrangement of nerve fibers in layers is called *myeloarchitectonics*. There are distinguished the following layers of nerve fibers:

- tangential layer
- dysfibrous layer
- suprastriate layer
- external stripe of Baillarger
- interstriate layer
- internal stripe of Baillarger
- infrastriate layer

The white matter, located beneath the gray matter, contains aggregations of multipolar neurons called **basal ganglia** (basal nuclei).

Cerebellum is a region of brain that plays important role in coordination of voluntary movements and maintenance of balance and posture. The white matter lies beneath the cerebellar cortex and contains subcortical cerebellar nuclei.

The cerebellar cortex consists of three layers:

1. molecular layer;
2. Purkinje cell layer (ganglionic);
3. granule cell layer.

The molecular layer, the outermost, is formed by cell bodies of the basket cells and the stellate cells. The *basket cells* are located in the lower third of the molecular layer. The basket cells are small, irregular in shape neurons; their dendrites branch longitudinally to the gyrus of cerebellum. The long axons of the basket cells pass in horizontal direction across the gyrus above the pyriform neurons (Purkinje cells). These axons give a rise to collaterals, which descend to the pyriform cells and together with other fibers form the **baskets of cerebellum**.
The generation of impulse in the axons of basket cells exerts inhibitory influence on the pyriform neurons (Purkinje cells).
The stellate neurons of the molecular layer are divided into the small and the large.

The processes of small stellate neurons contact with the dendrites of pyriform cells of the Purkinje cell layer.
The large stellate neurons have long and extensively branched dendrites and axons. The axons of large stellate neurons connect with the dendrites of Purkinje cells; some of them take part in formation of the baskets of cerebellum.
The neurons of the molecular layer are interneurons, which conduct inhibitory nerve impulses to the Purkinje cells.

Purkinje cell layer (ganglionic) consists of the one layer of large pyriform neurons, so-called Purkinje cells. The apex of Purkinje cell gives a rise to three dendrites, which have radial direction and give numerous branches. The axon extends from the wide basis of the Purkinje cell. The axons of Purkinje cells leave the cerebellar cortex and form the first link of the efferent inhibitory pathways.

The granule cell layer adjoins the white matter of cerebellum. The granule layer contains the several types of neurons:

1. granule cells;
2. stellate neurons;
3. neurons with long axons;
4. neurons with short axons;
5. horizontal cells.

The axons of granule cells pass into molecular layer, where they are divided into two branches, which are parallel to the gyrus. The axons of granule cells form numerous synapses with the dendrites of Purkinje cells, basket and stellate cells, thereby through the axons of granule cells the excitatory nerve impulses are conducted to numerous Purkinje cells. The widely branched dendrites of granule cells remain bird's leg; they form synapses with mossy fibers, thereby forming **glomerules of cerebellum.**

The afferent impulses are conducted to neurons of cerebellar cortex through the **mossy and climbing fibers.** The mossy fibers pass as a part of olivocerebellar and pontocerebellar tracts. Through the granule cells the mossy fibers conduct excitatory nerve impulses to the Purkinje cells.
The climbing fibers enter the cerebellar cortex as a part of vestibulocerebellar tract. Then the climbing fibers pass through the granule layer and conduct excitatory impulses immediately to the Purkinje cells. Degeneration of the Purkinje cells leads to cerebellar dysfunction.

The excitatory nerve impulses, conducted to cerebellum through the mossy fibers are realized by the granule cells and glomerules of cerebellum. The inhibition is provided by the basket cells of the molecular and granule layers. The stellate neurons with long axon provide the connection between different areas of cerebellar cortex. The stellate neurons with short axon are situated near the Purkinje cell layer. Their branched dendrites form synapses with the axons of granule cells; their axons pass into the granular layer to the glomerules of cerebellum and form synapses with terminal branches of the dendrites of granule cells above their synapses with the mossy fibers. This means that excitation of stellate neurons can block the nerve impulses conducted through the mossy fibers.

The fusiform horizontal cells have elongated cell body, from which two horizontal dendrites extend to the overlying layers. Their axons give collaterals to the granule layer and the white matter.

The cerebellar cortex contains glial cells. The granule layer contains fibrous and protoplsmatic astrocytes. The oligodendrocytes and the glial macrophages are found in all layers of cerebellar cortex. The Purkinje cell layer contains glial cells with dark nuclei, which form the Bergmann fibers supporting the branching of dendrites of the Purkinje cells.

Spinal cord is the part of central nervous system located within the vertebral canal. It is divided into 31 segment, each of them is connected to a pair of spinal nerves.

In a cross section, the spinal cord exhibits a butterfly-shaped inner substance, the gray matter, and a surrounding outer white substance.

The anterior median fissure and dorsal septum divide the spinal cord into two symmetric parts. The gray matter forms projections, which are called horns. There are distinguished anterior (ventral) horns, lateral horns and posterior (dorsal horns). The posterior (dorsal) roots enter the posterior horns, from the anterior horns the anterior (ventral) roots extend. The spinal canal is located in the center of gray matter.

The white matter is formed by myelinated and unmyelinated nerve fibers, which form the conducting tracts along the spinal cord. The white matter contains three pairs of funiculi: anterior funiculus, lateral funiculus and posterior funiculus.

The gray matter of spinal cord is formed by nerve cell bodies, unmyelinated nerve fibers and neuroglia. The main constituent of the gray matter is multipolar neurons. There are three types of multipolar neurons of the spinal cord:

- radicular neurons;
- fascicular neurons;
- interneurons.

Radicular neurons, their axons leave the spinal cord as a part of ventral roots.

Fascicular neurons, their axons pass into white matter and conduct nerve impulses from nuclei of the spinal cord to other segments of spinal cord or to brain, thereby forming the conducting tracts.

Interneurons, their processes form synapses within the gray matter of spinal cord.

The anterior horns are formed by large multipolar neurons. The main part of them is radicular motor neurons. These neurons form ventromedial, ventrolateral, dorsomedial, dorsolateral and central pairs of nuclei. The medial groups of nuclei innervate the trunk muscles. The lateral groups of nuclei are the most developed in cervical and lumbar intumescence and innervate the muscles of extremities.

The posterior horns are formed by thoracic nucleus, nucleus proprius, substantia spongiosa and substantia gelatinosa. The posterior horns contain interneurons of two types:

- **associative**, whose axons end within the one side of the spinal cord;
- **commussural,** whose axons end at the opposite side of spinal cord.

The interneurons of substantia spongiosa and substantia gelatinosa together with scattered interneurons provide connection between the sensory neurons of spinal ganglia and the motor neurons of anterior horns.

The nucleus proprius is located in the center of posterior horn. It consists of interneuros, whose axons pass through the anterior white commissure to the opposite side of spinal cord into the lateral funiculus of the white matter, where they become a part of ventral spinocerebellar and spinothalamic tracts.

The thoracic nucleus (Clarke) consists of large interneurons with widely branched dendrites. Their axons enter the lateral funiculus of the white matter of the same side and ascend to cerebellum as a part of dorsal spinocerebellar tract.

The lateral horns contain intermediolateral nucleus, formed by associative neurons of sympathetic reflex arch. The axons of neurons of the intermediolateral nucleus are located in so-called intermediate zone between the dorsal and the ventral horns; they ascend to the cerebellum as a part of ventral spinothalamic tract.

The bundles of nerve fibers, which provide the connection between different parts of nervous system are called conducting tracts (pathways) of spinal cord.

Spinal ganglion lies on the dorsal root of spinal nerve. The spinal ganglion is surrounded by a connective tissue capsule, from which thin septa extend into the parenchyma. The main functional unit of the spinal ganglion is pseudounipolar neuron. The cell bodies of these neurons are concentrated in the center of ganglion; the peripheral part is occupied by nerve cell processes. The dendrites of pseudounipolar neurons become a part of mixed spinal nerve and end as peripheral receptors. Their axons form the dorsal (sensory) roots, which conduct impulses to the spinal cord. The neurons of spinal ganglia are surrounded by the layer of glial cells, which are termed mantle cells or satellite cells.

SENSORY SYSTEMS. SENSORY ORGANS

Sensory system is a group of organs and structures, which provide the detection of different stimuli from external environment. Sensory system – is the analyzers of external and internal environment, which provide the adaptation of the organism to specific conditions.

Each analyzer consists of three parts:

- peripheral (receptive) part – is the organs, where the specialized receptive cells are located;
- conductive part – the chain of interneurons, through which the nerve impulse is conducted from receptors to the cortical centers;
- central part – the particular areas of brain cortex.

The types of receptors according to the nature of irritation:

- mechanoreceptors
- chemoreceptors
- photoreceptors
- thermoreceptors
- pain receptors.

Classification of sensory organs

The sensory organs are divided into three types on the basis of structure and function of their peripheral (receptive) part.

The first type is sensory organs, whose receptors are performed by specialized neurosensory cells (organ of vision, olfactory ogan), which transform external stimuli into nerve impulse.

The second type is sensory organs, whose receptors are the epithelial cells (sensoepithelial). They conduct the transformed stimulus to dendrites of the sensory neurons, which generate nerve impulse (organ of hearing, balance, taste).

The third type is the organs of proprioceptive (skeletal muscles, skin) and visceral sensory systems. Their peripheral parts consist of different incapsulted and non-incapsulated receptors (touch, pressure).

ORGAN OF VISION

Organ of vision – the eye – is the peripheral part of visual analyzer, in which the reception is provided by the neurons of retina. It consists of the eyeball and the accessory structures such as eyelids, lacrimal glands and extraocular muscles.

The eyeball consists of three layers or coats:

1. outer fibrous layer (corneoscleral coat);
2. vascular coat or uvea (choroid, iris, cilliary body)

3. retina

The layers of the eyeball and their derivatives form three functional apparatus:

1. dioptric apparatus (cornea, aqueous humor of anterior and posterior chambers, lens, vitreous body)
2. accommodative apparatus (iris, cilliary body)
3. receptive apparatus (retina).

The fibrous coat consists of two parts – opaque sclera and transparent cornea. The transitional zone between cornea and sclera is called **limb.**

Sclera is formed by dense regular connective tissue containing bundles of collagen fibers, between which fibroblasts and occasional elastic fibers are found. The sclera is divided into three rather ill-defined layers:

- the episcleral layer (episclera), the external layer, is the loose connective tissue adjacent to the periorbital fat.
- the substantia propria (sclera proper, also called Tenon's capsule), is the investing fascia of the eye and is composed of a dense network of thick collagen fibers.
- the suprachoroid lamina (lamina fusca), the inner aspect of the sclera, is located adjacent to the choroid and contains thinner collagen fibers and elastic fibers as well as fibroblasts, melanocytes, macrophages, and other connective tissue cells.

The sclera is covered by conjunctiva.

The dioptric apparatus of the eye

Cornea – is a transparent coat, referred to the dioptric apparatus of the eye. The five layers of the cornea are seen in a transverse section:

1. corneal epithelium;
2. anterior basement membrane (Bowman's membrane);
3. corneal stroma;
4. posterior basement membrane (Descemet's membrane);
5. corneal endothelium (posterior epithelium).

The corneal epithelium is stratified squamos nonkeratinized epithelium, which lie on the basal lamina. The epithelial cells adhere to neighboring cells via desmosomes. The corneal epithelium contains numerous free nerve endings, which explains the corneal reflex. The corneal epithelium has a remarkable regenerative capacity.

The anterior basement membrane (Bowman's membrane) lies beneath the basal lamina. The anterior basement membrane is an external part of corneal stroma. It takes part in protection of the eye from traumatic injuries and penetration of bacteria. The electron microscope examination reveals fibrillar structure of the anterior basement membrane.

The corneal stroma composed of about 60 thin lamellae. Each lamella consists of parallel bundles of collagen fibers. The collagen fibrils in each lamella are arranged at approximately right angles to those in the adjacent lamellae. The flattened fibroblasts are located between the lamellae. The ground substance contains corneal proteoglycans, which are sulfated glycosaminoglycans —

chiefly, keratan sulfate (lumican) and chondroitin sulfate. The components of ground substance and regular arrangement of collagen bundles provide the transparency of cornea. The corneal stroma does not contain blood vessels.

The posterior basement membrane (Descemet's membrane) is the basal lamina of corneal endothelial cells. It is vitreous light-refracting membrane. It consists of two layers – the external elastic and the internal cuticular. The characteristic features of the posterior basement membrane are strength, resistance to chemical agents and purulent effluent in case of corneal ulcer.

The corneal endothelium is a single layer of squamos cells, covering the surface of the cornea that faces the anterior chamber. It separates the corneal stroma from the aqueous humor of anterior chamber of the eye.

The Bowman's and the Descemet's membranes take part in metabolism of water; the metabolic processes in cornea are provided by diffusion of nutrients from the anterior chamber of the eye.

In case of inflammatory reactions, the blood capillaries and leukocytes migrate to the corneal stroma from limb, which leads to keratinization and opacity of the cornea and formation of leukoma.

Lens – is a transparent biconvex structure in the eye, which is connected to the ciliary body via fibers of the zonula ciliaris. The contraction of ciliary muscles causes the change of shape of the lens. The lens, by changing shape, functions to change the focal distance of the eye so that it can focuse on objects at various distances. The adjustment of the lens is known as **accommodation**. The lens is covered with a transparent lens capsule. The anterior wall of lens, under the capsule, is lined with simple squamos epithelium (lens epithelium). At the area of equator the epithelial cells elongate and form the cambial zone, which supply with new cells anterior and posterior portions of the lens. These cells transform into the **lens fibers**.

The proper substance of lens constitutes the bulk of the lens. It consists of the lens fibers, which are the modified cells of the lens epithelium. The central and transitional lens fibers do not contain nuclei and compose the dense **nucleus of lens**. The lens cortex is formed by the lens fibers, which contain nuclei. The lens fibers have a shape of hexahedral prim; their cytoplasm contains the transparent protein – **crystallin**.

Vitreous body – is a transparent, jelly-like substance, which is located between the lens and the retina. On histological specimen the vitreous body reveals reticular structure. The main portion of the vitreous body is a homogeneous gel containing approximately 99% water (the vitreous humor), collagen and glycosaminoglycans. The hyaloid canal (or Cloquet's canal), which is not always visible, runs through the center of the vitreous body from the optic disc to the posterior lens capsule. It is the remnant of the pathway of the hyaloid artery of the developing eye.

The vascular coat (uvea) consists of four layers:

1. suprachoroid lamina is located adjacent to the sclera. It is formed by loose connective tissue, containing numerous elastic fibers, fibroblasts and pigment cells (melanocytes);
2. choroid lamina consists of arteries and veins, between which loose connective tissue with pigment cells is located. It also contains bundles of the smooth muscles;
3. choriocapillary layer contains sinusoidal blood capillaries, between which the fibroblasts are located;
4. Bruch's membrane – a thin strip, which lies between the choriocapillary layer and the pigment layer of retina. Three layers are identified in Bruch's membrane: elastic layer, fibrous layer and basal lamina of pigment epithelium (cuticular layer).

Accommodative apparatus

Ciliary body is a derivate of both the vascular coat and the retina. It provides fixation and change of curvature of the lens, thereby taking part in the act of accommodation.

In a cross-section the ciliary body appears as triangle with a basis facing towards the anterior chamber of the eye. The ciliary body is divided into two layers:

1. ciliary corona, the inner;
2. ciliary ring, the outer.

From the ciliary corona the ciliary processes extend towards the lens; from the ciliary processes the fibers of zonulae ciliaris arise.

The main part of ciliary body is formed by the ciliary muscle, which takes an important part in accommodation. The ciliary muscle consists of bundles of the smooth muscle spread out in three directions – longitudinal, radial and circular. Contraction of the ciliary muscle causes relaxation of the zonular fibers. As a result, the convexity and refractivity of lens increase.

Iris is a derivate of the uvea. It arises from the anterior border of the ciliary body and is attached to the sclera about 2 mm posterior to the corneoscleral junction; it is a border between anterior and posterior chambers of the eye. The pupil is the central aperture of the iris. The iris consists of five layers:

1. anterior epithelium is the continuation of the corneal endothelium; it cinsists of one layer of flattened polygonal cells;
2. outer limiting (avascular) layer – is connective tissue, containing numerous fibroblasts and pigment cells; the differences in number and localization of pigment cells determine the color of the eye;
3. vascular layer contains numerous blood vessels surrounded by loose connective tissue with pigment cells (melanocytes); the sphincter pupillae muscle and the dilatator pupillae muscle are situated in this layer; the sphincter pupillae muscle is located near the papillary margin of the iris, the dilatator pupillae muscle – near the cilliary margin of the iris;
4. inner limiting layer has the same structure as the outer limiting layer;

5. posterior pigment epithelium is continuation of the epithelium of retina; it covers the ciliary body and processes too.

The iris functions as a diaphragm, ensuring that only the appropriate amount of light enters the eye.

Receptive apparatus of the eye

Retina consists of ten layers:

1. retinal pigment epithelium (RPE);
2. photoreceptor layer of rods and cones;
3. outer limiting membrane;
4. outer nuclear layer;
5. outer plexiform layer;
6. inner nuclear layer;
7. inner plexiform layer;
8. ganglion cell layer;
9. layer of optic nerve fibers;
10. inner limiting membrane.

The layers of retina are formed by nerve tissue and consist of neurons and glial cells.

The retinal pigment epithelium – is the outermost layer of retina that consists of one layer of hexahedral pigment epithelial cells. Their cytoplasm contains 1-2 nuclei; about 8-10 processes project for a short distance between the photoreceptor cells of the rods and cones. The pigment cells contain melanosomes, which migrate to the processes under intense illumination and return to cell body in the dark.

The pigment-containing processes of these cells surround the processes of photoreceptor cells, absorb light passing through the neural retina to prevent reflection and resultant glare. Besides this, the pigment epithelium serves as a major component of the blood-retina barrier, and phagocytoses and disposes of membranous discs from the rods and cones of the retinal photoreceptor cells etc.

The photoreceptor layer consists of modified dendrites of bipolar nerve cells called rods (the first cell type) and cones (the second cell type). By rods and cones the neurosensory cells perceive the light rays.

The rod and cone photoreceptors consist of the outer and the inner segments, connected together via the connecting cilium. The outer segment of the rod is cylindrical in shape and contains numerous closed membranous discs. These membranous discs contain the visual pigment – **rhodopsin**, which is composed of the protein opsin and the vitamin A aldehyde – A-retinal.

The outer segment of cone is conical in shape, it is wider and shorter than in rod, and contains half-discs, which are formed by the invagination of plasmolemma; the one end of the disc is closed, while the another is not. Membranes of the cone discs contain the visual pigment – **iodopsin,** which chemically differs from rhodopsin.

The connecting cilium is composed of nine peripheral microtubule doublets extending from a basal body.

The inner segment contains numerous mitochondria, endoplasmic reticulum and enzymes. The inner segment of cone differs from the inner segment of rod by the presence of ellipsoid – a lipid drop surrounded by mitochndria.

There are approximately 130 millions rods and 7 millions cones in human retina. Rods are the receptors of grey tones (a "black and white picture"); the cones are more sensitive to red, green and blue regions of visual spectrum. There are three types of cones containing different visual pigment molecules that are activated by the absorption of light at the blue (420 nm), green (531 nm), and red (588 nm) ranges in the color spectrum.

The mechanism of photoreception is connected with transformation of iodopsin and rhodopsin molecules under the action of light energy. It triggers the chain of chemical reactions, which change the permeability of plasma membranes of rods and cones thereby giving a rise to action potential. After the decay of visual pigment, it is resynthesized. The resynthesis of visual pigment occurs in the dark and in the presence of vitamin A. The lack of vitamin A in food can cause disorder of twilight vision (moon-blindness or nyctalopia). The color blindness (daltonism) is explained by genetically determined absence of one or more types of cones.

The outer limiting membrane is formed by glial cells - radial gliocytes, namely their external processes.

The outer nuclear layer is formed by cell bodies of photosensory neurons.

The outer plexiform layer contains the axons of photosensory neurons and the dendrites of bipolar neurons of the inner nuclear layer, which form synapses with each other.

The inner nuclear layer contains cell bodies of bipolar neurons and two types of associative neurons – horizontal and amacrine. Bipolar neurons connect rods and cones with neurons of ganglion layer. Each cone cell contacts with only one bipolar neuron, while each bipolar neuron contacts with several rod cells. Horizontal cells have numerous dendrites, via that they contact with central processes of neurosecretory cells.

The axon of horizontal cells contacts with synaptic structures between photoreceptive and bipolar cell. Here the numerous peculiar synapses are formed. The conduction of nerve impulse through such synapse and further by the horizontal cells can cause an effect of lateral inhibition, which increases the contrast of the image. The similar function is carried out by the amacrine neurons located in the inner plexiform layer. The amacrine neurons do not have axons, but posses the branched dendrites. The cell body of amacrine neuron plays a role of synaptic membrane.

The inner plexiform layer is formed by axons of the bipolar cells of the inner nuclear layer, dendrites of the amacrine cells and dendrites of multipolar nerve cells of the ganglion layer.

The ganglion cell layer is formed by cell bodies of the ganglion cells, which are the largest, multipolar neurons. They constitute the third component of the neuron chain of retina. The axons of ganglion cells unite into a layer of nerve fibers, which form the optic nerve. They run parallel to retinal surface and converge at the optic disc (so-called 'blind spot'), from which they leave the eye as an optic nerve.

The fovea appears as a small depression located at the posterior pole of the optical axis of the eye. Its central region is known as foveola. Except for the photoreceptor layer, most of the layers of the retina are markedly reduced or absent in this region. Here the photoreceptor is composed entirely of cones (approximately 4,000) that are longer and more slender and rodlike than they are elsewhere. In this area, the retina is specialized for discrimination of details and color vision. The macula lutea is the area surrounding the fovea, approximately 5.5 mm in diameter. It is yellowish because of the presence of yellow pigment (xanthophyll). The macula lutea contains approximately 17,000 cones and gains rods at its periphery. Here the retinal cells and their processes, especially the ganglion cells, are heaped up on the sides of the fovea so that light may pass unimpeded to this most sensitive area of the retina.

The inner limiting membrane consists of basal lamina separating the retina from the vitreous body.

Accessory structures of the eye are the eyelids, lacrimal glands and extraocular muscles.

The eyelids are derivates of the skinfolds. The internal surface of the eyelids is covered by mucosa called conjunctiva. The stratified squamos epithelium of conjunctiva contains goblet cells, which secrete mucus. Within each eyelid is dense connective tissue (tarsal plate), the orbicularis oculi muscle, sebaceous glands. Along the edges of eyelids the eyelashes and the apocrine glands of eyelashes are located. The glands of eyelashes are modified sweat glands with straight acini. The excretory ducts of sebaceous glands empty into the infundibulum of eyelash root. The tarsal glands (Meibomian glands) are long sebaceous glands embedded in the tarsal plates, appear as vertical yellow streaks in the tissue deep in the conjunctiva.

The lacrimal apparatus consists of lacrimal glands, lacrimal sac and nasolacrimal duct. Lacrimal glands – are compound serous-secreting tuboalveolar glands, whose secretion consists of 98% of water, 1,5% of sodium chloride, 0,5% of albumins and mucus. Tears contain the bactericidical substance – lysozyme.

The walls of lacrimal sac and nasolacrimal duct are lined with pseudostartified ciliated epithelium; the layer of loose connective tissue lies under the epithelium.

The small branched tubular glands empty into the lacrimal sac. The third, rudimentary, eyelid is located near the medial angle of palpebral fissure. It is covered with stratified squamos epithelium containing mucus-secreting cells. Tears keep the conjunctiva and corneal epithelium moist and wash foreign material from the eye.

The coordinated contraction of extraocular muscles provides movement of the eye within the orbit. Normally, the actions of the muscles of both eyes are coordinated so that the eyes move in parallel (called conjugate gaze). The extraocular muscles have a typical organization of skeletal muscle.

ORGAN OF HEARING AND BALANCE

The functions of organ of hearing and balance are perception of sound, linear and angular accelerations and gravitation. It consists of three divisions: the external ear, middle ear and internal ear.

The external ear consists of:

1. auricle;
2. external acoustic meatus;
3. tympanic membrane.

The auricle consists of elastic cartilage covered with a skin.

The external acoustic meatus is an air-filled tubular space that follows a slightly S-shaped course to the tympanic membrane. The wall of the lateral one third of the canal is cartilaginous and is continuous with the elastic cartilage of the auricle. The medial two thirds of the canal is contained within the temporal bone. The external acoustic meatus is covered with skin containing hair follicles and sebaceous glands. In deep layers of the skin the ceruminous glands, which secrete components of earwax, are located. The earwax lubricates the skin and coats the meatal hairs to impede the entry of foreign particles into the ear.

The tympanic membrane is a thin membrane, which separates the external acoustic meatus from the middle ear. The core of the tympanic membrane is formed by the lamina propria, which consists of two layers of collagen fibers: the outer radial and the inner circular. The surface of tympanic membrane facing the external acoustic meatus is covered by epidermis; the surface facing the middle ear – by mucosa, which is lined with simple squamos epithelium. The upper part of the tympanic membrane does not contain collagen fibers (Shrapnell's membrane).

The middle ear consists of:

1. tympanic cavity;
2. auditory ossicles;
3. auditory tube.

The tympanic cavity is an air-filled space within the temporal bone. The walls of tympanic cavity are covered by simple squamos, in some areas cuboidal or columnar epithelium. Two openings are found in the medial wall of the tympanic cavity - the oval (vestibular) window and the round (cochlear) window.

The oval window is closed by the footplate of stapes, the vibrations of which are transmitted to the perilymph of the scala vestibuli. The round window is closed by the fibrous membrane leading to the scala tympani.

The auditory ossicles

- maleus;
- incus;
- stapes;

They form the movable chain and transmit vibrations of the tympanic membrane to the oval window, from which the scala vestibuli begins. The auditory ossicles are formed by compact bone and covered with simple squamos epithelium.

The auditory tube connects the middle ear to the nasopharynx. It equalizes the pressure of the middle ear with atmospheric pressure. This tube is lined with pseudostratified ciliated epithelium, which can be transformed into the stratified squamos under the influence of chronic inflammation.

The inner ear is located within the petrous part of the temporal bone. It consists of two labyrinthine compartments, one contained within the other. The bony labyrinth is a complex system of interconnected cavities and canals. The

membranous labyrinth lies within the bony labyrinth and consists of a complex system of small sacs and tubules that also form a continuous space enclosed within a wall of epithelium and connective tissue. The perilymphatic space lies between the wall of the bony labyrinth and the wall of the membranous labyrinth. It is filled with fluid – the perilymph. The space within the membranous labyrinth also contains fluid – the endolymph. The perilymph and the endolymph are different in chemical composition. The membranous labyrinth is composed of two divisions: cochlear labyrinth and vestibular labyrinth. The vestibular labyrinth contains semicircular ducts, the utricle and the saccule.

The bony labyrinth consists of three connected spaces:

1. vestibule;
2. three semicircular canals;
3. cochlea.

The vestibule is a chamber, which forms the middle part of the labyrinth and connects the semicircular canals to cochlea.

The semicircular canals are arc-shaped canals, which extend from the wall of the vestibule and return to it. They occupy three planes in space – sagittal, frontal, horizontal, and lie at approximately right angles to each other. The end of each semicircular canal closest to the vestibule is expanded to form the ampulla. The three canals open into the vestibule through five orifices; the anterior and posterior semicircular canals join at one end to form the common bony limb.

The cochlea – is a blind-ending bony canal, which makes 2,5 turns around a central core of spongy bone. At the base the cochlear canal is wide, at the apex – narrow. Periosteum covers the internal surface of bony canal.

The membranous labyrinth is also consists of three parts:

1. utricle and saccule;
2. three semicircular canals;
3. cochlear canal.

There are six regoins in the membranous labyrinth, which contain the sensory cells – **hair cells** :

- **three** of these regions are located within the ampullae of semicircular canals and are called cristae ampullaris (**ampullary crests**);
- two of them are called maculae; one in the utricle (**macula of utricle**) and the other in the saccule (**macula of saccule**);
- the **spiral organ of Corti** is located in the cochlear duct.

The cochlear duct – is a spiral canal with triangular lumen, which blindly ends near the apex of bony cochlear canal and adheres to it by the spiral ligament. Due to the presence of cochlear duct, the cochlear duct is divided into three parallel compartments or scalae:

- scala media;
- scala vestibuli;
- scala tympani.

The scala media is the cochlear duct itself. The scala vestibuli and scala tympani are the perilymph-containing spaces above and below, respectively, the scala

media. The scala vestibuli and scala tympani communicate with each other at the apex of the cochlea through a small channel called **helicotrema**.

The scala media is an endolymph-containing space that is continuous with the lumen of the saccule and contains the spiral organ of Corti, which rests on its lower wall.

In transverse section the scala media is a triangular space, bounded by the upper medial, outer and lower walls. The upper medial wall facing to the scala vestibuli is formed by vestibular membrane. The vestibular membrane is thin-fibrillar connective tissue lamella, which is covered with simple squamos epithelium facing to the endolymph, and with endothelium facing to the perilymph.

The outer wall is formed by the spiral ligament. The spiral ligament is a thickening of periosteum, which is covered by the stria vascularis. The stria vascularis consists of pseudostratified epithelium, which contains light basal cells and high dark columnar cells. Between these cells blood capillaries are located. It is considered that the stria vascularis produces the endolymph and plays a significant role in nourishment of the spiral organ.

The lower wall or floor of the scala media is formed by a basilar membrane. It consists of thin collagen fibers, "strings". The basilar membrane increases in width and decreases in stiffness as it coils from the base to apex of the cochlea. The spiral organ of Corti rests on the basilar membrane and is overlain by the tectorial membrane.

The spiral organ of Corti is formed by the following cells:

1. supporting cells;
2. sensory cells (hair cells).

The types of supporting cells are the following:

1. pillar cells, inner and outer;
2. phalangeal cells (Deiters cells), inner and outer;
3. limiting cells (Hensen's cells), outer;
4. supporting cells (Claudius cells), outer.

The pillar cells form two layers. These cells contain elongated nucleus and expanded base, which lie on the basal lamina. The inner and the outer cells are arranged so that their bases are apart, while their apexes contact with each other, forming a triangular tunnel, the inner spiral tunnel. It serves as a boundary between the inner and the outer cells of spiral organ.

The phalangeal cells (Deiters cells), outer and inner. The outer cells are arranged into 3-5 layers; the inner cells form one layer. These cells are columnar in shape, their basal portion contains nucleus surrounded by bundles of tonofibrills. The phalangeal cells associated with the inner hair cells surround the cells completely. The phalangeal cells associated with the outer hair cells surround only the basal portion of the hair cell completely and send apical processes toward the endolymphatic space.

The outer limiting cells (Hensen's cells) – are cells of various sizes and shapes, so their nuclei are situated at different levels. The apical portion of outer limiting cells forms microvili; their cytoplasm contains glycogen. These cells carry out trophic function.

The outer supporting cells (Claudius cells) - are cuboidal cells, which gradually turn into the cells of stria vascularis.

The sensory hair cells are divided into:

- inner hair cells;
- outer hair cells.

The inner and the outer hair cells are surrounded by the phalangeal cells.

The inner hair cells are jug-shaped cells with expanded basal portion, which form a single row of cells. The apical potrion of these cells contains approximately 30-60 large specialized microvili – stereocilia. The stereocilia pass through the cuticle covering the apical surface of the hair cell.

The outer hair cells are columnar in shape and have round bases. They form 4-5 parallel rows. Their apical portions contains cuticular lamina and the stereocilia arranged in a letter V. By their apexes the stereocilia attach to the inner surface of tectorial membrane. The stereocilia are formed by numerous densely packed fibrils, which contain the contractive protein – actomyosin, due to that they return to initial position after the movement. The cytoplasm of hair cells is rich in oxidative enzymes, RNA, and glycogen.

The dendrites of sensory bipolar cells of the spiral ganglion approach the bases of outer and inner hair cells and form afferent nerve endings.

The tectorial membrane hangs freely above the spiral organ. It is a jelly-like spiral lamina. It extends throughout the whole spiral organ, laying above the apical portions of hair cells and contacting with the stereocilia. The tectorial membrane is formed by thin radially arranged collagen fibers and ground substance, which is rich in glucosaminoglycans.

Histophysiology of organ of hearing. The air vibrations are transmitted to the tympanic membrane and through the auditory ossicles achive the footplate of stapes; moving like a piston into the oval window, the stapes transmits the vibrations to the perilymph of the scala vestibuli. Through a small channel (helicotrema) at the apex of the cochlea the vibrations are transmitted to the perilymph of the scala tympani. The vibrations are extinguished by membrane of the round window. Vibrations of the perilymph of the scala vestibuli are transmitted through the vestibular membrane and the endolymph of the cochlear duct and involve the basilar and tectorial membranes. These vibrations correspond with frequency and intensity of sound. As a result, the stereocilia of the hair cells start moving, thereby causing the excitation of them. The interaction between acetylcholine contained in the endolymph and cholinoreceptor protein of the membrane of stereocilia originates the action potential. The nerve impulses are transmitted through the acoustic nerve to the central part of the auditory analyzer.

The vestibular part of membranous labyrinth consists of the utricle, saccule and three semicircular ducts with ampullary crests. Their wall is lined with simple squamos epithelium resting on the basal lamina with underlying layer of dense connective tissue. At the area of ampullary crests and the utricle and saccule the connective tissue layer thickens and forms an elevation, while the epithelium becomes cuboidal or columnar.

The maculae of the saccule and the utricle. The maculae are lined with epithelium, which rests on the basal lamina and contains sensory and supporting cells. The apical portions of hair cells are facing the lumen of the labyrinth. The bases of hair cells contact with nerve endings and do not reach the basal lamina.

The hair cells are divided into two types:

1. the first type is a pear-shaped cells with wide round bases, surrounded by nerve endings, which form a bowl-like sheath around them;
2. hair cells of the second type are columnar cells; the point nerve endings are situated near the bases of these cells, forming the synapses.

The apical portion of these cells is covered with cuticle, from which about 60-80 immovable cilia – the stereocilia and the one mobile cilium – the kinocilium arise. The kinocilium is always located diametrically to the bundle of stereocilia. If the kinocilium moves towards the stereocilia, the hair cell undergoes excitation; if the movement is in opposite direction, the hair cell is inhibited. The macula of saccule contains 18 thousands sensory cells; the macula of utricle – 33 thousands.

The supporting cells rest on the basal lamina between the sensory cells. The supporting cells contain large dark oval nuclei, numerous mitochondria. On the apical portion numerous microvili are found.

The epithelial surface is covered with jelly-like otolithic membrane containing inclusions, so-called otoliths, which consist of crystals of potassium carbonate. The otolithic membrane is a product of secretion of the supporting cells.

The macula of the utricle – is a receptor of linear accelerations and gravitation; the macula of the saccule – is a receptor of gravitation and vibration.

During the movement of head the otolithic membrane, like a flat stone, draws the cilia of sensory cells, leading to the generation of nerve impulses.

Ampullary crests look like a transverse folds into the ampule of semicircular duct, which is covered by the hair cells and the sensory cells. The apical portion of these cells is covered with gelatinous dome, which have an appearance of bell without lumen. The ampullar crests are the receptors of angular accelerations. During movement of the head or fast rotation of the body the movement of endolymph makes the dome easily change its postion, thereby stimulating the hair cells.

OLFACTORY ORGAN

The olfactory organ is a chemoreceptor. It perceives the molecules of odorous substances. Phylogenetically it is the oldest type of perception. The peripheral part of olfactory analyzer is located at the olafactory region of nasal cavity. The olfactory region is located on part of the dome of each nasal cavity and, to a variable extent, the contiguous lateral and medial nasal walls. Mucosa of the olfactory region appears yellowish.

The olafactory analyzer consists of three parts:

- peripheral part – the olfactory region of the nasal cavity;
- conductive part – olfactory bulb;

- central part – olfactory center in cerebral cortex.

Structure. The olfactory region is lined with specialized olfactory mucosa. In humans, the total surface area of the olfactory mucosa is only about 10 cm2. The olfactory epithelium consists of olfactory receptor cells, supporting cells, and basal cells. The olfactory epithelium is distinguished from the underlying lamina propria by the basal lamina. The surface of olfactory region facing the nasal cavity is covered with mucus.

Receptor cells are located between supporting cells. The receptor cells have long central process – axon and short peripheral process – dendrite. Their cell bodies are located in the middle of thickness of the olfactory epithelium; they contain light nuclei with one or two nucleoli and well-developed rough ER. The distal ends of dendritic processes dilate and form knob-like structures called the olfactory vesicles. A number of long, thin cilia (10 to 23) arise from the olfactory vesicle and extend radially in a plane parallel to the epithelial surface. The cilia of ofactory vesicles contain longitudinally oriented fibrils: 9 pairs of peripheric fibrils and 2 pairs of fibrils extended from the basal bodies. The cytoplasm of dendritic processes contains microtubules elongated along its long axis and mitochondria.

The olfactory cilia act like antenna for the molecules of odorous substances. The dendritic processes of the receptor cells can contract under the action of odorous substances. The basal domain of the cell gives rise to an unmyelinated axonal process that leaves the epithelial compartment. Collections of axons from olfactory receptor cells do not come together as a single nerve, but instead they are grouped into bundles that pass through a thin cribriform plate of the ethmoid bone, course through the dura and arachnoid matters, and finally are surrounded by pia matter, entering the olfactory bulb of the brain.

Supporting cells form multinuclear epithelial layer, within which the receptor cells are located. The apical portion of supporting cells contains numerous microvili. These cells reveal the signs of apocrine secretion and characterized by an intensive metabolism. Their cytoplasm contains mitochondria, ER, Golgi apparatus, granules, vacuoles and yellowish brown pigment, which causes the yellow color of the olfactory mucosa.

Basal cells rest on the basal lamina and form projection, which surround the bundles of axons of the receptor cells. These cells form cambial layer for renewal of cells of the olfactory mucosa.

Epithelium of the vomeronasal organ consists of the respiratory and receptor regions. The structure of receptor part is almost similar to that of the olfactory region. The main difference is that the olfactory vesicles of vomeronasal organ contain on their apical surfaces not cilia, but immobile microvili. The main function of vomeronasal organ is the regulation of sexual behavior.

The underlying loose connective of the olfactory region contains the acini of tuboalveolar (Bowman's) glands, which consist of secretory and myoepithelial cells. The secretion of these glands dissolves odorous substances, which interact with receptor cells. It causes the change of membrane potential, which is transmitted through the chain of neurons to the central part of olfactory analyzer.

ORGAN OF TASTE

The peripheral part of taste analyzer carries out the function of chemoreceptor. It is represented by an aggregation of taste buds located within the stratified epithelium of tongue papillae.

Structure. In histologic sections, taste buds appear as oval, pale-staining bodies that extend through the thickness of the epithelium. Three principal cell types are found in taste buds: neuroepithelial (sensory cells), supporting cells and basal (cambial) cells. A small opening onto the epithelial surface at the apex of the taste bud is called the taste pore, which leads to a small depression – taste fovea.

The neuroepithelial cells are spindle-like cells, whose cytoplasm contains smooth ER and mitochondria. The apical portion of these cells contains about 30-50 microvili, called taste brads. By these microvili the sensory cells perceive the stimuli. The molecules of food adsorb on the active centers of membranes of the microvilli. They selectively react on the substances with different tastes. The basal portions of receptor cells form synapses with afferent nerve fibers. The excitation is transmitted to the dendrites of sensory neurons.

The supporting cells – are various-shaped cells with large nuclei and well-developed organelles. They surround and isolate the sensory cells and nerve fibers at the basal portion of the taste bud. They also carry out secretory function by discharging secretion into the taste fovea. The supporting cells posses microvili on their apical surfaces, and do not form synapses with nerve fibers.

The basal cells rest on the basal lamina and, unlike sensory and supporting cells, do not reach the epithelial surface. Theses cells are small, contain small amounts of cytoplasm and organelles. They are considered to be the source of regeneration of sensory and supporting cells.

INTEGUMENTARY SYSTEM

The skin and its derivatives constitute the integumentary system. The skin forms the outer covering of the body and performs various functions. It protects the underlying tissues from injuring. The intact skin is impenetrable for microorganisms, numerous poisoning and toxic substances. The skin takes part in maintenance of homeostasis and regulation of water-salt metabolism. Due to the rich innervation, the skin represents an enormous receptive area containing numerous tactile, temperature and pain receptors. The skin protects the body from ultraviolet radiation. Besides these, the skin performs functions of thermoregulation, metabolism, vitamin D synthesis and blood deposition.

The derivatives of skin include hairs, nails, and glands (sebaceous, sweat, and mammary).

The skin consists of epidermis, dermis (the skin proper), and hypodermis (or subcutaneous fascia). The thickness of skin varies from 0,6 to 5mm.

Epidermis is composed of stratified squamos keratinized epithelium. The thickest layer of epidermis is located at the palms of the hands and at the soles of the feet. The skin of these areas does not contain hair follicles and glands and is called thick skin. Elsewhere, the skin possesses a much thinner epidermis and is

called thin skin. The five distinct layers can be identified in a thick skin: stratum basale, stratum spinosum, stratum granulosum, stratum lucidum, stratum corneum. In case of thin skin, the stratum lucidum is not observed.

The five types of cells constitute the epidermis: keratinocytes (epithelial cells), Langerhans' cells (intraepidermal macrophages), melanocytes, lymphocytes, and Merkel's cells. The main cells of epidermis are keratinocytes, which immediately undergo the process of keratinization. The special proteins resistant to mechanical and chemical impact, such as acid and alkaline types of keratines, filaggrin, involuctin, keratolinin etc, are synthesized within the keratinocytes and form the keratin tonofilaments called keratinosomes. Then, the nucleus and organelles of keratinocytes disappear; the spaces between keratinocytes are filled with cementing extracellular matrix, which is rich in lipids, and that's why impermeable for water. At the same time, the keratinocytes move from the stratum basale to stratum corneum, where they finish differentiation and are eventually sloughed off at the skin surface. The whole process of keratinization lasts approximately 3-4 weeks.

Stratum basale , also called stratum germinativum, is represented the single layer of cells, which rest on the basal lamina. It contains the stem cells from which new cells, the keratinocytes, arise by mitotic division. As new keratinocytes arise in this layer by mitotic division, they move into the next layer, thus beginning their process of upward migration. Besides the stem cells and keratinocytes, the stratum basale contains melanocytes, Merkel's cells, and Langerhans' cells.

The keratinocytes have a cuboidal or low columnar shape, basophilic cytoplasm and oval, rich in chromatin nucleus. Their cytoplasm contains keratine intermediate filaments and organelles; they also may contain various amounts of melanin.

The melanocytes – are pigment cells, which form processes branching towards the epidermal surface. On histological specimens the melanocytes are revealed by the silver impregnation method. The melanocytes synthesize melanin; their cytoplasm does not contain tonofibrils, but it is rich in ribosomes and melanosomes.

The Langenharns' cells are the type of macrophages, provide the immune defense. They are dendritic-appearing cells with cytoplasm containing Birbeck granules, which have an appearance of tennis racket. Langerhans' cells encounter and process antigens entering through the skin.

Stratum spinosum is formed by 5-10 layers of polygonal keratinocytes. Their cytoplasm contains tonofibrils, which take part in formatiom of desmosomes. The basal cells and cells of inner layers of stratum spinosum form the cambial zone of epidermis.

Stratum granulosum is formed by 3-4 layers of cells. At this layer filaggrin, a protein aggregating the keratin tonofilaments, is synthesized within the keratinocytes. As a result of aggregation of the keratin tonofilaments, the cytoplasm of keratinocytes stores the basophilic granules of keratohyaline. Involucrin and keratolinin form a protein layer under the plasmolemme, protecting it from action of hydrolytic enzymes of keratosomes and lysosomes, which are

activated by the Langenharns' cells. The appearance of keratohyaline granules is an indicative of the beginning of keratinization process.

Stratum lucidum is formed by 3-4 layers of squamos cells, within whose cytoplasm the nucleus and organelles are completely disrupted; the keratohyaline granules fuse into the refractile mass, which consists of aggregated keratin fibrils and amorphous matrix.

Stratum corneum of scores of layers of annucleate squamos cells largely filled with keratin filaments. Filaggrin provides the further aggregation of intermediate filaments within the keratinocytes. The keratinocytes store the air vesicles; the light cavity is appears at the site of nucleus. The intercellular lipid barrier and the keratinocytes provide impenetrability of the epidermis. The keratinocytes of stratum corneum are eventually sloughed off at the skin surface. The mechanism of desquamation is controlled by keratinosomes – the modificated lysosomes, which dissolve desmosomes and provide the separation of cornified cells from each other.

The stratum corneum is the layer that varies most in thickness, being thickest in thick skin. The thickness of this layer constitutes the principal difference between the epidermis of thick and thin skin.

The interrelated processes of differentiation and keratinization of keratinocytes constantly occur in the epidermis. These processes provide regular renewal of stratum corneum, which is characterized by mechanical and chemical resistance, high hydrolytic capability, poor heat conduction, and impenetrability for bacteria and their toxins.

Between the epidermis and dermis the basal lamina is located.

Dermis is a connective tissue core of the skin. The dermis is composed of two layers: the outer papillary layer and the inner reticular layer.

The papillary layer of dermis is formed by loose connective tissue, which projects into the epidermis and form fingerlike protrusions, dermal papillae. The connective tissue consists of collagen, elastic and reticular fibers, and cells represented by fibroblasts, macrophages, mast cells etc. The papillary layer is rich in vessels of microcirculatory bed, contains bundles of the smooth muscle cells. Contraction of the smooth muscles results in appearance of so-called "goose bumps". The contracted smooth muscles compress small blood vessels, thereby decreasing the heat emission of the body. The relief of papillary dermis is unique in each person; that explains the characteristic alternation of projections and depressions on the epidermal surface. The examination of fingerprints, dactylography, is used in criminology for person identification and for diagnostics of genetic anomalies, such as Down syndrome.

The reticular layer of dermis is formed by dense irregular connective tissue – a network of bundles of thick collagen fibers arranged in different directions. The cellular elements of the reticular layer are mainly represented by fibroblasts. The collagen fibers of this layer provide density of the skin. The hair follicles and glands of skin are located in the reticular layer of dermis.

In some areas of the skin the dermis contains pigment, which is stored in cytoplasm of dermal melanocytes. Unlike epidermal melanocytes, they only store, but do not synthesize melatonin.

The bundles of collagen fibers of derma continue in the hypodermis.

Hypodermis is formed by aggregations of adipocytes, which grow inwards the reticular layer of dermis. The hypodermis performs a function of shock absorber and limits the heat emission.

The skin derivatives

Sebaceous glands – are simple, branched, alveolar glands with holocrine type of secretion. The secretion of sebaceous glands – sebum – greases the skin surface and hairs, thereby preventing skin maceration and its affection by microorganisms. The secretion of sebaceous glands softens skin and hairs, imparts them elasticity. The glands secrete about 20g of sebum per day. Sebaceous glands develop as outgrowths of the external root sheath of the hair follicle, usually producing several glands per follicle. The most numerous sebaceous glands are located at the head, face and lower part of back; their absent in the skin of palms and soles.

Each sebaceous gland consists of secretory acinus and excretory duct. The acini of sebaceous glands are located in outer portion of the papillary layer of dermis, near the external root sheath of hair follicle. Their excretory ducts open at the bottom of infundibulum of hair follicle.

The secretory acinus of sebaceous gland is represented by a sac of about 0,2 to 2mm in size, which is surrounded by a basal lamina and consists of two types of cells – sebocytes. The outer germinative layer of cells rests immediately on the basal lamina. It consists of cuboidal progenitor cells with well-defined nucleus, which undergo proliferation by mitosis. Closer to the central portion of acinus the large polygonal, lipid-synthesizing cells are found.

The sebocyte produces and becomes filled with the fatty product while itsimultaneously undergoes programmed cell death (apoptosis) as the product fills the cell. Ultimately, both the secretory product and cell debris are discharged from the gland as sebum into the infundibulum of a hair follicle.

Sweat glands are simple tubular non-branched glands. Their secretion – the sweat – consists of 98% of water and 2% of mineral salts and organic components. The sweat glands produce 500ml of sweat per day. The sweat glands take part in water-salt metabolism, excretion of metabolic wastes (urea, uric acid, ammonia), and thermoregulation.

Each sweat gland consists of secretory acinus and excretory ducts. The secretory acinus appears as a tubule of 0,3-0,4 mm in diameter. The wall of tubule is lined with cuboidal or columnar (depending on the phase of secretion) epithelial cells. The secretory cells of sweat glands are divided into two types – the clear and dark cells. The function of clear cells is secretion of water and mineral salts; the dark cells secrete organic macromolecules. Externally the secretory cells of acinus are surrounded by myoepithelial cells. The contraction of myoepithelial cells stimulates the discharge of secretion. A basal lamina separates the epithelial cells of secretory acini from the reticular layer of dermis.

The excretory ducts of sweat glands, like a spiral, extend through the reticular and papillary layers of dermis, run through the all thickness of epidermis, and open at the epidermal surface by a sweat pore. The wall of the excretory ducts of sweat glands is lined with double-layer of cuboidal epithelium, which undergoes

transition into the stratified squamos one within the epidermis; within the stratum corneum the excretory ducts do not possess their own wall. The epithelial cells of excretory ducts reveal secretory activity.

On the basis of type of secretion two types of sweat glands are recognized: the eccrine and the apocrine sweat glands.

Apocrine sweat glands are limited to the axilla, areola, and nipple of the mammary gland; skin around the anus; and the external genitalia. They produce a secretion that contains protein, carbohydrate, ammonia, lipid, and certain organic compounds that may color the secretion. When secreted, the fluid is odorless;through bacterial action on the skin surface, it develops an acrid odor.

The ceruminous glands of the external acoustic meatus canal and the apocrine glands of eyelashes (glands of Moll) are also apocrine-type glands.

The secretory cells of merocrine glands release secretion without disruption of their apical portions.

Hairs are derived from downgrowths of epidermal epithelium during development. Hair follicles and hairs are present over almost the entire body; they are absent only from the sides and palmar surfaces of the hands, sides, and plantar surfaces of the feet, the lips, and the region around the urogenital orifices. Hair distribution is influenced to a considerable degree by sex hormones.

Each hair has a shaft. The hair shaft is elongated filamentous structure that projects from the hair follicle; the hair root is embedded into epidermis and dermis.

The hair shaft consists of two morphologically distinct zones - the outer cuticle and the inner cortex. The hair root consists of three zones – the inner medulla, the middle cortex, and the outer cuticle.

The medulla of hair root is formed by polygonal cells stratified in the form of coin column. The cytoplasm of these cells contains granules of trichhyaline, melanin, and air vesicles. As the cells of root medulla migrate from inner layers to the outer ones, they undergo the process of keratinization: trichohyaline transforms into keratin. The root cortex is mainly formed by keratinized cells, filled with keratin. The hair cuticle in lower part of root is formed by columnar cells.

The lower part the hair root expands and forms the hair bulb. The low-differentiated cells of hair bulb are enable to proliferation and are the source of regeneration (growth) of hair. The loose connective tissue projects into the hair bulb and forms so-called hair papilla.

The hair papilla contains vessels of microcirculatory bed, which provide nutrition of hair, and nerve fibers. The outer cells of hair bulb proliferate and form the internal root sheath – an epithelial layer, which surrounds the root cuticle. The internal root sheath consists of one or several layers of keratinized cells containing soft keratin. The lower portion of the internal root sheath consists of three layers: cuticle attached to the hair root, the internal (granule-containing) and external (pale) epithelial layers.

The internal epithelial sheath of hair root borders with its external epithelial sheath. The external epithelial sheath is the continuation of germinative layer of epidermis: closer to the skin surface it consists of several layers of glycogen-containing cells, which are reduced to one or two layers towards the hair bulb.

The external epithelial sheath is surrounded by a root dermal sheath (hair sac) – elements of connective tissue with inner circular and outer longitudinal direction of fibers. The hair sac contains the smooth muscle cells – m.erector pili, whose contraction makes the hair take a vertical position. The inner and the outer epithelial sheaths form the hair follicle.

Nails – are plates of keratinized cells containing hard keratin. The nail plate rests on the nail bed and is surrounded by folds of skin called nail cuticles.

The nail bed consists of epithelial cells that are continuous with the stratum basale and stratum spinosum of the epidermis. The proximal part of the nail, the nail root, is buried in a fold of epidermis and covers the cells of the germinative zone, or matrix. The matrix contains a variety of cells, including stem cells, epithelial cells, melanocytes, Merkel's cells, and Langerhans' cells. The stem cells of the matrix regularly divide, migrate toward the root of the nail, and there differentiate and produce the keratin of the nail. Nail keratin is a hard keratin, like that of the hair cortex. Unlike the soft keratin of the epidermis, it does not desquamate. The constant addition of new cells at the root and their keratinization account for nail growth.

As the nail plate grows, it moves over the nail bed. On the microscopic level, the nail plate contains closely packed interdigitating corneocytes lacking nuclei and organelles. The crescent-shaped white area near the root of the nail, the lunula, derives its color from the thick, opaque layer of partially keratinized matrix cells in this region. When the nail plate becomes fully keratinized, it is more transparent and takes on the coloring of the underlying vascular bed. The edge of the skin fold covering the root of the nail is the cuticle. The cuticle is also composed of hard keratin; therefore, it does not desquamate.A thickened epidermal layer,the hyponychium, secures the free edge of the nail plate at the fingertip.