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MEDICAL FACULTY

Department of «Histology, Embryology, Cytology»



NORMAL HISTOLOGY

Textbook

*Dedicated to 30 years
of Medical Faculty of Kyrgyz-Russian
Slavic University named after B.N. Yeltsin*



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The textbook is compiled considering the modern educational standard and curriculum in the discipline “Histology, embryology, cytology” for medical universities. Contains the main provisions, topics, information, and didactic materials necessary for the successful development of the private histology course.

The content of the lectures corresponds to the qualified characteristics of medical school graduates.

The material is intended for students of medical universities of the specialty “General Medicine” to organize and increase the efficiency of independent work in preparation for classes.

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Preface

The textbook “Normal Histology” provides foreign students with the essential information needed to study histology independently during practical classes in English. The manual presents all theoretical material divided into topics (systems) and provides the basic material in a concise form. It also includes modern information on the topics. The authors aimed to present a concise and accessible overview of the structure of organs and systems of the human body for foreign students. They express gratitude to M. M. Yakubova and A. Shamsudinov, leading specialists from the Department of Histology, Embryology, and Cytology, for their technical assistance in compiling this textbook.

O. P. Kalugina.

INTRODUCTION

Private histology studies the development, structure, and functions of organs and systems of the human body.

The cardiovascular system (CVS) is of particular importance in the vital activity of the human organism. Understanding the cardiovascular system's role in the human body is crucial for practical medicine. The heart and blood vessels are more susceptible to pathological processes than other systems. Currently, systemic sclerosis pathology and oncologic diseases are the most frequent and deadly. As an open living system, the human body constantly exchanges substances with the environment and receives information about the changing state of both the external and internal environments through sensory organs. The information received is used to adapt the organism to changing environmental conditions. The nervous and endocrine systems regulate the functions of all organs of the body, allowing the body to adapt. Food is necessary for the vital processes that take place in the digestive tract. Nutrients support the functioning of organs and body systems, while metabolic waste is excreted through the urinary system. The sexual system is responsible for reproductive processes. It is essential for doctors to have a good knowledge of English in order to access the latest articles and studies in medicine. English proficiency enables one to stay up-to-date with the rapidly changing trends in medicine.

NERVOUS SYSTEM

The nervous system is responsible for regulating all vital processes in the body and its interaction with the external environment. Anatomically, the nervous system is divided into 1) peripheral and 2) central.

The peripheral nervous system includes

- 1) spinal ganglia,
- 2) autonomic ganglia.

The central nervous system includes:

- 1) spinal cord,
- 2) cerebellum,
- 3) cerebral cortex.

Physiologically, the nervous system is divided into

- 1) somatic, innervating the whole body except internal organs, vessels, glands,
- 2) vegetative, innervating internal organs, vessels, glands.

The morphological substrate of reflex activity of the nervous system are reflex arcs consisting of a chain of neurons of different functional significance.

Development of the nervous system

The development of the nervous system involves three sources:

- 1) the neural tube,
- 2) the ganglionic plate (neural crest),
- 3) the mesenchyme.

Neurons and neuroglia of the spinal and autonomic ganglia, which make up the peripheral nervous system, are formed from the ganglion plate or neural crest.

The mesenchyme gives rise to the stroma and membranes of organs.

The central nervous system develops from the neural tube and is differentiated into the cerebral (cranial) and trunk sections.

The spinal cord is formed from the trunk section of the neural tube.

During human embryogenesis, the head (cranial) section of the neural tube is subdivided into three brain vesicles (anterior, middle, posterior) - this is the stage of 3 brain vesicles. Later, at the end of the fourth week of embryonic development, five brain vesicles (1, 2, 3, 4, 5) are formed. The two cerebral hemispheres are subsequently formed from the first brain vesicle. The intermediate brain develops from the second brain vesicle. followed by the midbrain from the third brain vesicle. The cerebellum develops from the fourth brain vesicle. The medulla oblongata from the fifth brain vesicle.

The neural tube consists of three cellular layers from inner to outer:

- 1) the ventricular zone (ependymal layer),
- 2) the intermediate zone (mantle layer),
- 3) the marginal zone (marginal layer).

1 The ependymal layer forms the ependymoglia (ependymocytes) that line the cerebrospinal canal and all the ventricles of the brain.

2. The grey matter of the brain develops from the mantle layer. The cells of the mantle layer differentiate into 2 types of cells:

- 1) neuroblasts - large cells with a single extension (axon) that later form neurons (nerve cells),
- 2) spongioblasts - small cells that differentiate into astroglia and oligodendroglia.

3. White matter develops from the marginal zone, including outgrowths of 1st and 2nd layer cells, later represented by myelinated and unmyelinated nerve fibres.

Peripheral Nervous System (PNS)

The peripheral nervous system comprises ganglia (nodes) and nerves. Ganglia are clusters of neurons located outside the Central Nervous System (CNS), in the periphery. There are two types of ganglia: spinal (sensory) ganglia, which are located along the course of spinal nerves, and autonomic ganglia.

The spinal (sensory) ganglion

Development. Develops from: 1) ganglionic lamina (neural crest) and 2) mesenchyme. The mesenchyme forms the capsule (DFICT) and stroma (LFICT). Bipolar neurons and gliocytes (oligodendroglia) differentiate from ganglion plate cells. Bipolar neurons become pseudounipolar as they mature. The processes of the neurons gradually converge and their bases fuse. Later, the branches repeatedly wrap around the pseudounipolar neuron, often forming a tangle.

Structure. From the outside, the ganglion is covered by a capsule consisting of dense fibrous irregular connective tissue (DFICT). There are layers of connective tissue from the capsule to the inside of the ganglion. The dorsal root ganglion is divided into anterior and posterior roots. The stroma consists of loose fibrous irregular connective tissue (LFICT).

The parenchyma is represented by:

- 1) pseudounipolar neurons,
- 2) nerve fibers,
- 3) oligodendroglia – mantle gliocytes.

Structure of the posterior root of the ganglion. Pseudounipolar neurons (bodies) are compactly arranged along the periphery of the posterior root of the ganglion. The processes of these cells are located in the center of the posterior root of the ganglion. Dendrites of pseudounipolar neurons go to the periphery and terminate there with receptors. The axons go to the posterior horns of the spinal cord. The dendrites and axons of the cells are covered by sheaths of oligodendroglial cells, which have rounded nuclei. The bodies of pseudounipolar neurons are surrounded by mantle gliocytes (oligodendroglial cells). Mantle gliocytes have rounded nuclei. The glial cells form a glial sheath around the neuron. From the outside, the glial sheath is covered by a connective tissue whose fibroblasts have oval nuclei.

Structure of the anterior root of the ganglion. The anterior root of the ganglion is represented by nerve fibers covered by neurolemmocytes (oligodendroglia). Neurons in the anterior root of

the ganglion are absent. Pseudounipolar neurons are responsible for pain, temperature and tactile sensitivity.

Autonomic ganglia

Autonomic ganglia are peripheral nerve centers, unlike spinal ganglia, which are not nerve centers. From the outside, the autonomic ganglion is covered by a connective tissue capsule from which layers of connective tissue extend into the node. The stroma of the autonomic ganglion consists of loose fibrous irregular connective tissue (LFICT).

The parenchyma is represented by:

- 1) multipolar neurons
- 2) nerve fibers – fleshy and fleshless
- 3) oligodendroglia.

Morphologically, 3 types of multipolar neurons can be distinguished:

- 1) type 1 Dogel cells
- 2) type 2 Dogel cells
- 3) type 3 Dogel cells.

1) Type 1 Dogel cells (long axon neurons) have many short-branched dendrites and a long axon (neurite) that extends outside the ganglion. They are large efferent, motor, multipolar neurons.

2) Dogel cells type 2 multipolar sensory neurons. Multiple dendrites and axon of equal length. The dendrites terminate with receptors, the axon – with a synapse at the type 1 Dogel cell. Type 2 Dogel cells are sensory neurons of local autonomic reflex arcs.

3) Type 3 Dogel cells are associative cells. They have multiple dendrites and an axon. The dendrites do not extend beyond the ganglion and the axon (neurite) is directed to other ganglia.

Each neuron and its branches are surrounded by a glial sheath of oligodendroglia. Beyond the glial sheath, there is a connective tissue sheath.

The peripheral autonomic ganglia contain local reflex arcs that consist of sensory (1st neuron), motor (2nd neuron), and possibly associative multipolar neurons (insertion neuron).

Central Nervous System

Spinal cord

Structure. From the outside, the spinal cord is covered by 3 membranes: 1) inner soft (pia mater), 2) arachnoid mater (middle), 3) outer hard (dura mater).

The pia mater and arachnoid mater are made up of loose fibrous irregular connective tissue with a large number of blood vessels that supply the brain. The dura mater is made up of dense fibrous irregular connective tissue (DFICT).

The spinal cord lies in the spinal canal. The spinal cord is made up of two symmetrical hemispheres. They are separated at the front by a deep medial slit and at the back by a connective tissue septum. The spinal cord is divided into:

- 1) grey matter (in the center, dark)
- 2) white matter (in the periphery, light).

The white matter surrounds the grey matter and is made up of:

- 1) nerve fibers (unmyelinated and myelinated fibers)
- 2) neuroglia – microglia, astroglia, oligodendroglia. There are no neurons.

On each side, the white matter is divided into 3 funiculi: 1) anterior, 2) lateral and 3) posterior. Between the posterior and lateral funiculi are strands of grey matter called the reticular formation. The grey matter has the shape of a butterfly or the capital H. In the center of the grey matter is the spinal canal. The central canal is lined by ependymocytes.

The grey matter is made up of:

- 1) multipolar neurons,
- 2) nerve fibers (myelinated, unmyelinated)
- 3) neuroglia – microglia and macroglia.

Multipolar neurons, similar in size, structure and function, are located in the grey matter in groups called nuclei. There are 3 horns (projections) in the grey matter:

- 1) anterior horn,
- 2) lateral horn
- 3) posterior horn.

The anterior horns contain motor neurons, the largest motor neurons, which are 100-150 μm in diameter. Two nuclei can be distinguished in the anterior horns: 1) medial nucleus, 2) lateral nucleus. The medial nucleus is closer to the medial slit. These are the motor nuclei. In the lateral horns there are 2 nuclei: 1) medial, 2) lateral. These are associative neurons. In the posterior horns, 2 nuclei and 2 substances are distinguished: 1) the nucleus proprius, 2) the nucleus dorsalis of Clarke, and the spongy and gelatinous substance.

The nucleus proprius is located in the middle of the posterior horn. It consists of small bundles of sensitive multipolar neurons. The nucleus proprius transmits pain, temperature and tactile sensitivity. Clark's dorsal nucleus transmits proprioceptive sensitivity (impulses from tendons, ligaments, skeletal muscles). The spongy substance contains a large number of small bundled neurons in the form of a wide network. The gelatinous substance contains fewer neurons but more neuroglia.

Cerebellum

The cerebellum is the central organ for balance and movement coordination. The surface of the cerebellum has many gyri and sulci.

The cerebellum consists of:

- 1) Grey matter (periphery),
- 2) White matter (center).

The white matter is made up of nerve fibers.

The grey matter or cerebellar cortex consists of 3 layers:

- 1) molecular layer (outer)
- 2) ganglionic layer (middle),
- 3) granular layer (inner).

The middle layer of the cerebellar cortex is the ganglionic layer, which contains only one type of multipolar neuron - Purkinje cells. These cells are the largest in size, pear-shaped, and arranged strictly in a single layer. From the Purkinje cells, 2-3 dendrites branch into the molecular layer. The base of the pear-shaped neurons has an axon that passes through the granular layer of the cortex into the white matter. Purkinje cells are the main cells responsible for coordinating movements. They are efferent neurons of the cerebellar cortex.

The molecular layer comprises two types of multipolar neurons:

- 1) basket cells
- 2) stellate cells – small, large.

Small stellate cells are located in the upper third of the molecular layer and have short dendrites and axons. Their axons make contact with the dendrites of Purkinje cells, and their function is inhibitory. Large stellate cells have a star-like shape and situated in the middle third of the molecular layer. They have long, branched dendrites and neurites (axons) and can form two types of contacts: 1) the axon connects to the dendrite of the Purkinje cell, and 2) the axon surrounds the body of the Purkinje cell in the form of a basket. Large stellate cells function as inhibitors, transmitting inhibitory impulses to dendrites and Purkinje cell bodies.

Basket cells, which are located in the lower third of the molecular layer, have a basket-like shape, long dendrites, and long axons. The axons braid around the pear-shaped neuron bodies, forming baskets around them. The basket cells have an inhibitory function, meaning that they transmit inhibitory nerve impulses to the bodies of Purkinje cells.

The granular layer is composed of three types of cells:

- 1) granule cells,
- 2) golgi cells,
- 3) fusiform cells.

From the white matter to the cerebellar cortex come 2 types of afferent fibers:

- 1) climbing fibers,
- 2) mossy fibers.

Granule cell has three to four short dendrites and a long axon. The axon extends into the molecular layer and then branches in T-shape, forming synapses with the dendrites of the cells. The dendrites terminate in the granular layer with terminal branches. Mossy fibers originating from the white matter approach the dendrites and form synapses. The points of contact between dendrites of cells and mossy fibers are referred to as cerebellar glomeruli. Cerebellar granule cells have an excitatory function, transmitting impulses to Purkinje cells.

The mossy fibers and climbing fibers are both types of excitatory afferent fibers that enter the cerebellar cortex from the white matter.

Climbing fibers ascend to the molecular layer and form synapses with the dendrites of Purkinje cells, transmitting excitation directly to them.

The second type of cells in the granular layer of the cerebellar cortex are inhibitory large stellate Golgi cells.

There are two types of Golgi cells:

- 1) Golgi cells with short axons,
- 2) Golgi cells with long axons (neurites).

Large stellate Golgi cells with short axon (short-axon cells) have long dendrites and short neurite. The dendrites extend to the molecular layer, where they form synapses with the axons of the granule cells. The short axons in the granular layer approach the dendrites of the granule cells and form an inhibitory synapse.

Large stellate Golgi cells with a long axon (long-axon cells) have short dendrites and a long neurite. The short dendrites branch in the granular layer and the long axon exits into the white matter. The function of Golgi cells is to exert an inhibitory effect on Purkinje cells.

The third type of cells in the granular layer of the cerebellum are fusiform horizontal Golgi cells, which are located between the ganglionic and granular layers. These cells have long dendrites that extend horizontally in both directions and terminate in the ganglionic and granular layers. The axon of these cells extends into the white matter. Their function is associative. The neuroglia of the cerebellar cortex is represented by Bergmann fibers (fibrous astrocytes), plasmatic astrocytes, oligodendroglia, and microglia (glial macrophages).

Cerebral cortex

The cerebral cortex is a layer of gray matter located on the surface of the white matter. It is 2–5 mm thick and contains 10–14 billion multipolar nerve cells. The cortex is composed of multipolar neurons, nerve fibers, and neuroglia.

Cytoarchitectonics refers to the structure and arrangement of nerve cells, while **myeloarchitectonics** pertains to the arrangement of nerve fibers. The cerebral cortex is composed of six distinct layers: the molecular layer, outer granular layer, and pyramidal layer, among others.

The cerebral cortex is composed of six distinct layers:

- 1) molecular layer,
- 2) outer granular layer,
- 3) outer pyramidal layer,
- 4) inner granular layer,
- 5) inner pyramidal layer (which consists of a layer of giant pyramids),

6) multiform layer (which consists of a layer of polymorphic cells).

1) The molecular layer is made up of small fusiform associative multipolar neurons.

2) The outer granular layer consists of small neurons of various shapes, including basket, stellate, oval, and pyramidal. The dendrites of these cells extend into the molecular layer, while their axons either go into the white matter or, forming an arc, ascend into the molecular layer.

3) The outer pyramidal layer is the widest layer of the cortex and contains small, medium, and large pyramidal neurons (10–40 μm).

4) The inner granular layer is composed of small stellate oval neurons. The dendrites and axons of these cells are located exclusively within this layer.

5) The inner pyramidal layer is formed by the largest pyramidal neurons, including the Betz cells (120 μm). The dendrites of these neurons extend up to the molecular layer, while their axons project into the white matter.

6) Multiform layer contains neurons of various shapes, including pyramidal, fusiform, spider-shaped, and polygonal. The dendrites of these cells extend into the molecular layer, while the axons project into the white matter.

In the majority of individuals, the left hemisphere is dominant and is responsible for speech, writing, reading, verbal memory, counting, and abstract logical thinking. Conversely, the right hemisphere is responsible for visual-imaginative, musical, olfactory, gustatory, sensual, and figurative thinking.

Types of cortex

There are 2 types of cortex:

- 1) granular, 2) agranular.

The granular cortex is characterized by strongly developed outer granular and inner granular layers (2nd and 4th layers). This type of cortex is located mainly in primary sensory regions, such as visual, auditory, and olfactory centers.

The agranular cortex is characterized by strongly developed outer pyramidal layer, inner pyramidal layer, and multiform layer (layers 3, 5, 6). It is located mainly in the motor cortical centers (the speech center). Neuroglia is represented by macroglia and microglia.

Myeloarchitectonics refers to the regular arrangement of nerve fibers. There are three types of nerve fibers: associative, commissural, and projection.

- 1) Associative fibers connect different parts of the cortex within one hemisphere.
- 2) Commissural fibers provide interconnections between two hemispheres.
- 3) Projection fibers connect the cortex with the lower parts of the central nervous system.

Cerebral meninges

The brain is covered by three membranes known as cerebral meninges. These include:

- 1) pia mater (inner),
- 2) arachnoid (middle),
- 3) dura mater (outer).

1) The pia mater is directly adjacent to the brain tissue and is formed by loose fibrous irregular connective tissue (LFICT). There are a large number of blood vessels that feed the brain.

2) The arachnoid membrane is represented by the LFICT and large blood vessels, whose branches penetrate the pia mater.

3) The dura mater is formed by dense fibrous irregular connective tissue (DFICT) containing many elastic fibers. In the cranial cavity, it is tightly fused with the periosteum.

The blood-brain barrier serves to separate the cells of the central nervous system from the blood and maintain the intercellular fluid of the brain and spinal cord. It is composed of three main components:

- 1) endothelial cells of the capillaries of the CNS,
- 2) a continuous basal membrane, and
- 3) fibrous astrocyte's processes.

The functions of the blood-brain barrier are:

- 1) protection from toxic substances
- 2) regulation of homeostasis in the brain and cerebrospinal fluid.

SENSORY ORGANS

The sense organs enable the organism to adapt to specific conditions of the external and internal environment. Classification of sense organs according to their development, structure and function. They are divided into 2 groups: 1) primary sense organs, 2) secondary sense organs.

Primary sensory organs are derivatives of the neural tube (brain vesicles). Reception in them is carried out by specialized nerve cells (neurosensory). This group includes the organ of sight and the organ of smell.

Secondary sensory organs develop from placodes (placode is a thickened part of the ectoderm). Sensation is perceived by sensory epithelial cells – specialized epithelial cells. They contain stereocilia, kinocilia and microvilli on their apical surface. This group includes the organ of hearing, the organ of equilibrium and the organ of taste.

The sensory organs are analyzers. According to I.P. Pavlov, analyzers consist of 3 parts: 1) peripheral part – receptors, 2) intermediate part – transmits impulses through conducting pathways, 3) central part – cerebral cortex, where analysis and synthesis of sensations takes place.

The organ of vision

The eye is the peripheral part of the visual analyzer. With the help of the visual organ (eye), a person receives 80–85% of the information about the surrounding world. This information allows us to orient ourselves in the space around us.

The visual organ consists of 1) the eyeball and 2) the auxiliary apparatus. The auxiliary apparatus includes the eyelids, the oculomotor muscles and the lacrimal apparatus. The eyeball consists of 3 layers: 1) outer – fibrous tunic consisting of cornea and sclera, 2) middle – vascular tunic, 3) inner – retina in which receptor function is performed

by neurons. The eyeball also contains the lens, vitreous body, anterior and posterior chamber.

Development of the eye

Sources of development: 1) neural tube, 2) dermal ectoderm, 3) mesenchyme. Three developmental stages are distinguished:

- Stage 1 – the optic vesicle stage,
- Stage 2 – the optic cup stage,
- Stage 3 – the eyeball stage.

1. Optic vesicle stage.

In the 4th week of embryogenesis, paired (2) protuberances - optic vesicles - form in the lateral walls of the developing intermediate brain (neural tube) and retain their connection to the brain. The optic vesicle grows towards the cutaneous ectoderm, with mesenchyme in between.

2. Optic cup stage.

The anterior part of the optic vesicle bulges into its cavity and takes the form of a double-walled optic cup. The part of the ectoderm opposite the lens thickens to form the lens placode. The mesenchyme in between.

3. The eyeball stage.

The inner wall of the optic cup forms the retina (9 layers), the outer wall is the retinal pigment layer. Myoneural tissue - muscles that dilate and constrict the pupil - forms from the edges of the optic cup (where the inner and outer walls meet). The lens placode invaginates and detaches from the dermal ectoderm to become the lens. The anterior corneal epithelium forms from the dermal ectoderm. The sclera, vascular tunic, vitreous body and cornea are formed from the mesenchyme surrounding the eye. The stalk of the eyeball forms the optic nerve, which travels to the brain. The development of the eye is not complete at birth and continues during postnatal ontogenesis.

Structure of the Eye

The outer fibrous membrane consists of two parts: 1) the sclera (the white coat), and 2) the cornea (the transparent anterior part).

The sclera is made up of a dense fibrous regular connective

tissue (DFRCT) that does not contain any blood vessels. The junction between the sclera and the cornea is known as the limbus, which contains the Schlemm's canal responsible for draining aqueous humor from the anterior chamber of the eye.

The cornea is the transparent anterior section of the eye, consisting of five layers:

- 1) corneal epithelium – SSNE
- 2) anterior limiting lamina - Bowman's membrane
- 3) substantia propria - DFRCT.
- 4) posterior limiting lamina - Descemet's membrane.
- 5) corneal endothelium – SSE

The cornea lacks blood vessels. The corneal epithelium is a stratified squamous non-keratinized epithelium (SSNE) with free nerve endings, and it has a high regenerative capacity. Bowman's membrane is represented by a dense fibrous irregular connective tissue (DFICT). The substantia propria consists of dense fibrous regular connective tissue (DFRCT) represented by collagen fibers arranged in parallel, with fibroblasts interspersed between them. The substantia propria lacks blood vessels and is nourished through the anterior chamber of the eye, which is situated between the cornea and the iris. Descemet's membrane is a dense fibrous irregular connective tissue in the form of a network (DFICT). The corneal endothelium is a simple squamous epithelium (SSE). Inflammation can lead to corneal opacity or blindness.

The vascular (middle) membrane provides nutrition to the eye and composed of three parts: the choroid, the ciliary body, and the iris.

The choroid is divided into four layers:

- 1) the supravascular, which consists of the LFICT.
- 2) the vascular layer consisting of arteries and veins,
- 3) the choriocapillary layer consisting of capillaries,
- 4) the basal layer known as Bruch's membrane.

The ciliary body is formed by the ciliary muscle, which is composed of smooth muscle cells arranged in three directions.

- outer meridional,
- middle radial,
- internal circular.

The ciliary muscle gives off the thin projections called the ciliary processes. The suspensory ligament (that consist of zonular fibers of Zinn) runs from these towards the lens.

The iris separates the anterior chamber of the eye from the posterior chamber. It is located in front of the lens and appears like a plate with a round hole in the center, known as the pupil. Its main function is to regulate the amount of light that enters the eye. The pupil narrows in the light and widens in the dark. Myoneural cells, including sphincters and dilators, are located in the iris. **The iris is composed of five layers:**

- 1) the anterior epithelium (SSE),
- 2) the external boundary layer,
- 3) the vascular layer which includes arteries and veins,
- 4) the inner boundary layer.
- 5) the pigmented epithelium

The outer boundary layer contains loose fibrous irregular connective tissue (LFICT), which has melanocytes. The amount of melanin in melanocytes determines eye color. In people who lack melanin due to certain health conditions (e.g. in albinism) the iris of the eyes appears as red due to visible blood vessels. The inner border layer has the same structure as the anterior layer, but it also contains myoneural cells.

The lens is a transparent biconvex disk held by a suspensory ligament and covered by a transparent capsule composed of connective tissue. The anterior surface of the lens is covered with a simple squamous epithelium, while the posterior surface is made up of crystalline lens fibers in the form of elongated cells. Epitheliocytes form the cambial zone of the lens at the equator. Throughout life, this zone generates new cells on the anterior and posterior surfaces of the lens. These new epitheliocytes develop into lens fibers that contain nuclei. The centrally located lens fibers lose their nuclei, shorten, and overlap to form the lens nucleus. There are no vessels or nerves inside the lens. The lens is elastic and contains a protein called crystallin. The posterior chamber of the eye, which is filled with fluid, is located between the lens and the iris.

The curvature of the crystalline lens can be altered. When viewing close objects, the ciliary muscles contract, the zonular ligaments relax, and the elastic lens becomes convex. When observing distant objects, the ciliary muscles relax, the zonular ligaments tighten, and the lens thickens. As a person ages, the lens loses its elasticity, resulting in age-related farsightedness. In such cases, double-convex plus glasses are required for close work. Additionally, the lens may become cloudy with age, leading to cataract. In such cases, the lens is replaced with an artificial one through transplantation.

Vitreous body is a transparent gelatinous substance that fills the space between the lens and retina. It is composed of vitrein protein arranged in a network of collagen fibers. The vitreous body refracts light rays and directs them to the retinal yellow spot (macula lutea), which is the area of the retina with the best vision. Additionally, the vitreous body contributes to the intraocular pressure and is involved in the metabolic processes of the retina. The vitreous body is devoid of vessels and nerves.

The retina is the innermost layer of the eye. It originates as a specialized part of the cerebral cortex and is brought to the periphery.

The cellular composition of the retina includes:

- 1) pigment epitheliocytes,
- 2) glia cells (Müller cells or fibrous astrocytes),
- 3) neurons.

The pigment epitheliocytes form the pigmented (outer) layer of the retina. The cells have a polygonal shape and are located on the basal Bruch's membrane. In humans, the number of pigment cells ranges from 4 to 6 million. These cells are flattened at the periphery of the retina and taller in the center of the yellow spot (macula lutea). Melanocytes contain melanin pigment in their light cytoplasm, which is poor in general organoids. The nuclei are rounded in shape, and the apical surface of melanocytes has processes (microvilli) that contain melanin pigment. The amount of pigment in the processes increases in the light, while in the dark, melanin pigment moves from the outgrowths into the cell body. These cells' processes surround the outer segments of rod and cone neurons.

Functions of pigment cells:

1) Protective – Pigment cells perform phagocytosis of outer segments of rod and cone neurons (80 discs and half-discs per day).

2) Transport – Pigment cells transport metabolites from the vasculature to photoreceptors.

3) Antioxidant defense – Melanosomes in pigment cells provide anti oxidant defense.

4) Participation in vitamin A metabolism - Pigment cells participate in vitamin A (retinol) metabolism and supply retinol for rhodopsin synthesis in rod neurons.

Neuroglia in the human retina are represented by Müller cells, which are fibrous astrocytes. These cells are long and narrow, with a fibre-like structure that runs radially from the outer to the inner border layer of the retina. The Müller cell has an elongated nucleus that lies at the level of the nuclei of bipolar neurons. It is a large neuroglial cell with external and internal outgrowths, also known as radial gliocytes. The Müller cell's outer outgrowths form the external limiting membrane (3rd retinal layer), while the inner outgrowths form the internal limiting membrane (10th retinal layer) at the border with the vitreous body. Müller cells have two main functions:

5) supportive,

6) trophic.

The retinal neurons (nerve cells). The retina is composed of three types of neurons:

1) outer rod and cone neurons (photoreceptor, modified bipolar neurons),

2) middle bipolar neurons,

3) inner ganglionic (multipolar) neurons.

Additionally, there are two types of multipolar associative neurons, horizontal cells and amacrine cells, which connect the other neurons in various ways. The horizontal cells are situated at the same level as the processes of the first and second neurons, while the amacrine cells are located at the same level as the processes of the second and third neurons.

The retina is composed of 10 layers, including:

1) the pigmented layer (outer layer),

- 2) the photoreceptive layer of rods and cones,
- 3) the external limiting membrane,
- 4) the outer nuclear layer,
- 5) the outer plexiform layer,
- 6) the inner nuclear layer,
- 7) the inner plexiform layer,
- 8) the ganglionic layer,
- 9) the nerve fiber layer,
- 10) internal limiting membrane.

The human eye's retina is an example of an inverted organ, where the receptors (rods and cones) face away from the incoming light. The deepest layer of the retina is composed of rods and cones, which face the pigment layer of the retina. The light ray travels from the internal limiting membrane to the layer of rods and cones. To reach the rod and cone layer, the ray must pass through the cornea, anterior and posterior chambers of the eye, lens, vitreous body, and the entire retinal thickness.

The retina is primarily composed of functional, light-receptive photoreceptor cells, which are classified as either rod or cone neurons based on the shape of their peripheral processes. A smaller portion of the retina, located on the inner side of the ciliary body and the posterior surface of the iris, is non-functional and lacks photoreceptors.

The retina is composed of a chain of three neurons (1, 2, 3), each consisting of three parts: dendrite, body, and axon. The bodies of these neurons form the nuclear and ganglionic layers. Specifically, the body of the first neuron forms the outer nuclear layer, the body of the second neuron forms the inner nuclear layer, and the body of the third neuron forms the ganglionic layer. The dendrites and axons of the neurons form the plexiform layers and the nerve fiber layer. The outer plexiform layer is formed by the axon of the first neuron and the dendrite of the second neuron. Horizontal nerve cells, which form inhibitory synapses, are located here for communication. The inner plexiform layer is formed by the axon of the second (bipolar) neuron and the dendrites of the third (ganglionic) neuron. The amacrine nerve cells, which lie here, exert inhibitory influence. The axons of large

multipolar ganglionic neurons (the third neuron) form a layer of nerve fibers that make up the optic nerve.

The point at which the optic nerve exits the eye is known as the blind spot. This area lacks photoreceptor cells and is where axons (nerve fibers) acquire myelin sheath and unite to form the optic nerve.

The external and internal limiting membranes are formed by processes of Müller cells. The pigment layer is formed by pigment epitheliocytes. The retina is composed of ten layers, with this being the first. The remaining nine layers are comprised of nerve cells.

The structure of photoreceptor, visual, and primary-sensing neurons is as follows: Light-sensitive neurons consist of two types, namely rod and cone photoreceptor neurons. Several rod cells connect to a single bipolar neuron, while one cone cell connects to one bipolar neuron. Multiple bipolar neurons connect to one ganglionic neuron. The human retina contains approximately 130 million rod neurons. The rod neurons are receptors of black and white (twilight) light and provide twilight vision (night vision). The human retina contains 6-7 million cone neurons, which are responsible for daylight vision and color perception.

Structure of Rod Cells

Rod neurons consist of three main parts: a stick-shaped modified dendrite (photoreceptor), a nucleus-containing part, and an axon. The modified dendrite is made up of two parts: an outer segment and an inner segment (segment) connected by a cilium.

The outer segment is a cylindrical structure consisting of approximately 1000 flat membrane disks arranged in a stack. These disks are closed, twinned membranes that are not connected to each other or to the cytolemma. They are formed by deep folds of the plasmalemma, which then separate from it and have the appearance of independent disks. The outer segment of rod neurons contains membrane disks that contain the visual pigment rhodopsin, composed of the protein opsin and retinol (vitamin A), which is essential for rod function. Rods are responsible for perceiving black and white and providing twilight and night vision. The formation of new disks

occurs at night, while destruction and phagocytosis of discs by pigment epitheliocytes occur during the daytime (afternoon) when they are not functioning. During the day, large amounts of vitamin A accumulate in the rod discs. Vitamin A has membranolytic properties and promotes the destruction of the discs. The mechanism of photoreception involves the breakdown of the pigment rhodopsin in the dark. The breakdown of rhodopsin is followed by its resynthesis in the dark and in the presence of vitamin A. Impaired twilight vision (chicken blindness) and disc destruction can result from a deficiency of vitamin A in the diet.

Structure of Cone Cells

The structure of cone neurons is composed of three distinct parts:

- 1) a modified dendrite that is cone-shaped and subdivided into outer and inner segments,
- 2) a nucleus-containing part,
- 3) an axon.

The dendrite terminates in a photoreceptor known as the cone. The outer segment is cone-shaped and contains membranous semidisks. The cone's membranous semidisks, which contain the visual pigment iodopsin, are formed by invagination of the cytolemma but remain connected to it and do not separate from it. The semidisks are not closed and the intradisc space communicates with the extracellular medium.

There are three types of cone neurons, each sensitive to one of the primary colors of the spectrum: blue, green, and red. While each color affects all three types of cones, the degree of sensitivity varies. The sensation of different shades of color in the cortex is due to the mixing of these primary colors in different proportions. Cones containing the pigment erythrolab are sensitive to red, those containing the pigment cyanolab are sensitive to blue, and those containing the pigment chlorolab are sensitive to green.

Color blindness, a disorder of color perception, is caused by the genetically determined absence of one or more types of cone neurons in the retina. Four types of color blindness are recognized: protanopia, which is a lack of sensitivity to red; tritanopia, which is a lack of sensitivity to blue; deuteranopia, which is a lack of sensitivity to green; and monochromacy, which is complete color blindness.

The inner segment of cone neurons contains an ellipsoid consisting of a large lipid droplet and mitochondria, which are tightly adhering to each other and surrounding the lipid droplet. Ellipsoids play a crucial role in color perception. The mechanism of photoreception is related to the breakdown of iodopsin pigment molecules under the action of light energy. An action potential occurs in cone neurons. The cone semidiscs undergo phagocytosis and new formation at night when their function ceases. The semidisc membranes undergo no renewal, only molecular renewal of proteins within them.

The retina contains a yellow spot (macula lutea), which is the site of best vision. At the center of this spot lies a central fossa, where all retinal layers are thinned except for the outer nuclear layer, which mainly consists of the bodies of cone neurons.

The auxiliary apparatus of the eye

The auxiliary apparatus of the eye comprises the eye muscles, eyelids, and lacrimal apparatus.

The eye muscles, represented by skeletal muscle fibers, perform the oculomotor function.

The eyelids have several distinguishing features: The conjunctiva covers the back of the eyelid. The skin on the front of the eyelid, known as the anterior cutaneous surface, is covered in hair and contains sebaceous glands. There are also 2-3 rows of eyelashes and ciliary glands, which are modified sweat glands, along the edge of the eyelid. The conjunctiva, which covers the posterior surface, is lined with stratified squamous non-keratinizing epithelium (SSNE).

The lacrimal apparatus of the eye consists of the lacrimal glands, lacrimal sac, and lacrimal-nasal duct. The lacrimal glands are serous, complex, alveolar-tubular glands. The lacrimal fluid continuously moistens the surface of the cornea, providing protection. The lacrimal sac and lacrimal-nasal duct walls are lined with stratified columnar epithelium.

Olfactory Organ

The olfactory system is composed of two systems: the main and the vomeronasal. Each system consists of three parts:

- 1) the peripheral (olfactory organs),
- 2) the intermediate (olfactory bulb and nerve fibers),
- 3) the central (cortex of the large hemispheres).

The main olfactory organ is located in the olfactory area, which mainly covers the upper part of the nasal cavity in humans. The olfactory organ is the olfactory epithelium that covers the mucous membrane of the upper part of the nasal cavity. It is a chemoreceptor that perceives the action of odoriferous substances. Humans have approximately 6 million olfactory cells.

Development. The olfactory organ develops from two sources: 1) thickenings of ectoderm – olfactory placodes, and 2) mesenchyme. Olfactory placodes, which are thickenings of the ectoderm near the head end of the neural tube, subsequently become embedded in the underlying mesenchyme. These placodes form the olfactory pits, which migrate to the region of the upper nasal cavity. During embryogenesis, in the fourth month of development, olfactory pits differentiate into olfactory, basal, and supporting cells. Olfactory cells form an axon and a dendrite during this process. The axons then unite with each other. Between 20 and 40 nerve bundles form the olfactory pathways, which direct signals to the olfactory bulbs in the brain. Synaptic contacts are made with the dendrites of mitral neurons in the olfactory bulbs.

Structure of the Olfactory Organ

The olfactory epithelium is a pseudostratified ciliated columnar epithelium that lies on a thick basal membrane. Connective tissue is located beneath the basal membrane. The surface of the olfactory epithelium facing the nasal cavity is covered with a layer of mucus. The olfactory epithelium comprises three types of cells:

- 1) receptor (neurosensory) olfactory cells,
- 2) supporting epitheliocytes,
- 3) basal epitheliocytes.

All of these cells are in contact with the basal membrane.

The olfactory cell is a type of neuron that consists of a short dendrite and a long axon. The receptor cell is located between supporting

epitheliocytes. It is spindle-shaped and has two processes: a dendrite and an axon. At the end of the dendrite, there is a thickening called the olfactory vesicle, which contains 10–12 motile olfactory cilia. These cilia have basal cilia and 9 peripheral and 2 central paired protofibrils. The olfactory cilia detect odorant molecules through continuous, automatic, pendulous movements. Immersed in a liquid secretion, they are moistened by the secretion of Bowman's glands, which are tubular-alveolar protein-mucous olfactory glands with a merocrine type of secretion. These glands are located in the underlying LFICT and their secretion moistens the surface of the olfactory epithelium. The nucleus-containing part of the olfactory cell occupies a median position. The cytoplasm contains several organelles of general importance, including mitochondria, the Golgi complex, and the granular endoplasmic network. The axon passes between supporting cells and is covered by a myelin-free sheath in the connective tissue layer. Bundles of axons, numbering between 20 and 40, are directed towards the olfactory bulb.

The supporting epitheliocytes are prism-shaped and located on the basal membrane. The nucleus is centrally located within the cell. The cytoplasm contains well-developed organoids of general importance, secretory granules. Additionally, the apical surface of the cell contains numerous microvilli. The cells possess both secretory and phagocytic abilities.

The supporting cells have three main functions:

- 1) secretion of an apocrine-type liquid,
- 2) isolation of olfactory cells from each other,
- 3) protection through phagocytosis.

The basal epitheliocytes are cuboidal in shape and are situated on the basal membrane. Basal cells are undifferentiated cells that serve as a source for the formation of olfactory epithelial cells. They have cytoplasmic outgrowths that surround the axons of olfactory cells and are capable of differentiating into supporting cells. Their function: they serve as a source of regeneration.

The vomeronasal organ (Jacobson's organ) is an accessory olfactory organ located as two tubes in the lower part of the nasal septum.

Development. It forms at the base of the nasal septum during embryogenesis, in the sixth week. The epithelium of the base of the nasal septum grows into connective tissue in the form of two tubes. By week 7, the tubes develop a cavity, and by week 21, receptor and support cells differentiate. From the receptor cell there are 2 processes: dendrites and axons. The dendrite thickens at the end, forming a knob, while the axon extends into the brain.

Structure of the vomeronasal organ

The organ's surface facing the nasal cavity is covered with mucus. The tubes' proximal end opens into the anterior third of the nasal septum, while the distal end ends blindly. The organ comprises pseudostratified epithelium, which is made up of three types of cells.

- 1) sensory, receptor cells,
- 2) supporting cells,
- 3) basal cells.

Receptor cells have an elongated shape, contain an oval nucleus and organoids of general importance. This neuron has a dendrite and an axon. At the end of the dendrite there is a thickening, the knob. Fixed microvilli branch from the knob. Microvilli detect the odor emitted by the opposite sex's sex glands. Axons combine to form unmyelinated cable-type fibers and are directed towards the brain.

Supporting cells have an elongated shape, an oval nucleus, and general organoids. Microvilli are present on the apical surface. These cells secrete a liquid containing odorant molecules.

Basal cells are poorly differentiated stem cells and are responsible for regenerating the vomeronasal epithelium through proliferation and differentiation.

The vomeronasal organ influences sexual behaviour and emotional state through the detection of pheromones produced by glands.

Secondary sensory organs

Gustatory Organ

The taste organ is represented by taste buds located in the stratified squamous non-keratinizing epithelium of the tongue papillae. There are three types of taste buds:

- 1) foliate, found on the lateral surface of the tongue in children and reduced in adults;
- 2) fungiform, located on the tip of the upper surface of the tongue;
- 3) circumvallate, situated at the root on the upper surface of the tongue.

The human tongue contains approximately 2000 taste buds.

Development. Taste buds develop during the 6th-7th week of human embryogenesis. The embryonic stratified epithelium of the tongue papillae (basal cells) serves as the source of development. This undergoes special differentiation to form the taste bud.

Structure. The taste bud has an ellipsoidal shape. The apex of the taste bud communicates with the surface of the tongue through the gustatory pore, which has a depression known as the gustatory fossa.

The taste bud is composed of three types of cells:

- 1) receptor cells (also known as gustatory cells or sensoepithelial cells),
- 2) supporting epitheliocytes,
- 3) basal epitheliocytes.

Gustatory cells are elongated and dark in color, and they are located on the basal membrane, separated from each other by supporting cells. The taste cell nuclei are oval and located near the cell base. The cytoplasm contains well-developed mitochondria and smooth endoplasmic network. Microvilli on the apical surface of the taste cells increase the perceptual surface. Sensitive neurons' dendrites originate on the cytolemma of the basal part of the cells. In the anterior part of the tongue's taste buds, a receptor protein sensitive to sweetness is found, while in the posterior part, a receptor protein sensitive to bitterness is found.

Supporting cells surround and insulate taste cells and nerve fibers. The supporting cells are sickle-shaped and light in color. The nucleus is oval and located in the basal part of the cell. The cytoplasm of these cells contains numerous mitochondria, ribosomes, and granular endoplasmic network membranes. Microvilli are present on the apical surface of the cells. These supporting cells are situated on the basal membrane.

Basal cells are short and conical in shape, lying on the basal membrane. Organoids are poorly developed in the cytoplasm of these cells. These cells are poorly differentiated and able to undergo mitotic division. Their function is regenerative, as they are the source of development for supporting and taste cells.

The ear

It is a secondary sensory organ, with reception carried out by specialized sense epithelial cells. The peripheral section of the vestibular analyzer (organ of balance), which includes two sacs and three semicircular canals, reacts to the body's position in space, linear and angular accelerations, and vibration. The auditory analyzer's peripheral section is represented by the hearing organ, which comprises the outer, middle, and inner ear and responds to sound. The human ear can perceive sounds ranging from 16 to 20,000 hertz.

Development The source of development is otic placodes, which are paired thickenings of the ectoderm at the level of the posterior cerebral vesicle. During the third week of embryogenesis, the otic placodes become embedded in the underlying mesenchyme. They separate from the dermal ectoderm and develop into auditory vesicles, each containing a fluid-filled cavity. Subsequently, the otic vesicle divides into two parts, with one developing into the organ of balance and the other into the organ of hearing. The otic vesicles are lined with pseudostratified epithelium. The epithelial cells of the receptor structures, including the acoustic spots, acoustic crests, and the organ of Corti, develop from the pseudostratified epithelium.

The organ of balance comprises the saccule, utricle, and three semicircular canals. At the junction of the semicircular canals with the utricle, there are extensions known as ampullae, which contain receptor areas called crista. The receptor areas in the utricle and saccule are referred to as acoustic spots or maculae. The semicircular canals are located in three mutually perpendicular planes. A duct connects the utricle and the saccule, which terminates in a thickening adjacent to the dura mater. Inflammation of the inner ear affects the dura mater. The saccule and utricle are lined with a simple squamous epithelium.

Structure of the acoustic macule

The acoustic macule of utricle and saccule are lined with epithelium located on the basal membrane. The surface of the epithelium is covered by an otolithic membrane made of a jelly-like substance, in which there are otoliths - calcium carbonate crystals. The auditory epithelium consists of two types of cells:

- 1) vestibular hair (sensoepithelial) cells – vestibulocytes
- 2) supporting cells.

1. Vestibular hair cells by structure are divided into 2 types:

- type 1 – pear-shaped vestibulocytes,
- type 2 – columnar vestibulocytes.

Type 1 cells pear-shaped vestibulocytes. Apical surface is covered with: stereocilia and kinocilia. Stereocilia are immobile and there are 60-80 of them. Kinocilia, on the other hand, are mobile and contain 9 pairs of peripheral and 1 pair of central microtubules, giving them the structure of a contractile cilia. Kinocilia are always positioned opposite the bundle of stereocilia. If the stereocilia move towards the kinocilium, the cell is stimulated, and if they move in the opposite direction, the cell is inhibited.

Type 1 cells (pear-shaped cells) are situated between supporting cells. The nucleus of pear-shaped vestibulocytes is round and located at their basal end. The cytoplasm contains ribosomes, mitochondria, and an endoplasmic network. Vestibulocytes, which are pear-shaped, have a wide rounded base at the basal end. The basal end is approached by numerous nerve fibers, which braid the cell in the shape of a bowl, forming a bowl-shaped case. These nerve fibers are sensitive nerve endings, also known as dendrites.

Type 2 cells are columnar vestibulocytes with a cylindrical shape. Their basal ends are approached by few nerve fibers, which form point synapses on their bases. The internal structure of columnar vestibulocytes is similar to that of pear-shaped vestibulocytes. Above the receptor epithelium surface, there is an otolith membrane that is 80-100 μm thick and contains calcium carbonate crystals. When the head moves, the otolith membrane may shift. The kinocilia and

stereocilia, are connected to the otolith membrane and can shift. Excitation occurs when the stereocilia move towards the kinocilia, while inhibition occurs when they move away. The cell's excitation or inhibition is then transmitted through synaptic contacts in its basal part to the dendrites of the sensory neuron that innervates the hair cell.

Supporting cells of acoustic macule are situated between the hair cells. The apical surface of the supporting cells has many microvilli, and the nucleus is oval. These cells contain a large number of mitochondria. The otolith membrane is secreted by vestibular supporting cells. The functions of supporting cells include support and trophic functions.

Functions of the acoustic maculae

- 1) the acoustic macule of saccule perceives vibrations
- 2) the acoustic macule of utricle perceives changes in the body's position, serves as a receptor for gravity and a location for perceiving linear accelerations.

The structure of the auditory ridges (cristae)

The cristae are located in the ampullae of the semicircular canals, which are lined with a simple squamous epithelium. In this area, the epithelium takes on a prismatic shape.

The cellular composition of the cristae

The crista is composed of two types of cells: vestibular hair cells and supporting cells. These cells have a similar structure to those found in the acoustic maculae. On the surface of the crista, there is a gelatinous dome called the otolith dome instead of the otolith membrane. The receptor epithelium is separated from the underlying connective tissue by the basal membrane. The connective tissue contains many blood capillaries and nerve fibers. The gelatinous otolith dome is secreted by vestibular supporting epitheliocytes.

The function of the crista. The crista is responsible for perceiving angular accelerations. When the head or body is moved rapidly, the gelatinous otolith dome can easily shift position, causing it to move relative to the crista. This movement causes the kinocilia to be pulled either towards or away from the stereocilia, resulting in excitatory and inhibitory impulses in some hair cells. These impulses are then

transmitted to the skeletal and oculomotor muscles. In humans, the loss of vestibular function can cause postural instability. The auditory cristae act as receptors for acceleration in forward horizontal motion and angular acceleration in body rotation.

The auditory system

The auditory system is the second most important sensory system after vision. In humans, hearing plays a crucial role in the development of speech. The hearing organ is composed of three parts: the outer ear, middle ear, and inner ear.

The outer ear comprises:

- the auricle,
- the external acoustic meatus,
- the tympanic membrane.

The middle ear is composed of

- the tympanic cavity,
- the auditory ossicles,
- the auditory tube (Eustachian tube).

The inner ear is made up of the bony labyrinth, which contains the membranous labyrinth. The membranous labyrinth is divided into two parts:

- the vestibular part, which contains the organ of balance (including acoustic maculae in the saccule and utricle, and cristae in the semicircular canals).
- the cochlear part, which contains the organ of hearing known as the spiral organ of Corti.

External ear

Includes the auricle, external acoustic meatus, and tympanic membrane.

1) The auricle consists of elastic cartilage covered by skin with hair and sebaceous glands. There are no sweat glands in the auricle.

2) The external acoustic meatus is formed by elastic cartilage and a bony part. The ear canal is covered with skin containing hair and ceruminous tubular glands that secrete earwax, which has bactericidal properties.

3) The tympanic membrane is oval, slightly concave in shape, 0.1 mm thick. It is composed of collagen fibers and partly elastic material, with fibroblasts interspersed between them. The structure of the tympanic membrane can be divided into two layers: the outer layer, which is composed of radially arranged fibers, and the inner layer, which is composed of circular fibers. The outer surface is lined with stratified squamous keratinizing epithelium, while the inner surface is lined with low columnar epithelium. Additionally, the handle of the malleus is attached to the inner surface, and small arteries and nerves run to the tympanic membrane from there.

Middle ear

It consists of the tympanic cavity, auditory ossicles, and auditory tube.

1) The tympanic cavity is a space covered with a simple squamous epithelium.

2) The auditory ossicles, namely the malleus, incus, and stapes, are formed by lamellar bone tissue and are connected to each other through joints. They transmit vibrations from the eardrum and amplify sound vibrations to the inner ear.

3) The auditory (Eustachian) tube connects the tympanic cavity to the nasopharynx. It is lined with pseudostratified epithelium, which can be transformed into stratified squamous in chronic inflammatory processes. The auditory tube regulates the air pressure in the tympanic cavity of the middle ear, balancing it with atmospheric pressure.

Inner ear

Consists of a bony labyrinth and a membranous labyrinth. The membranous labyrinth follows the course of the bony labyrinth. The membranous labyrinth includes the auditory part, the cochlea. The cochlea is a bony canal that makes 2.5 turns around the bony shaft and is 3.5 cm long. The bony cochlear canal is subdivided into 3 parts:

- 1) scala vestibuli
- 2) scala tympani
- 3) the cochlear canal.

The scala tympani and the scala vestibuli, contain perilymph and the cochlear membranous canal contains endolymph. On a transverse section, the cochlear canal has a triangular shape, with its sides formed by:

- 1) vestibular membrane (Reissner's membrane),
- 2) stria vascularis
- 3) basilar membrane.

The vestibular membrane, which forms the upper wall, is a connective tissue plate covered on both sides by a simple squamous epithelium.

The basilar membrane, which forms the lower wall, is a connective tissue plate or spiral membrane. The vascular band forms the lateral wall of the cochlear canal and is lined by pseudostratified epithelium. Within the epithelium, there are squamous light basal cells and high columnar dark cells with many mitochondria. Blood capillaries run between the cells.

The stria vascularis is situated on the spiral ligament. Its cells produce endolymph, which is essential for the nourishment of the spiral organ (Corti's organ). The primary role of the stria vascularis is to secrete endolymph that fills the membranous cochlear canal.

The Cortia organ, also known as the spiral, is responsible for perceiving sound vibrations. It is located on the inferior basilar membrane. The spiral organ contains two types of cells:

- 1) hair (sensoepithelial) cells, which are further divided into inner and outer cells,
- 2) supporting cells, which are divided into three types: internal, external, and pillar cells.

A tunnel is formed between the pillar cells, dividing them into inner and outer cells. The spiral organ's supporting epitheliocytes are located directly on the basal membrane. The pillar cells have a columnar shape, and a distinction is made between inner and outer cells. At the point of contact (apical ends), they converge at an acute angle to form a regular triangular channel - a tunnel filled with endolymph. Unmyelinated nerve fibers run from the neurons of the spiral ganglion to the hair receptor cells, crossing the tunnel that

extends spirally along the entire spiral organ.

Internal supporting cells

The internal supporting (phalangeal) epitheliocytes are situated inside the inner pillar cells. A ribbon-like outgrowth (phalanx) extends from the apical surface of the inner phalangeal cells, separating the inner hair cells from each other. The inner supporting cells have a columnar shape and their bases rest on the basal membrane. The bases of the inner hair (receptor) cells are located in a depression on the apical surface of the inner supporting cells.

The outer supporting cells are subdivided into 3 types:

- 1) Deiters cells – phalangeal cells,
- 2) Genzen cells – external border cells,
- 3) Claudius cells – external supporting cells.

1) **Deiters cells** are external phalangeal cells that have a columnar shape. Their basal end lies on the basal membrane, and on the apical surface, there is a cup-shaped depression where the base of the outer hair cell is located. A long outgrowth (flank) separates the outer hair cells from each other from the apical surface. Deiters cells are arranged in 3-4 rows in close proximity to the outer cells, forming pillars.

2) **Genzen cells** -the external border supporting cells, have a low columnar shape and their basal end lies on the basal membrane. These cells are shorter than Deiters cells and have microvilli on their apical surface. The nucleus is located in the center of the cell and the cytoplasm contains organoids of general significance and glycogen inclusions. Their function is trophic.

3) **Claudius cells** – the outer supporting cells, have a cubic shape and pass into the vascular band.

The hair receptor cells responsible for detecting sound waves in the ear are divided into two types: inner and outer hair epitheliocytes.

Inner hair cells have a distinctive jug or pear shape, with their round nuclei located in the expanded basal part of the cell. The cytoplasm contains organoids of general significance. These cells are arranged in a single layer along the entire spiral organ. The hair cells' rounded base rests on the indentations of the inner supporting (phalangeal) cells. The hair cells have a narrowed apical surface

covered by a cuticle, from which 30-60 stereocilia branch off. Stereocilia are short microvilli, also known as auditory hairs, arranged in 3-4 rows. They are immobile. There are a total of 3500 inner hair cells. The sensitive nerve fibers of spiral ganglion neurons approach the base of inner hair cells.

The outer hair cells are columnar in shape and arranged in 3-5 rows, with a total number ranging from 12,000 to 20,000. They rest on the cup-shaped indentations of the outer supporting cells and have a cuticle on their apical surface, from which 60-70 immobile stereocilia depart. Stereocilia are short microvilli arranged in several rows. The tips of stereocilia attach to the inner surface of the gelatinous membrane that overhangs the spiral organ. The sensitive nerve fibers of spiral ganglion neurons approach the base of the outer hair cells.

The tectorial membrane is a plate of connective tissue made up of collagen fibers arranged radially. Its inner edge is attached to the spiral crista, while its outer edge hangs freely over the spiral organ. As the spiral organ ossicles, the stereocilia of the hair cells come into contact with the tectorial membrane, contributing to the generation of sound impulses. The spiral ganglion is where a sensitive pseudounipolar neuron is located. The hair cells located in the lower whorls of the cochlea are irritated by high sounds, while the hair cells of the apex of the cochlea are irritated by low sounds. It is important to note that only the outer hair cells are sensitive to high sounds.

When a sound wave enters the ear, it causes the eardrum to vibrate, which in turn transmits the vibrations to the malleus, anvil, and stirrup. These vibrations cause the perilymph, endolymph, and basal membrane with hair cells to vibrate. The oscillation of the basal membrane depends on the frequency of the sound, with high frequencies causing oscillation at the base of the cochlea and low frequencies causing oscillation at the apex. The cochlear organ and its hair cells oscillate along with the basal membrane. The receptor cells' hair cells interact with the covering membrane, causing a deflection of the stereocilia, resulting in the emergence of a receptor potential (microphone effect). Afferent information is transmitted along the auditory nerve to the central parts of the auditory analyzer.

Weak sounds are perceived by inner hair cells, while high sounds are perceived by outer hair cells. Inner and outer hair cells exhibit varying sensitivity to damaging effects. Therefore, administering large doses of streptomycin damages internal hair cells, while quinine damages external hair cells. Exposure to loud sounds, both short-term and long-term, can result in hearing loss. The combination of noise and vibration, blasting, and shaking can cause hemorrhages in the tympanic cavity, semicircular canals, and the area of the stria and scallop. The degeneration of cells in the spiral ganglion and changes in the nerve fibers of the conducting pathway progress with age.

CARDIOVASCULAR SYSTEM

This system includes the heart, blood vessels, and lymphatic vessels.

Classification of blood vessels:

- 1) arteries,
- 2) veins,
- 3) microcirculatory vessels: arterioles, venules, capillaries, arteriovenular anastomoses.

Development of blood vessels. The source of their development is the mesenchyme. At 2-3 weeks of embryogenesis, clusters of mesenchymal cells appear in the wall of the yolk sac. Within the clusters, mesenchymal cells thicken, flatten, elongate, and form blood islets. Cells at the periphery of the blood islets differentiate into angioblasts. Angioblasts are flattened cells that connect with each other.

Cells in the center of the islet round out and differentiate into blood stem cells. Angioblasts then differentiate into vascular endotheliocytes, and stem cells differentiate into croca cells. From the mesenchyme, pericytes, fibroblasts, smooth myocytes, and adventitial cells of the vascular wall arise.

Blood vessels are a system of closed tubes of various diameters. The closed network of blood vessels and the heart provides blood circulation in the body.

Vessels of the microcirculatory system.

The exchange of substances between blood and tissues takes place through the walls of these vessels, so the microcirculatory channel is called the exchange link of the vascular system. The constant exchange of water and various substances between blood and tissues is the process of microcirculation. Microcirculatory vessels include: 1) hemocapillaries, 2) lymphatic capillaries, 3) arterioles, 4) venules, and 5) arterio-venular anastomoses.

Hemocapillaries.

Classification by diameter:

- 1) small – diameter – 4.5–7 microns – in striated muscles, nerves, lungs,
- 2) large – diameter – 7–11 microns – in skin, mucous membranes,
- 3) large ones are divided into 2 types:
 - 1) sinusoidal (diameter 20–30 microns) – in hematopoietic organs, endocrine glands, liver,
 - 2) lacunae (diameter 30–60 microns) – in placenta.

In every tissue there are capillaries in a collapsed state. They are called non-functional, only blood plasma passes through them. When the functional load on the organ increases, non-functional capillaries can turn into functional capillaries.

The function of capillaries is the exchange of substances and gases between the lumen of capillaries and surrounding tissues due to 1) thin capillary wall, 2) slow blood flow, 3) low pressure, and 4) large area of contact with surrounding tissues.

Classification of capillaries based on the structure of the endothelium and basement membrane. There are 3 types of capillaries:
Type 1 – with continuous basal membrane, somatic,
Type 2 – with partially discontinuous basal membrane, fenestrated,
Type 3 – with discontinuous basal membrane, perforated.

Capillaries with a continuous basement membrane are somatic capillaries.

The capillary wall consists of 3 types of cells:

- 1) endotheliocytes – the inner layer,
- 2) pericytes – the middle layer
- 3) adventitial cells – the outer layer.

The inner layer is represented by a single layer of endothelial cells located on the basal membrane. Endotheliocytes are flat epithelial cells that form a continuous layer. They are interconnected by tight contacts. The cytoplasm of endotheliocytes is poor in organs of general importance. The nucleus is oval. The solid, continuous endothelial layer in the brain, for example, is necessary for the impermeability of the blood-brain barrier. The basement membrane of the capillary endothelium is continuous. It is a thin fibrillar plate 30–35 nm thick.

The middle layer is composed of pericytes. Pericytes are located in the clefts of the basal membrane and have a basket-shaped outgrowth. Pericyte processes contain contractile filaments. Pericyte processes include endotheliocytes. Pericytes have the ability to swell and contract, regulating changes in the diameter of blood capillaries. These cells can differentiate into smooth muscle cells.

The outer layer consists of adventitial cells. Adventitial cells are poorly differentiated connective tissue cells located outside the pericytes. They are spindle-shaped. The organelles are poorly developed, the nucleus is oval. These cells can differentiate into fibroblasts, lipocytes.

Somatic capillaries are the capillaries of skeletal muscles, lungs, mucous membranes, nerve trunks, brain and skin. They are the most common type of capillaries. The diameter of their lumen is 6–11 microns.

Capillaries with partially discontinuous basal membrane – fenestrated.

The wall of a fenestrated hemocapillary consists of 3 layers: 1) inner – endothelial, 2) middle – pericyte layer, 3) outer – adventitial.

The inner layer of the hemocapillary is represented by endotheliocytes, which can thin to form fenestrae. Fenestrae are localized thinning of endotheliocyte cytoplasm. The basement membrane is thinned and partially interrupted in the area of endotheliocyte fenestrae.

Pericytes of the middle layer are located between the endotheliocytes and the basement membrane. On the outside, there are adventitial cells.

The fenestrated type of capillaries is characterized by the presence of fenestrae in the endothelium and a partially discontinuous basal membrane. These are capillaries of renal tubules (for filtration of blood and formation of primary urine), capillaries of intestinal villi, pituitary gland, endocrine organs. The presence of fenestra in capillaries facilitates the course of metabolic processes.

Capillaries with discontinuous basal membrane – perforated.

The wall of hemocapillaries is represented by 3 layers: 1) inner – endothelium, 2) middle – pericytes, 3) outer – adventitial cells.

The endothelium of such capillaries has slit-like pores. The basement membrane is interrupted. Pericytes are located in the clefts of the basal membrane.

The outer layer is represented by adventitial cells.

Capillaries of this type are very wide – sinusoidal. Sinusoidal capillaries are found in red bone marrow, spleen, liver. Through the pores in the wall of capillaries of hematopoietic organs in the blood come mature blood cells.

Lymph capillaries

The wall of lymph capillaries is formed only by endotheliocytes. Basal membrane and pericytes are absent. The lumen of lymph capillaries (20-30 microns) is several times wider than that of blood capillaries. Lymphatic capillaries start blindly, are located next to blood capillaries and are part of the microcirculatory channel.

Lymph capillaries are different from blood capillaries:

- 1) the basal membrane is absent,
- 2) endotheliocytes are 3–4 times larger,
- 3) no pericytes,
- 4) are located on outgrowth of collagen fibers,
- 5) larger in diameter,
- 6) start blindly,
- 7) lymphatic capillaries form a network.

Venules

Postcapillary venules are 30–50 μm in diameter and collect blood from the capillary channel. The wall of venules consists of endotheliocytes and loose fibrous irregular connective tissue (LFICT) of the outer layer. Distinguishing features:

1. endotheliocytes are shorter,
2. endotheliocyte nuclei are round,
3. prominent outer connective tissue layer.

Venules perform:

- 1) drainage function – influx of metabolic products from the

connective tissue into the lumen of the venule, removal of products of tissue metabolism,

2) migration of blood-forming elements (leukocytes) from the venules into the surrounding tissue,

3) storage of blood due to the distensibility of these vessels.

Arterioles

The diameter of arterioles is 50-100 microns. The wall of arterioles consists of 3 sheaths: 1) inner, 2) middle, 3) outer.

The inner sheath consists of 3 layers:

- 1) endothelium lying on the basal membrane,
- 2) individual cells of the subendothelial layer,
- 3) thin internal elastic membrane.

All 3 layers of the inner sheath are greatly thinned.

The middle layer consists of 1–2 layers of smooth muscle cells arranged in a circle.

The outer membrane consists of a thin layer of loose fibrous irregular connective tissue (LFICT).

Functionally, arterioles are the «faucets of the vascular system» that regulate blood flow to organs through contraction of circularly arranged myocytes. (I.M. Sechenov).

Arteriovenous anastomose.

They allow direct blood flow from arterioles to venules, bypassing capillaries. The path of blood flow through the anastomoses is shorter, so the anastomoses are called shunts. Arteriovenous anastomoses are larger than 30 μm in diameter.

Functions of arteriovenous anastomoses:

- 1) regulation of blood flow in capillaries – local peripheral blood flow,
- 2) participate in blood redistribution,
- 3) regulate blood pressure – increase intravenous pressure,
- 4) participate in thermoregulation,
- 5) arterialized of venous blood,

- 6) when capillaries are compressed by a pathological process, blood from arterioles immediately flows into venules,
- 7) regulation of the flow of tissue fluid into the venous channel,
- 8) mobilization of stored blood.

Arteries

Classification of arteries:

- 1) elastic arteries (aorta, pulmonary artery),
- 2) mixed arteries (carotid, subclavian),
- 3) muscular arteries (medium and small caliber arteries).

The classification of arteries is based on the ratio of the number of smooth muscle cells (myocytes) and elastic fibers in the middle sheath of the artery. The walls of all arteries consist of 3 layers: 1) inner, 2) middle, and 3) outer.

The lumen of arteries is usually gaping due to the presence of elastic membranes in the wall. The elastic membranes of the arteries prevent the arteries from collapsing, which accounts for their permanent gap.

Elastic artery

The arterial wall consists of 3 layers: 1) inner, 2) middle, 3) outer.

1. The inner sheath contains 2 layers: 1) endothelial layer, 2) subendothelial layer.

The endothelial layer is represented by a layer of endothelial cells located on the basement membrane.

The subendothelial layer consists of loose fibrous irregular connective tissue (LFICT).

2. The media is composed of 2 components:

1) elastic endomembranes (50-70) interconnected by elastic fibers forming an elastic network.

2) individual smooth muscle cells, arranged obliquely.

3. The outer sheath is formed by loose fibrous irregular connective tissue (LFICT), which contains feeding blood vessels.

Arteries of mixed type (muscular-elastic).

The arterial wall consists of 3 layers: 1) inner, 2) middle, 3) outer.

1. The inner membrane consists of 3 sheaths:

- 1) endothelial layer – a layer of endothelial cells located on the basal membrane,
- 2) the subendothelial layer consists of loose fibrous irregular connective tissue (LFICT),
- 3) an internal elastic membrane. This membrane is located at the junction of the inner and middle sheaths and is distinct.

2. The middle layer consists of an equal number of 1) spirally arranged elastic fibers (50%), 2) smooth muscle cells, spirally arranged (50%).

3. The outer sheath is composed of 2 layers:

1. an outer elastic membrane, which is weaker than the inner elastic membrane,
2. a loose, fibrous, irregular connective tissue (RVNST) in which the vessels of the vasculature pass.

The artery is of the muscular type.

The arterial wall consists of 3 layers: 1) inner, 2) middle, 3) outer.

The inner layer consists of 3 layers:

1. endothelial layer – a layer of endothelial cells lying on the basal membrane,
2. subendothelial layer – LFICT,
3. inner elastic membrane, clearly defined.

The middle layer contains:

1. numerous obliquely arranged smooth muscle cells
2. an insignificant number of elastic fibers with radial and arcuate arrangement.

The outer sheath consists of

1. Outer elastic membrane, thinner than the inner elastic membrane, composed of longitudinal elastic fibers in the form of a continuous elastic lamina.

2. Loose fibrous irregular connective tissue (LFICT), in which the fibers have an oblique and longitudinal direction. Blood vessels nourishing the wall and nerves are found in this layer.

Veins

Differences between veins and arteries:

- 1) veins lack inner and outer elastic membranes,
- 2) veins have valves in their walls – thin folds of the inner venous layer,
- 3) veins are larger in diameter than arteries,
- 4) irregular lumen in veins,
- 5) more underdeveloped smooth muscle cells in the middle venous layer,
- 6) smooth muscle cells are arranged in bundles,
- 7) well-developed outer sheath, the thickest sheath.

However, cerebral veins, cerebral veins, brain veins, iliac veins, iliac veins, subcostal veins, hollow veins, unnamed veins and veins of internal organs do not have valves.

The classification of veins depends on the degree of development of smooth muscle cells. Veins are divided into 2 groups:

1. muscle-free veins,
2. veins of muscular type.

Muscle veins are divided into 3 types:

- 1) veins with weak myocyte development,
- 2) veins with medium myocyte development,
- 3) veins with strong myocyte development.

Muscle-free veins have two layers:

- 1) inner layer consisting of endothelial (endothelium) and subendothelial (LFICT) layers,
- 2) the outer layer consisting of the LFICT.

Smooth muscle cells are absent in muscle-free veins. Muscle-free veins are found in dura mater, brain, retina, placenta, and bone tissue.

Muscular veins with poorly developed myocytes.

The vein wall consists of 3 layers: 1) inner, 2) middle, 3) outer. The inner layer consists of 2 layers:

- 1) endothelial layer – a layer of endotheliocytes located on the basal membrane,
- 2) subendothelial layer – LFICT, poorly developed.

The middle layer contains poorly developed bundles of smooth myocytes arranged in a circle. Between the bundles of myocytes are layers of LFICT.

The outer layer consists of loose, fibrous, irregular connective tissue (LFICT). The outer layer is 5-6 times thicker than the middle and inner layers combined. Veins with weak myocyte development are small and medium caliber veins of the face, neck and upper body; a large caliber vein is the superior vena cava.

Muscle type vein with medium myocyte development.

The vein wall consists of 3 layers: 1) inner, 2) middle, 3) outer.

The inner layer consists of 2 layers:

- 1) the endothelial layer is represented by a layer of endotheliocytes located on the basal membrane,
- 2) the subendothelial layer consists of LFICT.

Due to the inner layer, valves – thin folds – are formed in the vein. The valves in the veins prevent reflux of venous blood and promote unidirectional blood flow.

The middle layer contains bundles of smooth muscle cells arranged in a circular pattern. Between the myocytes are layers of LFICT.

The outer layer contains longitudinally arranged bundles of smooth myocytes and LFICT and is 2-3 times thicker than the middle and inner layers combined. An example of a medium caliber vein with medium myocyte development is the brachial vein.

Muscular vein with strong myocyte development.

The vein wall consists of 3 layers: 1) inner, 2) middle, 3) outer.

The inner layer contains 2 layers:

1. endothelial – a layer of endotheliocytes lying on the basal membrane.
2. the subendothelial layer is represented by loose, fibrous, irregular connective tissue (LFICT), which is well developed. It contains numerous bundles of smooth myocytes arranged longitudinally.

Valves are formed at the expense of the inner layer. The valves are arranged in such a way that when the blood moves toward the heart, their flaps press against the wall and allow the blood to pass, and when the blood moves in the opposite direction, the valves close.

The middle layer is made up of bundles of smooth muscle cells arranged in a circle. Between the myocytes is a loose, fibrous, irregular connective tissue (LFICT).

The outer layer is composed of 1) loose fibrous irregular connective tissue (LFICT), and 2) numerous bundles of smooth myocytes arranged longitudinally. The outer layer is 6-7 times thicker than the inner and middle layers combined.

Veins of muscular type with strong development of myocytes are located in the lower part of the body and in the lower extremities. This type of veins includes femoral veins, inferior vena cava. In these veins, smooth muscle cells are present in all three layers.

The Heart

The heart is the central organ in the circulatory system. Through its ability to contract, the heart propels blood.

The wall of the heart has 3 layers:

- 1) the inner one is the endocardium,
- 2) the middle one is the myocardium,
- 3) the outer epicardium.

Development. In human embryogenesis, the heart is formed at the beginning of the 3rd week from 2 sources: 1) mesenchyme, 2) visceral layer of the splanchnotome – myoepicardial plate. The endocardium of the heart is formed from the mesenchyme. Cells of the myoepicardial plate differentiate in 2 directions: 1) from the inner part, the myocardium of the heart is formed, and 2) from the outer part, the mesothelium that lines the epicardium of the heart is formed. The valves of the heart develop from the endocardium.

Endocardium

Consists of 4 layers:

- 1) the endothelial layer,

- 2) the subendothelial layer
- 3) the muscular elastic layer
- 4) the outer connective tissue layer.

There are no blood vessels in the endocardium. The valves of the heart are formed by the endocardium.

1. The endothelial layer is represented by the endothelium, which lies on the basal membrane.
2. The subendothelial layer is formed by loose fibrous irregular connective tissue (LFICT).
3. The muscular elastic layer consists of smooth myocytes and elastic fibers arranged in a network.
4. The outer connective tissue layer consists of loose fibrous irregular connective tissue (LFICT).

The endocardium is diffusely nourished by blood in the atrial and ventricular cavities.

Myocardium

The middle muscular membrane of the heart. The myocardium consists of transverse striated muscle cells – cardiomyocytes, between which there are layers of loose, fibrous, irregular connective tissue (LFICT) with blood vessels.

There are 3 types of cardiac myocytes:

- 1) typical, contractile, working,
- 2) atypical, conducting, Purkinje fibers,
- 3) secretory, endocrine.

1. **Typical**, contractile, working cardiomyocytes are rectangular in shape. They contain myofibrils and numerous mitochondria. Cardiomyocytes communicate with each other through sarcoplasmic reticulum. There are 2 types of contacts in the insertion discs – 1) desmosome, 2) nexus – slit contact.

Desmosomes contribute to firm adhesion of contractile cardiomyocytes to functional muscle fibers. Nexuses provide conduction from one cell to another. There are anastomoses between cardiomyocytes, giving the myocardium a network-like structure. An anastomosis may be a fragment of cardiomyocyte cytoplasm or

a modified cardiomyocyte. Typical cardiomyocytes lose the ability to divide by mitosis. The main mode of regeneration is 1) hypertrophy – increase in cell volume, and 2) replacement by connective tissue when cardiomyocytes die.

Typical, contractile, working cardiomyocytes provide contraction of the heart.

2. **Atypical** conducting cardiomyocytes or Purkinje fibers have a polygonal shape. Organelles of general importance are poorly expressed, few myofibrils are oriented in different directions. Atypical cardiomyocytes form the conduction system of the heart. Purkinje fibers transmit excitation to contractile (working) cardiomyocytes. A number of drugs and other factors that can lead to arrhythmias and heart block have an unfavorable effect on the conducting cardiomyocytes. The presence of its own conducting system in the heart provides a rhythmic change of systolic contractions and diastole atria, ventricles, the work of the valve apparatus.

3. **Secretory**, endocrine cardiomyocytes are located in the atrium, contain many processes. The cytoplasm is well-developed granular endoplasmic network, poorly developed myofibrils, contain secretory granules.

Functions:

- 1) produce a hormone, atrial natriuretic factor (ANF),
- 2) regulates blood pressure,
- 3) regulates water and salt metabolism,
- 4) regulates urine output,
- 5) stimulates contraction of the cardiac muscle.

The epicardium and pericardium form the serous membrane, which includes 2 layers: 1) mesothelium, 2) connective tissue base (LFICT). Between the epicardium and the pericardium is a slit-like cavity filled with a small amount of fluid, which has a lubricating function. The pericardium develops from the parietal leaflet of the splanchnotome.

ORGANS OF HEMATOPOIESIS AND IMMUNE DEFENSE

The organs of hematopoiesis are divided into: 1) central and 2) peripheral. Central (antigen-independent) organs include: 1) red bone marrow, 2) thymus. The peripheral (antigen-dependent) organs of hematopoiesis include: 1) spleen, 2) lymph nodes. Myeloid and lymphoid organs of hematopoiesis are distinguished. Myeloid organs of hematopoiesis are represented by myeloid tissues. They include the red bone marrow, in which all blood formations (erythrocytes, leukocytes, platelets) develop. Lymphoid organs of hematopoiesis are represented by lymphoid tissues. They include thymus, spleen, lymph nodes, in which only lymphocytes develop.

There are three types of hematopoiesis:

- 1) mesoblastic hematopoiesis occurs in the yolk sac during embryogenesis,
- 2) hepatolienal hematopoiesis – in the liver and spleen,
- 3) medullary hematopoiesis occurs in the red bone marrow during embryogenesis and from birth to the end of life.

Red bone marrow

In the adult body, bone marrow is divided into red and yellow marrow. Red marrow is found in the epiphyses of tubular bones, the shoulder blades, the sternum, the vertebrae, and the bones of the skull. Yellow marrow is found in the diaphyses of long bones. It is represented by adipose tissue. Under normal conditions, yellow bone marrow does not perform hematopoietic function, only in case of large blood loss it can perform hematopoietic function.

Red bone marrow is the central organ of hematopoiesis in which red blood cells, platelets, leukocytes and T-lymphocyte precursors develop from stem cells. It is an antigen-independent organ. The source of its development is mesenchyme. Stroma – reticular tissue.

Parenchyma – developing hematopoietic blood cells from 6 classes of hematopoiesis (stem, semistem, unipotent, blasts, mature and mature cells). Developing blood cells are located in the red bone marrow in groups (islets, «nests») and are localized near sinusoidal capillaries with a discontinuous basement membrane. Under normal conditions, only mature blood formations can penetrate the wall of sinusoidal capillaries. Bone marrow has a high physiological and reparative regenerative capacity.

Thymus (goiter, thymus gland)

The thymus is the central organ of lymphocytopoiesis and immune defense of the body. It is an antigen-independent organ. Antigen-independent differentiation of T-lymphocyte precursors into T-lymphocytes (killer, helper, suppressor) takes place in the thymus.

Sources of development: 1) 3.4 pairs of gill pouches
2) mesenchyme.

Development. Laying of thymus in human occurs in the 4th-5th week of embryogenesis in the epithelium of pharyngeal intestine, in the area of 3rd and 4th pairs of gill pockets in the form of protrusions of multilayered epithelium. Later, these protrusions fuse to form a common epithelial stroma. Around this stroma, a connective tissue capsule is formed from the surrounding mesenchyme. From the capsule, trabeculae extend deep into the stroma along with sinusoidal capillaries with a discontinuous basement membrane. The trabeculae divide the stroma into lobules. The lobules distinguish between cortical and medullary substance, which is populated by T lymphocytes. Hematopoiesis in the thymus begins in the 9th-10th week of embryogenesis.

Structure. The thymus is covered from the outside by a capsule, a dense fibrous irregular connective tissue. From the capsule, the connective tissue divides the thymus into lobules. A lobe is a structural-functional unit of the thymus.

The stroma of the lobule is a stratified squamous partially keratinized epithelium. In the center of the lobule, the epithelial cells of the stroma become keratinized and layer on each other to form

Hassall's corpuscles. Hassall's corpuscles or stratified epithelial corpuscles are concentric layering of partially keratinized epithelial cells.

The parenchyma of the lobule consists of cortical (peripheral) and cerebral (central) substance.

The cortical substance is darker and densely populated with mature small T lymphocytes (killer, helper, suppressor).

The medullary substance of the thymus lobules is lighter in color because there are few T lymphocytes present. Epithelial layered thymic cells (Hassall's) are found in the middle part of the brain matter. Mature T lymphocytes leave the thymus and fall with the bloodstream into the spleen, lymph nodes. The cortical substance of the thymus, unlike the cerebral substance, has an independent microcirculatory channel. In the cerebral substance, mature lymphocytes can leave and return to the thymus, i.e. recirculate. There are 2 types of involution in the thymus: 1) **accidental** (temporary) involution, 2) **age-related** (permanent) involution.

Age-related involution of the thymus gland

The thymus reaches its maximum development at the age of 3 years. From the age of 3 to the age of 20, the thymus is in a stable state. After the age of 20, there is age-related involution of the thymus – reverse development. Age-related (permanent) involution of the thymus is a decrease in the number of lymphocytes in the cortical substance and erasure of the boundary between the cortical and cerebral substance. Connective tissue overgrows and fatty tissue develops, T lymphocytes disappear. If the thymus does not undergo age-related involution, such people are characterized by reduced resistance to infections, if the adrenal cortex secretes an insufficient amount of glucocorticoids.

Accidental (temporary) involution of the thymus

The thymus retains its largest mass and lobular histologic structure during the first years of life. Accidental (temporary) involution can occur due to the effect of various extremely strong stimuli (trauma, starvation, infection, intoxication, disease). In the case of accidental

(temporary) involution, there is a release of T-lymphocytes into the blood and mass death of lymphocytes in the cortical substance. The boundary between the cortical and cerebral substance becomes invisible. The cortical substance of the thymus lobules becomes as light as the brain substance. The accidental (temporary) involution of the thymus continues as long as the disease or stress persists. After that, the state of the cortical and cerebral matter returns to normal, i.e., the boundary between the cortical and cerebral matter becomes visible.

The functions of the thymus are

- 1) hematopoietic – antigen-independent differentiation of precursors of T lymphocytes
- 2) hormonal – the stroma secretes the hormone thymosin, which stimulates proliferation and differentiation of lymphocytes in peripheral hematopoietic organs, as well as insulin-like factor, calcitonin-like factor, and body growth factor.

Peripheral organs of hematopoietic.

The spleen is a peripheral organ of hematopoiesis, an important hematopoietic and protective organ, which participates in protective reactions to antigens entering the bloodstream, destroying old and damaged erythrocytes and platelets. In the spleen there is antigen-dependent proliferation, differentiation of T and B lymphocytes.

Sources of spleen development – mesenchyme, visceral sheet of the splanchnotome forms the mesothelium of the serous membrane.

Development. The spleen is formed in the 5th week of embryogenesis from mesenchyme. Peripheral mesenchymal cells form a capsule from which trabeculae branch off. The central mesenchymal cells form the stroma of the spleen and the islets with hematopoietic cells.

Structure of the spleen. The spleen is externally covered with peritoneal-serous membrane. The serous membrane is represented by mesothelium and connective tissue. Deeper is the capsule. Spleen trabeculae branch inward from the capsule. The capsule consists of dense fibrous irregular connective tissue (DFICT). Between the fibers

of the capsule are a small number of smooth muscle cells – myocytes. The stroma consists of reticular tissue. The parenchyma is represented by white and red pulp.

White pulp of the spleen

The white pulp is represented by lymphatic follicles (nodules) in which the central artery is located eccentrically. Four zones are distinguished in the lymphatic follicle:

- 1) periarterial,
- 2) reproductive center,
- 3) mantle,
- 4) marginal zone.

The periarterial zone is located around the central artery, where proliferation, activation and antigen-dependent differentiation of T lymphocytes from the thymus take place, i.e. this zone consists only of T-lymphocytes. As a result of differentiation, effector cells are formed: T-helper cells, T-suppressor cells, T-killer cells, and memory cells, which enter the general bloodstream to participate in immune reactions.

The luminal center is the area of B lymphocytes. In the luminal center, B lymphocytes from the red bone marrow undergo proliferation and antigen-dependent differentiation. As a result, plasmocytes and memory cells are formed, which are released into the bloodstream and from the blood into the connective tissue, where they participate in immune reactions.

The mantle zone consists of T and B lymphocytes, i.e. it is a mixed zone.

The marginal zone contains T and B lymphocytes, i.e. it is a mixed zone. This zone is located on the border between the white and red pulp. The marginal zone is the site of immune response formation and is richly vascularized.

The red pulp of the spleen

The red pulp consists of: 1) numerous blood vessels and 2) blood cells (red blood cells). Some of the red blood cells are in a state of

degeneration or complete disintegration. Such erythrocytes are phagocytized by macrophages, which carry some of the hemoglobin (iron) to the red bone marrow for erythropoiesis. The spleen is entered by the splenic artery, which branches into the trabecular arteries. The trabecular arteries branch into: 1) pulpal arteries, which run along the red pulp, and 2) central arteries, which run along the white pulp (eccentrically in the lymph follicle). After the central artery leaves the lymphatic follicle (nodule), it splits into brush arterioles. In the wall of the brush arterioles (at the ends) there are thickenings called sleeves, couplings. These thickenings consist of reticular fibers and reticular cells. They are arterial sphincters of the spleen, the contraction of which stops the flow of arterial blood. The part of the arteriole that passes inside the arterial cuff is called the ellipsoid arteriole, from which numerous capillaries branch off.

There are 2 systems of blood supply to the spleen:

1) **closed** – the ends of the capillaries open into venous sinuses (sinusoidal hemocapillaries with discontinuous basement membrane). The closed (fast) blood supply system delivers oxygen to the tissues.

2) **open** – capillaries pour blood directly into reticular tissues. The open (slow) system brings red blood cells and antigens into contact with macrophages. Old and damaged red blood cells are taken up by macrophages.

Functions of the spleen:

- 1) hematopoietic function – antigen-dependent differentiation of T- and B-lymphocytes,
- 2) protective function – phagocytosis and immune defense,
- 3) blood-destroying function – destruction of old red blood cells, «red blood cell graveyard»,
- 4) blood storage,
- 5) universal hematopoietic organ in embryogenesis,
- 6) antitumor – inhibits the growth of some tumors in the body.

Lymph nodes

Lymph nodes are organs located along the course of lymphatic vessels. They are antigen-dependent organs. Antigen-dependent

proliferation and differentiation of T- and B-lymphocytes takes place in lymph nodes. They are organs of lymphocytopoiesis, immune defense and deposition of flowing lymph. Lymph flowing through lymph nodes is 95–99% purified from antigens and foreign particles, excess water, proteins, fats, enriched with lymphocytes and antibodies.

Development of lymph nodes takes place in 8–10 weeks of embryogenesis from mesenchyme along the course of lymphatic vessels. By the end of the 16th week, lymphocytes are infiltrated and clusters – lymph nodes – are formed.

Structure of a lymph node

From the outside, the node is covered by a connective tissue capsule. The capsule is formed by dense fibrous irregular connective tissue. (DFICT). Trabeculae extend inward from the capsule. The stroma is formed by reticular tissue consisting of reticular cells and reticular fibers. The parenchyma of a lymph node is represented by cortical and medullar substance. In the cortical (darker, peripheral) substance, 2 zones are distinguished: 1) cortical and 2) paracortical zones.

The cortical zone is represented by lymphatic follicles consisting of B lymphocytes (B zone), which come here from the red bone marrow with the blood stream. The B-lymphocytes of the lymph node are exposed to antigens.

The lymph follicle is a rounded formation consisting of B-lymphoblasts in the central (lighter) part and small B-lymphocytes in the peripheral (darker) part. The central part, due to the presence of cells in various stages of division, used to be called the center of reproduction (bright center). In the central part there can be accumulation of phagocytic cells (macrophages) during intoxication of the organism, especially of microbial origin, which indicates high reactivity of this part. Therefore, the central part of the follicle is often called the reactive center. Macrophages of luminal centers can phagocytize dying cells and cause antigen-dependent differentiation of B lymphocytes into plasmocytes and memory cells.

The paracortical zone – thymus-dependent zone (T zone)

contains a significant number of T-lymphocytes. In this zone there is a proliferation of T-lymphocytes that come here from the thymus with the bloodstream. Here, under the influence of antigens, T-lymphocytes differentiate and form T-helpers, T-suppressors, T-killers and memory cells. T-helpers stimulate the development and function of B lymphocytes, activate their production of antibodies. T-suppressors inhibit the development and function of B lymphocytes, suppress their antibody production. T-killers carry out cellular immunity, they are cell «killers», i.e. they kill genetically foreign cells (in organ transplantation).

Medulla (lighter, central) substance is represented by cerebral cords (cords) containing B-lymphocytes (B-zone).

Lymphatic sinuses

Sinuses are spaces in the lymph node bounded on one side by the capsule and trabeculae and on the other side by follicles and medullary cords. The sinuses contain macrophages, which phagocytize antigens in the lymph flowing in the sinuses. The lymph node distinguishes 4 types of sinuses: 1) marginal sinus, 2) intermediate cortical sinus, 3) intermediate cerebral sinus, 4) central (portal) sinus

1. The marginal (subcapsular) sinus is located between the capsule and the lymphatic follicle.
2. The intermediate cortical sinus is located between the trabeculae and the lymphatic follicles.
3. The intermediate medullary sinus is bounded by the trabeculae and the cerebral foramen.
4. The central (portal) sinus is located in the area of the lymph node gate, from which the lymphatic vessels originate.

From the lymphatic vessels, lymph enters first the marginal sinus, then the intermediate cortical sinus, then the intermediate cerebral sinus, then the central sinus and the outflow lymphatic vessel. The slow flow of lymph through the sinuses facilitates phagocytosis of antigens. The sinus lymph receives antibodies and lymphocytes from the lymph nodes. The paranasal sinuses act as a protective filter where antigens are trapped by macrophages.

Functions of lymph nodes:

- 1) hematopoietic function (lymphopoiesis) – antigen-dependent differentiation of lymphocytes,
- 2) protective – phagocytosis, immune defense,
- 3) lymph is enriched with lymphocytes,
- 4) lymph storage.

THE ENDOCRINE SYSTEM

In the human body, the endocrine system is represented by a set of organs, parts of organs, individual cells that secrete hormones into the bloodstream, lymph or interstitial fluid. All functions of the human body are regulated by the endocrine and nervous systems. The endocrine system regulates general processes: metabolism, development of germ cells, growth of the human body. The endocrine system includes endocrine glands that do not have excretory ducts. The peculiarity of the endocrine glands is the abundance of sinusoidal hemocapillaries, a rich vascularization (blood supply). Each cell of the endocrine glands contacts the capillaries. Substances secreted by cells are called hormones. The endocrine system is regulated by the cerebral cortex. The endocrine system regulates itself with the help of hormones.

Properties of hormones

1. High biological activity, small doses cause a pronounced effect.
2. Specificity of action – act directly on target cells.
3. Distance of action – realization of the effect at a distance
4. Species non-specificity

Classification of the endocrine system:

I. Central organs – hypothalamus, pituitary gland, epiphysis

II. Peripheral organs:

1. Adenohypophysis-dependent glands – thyroid gland, adrenal cortex, sex glands.
2. Adenohypophysis independent glands – parathyroid glands, calcitoninocytes of the thyroid gland, glomerular zone of the adrenal cortex, adrenal medulla, enterocytes of the gastrointestinal tract, respiratory organs, urinary system.

Hypothalamus

The hypothalamus develops from the embryonic diencephalon. It regulates all organs of the endocrine system. There are anterior, middle and posterior divisions of the hypothalamus. The hypothalamus is connected to the pituitary gland through the pituitary pedicle. Clusters of nerve and neurosecretory cells of the hypothalamus form nuclei. Nuclei of the anterior hypothalamus:

1. Supraoptic
2. Paraventricular

Supraoptic nuclei are formed by neurosecretory cells secreting vasopressin or antidiuretic hormone (ADH). The axons of the neurosecretory cells descend into the posterior lobe of the pituitary gland with the help of the pituitary pedicle and form axon-vascular synapses.

Functions of vasopressin (ADH):

1. Causes vasoconstriction
2. Increases blood pressure
3. Increases reabsorption (reverse absorption) of water from the renal tubules
4. Reduces diuresis (urination)

Paraventricular nuclei are formed by large neurosecretory cells secreting oxytocin.

Functions of oxytocin:

1. Contraction of the uterine myometrium
2. Contraction of myoepithelial cells of the end sections of the mammary glands
3. Increases milk secretion
4. Contraction of smooth muscle cells of the male vas deferens.

These two hormones (vasopressin, oxytocin) are transported axonally into the posterior lobe of the pituitary gland and deposited in the form of Herring bodies near blood vessels.

In the middle part of the hypothalamus there are nuclei:

1. Arcuate (infundibular)
2. Ventromedial

Secretory neurons of these nuclei produce hypothalamic

adenohypophysiotropic hormones. Hypothalamic neurohormones are also called releasing hormones, or releasing factors. Adenohypophysiotropic hormones affect the adenohypophysis. Neurohormones that stimulate the release of pituitary tropic hormones are called liberins, neurohormones that inhibit the release of pituitary tropic hormones are called statins. Under the action of statins, the secretion of hormones of the adenohypophysis stops.

Pituitary gland

The pituitary gland (pea gland) together with the hypothalamus forms the hypothalamic – pituitary neurosecretory system. In humans, the pituitary gland mass is very small, about 0.5 grams, but its functioning is vital for the body.

Parts of the pituitary gland:

- I. Adenohypophysis, which develops from the epithelium of the oral cavity of the embryo
- II. Neurohypophysis – an outgrowth of the diencephalon

The adenohypophysis includes 3 components:

1. Pars anterior
2. Pars intermedia
3. Pars tuberalis

The neurohypophysis forms the posterior lobe of the pituitary gland.

Development of the pituitary gland

The development of the pituitary gland occurs in three stages from different sources (ectoderm, neural tube).

Stage 1. At the 4th week of embryogenesis, an epithelial protrusion forms in the roof of the oral cavity in the form of a pituitary Ratke pouch – the rudiment of the adenohypophysis. A funnel – shaped protrusion grows down from the diencephalon – the rudiment of the neurohypophysis.

Stage 2. The Ratke pouch begins to lose contact with the epithelium

of the oral cavity and two walls are formed: anterior and posterior. The rudiment of the funnel lengthens and contacts the Ratke pouch.

Stage 3. The Ratke pouch completely loses its connection with the epithelium of the oral cavity. The anterior wall of the Ratke pouch thickens and turns into the anterior lobe of the adenohypophysis. An intermediate lobe of the adenohypophysis is formed from the posterior wall of the Ratke pouch. The neuroglia of the distal end of the funnel grows and forms the posterior lobe of the pituitary gland (neurohypophysis). The proximal part of the funnel narrows and turns into a pituitary pedicle connecting the pituitary gland with the hypothalamus. The mesenchyme forms the capsule and stroma of the pituitary gland. The adenohypophysis has an ectodermal origin. The neurohypophysis has a neural origin, it is formed as a glial protrusion of the diencephalon.

Structure of the adenohypophysis

In the adenohypophysis, the anterior, middle (or intermediate) lobes and the tuberal part are distinguished.

The structure of the anterior lobe of the adenohypophysis

The anterior lobe is covered with a capsule – dense fibrous irregular connective tissue (DFICT). Layers of loose fibrous unformed connective tissue (LFICT), forming the stroma of the lobe, depart from the capsule into the depths. Sinusoidal fenestrated capillaries pass through the layers of the LFICT. The parenchyma of the anterior lobe is formed by strands of epithelial glandular cells (adenocytes) located between the layers of LFICT. Epithelial strands are called trabeculae. The trabeculae are strongly branched and intertwined into a network. The anterior lobe has a trabecular structure. In each trabecula, several varieties of glandular cells can be distinguished – endocrinocytes (adenocytes).

Classification of the adenocytes

Anterior lobe cells are divided into

- 1) Chromophobic (main)
- 2) Chromophilic.

The chromophobic (main) endocrinocytes make up 60%, they are small in size, they do not contain any stainable granules, the cytoplasm does not stain, it does not perceive the dye. They are located in the middle of the trabeculae. The chromophobic cells are the following 1 – reserve cambial cells, 2 – young chromophilic cells that have not yet accumulated secretory granules, 3 – mature chromophilic cells that have already isolated secretory granules. Due to the quantitative predominance of the chromophobic cells in the composition of the trabeculae, they are referred to as the main cells, even though they are not functionally active.

The chromophilic endocrinocytes

They are classified as acidophilic or basophilic depending on the staining ability of their secretion granules.

Acidophils are located at the periphery of the trabeculae and represent 30-35% of the total number of adenocytes within the anterior pituitary. They are medium-sized, rounded cells with a well-developed granular endoplasmic reticulum. The nuclei are located in the centre of the cells. The cytoplasm contains large acidophilic granules. There are two types of acidophilic cells: 1) somatotropocytes, 2) lactotropocytes.

Somatotropocytes produce somatotropic hormone (STH, growth hormone), which stimulates body growth in childhood and adolescence.

Lactotropocytes (mammatropocytes) produce lactotropic hormone (LH, prolactin). Its functions are 1) stimulates milk synthesis in the mammary glands, 2) stimulates progesterone production in the yellow body of the ovary.

Basophils are located on the periphery of the trabeculae. They make up 4-10% of the total number of adenocytes in the anterior pituitary. These cells are large in size. The cytoplasm contains basophilic granules. There are three types of basophils: 1) gonadotropocytes, 2) thyrotropocytes, 3) corticotropocytes.

Gonadotropocytes are oval-shaped with an eccentrically located nucleus. In the centre of the cell is the macula. This contains the Golgi complex. In the cytoplasm, the granular ER is well developed.

There are two groups of gonadotropocytes: 1) folliculotropocytes, which produce the follicle-stimulating hormone (FSH),

and 2) luteotropocytes, which produce the luteinising hormone (LT).

Follicle-stimulating hormone affects spermatogenesis in the male body and the growth of follicles and the release of oestrogen in the ovary in the female body. Luteinising hormone stimulates the production of testosterone in the male sex glands and the development and function of the corpus luteum in the female sex glands.

Castration cells appear in the anterior lobe of the pituitary gland when the sex glands do not produce enough sex hormones. The macula of the gonadotropocytes then increases in size, pushing the cytoplasm and nucleus to the periphery. At the same time, the cell becomes hypertrophic, takes on a ring shape and actively secretes gonadotropin to increase the production of sex hormones.

Thyrotropocytes are irregular-shaped and contain small secretory basophilic granules. They produce thyroid-stimulating hormone (TSH), which stimulates the release of thyroxine by the thyroid.

Thyroidectomy cells appear in the pituitary gland when there is a decrease in the function of the thyroid gland. The cytoplasm of these cells contains a large number of vacuoles. Thyroid stimulating hormone production increases.

Corticotropocytes are irregular-shaped cells. In the cytoplasm there are small basophilic secretory granules in the form of a bubble with a dense core surrounded by a membrane. There is a bright rim between the membrane and the core. The corticotropocytes produce adrenocorticotrophic hormone (ACTH), which activates the cells of the fascicular and reticular zones of the adrenal cortex.

Epiphysis

Epiphysis (pineal gland). It develops in the 5th-6th week of embryogenesis as a bulge of the midbrain. The epiphysis reaches its maximum development in children up to 7 years of age.

Structure. The epiphysis is covered by a connective tissue capsule from which septa form lobules. The stroma is a loose fibrous irregular connective tissue (LFICT). The parenchyma consists of 2 types of cells: 1) pinealocytes, 2) fibrous astrocytes – neuroglia.

Pinealocytes are polygonal cells with processes. There are

secretory granules in the processes and in the cell body. Pinealocytes are neurosecretory cells. The pinealocytes secrete the following neurohormones: 1) Serotonin, which is converted to melatonin. Serotonin is synthesized during the day and melatonin during the night. Serotonin acts on vascular smooth muscle and increases blood pressure. 2) Antigonadotropin – inhibits the premature development of the sexual system, inhibits the secretion of luteinizing hormone (LH) in the pituitary gland. 3) Kalitropin – increases the level of potassium in the blood, participates in the regulation of mineral metabolism. Fibrous astrocytes have long processes and perform a supporting function.

Age-related changes. With age, the deposition of phosphate and carbonate salts in the stroma of the epiphysis increases in the form of layered spheres called «cerebral sand». In the parenchyma of the gland there is death of pinealocytes, the number of astrocytes increases.

Peripheral endocrine glands

The following peripheral glands are found in the human body:

- 1) thyroid gland,
- 2) parathyroid glands,
- 3) adrenal glands.

Thyroid gland

Development: 3-4 weeks of embryogenesis on the ventral wall of the pharyngeal gut between the I and II pair of gill pouches forms an unpaired bulge – the rudiment of the thyroid gland. Further, the bulge reaches the level of the III and IV pouches, thickens and bifurcates, giving rise to the right and left lobes of the thyroid. A capsule and stroma are formed from the surrounding mesenchyme. Neural crest cells (neuroectoderm) differentiate into calcitoninocytes (parafollicular cells).

Structure. The thyroid gland is covered by a capsule – dense fibrous irregular connective tissue (DFICT). Connective tissue trabeculae separate from the capsule and divide the gland into lobules. The glandular stroma is represented by loose fibrous irregular connective tissue (LFICT).

The parenchyma of the gland is represented by 1) follicular cells (thyrocytes) and parafollicular cells (calcitoninocytes, K-cells). The structural and functional unit of the thyroid gland is the follicle. Follicles are closed vesicles. Between follicles are interfollicular islands formed by clusters of parafollicular cells (K-cells).

Structure of the follicle. The follicle wall is formed by a monolayer of epithelium on the basal membrane. The cells of the follicle are called follicular endocrinocytes or thyrocytes. The follicular cavity is filled with colloid, which has a liquid, semi-liquid or viscous consistency, depending on its functional state. The structure of thyrocytes depends on the functional state of the thyroid gland: normal, hyperfunction, hypofunction. Thyrocytes in normal functional state have a cubic shape. There are microvilli on the apical surface of thyrocytes. Granular ER, lysosomes, Golgi complex are well developed in cytoplasm of thyrocytes. Nuclei of thyrocytes are round. Colloid has semi-liquid consistency. The shape of thyrocytes changes depending on the functional activity of the thyroid gland. In hyperfunction thyrocytes have a prismatic shape. On their apical surface the number of microvilli increases. The colloid becomes fluid. In hypothyroidism, thyrocytes have a flat shape. Their nuclei are flattened. The colloid is thick, the size of the follicles increases. Outside the follicles there are braided sinusoidal fenestrated blood capillaries.

The thyroid secretory cycle consists of 4 phases:

- 1) uptake of precursors;
- 2) synthesis of the secreted hormone – thyroxine;
- 3) release of hormone into the follicular cavity in the form of colloid;
- 4) release of the hormone through the basal part of the cell into the blood capillaries.

A morphological peculiarity of the thyroid gland is the release of thyroxine hormone not directly into the blood, but first into the follicular cavity, where it gradually accumulates in the form of colloid. The colloid is then absorbed by cells and released into the blood.

Phase 1 – absorption of initial substances is characterized by the entry of iodine ions and other substances into thyrocytes.

Phase 2 – synthesis of hormone takes place in EPS,

Phase 3 – hormone is released into colloid.

Phase 4 – hormone is excreted from colloid into blood capillaries.

In hyperfunction, excretion of hormone into blood is increased.

In hypofunction, hormone excretion is delayed. Thyroid hormone increases thyroid function. Parafollicular cells (calcitoninocytes, K-cells) are larger and lighter in color than thyrocytes. They are usually found in groups in interfollicular islands or singly in the follicle wall. Calcitoninocytes in the follicle wall are triangular in shape and round in the islets. The cytoplasm of K cells is well developed EPS, many secretory granules. Calcitoninocytes produce the hormone calcitonin, which lowers the level of calcium in the blood. Calcitonin reduces the activity of osteoclasts in bone tissue.

Functions of thyroxine hormone:

- 1) increases metabolism, fat and carbohydrate metabolism, gas exchange
- 2) increases protein synthesis
- 3) influences development, growth, differentiation of cells and tissues
- 4) accelerates the development of bones
- 5) influences histogenesis of nervous tissue
- 6) promotes regeneration of organs and tissues

In the composition of thyroxine contains iodine as an obligatory component, so the intake of iodine with drinking water and food in the body is necessary for normal functional activity of the thyroid gland.

Parathyroid glands

Development. Parathyroid glands develop in the 5th week of embryogenesis from the protrusions of the epithelium of the 3 and 4 pairs of gill pouches. In the 7th–8th week, these protrusions are tied off from the walls of the gill pouches, and the parenchyma of the parathyroid glands develops from each of them. The capsule and stroma develop from the mesenchyme. Thus, 4 parathyroid glands are formed, which are anatomically closely related to the thyroid gland.

Structure. Each gland is covered by a connective tissue capsule (DFICT) from which interlayers extend deep. The stroma consists of loose fibrous irregular connective tissue (LFICT) containing sinusoidal fenestrated blood capillaries. The parenchyma of the gland is formed by epithelial strands (trabeculae) composed of parathyrocytes. There are 3 types of cells among the parathyrocytes:

- 1 – main (young),
- 2 – intermediate (aging),
- 3 – acidophilic (oxyphilic, old).

These cells represent the aging stages of parathyrocytes. The main cells are polygonal in shape. Cytoplasm is basophilic, secretory granules are contained, EPS is well developed. The main cells secrete the hormone parathyrin, which increases the calcium content in the blood, removes calcium from the bones into the blood. In intermediate cells, the basophilia of the cytoplasm is attenuated due to a reduced amount of endoplasmic reticulum. Acidophilic cells are smaller than the main cells. The cytoplasm is oxyphilic and contains a large number of mitochondria. They are an older form of main cells. When the parathyroid glands are accidentally removed during thyroid surgery, convulsions begin and death occurs due to impaired myocardial contractility. The seizures are caused by a lack of calcium in the blood.

Adrenal glands

The adrenal glands are paired glands consisting of cortical and medullar substance.

Development. The sources of development of the adrenal glands are:

- 1) coelomic epithelium (cortical substance),
- 2) neural crest cells (brain substance),
- 3) mesenchyme (capsule, stroma).

The adrenal cortex develops in the 5th week of embryogenesis from the coelomic epithelium in the region of the root of the mesentery – the interrenal body. The brain substance of the adrenal glands is formed in the 6th-7th week of embryogenesis from the neural crest. Sympathoblasts migrate to the interstitial space, proliferate,

and differentiate into chromaffin cells. Connective tissue and vessels develop from the mesenchyme.

Structure. The adrenal glands are covered by a capsule of DFICT. The **stroma** is LFICT. The **parenchyma** is represented by cortical and medullar substance. The adrenal cortex consists of strands of epithelial cells – endocrinocytes. Between the strands of epithelial cells there are layers of loose connective tissue in which there are sinusoidal fenestrated blood capillaries. In the adrenal cortex, depending on the location and shape of the epithelial strands, 3 zones are distinguished: 1) glomerular, 2) fasciculata, 3) reticular.

Glomerular zone. The epithelial strands of this zone are coiled into tubules. Endocrinocytes are small, cubic or conical in shape. Nuclei are rounded. The cytoplasm is well developed smooth EPS, there are lipid inclusions. The function of the tubular zone is the secretion of mineralocorticoids (aldosterone), under the influence of which occurs 1) reabsorption of sodium ions from renal tubules into blood capillaries, 2) increases inflammation, 3) affects water-salt metabolism. The fascicular zone is pituitary dependent. The sudanophobic layer is located at the boundary between the tubular and buccal zones. The sudanophobic layer consists of cuboidal cells. There are no lipid inclusions in these cells, so they are not stained with Sudan. Significance of the sudanophobic layer: Its cells are a source of regeneration for the cortical endocrinocytes of the bundle and reticular zones.

The zona fasciculata consists of prismatic endocrinocytes forming parallel strands or bundles. The cytoplasm of endocrinocytes contains a large number of lipid inclusions, smooth EPS is well developed. Functions of the zona fasciculata: synthesis of corticosteroids called glucocorticoids (cortisone, hydrocortisone). Functions of glucocorticoids: 1) regulation of metabolism of carbohydrates, proteins, lipids, 2) providing gluconeogenesis, 3) attenuation of inflammatory reaction, 4) providing adaptation of the body to chronic stress. The zona fasciculata is pituitary dependent, stimulated by adenohipophysitis ACTH.

Reticularis zone of the adrenal cortex, consists of endocrinocytes forming a network. The cells are small. There are fewer lipid inclusions

in the cytoplasm of the cells. The shape of the cells is variable. Function of the reticular zone: 1) secretion of androgenic hormone (male sex hormone), 2) secretion of estrogen and progesterone (female sex hormones). The reticular zone is pituitary dependent, influenced by the adenohypophysis ACTH.

Medulla of adrenal gland

Stroma – LFICT. **Parenchyma** – chromaffin cells – light and dark cells. Chromaffin cells are modified nerve cells. They are large cells with rounded shape. The cytoplasm contains granules surrounded by a membrane, granular EPS is well developed. Adrenaline and noradrenaline (catecholamines) accumulate in the granules. Two types of cells are distinguished: 1) light chromaffinocytes producing adrenaline, 2) dark chromaffinocytes producing noradrenaline. Adrenaline and noradrenaline have similar physiological effects, causing vasoconstriction and increasing blood pressure. Adrenaline increases heart function, increases heart rate, increases blood sugar content, dilates cerebral vessels and skeletal muscles, provides adaptation to acute stress – stimulates the breakdown of carbohydrates and fats for energy supply of intensive muscle activity. During sudden cold, pain and stress, the release of adrenaline and noradrenaline increases.

Diffuse Endocrine System

Diffuse endocrine system (DES) is represented by individual endocrine cells of neurogenic (APUD) and non-neurogenic origin scattered in different organs. The name of the group of endocrine cells that make up the APUD system (apudocytes) comes from the first letters of the English words – Amine Precursors Uptake and Decarboxylation, which means – uptake and decarboxylation of amine precursors. The cells of this system combine characteristics of both neural and endocrine cells. Most of the individual endocrine cells are endocrinocytes of neural origin, i.e. they develop from the neural crest. The APUD system was first described by the English scientist Pierce. They are present in the epithelium of the respiratory and urinary tracts,

in the thyroid gland (calcitoninocytes), in the brain substance of the adrenal gland, in the pineal gland. Especially many cells of APUD system in the epithelium of gastrointestinal tract (endocrine cells of various types).

Sources of development of endocrinocytes APUD system.

They are:

- 1 – neuroectoderm (hypothalamus, pineal gland, adrenal gland)
- 2 – dermal ectoderm (adenohypophysis, Merkel cells)
- 3 – intestinal ectoderm (endocrinocytes of the gastrointestinal tract)
- 4 – mesoderm (atrial endocrine cardiomyocytes, Leydig cells, endocrinocytes of the theca of the ovarian follicle)
- 5 – mesenchyme (labrocytes).

Endocrine cells of neurogenic origin

They are a minority. They are Leydig cells in the male glands and endocrinocytes of the theca of the ovarian follicle. They secrete steroid hormones and develop from the coelomic epithelium.

Individual hormone-producing cells have paracrine and remote effects. Paracrine effects are effects on nearby target cells in a given organ.

Distant effects occur when hormones from the cell are secreted into the bloodstream and transported to those organs whose cells have receptors for that hormone, i.e. are located in another organ.

DIGESTIVE SYSTEM

In the digestive system there are 3 sections: anterior, middle and posterior.

The anterior part includes: the oral cavity and its derivatives: (lips, cheeks, gums, hard palate, soft palate, tonsils, tongue, salivary glands, teeth, pharynx, esophagus).

The anterior compartment is where most of the mechanical processing of food takes place. The middle section includes: stomach, small and large intestines, liver, pancreas.

In the middle section there is chemical processing of food, absorption of waste products, formation of feces. The posterior section includes: the anal section of the rectum. In the posterior section there is evacuation of fecal masses.

Development. Sources of development: dermal ectoderm, entoderm, mesoderm, mesenchyme. Dermal ectoderm participates in the formation of stratified epithelium. Entoderm forms simple epithelium, parenchyma of liver and pancreas. Mesoderm forms skeletal muscle tissue (myotome), mesothelium of serous membrane (visceral layer of splanchnotome). Mesenchyme is the source of connective tissue development.

The structure of the digestive tract

The wall of the digestive tube contains 4 layers: 1) mucosa, 2) submucosa, 3) muscular, 4) adventitial or serosa.

1. **The mucosa** consists of 3 layers: 1) epithelium, 2) lamina propria, 3) muscular lamina.

2. **The epithelium** in the anterior and posterior sections is stratified squamous, in the middle section – simple columnar.

3. **The lamina propria** of the mucous membrane consists of loose fibrous irregular connective tissue. It can contain simple glands, blood vessels.

The muscular lamina of the mucosa consists of 1–3 layers of smooth muscle cells.

This membrane is called mucous because its epithelial surface is moistened by mucus secreted by glands.

The submucosa is represented by loose fibrous irregular connective tissue (LFICT), in some parts of the digestive tube there are compound glands (esophagus, duodenum).

The muscular layer consists of 2 layers (in the stomach of 3 layers) of muscle elements: inner - circular, outer – longitudinal. In the anterior and posterior parts of the digestive tract, the muscle tissue is skeletal (transversely striated), in the middle - smooth. The contractions of the muscular mantle facilitate the movement and passage of food.

The outer membrane is either serous or adventitial.

The serous membrane is mesothelium on a connective base. The adventitial membrane is made up of loose fibrous irregular connective tissue (LFICT).

Anterior digestive system includes: 1) oral cavity (lips, cheeks, gums, hard and soft palate, tonsils, tongue, salivary glands, teeth), 2) pharynx, 3) esophagus.

Lips.

There are 3 parts of the lip - 1) cutaneous, 2) intermediate, 3) mucous.

1) The cutaneous part of the lip has the structure of thin skin: stratified squamous keratinized epithelium (4 layers), connecting base.

2) The intermediate part is epithelium (SSKE) and connective tissue with numerous capillaries.

3) The mucosa is covered by a mucous membrane composed of stratified squamous non-keratinized epithelium (SSNE) and the lamina propria (LFICT). Below it is the submucosal base (LFICT), which contains complex glands. Deeper is the circular muscle of the mouth (striated muscle).

The cheek is divided into 3 zones: 1) maxillary, 2) mandibular, 3) intermediate.

It consists of: 1) mucosa, 2) submucosa, 3) muscularis.

The mucosa is composed of 2 layers: 1) stratified non-keratinized squamous epithelium (SSNE), 2) lamina propria (LFICT).

The submucosa is represented by the LFICT, which contains complex glands. The muscular layer is represented by buccinator muscle (striated muscle). The cheek is externally covered with skin and internally lined with mucous membrane.

Gums

The mucous membrane is lined with: 1) stratified squamous partially keratinized epithelium (SSPKE), 2) lamina propria (LFICT) is firmly attached to the bones of the upper and lower jaws. The gingiva is well supplied with blood and richly innervated.

The hard palate consists of: 1) a bony base, 2) a mucosa tightly attached to the bone. There is no submucosa. The mucosa consists of 2 layers:

- 1) SSNE, partially keratinized epithelium,
- 2) A lamina propria (LFICT) fused to the periosteum.

The soft palate includes: 1) mucosa, 2) submucosal base, the mucosa consists of SSNE, lamina propria (LFICT). The submucosal base is the LFICT, which contains complex glands.

The tonsils. At the border of the oral cavity and pharynx as a part of the mucous membrane are located tonsils - clusters of lymphoid tissue. Tonsils ensure the development of lymphocytes, perform a protective function. They are covered with SSNE – stratified squamous non-keratinized epithelium. The lamina propria (LFICT) contains lymphatic follicles. The submucosa is represented by the LFICT, in which complex glands are found. Outside the submucosa are the striated muscles of the pharynx.

The tongue is a muscular organ that performs the following functions: 1) mechanical processing and swallowing of food, 2) sound production (speech organ), 3) perception of taste stimuli (taste organ), 4) salivation, 5) immune defense against foreign antigens (lysozyme). The tongue is divided into the upper, lateral, and lower surfaces.

Tongue Development. The tongue develops from several rudiments that take the form of tubercles. These tubercles are located at the bottom of the primary oral cavity in the area of the central parts of the I, II, III gill arches. The first to appear, in the fourth week, is the unpaired lingual tubercle located on the ventral side between the first and second gill arches. The back of the tongue develops from this tubercle. Subsequently, two paired thickenings, called lateral lingual tubercles, are formed in front of the unpaired tubercle at the level of the first (mandibular) gill arch. These tubercles join to form the body and tip of the tongue. At the level of the second and third gill arches, there is a thickening of the mucous membrane known as the bracket, from which the root of the tongue develops. All these rudiments of the tongue join together to form a single organ - the tongue. The muscles of the tongue develop from the myotomes of the dorsal mesoderm.

Structure of the tongue. The following membranes are distinguished in the tongue from the upper to the lower surface: 1) mucosa, 2) muscular layer, 3) submucosa, 4) mucosa.

I. **The mucosa** is composed of: stratified non-keratinized squamous epithelium (SSNE), partially SSPE (in filiform papillae), lamina propria (LFICT).

On the upper and lateral surfaces of the tongue, the mucosal layer forms numerous projections - papillae. There are 4 types of papillae: 1) filiform, 2) fungiform, 3) foliate, 4) circumvallate- not raised above the surface of the tongue.

Filiform papillae are the smallest and most numerous. They cover the upper surface of the tongue, are conical in shape, and do not contain taste buds. The filiform papillae rise above the level of the mucosa and are covered with stratified squamous partially keratinized epithelium (SSPE). In some diseases, keratinized scales remain on the surface of the filiform papillae - a "white plaque" is formed. The base of each papilla is formed by a connective tissue papilla, which is formed by its own layer of mucous layer.

The fungiform papillae of the tongue are few, larger and located at the tip of the tongue. They are covered with stratified squamous non-keratinized epithelium (SSNE). In the thickness of the epithelium are taste buds that perceive sweet taste.

Foliated papillae are present only in young children, located on the lateral surfaces of the tongue, have the shape of a leaf. They are covered with stratified squamous non-keratinized epithelium (SSNE), in the thickness of which there are no taste buds. In adults, the foliated papillae are redivided and adipose tissue develops in their place.

Circumvallate papillae (papillae surrounded by a shaft), located on the upper surface of the root of the tongue, do not rise above the level of the mucous membrane. The papillae are covered with stratified squamous non-keratinized epithelium, in which are located taste buds that perceive salty, sour, bitter tastes. Around the papilla is a narrow-slit groove. The groove separates the papilla from the roller - thickening of the mucous membrane surrounding the papilla. In the connective tissue of the papillae are bundles of smooth muscle cells. The contraction of these bundles provides the convergence of the papilla with the roll, which contributes to the contact of food substances with the taste buds.

II. **The muscular layer** of the tongue is represented by skeletal muscles arranged vertically, longitudinally, and transversely.

III. **The submucosa** is represented by the LFICT.

IV. **The mucosa of the lower surface** is characterized by the absence of papillae.

The salivary glands of the tongue are divided into 3 types:

- 1) Protein Ebner's glands,
- 2) Mucous Weber's glands
- 3) Nuhn's mixed glands.

1) **Ebner's protein glands** are simple tubular branching glands. The terminal part consists of cone-shaped cells that secrete a protein secretion. The excretory ducts open into the furrows of the vallated papillae.

2) **The mucous glands of Weber** are simple alveolar-tubular branched glands. The terminal part is composed of mucous cells. The exit ducts are lined with stratified epithelium and open at the root of the tongue.

3) **Mixed Nuhn's glands** are - simple alveolar-tubular branched glands are located in the anterior part of the tongue. The excretory

ducts open under the tongue. The secretory part consists of protein and mucous cells.

The main salivary glands

There are 3 pairs of salivary glands: 1) parotid, 2) submandibular, 3) sublingual

Sources of development: ectoderm, mesenchyme.

General structure. These are complex branched alveolar or alveolar-tubular merocrine glands. Each major salivary gland is covered by a connective tissue capsule (DFICT) and consists of secretory terminal sections and excretory ducts. There are 3 types of excretory ducts and terminal compartments: 1) protein (serous) containing protein cells (serocytes) that produce protein secretion, 2) mucus (mucous) containing mucus cells (mucocytes) that produce mucus secretion, mixed (protein-mucus) terminals sections containing serocytes and mucocytes that produce protein-mucus secretion.

The excretory ducts of the salivary glands are divided into: 1) intercalated, 2) striated, 3) intralobular, 4) interlobular, and 5) common duct.

1) **The intercalated ducts** are lined with squamous or cuboidal epithelium. The second layer in them is formed by myoepithelial cells.

2) **Striated ducts** are lined with single layer cylindrical epithelium. Basal parts of epithelial cells have basal striations formed by mitochondria and folds of cytolemma. Mitochondria are perpendicular to the basal membrane. Myoepitheliocytes make up the second layer.

3) **Intralobular ducts** are lined by a bilayer cuboidal epithelium.

4) **The interlobular ducts** are lined with stratified cuboidal epithelium.

5) **The common excretory duct** is lined by stratified squamous non-keratinized epithelium (SSNE).

The distribution of terminal segments in the major salivary glands is as follows:

1) The parotid gland has only protein (serous) terminal secretory compartments.

2) The submandibular gland has two types of end sections – 1. protein (serous), 2. protein-mucus (mixed).

3) The sublingual gland has three types of end sections - 1. protein (mucous), 2. mixed (protein-mucous), 3. mucous.

The parotid salivary gland is a complex branched alveolar merocrine gland that secretes a proteinaceous secretion into the oral cavity. The common excretory duct opens into the oral cavity at the level of the second upper large molar.

The protein ends of the parotid gland are composed of 2 types of cells: 1) protein cells (serocytes), 2) myoepithelial cells. Serocytes have a conical shape. The cytoplasm contains secretory granules that secrete proteins. Myoepithelial cells or myoepitheliocytes are basket-shaped, located between the base of serocytes and the basement membrane. Their contractions facilitate the secretion of secretions from the secretory compartments.

The submandibular salivary gland is a complex branched alveolar tubular merocrine gland. The common terminal duct opens under the tongue. Two types of terminal compartments are distinguished: 1) protein, 2) protein-mucus (mixed).

Protein-mucus (mixed) end sections consist of 2 types of cells: 1) serocytes (protein cells) and 2) mucocytes (mucus cells). Mucus cells are larger than protein cells and are pale in color. The nuclei of mucocytes are located at their base and are greatly flattened. A small number of protein cells cover the mucous cells in the form of a serous demiluni- Gianuzzi. Myoepithelial cells are located outside of the demilunar Gianuzzi cells.

The sublingual gland is a complex branched alveolar tubular merocrine gland. The common duct opens next to the duct of the submandibular salivary gland. By the nature of secretion – it is a mixed, mucous-protein gland, with the predominance of the mucous component. It has terminal secretory compartments of three types: 1) protein, 2) mucus, and 3) mixed. Myoepithelial cells form the outer layer in all types of terminal compartments.

Saliva has several functions, including antibacterial properties due to lysozyme, stimulation of regeneration due to epithelial growth

factor, and the initial stage of carbohydrate digestion due to enzymes such as amylase and maltase.

Teeth

In humans, primary teeth (which fall out – 20) are the first to form, followed by permanent teeth – 32.

Development of teeth. Sources of teeth development: 1 – ectoderm (enamel, cuticle), 2 – mesenchyme (dentin, cementum, pulp). There are 3 stages of development:

- Stage 1 – the stage of formation of dental buds.
- Stage 2 – the stage of differentiation of dental buds.
- Stage 3 – the stage of histogenesis of dental tissues.

Stage 1 – formation of dental buds

In humans, the development of primary teeth begins at the end of the 2nd month of intrauterine life. An epithelial structure is formed in the oral cavity. This is called the dental plate. On the inner surface of the dental plate, epithelial tooth buds appear from which enamel organs develop. Subsequently, mesenchyme grows toward each bud, which extends into the enamel organ. The mesenchyme forms the dental papilla. These 3 components make up the dental bud: 1) enamel organ, 2) dental papilla, 3) dental sac. The enamel organ takes the form of a double-walled cup.

Stage 2 – Differentiation of tooth buds

The enamel organ gradually separates from the tooth plate. The epithelial cells of the enamel organ differentiate into three types: inner, outer, and intermediate. The inner cells, adjacent to the dental papilla, become prismatic and are called enameloblasts, which later form the enamel of the tooth. The outer cells of the enamel organ flatten and become flat. The cells of the intermediate layer between the outer and inner cells become star-shaped and form the pulp of the enamel organ. The pulp of the enamel organ resembles a wide network. The cells remain connected to each other by processes. The enamel organ pulp

also forms the enamel cuticle. The outer cells of the enamel organ also participate in the formation of the enamel cuticle that covers the tooth. Odontoblasts differentiate from the dental papilla and subsequently form the dentin of the tooth. The mesenchyme surrounding the papilla thickens to form the pulp.

In the 3rd month of embryogenesis the tooth enamel organ separates from the tooth plate. As a result of stage 2 – differentiation of dental buds, the enamel organ is divided into 3 components:

- 1 – outer layer – outer enamel epithelium formed by squamous cells
- 2 – central part – pulp of the enamel organ
- 3 – inner epithelium – enameloblasts.

The cells of the dental papilla form odontoblasts. The dental sac is divided into 2 layers – inner and outer. The cementum develops from the inner layer and the periodontium from the outer layer.

Stage 3 – histogenesis of dental tissues.

Development of dentin (dentinogenesis). At the earliest, at the end of the 4th month of embryonic life, dentin appears. Odontoblasts participate in dentin formation. There are 2 developmental stages:

- Stage 1 – stage of organic matrix formation (Korff, Ebner fibers).
- Stage 2 – the stage of mineralization – deposition of inorganic substances.

Stage 1 – Formation of organic matrix.

Odontoblasts (dentinoblasts) are pear-shaped, contain well-developed granular endoplasmic reticulum and Golgi apparatus. Odontoblasts have processes. Odontoblasts secrete organic components of future dentin (collagen, glycoproteins, proteoglycans) through their processes, forming the organic matrix of dentin. The outgrowths of the odontoblasts elongate, and the bodies of the odontoblasts move further away from the surface toward the center. The dentinoblasts form thin precollagen fibers that run radially between the odontoblasts and enameloblasts. The precollagen fibers then become collagen fibers. These fibers are called Korff fibers and are involved in the formation of

coated dentin. Later, odontoblasts synthesize longitudinal tangential fibers. These new fibers are called Ebner fibers. These fibers form immediately as collagen fibers, bypassing the precollagen fiber stage. Peri-pulpal dentin is formed at the expense of tangential Ebner fibers. When the main substance of dentin is formed, odontoblasts leave their thin processes in it – Toms fibers, which are located in the cavity of dentinal tubules. The outgrowths of the odontoblasts begin to branch. The odontoblasts themselves are not a part of the basic substance of the dentine formed by them, but remain in the outer parts of the dental papilla, and then – in the pulp.

Stage 2 – Mineralization

Odontoblasts play an important role in the process of mineralization (calcification) of dentin. With the help of their processes, odontoblasts contribute to the transport of mineral salts from the blood into the basic substance of the developing dentin. Mineralization of dentin begins at the end of the 5th month of embryogenesis. Normally, the innermost part of the dentin facing the dental pulp, which is directly adjacent to the odontoblast layer, is not mineralized. This zone of abnormal dentin is called predentin.

Chemically, the process of mineralization (calcification) consists in the deposition of mineral salts (phosphoric acid, calcium) in the organic matrix of dentin, which are deposited only in the amorphous cementing substance. There is no mineralization of Korff, Ebner and Toms collagen fibers, which are deposited in the dentinal tubules.

Dentin is characterized by a globular form of mineralization, which is absent in bone, where calcium salts are deposited in the form of tiny crystals. Deposition of mineral salts in the main substance of dentin occurs in the form of globules (spheres or calcospherites). Mineral salts are deposited in the form of lumps and grains, which merge with each other to form spheres – globules. Dentin becomes hard, mineralized. Areas of non-mineralized dentin, called interglobular spaces, may remain between these globules. Interglobular spaces play an important role in the metabolism of dentin.

Pulp development.

Parallel to the development of dentin is the process of differentiation of the dental pulp. The pulp develops from the mesenchyme of the papilla. This process begins at the apex of the papilla, where odontoblasts first appear. Simultaneously with the formation of odontoblasts at the periphery of the papilla, differentiation of mesenchymal cells occurs. Mesenchymal cells increase in size and begin to move away from each other. Even before the first odontoblasts appear, a blood vessel grows into the basal part of the dental papilla. Almost simultaneously, nerve fibers grow into the dental papilla. Cells from the central parts of the mesenchymal papilla form the dental pulp – a loose, fibrous, unformed connective tissue of the tooth, rich in blood vessels and nerves. Deep within the papilla, mesenchymal cells gradually transform into connective tissue pulp cells. Fibroblasts form an intercellular substance that contains precollagen, collagen fibers, and other components of the pulp intercellular substance.

Enamel development (enamelogenesis)

After dentin formation, enamel formation begins. The supply of nutrients to the ameloblasts stops as a result of dentin mineralization. Nutrients to ameloblasts (adamantoblasts) begin to come from the intermediate layer (pulp) of the enamel organ. There are two stages in the development of enamel:

- Stage 1 – the stage of formation of organic matrix – enamel prisms.
- Stage 2 – mineralization stage.

Stage 1 – organic matrix formation

The first enamel buds appear in the 5th month of embryogenesis. Due to the change in the source of nourishment of adamantoblasts (previously dental papilla, later pulp of enamel organ), there is a movement of the nucleus and cell organelles (centrosome, lamellar complex) to the opposite end of the cell. As a result, the nucleus moves from the basal part of the ameloblast, the centrosome and the Golgi lamellar complex move to the apical part of the cell. This

causes a pole change, the apical pole of the ameloblasts becomes the basal pole and the basal pole becomes the apical pole towards dentin. This process of moving or changing poles is called inversion. After this change in cell poles, the ameloblasts begin to feed from the intermediate layer side of the epithelial enamel organ instead of from the dentin side. Mature ameloblasts are prismatic in shape. Protein begins to be synthesized on the granular ER of ameloblasts.

The protein granules move to the apical pole of the cell and form cuticular arches. These arches elongate as the number of granules increases and then give rise to enamel prisms. As the length of the prisms increases, the ameloblasts become shorter (cubic, flat), i. e., they become smaller and move away from the dentin. At the end

of this stage, the ameloblasts are reduced and S-shaped enamel prisms are formed in their place. Each ameloblast follows an S-shaped trajectory and becomes an S-shaped prism. The formation of enamel also follows the general principle (for hard tissues):

1 – first, ameloblasts accumulate in their granules and release the components of the organic matrix of enamel through outgrowths.

2 – then a rapid mineralization of the enamel takes place. Ameloblasts also secrete special proteins – amelogenins, which contribute to the high rate of mineralization.

The second stage of enamel formation is mineralization.

Mineralization of enamel starts from the surface of enamel prisms and spreads to their central parts, i. e. from the dentin-enamel junction to the enamel surface.

Development of cementum (cementogenesis).

The development of cementum occurs in the 4th month after birth from the mesenchyme that forms the dental pouch. Two layers are distinguished in the periodontal pocket: 1 – denser – the outer layer, 2 – looser – the inner layer. In the inner layer of the dental pouch there is a process of cementum development, which includes 2 stages: 1 – formation of organic matrix, 2 – mineralization. Cells of the inner layer of the periodontal pocket differentiate into cementoblasts. Shortly

before the eruption of teeth in the area of future roots, cementoblasts form cement, which is deposited on the dentin. The cementoblasts coat themselves with the products of their secretion and become cementocytes. In some areas, the cementocytes die, leaving acellular cementum.

Development of the periodontium

The periodontium develops from the outer, denser layer of the periodontium. The dense connective tissue (DFRCT) of the periodontium – the periodontal ligament – develops from the mesenchyme of the periodontal pocket. The bundles of collagen fibers of the periodontium (peri-cementum) with one of their ends are woven into the basic substance of the developing cementum, and with the other ends they pass into the basic substance of the alveolar bone. This ensures that the root is firmly attached to the wall of the bony alveolus. The alveolar bone is formed from the surrounding mesenchyme rudiments in parallel with tooth formation. Thus, enamel develops from the oral epithelium, while dentin, cementum, pulp, and periodontium are derived from the mesenchyme.

The establishment of permanent teeth occurs at the end of the 4th or beginning of the 5th month of embryogenesis. Permanent teeth are formed from the dental plate and the surrounding mesenchyme. Initially, both primary and permanent teeth are located in a common alveolus. Then a bony septum appears between them. The permanent tooth develops very slowly. At the age of 6–7 years, osteoclasts destroy the bony septum and root of the primary tooth, and the permanent tooth begins to develop rapidly.

Tooth structure.

The tooth is made up of hard and soft tissues. Hard tissues of the tooth: enamel, dentin, cementum. Soft tissues of the tooth – pulp. The supporting or supporting apparatus of the tooth is called paradontium. The paradontium includes: cementum, periodontium, bony alveolus.

Hard tissues of the tooth

Enamel is the hardest part of the tooth and the whole body. It contains 97% inorganic substances (calcium salts) and 3% organic substances (amino acids, lipids, mucopolysaccharides). Enamel covers the crown of the tooth (the visible part). On the outside, the enamel is covered by a thin cuticle (Nasmyth's sheath), which is gradually eroded on the chewing surface.

Enamel consists of 1) enamel prisms and 2) the interprismatic substance (less calcified) that holds them together. There are no cells in enamel. Enamel is a non-cellular structure. The structural elements of enamel are enamel prisms formed by hydroxyapatite crystals and an organic matrix. The enamel prisms have an S-shaped curvature and are perpendicular to the dentinenamel junction throughout the enamel thickness. Due to the S-shaped course, the enamel prisms are perceived as bands running in a radial direction. These bands are called Gunther – Schragger bands, which appear as dark and light bands. Tangential lines (parallel to the surface) are also observed in enamel. These are called Retzius lines. The appearance of Retzius lines is explained by periodic weakening of mineralization. Retzius lines are lines with reduced deposition of calcium salts, i. e. with reduced mineralization.

Retzius lines are a reflection of the diurnal rhythm in the deposition of calcium salts during the development of enamel prisms, i. e. different intensity of their mineralization during the day and night.

Peculiar structures of normal enamel are enamel plates and enamel bundles. They are areas of insufficiently mineralized interprismatic substance that differ in shape. Enamel plates are thin sheet-like structures that run through the entire thickness of the enamel. Enamel bundles are located at the dentine-enamel junction and penetrate only the interior of the enamel. Enamel laminae and enamel bundles, which are composed of organic matter, can serve as entry points for enamel-destroying bacteria.

Enamel spindles are found in the enamel. Enamel spindles are bulbous thickenings of dentin fibers at the point where dentin tubules penetrate the enamel through which nutrients enter the enamel. Enamel

spindles are formed by outgrowths of odontoblasts (Thoms fibers) that penetrate the lower layer of enamel between enamel prisms. Enamel spindles are hypomineralized areas of enamel.

Enamel is permeable to water, amino acids, ions, glucose, dyes, urea, and other substances directly from saliva. Saliva affects the permeability of enamel. The permeability of enamel increases under the influence of acids, alcohol and deficiency of dietary salts of phosphorus, calcium, fluorine. A lack of nutrients and vitamins causes enamel to break down

Enamel cuticle (Nasmyth's sheath). The enamel cuticle is a thin organic layer that covers the enamel. The enamel cuticle develops from the pulp of the enamel organ (intermediate and superficial layers). Nasmyth's enamel is very resistant to the action of acids, but is easily eroded by chewing. In the enamel of adult teeth, it is preserved only on the lateral surfaces of the crown of the tooth. The cuticle protects the enamel from the harmful effects of various chemicals. Enamel does not regenerate.

Dentin is the main mass of the tooth. In humans, dentin is covered by enamel in the crown area and by cementum in the root area. In a normal tooth, dentin is not in contact with the external environment and the tissues surrounding the tooth.

Dentin is similar in structure and properties to coarse-fiber bone, but differs from it in the absence of cells. The cells that form dentin (odontoblasts) are located in the peripheral pulp layer, and only the outgrowths of the cells remain in the dentin. Dentin is 28% organic (collagen, lipids, mucopolysaccharides) and 72% inorganic (calcium phosphate, calcium fluoride, calcium carbonate, magnesium, sodium).

Dentin consists of 1) the basic (non-cellular) substance, 2) the dentin tubules. There are no cells in dentin. Dentin tubules look like thin tubes that run radially from the pulp to the enamel or cementum. Under normal conditions, the lumen of dentin tubules is filled with outgrowths of odontoblasts - Tom's fibers. The wall of the dentinal tubule is formed by the basic substance of dentin. In the thickness of the dentin, the dentinal tubules and the Thoms fibers within them branch out and give lateral processes. Unmyelinated nerve fibers also

pass through the dentinal tubules. Trophic processes are carried out through these tubules.

The interglobular spaces are of great importance in the metabolism of dentin. Interglobular spaces are unusual areas of the main substance of dentin, which have the shape of spherical cavities. The cavities are filled with collagen fibers and amorphous substances (glycoproteins). Especially many interglobular spaces in the root, at the border with the cementum, where they have the appearance of black grains, forming a granular layer of Toms.

Core substance of dentin.

The ground substance is located between the dentin tubules and is composed of: 1) collagen fibers and 2) cement substance. The location of these fibers varies from dentin to dentin.

Layers of dentin.

There are three layers of dentin:

- 1 – Mantle, the outer layer,
- 2 – periopulpal, the inner layer,
- 3 – predentin.

I. **Mantle**, the outer layer, contains

- 1 – collagen fibers that run in a radial direction, perpendicular to the tooth surface. These fibers are called Korf fibers.
- 2 – dentin tubules with outgrowths of odontoblasts and mineralized substances.

II. **The peri-pulpal** dentin contains:

- 1 – collagen fibers that run tangentially, parallel to the tooth surface, perpendicular to the dentinal tubules. These collagen fibers are called Ebner fibers.
- 2 – dentin tubules with Toms fibers and mineralized amorphous cement.

Mineral salts (calcium salts) are deposited in the amorphous cement substance between the collagen fibers. Deposition of dentin by odontoblasts continues throughout life and increases with tooth damage.

III. **Predentin** is the innermost zone facing the pulp. Predentin is immediately adjacent to the odontoblast layer. The dentin fibers pass through the predentin. Predentin is a zone of non-mineralized dentin that is normally never mineralized. This zone is a place of constant dentin growth. At the expense of the predentin, there is appositional dentin growth and tooth growth.

Dentin growth in adult teeth does not stop and continues throughout life, although at a slower rate. The dentin that develops after the teeth have erupted is called irregular, secondary dentin. Secondary dentin differs from regular primary dentin (formed during embryogenesis of the tooth) by less regular structure of dentin tubules (changes in the course and number of tubules), collagen fibers and irregularities in the type of mineralization (strong or insufficient). The production of secondary dentin increases when the enamel is destroyed (caries). Secondary dentin is called irregular, i.e. it does not have the correct structure.

Transparent dentin

In older or decayed teeth, areas of dentin are observed where calcium salts are deposited in and around the outgrowths of the odontoblasts. This results in the closure of the lumen of some dentinal tubules. Due to the deposition of calcium salts in the dentinal tubules, the refractive indices of the tubules and the main substance of the dentin are equalized, and therefore such areas of dentin appear transparent. This is called transparent or sclerosed dentin. The appearance of transparent dentin in caries can be considered as a reaction of the tooth to the action of various harmful agents, which protects the pulp from irritation and penetration of infection.

«Dead traces»

In caries, the death of odontoblast outgrowths in the dentinal tubules can also be observed. The cavities of dentin tubules are filled with air and other gaseous substances. Therefore, groups of such dentinal tubules are called «dead paths».

In dentin, there are weakly mineralized areas in the form of thin bands with a tangential direction. These bands are called Owen's lines.

Structure of cementum

Cement covers the dentin of the root. The chemical composition of cementum is similar to that of coarse bone. It contains 30% organic substances and 70% inorganic substances (calcium phosphoric acid, calcium carbonate). Cementum is the only hard tissue of the tooth that can contain cells.

Types of cementum

There are two types of cementum: 1 – acellular (primary), 2 – cellular (secondary).

I. **In acellular (primary) cementum** there are no cells and their processes. Acellular cement consists of: 1) collagen fibers and 2) an amorphous substance (calcium salts). Collagen fibers run in radial and longitudinal directions. Radial collagen fibers continue into bundles of periodontal collagen fibers called Sharpeian fibers.

II. **Cellular cementum.** Cellular cement is similar in structure and composition to coarse-fiber bone, but unlike bone, it does not contain blood vessels. The cement is diffusely supplied by periodontal blood vessels. Cellular secondary cement contains: 1) cells – cementocytes, with numerous processes, 2) collagen fibers, less ordered, 3) amorphous substance, mineralized.

Cementocytes are located in lacunae from which tubules branch off. Inside the tubules there are processes of cementocytes. Through the tubules, there is an exchange of substances between cement and dentin. Collagen fibers have no specific orientation. The cementum of the tooth is poorly regenerated, does not undergo permanent remodeling, and is avascular.

Soft tissues of the tooth.

Structure of the pulp. The pulp is composed of 4 layers:

- 1 – odontoblastic (peripheral),
- 2 – Weil's layer – acellular, only protuberances,
- 3 – subodontoblastic (intermediate),
- 4 – central – LFICT.

- I. The peripheral or odontoblastic layer is composed of odontoblasts. Odontoblasts are pear-shaped and have many processes. The long processes penetrate the dentin tubules. There are collagen fibers between the cells. Elastic fibers are not found in the pulp. The function of odontoblasts is similar to that of osteoblasts in bone. They produce substances that form dentin.
- II. The Weil's layer is represented by collagen fibers and outgrowths of odontoblasts.
- III. The subodontoblastic (intermediate) layer consists of subodontoblasts – precursors of odontoblasts, star-shaped, poorly differentiated cells.
- IV. The central layer consists of LFICT, nerve vessels or DFICT. The central layer of the crown pulp contains LFICT, while the adult root pulp contains DFICT.
The pulp has the following functions:
 1. trophic,
 2. dentin forming,
 3. protective or barrier function,
 4. plastic,
 5. sensory irritation.

The intercellular substance of the pulp includes collagen fibers and basic substance: glycosaminoglycans, proteoglycans, glycoproteins. Cells are represented by fibroblasts, macrophages, adventitial and denticle cells.

Denticles

Sometimes pieces of dentin are found in the pulp – these are denticles (calcified structures). The source of their development are ectopically («wrongly») located odontoblasts. According to their location in the pulp, denticles are divided into 1) free, located in the center of the pulp, 2) walled – maintaining the connection with the dentin-enamel junction, 3) interstitial – penetrating into the dentin. A distinction is made between true and false dentin. True dentin has the structure of dentin. False denticles (petrificates) are foci of organic calcification in the pulp tissue. Petrificate – diffuse areas of

calcification found in the root on the periphery of nerve fibers and vessels, as well as in the wall of vessels. Denticles can pinch nerve fibers, blood vessels and cause pulp pain. Causes of tartar formation – 1) metabolic disorders (aging, local inflammatory processes, endocrine diseases), 2) lack of nutrients (protein, vitamins).

Periodontium

The tooth is attached to the dental alveolus by the periodontium, which consists of the cementum, the periodontium, and the wall of the dental alveolus, which is the supporting apparatus of the tooth. The periodontium consists of bundles of collagen fibers (DFRCT-70%) attached to the cementum at one end and to the wall of the alveolus at the other. Between the bundles of dense connective tissue are interlayers of loose connective tissue (LFICT – 30%) through which blood vessels pass.

Bundles of dense connective tissue have a different location. At the edges of the alveolus, the bundles have a horizontal direction and form the circular ligament of the tooth. In the lateral sections of the periodontal space, the bundles of collagen fibers have an oblique arrangement, with their upper ends attached to the alveolar bone and their lower ends attached to the cementum. In the region of the root apex, the collagen fibril bundles have a radial direction. The bundle of periodontal fibers running in horizontal, oblique and radial directions limits the possibility of tooth movement during chewing. Destruction of these fibers, for example, in paradontosis, causes an increase in tooth mobility. In an adult, the bundles of collagen fibers of the periodontium run uninterrupted across the entire width of the periodontal space. In children, the bundles of collagen fibers are interrupted in the middle of the width of the periodontal space. Between the bundles of collagen fibers lies loose fibrous irregular connective tissue containing blood vessels and nerve endings.

Blood vessels of the periodontium nourish the cement. Functions of the periodontium – fixation, participation in eruption of teeth, support, trophic, reparative, sensory, protective.

Eruption of teeth

Several causes are distinguished: 1) increased pressure in the dental papilla – increase in intrapapillary pressure, 2) deposition of newly formed bone tissue at the bottom of the dental alveolus, 3) osteoclasts destroy the bony septum located between the milk tooth and the rudiment of the permanent tooth, 4) resorption (destruction) of the roots of milk teeth.

Age-related changes in teeth.

With age, the enamel and dentin on the chewing surface wear away. Enamel becomes dull, cracks may appear, and mineralized plaque may be deposited. The organic content of enamel, dentin and cementum decreases and the inorganic content increases. The permeability of enamel, dentin and cementum to water, glucose, enzymes, ions, amino acids decreases. With age, the formation of secondary dentin ceases and the formation of cementum increases. The pulp atrophies due to sclerotic changes in the blood vessels and deterioration of nutrition. The number of cells in the pulp decreases and the collagen fibers become coarse.

Esophagus

Sources of development:

1. prechordal plate in the entoderm of the foregut,
2. mesenchyme,
3. mesoderm (myotome of dorsal mesoderm, visceral leaflet of splanchnotome).

The esophageal epithelium develops from the prechordal plate.

Smooth muscle tissue, loose fibrous irregular connective tissue (LFICT), develops from the mesenchyme. Skeletal (striated) muscle tissue develops from the myotome of the dorsal mesoderm.

The mesothelium of the peritoneum develops from the visceral sheath of the splanchnotome.

Structure of the esophagus

The esophagus consists of 4 membranes: 1) mucosa, 2) submucosa, 3) muscularis, 4) adventitial (serous) membrane.

I. The mucosa consists of 1) stratified squamous non-keratinized epithelium, 2) lamina propria consisting of loose fibrous irregular connective tissue, 3) muscular lamina represented by smooth muscle tissue.

The mucous membrane together with the submucosa forms 7–10 longitudinally arranged folds in the esophagus. As food passes through, the folds are spread apart. The epithelium of the esophagus is represented by the stratified squamous non-keratinized epithelium (SSNE), in which 3 layers are distinguished: 1) basal, 2) spinous, 3) superficial. The epithelium may undergo keratinization in elderly people.

The lamina propria of the esophageal mucosa consists of: 1) loose, fibrous irregular connective tissue (LFICT), 2) cardiac mucosal glands located in the upper and lower parts of the esophagus. There are no cardiac mucosal glands in the middle part of the esophagus.

The cardiac mucosal glands are simple branched tubular glands. Their ends are formed by cuboidal epithelium and endocrine cells. The epithelium of the ducts is formed by cylindrical epithelium. Diverticula, cysts, ulcers and tumors of the esophagus are most often formed at the sites of adenoids.

Muscular lamina of the mucous membrane. In the upper part of the esophagus it is represented by separate longitudinal bundles of smooth myocytes. In the middle part there is a muscular lamina with longitudinal smooth muscle cells. In the lower part, the muscle lamina consists of 2 layers: 1) the inner circular layer of myocytes, 2) the outer longitudinal layer of myocytes. The contraction of the myocytes of the muscular lamina facilitates the passage of food through the esophagus into the stomach.

II. The submucosal base is composed of LFICT. Throughout the esophagus, the submucosal base contains its own submucosal glands. The submucosal glands of the esophagus are complex alveolar-tubular branching mucosal glands. The terminals of the glands are composed of mucosal cells (mucocytes). The secretory cells are surrounded by myoepithelial cells. The secreted mucus facilitates the passage of the food clump.

III. The muscularis consists of 2 layers: 1) inner circular, 2) outer longitudinal, separated by layers of LFICT. In the upper part of the muscle sheath is represented by skeletal (striated) muscle tissue. In the middle part – skeletal and smooth muscle tissue, in the lower part – smooth muscle tissue. The contraction of the muscular tissues promotes the movement of the food lump from the esophagus to the stomach.

IV. The adventitial sheath is formed by the LFICT and is located in the upper and middle part of the esophagus. The lower part of the esophagus is covered by a serous membrane formed by mesothelium (SSKE) and underlying connective tissue (LFICT).

Organs of the middle part of the digestive tract

Stomach

Sources of development: 1) entoderm forms a simple, single-row cylindrical epithelium, 2) mesenchyme forms smooth muscle tissue and loose fibrous irregular connective tissue, 3) mesoderm – visceral layer of the splanchnotome forms the mesothelium of the serous membrane.

Structure of the stomach

The stomach is divided into cardiac, fundal and pyloric sections. The stomach wall consists of 4 layers: 1) mucous, 2) submucous, 3) muscular, 4) serous.

I. The mucosa consists of 3 layers: 1) simple single-row cylindrical epithelium, 2) lamina propria of the mucosa, 3) lamina muscularis.

Depressions of the epithelium in the lamina propria are called gastric fossae. The epithelium is a simple cylindrical gland. All the epithelial cells of the stomach constantly secrete a mucoid (slimy) secretion. Mucus is a protective substance for the stomach wall. The amount of mucus in the stomach increases when irritating substances (alcohol, mustard, acid) enter the stomach. The lamina propria of the mucous membrane is a loose, fibrous, irregular connective tissue (LFICT) in which the gastric glands are located. The muscular lamina of the gastric mucosa consists of 3 layers of smooth muscle cells:

1) inner – circular, 2) middle – longitudinal, 3) outer – circular. The contraction of myocytes of the mucosa contributes to the excretion of secretions from the glands of the stomach.

II. The submucosal base of the stomach consists of LFICT.

III. The muscularis consists of 3 layers of smooth myocytes: 1) inner oblique, 2) middle circular, and 3) outer longitudinal. There are interlayers of LFICT between the layers of the muscularis.

IV. The serous membrane of the stomach consists of mesothelium (simple squamous epithelium) on a base of connective tissue (LFICT). The LFICT is adjacent to the muscularis of the stomach. The connective tissue base is covered by mesothelium on the surface.

Gastric glands

The glands of the stomach are divided into: 1) intrinsic glands located in the body and fundus of the stomach, 2) cardiac glands located in the cardiac portion, 3) pyloric glands located in the pyloric portion.

The glands of the stomach are located in the intrinsic lamina of the mucosa.

I. The intrinsic (fundal) glands of the stomach. By structure, the intrinsic glands are simple tubular unbranched glands. The outlet ducts of the glands open at the bottom of the gastric fossa. The secretory end sections of the intrinsic glands contain 5 types of cells: 1) main, 2) parietal, 3) mucous neck, 4) stem, 5) endocrine.

1. The chief cells are prismatic. Microvilli are present on the apical surface. In the basophilic cytoplasm there is a well-developed granular endoplasmic network with secretory granules. The function of the main cells is to secrete pepsinogen, which in an acidic environment is converted into the active form – pepsin, the main component of gastric juice.
2. Parietal cells are located outside the main cells and mucosal additive cells. Oblique (parietal) cells are irregularly shaped, acidophilic cytoplasm. The cytoplasm contains intracellular tubules. The function of the parietal cells is to secrete chloride,

which serves as a material for the formation of hydrochloric acid, and internal Kastl factor, which is necessary for the absorption of vitamin B12 in the small intestine. Factor Kastl is an enzyme that converts the inactive form of vitamin B12 from food into the active, absorbable form.

3. Mucosal neck cells are located in the neck of the gland, have a triangular shape. Function – are the source of regeneration of the gastric epithelium. These cells proliferate and differentiate into all types of glandular cells. This ensures constant renewal of the epithelium.
4. Stem cells are located in the body of the gland, have a prismatic shape, the nucleus is flattened and pushed to the basal part of the cell. The apical part of mucosal accessory cells contains granules of mucosal secretion (mucin). The function of these cells is mucus secretion.
5. Endocrine cells (argentaffin, enterochromaffin, argyrophilic, Kulchitsky cells). A characteristic feature of these cells is the presence of secretory granules in the cytoplasm. Several cell types are distinguished:

EC cells secrete serotonin and melatonin. Serotonin stimulates secretion of digestive enzymes, mucus secretion, motor activity. Melatonin regulates functional activity depending on the action of the light cycle.

G-cells (gastrin-producing) secrete gastrin, which stimulates the secretion of hydrochloric acid.

ECL – cells produce histamine, which stimulates the secretion of hydrochloric acid.

P-cells secrete bombesin, which stimulates the secretion of hydrochloric acid.

D-cells secrete somatostatin which inhibits gastric secretory activity.

D1-cells secrete vasointerstitial peptide (VIP), which dilates blood vessels, lowers blood pressure, and stimulates the release of pancreatic hormones.

A-cells synthesize glucagon, which breaks down glycogen into glucose and raises blood sugar.

II. **The gastric cardiac glands** are simple tubular branching glands. The terminal secretory portions of the glands contain all 5 cell types, but many mucosal accessory cells and few chief and parietal cells. The function is to secrete a mucous secretion.

III. **The pyloric glands** are simple tubular glands with highly branched terminal sections. The secretory terminals of the glands contain 4 types of cells, no parietal cells. The terminals contain many mucosal accessory cells, few principal cells. The function is to secrete mucus.

Functions of the stomach:

- 1) secretory – production by glands of gastric juice, which performs chemical breakdown of food
- 2) mechanical – contraction of muscle tissue provides mixing of food with gastric juice and progression to the 12-intestines
- 3) absorptive – absorption of water, salt, alcohol, drugs through the stomach wall
- 4) antianemic – production of Castl factor, without which iron deficiency anemia develops
- 5) excretory – excretion of urea, ammonia from the blood into the stomach
- 6) endocrine – production of hormone-like substances that regulate digestion
- 7) protective – prevents the penetration of microbes into the blood, protects the mucous membrane of the stomach from the harmful effects of hydrochloric acid, prevents self-digestion.

The small intestine

The small intestine is divided into 3 sections: 1) duodenum, 2) jejunum, 3) ileum.

Sources of development: intestinal endoderm, mesenchyme, mesoderm - visceral layer of the splanchnotome. Intestinal endoderm forms a simple columnar epithelium. The mesenchyme forms smooth muscle tissue and loose fibrous irregular connective tissue. The visceral layer of the splanchnotome forms the mesothelium of the serous membrane.

Structure of the small intestine

The wall of the small intestine is composed of 4 layers: the mucosa, submucosa, muscular, and serosa.

I. The mucosa is uneven and contains folds, villi, and crypts. The folds of the mucous membrane are circular and formed by the mucous membrane and submucosa. The villi are finger-like protrusions that extend from all layers of the mucosa. In the duodenum, the villi are broad and short, while in the jejunum and ileum, they are narrower and taller. Crypts are tubular recesses in the epithelium of the mucosa's lamina propria.

The mucous membrane comprises three layers: 1) a simple columnar epithelium, 2) a lamina propria consisting of LFICT and lymph nodules, 3) a muscular lamina (or muscularis mucosae) consisting of smooth muscle tissue (SMT) that includes two layers - inner circular and outer longitudinal.

II. The submucosa is formed by the LFICT. The submucosa of the duodenum contains Brunner's glands, which are complex branched tubular and secrete mucus.

III. The muscular wall of the intestine consists of two layers of smooth muscle tissue: an inner circular layer and an outer longitudinal layer.

Contractions of the circular layer cause intestinal spasms, while peristaltic movements are caused by orderly contractions of both layers.

IV. The small intestine's serous membrane comprises a connective tissue (LFICT) covered by mesothelium, a simple squamous epithelium. The serosa covers the small intestine externally on all sides except the duodenum, which is covered by peritoneum only in the front, while the rest of it is covered by the adventitia.

Structure of the intestinal villi

The intestinal villi are lined with a simple columnar epithelium. The epithelium contains three types of cells: border cells (or absorptive cells), goblet cells, and endocrine cells.

Absorptive cells have a cylindrical shape and microvilli on their apical surface, which increases the area of absorption. The surface of microvilli is covered by a glycocalyx composed of polysaccharides, oligosaccharides, glycoproteins, glycolipids, and digestive enzymes. The cytoplasm of absorptive enterocytes contains a well-developed granular endoplasmic reticulum and lysosomes.

The functions of absorptive enterocytes are to produce digestive enzymes for wall-to-wall digestion and to absorb breakdown products.

Goblet cells are unicellular endoepithelial mucosal glands. They have a distinctive goblet shape and well-developed smooth endoplasmic reticulum and Golgi apparatus in cytoplasm. Mucous secretion granules accumulate in the apical part of the cell, and they are released through merocrine secretion. Goblet cells release their mucous secretion when food enters the intestine. The number of goblet cells increases from the duodenum to the ileum. The mucus secreted by the goblet cells moistens the surface of the mucosa of the small intestine, promoting the movement of food.

Endocrine cells. Endocrinocytes, also known as argentaffin cells, or basal granular cells, are located in the epithelium of the villi and crypts. These cells contain granules with hormones in their basal part. There are seven types of endocrine cells that secrete different hormones

- 1) EC-cells produce serotonin, motilin and substance P.
- 2) A-cells produce enteroglucagon.
- 3) S-cells produce secretin.
- 4) G-cells secrete gastrin.
- 5) D-cells produce somatostatin.
- 6) J-cells – cholecystokinin, pancreosimine.
- 7) D1-cells are VIP (Vasoactive intestinal polypeptide).

The structure of the intestinal crypt

The epithelial lining of crypt is composed of five types of cells: border cells (or absorptive cells), goblet cells, endocrine cells, Paneth cells (apical granular cells), and non-border cells (or stem cells).

While the absorptive, goblet, and endocrine cells have the same structure as those found in the villi, Paneth cells (cells with acidophilic granularity) are only present in the epithelium of crypts and are absent in villi. The apical part of Paneth cells contains acidophilic granules that stain bright red with eosin.

Paneth cells have several functions, including:

- 1) the secretion of dipeptidases (erepsin) that break dipeptides to aminoacids,
- 2) a secretion that neutralizes the hydrochloric acid of intestinal contents,
- 3) the secretion of lysozyme, which has antimicrobial action.

Stem cells are undifferentiated cells

These intestinal stem cells and serve as a source of regeneration for crypt and villus epithelial cells. The epithelium of crypts and villi is renewed every 5-6 days due to the stem cells, which divide and differentiate into all types of intestinal epithelial cells.

The functions of small intestine:

1. the chemical processing of food, including the breakdown of proteins, lipids, and carbohydrates;
2. 3the absorption of the breakdown products into the stroma of villi;
3. the motor function is responsible for the mechanical mixing and pushing of chyme;
4. the endocrine – production of biologically active substances.

The large intestine

The large intestine is made up of 2 main parts: 1) the colon and 2) the rectum. The colon is in turn subdivided into: cecum with vermiform appendix, the ascending, transverse, descending and sigmoid colons.

Sources of development: ectoderm, endoderm, mesenchyme, mesoderm. The stratified squamous nonkeratinized epithelium of

the anal rectum develops from the ectoderm. The simple columnar epithelium of the colon develops from the endoderm. Smooth muscle tissue and loose fibrous irregular connective tissue develop from the mesenchyme. The mesothelium of the serous membrane develops from the mesoderm, the visceral leaflet of the splanchnotome.

The colon

The wall of colon is composed of 4 layers: the mucosa, submucosa, muscular, and serosa.

I. The mucosa is irregular and contains folds and crypts, but no villi. The folds, which run circularly, are formed by the mucosa and submucosa. Additionally, the crypts in the colon are wider than those in the small intestine and contain numerous goblet cells. The mucosa is made up of 3 layers: 1) simple columnar epithelium, 2) lamina propria consisting of LFICT, 3) muscular lamina (or muscularis mucosae) which is represented by two layers of smooth myocytes: the internal circular and the external longitudinal. There are interlayers of LFICT between the layers.

II. The submucosa is composed of LFICT and numerous lymph nodules.

III. The muscular sheath of the colon is composed of two layers of smooth myocytes. The inner layer is circular and continuous, while the outer layer is longitudinal and represented by three ribbons, which are bundles of smooth myocytes. Between these ribbons, there are bulges known as haustrae.

IV. The colon is covered by a serous membrane from the outside. The composition of the serous membrane is such that it consists of a connective tissue base that is covered with mesothelium.

Structure of the intestinal crypts of the colon

The structure of the intestinal crypts of the colon is similar to that of the small intestine, with the epithelium containing five types of epithelial cells, namely:

- 1) border cells (or absorptive cells),
- 2) goblet cells (which are the most numerous),

- 3) endocrine cells,
- 4) Paneth cells (apical granular cells),
- 5) undifferentiated cells.

The large intestine presents some differences when compared to the small intestine:

- 1) it does not have villi in the mucosa.
- 2) there is a significant predominance of goblet cells in the crypt epithelium.
- 3) the outer longitudinal layer of the muscular membrane is divided into three ribbons (Taenia coli) that are not continuous.
- 4) the presence of haustra on the external surface and semilunar folds on the internal surface.

Colon functions:

- 1) formation of feces and the intensive absorption of water from the chyme,
- 2) the evacuation of fecal matter,
- 3) the production of mucus, which facilitates the movement of chyme along the intestine,
- 4) excreting salts of heavy metals, urea, and metabolic products.
- 5) synthesis of vitamins B and K with the participation of bacterial flora that is constantly present in the intestine,
- 6) bacteria in the intestine also assist in the partial digestion of fiber.

Rectum

The rectum is divided into 2 sections: 1) pelvic and 2) anal. The anal region is divided into 3 zones: 1) columnar, 2) intermediate, 3) cutaneous.

Pelvic region

The pelvic wall of the rectum consists of 4 layers: 1) mucosa, 2) submucosa, 3) muscular, 4) serous.

I. The mucosa is made up of 3 layers: 1) a simple columnar epithelium, 2) the lamina propria, which is formed by LFICT, 3) the muscular lamina (or muscularis mucosae) is composed of two

layers of smooth myocytes, with an inner circular layer and an outer longitudinal layer.

The pelvic mucosal epithelium contains intestinal crypts that consist of five types of cells: border cells (or absorptive cells), goblet cells, endocrine cells, Paneth cells, and undifferentiated cells.

II. The submucosa is well-developed and is represented by LFICT.

III. The muscular sheath is composed of two layers of smooth muscle tissue: an inner circular layer and an outer longitudinal layer that are continuous and not divided into bands.

IV. The serous membrane composed of a connective tissue base and mesothelium.

The anal canal

The anal canal is composed of 4 layers, namely the mucosa, submucosa, muscular layer, and adventitia.

I. The mucosa consists of 3 layers:

- 1) Epithelium,
- 2) lamina propria,
- 3) muscular plate (muscularis mucosae).

1) The columnar zone epithelium is stratified cuboidal, while the intermediate zone epithelium is stratified squamous non-keratinized (SSNE), and the cutaneous zone epithelium is stratified squamous keratinized (SSKE).

2) The lamina propria of the mucosa is formed by the LFICT, which contains solitary lymphatic follicles.

3) The muscular lamina consists of a single layer of longitudinal myocytes.

II. The submucosa is represented by the LFICT, which contains hemorrhoidal veins. Prolonged stasis of blood in the veins can sometimes lead to the development of varicose veins, which are characterized by bulges in the anal canal known as hemorrhoidal nodes.

III. The muscular layer comprises an inner circular and outer longitudinal layer of smooth muscle tissue. The thickenings of the circular layer are called the sphincters of the rectum. The outer sphincter is made up of skeletal muscle tissue.

IV The adventitial layer is composed of the LFICT.

The liver

The liver is the largest gland in the digestive system.

Development. The liver develops from the endoderm of the middle portion of the foregut. In the 3rd week of embryogenesis the hepatic bud forms on the ventral wall of the foregut. The hepatic bud is then divided into cranial (upper) and caudal (lower) sections.

The liver develops from the cranial part and the gallbladder from the caudal part. Connective tissue and blood vessels develop from the mesenchyme.

From the second half of embryogenesis, the liver forms lobules - structural and functional units.

The structure of the liver

The liver is covered by a capsule of dense fibrous irregular connective tissue (DFICT). The capsule (Glisson's) is covered by the visceral layer of the peritoneum (connective tissue-based mesothelium).

Stroma – loose fibrous irregular connective tissue (LFICT), poorly developed in humans.

Parenchyma – Liver lobules, which are a structural and functional unit of the liver. The number of lobules in the human liver reaches 500 000.

The classic hepatic lobule has a hexagonal prism shape with the central vein (vein of non-muscular type) located in the center. Triads, consisting of interlobular artery, interlobular vein, and interlobular bile duct, are located at the corners of the lobule. The interlobular connective tissue is poorly developed, resulting in poor delimitation of the hepatic lobules. This structure is typical of a healthy human liver. Blood vessels and bile ducts pass through the interlobular connective tissue.

The liver has two histofunctional units: the hepatic acinus and the portal lobule.

1. The hepatic acinus is rhombus-shaped, with central veins located at the acute corners and triads at the obtuse corners. It includes segments of two adjacent classical hepatic lobules.
2. The portal lobule is triangular in shape, with triads in the center

and central veins at the corners. It includes segments of three adjacent classical hepatic lobules.

Blood supply in liver

The liver's blood supply can be divided into three parts: the system of blood inflow to the lobules, the system of intra-lobular blood circulation, and the system of blood outflow from the lobules.

1. The system of blood inflow to the lobules is made up of the portal vein and hepatic artery, which are further divided within the liver. The blood vessels include lobular, segmental, interlobular, and circumlobular arteries and veins, which are accompanied by bile ducts.

2. The system of intra-lobular blood circulation is represented by sinusoidal capillaries with a discontinuous basal membrane. Mixed blood flows through these capillaries from the periphery to the center of the lobules.

3. The lobules' blood outflow system comprises central veins, collecting veins, and hepatic veins. These vessels are not accompanied by arteries or bile ducts.

Structure of a liver lobule.

A liver lobule consists of three components: 1) hepatic cords (trabeculae), 2) sinusoidal capillaries, 3) central vein.

Hepatic cords are formed by hepatocytes arranged in two rows and connected to each other by desmosomes and 'lock' type junctions, without a basal membrane. There are slit-like spaces between hepatocytes of adjacent rows without their own wall. These spaces are called bile capillaries.

1. Hepatocytes are large, polygonal-shaped cells. All general organelles are present in the cytoplasm of hepatocytes (the endoplasmic reticulum is well-developed, as is the Golgi complex, mitochondria, and lysosomes), as well as inclusions such as glycogen, lipids, and proteins. The hepatocyte has two surfaces (sides): 1) biliary, 2) vascular. Hepatocytes have microvilli on their biliary and vascular surfaces.

The biliary side faces the gaps between adjacent hepatocytes, forming bile capillaries. The vascular side faces the sinusoidal capillary.

Bile capillaries do not have their own wall. Their wall is formed by the biliary sides of adjacent hepatocytes, which have indentations that together form the lumen of the bile capillary. The bile capillaries begin blindly in the central part of the hepatic lobule and are located inside it. Bile is produced by hepatocytes during the day. It flows through the bile capillaries from the center of the lobule to its periphery.

2. Sinusoidal hemocapillaries with a discontinuous basal membrane are almost devoid of basal membrane. The capillary wall contains two types of cells: endotheliocytes (squamous cells) and Kupffer cells, which are stellate macrophages. Kupffer cells originate from monocytes, are capable of phagocytosis, and have an outgrowth shape. They are capable of amoeboid movement and can exit into the lumen of the hemocapillary.

Around capillaries, there is a narrow space called the Disse space, located between them and surrounding cells. One wall of the Disse space is formed by the vascular side of hepatocytes, and the other by the wall of the sinusoidal capillary. The Disse space contains outgrowths of Kupffer cells, microvilli of hepatocytes, outgrowths of perisinusoidal lipocytes, and argyrophilic fibers.

Lipocytes, also known as fat-accumulating or fat-storing cells, are located between neighboring hepatocytes. These cells are small in size and contain small fat droplets, as well as many ribosomes. The functions of lipocytes are: 1) to deposit fat-soluble vitamins and 2) to form fibers.

The hepatohematous (blood-liver) barrier consists of three components: the endothelium of sinusoidal capillaries, stellate macrophages (Kupffer cells), and structures in the perisinusoidal space. Hepatocytes release glycogen, proteins, urea, vitamins, and fats into the blood during the night. The amount of glycogen in hepatocytes increases 4-5 hours after a meal, reaching a maximum in 10-12 hours. Glycogen gradually transforms into glucose and disappears from the cytoplasm of cells within 24-28 hours after a meal. There is no direct connection between blood and biliary capillaries, as they are separated from each other by hepatic and endothelial cells.

The biliary tracts include:

- 1) circumvillous bile ducts lined with cuboidal epithelium,
- 2) interlobular bile ducts also lined with cuboidal epithelium,
- 3) segmental bile ducts lined with columnar epithelium,
- 4) lobular bile ducts also lined with columnar epithelium, and
- 5) the common hepatic duct lined with columnar epithelium.
- 6) The cystic duct lined with columnar epithelium.
- 7) The common bile duct lined with columnar epithelium.

Structure of the gallbladder

The gallbladder wall is composed of three layers: the mucous, muscular, and adventitial.

The gallbladder is covered with peritoneum from the side of the abdominal cavity, which is mesothelium on a connective tissue base. The submucosa is not present.

The mucosa is composed of two layers: a simple columnar epithelium and the lamina propria, which consists of loose fibrous irregular connective tissue (LFICT). The mucosa forms numerous folds. The microvilli of the columnar epithelium allows for the reabsorption of water from the bile in the gallbladder.

The gallbladder's muscular layer is composed of bundles of smooth myocytes, with a predominance of circular direction.

The adventitia is made up of dense fibrous irregular connective tissue (DFICT).

Liver Functions

The liver is responsible for a variety of functions, all of which are associated with complex biochemical processes. It is often referred to as the biochemical laboratory of the body.

The following functions are distinguished:

- 1) bile formation - bile is necessary for the absorption of fats.
- 2) glycogen is formed during the metabolism of carbohydrates, which is the main source of maintaining a constant concentration of glucose in the blood.
- 3) blood plasma proteins such as fibrinogen, albumin, and prothrombin are synthesized during protein metabolism.

- 4) cholesterol, a component of cell membranes, is metabolized.
- 5) The liver has several functions, including participation in the metabolism of vitamins such as fat-soluble vitamins A, D, E, K, B2, and nicotinic acid.
- 6) hematopoietic function during embryogenesis;
- 7) deposits 20% of the total blood mass,
- 8) forms urea,
- 9) detoxifies hormones, toxins, and drugs,
- 10) a protective function - stellate macrophages phagocytize bacteria and microbes.

Liver regeneration

The liver has the capacity for physiological and reparative regeneration. Foods rich in carbohydrates and proteins stimulate liver regeneration. Regeneration processes occur through hepatocyte multiplication and compensatory hypertrophy. However, the high regenerative capacity of the liver is not characteristic of humans.

Pancreas

The pancreas is a gland that contains both exocrine and endocrine parts. It develops from the endoderm and mesenchyme. During embryogenesis, outgrowths form in the wall of the foregut in the third or fourth week. The dorsal bud and two ventral buds fuse together as a result of a 180-degree turn. The head of the pancreas is formed from the ventral buds, while the body and tail are formed from the dorsal bud. During the third month of intrauterine development, endodermal buds differentiate into the exocrine and endocrine sections of the pancreas.

The exocrine sections first form a system of excretory ducts, followed by the terminal secretory sections, known as pancreatic acini. In the endocrine divisions, islets of Langerhans are formed from buds that branch off from the wall of the excretory ducts.

The pancreas's capsule, connective tissue stroma, and blood vessels develop from the mesenchyme. By birth, the pancreas's exocrine and endocrine parts have a differentiated structure. However, this organ's further complication occurs postnatally.

Structure

The pancreas is divided into three parts: the head, body, and tail. It is covered by a connective tissue capsule (DFICT) that is fused with the visceral layer of the peritoneum (mesothelium on connective tissue base). The pancreas is composed of stroma and parenchyma. The stroma is made up of loose fibrous irregular connective tissue (LFICT). The gland's parenchyma is composed of epithelial tissue, which is divided into lobules. These lobules consist of both exocrine and endocrine components. The exocrine portion accounts for 97% of the gland's mass, while the endocrine portion accounts for the remaining 3%.

The exocrine part of the pancreas

It is a compound alveolar-tubular gland with a lobular structure. The structural and functional unit of the exocrine part is the pancreatic acinus. The exocrine part is represented by the pancreatic acinus and the excretory ducts. The acinus consists of a secretory part and an intercalated duct. The secretory part looks like a sac and consists of 8–12 acinar cells. Acinar cells are pyramidal in shape. The cell is divided into 2 parts – 1) basal – wide, 2) apical – narrow. The cytolemma on the basal surface of the cells forms folds, and on the apical surface – microvilli. The basal part of acinar cells is called homogeneous zone, it is strongly basophilic stained. The broad part is located on the basal membrane. In the homogeneous zone there is a well-developed granular endoplasmic reticulum (ergastoplasm), rich in ribosomes. This is where the synthesis of pancreatic enzymes takes place. The nucleus is round and located in the basal part of the cell. Above the nucleus is the Golgi complex. Mitochondria are scattered throughout the cytoplasm. The apical, narrow part of acinar cells is called the zymogenic zone and is stained acidophilic. This zone contains large secretory granules – zymogenic granules. Zymogenic granules contain enzymes synthesized in the cells in an inactive form, i.e. as zymogen. The cell structure can change at different stages of the

secretory cycle. Phases of the secretory cycle (4):

- 1 – Phase of uptake of precursors
- 2 – Secretion synthesis phase
- 3 – Secretion accumulation phase
- 4 – Phase of merocrine secretion.

The average duration of the secretory cycle is 1.5–2 hours. During starvation, the number of zymogenic granules in the cytoplasm of pancreatic cells increases. A few minutes after eating, there is an intense release of secretory granules from the cells. The function of pancreatic cells (acinar cells, acinar cells) is to synthesize the proteins of digestive enzymes (trypsin, amylase, lipase and others).

Intercalated duct

The intercalated duct is part of the pancreatic acinus. The wall of the intercalated duct is lined with a simple squamous epithelium that lies on the basal membrane. There are 3 types of acinus, which differ in the position of the intercalated ducts in relation to the secretory end segments.

Type 1 acinus - the secretory end section is located at the end of the intercalated duct.

2nd type of acinus – the secretory end section is attached laterally to the intercalated duct, sharing a common basal membrane.

3rd type of acinus – the intercalated duct is located on the apical surface of the secretory terminal cells. The cells of the intercalated duct located inside the acinus are called centroacinar cells. Centroacinar cells have an irregular, flattened shape and their oval nucleus is surrounded by organelle-poor cytoplasm.

The excretory ducts of the exocrine part of the pancreas include:

- 1 – intercalated ducts, lined with a simple squamous epithelium,
- 2 – inter-acinar ducts are lined with a simple cuboidal epithelium,
- 3 – intralobular ducts - simple cuboidal epithelium,
- 4 – interlobular ducts - simple columnar epithelium,
- 5 – common duct - simple columnar epithelium.

The common duct opens into the duodenum. The ducts are surrounded by loose fibrous irregular connective tissue (LFICT) in

which blood capillaries and nerve fibers run. The epithelium of the ducts contains goblet cells as well as endocrine cells that produce pancreosimine and cholecystokinin.

The endocrine part of pancreas is made up of pancreatic islets, also known as islets of Langerhans. These islets consist of endocrine cells and blood capillaries of the fenestrated type. The islets are rounded in shape and contain 5 main types of endocrine cells:

- 1) B-cells (basophilic) – 70–75%
- 2) A-cells (acidophilic) – 20–25%
- 3) D-cells (dendritic) – 5–10%
- 4) D1-cells (argyrophilic) – 2–5%
- 5) PP-cells – 2–5%

B-cells, also known as insulocytes, constitute 70–75% of the total number of cells in the islet and are located in the center. They have a cubic shape. The cytoplasm contains basophilic granules surrounded by a light rim. These granules contain the hormone insulin, which facilitates the assimilation of blood glucose by tissue cells, reduces blood glucose levels, and has a hypoglycemic effect.

A-cells, also known as glucagonocytes, which are located on the periphery and constitute 20–25% of all cells in the islet. These cells have a rounded shape and contain oxyphilic (acidophilic) granules surrounded by a light rim that accumulate the hormone glucagon. Glucagon breaks down glycogen and increases the sugar content in the blood, resulting in a hyperglycemic effect.

D-cells (Dendritic cells) make up 5-10% of all cells in the islet and are located in the periphery. They have a pear-shaped or stellate shape and contain granules without a light rim. These granules contain the hormone somatostatin, which inhibits the release of insulin by B cells and glucagon by A cells, as well as suppressing the synthesis of enzymes by pancreatic cells.

D1-cells, also known as VIP cells (Vasoactive intestinal polypeptide) or argyrophilic cells, are located in the periphery of the islet and make up a small percentage (2-5%) of the total number of cells. The cytoplasm of these cells contains argyrophilic granules with a narrow light-colored rim that contain vasoactive intestinal

polypeptide (VIP). This peptide is responsible for dilating blood vessels and lowering blood pressure.

PP-cells, which also make up 2-5% of the total number of cells in the islet, are typically found at the periphery of the islet. The pancreas has a polygonal shape and contains small granules in the cytoplasm with a narrow light-colored rim. These granules contain pancreatic polypeptide, which stimulates the secretion of pancreatic and gastric juices.

Pancreatic regeneration occurs through intracellular renewal of organoids, and mitotic activity of pancreatic cells is low. It is important to note that after the death of glandular cells, they do not regenerate.

The functions of pancreas

The pancreas has two main functions: exocrine and endocrine. The exocrine part produces pancreatic juice, which contains enzymes that regulate carbohydrate, protein, and fat metabolism. This juice flows through a system of excretory ducts into the duodenum. The endocrine part synthesizes hormones such as insulin, glucagon, somatostatin, vasoactive intestinal polypeptide, and pancreatic polypeptide.

RESPIRATORY SYSTEM

The respiratory system consists of: 1) airways 2) respiratory system.

I. **The airways** include: 1) nasal cavity, 2) nasopharynx, 3) larynx, 4) trachea, 5) bronchi – large, medium, small, 6) terminal bronchioles.

II. **Respiratory division.** The morphofunctional unit of the respiratory part of the lung is the acinus. The acinus contains respiratory bronchioles of the 1st order, which branch into respiratory bronchioles of the 2nd order, which divide into respiratory bronchioles of the 3rd order. They continue into alveolar passages, then into alveolar sacs, which end in alveoli (1st, 2nd, 3rd order respiratory bronchioles, alveolar passages, alveolar sacs, alveoli). The acinuses are separated from each other by layers of loose fibrous irregular connective tissue (LFICT). 12-18 acinuses form a lobule.

Development of the respiratory organs. There are 3 developmental stages:

Stage 1 – glandular stage.

Stage 2 – tubular stage.

Stage 3 – alveolar stage.

Sources of development:

- 1) Entoderm forms the singular multi-row ciliated epithelium (SMCE) of the acinar epithelium.
- 2) The mesenchyme forms the stroma (LFICT), smooth muscle tissue (SMT), and cartilage tissue.
- 3) The splanchnotome differentiates into the mesothelium single layer single row squamous epithelium (SSSE) of the pleura.

I. Glandular stage

In the 3rd week of embryogenesis, an unpaired protrusion of epithelium into the underlying mesenchyme appears from the ventral wall of the foregut, which divides into two sacs in the distal part. The

upper part gives rise to the larynx and trachea. The distal part splits into many smaller bulges, giving rise to the rudiments of the right and left lungs. Mesenchyme surrounds the rudiments. During this stage of development, the lung resembles a gland, which continues until the 16th week (month 4) of embryogenesis, forming the airways.

II. Canalicular stage

At the beginning of the 5th month of embryogenesis, the bronchioles and alveolar passages differentiate from the lung sacs.

III. Alveolar stage

From the 6th month until birth, alveolar sacs and alveoli are formed. Mesenchyme is also differentiated from it, forming smooth muscle tissue, hyaline and elastic cartilage, loose fibrous irregular connective tissue (LFICT), blood vessels, nerves. Alveoli have the appearance of collapsed bubbles that open with the first breath of the newborn and are filled with air.

Airways

The wall of the airways (trachea, bronchi) consists of 4 layers: 1) mucous layer, 2) submucosal layer, 3) cartilaginous layer, 4) adventitial layer.

I. The mucous membrane consists of 3 parts: 1) epithelium, 2) lamina propria, 3) muscular layer.

1. The structure of the epithelium is different. In the cutaneous part of the nasal vestibule – stratified squamous keratinized epithelium (SSKE), in the transitional part of the nasal cavity – SSNE, starting from the respiratory region of the nose and throughout the airways – single layer multi-row ciliated epithelium (SMCE).

2. The lamina propria is represented by loose fibrous irregular connective tissue (LFICT), rich in longitudinally directed elastic fibers.

3. The muscular layer of the mucosa consists of circularly arranged myocytes, which is most pronounced in small bronchi.

II. The submucosal membrane is represented by LFICT, which contains complex branched protein mucous glands.

III. The cartilaginous membrane consists of: in the

trachea – C-shaped rings of hyaline cartilage, in large bronchi – hyaline plates, in medium bronchi – islands of elastic cartilage.

IV. The adventitial layer is represented by loose fibrous irregular connective tissue (LFICT).

Single layer multi-row ciliated epithelium (SMCE).

7 cell types are distinguished:

- 1 – ciliated cells
- 2 – goblet cells
- 3 – endocrine cells
- 4 – basal cells
- 5 – secretory cells (Clara)
- 6 – ciliated cells
- 7 – brush cells

1. The ciliated cell is prismatic. The apical surface contains cilia (approximately 250 cilia). Cilia are specialized organoids consisting of an axoneme and basal telomeres. The axoneme consists of microtubules (9 pairs in the periphery and one pair in the center – $(9 \times 2) + 2$). The basal celom consists of 9 triplets of microtubules $(9 \times 3) + 0$ located along the periphery. The basal cilia are arranged at right angles to each other. The oscillatory movement of the cilia occurs in the direction opposite to the inhaled air and is most intense at air temperatures of 18-33 C°. The number of ciliated cells decreases as the diameter of the bronchi decreases, and the height of the cells also decreases. Their function is mechanical protection. Ciliated cells remove mucus, bacteria and dust particles that settle on the surface of the mucous membrane by oscillating the cilia. At low or high air temperature, the cilia stick together and their movement stops (smoking), resulting in the inflammatory process (lung cancer, tracheitis, bronchitis).

2. The goblet cell is goblet-shaped. They are pale and large cells that secrete a mucous secretion. The goblet cell is a unicellular endoepithelial mucous gland. The mucous secretion moistens the mucous layer, creates conditions for the adhesion of dust particles that come in with the air and are removed by coughing. Mucus also has a bactericidal effect, neutralizing many airborne microorganisms. The

number of goblet cells decreases as the lumen of the respiratory tract decreases. The function is secretory.

3. The endocrine cell has a pyramidal shape. The basal part of the cell contains secretory granules. Endocrine cells secrete hormones (dopamine, serotonin, norepinephrine) that regulate the contraction of myocytes, the smooth muscle cells of the airways. The function is endocrine.

4. The basal cell is conical in shape. It is a poorly differentiated (cambial) cell that is a source of regeneration of the airway epithelium. Mitotic division of basal cells renews the bronchial epithelium. The function is regenerative.

5. The Clara's secretory cell is a large cell with a dome-shaped apex. The cytoplasm has a well-developed smooth endoplasmic reticulum and contains secretory granules. Clara secretory cells produce enzymes that break down surfactant. The number of Clara secretory cells increases as the airway lumen decreases. The function is secretory.

6. The unciliated cell has a prismatic shape. The apical part contains clusters of glycogen granules. Function – unknown.

7. The brush cell has a barrel shape. On the apical surface are microvilli that form a rim. These cells respond to changes in the chemical composition of the air. Function – chemoreceptor.

Larynx.

The wall of the larynx consists of 3 layers: 1) mucosal layer, 2) fibrous cartilaginous layer, 3) adventitial layer. The mucosal layer consists of 2 layers: 1) epithelium, 2) the lamina propria of the mucosal layer. In the middle part of the larynx there are folds of the mucous membrane forming true and false vocal cords.

1. The epithelium in the area of the vocal cords is represented by stratified squamous non-keratinized epithelium (SSNE), and the rest of the mucosa is covered by single-layered multi-row ciliated epithelium (SMCE). The epithelium lies on the basement membrane. In the single-layered multi-row ciliated (mesenteric) epithelium, 4 types of cells are distinguished: 1) ciliated, 2) goblet, 3) endocrine, 4) basal cells.

2. The lamina propria of the mucosa is represented by loose fibrous irregular connective tissue (LFICT), which contains elastic fibers that have no definite direction. The lamina propria contains lymphoid follicles, which form the laryngeal tonsil and mixed (protein-mucus) glands.

Lamina propria

The mucous membrane of the larynx has structural features in the area of the true and false vocal cords. The vocal cords are folds of the mucous membrane that protrude into the lumen of the larynx. As part of the lamina propria of the mucous layer of the true vocal cords, there are also transverse striated muscles. Between the folds is the vocal slit. When the transverse striated muscle contracts, the vocal slit narrows, and when it relaxes, it widens. The change in size of the vocal cords affects the pitch of the sound produced by the air passing through the larynx. The false vocal cords contain smooth muscle cells.

The fibrocartilaginous layer of the larynx consists of hyaline and elastic cartilage surrounded by dense fibrous irregular connective tissue (DFICT).

The adventitial layer consists of loose fibrous irregular connective tissue (LFICT), which contains blood vessels.

The functions of the larynx are 1) air conduction, 2) vocalization, 3) thermoregulation – warming or cooling of inhaled air by blood vessels.

Epiglottis

The epiglottis separates the larynx from the pharynx. It consists of a mucous membrane covered by elastic cartilage. The mucosal membrane is represented by 1) epithelium – stratified squamous non-keratinized epithelium (SSNE), 2) lamina propria of the mucous layer consisting of LFICT. The function of the epiglottis is to close the entrance to the larynx during swallowing.

Trachea

The trachea is a hollow tubular organ. The tracheal wall consists of 4 membranes: 1) mucosal layer, 2) submucosal layer, 3) fibrous cartilaginous layer, 4) adventitial layer.

I. The mucosa consists of 3 layers: 1) epithelium – SMCE, 2) lamina propria of the mucosa, 3) bundles of smooth myocytes.

1. There are 4 types of cells in the single-layered multi-row ciliated prismatic epithelium (SMCPE): 1) ciliated cells – many cells, 2) goblet cells – also many cells, 3) endocrine cells, 4) basal cells.

2. The lamina propria of the tracheal mucosa consists of loose fibrous irregular connective tissue (LFICT) containing longitudinally oriented elastic fibers and lymphatic follicles.

3. The mucosa contains separate circularly arranged bundles of smooth muscle cells – myocytes.

II. The submucosa of the trachea is represented by loose fibrous irregular connective tissue (LFICT). Numerous complex branched alveolar tubular mixed protein mucous glands are located in the submucosa.

III. The fibrous cartilaginous layer of the trachea consists of 16-20 hyaline cartilaginous semicircles that are not closed on the posterior wall of the trachea. The free ends of the cartilaginous semicircles are connected by bundles of smooth muscle cells – myocytes. The esophagus is connected to the posterior wall of the trachea. Thanks to the smooth muscular tissue of the trachea, when swallowing, food chunks passing through the esophagus do not encounter any obstacles. Vertically, the tracheal semicircles are connected by dense fibrous irregular connective tissue (DFICT).

IV. The adventitial layer of the trachea is formed by loose fibrous irregular connective tissue (LFICT).

Functions of the trachea: 1) air conduction, 2) thermoregulation – warming or cooling of inhaled air by blood vessels.

Main bronchi

The trachea is divided into the main bronchi. The wall of the main bronchi is similar in structure to the wall of the trachea, but there are differences in the fibrous-cartilaginous membrane. The fibrous-cartilaginous membrane of the main bronchi consists of closed hyaline cartilaginous rings instead of C-shaped rings.

Lungs

The lungs contain bronchi of various calibers (primary, secondary, tertiary), terminal bronchioles and respiratory tract represented by acinus. The surface of lungs is covered with serous membrane – visceral pleura. The pleura consists of 2 layers: 1) mesothelium – single-layered single-row squamous epithelium (SSSE), 2) base of connective tissue – loose fibrous irregular connective tissue (LFICT).

Primary bronchi

Their wall consists of 4 membranes: 1) mucous 2) submucosa, 3) fibrous cartilaginous, 4) adventitia.

I. The mucous membrane consists of 3 layers: 1) epithelium – SMCE, 2) lamina propria of the mucous layer, 3) muscular layer of the mucous layer.

1. The epithelium is represented by a single layer multi-row ciliated prismatic (mesenteric) epithelium (SMCPE). The epithelium consists of 7 types of cells: 1) ciliated cells, 2) goblet cells, 3) endocrine cells, 4) basal cells, 5) secretory Clara cells, 6) brush cells, 7) unciliated cells.

2. The lamina propria of the mucous layer of the large bronchi consists of loose fibrous irregular connective tissue (LFICT), in which there are longitudinally oriented elastic fibers and lymphatic follicles.

3. The muscular lamina of the mucosa is formed by circularly arranged smooth muscle cells – myocytes, which form a thin lamina.

II. The submucosal base of large bronchi is formed by loose fibrous irregular connective tissue (LFICT), which contains complex branched alveolar-tubular mixed protein mucous glands. Mucus secretion has bactericidal and bacteriostatic properties.

III. The fibrous cartilaginous layer is composed of hyaline cartilage plates. The hyaline cartilaginous plates are interconnected by dense, fibrous irregular connective tissue.

IV. The adventitial layer is made up of loose fibrous irregular connective tissue.

Secondary bronchi

The wall of the middle bronchus consists of 4 membranes: 1) mucous, 2) submucosal, 3) fibrous cartilaginous, 4) adventitia.

I. The mucous membrane consists of 3 layers: 1) epithelium – SMCE, 2) lamina propria of the mucous layer, 3) muscular layer of the mucous layer.

1. The epithelium is represented by a single layer multi-row ciliated low prismatic epithelium (SMCE) containing 7 types of cells. In contrast to the epithelium of large bronchi, the height of the epithelium decreases, the number of goblet and ciliated cells decreases, and the number of secretory Clara cells increases.

2. The lamina propria of the middle bronchial mucosa is represented by loose fibrous irregular connective tissue (LFICT), in which the number of longitudinally arranged elastic fibers increases.

3. The muscular membrane of the middle bronchial mucosa is thickened and represented by obliquely arranged smooth muscle cells.

II. The submucosal membrane consists of loose fibrous irregular connective tissue in which the number of complex branched alveolar tubular mixed protein mucous glands decreases.

III. The fibrous-cartilaginous membrane of the middle bronchus is represented by elastic cartilaginous islands. The cartilage becomes elastic in the form of small islets. Elastic islets are interconnected by dense fibrous irregular connective tissue (DFICT).

IV. The adventitia of secondary bronchi represented by loose fibrous irregular connective tissue (LFICT).

Tertiary bronchus

The wall of the tertiary bronchus consists of 2 membranes: 1) mucous, 2) thickened adventitial.

I. The mucous consists of 3 layers: 1) epithelium, 2) lamina propria of the mucous layer, 3) muscular layer of the mucous layer.

The mucous membrane of small bronchi forms numerous folds.

1. The epithelium of small bronchi is represented by a single layer double-row ciliated cubic epithelium containing 7 types of cells. The number of goblet and ciliated cells decreases, the number of secretory Clara cells increases.

2. The lamina propria of the mucous layer of tertiary bronchi consists of loose fibrous irregular connective tissue (LFICT), in which the number of longitudinally arranged elastic fibers increases.

3. The muscular lamina of the tertiary bronchial mucosa is the thickest and is represented by co-circularly arranged smooth muscle cells. Smooth muscle tissue of tertiary bronchi is very sensitive to the concentration of carbon dioxide in the air. An increase in the concentration of carbon dioxide in the air causes the small bronchi to dilate. The muscular lamina regulates the passage of air during inhalation and exhalation. When the muscular lamella spasms, breathing becomes difficult (choking attacks in bronchial asthma). In small bronchi, complex mixed glands and cartilaginous tissue disappear, i.e. glands and cartilage are absent.

II. The adventitial membrane thickens and consists of loose fibrous irregular connective tissue (LFICT).

Regularities of the bronchial tree:

1. Lymphoid follicles are present throughout the mucosa and submucosa and carry out local defense reactions.
2. The height of the mucosal epithelium decreases as the caliber of the bronchi decreases.
3. The composition of the epithelium changes: the number of goblet and ciliated cells decreases as the bronchial caliber decreases.
4. The most pronounced folding of the mucosa occurs in tertiary bronchi.
5. The muscular lamina thickens (increases), reaching a maximum in tertiary bronchi.
6. Cartilage changes (fragments):
 - in the trachea – C-shaped half rings of hyaline cartilage
 - in primary bronchi – plates of hyaline cartilage
 - in secondary bronchi – islands of elastic cartilage
 - in tertiary bronchi – no cartilage in the wall – arranged longitudinally.

7. The number of elastic fibers increases as the caliber of the bronchi decreases. The bronchial tree of tertiary bronchi ends in terminal bronchioles.

Terminal (end) bronchioles

The wall of terminal bronchioles consists of 2 membranes:
1) mucous, 2) adventitial -LFICT.

The mucous consists of 3 layers: 1) epithelium, 2) lamina propria of the mucous layer, 3) separate bundles of smooth muscle cells.

1. The epithelium is represented by a single layer single-row ciliated low-cubic epithelium containing 7 types of cells.
2. The lamina propria of the mucosa contains loose fibrous irregular connective tissue (LFICT) in which elastic fibers are located longitudinally.
3. Bundles of smooth muscle cells are located between the elastic fibers.

Respiratory portion of the lung.

The respiratory portion of the lung begins at the acinus of the lung. The acinus is a structural and functional unit of the lung. The acinus consists of

1. 1st order respiratory bronchioles;
2. 2nd order respiratory bronchioles;
3. 3rd order respiratory bronchiole;
4. alveolar passages;
5. alveolar sacs;
6. alveoli.

The acinus resembles a cone or pyramid in shape. The acini are separated from each other by loose, fibrous irregular connective tissue (LFICT) containing blood vessels. 12-18 acini surrounded by LFICT form a pulmonary lobule.

Respiratory bronchioles.

The wall of respiratory bronchioles consists of 2 membranes:

1) mucous, 2) adventitial – LFICT.

The mucous membrane of respiratory bronchioles is represented by 3 layers: 1) epithelium, 2) lamina propria of mucous membrane – LFICT, 3) separately circularly arranged bundles of smooth myocytes. The epithelium of the mucous layer of respiratory bronchioles is represented by a single-layer single-row cubic unciliated epithelium.

Alveoli.

The main structural element of the lung is the alveolus. Alveoli are closely adjacent to each other and have the form of unenclosed (open) vesicles. Between them are interalveolar septa (LFICT), through which small blood capillaries pass. There are connections between the alveoli. These are called alveolar Kon's pores, which allow air to pass from one alveolus to another. The inside of the alveoli is lined with a single layer of epithelium – the alveolar epithelium. The alveolar epithelium contains 3 types of cells:

- 1) Type I alveolocytes
- 2) Type II alveolocytes
- 3) Alveolar macrophage.

The alveolar macrophage has an outgrowth shape. In their cytoplasm, lysosomes are well developed and there are lipid inclusions – lipid droplets. When lipids are oxidized in macrophages, heat is released, which warms the inhaled air. Alveolar macrophages are derived from monocytes (their developmental source) and are part of the macrophage system. They can migrate from the alveoli into the interstitial tissue. Function of alveolar macrophages:

- 1) protective – phagocytize microbes, dust particles
- 2) warm the air by releasing heat energy
- 3) synthesize lysozyme, interferon, pyrogen.

Type II alveolocytes

These are large secretory cells. They are cubic in shape and have short microvilli. Type II alveolocytes make up only 5% of the total number of cells lining the inner surface of the alveolar wall. These cells are also called secretory cells because of their ability

to synthesize surfactant. The cytoplasm has a well-developed endoplasmic reticulum, ribosomes, and contains lamellar osmiophilic cells (surfactant inclusions), which are markers of type II alveolocytes. Function of Type II alveolocytes: secrete surfactant alveolar complex. Type II alveolocytes are both secreting and proliferating cells. They can divide by mitosis and differentiate into Type I alveolocytes.

Alveolar surfactant complex

The surfactant layer covers the inner surface of the alveolar wall and consists of 2 phases: 1) surface membrane (apophase), 2) fluid (hypophase).

1. The membrane component consists of phospholipids and proteins, similar in structure to cell membranes.

2. Deeper is the hypophase – a liquid component consisting of glycoproteins, lipoproteins.

The thickness of the surfactant layer is 20-30 nm. Normally, surfactant synthesis begins during embryogenesis. If surfactant is absent from the lungs at birth (congenital distress syndrome), the child cannot take its first breath independently because the alveoli are stuck together due to the lack of surfactant.

Functions of the surfactant-alveolar complex:

1. Prevents the walls of the alveoli from sticking together during exhalation. If the alveoli were to stick together, inhalation would be impossible and death would occur within 5 minutes. Surfactant maintains the surface tension of the alveoli, preventing them from collapsing during exhalation.

2. Prevents transudation (entry) of fluid from interstitial tissue, capillaries in the lumen of the alveoli.

3. Prevents penetration of microbes from the inhaled air through the alveolar wall into the surrounding connective (interstitial) tissue, blood capillaries.

4. Protective, bactericidal function.

Type I alveolocytes.

These are respiratory squamous epithelial cells. Type I alveolocytes have a flattened elongated shape and lie on the basal membrane.

Respiratory pneumocytes have short processes (microforaminae) on the apical surface. Type I alveolocytes are divided into 2 parts: 1) nucleated part – thicker, 5 μm thick, 2) non-nucleated part – thin, 0.2 μm thick.

Organelles are located near the nucleus. In the nucleus-free part there are many pinocytotic vesicles. Type I alveolocytes lie on a thin (0.1 μm thick) basal membrane. With their nucleus-free part, they adhere to the basal (nucleus-free) areas (0.2 μm thick) of the endothelial cells of blood capillaries. In these areas, the basal membranes of type I alveolocytes and endothelium may fuse. The partition between the air of the alveoli and the lumen of the capillary is called the aerogematic barrier (air-blood barrier), where gas exchange takes place. Due to the difference in partial pressures of oxygen and carbon dioxide in the alveolar air and in the blood, gas exchange between air and blood occurs by diffusion.

Aerogematic barrier.

The composition of the aerogematic barrier includes

- 1) surfactant membrane phase
- 2) surfactant hypophase
- 3) nucleus-free part of type I alveolocytes (thickness 0.2 microns)
- 4) basal membrane – common to type I alveolocytes and endothelium, thickness 0.1 μm
- 5) nuclear-free part (cytoplasmic protrusion) of the endothelium of blood capillaries, thickness 0.2 μm .
- 6) erythrocyte wall.

The aerochemical barrier appears to be extremely thin (about 0.5 μm). This favors gas exchange. Type I alveolocytes constitute 95% of the total number of cells lining the inner surface of the alveolar wall. Respiratory pneumocytes (type I alveolocytes) are highly specialized cells that have lost the ability to divide by mitosis. The developmental source of Type I alveolocytes are Type II alveolocytes. Type I alveolocyte function: Respiratory function – gas exchange between the air of the alveoli and the hemoglobin of the red blood cells.

Functions of the Respiratory System:

- 1) respiratory Function
- 2) non-respiratory functions.

1. The respiratory function includes the gas exchange function. Gas exchange is performed by the pulmonary alveoli between the hemoglobin of the red blood cells and the air of the alveoli, i.e., the absorption of oxygen from the inhaled air and its delivery to the blood, and the removal of carbon dioxide from the body.

2. Non-respiratory functions include

- 1) humidifying the inhaled air,
- 2) purification of inhaled air from bacteria and dust
- 3) thermoregulation
- 4) voice formation
- 5) olfactory function
- 6) immune defense
- 7) involvement in water-salt and lipid metabolism
- 8) blood coagulation
- 9) hormonal function
- 10) air conduction
- 11) synthesis of lysozyme, interferon and pyrogen by lung macrophages
- 12) blood deposition in vessels
- 13) participation in the elimination of volatile substances from the body (acetone, ammonia, alcohol vapors)
- 14) destruction of small blood clots in pulmonary vessels
- 15) inactivation of serotonin.

SKIN AND IT'S DERIVATIVES

The skin is an organ of the body's covering system. Of the derivatives (appendages) of the skin, humans have sweat glands, sebaceous glands, hair, nails. The skin is composed of 2 components:

- 1) epidermis 2) dermis. Under the dermis is the hypodermis – subcutaneous fatty tissue. Sources of skin development:
 - 1) Skin ectoderm. From it develops the epidermis of the skin and skin appendages.
 - 2) Dermatome – somite of dorsal mesoderm. It gives rise to the dermis of the skin itself.
 - 3) Neural crest. It gives rise to melanocytes and Merkel cells of the epidermis.
 - 4) Monocytes are the source for the development of intraepidermal macrophages (Langerhans cells).

Epidermis

The epidermis is represented by stratified squamous keratinizing epithelium (SSKE). Based on the different structure and thickness of the epidermis, the skin is divided into «thick» and «thin» skin. «Thick skin covers the palms and soles of the feet. «Thin skin covers the rest of the body. The epidermis of thick skin has 5 layers of cells:

- 1) basal layer
- 2) spinosa layer
- 3) granular layer
- 4) lucidum layer
- 5) stratum corneum – very thick, keratinized cells in 15-20 layers.

In the epidermis of «thin» skin there is no corneum layer. In addition, the stratum corneum is thin and contains only 3-4 rows of keratinized cells. The basal layer of the epidermis contains 4 types of cells:

- 1) keratinocytes

- 2) melanocytes
- 3) merkel cells
- 4) Langerhans cells.

1. Keratinocytes have a prismatic shape and lie on the basal membrane. They are connected to each other by desmosomes and to the basement membrane by semi-desmosomes. The cytoplasm is basophilic. It contains organoids of general significance and tonofibrils (organoid of special significance). Keratinocytes proliferate by mitosis. Therefore, the basal layer is also called the growth layer. Basal keratinocytes migrate to the stratum spinosum as they differentiate. Functions of keratinocytes: regenerative, keratin synthesis.

Melanocytes

These are pigment cells of a neuroglial nature. Melanocytes are multibranched, have no desmosomes and are free. Their cytoplasm is poorly developed organelles, containing large quantities of melanin granules. The main characteristic is the presence of melanosomes containing the pigment melanin. Melanocytes synthesize melanin pigment with the help of DOPA oxidase. Melanin pigment has the ability to trap ultraviolet rays. UV rays stimulate melanin synthesis in melanocytes and vitamin D synthesis in keratinocytes. There is one melanocyte for every 10 keratinocytes. When the intensity of solar radiation is high, there is a compensatory increase in melanin synthesis in the melanocytes of the epidermis, which is externally perceived as a tan. This protective pigmentation of the skin develops under the action of ultraviolet rays. Melanin can be transferred to keratinocytes by outgrowth. People of different races (different skin colors) have different numbers of melanosomes in their cells, while the number of melanocytes in the epidermis is the same for everyone. Dark-skinned people have many large melanosomes with high melanin content in their melanocytes. Melanin protects the underlying tissue by absorbing UV rays. Under pathological conditions, malignant tumors – melanomas – are formed from melanocytes. Function of melanocytes: protection of skin tissue from UV rays.

Merkel cells

These are tactile epitheliocytes. They are of neuroglial origin. Their shape is rounded. Merkel cells are located in the basal layer of the epidermis (especially in the fingertips). Merkel cells form desmosomal contacts with adjacent keratinocytes. Merkel cells themselves are approached by the endings of the dendrites of sensitive neurons. Merkel cells are a type of mechanoreceptor. They are capable of perceiving very light touch, i.e. they are responsible for tactile sensitivity or touch. The function is receptor based.

Langerhans cells

These are large intraepidermal macrophages. They have a dendritically shape and are located in the stratum basale of the epidermis. In the epidermis, the processes reach the granular layer. The source of their development are monocytes. Langerhans cells are able to migrate from the epidermis to the dermis. They do not form desmosomal contacts with neighboring cells. The cytoplasm has many lysosomes and contains Birbeck granules, which have the appearance of a «tennis racket». Functions: 1) phagocytosis of antigenic particles trapped in the epidermis, 2) stimulation of proliferation and differentiation of keratinocytes.

The stratum spinosum is composed of polygonal keratinocytes. The cells have numerous short processes («spines»). The keratinocytes are interconnected by desmosomes. This gives the cells a spiky shape. In the cytoplasm of keratinocytes the number of keratin tonofibrils increases, keratinosomes appear – dense granules surrounded by a membrane. They begin to synthesize lipids, which later take part in the binding of cells to each other. Langerhans cells are located between the keratinocytes. The stratum spinosum and stratum basale are the growth zone, due to which the epidermis is constantly renewed (every 3-4 weeks) (physiological regeneration). With further differentiation, the cells of the spinous layer migrate to the next granular layer.

The granular layer consists of oval keratinocytes. In the cytoplasm of keratinocytes, organelles begin to disintegrate and large granules containing the protein keratohyalin are formed. Keratohyalin granules

fill the cytoplasm of keratinocytes, giving them a granular appearance. The nuclei become pyknotic. Keratin tonofibrils are packed into keratohyalin granules. The formation of keratohyalin granules is the 1st stage of keratinization. The formation of keratinosomes continues in the keratinocytes of the granular layer. The synthesis of specific lipids continues in the keratinosomes. The number of desmosomes between the granular layer cells decreases. With further differentiation, the cells of the granular layer migrate to the next shiny layer.

The lucidum layer is formed by flat keratinocytes in which nuclei and organelles are completely destroyed, and keratohyalin granules coalesce into a light-refracting mass. Cell borders become indistinguishable and the entire layer is perceived as a shiny band. The keratohyalin granules coalesce into a continuous mass called eleidin. Eleidin formation is the 2nd stage of keratinization. Eleidin refracts light well. There are no desmosomes between the cells, they are connected by a cementing substance. With further differentiation (cornification, keratinization), the cells of the stratum corneum flatten and move to the next stratum corneum. In the epidermis of «thin» skin, the stratum corneum is absent.

The corneum layer consists of horny scales. They have the shape of flat polyhedrons (14-cornered scales) covered with cytolemma. In the center of the scale there is an air bubble. The entire interior of the scale is filled with keratin fibrils. The keratinized structures of cornified scales are soft keratin. The formation of soft keratin is the 3rd stage of keratinization. This keratin is called soft keratin because it retains the ability to dissolve in acids and alkalis, unlike the hard keratin of nails and hair. Horn scales look like light-colored cells that do not contain any organelles inside and are completely filled with horny substance – soft keratin. The connection between horny scales weakens and their sloughing (desquamation) from the surface of the epidermis occurs. The process of keratinization lasts 3-4 weeks and includes the following processes

- 1) The content of keratinous tonofibrils in the cells gradually increases until they completely fill the cell volume,
- 2) From the middle of the process, all organelles, including the nucleus, are gradually reduced and disappear,

3) Lipids are synthesized in special organelles – keratinosomes, which bind keratinocytes together in the shiny and corneum layers,

4) Keratolinin protein is synthesized and accumulates under the plasmalemma, forming a thick shell of horny scales,

5) Cell shape changes – rounded cells become flat horny scales resembling 14-sided prisms.

The dermis, or actual skin, consists of 2 layers: 1) papillary, 2) reticular.

1. The papillary layer consists of loose fibrous unformed connective tissue containing many blood vessels. Smooth muscle cells are also found here. Smooth muscle cells in the dermis form not only muscles that lift the hair, but also bundles that are not associated with hair. The contraction of these and other bundles in the cold leads to the appearance of «gooseflesh». This is accompanied by compression of the lumen of nearby small blood vessels, resulting in reduced heat loss. There are pigment cells – chromatophores, they accumulate pigment. The cells are dendritically shape. The papillary layer is located directly under the epidermis. This layer gets its name from the numerous papillae that extend into the epithelium. The largest number of papillae is found in the skin of the palms. The connective tissue of the papillary layer is separated from the epidermis by the basal membrane. The papillary layer of the dermis determines a strictly individual character of the arrangement of furrows and lines on the surface of the palms. And this is the basis of dactyloscopy – a method of determining the identity of a person on the basis of fingerprints, as well as the connection of the pattern with human genetic diseases – Down’s disease. The function of the papillary layer is trophic, it supplies the epidermis with nutrients.

2. The papillary layer of the dermis is formed by dense fibrous irregular connective tissue (DFICT). Bundles of collagen fibers run in 2 directions – some parallel to the skin surface, others oblique. Elastic fibers repeat the course of collagen fibers. Together they form a network. The function of the papillary layer is to provide mechanical strength to the skin.

The hypodermis or subcutaneous adipose tissue is represented by white adipose tissue. The subcutaneous tissue represents the body’s fat

depot and also provides its thermoregulation. Hypodermis reduces the effect of various mechanical factors on the skin. Hypodermis on thick skin is preserved even with an extreme degree of exhaustion of the body. Functions of the hypodermis:

- 1) Storage of fatty tissue
- 2) Cushioning the skin from mechanical damage
- 3) Participation in thermoregulation.

Sweat glands

They are simple unbranched tubular glands with merocrine or apocrine type of secretion. It consists of: 1) the terminal secretory section, a long tube twisted into a tangle, 2) the excretory duct, straight or slightly convoluted.

The source of development is the ectoderm, as an embedding of the epidermis in the underlying connective tissue. Sweat glands begin to function after birth.

I. The terminal secretory sections are located at the boundary between the reticular layer of the dermis and the hypodermis. These sections contain 2 types of cells: 1) secretory cells, 2) myoepithelial cells.

1. The secretory cells are prismatic before secretion and cubic after secretion. Sweat gland secretion: sweat contains 98% water, 2% - organic and inorganic substances. 500 ml of sweat is secreted daily.

2. Myoepithelial cells are dendritically shaped. They are located between the basal membrane and the basal end of the secretory cells. Their processes contain contractile myofibrils that contract to release secretion from the secretory cells.

II. The duct of the sweat gland, which passes through the dermis, is lined with two layers of cuboidal epithelium. When passing through the epidermis, it acquires a twisted (corkscrew) course and is lined with stratified squamous non-keratinized epithelium (SSNE) and opens with a sweat pore on the surface of the epidermis. According to the type of secretion, sweat glands are divided into 2 types:

- 1) Merocrine – in most of the skin (especially the skin of the palms and soles)
- 2) Apocrine – in the skin of the armpits and anogenital area.

Apocrine sweat glands differ from merocrine glands by the following features: 1) They secrete secretion of apocrine type. Secretion of secretion is accompanied by destruction of apical sections of secretory cells, while in merocrine glands secretion of secretion occurs diffusely, without destruction of cytolemma. 2) The secretion of apocrine glands (sweat) contains more organic substances than in merocrine glands. The decomposition of these substances produces a characteristic pungent odor on the surface of the skin. 3) The excretory ducts of the apocrine glands open together with the ducts of the sebaceous glands into the hair follicle. 4) They are located in specific areas (axillae, anus, inguinal folds). 5) Functionally related to the sexual system (increased sweating during menstruation, pregnancy). 6) Eventually develop during puberty. 7) One type of apocrine glands are ceruminous glands located in the external auditory canal that secrete earwax. 8) Apocrine glands are distinguished from merocrine glands by their slightly larger size.

Functions of sweat glands:

- 1) Involved in thermoregulation – as sweat evaporates, the skin's surface cools.
- 2) Water and salt metabolism
- 3) Excretion with sweat of products of nitrogen metabolism (urea, uric acid, ammonia). In conditions of renal failure can compensate for impaired excretory function of the kidneys.

Sebaceous gland

These are simple branched alveolar holocrine glands. They consist of: 1) terminal divisions and 2) excretory ducts.

I. The terminal divisions lie at the junction of the reticular and papillary layers of the dermis. Secretory end sections of sebaceous glands contain secretory cells – sebocytes of 3 types:

- 1) Cambial, undifferentiated,
 - 2) Differentiated,
 - 3) Necrotic cells.
1. Cambial cells are located on the basal membrane. They are capable of mitosis.
 2. Some cells are displaced from the basal membrane and become

differentiating cells. Lipids are synthesized on the smooth endoplasmic reticulum of these cells, and fatty inclusions accumulate in the cytoplasm.

3. The sebocytes move to the center of the terminal compartment. Here sebocytes die by the mechanism of apoptosis. Sebocytes undergo steatosis. They are completely destroyed by secretion. They are necrotic, disintegrating cells. According to the type of secretion, sebaceous glands are holocrine. Sebocytes are completely destroyed under the influence of their own lysosomal enzymes and turn into a secretion – sebum. Sebum is a mixture of degenerated and destroyed sebocytes.

II. The duct of the sebaceous gland is very short and lined with stratified squamous non-keratinized epithelium (SSNE). The duct opens into the hair follicle. One hair is associated with 1-3 glands. Most sebaceous glands are associated with the hair. There are no sebaceous glands in the «thick» skin of the palms and soles. Sebaceous glands are most abundant on the scalp. Sebocyte differentiation is stimulated by the sex hormones testosterone and progesterone. The sebaceous glands finally develop at the onset of puberty. An excess of sex hormones, when the division and maturation of sebocytes occurs at an increased rate, can block the sebaceous gland ducts. The sebum accumulated in the sebaceous gland becomes a breeding ground for microorganisms, resulting in an inflammatory process that manifests itself as blackheads (acne). The secretion of sebum on the surface of the skin increases when the muscle that lifts the hair is contracted, i.e. when the body cools down.

The function of sebaceous glands:

1) Sebaceous gland secretion (sebum) serves as a greasy lubricant for the epidermis and hair. In a day, the human sebaceous glands secrete 20 grams of sebum. Sebum softens the skin, makes it impervious to water, and facilitates friction between touching surfaces.

2) Sebum has an antimicrobial (bactericidal) effect, preventing the development of microbes on the surface of the skin, as sebum has an acidic reaction. The breakdown of fat produces fatty acids that can kill microorganisms.

3) Limits heat loss.

Hair

These are keratinized epithelial appendages of the skin. Hair is distributed over the entire surface of «thin» skin. On «thick» skin, hair is absent (palms, soles). Hair length ranges from a few millimeters to 1.5–2.0 meters. The rate of hair growth is 0.3 to 0.4 mm/day. Androgens accelerate the growth of facial hair (moustache, beard). Cutting and shaving do not affect the rate of hair growth or the amount of hair. The lifespan of a hair ranges from a few months to 2–6 years. A new hair usually grows to replace the hair that has fallen out. Hair development begins in the 3rd month of embryogenesis. The epidermis, in the form of strands, grows into the underlying connective tissue. The ends of the epithelial strands elongate. They become hair follicles. Connective tissue grows into the hair follicle and a hair papilla is formed. The hair bulb is nourished by the blood capillaries of the hair papilla. Hair growth begins with the proliferation (mitotic division) of hair follicle cells. After birth, new hair follicles are not formed and hair growth occurs at the expense of previously formed follicles. There are 3 types of hair: 1) long hair – the hair of the head, beard, moustache, armpits, pubic hair 2) bristly hair – the hair of the eyebrows, eyelashes, external auditory canal, nasal vestibule 3) downy hair – the hair of the rest of the skin.

Hair structure

Hair is divided into 2 parts: 1) the shaft, 2) the root. The shaft is above the surface of the skin (visible part). The root of the hair is hidden in the skin (invisible part). The root of the hair ends in an extension called the hair follicle. The hair papilla, a loose fibrous irregular connective tissue with blood capillaries, extends into the hair follicle from underneath. The hair papilla nourishes the hair follicle. The hair follicle is the growing part of the hair. It consists of: 1) reproductive keratinocytes, 2) melanocytes. Melanocytes synthesize the pigment melanin, which determines the color of the hair. The hair root is located in the epithelial hair sac (hair follicle), which is surrounded by the hair bulb.

Hair complex

This complex includes

- 1 – the hair itself
- 2 – hair follicle
- 3 – capillary bulb – connective tissue pouch around the hair follicle
- 4 – sebaceous glands and muscles that lift the hair.

The hair itself

There are 3 parts to the hair:

- 1 – Hair follicle – the expanded base of the hair
- 2 – Hair root – up to the exit of the hair in the hair pit
- 3 – Hair shaft – the free (visible) part of the hair.

1. The hair follicle consists of keratinocytes: basal and spiny. The basal and spiny keratinocytes of the hair follicle actively divide by mitosis (every 1-3 days), so they are called the hair matrix. Melanocytes, Langerhans cells and Merkel cells are also found in the bulb.

2. Structure of the hair root. The hair root consists of 3 parts: 1) medulla, 2) cortex, and 3) hair cuticle.

1. The medulla is the innermost (central) layer of the hair. It is found in long and bristly root hairs. There is no medulla in the root of downy hair. Medulla at the root level consists of progressively keratinizing keratinocytes. The cells have a polygonal or flattened shape, a flattened nucleus, and are arranged in «coin columns». The medullary keratinocytes contain: 1) melanin pigment from the melanocytes of the hair follicle, 2) soft keratin, and 3) air bubbles. The cells of the medullary substance are formed by mitotic division (proliferation) of hair bulb cells. Above the sebaceous duct, the cells lose their nucleus and transform into polygonal keratinized scales containing pigment, air bubbles, and soft keratin.

2. The cortex is formed by the proliferation of hair follicle cells. The cortical cells near the follicle are prismatic and perpendicular to the longitudinal axis of the hair. Gradually, the cells lose their nucleus and turn into keratinized scales containing melanin pigment, hard keratin and air bubbles. The cortical substance of the hair consists of

flat keratin scales throughout most of the root and the entire hair shaft. The more developed the cortex, the stronger and more elastic the hair due to the hard keratin content.

3. The cuticle is directly adjacent to the cortex. It is formed by the proliferation of hair follicle cells. Cuticle cells near the hair follicle have a prismatic shape and are perpendicular to the hair surface. As they move away from the hair follicle, the cuticle cells lose their nucleus and become horny scales. The keratin scales take on a slanting (shingle-like) position and contain hard keratin. There is no melanin pigment in the keratin scales of the hair cuticle.

The hair shaft is made up of: 1) cortex, 2) cuticle. The hair shaft has no medulla. The cortex and cuticle of the hair shaft consist of very flat horny scales containing hard keratin. At the point where the hair root joins the hair shaft, the epidermis of the skin forms a small depression called the hair follicle. Here the hair, leaving the follicle, appears above the surface of the skin. The exit duct of the sebaceous gland opens in the hair follicle.

The hair follicle consists of 2 parts:

- 1) The outer epithelial root sheath,
- 2) The inner epithelial root sheath.

The inner epithelial sheath surrounds the hair root and disappears at the level of the sebaceous duct. The inner epithelial root sheath is also a derivative of the hair bulb. In the lower parts of the inner root sheath, 3 layers are distinguished: 1) cuticle, 2) granulose epithelial layer of Hexley – middle layer, 3) pale epithelial layer of Henle – outer layer. In the middle and upper parts of the inner root sheath, all three layers merge and consist only of fully keratinized cells containing soft keratin.

1. The cuticle of the inner epithelial root sheath consists of a single layer of keratinized cells. These cells adhere closely to the cuticle and contain soft keratin.

2. The granular layer of Hexley consists of 1–2 rows of squamous cells containing keratohyalin granules.

3. The pale layer of Henle consists of a single row of squamous cells containing soft keratin.

The external epithelial root sheath consists of the basal and spiny layers of the epidermis, i.e. it is an extension of the epidermal growth layer of the skin deep into the dermis. The outer root sheath continues to the hair follicle. May participate in the regeneration of the epidermis.

The dermal root sheath is the connective tissue sheath of the hair. It consists of 3 layers: 1) basal membrane, 2) inner circular layer of collagen fibers consisting of circularly arranged collagen fibers, 3) outer longitudinal layer formed by longitudinal collagen fibers. The hair follicle on the surface of the skin forms an extension – a funnel into which the ducts of the sebaceous glands enter.

The arrector pili muscle is composed of smooth muscle cells and has an oblique orientation. One end of the muscle is woven into the hair follicle and the other end is woven into the papillary layer of the dermis. When the muscle contracts, the hair takes a perpendicular direction to the surface of the skin (the hair «stands up»). Also, when the muscle contracts, it compresses the skin and blood vessels, resulting in the formation of bumps on the surface of the skin («goose skin»). This reduces the body's transfer of heat through the skin to the environment. The muscle that lifts the hair is absent in downy hair, bristly hair, beard hair, mustache, armpits, and pubic hair.

During a person's lifetime, hair undergoes a periodic change – old hair stops growing and falls out, and new hair grows in its place. The life span of a hair is from a few months to 2–4 years. The processes of hair change are

- 1) The hair papilla of the hair is reduced (atrophied).
- 2) Hair follicle cells do not divide by mitosis.
- 3) The hair bulb becomes keratinized and turns into a hair bulb.
- 4) The hair bulb separates from the hair papilla.
- 5) The inner epithelial root sheath is destroyed, while the outer epithelial root sheath is preserved.
- 6) Growth of old hair stops.
- 7) The hair falls out.

The growth of a new hair begins with the formation of a hair papilla, which gives rise to a new hair follicle. The new hair grows from this follicle through cell proliferation. As the new hair grows,

it displaces the old hair, i.e. the growing hair pushes out the hair bulb along with the old hair. There are many reasons for premature hair loss: genetic predisposition, the influence of the male hormone testosterone, which makes men much more susceptible to baldness, especially in the frontal-parietal area.

Graying of the hair

The most common cause is constant nervous overload – stress. Released adrenaline constricts blood vessels, including those that feed the hair follicle. The production of melanin in melanocytes decreases. If the nutritional disorder is severe (acute stress), the hair follicle atrophies and dies, hair falls out.

The nail

The nail is a plate of hard keratin that lies on the nail bed. The nail is a derivative of the epidermis of the skin. The nail plate is divided into the root, body and edge. The free end of the nail plate that protrudes from the nail bed is called the edge (protrusion) of the nail. The nail plate is made of tightly adhering horny scales containing hard keratin. The nail bed consists of: 1) epithelium and 2) connective tissue.

1. The epithelium of the nail bed is represented by the growth layer of the epidermis – the basal layer and the stratum spinosum. The underlying nail plate is the corneum layer of the epidermis. The part of the nail bed epithelium that supports the nail root is called the nail matrix. The nail matrix is where cell proliferation takes place. It is the site of nail growth. The granular and shiny layers are absent in the area of the nail matrix. This is characteristic of the process of hard keratin formation. The growth layer passes into the stratum corneum.

2. The connective tissue of the nail bed is represented by a dense fibrous irregular tissue (DFICT) in which blood vessels pass. The base of the connective tissue contains collagen fibers arranged longitudinally and perpendicularly.

Skin Functions

- 1) Protective, barrier
- 2) Involved in water and salt metabolism – 500 ml of sweat is excreted through the skin daily.
- 3) Involved in heat metabolism
- 4) Vitamin D is synthesized under the influence of ultraviolet rays.
- 5) Up to 1 liter of blood is deposited in the skin vessels
- 6) Skin is a receptor field, it contains tactile, temperature, pain nerve endings.
- 7) Healthy skin is impermeable to microorganisms, toxic substances.
- 8) Chlorides, lactic acid and nitrogen metabolites are excreted through the skin with sweat.
- 9) Skin is a carrier of secondary sexual characteristics.

URINARY SYSTEM

The urinary system includes: 1) urine-producing organs – kidneys, 2) urinary tracts – ureters, bladder, urethra.

Development.

During embryogenesis, 3 kidneys are laid down: 1) the premammary or head kidney, 2) the primary kidney or Wolff's body, 3) the secondary kidney, the permanent, final or pelvic kidney.

Sources of development: 1) mesoderm – nephropogonotome, 2) mesenchyme.

The prekidney

In the human embryo, the nephropogonotome consists of 3 divisions: 1) cranial (front, head) – 8-10 segmental pedicles, 2) trunk – 25-30 segmental pedicles, 3) caudal – metanephrogenic tissue, non-segmented part. In the nephropogonotome, the cranial and truncal parts are segmented (40 segments), and the caudal part is unsegmented. In the 3rd week of embryogenesis, the pronephros is formed from 8-10 pairs of anterior (head) segmental legs. The segmental legs are tied (separated) from the mesodermal somite and turn into straight tubes – protonephridia. One blindly closed end they open as a whole, and the second end connects with each other, forming the mesonephral (Wolff's) duct. Blood plasma is filtered from the capillary tubule as a whole. This filtrate (primary urine) flows into the protonephridia and from there into the mesonephral (Wolff) duct. The precuneus exists for only 40 hours and does not function. Soon (after 40 hours), the nonfunctional precuneus is reduced. Only the mesonephric duct remains, growing caudally.

Primary kidney (mesonephros)

This kidney develops at the end of the 3rd week from 20-25 pairs of trunk segmental pedicles. The segmental pedicles separate (detach) from the mesodermal somites and splanchnotome and become the tubules of the primary kidney – metanephridia (convoluted tubules). One end of the tubules (metanephridia) is connected with the mesonephric duct, and the second (blind) end is in contact with the capillary bed, forming around it a double-layered capsule – the renal capsule. Blood plasma is filtered from the capillary beds into the renal tubular capsule. The filtrate (primary urine) flows into the metanephridia and the mesonephric duct. In the 2nd month of embryogenesis, the primary kidney reaches its maximum development and functions until the 4th month of embryogenesis. The urinary process in the primary kidney is slow due to low fetal arterial pressure. From the 3rd to the 5th month, the primary kidney gradually degenerates. The final kidney is implanted in the fetus in the 2nd month of embryogenesis, but its development ends only after birth. The secondary kidney begins to function in the second half (4th month) of embryogenesis.

There are 3 sources for the development of the terminal kidney: 1) the mesonephric duct, 2) metanephrogenic (unsegmented) tissue, and 3) mesenchyme. The mesonephric duct forms an outgrowth from which the ureter, lobules, calyces, and collecting ducts are formed. From the metanephrogenic tissue, the urinary tubules of the kidney – nephrons differentiate. At one end of them are formed capsules, which cover the vascular tubules. At the other end they are connected with collecting tubules. The stroma of the final kidneys develops from mesenchyme. The final formation of the kidney is completed by puberty.

Structure of the kidney

The kidney is covered by a capsule and a serous membrane. The capsule is represented by dense fibrous irregular connective tissue (DFICT). The renal stroma is composed of loose fibrous irregular connective tissue (LFICT).

Kidney parenchyma: 1) cortical substance (darker, located below the capsule), 2) cerebral substance (lighter, located below the cortical substance). The cerebral substance is divided into 8-12 pyramids and penetrates into the cortical substance, forming Ferrein's cerebral rays, consisting of collecting tubes. In turn, the cortical substance penetrates between the bases of pyramids in the form of renal columns – Bertini columns.

The structural and functional unit of the kidney is the nephron. There are about 1 million of them in each kidney. In the nephron we distinguish: 1) tubular capsule – Bowman-Schumlersky capsule, 2) proximal convoluted tubule, 3) loop of Henle – descending and ascending part, 4) distal convoluted tubule.

The distal convoluted tubule drains into the collecting duct. The collecting ducts are part of the medullary rays of Ferrein. The renal medulla includes the convoluted tubule and the surrounding capsule.

Types of nephrons: 1) cortical nephrons – 80%, 2) perimembranous (juxtamedullary) – 20%. Cortical nephrons (80% of them) are located almost entirely in the cortical substance, and only the knees of loops of Henle are located in the cerebral substance. Pericerebral nephrons (20%) are located in the kidney so that their renal tubules, proximal and distal parts are in the cortex on the border with the brain matter, and loops of Henle are in the brain matter. The cortex and medulla are formed by different sections of nephrons.

Blood supply to the kidney.

In the kidney, a conventional distinction is made between: 1) the cortical blood supply, which serves the cortical nephrons, and 2) the juxtamedullary blood supply, which is associated with the pericardial nephrons.

The cortical blood supply system consists of:

- 1) the renal artery,
- 2) the interlobular artery
- 3) the arch artery, which lies at the boundary between the cortex and the medulla,
- 4) the interlobular artery,

- 5) the innominate arteriole is wide,
- 6) primary capillary network (50-100 capillaries of the fenestrated type), forming the vascular tubercle of the renal tubule of the nephron, the pressure in the capillaries is high – 70–90 mm of mercury column,
- 7) the outflow arteriole is narrow, 2 times smaller in diameter than the inflow arteriole,
- 8) secondary capillary network – low pressure – 10–12 mmHg,
- 9) stellate vein,
- 10) interlobular vein,
- 11) arched vein,
- 12) interlobular vein,
- 13) renal vein.

Together, these vessels form the cortical circulation of the kidney. Cortical nephrons are actively involved in urine formation due to the characteristics of the cortical circulation.

Characteristics of cortical circulation: 1) high blood pressure (70–90 mmHg) in the capillaries of the primary (miraculous) network – vascular tubules, 2) low blood pressure (10–12 mmHg) in the capillaries of the secondary (peritubular) network.

The juxtamedullary blood supply system is

- 1) the renal artery,
- 2) the interlobular artery
- 3) the arch artery,
- 4) the interlobular artery,
- 5) the supplying arteriole,
- 6) primary capillary (wonderful network, blood pressure 40 mmHg,
- 7) the supplying arteriole is equal to or larger in diameter than the receiving arteriole,
- 8) straight artery, no secondary capillary network
- 9) straight vein,
- 10) curved vein,
- 11) interlobular vein,
- 12) renal vein.

Characteristics of juxtamedullary circulation:

1) The feeding arteriole and the feeding arteriole are the same size or the feeding arteriole is larger and the feeding arteriole is smaller.

2) Blood pressure in capillaries of vascular tubules – primary (miraculous) network is lower – 40 mmHg, than in vascular tubules of cortical nephrons.

3) Carrying arterioles do not divide into secondary capillary network, but arteriolovenular anastomoses are formed.

4) No secondary capillary network.

5) No interlobular veins.

The juxtamedullary nephrons do not normally participate in urine production. The juxtamedullary vasculature is shorter than the cortical vasculature and is a kind of shunt (pathway) through which blood can be drained, bypassing the cortical substance. This pathway is important because when blood pressure rises (during heavy physical work, physical exertion), blood flow to the kidneys increases sharply. The juxtamedullary circulatory system acts as a shunt, i.e. it is the shortest and easiest way to transfer blood from arteries to veins through the kidneys in conditions of their strong blood filling.

The main stages (processes) of urine formation in the kidneys

Urine formation is a complex biological process that takes place in nephrons, i.e. it is the result of active activity of nephron cells. There are three stages of urine formation:

Phase 1 – filtration,

Phase 2 – reabsorption,

Phase 3 – acidification of urine, secretion.

The first phase of urine formation – filtration, occurs in the renal (malpighian) corpuscles, which are a set of capillaries and capsules Bowman – Shumlansky. In them, filtration of blood plasma from capillaries into the lumen of the capsule occurs – the formation of primary urine (100–180 liters per day).

The second phase of urine formation – reabsorption of water and dissolved substances (sugar, protein, salts), is carried out in the tubules of nephrons and collecting ducts – formation of secondary

urine (1.5–2 liters per day).

The third (final) phase of urine formation – acidification of urine or secretory phase is carried out in the collecting ducts, where the reaction of urine becomes slightly acidic.

Histophysiology of the nephron

The nephron begins with the medulla. The medulla is composed of: 1) the convoluted tubule and 2) the Bowman-Schummlansky capsule.

The Bowman-Schummlansky capsule has the shape of a double-walled bowl and consists of 2 layers: 1) outer and 2) inner. Between the outer and inner sheets there is a slit-shaped (30-50 nm) cavity – the capsule cavity, which merges into the lumen of the proximal convoluted tubule of the nephron.

The outer leaflet of the capsule is lined with a single layer of squamous and cuboidal epithelial cells located on the basal membrane. The epithelium of the outer capsule leaflet merges with the epithelium of the proximal nephron.

The inner layer of the capsule forms deep folds, penetrates between the capillaries of the vascular bed and covers them from almost all sides. The inner layer of Bowman-Shumlansky capsule is represented by irregularly shaped epithelial cells – podocytes.

Large projections – cytotrabeculae, from which small projections – cytopodia, attached to the basal membrane, emerge from the bodies of podocytes. The vascular tubercle – the tubercle of the primary capillary network is represented by 50-100 capillaries of the fenestrated type. The endothelium of the capillaries of the vascular tubercle consists of flat endotheliocytes with numerous fenestrations in the cytoplasm of the size of 0.1 μm . 1) The renal medulla contains the filtration barrier, where the first phase of urine formation, filtration, takes place. The filtration barrier consists of 3 components

- 1) Fenestrated capillary endotheliocytes (cytoplasmic projections).
- 2) Three-layered common basement membrane for endothelium and podocytes.
- 3) Podocytes of the inner leaflet of the capsule (cytotrabeculae and cytopodia).

The 300 nm thick basement membrane is common to the endothelium of blood capillaries and the podocytes of the internal capsule. It consists of 3 layers:

- 1) Inner – light, friable
- 2) Middle – dark, dense
- 3) Outer – light, friable.

The middle layer contains thin collagen fibers that form a mesh with a cell diameter of 4-7 nm. Under normal conditions, blood components (erythrocytes, leukocytes, platelets), large and medium molecular weight plasma proteins (fibrinogen, immunoglobulins) do not pass through the filtration barrier. The kidney filter has a selective permeability, retaining everything larger than the size of cells (7 nm) in the middle layer of the basal membrane and passing only substances whose diameter is smaller than 7 nm. The following components of blood plasma normally pass through the filtration barrier: water, glucose, low molecular weight proteins, electrolytes, products of nitrogen metabolism. All these components of blood plasma constitute primary urine. During the day, the kidneys produce 100-180 liters of primary urine (primary filtrate). Of great importance for effective filtration is the large diameter of the inflow and small diameter of the outflow arterioles, which creates high filtration pressure (70-80 mmHg), as well as a large number of capillaries (50-100) inside the tubule. Effective filtration of plasma, which is carried out continuously by the kidneys, contributes to the maximum removal of harmful metabolic products – waste products from the body. In places, where podocytes of the inner leaflet of the capsule cannot penetrate between the capillaries of the vascular tubercle, there is a third type of cells – mesangiocytes.

There are 3 types of mesangiocytes: 1) smooth muscle, 2) macrophagic, 3) transient – monocytes from the blood stream. They have an outgrowth form. Smooth muscle mesangiocytes are capable of contraction and fiber formation. Macrophagic mesangiocytes are capable of phagocytosis and have a protective function.

The reabsorption phase is the second phase of urine formation. It takes place in the renal tubules. Reabsorption begins in the proximal

convoluted tubule of the nephron. The wall of the proximal convoluted tubule of the nephron is formed by a single layer of prismatic (cylindrical) ciliated epithelium. These cells have a turbid cytoplasm, on their apical surface there is a «brush» border (microvilli), on the basal surface – basal striations (folds of cytolemma, between which mitochondria are located perpendicularly). There are 2 types of resorption: 1) obligatory, 2) facultative.

Reabsorption is the reabsorption into the blood (into the capillaries of the secondary network) from primary urine of a number of substances contained in it. The «brush» border of the epithelium of the proximal nephron provides obligatory reabsorption – complete reabsorption of proteins and glucose. The basal striation of the epithelium of the proximal nephron provides facultative reabsorption of a part of water due to the folds of the cytolemma and electrolytes due to mitochondria.

Pale cells are poor in organelles. In the basal part of the cells there are folds of plasmolemma. Passive reabsorption of a part of water from urine into blood is carried out in collecting tubes with the help of light cells. The reabsorption of water in the collecting tubules is influenced by the antidiuretic hormone (ADH) of the hypothalamus. In the presence of this hormone, the walls of the collecting tubes become permeable to water, as ADH (vasopressin) increases the permeability of the wall to water. Under the influence of ADH (vasopressin), water reabsorption in the collecting ducts increases. The dark cells of the collecting ducts are ultrastructurally similar to the parietal cells of the gastric glands. The dark cells secrete hydrochloric acid, which acidifies the final urine.

The third and final stage of urine formation is the acidification of the urine. The dark cells of the collecting ducts acidify the urine. The amount of final, secondary urine decreases to 1.5 – 2 liters per day.

The endocrine apparatus of the kidneys includes 2 apparatuses: 1) juxtaglomerular apparatus (JGA), 2) prostaglandin apparatus. The juxtaglomerular apparatus consists of 3 components:

- 1) The juxtaglomerular cells,
- 2) The dense patch,
- 3) Juxtavascular cells.

1. Juxtaglomerular cells or juxtaglomerular myocytes (myoid endocrinocytes) are baroreceptors, modified smooth muscle cells located in the medial wall of inflow and outflow arterioles under the endothelium.

They have a cubic shape, a light-colored cytoplasm, and large secretory (renin) granules. The secretory granules contain renin. Function of the juxtaglomerular cells: They secrete renin into the blood. The signal for the secretion of renin into the blood is a decrease in blood pressure in the supplying arterioles of the vascular beds. Renin has a vasoconstrictive effect, causes an increase in blood pressure, stimulates the production of aldosterone hormone in the adrenal cortex. Under the influence of aldosterone, the reabsorption of sodium and chlorine in the distal tubules of the nephron increases. Juxtaglomerular cells are the main type of cells that produce renin.

2. The dense patch is located in the section of the wall of the distal tubule of the nephron that lies between the efferent and efferent arterioles, adjacent to the renal medulla. The cells in the dense patch are cylindrical, 15–40 in number, lack basal striation, and the basal membrane is absent. These cells are osmoreceptors. The dense patch epitheliocytes sense changes in urinary sodium concentration and influence the juxtaglomerular cells that regulate renin production. Function of the dense patch: The dense patch is a «sodium receptor» that senses changes in urinary sodium and acts on juxtaglomerular myocytes that secrete renin. When there is a lot of sodium in the urine, the dense patch cells act on juxtaglomerular cells that synthesize renin. Under the influence of renin, aldosterone is secreted by the adrenal cortex. Under the influence of aldosterone, the reabsorption of sodium in the urine is increased. This leads to a decrease in the sodium content of the primary urine and stops the excitation of the cells of the juxtavascular zone.

3. Juxtavascular or Gurmagtig cells are located in the triangular space between the inflow and outflow arterioles and the dense patch. The cells are oval or irregularly shaped and form long processes that contact mesangiocytes of the vascular tubercle. Function of juxtavascular cells: The Gurmagtig cells and mesangial cells are

capable of producing renin when juxtaglomerular cells are depleted. These cells have a phagocytic capacity.

The prostaglandin apparatus consists of 2 components:

Luminal cells of the collecting ducts, which are capable of producing prostaglandins

Interstitial cells of the renal medulla.

Interstitial cells develop from mesenchyme. They are located in the stroma of cerebral pyramids in a horizontal direction. The cells have the form of processes. One of their processes braids the descending part of the loop of Henle, and the other process – a blood capillary. Interstitial cells contain prostaglandin granules.

Interstitial cell function: synthesizes prostaglandins. Prostaglandins have: 1) vasodilatory effect, 2) antihypertensive effect, i.e. reduce blood pressure, 3) reduce sodium reabsorption from the renal tubules, thus increasing the amount of sodium in the urine. Prostaglandin and juxtaglomerular apparatus regulate renal blood flow and affect urine formation.

Functions of the kidneys: 1) urine formation, 2) maintenance of water-salt balance, 3) maintenance of acid-base balance, 4) excretion of waste products from the body, 5) maintenance of homeostasis, 6) endocrine function – regulates blood pressure, regulates erythropoiesis.

Urinary Tract

The urinary tract includes: 1) renal calyx and pelvis, 2) ureters, 3) bladder, 4) urethra.

The ureter consists of 4 layers: 1) mucosa, 2) submucosa, 3) muscle, 4) adventitia.

The mucosa forms 10–12 longitudinal folds and consists of 2 layers: 1) multilayered transitional epithelium, 2) intrinsic lamina of the mucosa. Stratified transitional epithelium is represented by 3 layers: 1) basal – cambial, 2) intermediate, 3) superficial – multinucleate.

The lamina propria of the mucosa is represented by loose fibrous irregular connective tissue (LFICT). The submucosal base is formed by loose fibrous irregular connective tissue (LFICT). The lower part of

the ureter contains complex branched alveolar tubular mucous glands.

The muscular mantle consists of smooth muscle cells. In the upper part it consists of 2 layers: 1) internal – longitudinal, 2) external – circular. In the lower part there are 3 layers: 1) inner – longitudinal, 2) middle – circular, 3) outer – longitudinal. The muscular layer of the ureter at the point of passage through the wall of the bladder contains smooth muscle cells, which are located only in one direction – in the longitudinal direction. When they contract, they open the ureteral orifice regardless of the state of the smooth muscle of the bladder.

The adventitial layer covers the ureter from the outside and is represented by loose fibrous irregular connective tissue (LFICT).

The bladder consists of 4 layers: 1) mucosa, 2) submucosa, 3) muscular, and 4) adventitial or serosa.

1. The mucosa forms folds in an empty bladder. The mucosa consists of 2 layers: 1) stratified transitional epithelium, 2) the intrinsic lamina of the LFICT mucosa. The mucosa has no folds in the triangle between the ureteral inlet and outlet. There are small mucosal glands in the intrinsic lamina. The submucosal base is absent in this triangle.

2. The submucosal base is represented by loose fibrous irregular connective tissue.

3. The muscular membrane consists of 3 layers: 1) inner – longitudinal, 2) middle – circular, 3) outer – longitudinal. The muscular sphincter is formed from the circular layer in the bladder neck. Smooth muscle cells have the shape of a divided spindle.

4. The adventitial layer is represented by loose fibrous irregular connective tissue (LFICT). In the area of the bladder floor there is a serous membrane. The serous membrane is mesothelium based on connective tissue (LFICT). The mesothelium is a simple, single-row, squamous, secreted epithelium.

MALE REPRODUCTIVE SYSTEM

The male reproductive system comprises:

- 1) the testes or testicles,
- 2) ejaculatory tracts (including the seminiferous tubules, rete testis, ejaculatory tubules, epididymal duct, and ejaculatory duct),
- 3) prostate gland,
- 4) penis.

The male sexual system develops in close proximity to the urinary system.

Sources of development:

- 1) yolk sac gonoblasts (extraembryonic endoderm),
- 2) tubules of primary kidney (nephrogonotome),
- 3) gonadal ridge (visceral layer of mesoderm),
- 4) mesenchyme.

The development of the male reproductive system includes 2 phases: 1) an indifferent phase in which the female and male reproductive systems develop in the same way, 2) a differentiated phase.

The indifferent phase

During the third week of embryogenesis gonoblasts (primary germ cells) form in the yolk sac wall (extra-embryonic endoderm). Gonoblasts, which are rounded and large in shape, contain glycogen inclusions in their cytoplasm and are capable of dividing through mitosis. These cells migrate towards the gonadal ridge via two methods: 1) passively, with the blood flow, or 2) actively, with the help of pseudopods.

During the fourth week of embryonic development, there is an appearance of thickenings on the surfaces of primary kidneys. These thickenings are referred to as gonadal ridges, and they stem from the coelomic epithelium, specifically the visceral splanchnotome layer.

At the same time, gonoblasts are introduced into the gonadal ridges due to a secretion of a chemical that causes a positive chemotaxis by cells of the genital cords. Following this, the genital cords are separated from the gonadal ridge. Next, sexual cords composed of coelomic epithelium and gonoblasts extend from the genital ridges towards the primary kidney. The Müllerian duct differentiates from the Wolffian duct.

Differentiated phase

The differentiated phase starts during the 6th week of embryonic development. Male differentiation is primarily influenced by the Y chromosome. The signal encoded in the Y chromosome plays a major role in this process. The signal encoded in the Y chromosome plays a major role in this process. The sex-determining gene on the Y chromosome ensures male development of the embryo. The coelomic cells produce the primary male sex hormone, inhibin, under the influence of this gene. This hormone causes the paramesonephral (Müllerian) duct to atrophy, leaving only the hydatid Morgagni in the upper part and the male uterus in the lower part.

During the 9th week of embryonic development, the mesenchyme between the genital ridges develops into interstitial cells under the influence of the sex-determining gene. Interstitial cells, which originate from mesenchyme, produce the male sex hormone testosterone, which is necessary for male differentiation. By the end of embryonic development, there is intense development of interstitial cells, also known as Leydig cells.

During male mesenchyme development, it grows between the genital ridge and the genital cords, separating the genital cords from the genital ridge that gave them origin. This mesenchyme forms the future capsule of the testis - the tunica albuginea.

In the further course, the genital cords form proximal sections:

1) convoluted seminiferous tubules of the testis: a) gonocytes differentiate into spermatogenic cells (spermatogonia, spermatocytes, spermatids, spermatozoa), b) coelomic epithelium differentiates into supporting cells (Sertoli cells).

2) distal sections: straight tubules of the testis, in which gonocytes are reduced and disappear,

3) rete testis, in which gonocytes atrophy.

The genital cords fuse with the primary kidney tubules. The primary kidney tubules form 12–15 seminiferous tubules. The visceral layer of the splanchnotome forms the serous membrane of the testis. The prostate gland and seminal vesicles develop as outgrowths of the urethral sinus.

The mesonephric (Wolffian) duct forms: 1) the epididymal duct - head, body, tail from the upper and middle thirds, and 2) the vas deferens from the lower third. After 22 weeks, gonocytes transform into spermatogonia, losing their cytoplasmic glycogen. The mesenchyme forms the stroma of the testis, Leydig cells, myocytes, connective tissue septa, and tunica albuginea.

Testis

Structure of the Testis. The testis is covered by a serous membrane called the mesothelium, which is supported by connective tissue. Underneath the mesothelium lies the tunica albuginea, a dense fibrous irregular connective tissue (DFICT). Radial connective tissue partitions (septa) extend from the tunica albuginea into the testis, dividing it into lobules (250 lobules). Each lobule contains 1-4 convoluted seminiferous tubules.

The seminiferous tubules in the testis number between 350-400. The stroma of the testis is a loose fibrous irregular connective tissue (LFICT). The convoluted seminiferous tubules lead into straight tubules, which then form a rete testis. From this rete testis, 12-15 efferent ductules emerge and enter the epididymal duct, which then leads to the vas deferens.

In the stroma of the testis (LFICT), there are interstitial cells such as glundulocytes, endocrine cells, and Leydig cells, which are located between the convoluted seminal tubules and accumulate around the blood capillaries. Leydig cells are large, rounded cells with a weakly oxyphilic cytoplasm, a well-developed smooth endoplasmic reticulum (SER), mitochondria, and glycoprotein inclusions.

Their primary function is to produce the male sex hormone testosterone, which is regulated by the adenohipophysis hormone lutropin.

The convoluted seminiferous tubules

In the convoluted seminiferous tubules of the adult male reproductive system, spermatogenesis takes place. The fully developed convoluted seminiferous tubule is lined with two types of cells resting on the basal membrane:

- 1) supporting cells - Sertoli cells, sustentocytes, lying on the basal membrane,
- 2) cells of the germinal epithelium at different stages of spermatogenesis.

Within the germinal epithelium (developing germ cells), the following can be distinguished:

1. Spermatogonia, located on the basal membrane,
2. First and second order spermatocytes, located in the second layer,
3. Spermatids are located in the third layer,
4. Spermatozoa are found in the fourth layer.

The convoluted seminiferous tubule is lined with an epitheliospermatogenic layer on the inside and covered with its own membrane on the outside.

Types of spermatogenic cells:

1. Spermatogonia - capable of mitotic divisions (2 weeks),
2. Spermatocytes - cells in the state of meiosis (1 month),
3. Spermatids are haploid cells that do not divide further (1 month)
4. Spermatozoa are male gametes (1-3 weeks).

Supporting cells, known as sustentocytes or Sertoli cells, are large pyramid-shaped cells. Their cytoplasm contains well-developed smooth endoplasmic reticulum, mitochondria, ribosomes, and lipid and carbohydrate inclusions. On the lateral surfaces of the sustentocytes, there are invaginations in which maturing germ cells - spermatocytes of the 1st and 2nd order, spermatids – are located. Spermatozoa exit into the lumen of the tubule, but they are immobile and incapable of fertilization. Each spermatogonium gives rise to 4 spermatids, which then develop into spermatozoa. In humans, spermatogenesis takes

approximately 64–75 days.

Functions of Sertoli cells include:

- 1) trophic -providing nourishment to developing germ cells,
- 2) forming part of the blood-testis barrier,
- 3) phagocytosis of degenerating germ cells,
- 4) mechanical support for germ cells,
- 5) exocrine - producing a fluid secretion that fills the convoluted seminiferous tubules,
- 6) endocrine - producing: 1. Inhibin, 2. Factor that stimulates the division of sex cells, 3. Androgen-binding protein that transports testosterone to spermatids,
- 7) Protective - prevents toxins, bacteria, and antigens from passing through.

The wall of the coiled seminiferous tubules consists of three layers:

1. the inner basal layer,
2. the middle myoid layer,
3. the outer fibrous layer.

1. The basal layer is located beneath the basal membrane, upon which the epitheliogermlinal layer rests. The inner basal layer consists of a network of thin collagen fibers.

2. The myoid middle layer is composed of myoid cells. Myoid cells provide rhythmic contractions of the tubular wall.

3. The fibrous layer consists of two layers: 1) the inner layer is represented by collagen fibers, 2) the outer layer is represented by fibroblast-like cells.

The blood-testis barrier is a collection of structures located between the capillary lumen and the convoluted seminiferous tubules. It consists of three components:

- 1) the wall of the blood capillary - endothelium and basal membrane,
- 2) the basement membrane of the convoluted seminiferous tubule consisting of three layers: basal, myoid, and fibrous.
- 3) the sustentocyte lying on the basal membrane.

The Functions of the blood-testis barrier:

- 1) It helps maintain a constant concentration of nutrients and

hormones necessary for normal spermatogenesis.

2) It protects developing germ cells from harmful substances such as toxins, bacteria, and antigens.

Spermatogenesis is highly sensitive to damaging factors such as intoxication, vitamin deficiencies, malnutrition, high temperature, fever, and radioactive exposure. These factors can weaken or even halt spermatogenesis, leading to the death of spermatozoa, spermatids, and spermatocytes, while spermatogonia are preserved. In these circumstances, Sertoli cells remain functional.

The functions of the testis

1) The generative function involves the development of male gametes (spermatogenesis)

2) The endocrine function involves the production of hormones such as testosterone and inhibin. Testosterone plays a crucial role in the final stages of spermatogenesis.

Spermatogenesis can continue until a man reaches 80 years of age.

The seminal ducts include:

- 1) the straight tubules
- 2) tubules of the rete testis
- 3) the efferent tubules
- 4) the epididymal duct
- 5) vas deferens
- 6) the ejaculatory duct.

All the seminal ducts are composed of 3 layers:

- 1) a mucous membrane consisting of an epithelium and a lamina propria (LFICT),
- 2) muscular layer, represented by smooth muscle tissue - round myocytes
- 3) adventia consisting of loose fibrous irregular connective tissue (LFICT).

The straight tubules are made up of 3 layers:

- 1) the mucosa, which includes:
 - (a) the simple columnar epithelium,
 - (b) the lamina propria of the mucosa (LFICT),
- 2) muscular layer consisting of a circular layer of myocytes,

3) adventia (LFICT).

The rete testis consists of 3 layers:

- 1) mucosa - (a) simple cubic epithelium and simple squamous epithelium, (b) lamina propria (LFICT),
- 2) muscular layer consisting of circular smooth muscle cells,
- 3) adventia layer (LFICT).

The efferent tubules are made up of 3 layers:

- 1) mucosa, in the epithelium 2 types of cells are distinguished:
 1. high - ciliated cells with fixed cilia (stereocilia) on the apical surface,
 2. low - cuboidal glandular cells secreting mucus (apocrine type).The lamina propria is formed by LFICT.
- 2) the muscular layer consists of circular myocytes,
- 3) adventitia (LFICT).

The epididymal duct is made up of 3 layers:

- 1) mucosa:
 - (a) the pseudostratified columnar epithelium, represented by 2 types of cells: 1) ciliated columnar cells, 2) basal cells (stem), triangular in shape,
 - (b) lamina propria (LFICT),
- 2) muscular layer, formed by a circular layer of myocytes, allows sperm to be propelled,
- 3) adventitia (LFICT).

The functions of the epididymal duct are:

- 1) acts as a reservoir for spermatozoa,
- 2) produces fluid that dilutes the sperm
- 3) forms a glycocalyx that coats the sperm to inactivate them
- 4) sperm mature and become motile.

The vas deferens is formed by 3 layers:

- 1) the mucous membrane, consisting of the pseudostratified columnar epithelium, the lamina propria (LFICT),
- 2) the muscular layer consisting of 3 layers of myocytes:
 - a) inner longitudinal,
 - b) middle circular
 - c) outer longitudinal.

Contraction of the smooth muscle cells ensures ejaculation

of sperm.

3) Adventitia (LFICT).

The ejaculatory duct is made up of 3 layers:

- 1) the mucous membrane, consisting of the pseudostratified columnar epithelium, the lamina propria (LFICT),
- 2) the muscular layer consisting of 2 layers:
 - a) internal circular,
 - b) external longitudinal
- 3) adventitial sheath composed of the LFICT.

The accessory glands of the male reproductive system

The accessory glands include the seminal vesicles and the prostate.

Seminal vesicles develop as a bulge in the wall of the ejaculatory duct in its distal part. In the wall of seminal vesicles 3 layers are distinguished:

- 1) the mucosa is represented by a pseudostratified columnar epithelium (secretory cells secrete mucous secretion), its lamina propria (LFICT with mucous glands),
- 2) muscular layer consists of 2 layers of myocytes:
 - a) inner circular,
 - b) outer longitudinal
- 3) adventitia (DFICT).

Function of the seminal vesicles: the secretion of the seminal vesicles liquefies the semen.

Prostate gland

The prostate covers the upper part of the urethra and is a glandular-muscular organ.

Development. The glandular tissue of the prostate develops from the protrusion of the epithelium of the urethral wall. Smooth muscular and connective tissue (LFICT, DFICT) develop from the mesenchyme.

Structure. The prostate is covered by a connective tissue capsule of dense fibrous irregular connective tissue (DFICT). The prostate is a lobulated gland.

The stroma of the gland is formed by:

- 1) loose fibrous irregular connective tissue (LFICT),
- 2) smooth muscle tissue that divides it into lobules.

Each lobule and gland is surrounded by longitudinal and circular layers of smooth muscle cells that contract and expel secretions from the prostate during ejaculation.

The parenchyma of the prostate consists of numerous (30-50) compound branched tubuloalveolar mucous glands with ducts that open into the urethra. The glands are arranged in three groups around the urethra.

The prostate gland consists of 2 parts: 1) the terminal parts and 2) the excretory ducts. The terminal parts are lined by 2 types of epitheliocytes:

- 1) columnar mucocytes, which produce a fluid mucus secretion,
- 2) basal cells, triangular in shape, which are the source of regeneration.

The excretory ducts are lined by a pseudostratified columnar epithelium. There are layers of loose fibrous irregular connective tissue (LFICT) and smooth muscle tissue (SMT) around the end sections and excretory ducts of the prostate.

The functions of the prostatic gland are:

- 1) produces a secretion that dilutes sperm,
- 2) produces a factor that stimulates the growth of nerve fibres.

The prostate is dependent on testosterone from the testes and atrophies after castration. Removal of the prostate affects spermatogenesis and testosterone production in the testes. With age (after 50–60 years), the prostate begins to atrophy and connective tissue begins to overgrow.

FEMALE REPRODUCTIVE SYSTEM

The female reproductive system consists of 1) ovaries, 2) fallopian tubes, 3) uterus, 4) vagina, 5) external genitalia, 6) mammary glands.

Sources of development: 1) yolk sac gonoblasts (extraembryonic endoderm), 2) gonadal ridge (visceral layer of mesoderm), 3) tubules of primary kidney (nephrogonotome), 4) mesenchyme.

The development of the female reproductive system includes 2 phases: 1) an indifferent phase in which the female and male reproductive systems develop in the same way, 2) a differentiated phase.

1. **The indifferent phase** occurs during the third week of embryogenesis when gonoblasts, i.e. primary germ cells, form in the yolk sac wall (extra-embryonic endoderm). Gonoblasts, which are rounded and large in shape, contain glycogen inclusions in their cytoplasm and are capable of dividing through mitosis. These cells migrate towards the gonadal ridge via two methods: 1) passively, with the blood flow, or 2) actively, with the help of pseudopods.

During the fourth week of embryonic development, there is an appearance of thickenings on the surfaces of primary kidneys. These thickenings are referred to as gonadal ridges, and they stem from the coelomic epithelium, specifically the visceral splanchnotome layer. At the same time, gonoblasts are introduced into the gonadal ridges due to a secretion of a chemical that causes a positive chemotaxis by cells of the genital cords. Following this, the genital cords are separated from the gonadal ridge. Next, sexual cords composed of coelomic epithelium and gonoblasts extend from the genital ridges towards the primary kidney. The Müllerian duct differentiates from the Wolffian duct.

2. During embryogenesis, the second stage – **the differentiation** based on a female type starts at 7–8 weeks. The mesenchyme obliterates the ends of the genital cords and advances towards the primary kidney, thus reducing the tubules of the primary kidney. Afterward, the mesenchyme gives rise to the ovarian medulla.

As development proceeds, the expanding mesenchyme splits the upper parts of the genital cords into islets called genital balls. These genital balls eventually become the follicles of the ovarian cortex, while gonocytes form ovogonies.

Each follicle is composed of an ovogonium and flattened follicular cells. During 3–4 months of embryogenesis, ovogonia enter a phase of minor growth and become primary oocytes at the leptotene stage. By the end of embryogenesis, 350–400 thousand follicles are formed, comprising future germ cells and follicular cells. Additionally, the mesenchyme proliferates between the genital ridge and the gonadal cords, leading to their separation. This layer of mesenchyme develops a protein-rich, connective tissue shell. The remnants of the genital ridge are maintained superficially in the form of inactive epithelium.

The mesonephric (Wolf's) duct atrophies under the influence of expanding mesenchyme, resulting in the preservation of its upper part, the paraephoron, and lower part, the epophoron, as epithelial strands. The paramesonephric (Müller) duct differentiates, with the fallopian tubes developing from its upper portion and the uterus and vagina from the lower portion, which later merge. The fallopian tubes, uterus, and vagina's connective and smooth muscle tissues derive from the mesenchyme. The mesothelium in the serous membrane of the fallopian tubes and uterus develops from the visceral layer of the splanchnotome, (ventral mesoderm).

The structure of the ovary

The exterior is enveloped with a germinal epithelium, reminiscence of embryonic gonadal ridge. This layer is represented by a single layer simple squamous epithelium. The tunica albuginea that lies beneath the germinal epithelium is a dense fibrous irregular connective tissue. The ovarian stroma, made up of loose fibrous irregular connective tissue (LFICT). The ovary's parenchyma comprises the medulla in the center and the cortex on the periphery. The medulla of the ovary contains loose fibrous irregular connective tissue (LFICT). The cortex forms 1) follicles with varying degrees of maturation, as well as 2) atretic, yellow, and white bodies.

The follicles of the cortex are divided according to their stage of development and structure into 1) primordial follicles, 2) growing follicles, 3) mature follicles (Graafian follicles).

The primordial follicle

The primordial follicle consists of: 1) oocyte of the first order, in the stage of diplonema, 2) follicular cells – layer of squamous epithelial cells on the basement membrane. These tiny follicles are considered dormant since they stop developing before puberty. All primordial follicles are formed in the ovaries of a human fetus from the 6th to the 9th months of embryogenesis.

Growing follicles

Characterized by the fact that:

- 1) the first-order oocyte grows in this follicle
- 2) zona pellucida consisting of glycosaminoglycans, mucoproteins and proteins is formed around the oocyte.
- 3) follicular cells, which are located in a layer on the basal membrane, change their shape and become cubic, prismatic. These cells synthesize substances necessary for the growth and development of the oocyte.
- 4) the size of the follicle increases.
- 5) a connective tissue membrane begins to form around the follicle.

In the following, the growth of the follicles is influenced by the pituitary hormone FSH, in the phase of large growth. This phase is characterized by the fact that:

- 1) the first-order oocyte stops growing
- 2) several layers of follicular cells are formed due to increased mitotic division, the follicular epithelium becomes multilayered
- 3) follicular cells secrete follicular fluid containing estrogen, a female sex hormone, which accumulates in the cavities of the follicle; several small fluid-filled cavities appear
- 4) the size of the follicle increases as the cavities are filled with follicular fluid.
- 5) the connective tissue membrane surrounding the outside of the

follicle is called the theca.

The theca of the follicle consists of 2 layers: 1) inner and 2) outer. The inner theca consists of loose fibrous irregular connective tissue (LFICT) with numerous blood vessels, around which are interstitial cells of mesenchymal origin. The outer theca is represented by dense fibrous irregular connective tissue (DFICT).

Every 28 days, typically only a single follicle reaches maturity in the ovaries.

A mature **Graafian follicle** is identified by following features:

- 1) the follicle has reached its maximum growth
- 2) the oocyte of the 1st order is situated eccentrically, but remains connected to the follicle wall via an egg-bearing tubercle
- 3) there is another layer of follicular cells surrounding the oocyte, known as the corona radiata, which penetrates into the oocyte. The corona radiata serves as the third shell of the oocyte – 1st order (cytolemma, zona pellucida, radiant crown).
- 4) an egg-bearing tubercle forms when one of the follicular cells adjacent to the oocyte of the first order is pushed to one of the poles.
- 5) the remaining follicular cells form a granulosa layer, which consists of the follicular cells lying in one or more layers.
- 6) in the follicle, one large cavity fills with the hormone estrogen as a result of the fusion of small cavities.
- 7) the follicle enlarged rapidly owing to the proliferation of granulosa layer cells (follicular cells) and the growth of the follicle cavity, with a diameter reaching 2-3 cm.
- 8) the overgrown follicle causes a protrusion in the zona pellucida of the ovary, rising above its surface.
- 9) the blood vessels in the inner and outer layers of the theca are highly developed.

Functions of granulosa layer follicle cells:

- 1) barrier,
- 2) trophic,
- 3) the formation of follicular fluid and production of estrogen.
- 4) After two weeks, one of these follicles completes its ovulation development.

Atretic Follicles

Not all follicles that undergo a period of great growth successfully mature. Conventionally, all developing follicles, except one, undergo cell death known as atresia, resulting in the formation of atretic follicles. Follicular cells of the granulosa layer of the follicle secrete gonadocrinin hormone, which actively limits the growth and maturation of oocytes, leading to their death. The highest concentration of gonadocrinin hormone is typically found in mature follicles. If a mature follicle fails to undergo ovulation, the gonadocrinin secreted by it causes its atresia or death. Atresia is a type of restructuring characterized by:

- 1) the death of the follicular oocyte and its fragments' absorption by macrophages,
- 2) preservation of the zona pellucida, center positioning with shrinkage and thickening,
- 3) reduction or atrophy of follicular cells of the granulosa layer, and
- 4) multiplication and enlargement of interstitial cells of the inner theca.

The structure of the atretic body

At the center of the atretic body lies a wrinkled zona pellucida alongside hypertrophied interstitial cells and loose fibrous irregular connective tissue that contains blood vessels. These interstitial cells are large and rounded in shape, with a well-developed smooth endoplasmic reticulum, mitochondria and lipid inclusions.

Functions of the atretic body

- 1) hormone production by interstitial cells,
- 2) prevention of superovulation to allow only one mature follicle, and
- 3) ensuring oocyte maturation of a more complete follicle.

During menopause, the body undergoes changes that cause the atresia process to worsen. This is because the hormonal function of the ovaries is depressed.

Haematofollicular barrier

The haematofollicular barrier separates female germ cells from the microenvironment to create optimal conditions for ovocyte metabolism. It is composed of

- 1) vessels within the microcirculatory channel.
- 2) theca (connective tissue),
- 3) basal membrane,
- 4) follicular epithelium,
- 5) zona pellucida (glistening sheath).

Ovulation

Ovulation occurs when a mature (Graafian) follicle ruptures, releasing a first-order oocyte that is surrounded by follicular epithelium (“radiate corona”) into the abdominal cavity.

Main causes of ovulation include:

- 1) a rise in the blood concentration of adenohipophysis luteinizing hormone (LH)
- 2) increased blood flow to the capillaries within the inner theca of the mature follicle
- 3) an increase in intrafollicular pressure due to higher content of follicular fluid in the follicular cavity.
- 4) proteolytic enzymes thin and loosen the follicular membrane and ovarian outer layer.
- 5) release of oxytocin as a result of irritation of nerve endings associated with pressure on the follicle wall.

In humans, preparation for ovulation and rupture of the follicle lasts about 12 hours. As a result of these factors, the mature Graafian follicle’s wall and ovarian outer layer rupture, and the 1st order oocyte is released into the abdominal cavity.

The corpus luteum (yellow body)

The corpus luteum, a temporary endocrine gland, develops after ovulation in place of the burst follicle due to the influence of luteinizing hormone (lutropin) and prolactin of the adenohipophysis. The process

of corpus luteum development comprises four stages:

- 1) vascularization and proliferation stage,
- 2) glandular metamorphosis stage,
- 3) blossoming stage, and
- 4) reverse development stage.

Stage 1 – Proliferation and Vascularization. Following ovulation, blood flows from the damaged vessels of the inner layer of theca into the cavity of the empty follicle. This results in the formation of a blood clot that is eventually replaced by a connective tissue scar (DFICT). The remaining follicular cells in the granular layer of the ruptured follicle undergo rapid division (proliferation) and increase in number. Blood vessels from the inner layer of theca expand and grow between the proliferating follicular cells (vascularization).

Stage 2 – The stage of glandular metamorphosis. Follicular cells grow in size and differentiate into luteal cells (luteocytes). The latter accumulate lutein, a yellow pigment.

Stage 3 – The blossoming stage. Luteal cells produce progesterone actively during this stage. The duration of this stage varies depending on whether or not pregnancy happens. If there's no pregnancy nor fertilization, this stage will last 12-14 days, and the corpus luteum is referred to as the menstrual corpus luteum, which measures 2 cm. On the other hand, if both fertilization and pregnancy happened, the pregnancy corpus luteum is created, which enlarges to 5-6 cm. For approximately four months, the corpus luteum hormone progesterone maintains pregnancy until the placenta synthesizes progesterone and prolactin. Therefore, 2 types of corpus luteum are distinguished: 1) the pregnancy corpus luteum, 2) the menstrual corpus luteum.

Progesterone inhibits the entry of oocytes into the stage of great growth, i.e. as long as the corpus luteum is present, the oocytes cannot enter the stage of great growth of the ovarian follicles.

Stage 4 – The stage of reverse development (involution). Over time, the corpus luteum, surrounded by fibrous connective tissue, will degenerate in both cases. Luteal cells will atrophy and die, while the connective tissue at the central scar will overgrow. Consequently, in

place of the previous corpus luteum, a white body (corpus albicans) - a connective tissue scar (DFICT) – will form. The corpus luteum can persist for several months or even years before undergoing resorption.

The ovary serves two main functions: 1) generative, which involves oogenesis, and 2) endocrine, which involves the secretion of sex hormones such as estrogen, progesterone, and gonadocinin. The ovarian functions are under the regulation of adenohipophysis hormones, namely FSH, LH, and prolactin.

Fallopian Tubes

The fallopian tubes are a pair of organs that carry the sex cells from the ovaries to the uterus. They develop from the upper part of the paramesonephric (Müllerian) ducts.

Structure. The wall of the fallopian tube comprises three layers: 1) mucous, 2) muscular, and 3) serous.

1) The mucosa membrane arranged in longitudinal folds and comprises two layers: 1) epithelium and 2) mucosal lamina propria, which is composed of loose fibrous irregular connective tissue (LFICT). The mucosal epithelium is a simple columnar epithelium that encompasses two types of cells: 1) ciliated cells, which facilitate ovum movement, and 2) secretory cells, which secrete a mucous secretion.

2) The muscular layer consists of 2 layers of smooth myocytes: the inner circular, the outer longitudinal.

3) The serous layer covers the outside of the fallopian tubes and consists of mesothelium on a base of connective tissue.

The proximal end of the fallopian tubes expands to form infundibulum, which terminate in fimbriae. These fimbriae are composed of connective tissue and blood vessels. Filling with blood during ovulation, they lengthen and move over the ovary, covering it. As a result, the ovum enters the fallopian tube where fertilization occurs.

The fallopian tube functions: 1) ovogenesis - maturation stage, 2) fertilization.

Uterus

The uterus is a muscular organ that is responsible for the intrauterine development of the fetus (implantation and pregnancy).

Development. The uterus is formed from the distal parts of the paramesonephric ducts, known as the Mullerian ducts, when they join.

Structure. The wall of the uterus has three layers: 1) the mucous membrane or endometrium, 2) the muscular membrane or myometrium, 3) the serous membrane or perimetrium.

1. The endometrium comprises two layers:

1) the simple columnar epithelium;

2) the lamina propria, which is composed of loose fibrous irregular connective tissue (LFICT) and contains simple tubular unbranched uterine glands.

The endometrial epithelium comprises two types of cells: ciliated cells situated around the uterine gland orifices, and glandular (mucous, secretory) cells. Mucous exocrinocytes possess microvilli on their apical surface. During high estrogen concentrations, microvilli are at their maximum number and height. They may secrete uterine mucus in addition to ciliated epitheliocytes.

The uterine glands, in conjunction with mucous exocrinocytes, secrete a protein-glycosaminoglycan complex called uterine fluid. Relaxin is contained within the uterine gland cells on the eve of labour, enabling relaxation of the pubic joint to facilitate the baby's delivery.

Certain connective tissue cells undergo differentiation into decidual cells, which are characterized by their large, spherical morphology and cytoplasmic inclusions of lipoproteins and glycogen. The quantity of decidual cells augments during gestation in the secretory phase of the menstrual cycle. Their main function consists of supplying histotrophic nutrition to the developing embryo following implantation

The endometrium is divided into two layers based on how it responds to ovarian hormones: the functional layer and the basal layer.

The functional (superficial) layer includes a simple columnar epithelium, lamina propria, uterine glands, spiral arteries except for the bottom of the glands. Ovarian hormones have a considerable influence on the functional layer of the endometrium.

The endometrial functional layer is shed each month due to hormonal changes during menstruation and childbirth. It is responsible

for the implantation and development of the embryo, as well as the formation of the placenta.

The basal layer, consisting of lamina propria, uterine gland bases, and direct arteries. The basal layer of the endometrium remains unaffected by ovarian hormones. This layer is permanent and not subject to rejection. It contains uterine gland lobules that facilitate the restoration of the functional layer once it sheds, thereby promoting endometrial regeneration.

The myometrium comprises of three layers of smooth muscle cells: 1) the submucosal – internal oblique, 2) the vascular – middle circular, 3) the supravascular – external oblique, which contain myocytes with oblique direction, perpendicular to the submucosal internal oblique layer. The crossing of myocytes is significant in regulating blood circulation intensity during menstruation and labour. During labour, oxytocin stimulates myocyte contraction. There is a layer of connective tissue between myocytes. The uterus, a powerful muscular organ, maintains a constant state of tone. Its body contracts, accompanied by the opening of the cervix. Estrogens facilitate dilation of the cervix. During pregnancy, myocytes undergo significant hypertrophy, with a length of up to 500 μm , branching out and forming a network.

The perimetrium is represented by mesothelium and loose fibrous irregular connective tissue attached to the uterine myometrium.

The parametrium is localized anteriorly and on the sides of the cervix, comprising white adipose tissue.

The cervix is a cylindrical structure comprising three layers- 1) the mucous layer lining the cervical canal, 2) the muscular layer, and 3) the mucous layer covering the vaginal part of the cervix.

1. The cervical canal's mucous layer is folded and comprises of two layers: 1) glandular and ciliated epithelium of simple columnar epithelium, which secrete mucus, and 2) the lamina propria containing simple, large, branched tubular mucous glands that secrete mucus. The glands' secretion is of alkaline nature and is thick and tenacious. This secretion fills the cervical canal and forms a mucous plug, which mechanically and bactericidally prevents the entry of microbes into the cervix.

2. The muscular layer consists of a dense, circular layer of smooth

muscle cells that constitute the uterine sphincter. The contraction of this sphincter expels mucus secreted by the cervical glands into the cervical canal, forming a plug that occludes the canal. Upon relaxation of the sphincter, the cervical lumen expands, allowing for aspiration (suction) of sperm trapped within the vagina into the uterus. The small number of longitudinal bundles of smooth muscle cells situated on the exterior of the vaginal portion of the cervix are an elongation of the muscular layer of the vagina.

3. The mucous layer of vaginal part of the cervix consists of two layers:

- 1) a stratified squamous (nonkeratinized) epithelium comprising of basal, intermediate, and superficial (functional) layers,
- 2) the lamina propria that is represented by loose fibrous irregular connective tissue (LFICT).

The boundary between the stratified and columnar epithelium of the cervical mucosa is always distinct. Atypical epithelial cell growth and the development of cervical cancer are commonly observed in the region where two epithelia make contact.

The vagina

The vaginal wall comprises three layers: (1) mucous, (2) muscular, and (3) adventitial.

1. The mucous membrane is folded and composed of two layers: (1) stratified squamous epithelium and (2) lamina propria.

The stratified squamous epithelium, which partially keratinises, is comprised of three layers: (1) basal, (2) intermediate, and (3) superficial (functional). The cells within the superficial layer possess keratohyalin granules, an indicator of keratinization. However, complete keratinization of the cells does not take place under normal circumstances. In addition, glycogen inclusions can be found within these cells. Microbes that reside within the vagina prompt the breakdown of glycogen. Due to the breakdown of glycogen, lactic acid is generated, leading to the acidic nature of vaginal mucus. This provides bactericidal properties, safeguarding the vagina from the growth of pathogenic microorganisms.

The lamina propria of the mucosa consists of loose fibrous

irregular connective tissue (LFICT), in which elastic fibres form superficial and deep networks. Glands in the vaginal wall are absent.

2. The muscular layer of the vagina consists of longitudinal smooth myocytes. There are a small number of circularly arranged smooth myocytes in the middle part of the muscular sheath.

3. The vaginal adventitial layer consists of loose fibrous irregular connective tissue.

Sexual cycle

Ovarian and Menstrual Cycles. The female reproductive system changes cyclically. The alterations occurring in the uterine endometrium during this process are known as the menstrual cycle, which leads to periodic uterine bleeding as the functional layer of the endometrium is rejected.

The average menstrual cycle lasts 28 days. From the age of 13-15 to 40-45 years, a woman's body goes through cyclical morphological rearrangements of the reproductive system in preparation for pregnancy. This physiological process results in uterine bleeding (menstruation) in the absence of fertilization. During each ovarian cycle, the sex cell matures and the mature follicle ovulates, leading to the development of the corpus luteum. Simultaneously, the uterine mucous membrane undergoes restructuring. These processes are interrelated, synchronized, and regulated by the hypothalamic-pituitary endocrine system. During the menstrual cycle, three distinct phases occur:

- 1) the menstrual phase (desquamation) from day 1 to day 4,
- 2) the postmenstrual phase (proliferation) from day 5 to day 14, and
- 3) the premenstrual phase (secretion) from day 15 to day 28.

Follicular development is advanced in one of the two ovaries, and ovulation alternates between ovaries from cycle to cycle. As a result, ovulation typically occurs in a single ovary.

The premenstrual (secretory) phase lasts about 14 days and marks the end of the female reproductive system's preparation for pregnancy. After ovulation, under the influence of luteinising hormone from the adenohypophysis, the corpus luteum develops in place of

the ruptured follicle and the release of progesterone begins, under the influence of which the premenstrual phase takes place. Under the influence of progesterone, the following processes are initiated:

- 1) uterine glands become twisted and secrete thick mucus that contains ample glycogen necessary for implantation, trophicity, and activation of embryo development.

- 2) the cells lining the gland openings become ciliated.

- 3) certain cells of the connective tissue stroma differentiate into decidual cells.

- 4) the thickness of the endometrium increases due to hyperaemia and the accumulation of oedematous fluid in the endometrial lamina propria.

- 5) The supply of blood to the endometrium increases, leading to the full development of endometrial blood vessels. Spiral arteries become larger, twist and form a dense network of capillaries that branch out in the functional layer of the endometrium. Straight arteries create capillaries that feed the basal layer of the endometrium.

During the secretory phase, the endometrium is readied for the potential implantation of the embryo. If fertilization takes place, the enlarged state of the endometrium is sustained for a duration of 6-8 weeks. The endometrium contributes to the development of the uterine component of the placenta, which is then detached from the uterine wall and expelled from the cavity after birth. If fertilization has not occurred, the functional layer of the endometrium is destroyed and shed with the unfertilized egg during the following menstrual cycle and is removed from the uterine cavity.

The desquamation phase of the menstrual cycle takes place over a duration of four days. During this phase, it is noteworthy that:

- 1) the ovarian corpus luteum experiences a regression, leading to the cessation of progesterone secretion.

- 2) the ovarian follicles do not undergo significant growth or secrete estrogens due to progesterone inhibition, resulting in the absence of ovarian hormones.

- 3) the secretion of luteinising hormone ceases.

- 4) hypothalamic hormones including vasopressin and oxytocin are

secreted.

5) the hormone vasopressin causes spasm of the spiral arteries in the functional layer of the endometrium, leaving the straight arteries unaffected, so the basal layer of the endometrium continues to receive an adequate supply of blood.

6) the blood supply to the functional layer of the endometrium becomes disrupted, resulting in a reduction in blood flow (ischaemic phase).

7) thromboses develop in spiral (twisted) arteries and cause the vessel walls to lose elasticity and strength.

8) nutrition to the functional layer is also affected.

9) as a result of ischemia, the functional layer experiences necrotic changes which ultimately lead to its death.

10) following prolonged spasm, spiral (tortuous) arteries redilate, resulting in an increase in blood flow to the endometrium.

11) however, due to the brittleness of the walls of these vessels, several ruptures occur.

12) consequently, blood from these ruptured arteries flows out between the basal and functional layers of the endometrium, causing haemorrhage.

13) subsequently, the necrotising functional layer is expelled. The shedding of necrotic tissue results in desquamation.

14) this leads to uterine bleeding, characterized by bloody discharge from the genital tract and signifying the onset of menstruation. As the blood flows out of the spiral arteries, it separates the necrotic functional layer of the endometrium from the basal layer. Ultimately, the detached functional layer is expelled from the uterus alongside menstrual blood.

15) at the conclusion of menstruation, the endometrium retains a slender basal layer containing the deep-end portions or lobules of the uterine glands.

The proliferation or postmenstrual phase takes place from the 5th to the 14th day of the menstrual cycle, succeeding the menstrual phase. The endometrium in this phase is limited to the basal layer, with the distal regions of the uterine glands remaining intact. The growing follicles in the ovary produce estrogens by the 7th day of the cycle,

which trigger the proliferation of the uterine epithelium characterized by following processes.

- 1) The epithelium of the uterine gland lobules located in the basal layer of the uterine endometrium proliferates intensely through mitosis.
- 2) Uterine glands undergo rapid growth but remain narrow, straight, and do not secrete.
- 3) As a result of active cell proliferation, a new epithelial covering for the uterine mucosa is created.
- 4) The endometrial stroma regenerates and significantly expands, restoring the lamina propria of functional layer.
- 5) The covering epithelium comprises unciliated cells,
- 6) Blood vessels extend from the basal layer into the functional layer, but they are few in number and poorly branched,
- 7) The entire functional layer of the uterine endometrium is restored.

Therefore, the proliferation phase is determined by the influence of ovarian estrogens, and the secretion phase is influenced by progesterone. Ovulation takes place in the ovary on days 12 to 17 of the menstrual cycle, which is the midpoint between two regular menstrual periods. In most sexually mature females, menstruation occurs at regular intervals of 28 days.

Mammary Glands

Mammary glands are modified sweat glands, deriving from the skin. Mammary gland development originates from two sources: 1) cutaneous ectoderm, and 2) mesenchyme.

During **development**, thickenings of cutaneous ectoderm (milk lines) arise in the 6th week of embryogenesis. These lines give rise to epithelial tracts, which grow into the underlying mesenchyme. The mammary ducts branch into the excretory ducts and alveolar passages. This process continues until the 6th month of embryogenesis. In adolescent females, the advancement and maturation of mammary glands take place with the mediation of estrogen. During pregnancy and lactation, the mammary gland forms alveoli at the ends of the epithelial strands, which are the terminal secretory sections of the alveolar tubular glands.

Structure. The mammary gland is comprised of about 15-20 distinct lobules, which are each surrounded by connective and adipose tissue layers. Within each lobe lies a relatively complex, branched, alveolar-tubular apocrine gland. The excretory duct opens onto the surface of the nipple, i.e. 15-20 ducts open onto the surface of the nipple. The mammary gland consists of 2 parts: 1) the ducts of the mammary gland, and 2) the terminal secretory sections. The excretory ducts include:

- 1) common excretory duct
- 2) milk sinus – a reservoir for milk,
- 3) milk ducts,
- 4) branched alveolar milk ducts.

There are no secretory sections present in the mammary gland of non-lactating females. Development of the mammary gland in girls is incomplete and only reaches maturity during pregnancy and lactation (lactating mammary gland). The terminal secretory sections, known as alveoli, are formed in the lactating gland. The alveolar wall is comprised of two types of cells: lactocytes and myoepitheliocytes. Lactocytes are located in a single layer on the basal membrane. The lactocytes are prismatic in shape. Microvilli are found on the apical surface of the lactocytes. The cytoplasm of the lactocytes contains a well-developed, smooth, and granular endoplasmic reticulum, mitochondria, and inclusions such as fat droplets. Desmosomes connect the lactocytes to each other. Myoepitheliocytes, with their outgrowths, cover the alveolus externally. The alveoli are hollow sacs. The myoepitheliocyte contraction is a factor in milk secretion. Milk is released into the alveolar lumen via the apocrine type. This milk has a complex composition that includes proteins (casein), lipids (triglycerides), sugars (lactose), immunoglobulins, vitamins, salts, and water. All these components are present in breast milk, which is the most valuable and crucial nutrition for babies.

Lactocyte secretory function is stimulated by lactotropic hormone of the adenohypophysis. Milk secretion in the alveoli begins in the second half of pregnancy, and hypothalamic oxytocin stimulates milk secretion by inducing contraction of the myoepithelial cells of the

secretory end sections of the mammary glands. After secretion, the lactocytes regenerate and a new cycle of secretion is initiated. The alveoli discharge milk into alveolar passages.

The alveolar passages comprise a simple cuboidal epithelium and contain myoepitheliocytes. The milk ducts feature two-layer cuboidal epithelium while the milk sinuses are lined with three-layered cuboidal epithelium. The common duct presents stratified squamous nonkeratinized epithelium. Bundles of smooth muscle tissue in the connective and adipose tissue along the outlet ducts contribute to milk production by contracting. The epidermis in the areola region heavily pigments owing to the accumulation of melanocytes. Encapsulated nerve endings (mechanoreceptors) are abundant in the papillary dermis layer. The mammary glands furnish the required nourishment to the baby after birth, once the placental blood stops providing nutrients.

The mammary glands secretory activity is regulated by estrogens, progesterone, prolactin, oxytocin and other hormones. As age advances and synthesis of sex hormones reduces, gradual involution of the mammary glands takes place.

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