MINISTRY OF HEALTH OF UKRAINE

ODESA NATIONAL MEDICAL UNIVERSITY

Faculty of **Dentistry**

Department of **Histology, Cytology, Embryology and Pathological Morphology with a course in Forensic Medicine**

APPROVED

Vice-rector for scientific and pedagogical work

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September 4, 2023

METHODOLOGICAL RECOMMENDATION

FOR LECTURES CLASSES

FROM EDUCATIONAL DISCIPLINE

Faculty of Dentistry, course 1, 2

Educational discipline - **"Histology, cytology and embryology."**

Approved:

At the meeting of the Department of Histology, Cytology, Embryology and Pathological Morphology with the course of Forensic Medicine of Odesa National Medical University

Protocol No. 1 of September 1, 2023

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Theme: «Introduction to the course of histology, cytology and embryology.»- 2h.

1.Relevance of the topic

Like other science histology, cytology and embryology use special research methods to solve their inherent tasks, which allow learning the macro-, micro-and ultrastructure, molecular organization, and histophysiology of cells and their components, which are necessary for the future doctor to understand the patterns of formation of multicellular organisms, the functioning of tissues, organs, and systems, the emergence of adaptive or pathological morphofunctional changes in cells under the influence of various factors of the external and internal environment.

The development of histology, cytology, and embryology is inextricably linked with the improvement of research methods. Histological examination of biological objects is used in the practice of a laboratory assistant, pathologist, physician.

A cell is an elementary living system; it is a structural, functional, and genetic unit of the human body. Cells provide reproduction, the transmission of hereditary information, growth of the organism, adaptation, and regeneration processes.

The largest number of diseases are accompanied by a violation of the structure and functions of cellular elements, therefore, without knowledge of the structure of cells, tissues, and organs, it is impossible to imagine and explain the mechanism of development of pathological processes in the body. In the hospital, histochemical and cytological examinations of biopsies of different organs are widespread, which help the doctor to make or clarify the diagnosis, and, as a result, to choose a method of treatment.

2. Objectives of the lecture:

a) Learning:

- interpretation and use of the main research methods in histology, cytology, and embryology at the present stage;

- analysis of the structural organization of cells and their derivatives;

- modern ideas about the morpho-functional organization of the animal cell;

- interpretation of relationships between structural elements of cells, assessment of their functional state, interpretation of age-related changes, mechanisms of regeneration, adaptation to the action of various factors.

b) educational:

-to bring to the students the importance of studying the subject and its significance in the process of forming him as a doctor;

- to acquaint students with the basic research methods in histology, cytology, and embryology, to determine their significance for practical medicine;

- to form students' professional significance of the topic. Discuss the issue of deontology.

3. Plan and organizational structure of the lectures.

№№	The main stages of the lecture and their content	Goal of the lecture	Lecture type. Lecture equipment	Time management
1	2	3	4	5
I. 1. 2. II	*Preparatory stage.* Determination of the learning goal. Providing positive motivation. *The main stage.* Teaching lecture material according to the plan: 1.Modern research methods in histology, cytology and embryology		Tables. Slides.	5% 85-95%

III.	2.Morphofunctional characteristics of cells *The final stage.* Summary of the lecture. General conclusions. Lecturer's answer to possible questions. Self-study assignment.	I. Descriptive. II. Analytical - synthetic, high quality.	In accordance with the publication "Guidelines for the planning, preparation and analysis of lectures." List of literature, questions, tasks.	5%

4. Content of the lecture material:

- structural and logical scheme of the content of the topic;

- text of the lecture. (attached)

5. Materials for activating students during the lecture:

- questions

- tasks

- problem situations

Questions:

• Research methods used in modern histology, cytology and embryology.

• Vital research methods. In vivo and in vitro cultivation.

• Basic principles of preparation of specimens for light microscopy. General organization of the cell.

• Synthetic cell apparatus. Cytoskeleton.

• Nuclear apparatus.

• Cell and cell life cycle. Cell aging.

• The main morphofunctional and physicochemical changes in cells during aging.

6. General material and methodological support of the lecture:

- classrooms;

- equipment;

- equipment;

- illustrative materials.

List of recommended literature .

The main one:

1. Lutsyk O.D., Tchaikovsky Y.B. Histology, cytology, embryology Vinnytsia, New Book, 2018.
2. Barinov E.F., Tchaikovsky Y.B. General histology and embryology of internal organs: textbook.Kyiv: Medicine; 2013
3. Wojciech Pawlina. Histology: textbook and atlas. WSV: Medicine, 2021.

Additional:

1. Histology and embryology of internal organs: textbook / E.F. Barinov, Y.B. Tchaikovsky, O.M. Sulaeva et al.
2. Cytology of human organs and tissues edited by L.S.Bolgova. Kyiv: Book-plus, 2018, p.288

Addition

Theme: «Introduction to the course of histology, cytology and embryology.»

Histology is the study of the microscopic anatomy of cells and tissues. Histology is an essential tool of biology and medicine.

Subdivisions of histology

Cytology is a science that is about the structure and functions of cells and their derivatives, their reproduction, and interactions.

General histology examines the composition of each of the tissue types, including the nature of its cells and extracellular matrix.

Special histology is a science which is about the structure of organ systems.

Embryology is a science which is about the development of an embryo from the fertilization of the ovum to the fetal stage.

Fundamental theoretical problems of histology:

-studying rules of cyto- and histogenesis, structures, and functions of cells and tissues;

- studying rules of differentiation and regeneration of tissues;

- finding out of the role of nervous, endocrine, immune systems of the organism in the regulation of processes of cells, tissues, and organs and their functioning;

- research of age changes of cells, tissues, organs;

- research of adaptation of cells, tissues, and organs to the action of various biological, physical, chemical, and other factors;

- studying of processes of morphogenesis in system mother-fetus;

- research of features of human embryogenesis.

The cell theory refers to the idea that cells are the basic unit of structure in every living thing. The development of this theory during the mid 17th century was made possible by advances in microscopy. This theory is one of the foundations of biology. Credit for developing cell theory is usually given to three scientists: Theodor Schwann, Matthias Jacob Schleiden, and Rudolf Virchow.

Cell theory states:

-that cell is the basic unit of the living system;

-that all organisms consist of at least one cell;

- that cells in multicellular organisms are often specialized;

- that all cells come from previous cells.

Cell

The cell is the structural and functional unit of the organism.

Except cells, in an organism, there are their derivatives, which have no cellular structure (extracellular matrix, postcellular structures, symplast, syncytium).

Extracellular matrix is produced by cells and excreted to the extracellular space within tissues, serving as a scaffolding to hold tissues together and helping to determine their characteristics.

Postcellular structures are derivatives of cells which during a differentiation (more often owing to loss of a nucleus and a part of organelles) have lost the major signs of cells, but have got a number of properties necessary for execution by them are specialized functions. The postcellular structures in humans are erythrocytes, platelets, horny cells of the epidermis.

Symplasts are the structures formed as a result of cell fusion with loss of their borders and formation of uniform cytoplasmic mass in which there nuclei. Symplasts are osteoclasts of bone, an external layer of trophoblast, and fibers of skeletal muscle tissue.

Syncytium is the structure arising owing to incomplete cytotomia at cell division with preservation of connection between elements of cells by means of cytoplasmic bridges (seminiferous epithelium in the seminiferous tubules of testis).

Overview of methods used in histology

Modern histology has a wide arsenal of various methods of research. All these methods are connected by the requirement of application of the special device-microscope, and all of them are microscopic methods.

Light microscopy

Conventional light, phase contrast, polarizing, confocal, and fluorescence microscopy are all based on the interaction of photons and tissue components.

With the light microscope, stained preparations are usually examined by transillumination. The microscope is composed of both mechanical and optical parts.

The optical components consist of three systems of lenses: condenser, objective, and ocular. The condenser collects and focuses the illumination to produce a cone of light that illuminates the object to be observed. The objective lens enlarges and projects the illuminated image of the object in the direction of the ocular lens. The ocular lens (eyepiece) further magnifies this image and projects it onto the viewer's retina or photographic plate. The total magnification is obtained by multiplying the magnifying power of the objective and ocular lenses.

The critical factor in obtaining a crisp, detailed image with the microscope is its resolving power, that is, the smallest distance between two particles at which they can be seen as separate objects. The maximal resolving power of the light microscope is around 0.1 nm; this permits good images to be magnified in 1000-1500 times. Objects smaller than 0.1 nm cannot be distinguished with this instrument.

The quality of the image – its clarity and richness of detail- depends on the microscope's resolving power. The magnification is independent of its resolving power and is of value only when accompanied by high resolution. The resolving power of a microscope depends mainly on the quality of its objective lens. The ocular lens only enlarges the image obtained by the objective; it doesn't improve resolution.

Phase-contrast microscopy

Unstained biological specimens are usually transparent and difficult to view in detail since all parts of the specimen have almost the same optical density. Phase-contrast microscopy, however, uses a lens system that produces visible images from transparent objects.

The principle of phase contrast microscopy is based on the fact that light changes its speed and direction when passing through cellular and extracellular structures with different refractive indices. These changes cause the structures to appear lighter or darker relative to each other. Differential interference optics produces an apparently three-dimensional image of living cells and tissues.

Polarizing microscopy

When normal light passes through a polarizing filter, it exits vibrating in only one direction. If a second filter is spaced in the microscope above the first one, with its main axis perpendicular to the first filter, no light passes through, resulting in a dark field effect. If tissue structures containing oriented molecules (such as cellulose, collagen, microtubules, and microfilaments) are located between two Polaroid Filters, their repetitive, oriented molecular structure allows them to rotate the axis of the light emerging from the background. Consequently, they appear as bright structures against a dark background. The ability to rotate the direction of vibration of polarized light is called birefringence and is present in crystalline or substances containing oriented molecules.

Confocal microscopy

This type of microscopy uses lasers and computers to produce three-dimensional images of living cells and tissue slices. Because of the way in which the image is produced, the investigator can visually dissect through the specimen, observing structures above and below others. Storing information from each visual plane of the section in a computer allows a three-dimensional image to be reconstructed.

Fluorescence microscopy

When certain fluorescence substances are irradiated by the light of a proper wavelength, they emit light with a longer wavelength. In fluorescence microscopy, tissue sections are usually irradiated with ultraviolet light so that the emission is in the visible portion of the spectrum. The fluorescent substances appear as brilliant, shiny particles on a dark background. A microscope with a strong ultraviolet light source is used, and special filters that eliminate ultraviolet light are used after the objective lens to protect the observers' eyes.

Some naturally fluorescent substances are normal constituents of cells, e.g., vitamin A, vitamin B2, and porphyrins. Other fluorescent compounds that have an affinity for tissues and cells are used ad fluorescent stains. Acridine orange is most widely used because it can combine with DNA and RNA. When observed in the fluorescence microscope, the DNA-acridine orange complex emits a reddish-orange light. It is thus possible to identify and localize nucleic acids in the cells.

Electron microscopy

Both transmission and scanning electron microscopy are based on the interaction of electrons and tissue components.

The electron microscope is an imaging system that permits high resolution (0.1nm). In practice, a resolution of 1nm in tissue sections is considered satisfactory. This by itself permits enlargements to be obtained up to 400 times greater than those achieved with light microscopes.

The electron microscope functions on the principle that a beam of electrons can be deflected by electromagnetic fields in a manner similar to light deflection in glass lenses. Electrons are produced by high-temperature heating of a metallic filament (cathode) in a vacuum. The emitted electrons are then submitted to a potential difference of approximately 60-100kV or more between the cathode and the anode. The anode is a metallic plate with a small hole in its center. Electrons are accelerated from the cathode to the anode. Some of these particles pass through the central opening in the anode, forming a constant stream (or beam) of electrons. The beam is deflected by electromagnetic lenses in a way roughly analogous to what occurs in the optical microscope. Thus, the condenser focuses the beam at the object plane and the objective lens forms an image of the object. The image obtained is further enlarged by one or two projecting lenses and is finally seen on a fluorescent screen or is projected onto photographic plates.

Because electron microscopy requires a much thinner section (0.02-0.1nm), embedding is performed with a hard epoxy plastic. The blocks thus obtained are so hard that glasses are diamond knives are usually necessary to section them. Since the electron beam in the microscope cannot penetrate glass, the extremely thin sections are collected on small metal grids. Those portions of the section spanning the holes in the mesh of a grid can be examined in the microscope.

Radioautography

Radioautography permits the localization of radioactive substances in tissues by means of the effect of emitted radiation on photographic emulsions. Silver bromide crystals present in the emulsion act as microdetectors of radioactivity. In radioautography, tissue sections from animals previously treated with radioactive compounds are covered with a photographic emulsion and stored in a lightproof box in a refrigerator. After various exposure times, the slides are developed

photographically and examined. All silver bromide crystals hit by radiation are reduced to small black granules of elemental silver, which reveal the existence of radioactivity in the tissue structures in close proximity to these granules. This procedure can be used in both light and electron microscopy. By localizing radioactivity in tissue components it is possible to obtain data on the sequence of events occurring in tissues. Thus, if a radioactive protein precursor is given to a protein-synthesizing cell, its pathway can be followed in the cell after varying periods of time. Furthermore, the intensity of the process is proportional to the number of granules formed over the tissue components.

Immunohistochemical method

The Immunohistochemical method is based on the reactions antigen-antibody. Every cell of an organism has specific antigen composition which is determined by proteins mostly. It is possible to get by immunization specific antibodies proper to the antigens. Antibodies contact with fluorochromes or enzymes. After processing of the explored histological specimens in the places of localization of the proper antigens the molecules of the marked antibodies, which expose either thanks to luminescence or on the basis of laying of the products of the histochemical reaction, are concentrated. By this method, it is possible to identify any cells or substances (like hormones), produced by those or other cells.

Tissue preparation

Fixation

Chemical fixation with formaldehyde or other chemicals.

Chemical fixatives are used to preserve tissue from degradation, and to maintain the structure of the cell and subcellular components such as cell organelles. The most common fixative for light microscopy is 10% neutral buffered formalin. For electron microscopy, the most commonly used fixative is glutaraldehyde, usually as a 2,5% solution in mainly by irreversibly cross-linking proteins. This process, while preserving the structural integrity of the cells and tissue, can damage the biological functionality of proteins, particularly enzymes, and can also denature them to a certain extent. This can be detrimental to certain histological techniques. Further fixatives are often used for electron microscopies such as osmium tetroxide or uranyl acetate.

Processing

Tissue processing aims to remove water from tissues and replace it with a medium that solidifies to allow thin sections to be cut. Biological tissue must be supported in a hard matrix to allow sufficiently thin sections to be cut, typically 5 nm thick for light microscopy and 80-100nm thick for electron microscopy.

For light microscopy, paraffin wax is most frequently used. Since it is immiscible with water, the main constituent of biological tissue, water must first be removed in the process of dehydration. Samples are transferred through baths of progressively more concentrated ethanol to remove the water. This is followed by a hydrophobic clearing agent (such as xylene) to remove the alcohol, and finally, molten paraffin wax, the infiltration agent, which replaces the xylene. Paraffin wax does not provide a sufficiently hard matrix for cutting very thin sections for electron microscopy. Instead, resins are used. Epoxy resins are the most commonly employed embedding media, but acrylic resins are also used, particularly where immunohistochemistry is required.

Thicker sections of resin-embedded tissue can also be cut for light microscopy. Again, the immiscibility of most epoxy and acrylic resins with water necessitates the use of dehydration, usually with ethanol.

Embedding

After the tissues have been dehydrated, cleared, and infiltrated with the embedding material, they are ready for external embedding. During this process, the tissue samples are placed into molds embedding. During this process, the tissue samples are placed into molds along with liquid embedding material which is then hardened. This is achieved by cooling in the case of paraffin wax and heating in the case of the epoxy resins. The acrylic resins are polymerized by heat, ultraviolet light, or chemical catalysts. The hardened blocks containing the tissue samples are then ready to be sectioned. Because formalin-fixed, paraffin-embedded (FFPE) tissues may be stored indefinitely at room temperature, and nucleic acids may be recovered from the decades after fixation, making FFPE tissues an important resource for historical studies in medicine.

Sectioning

For light microscopy, a steel knife mounted in a microtome is used to cut 10-micrometer-thick tissue sections which are mounted on a glass microscope slide. For transmission electron microscopy, a diamond knife mounted in an ultramicrotome is used to cut 50-micrometer-thick tissue sections which are mounted on a 3-millimeter-diameter copper grid. Then the mounted sections are treated with the appropriate stain.

Staining

Biological tissue has little inherent contrast in either the light or electron microscope. Staining is employed to give both contrasts to the tissue as well as highlighting particular features of interest. Where the underlying mechanistic chemistry of staining is understood, the term histochemistry is used.

Hematoxylin and Eosin are the most commonly used light microscopical stains in histology and histopathology. Hematoxylin, a basic dye, stains nuclei blue due to an affinity to nucleic acids in the cell nucleus; eosin, an acidic dye, stains the cytoplasm in pink color.

Special staining

There are hundreds of other techniques that have been used to selectively stain cells and cellular components. Other compounds used to color tissue sections include safranin, Congo red, silver salts, and numerous natural and artificial dyes that were usually originated from the development of dyes for the textile industry.

Cytology *(Greek kytos "a hollow", -logia "study")* is the study of cells.

Cytology is the branch of life sciences that deals with the study of cells, derivatives of cells in terms of their structure, function, chemistry, reproduction and adaptation to various conditions of external environment.

All pathological processes in living organisms are accompanied by morphological and functional changes at the cellular level.

Cell is the basic structural and functional unit of all multicellular organisms. The processes we associate with the daily activities of organisms – protection,

digestion, elimination of wastes, movements, reproduction and even death – are all reflections of similar processes occurring within each of the billion cells that constitute the organism.

Cell is surrounded by a plasma membrane that separates it from external environment. Cell can be divided into two major compartments: the cytoplasm and the nucleus. The cytoplasm contains organelles and inclusions in the aqueous gel called cytoplasmic matrix.

Cells of all living organisms are divided into two types:

eukaryotic cells – contain nucleus;

prokaryotic cells – do not contain nucleus.

Those organisms which are composed of eukaryotic cells are named eukaryotes, whilst those composed of prokaryotic cells are referred to as prokaryotes. Most of the living organisms including animals and humans are eukaryotes; the only two examples of prokaryotes are viruses and cyanobacteria.

CELL THEORY. NON-CELLULAR STRUCTURES

Cell theory is the theoretical foundation of biology and medicine; it reflects the quintessence of all concepts of structure and functioning of cell as a basic unit of living organisms.

Actual postulates of the cell theory

1. Cell is a basic structural unit of all living organisms. It is capable of reproduction, metabolic activity (consumption and production of energy), sensitivity, adaptation and modification.

2. Cells of different organisms have the similar general organization; use the similar mechanisms for synthesis, transport and reproduction. The variability of different cells is determined by specific functions they carry out.

3. The cell reproduction occurs only by a division of maternal cell.

4. Cells constitute the organism. Multicellular organisms are extremely complicated “ensembles” of various specialized cells that compose integrated systems of tissues, organs and systems of organs.

Non-cellular structures

In animal organisms, despite cells, there are also found non-cellular structures that are derivatives of cells.

Non-cellular structures are divided into two types:

1) nucleated;

2) unnucleated.

Nucleated non-cellular structures arise as a result of fusion of several cells or incomplete cell division. Such structures are symplasts and syncytia.

Symplast is a large structure which consists of cytoplasm and numerous nuclei. Symplasts are found in skeletal muscle and the trophoblast of placenta.

Syncytium arises as a result of incomplete cell division, when new-formed cells do not separate from the maternal one and remain connected by cytoplasmic bridges. Such temporary structures can be found at one of stages of male germ cells formation.

Unnucleated non-cellular structures are products which are synthesized by cells. The most common examples of such structures are fibers and ground substance of connective tissue, which are produced by cells called fibroblasts. The blood plasma is also referred to as unnucleated non-cellular structure.

It is necessary to mention that unnucleated cells are also found in human body. Such “cells”, like red blood cells, platelets and keratinized cells of epidermis, are often called post-cellular structures, hence they have lost their nuclei in the process of their development. These cells carry out limited functions and are incapable of reproduction.

THE GENERAL STRUCTURE OF CELL

EUKARYOTIC CELL CONSISTS OF THREE MAJOR COMPONENTS:

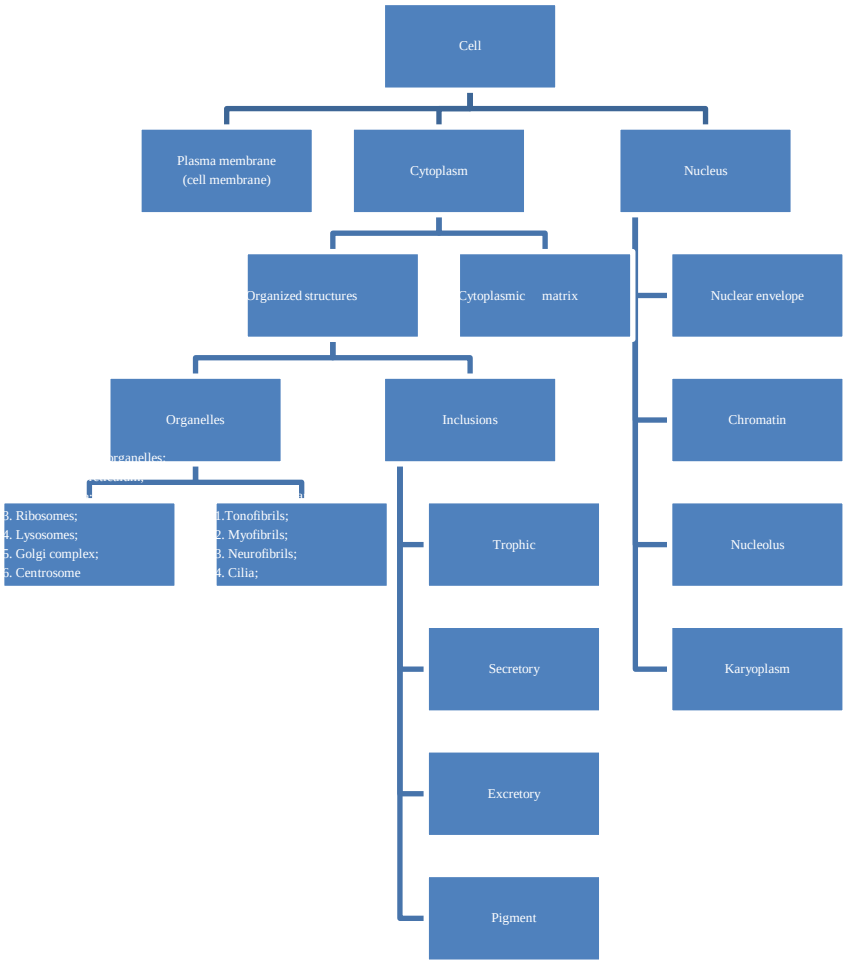
Plasma membrane; 2. Cytoplasm; 3. Nucleus.

Plasma membrane (plasmalemma, cell membrane) separates cell cytoplasm from neighboring cells or external environment.

Cytoplasm consists of cytoplasmic matrix and organized structures (organelles and inclusions).

Nucleus consists of nuclear envelope, karyoplasm, chromatin (chromosomes), and nucleolus.

All named components of cell interact with each other making it functioning as an integrated structure.



Scheme 1. Structural components of cell

PLASMA MEMBRANE

Plasma membrane (plasmalemma) represents the peripheral structure that forms an external covering of cell, and simultaneously separates and provides its interaction with external environment.

Structure

Plasma membrane consists of three layers:

1) external layer – glycocalyx;

2) lipid bilayer;

3) internal layer – cortical layer of cytoplasm.

Glycocalyx is formed by complexes of glycolipids and glycoproteins associated with the lipid bilayer. It is 3-4nm thick. Long branched carbohydrate chains form complexes with lipids and proteins that are the part of the lipid bilayer. The glycocalyx can be found in almost all animal cells. Polysaccharide chains of glycocalyx perform the function receptive apparatus, which helps cells "recognize" each other and interact with external microenvironment.

Lipid bilayer (biological membrane). The current interpretation of the molecular organization of the plasma membrane is reflected by the modified fluid-mosaic model devised by SJ Singer and GL Nicolson. According to this model the plasma membrane consists of phospholipid, cholesterol and protein molecules. The hydrophobic tails of phospholipids face each other, whilst the hydrophilic heads are, oppositely, pushed away from each other, thereby forming the lipid bilayer.

In most plasma membranes proteins constitute approximately half of the total membrane mass. Most of the proteins are embedded within the lipid bilayer or pass through it completely. Such proteins are called **integral** membrane proteins. The proteins of second type – semi-integral proteins- are partially embedded within the lipid bilayer. The third type of proteins is peripheral proteins, which are associated with lipid bilayer by strong ionic interactions. Hence the plasma membrane is dynamic structure the protein molecules can change their position within lipid bilayer depending on functional condition of cell.

Lability of components of the plasma membrane depends on number of cholesterol molecules it contains. Cholesterol molecules facilitate movements of proteins within lipid bilayer. The thickness of the lipid bilayer is about 5-7nm.

Cortical layer is the densest layer the plasma membrane (sometimes it is described as an outer layer of cytoplasm). This layer contains numerous microfilaments and microtubules that form a well-arranged network. Microfilaments and microtubules of the cortical layer form a cytoskeleton, provide movements of cell, and take part in exocytosis. The thickness of cortical layer is about 1 nm.

Functions of the plasma membrane

The main functions of the plasma membrane are:

delimiting;

transport;

receptivity;

formation of cell-to-cell junctions.

Delimiting and transport

Being separated from external environment, cell maintains its individuality; whilst due to the cell transport it can keep functioning. These two contradictory processes complement each other and provide maintenance of homeostasis of cell.

The transport of substances within and out of cell can be of two types: active transport and passive transport.

- Active transport uses energy of ATP to pump molecules against the concentration gradient (transport occurs from a low concentration of solute to a high concentration of solute).

- Passive transport does not require the ATP energy. It goes down the concentration gradient (from high to low concentration in order to maintain ionic equilibrium of cell).

Endocytosis is general term for process of transport in which substances **enter** the cell.

Exocytosis is general term for process of transport in which substances **leave** the cell.

In general two main mechanism of endocytosis are recognized in the cell:

Phagocytosis – is an uptake and ingestion of large molecules like bacteria and particles of other cells.

Pinocytosis – is ingestion of fluid and small protein molecules via small vesicles.

- Endocytosis includes the following sequential stages:

Sorption – an ingested molecule binds to a receptive protein molecule of the plasma membrane.

Invagination of the plasma membrane and formation of vesicles.

Separation of transport vesicles from the plasma membrane (sometimes a few vesicles can fuse with each other);

Digestion of the ingested molecules using lysosomal hydrolytic enzymes.

In some cases the molecule ingested by one side of the plasma membrane is surrounded by a transport vesicle and just passes across the cytoplasm and then it is ejected through the opposite side of the plasma membrane. This process is called **cytopempsis**.

Exocytosis is a process by which the cell releases molecules to the extracellular space.

There are the following types of exocytosis recognized in the cell:

secretion;

excretion;

recretion;

clasmatosis.

Term ***secretion*** refers to an ejection of substances which are the products of synthesis of the cell. The products of secretion are essential for functioning of organs and systems of the organism.

Excretion is an ejection of toxic waste products, which need to be removed out of the organism.

Recretion is a process of removing molecules out of the cell, in which the chemical structure of ejected substance is not affected by the process of cell metabolism (water, mineral salts).

Clasmatosis is a process in which the cell ejects its own components (impaired organelles etc.).

- Exocytosis includes four sequential stages:

Storage of molecules produced by the cell for export in sacs and vesicles of the Golgi complex and their sorting and packaging into transport vesicles;

Intracellular traffic of the transport vesicles towards the plasma membrane;

Fusion of membrane of the transport vesicle with the plasma membrane;

Discharge of contents of the transport vesicles to the extracellular space.

Receptivity

A cell reception of external stimuli is provided by the specialized receptor proteins of its plasma membrane. A carbohydrate chain bounded to the receptor protein determines the selectivity of cell interaction with one or another stimulus. The complex processes of intercellular recognition and interaction are essential for living of multicellular organisms.

Cell-to-cell junctions (contacts)

The junctions between neighboring cells in tissues and organs of multicellular organisms are represented by complex specialized structures called cell-to-cell junctions.

In general, all cell-to-cell junctions are divided into three groups depending on their functional role:

Anchoring junctions

Occluding (tight) junctions

Communicating junctions

~ **The anchoring junctions** include a) simple junction; b) adherens junction; c) desmosome.

• Simple junction: the plasma membranes of two neighboring cells approach each other to the distance of 15-20 nm. Any specific structures of the cell cytoplasm are not involved in formation of this type of junction. Interdigitation is one of the examples of the simple junction.

• Adherens junction: the projections of the plasma membrane of one cell interlock with the invaginations of the plasma membrane of neighboring cell, providing the mechanical adhesion between adjoining cells. This type of cell-to-cell junction is widely found in epithelial tissue, where it provides the formation continuous cell layer. The neighboring cells remain distance of 10-20 nm.

• Desmosome is a junctional complex that represents localized spot-like adhesions of 0,5 μm in diameter arranged at the lateral sides of the plasma membrane. Electron microscopy reveals that the desmosome has a complex structure. On the cytoplasmic side of the plasma membrane of each of the adjoining cells is a disc-shaped structure consisting of very dense material called the desmosomal attachment plaque. This structure anchors intermediate filaments. The filaments appear to loop through the attachment plaques and extend back out into the cytoplasm. They are thought to play a role in dissipating physical forces throughout the cell from the attachment site.

~ **Tight (occluding) junction** is a zone, also named zonula occludens, in which the plasma membranes of adjoining cells come in close contact to seal off the intracellular space. The zonula occludens appears not as a continuous seal but as a series of focal fusions between two cells. At high resolution it was estimated that these focal fusions are created by globules of special integral proteins of adjoining cells, which are arranged in lines. These lines of globules can cross over, thereby forming a network. From the side of cytoplasm this zone reveals numerous fibrils with diameter of 7 nm, which are oriented parallel to the surface of plasma membrane. The zone of such contact is impenetrable for molecules and ions. Tight junctions are usually found in epithelia, especially stomach and intestinal epithelia.

~ **Communicating junctions include**:

a) *gap junction* represents a communicating junction between adjoining cells through the special protein complexes – connexons, which form channels for transport of ions and molecules from cell to cell. The distance between the plasma membranes of two cells is 2-3nm. The area of the zone of connection measures 0,5-3 μm. Each connexon contains six subunits of an integral membrane protein connexin that is paired with a similar structure from the adjacent membrane. The pairs of connexons bridge the extracellular space between adjacent cells. The connexon in on cell membrane is aligned to dock with a corresponding connexon on a membrane of an adjacent cell, thus, allowing the communication between the cells. Such type of cell-to-cell junctions can be found in all types of tissues.

Synapses

Synapse is a special type of cell-to-cell junctions that allows only unidirectional transmission of impulses from one cell to another. This type of junction is characteristic only for the cells of nerve tissue.

MEMBRANES OF CELL

Biological membrane is a structural and functional unit of all cell membranes.

Structural and functional characteristics of biological membranes

All biological membranes represent thin (6-10nm) layers consisting of lipoproteins. The main chemical components of cell membranes are lipids (about 40%), proteins (about 60%), and, besides these, there are also found carbohydrates (about 5-10%).

Lipids constitute a big group of organic substances, which are almost not soluble in water (hydrophobic), and soluble in organic solvents and fats (lipophylic). The lipids of cell membranes are represented by phospholipids (glycerophosphates), sphingolipids, and steroid lipids – cholesterol.

The molecules of lipids of biological membrane are subdivided into two functionally different parts:

Hydrophobic part – unpolarized, uncharged, consists of fatty acids (tails);

Hydrophilic part – polarized, charged (heads).

In molecules of membrane proteins are usually also distinguished two parts:

polarized part – rich in charged amino acids;

unpolarized part – contains neutral amino acids (glycine, alanine, valine, leucine).

Depending on their location in relation to a lipid layer of membrane, the protein molecules are subdivided into:

integral proteins – totally embedded into the lipid layer;

semi-integral proteins – partially embedded into the lipid layer;

peripheral – attached to the outer surface of lipid layer.

On the basis of their biological function, the membrane proteins are subdivided into:

enzymes;

carrying proteins;

receptors;

structural proteins.

Carbohydrates are associated with membrane proteins (glycoproteins) or lipids (glycolipids). The amount of carbohydrates in membrane is the smallest one.

cytoplasm and its components

The cytoplasm represents a complex colloid system which is composed of cytoplasmic matrix (hyaloplasm), organelles, and inclusions.

Cytoplasmic matrix is a complex colloid system which is composed of various biopolymers (proteins, nucleonic acids, polysaccharides). It may change from fluid (sol) to elastic (gel) and back again to being fluid.

♦ The cytoplasmic matrix consists of water with dissolved organic and inorganic substances, and a trabecular network of 2-3nm thick protein fibers.

♦ The function of cytoplasmic matrix is to form the environment into which all structures of cell are embedded, and provide chemical interaction between them.

A lot of types of intracellular transport occur through the cytoplasmic matrix (transport of amono acids, fatty acids, nucleotides, sugars). The cytoplasmic constitutes for 50% of the total volume of cytoplasm.

Organelles and inclusions. Organelles are permanent and essential microstructures of all cells, which provide performing of vital functions of cells.

On the basis of their size, the organelles are subdivided into:

microscopic – visible under the light microscope;

submicroscopic – distinguishable only under the electron microscope.

On the basis of presence of membrane, the organelles are subdivided into:

membrane-limited;

non- membrane-limited.

♦Membranous organelles: 1) mitochondria 2) lysosomes 3) peroxisomes 4) Endoplasmic reticulum 5) Golgi complex	♦Nonmembranous organelles: 1) ribosomes, 2) microfilaments, 3)microtubules, 4) centrosome.

Depending on their function, all organelles are subdivided into:

♦General-function organelles– Mitochondria, lysosomes, peroxisomes, Endoplasmic reticulum, Golgi complex, ribosomes, microtubules, Microfilaments, centrosome.	♦Special function organelles –are derived from general function organelles, and are found only in particular types of cells: Cilia, flagella, myofibrils (muscle cells), neurofibrils (nerve cells).

MEMBRANOUS ORGANELLES

Mitochondria

Mitochondria are general-function, membrane-limited, microscopic organelle.

- ♦ Sizes: 0,5μm thick, 1-10 μm long;
- ♦Shape: oval, elongated
- ♦ Structure: it is surrounded by two membranes of 7nm thick:

Outer smooth membrane separates mitochondria from cytoplasmic matrtix; appears as a closed sac.

Inner mitochondrial membrane forms folds, named crists, facing inside the mitochondrion, and encloses the inner content of mitochondrion – mitochondrial matrix. Mitochondrial matrix is an electron-dense substance, containing thin filaments of 2-3nm thick and granules with a diameter of 15-20 nm. The filaments represent the DNA molecules, the granules are mitochondrial ribosomes.

♦ Functions of mitochondria:

Synthesis and storage of ATP energy, which occurs as a result of oxidative phosphorylation.

Synthesis of proteins. Mitochondria possess its autonomic system of protein synthesis. They are the unique organelles which have molecules of their own DNA, which is free of histone proteins. The processes of formation of ribosomes and synthesis of proteins that are not encoded by nucleus also occur within the ribosomes. These proteins are used for mitochondrial enzyme systems.

Regulation of water balance.

Lysosomes

Lysosomes are submicroscopic, general-function, membranous organelles.

♦Size: 0,2-0,4μm

♦ Shape: oval, spherical

♦ Structure: lysosomes contain proteolytic enzymes (it is known more than 60), which break down various biopolymers. These enzymes are enclosed in membranous sac, which prevents them from entering the cytoplasmic matrix.

The four types of lysosomes are distinguished:

Primary lysosomes;

Secondary lysosomes (phagolysosomes);

Autophagosomes;

Residual bodies.

Primary lysosomes are small (20-25) μm membrane-limited vesicles, filled with inactive hydrolytic enzymes (marker – acidic phosphatase).

Secondary lysosomes (phagosomes) are formed as a result of fusion between primary lysosomes and phagocytic vesicles. The enzymes of primary lysosome contact with biopolymers and break them down into monomers. The last ones are transported through the membrane to the cytoplasmic matrix, where they are involved in several metabolic processes.

Autophagosomes are constantly found in plant and animal cells. Their structure remains that of the secondary lysosomes, the difference is that the

vesicles contain fragments or even full cytoplasmic structures, like mitochondria, ribosomes, or glycogen granules.

Residual bodies contain the rests which were not totally dissolved, and small amount of hydrolytic enzymes.

♦Functions: digestion of biogenic macromolecules, modification of products, produced by a cell, using hydrolases.

Peroxisomes

Peroxisomes are submicroscopic, membranous, general-function organelles.

♦Size: 0,3-1,5μm.

♦ Shape: oval.

♦ Structure: peroxisomes are membrane-bounded bodies filled with granular matrix. The central part of the matrix of peroxisomes usually reveals crystalloid structures which consist of fibrils and tubules.

Peroxisomes are formed at the extended portions of cisterns of Endoplasmic reticulum. They are especially numerous in the cells of liver and kidneys. The matrix of peroxisomes is composed of oxidative enzymes, particularly catalase and other peroxidases. The catalase breaks down the hydrogen peroxide, which is toxic substance, thus protecting the cell.

♦Function: utilization of hydrogen peroxide, breakdown of ethanol, uric acid, oxidation of fatty acids.

Endoplasmic reticulum

Endoplasmic reticulum is a submicroscopic, general-function, membrane-bounded organelle.

The two types of endoplasmic reticulum are distinguished:

Smooth endoplasmic reticulum (sER) consists of short anastomosing tubules.

♦ Size: the diameter of tubules is 50-100 nm.

♦ Functions: lipid and steroid metabolism (synthesis of phospholipids, fatty acids, steroids, cholesterol), carbohydrate metabolism (glycogen metabolism); detoxification of noxious substances; sequestering of Ca^{2+} ions (in muscle tissue).

2) ***Rough endoplasmic reticulum (rER)*** appears as a series of interconnected, membrane-limited, flattened sacs called cisternae, with ribosomes attached to the exterior surface of the membrane.

♦ Size: the diameter of cisternae varies from 20 to 1000nm.

♦ Functions: due to the presence of ribosomes, rough endoplasmic reticulum carries out the function of protein synthesis (90%-for export, 10%- for cell itself). Rough endoplasmic is also involved in formation of membranous structures of the cell.

Golgi apparatus (complex)

Golgi apparatus is a microscopic, general-function, membrane-bounded organelle, which is responsible for the final modifications and formation of all substances produced by the cell.

♦ Structure: Golgi apparatus is represented by a series if stacked, flattened, membrane-limited sacs or cisternae, with a diameter of 25 nm, and tubular extensions. A stack of sacs and cisternae is named **dictyosome**.

Each dictyosome consists of densely packed 5-10 interconnected flattened sacs and cisternae, which are separated by a tin layer of cytoplasmic matrix. Each cistern has a changing thickness; in its central part the membranes are closely attached to one another, while the peripheral part forms extensions, named ampullae. Besides cisternae, numerous vesicles are also found in Golgi complex.

Each dictyosome consists of proximal (cis-face) and distal part (trans-face). The proximal part faces nucleus; the distal part – plasma membrane.

♦Functions: Golgi apparatus functions in post-translational modification, sorting, and packaging of proteins, segregation and modification of lipids and carbohydrates, formation of polysaccharides and mucopolysaccharides, formation of primary lysosomes.

NONMEMBRANOUS ORGANELLES

Ribosomes

Ribosomes are submicroscopic, general-function, nonmembranous organelles, which represent elementary units of synthesis of protein and polypeptide molecules.

♦ Size of functioning ribosome: 25x20x20 nm.

♦ Shape: resembles mushroom

♦ Structure: ribosomes represent complex ribonucleoproteins, which are composed of proteins and RNA molecules in a ratio of 1:1.

The ribosome consists of two subunits:

small subunit;

large subunit.

Each subunit is composed of ribonucleoprotein cord, in which rRNA interacts with different proteins.

Ribosomes can form clusters connected with messenger RNA - polysomes. Solitary ribosomes and polysomes can also lie freely within the cytoplasm or be bounded to the membrane of rough ER. .

♦ Function – protein synthesis. Free ribosomes produce proteins for the cell itself (proteins of cell membranes, enzymes); while the ribosomes associated with rough ER produce proteins for export (secretion).

Centrosome

Centrosome is a microscopic, general-function, nonmembranous organelle which participates in formation of mitotic spindle and serves as the main microtubule-organizing center (MTOC).

This organelle is found in all somatic cells of animals and humans, except female germ cells (oocytes).

♦ Structure: centrosome is composed of two centrioles surrounded by centrosphere. In the cell, which is not preparing for division, the centrosome is found near the nucleus. A pair centriole is called diplosome.

Centrioles are built from circumferentially disposed nine microtubule triplets, which form a hollow cylinder of 0,2μm wide and 0,3-0,5 μm long. The triplets are connected via special structures-“handles”. The “handles” are composed of protein ***dynenin***. Dynein is characterized by ATPase activity, which provides the movement of centrioles. The system of microtubules in centrioles can be described by a formula: (9x3)+0, showing the absence of microtubules in the center of centriole.

A maternal and a daughter centriole are distinguished in the diplosome. The end of daughter centriole is directed perpendicularly to the surface of maternal centriole. Each centriole is surrounded by fibrillar matrix, sometimes there are also found accessory structures, which are not connected to centrioles – satellites.

Centrosphere – is a cytoplasmic matrix which surrounds centrioles and lacks organelles. The centrosphere is penetrated by microtubules.

When the cell is preparing for division, the centrioles of diplosome move to the opposite ends of the cell, and each of them gives a rise to one new centriole. This process is called duplication.

♦ Functions: centrioles participate in induction, polymerization of tubulins and formation of microtubules. Before mitosis centriole is one of the centers of polymerization of microtubules of the mitotic spindle. Centriole – is a growth center of microtubules, and axoneme of cilia and flagella.

Microfilaments

Microfilaments are submicroscopic, general-function, nonmembranous organelles, which act as **cytoskeleton** of the cell.

Depending on their structure and functions the microfilaments are subdivided into three types:

1) Proper filaments;

2) Intermediate filaments.

• **Proper filaments** are present in virtually all types of cells and localized in the cortical layer of cytoplasm (immediately under the plasma membrane).

♦ Structure: proper filaments are thin filaments of 5-7nm in diameter which consist of proteins: actin, myosin, tropomyosin, α-actinin.

♦ Functions: proper microfilaments serve as intracellular contractile apparatus, which provides not only cell motility, but also intracellular movements, like flow of cytoplasm, movements of mitochondria and transport vesicles, and cytokinesis during cell division.

• **Intermediate filaments** are composed of proteins.

♦ Structure: intermediate filaments represent thin filaments which form bundles of 10-15nm in diameter. The cells of different types of tissues are characterized by the specific protein that composes their intermediate filaments. For example, intermediate filaments of epithelial cells are composed of keratin protein, those of the connective tissue – of desmin protein.

♦ Function: are responsible for maintenance of the shape of cell.

Microtubules

Microtubules are submicroscopic, membranous organelles, which build elastic and, at the same time, stable cytoskeleton.

♦ Structure: microtubules are built of globular proteins – tubulins, polymerizing in an end-to-end fashion, and thereby forming rounded subunits of 5nm. The wall of microtubule is composed of densely packed subunits; 13 subunits form one circle of microtubule. The external diameter of microtubule measures approximately 24nm, the lumen of microtubule – 15nm. Microtubules compose highly organized organelles, like centrosome and basal bodies, are the principal components of cilia and flagella.

♦ Function: maintenance of cell shape, cell movement, movement of chromosomes during mitosis and meiosis, movement of cilia and flagella.

Cilia and flagella

Cilia and flagella are specialized organelles that can be found in particular cells of different organisms.

Cilia represent thin cylindrical projections of cytoplasm.

♦ Size: 200nm wide and 5-10μm high.

♦ Structure: cilium, from its basis to apex, is covered by a plasma membrane. The core of cilium is represented by axial filament (axoneme). Axoneme is a complex structure that consists predominantly of microtubules. The proximal part of cilia (basal body) is embedded into the cytoplasm. The diameters of axoneme and basal body measure approximately 150 nm.

Axoneme (axial filament) is composed of 9 microtubule duplets connected via “handles”. A pair of central microtubules is located in the center of axoneme. A system of microtubules of axoneme is described by formula: (9x2)+2.

Basal body consists of 9 microtubule triplets connected via “handles”. The system of microtubules of basal body is described by formula: (9x3)+0, as that of the centriole. Sometimes even two basal bodies, lying at the right angle to one another, can be found in the base of axoneme.

Axonemes and basal bodies are structurally interconnected: two microtubules of basal body’s triplet are at the same time the microtubules of axoneme’s duplets.

Flagella are thin cylindrical projections of cytoplasm, whose structure resembles that of the cilia.

♦ Size: diameter: 200nm, length: 150μm.

Like cilia, flagella are composed of axoneme and basal body.

♦ Functions: the cells that possess cilia and flagella are capable of movement. Immotile cells can move liquid or small particles by the movement of their cilia.

Inclusions

Cytoplasmic inclusions are temporary components of the cell, as they can appear or disappear depending on metabolic activity of the cell.

The following types of inclusions are distinguished:

1. Secretory;

2. Trophic;

3. Excretory;

4. Pigment.

Secretory inclusions are rounded structures of different shapes that contain biologically active substances formed as a result of secretory activity of the cell (hormones, secretions etc).

Trophic inclusions can include droplets of neutral fats, glycogen and protein molecules.

Excretory inclusions do not contain any enzymes or biologically active substances, and are waste products that should be removed out of the cell.

Pigment inclusions could be exogenous (carotene, dust particles, dyes) or endogenous (hemoglobin, hemosiderin, bilirubin, melanin, lipofuscin). Presence of pigment inclusions usually changes the color of tissue.

THE CELL NUCLEUS

The nucleus is a membrane-limited compartment that contains genetic information of the cell.

Structure and chemical composition of the nucleus

The nucleus consists of chromatin (chromosomes), nucleolus, karyoplasm (nucleoplasm) and nuclear envelope.

Most of cells which can undergo division possess only one nucleus. But there are also found cells with two (liver cells) and even several nuclei (osteoclasts of the bone tissue).

♦ Size – varies from 3-4 to 40 μm

Each type of cell is characterized by a constant ratio of the size of nucleus to the volume of cytoplasm. This ratio is called **index of Hertwig.** Depending on the index of Hertwig all cells are divided into two groups:

nuclear cells –are characterized by high index of Hertwig;

cytoplasmic cells – are characterized by low index of Hertwig.

♦ Shape of the nucleus varies among different types of cells. It can be spherical, bean-shaped, circular, segmented etc.

♦ Localization – the nucleus always has its distinct position in the cell cytoplasm. For example, in columnar cells of stomach it occupies the basal portion of the cytoplasm.

The nucleus can be found two functional conditions:

mitosis (the process of division)

interphase (the period between divisions).

During the interphase the nucleus of living cell appears empty and exhibits only the nucleolus. The other structures of the nuclei could be revealed only if it is affected by an injurious agent and undergoes paranecrosis (a reversible condition between life and death). From this condition the cell can return to life or die.

Dying cells have visible nuclear alterations. These include:

1) karyopyknosis – condensation of chromatin leading to shrinkage of the nucleus (it appears as dense basophilic mass);

2) karyorrhexis – fragmentations of nuclei;

3) karyolysis - the disappearance of nuclei due to complete dissolution of DNA.

Functions of the nucleus: 1) keeping and transfer of hereditary information; 2) control of cell growth, metabolism and reproduction.

Chromatin

Chromatin is a complex of DNA, RNA and proteins, which is responsible for the characteristic basophilia of the interphase nucleus.

Structurally chromatin is an analogue of chromosomes.

Two forms of chromatin are found in the nucleus:

heterochromatin;

euchromatin.

Heterochromatin is a highly **condensed** chromatin, which **stains** with hematoxylin and basic dyes. It is **evident** in the light microscope. Heterochromatin is divided into:

structural;

facultative.

Structural heterochromatin represents the areas of chromosomes that always remain condensed.

Facultative heterochromatin is capable of decondensation and can transform into euchromatin. Heterochromatin predominates in metabolically **inactive** cells.

Euchromatin is a **dispersed** form of chromatin. It is found during the interphase and represents **decondensed** areas of chromosomes. This type of chromatin **does not stain** with histological dyes and is **not evident** in the light microscope. Euchromatin indicates **active** chromatin – it can be used for reading and transcription of genetic information.

During mitosis all euchromatin becomes maximally condensed and forms chromosomes. In this period the chromosomes do not carry out any synthetic functions. The chromosomes can be found in functional conditions:

active (working) – when the chromosomes are decondensed and the processes of transcription and replication occur within the nucleus.

inactive – when the chromosomes are maximally condensed and carry out the function of distribution and passage of genetic information to the daughter cell.

In some cases the whole chromosome, even during the interphase, remains condensed. For example, one of the X-chromosomes of females is condensed at the early stages of embryogenesis and does not function. This X-chromosome was named the Barr body.

In different cells the sex chromatin appears differently:

1) in neutrophilic leukocytes it looks like a drumstick;

2) in epithelial cells of mucosa it is spherical structure adjacent to the nuclear envelope.

A series of electron-microscopic examinations revealed that the interphase chromatin is composed elementary chromosome fibrils with thickness of 20-25 nm.

The chemical composition of the chromatin fibrils includes complexes desoxyribonucleotids which are composed of:

DNA;

Specialized chromosome proteins;

RNA.

The ratio between amounts of DNA, proteins and RNA is 1:1,3:0,2. The DNA constitute 30-40% of chromatin mass. The total length of all DNA molecules in all chromosomes in one human cell is about 170 cm.

The proteins of chromatin constitute 60-70% of its dry mass. They include two types:

histone proteins;

non-histone proteins.

♦*Histone proteins* are alkaline proteins, which contain basic amino acids (mostly lysine and arginine). Histone proteins are unequally distributed along the DNA molecule. One protein possesses 8 histone molecules which form nucleosome. These 10-nm-diameter particles represent the first level of chromatin folding and are formed by the coiling of the DNA molecule around a protein core. This step shortens the DNA molecule by approximately sevenfold relative to the unfolded DNA molecule.

♦ Non-histone proteins constitute 20% of the number of histone proteins. In the interphase nucleus non-histone proteins form a structural network called protein matrix. This matrix is a foundation that determines morphology and metabolism of the nucleus.

Besides chromatin, the nucleus also possesses perichromatin fibrils, perichromatin and interchromatin granules. These structures contain RNA and are found in almost all nuclei.

Perichromatin fibrils are 3-5 nm thick; perichromatin granules measure 45 nm in diameter; interchromatin granules - 21-25 nm in diameter.

Nucleolus

Nucleolus is the densest structure of nucleus, which is well-evident in unstained cell. Nucleolus is a derivative of chromosome, one of its locus with the highest concentration of the most transcriptionally active RNA. Nucleolus is not an independent structure or organelle.

♦ Size - 1-5 μm.

♦Shape - spherical.

Examined under the electron microscope, nucleolus exhibit two morphologically different parts:

1) granular material (pars granulosa);

2) fibrillar material (pars fibrosa).

Granular material consists of granules with diameter of 15-20 nm. These granules represent the subunits of ribosomes. The granular material occupies the peripheral part of nucleolus.

Fibrillar material occupies the central part of nucleolus and represents the ribonucleoprotein cords of precursors of ribosomes.

The ultrastructure of nucleolus depends on the activity of RNA synthesis: if the RNA is actively synthesized the nucleolus contains numerous granules; if the RNA is not actively produced the nucleolus appears as dense basophilic fibrillar cord.

Nuclear envelope

The nuclear envelope consists of:

Outer nuclear membrane;

Inner nuclear membrane;

Perinuclear cisternal space of 20-60 nm width.

Each membrane of the nucleus is 7-8 nm thick. In general, the nuclear envelope appears as hollow double-layered sac, which separates the contents of nucleus from cytoplasm.

The outer nuclear membrane immediately contacts with the cytoplasm, resembles the membrane of the endoplasmic reticulum and, in fact, continues with the rER membrane. Polyribosomes are usually attached to the cytoplasmic side of the outer nuclear membrane. It's surface is not smooth and exhibits numerous projections, vesicles and tubules towards the cytoplasm.

The inner nuclear membrane is supported by rigid network of intermediate filaments (fibrous lamina). It contains several lamina-associated proteins that bind to chromosomes.

The two membranes of the envelope are perforated by **nuclear pores**. The nuclear pores are formed from the merging of the inner and outer membranes of the nuclear envelope. At numerous sites, the paired membranes are perforated by 70-80nm "openings" through the envelope. These opening are filled with complex globular and fibrillar structures. The complex of membrane perforations and these structures is known as nuclear pore complex.

The nuclear pore complex (NPC) is composed of about 50 different nuclear pore proteins (nucleoporines).

This central framework is inserted between the **cytoplasmic ring** and the **nuclear ring.** From the cytoplasmic ring, eight short **protein fibrils** protrude into the

cytoplasm and point toward the center of the structure. The nucleoplasmic ring complex anchors a **nuclear basket** (or nuclear "cage" that resembles a fish trap) assembled from eight thin filaments joined distally by an adjustable **terminal ring**. The cylinder shaped central framework encircles the **central pore** of the NPC, which acts as a close-fitting diaphragm or gated channel. In addition, each NPC contains one or more water-filled channels for transport of small molecules.

♦Functions:

Barrier – separates contents of nucleus from contents of cytoplasm, provides selective transport of macromolecules between nucleus and cytoplasm.

Control of intranuclear order – fixation of chromosome material within the three-dimensional lumen of nucleus.

Karyoplasm

Karyoplasm is a fluid component of nucleus, into which all components of nucleus are embedded. Karyoplasm is a nuclear analog of cell cytoplasm.

Cell cycle

The cell cycle represents a self-regulated sequence of events that controls cell growth and cell division. For renewing cell populations, the goal of the cell cycle is to produce two daughter cells, each containing

chromosomes identical to those of the parental cell. The cell cycle consists of two principal phases: the interphase, representing continuous growth of the cell, and the M phase (mitosis), characterized by the partition of the genome. The interphase is subdivided into three phases, G1 (gap1) phase, S (synthesis) phase, and G2 (gap2) phase.

The G1 phase is usually the longest and the most variable phase of the cell cycle, and it begins at the end of M phase. During the G1 phase, the cell gathers nutrients and synthesizes RNA and proteins necessary for DNA synthesis and chromosome replication.

In the S phase, DNA is replicated. Initiation of DNA synthesis marks the beginning of the S phase, which is about 7.5 to 10 hours in duration. The DNA of the cell is doubled during the S phase, and new chromatids are formed that will become obvious at prophase or metaphase of the mitotic division.

In the G2 phase, the cell prepares for cell division. During this phase, the cell examines its replicated DNA in preparation for cell division. This is a period of

cell growth and reorganization of cytoplasmic organelles before entering the mitotic cycle.

The G2 phase may be as short as 1 hour in rapidly dividing cells or of nearly indefinite duration in some

polyploid cells and in cells such as the primary oocyte that are arrested in G2 for extended periods.

There are some cells in the human which stay out of cycle – cells of G_0-period. They do not enter the S-phase of interphase, and do not divide.

There are the following types of such cells:

1. Stem cells – immature, low-differentiated cells which retain their ability to divide, but stay in a **G_0-period** for a long time.

2. Cells that lost their capacity of division but undergo specialization and differentiation. Such cells are subdivided into two types:

a) cells that started their differentiation and irreversibly lost their capacity of division (mature blood cells, cells of epidermis);

b) cells that even after differentiation can return to the cell cycle and divide (hepatocytes of liver).

3. Highly differentiated and specialized cell that irreversibly lose their capacity of division; their life span is the as the life of an organism (nerve cells).

MITOSIS

Mitosis is nuclear division plus cytokinesis, and produces two identical daughter cells during prophase, metaphase, anaphase, and telophase. Interphase is often included in discussions of mitosis, but interphase is technically not part of mitosis, but rather encompasses stages G1, S, and G2 of the cell cycle.

1 Prophase. Chromatin in the nucleus begins to condense and becomes visible in the light microscope as chromosomes. The nucleolus disappears. Centrioles begin moving to opposite ends of the cell and fibers extend from the centromeres. Some fibers cross the cell to form the mitotic spindle. The nuclear membrane dissolves, marking the beginning of prometaphase. Proteins attach to the centromeres

creating the kinetochores. Microtubules attach at the kinetochores and the chromosomes begin moving.

2. Metaphase. Spindle fibers align the chromosomes along the middle of the cell nucleus. This line is referred to as the metaphase plate. This organization helps to ensure that in the next phase, when the chromosomes are separated, each new nucleus will receive one copy of each chromosome.

3. Anaphase. The paired chromosomes separate at the kinetochores and move to opposite sides of the cell. Motion results from a combination of kinetochore movement along the spindle microtubules and through the physical interaction of polar microtubules.

4. Telophase. Chromatids arrive at opposite poles of cell, and new membranes form around the daughter nuclei. The chromosomes disperse and are no longer visible under the light microscope. The spindle fibers disperse, and cytokinesis or the partitioning of the cell may also begin during this stage. In animal cells, **cytokinesis** results when a fiber ring composed of a protein called actin around the center of the cell contracts pinching the cell into two daughter cells, each with one nucleus.

Chromosomes

During mitotic division, chromatin undergo condensation to form chromosomes. Each chromosome is formed by two chromatids that are joined together at a point called the centromere. The double nature of the chromosome is produced in the preceding synthetic (S) phase of the cell cycle, during which DNA is replicated in anticipation of the next mitotic division. The area located at each end of the chromosome is called the telomere. Telomeres shorten with each cell division. Recent studies indicate that telomere length is an important indicator of the lifespan of the cell. With the exception of the mature gametes, the egg and sperm, human cells contain 46 chromosomes organized as 23 homologous pairs (each chromosome in the pair has the designated X and Y. Females contain two X chromosomes; males contain one X and one Y chromosome. The chromosomal number, 46, is found in most of the somatic cells of the body and is called the

diploid (2n) number. To simplify the description of chromosomal number and DNA changes during mitosis and meiosis, we use the lower case letter (n) for chromosome number and lower case letter (d) for DNA content.

ENDOMITOSIS

Endomitosis is mitosis taking place without dissolution of the nuclear membrane, and not followed by cytoplasmic division, resulting in doubling of the number of chromosomes within the nucleus.

Meiosis

Meiosis is a specialized type of cell division that reduces the chromosome number by half, creating four haploid cells, each genetically distinct from the parent cell that gave rise to them. Meiosis includes two sequential mitotic divisions without interphase between them. The characteristic feature of meiosis is crossing over – an exchange of genetic material between homologous chromosomes.

ODESA NATIONAL MEDICAL UNIVERSITY

DEPARTMENT OF HISTOLOGY, CYTOLOGY AND EMBRYOLOGY

METHODICAL RECOMMENDATION OF LECTURES

for dentistry faculty

THEME: «Basics of general and comparative embryology.»

Approved on the methodical conference of department

«____»_____ 20___., protocol №_____

Head of Department, doc._____ Tiron O.I.

Approved on the methodical conference of department

«____»_____ 20___., protocol №_____

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Head of Department, doc._____ Tiron O.I.

Theme: "Basics of general and comperative embryology." -2h.

1.Relevance of the topic.

Recently, embryology has come into ever closer contact with two biological disciplines: cytology and genetics. The study of the basics of embryonic development is important for understanding the sources and mechanisms of formation of tissues (histogenesis) and organs (organogenesis) of a person.

The study of human embryonic development makes it possible to establish the characteristics of the development of the human embryo. Knowledge of the processes of fertilization, cleavage, implantation, gastrulation, as well as the developmental features of the placenta, extraembryonic membranes and organs of the embryo is necessary for the future doctor for the rational prevention of fetal anomalies and malformations.
It makes it possible to think over and evaluate the entire cycle of biological phenomena accompanying pregnancy, to prevent the consequences of the adverse effects of environmental factors and everyday life. The rational management of pregnant women, the management of childbirth, the implementation of many therapeutic and preventive measures in obstetrics, pediatrics and gynecology is impossible without a deep knowledge of embryology.

2. Objectives of the lecture:

a) learning:

- analysis of the main stages of embryology;

- modern ideas about the male and female gamets;

- process of formation of embryonic germ layers;

- the origin of tissues and organs;

b) educational:

- to bring to the students the importance of studying the structural and functional features of general embryology for the getting of basic knowledge about the origin of germ layers;

- to interpret the morphological and functional features of organs and disorders of the stages of human development, to determine their significance for practical medicine;

- to form students' professional significance of the topic. Discuss the issues of deontology.

3. Plan and organizational structure of the lecture.

№№	The main stages of the lecture and their content	Objectives in levels of abstraction	Lecture type. Lecture equipment	Time management
1	2	3	4	5
I. 1. 2. II	*Preparatory stage.* Determination of the learning goal. Providing positive motivation. *The main stage* Presentation of the		Tables. Slides.	5% 85-95%

III.	lecture material according to the plan: 1. Morpho-functional characteristics of the male and female gamets. 2. Germ layers. Origin. Structure. Functions. 3. Critical periods of human embryogenesis. *The final stage.* Summary of the lecture. General conclusions. Lecturer's answer to possible questions. Self-study assignments.	I. Descriptive. II. Analytical - synthetic, high quality.	In accordance with the publication "Guidelines for the planning, preparation and analysis of lectures." List of literature, question, task.	5%

4. Content of the lecture material:

- structural and logical scheme of the content of the topic;

- the text of the lecture. (Provided)

5. Materials for activating students during the lecture:

1) One fetus usually develops in a woman's uterus, however, in about 1% of pregnancies, multiple twin fetuses develop and are born. Identical twins develop from a single fertilized cell. It occurs rather at the blastocyst stage as a result of the division of the embryoblast into two symmetrical parts.Some embryologists believe that symmetrical separation of the embryo is possible during gastrulation - at the stage of development of the embryonic shield. Identical twins share a common placenta, a common or separate amniotic membrane, always of the same sex. Fraternal twins occur when two or more eggs are fertilized at the same time.

Each has its own placenta, amnion and develops independently. They can be of the same gender or different.

2) In medical practice, the procedure of artificial (in vitro) fertilization is now widely used to treat male and female infertility. The first child conceived outside the mother's body - Louise Brown - was born in 1976. In Great Britain. Her godparents were the English embryologists Edwards and Stentow.

3) In connection with the development of modern reproductive technologies, a new medical and legal concept has appeared - surrogacy. Ovocytes are obtained from a woman; using the sperm of the husband or donor, in vitro fertilization is performed; an embryo at the stage of 18-32 blastomeres is implanted into the uterus of another woman who will carry the fetus until the moment of birth.

When carrying out in vitro fertilization, it is possible to choose the sex of the unborn child: one blastomere is removed from the obtained several blastocysts, analyzing the chromosome sets of these cells, the presence of the X or Y-sex chromosome is established, blastocysts with the desired chromosome set are inserted into the uterus.

4) Embryological knowledge is necessary for future doctors for the rational prevention of fetal anomalies and malformations, as well as for the prevention of adverse effects of environmental factors and everyday life during pregnancy.

Questions:

1.Male gamets. Structure. Functions.

2.Female gamets. Classification. Structure. Functions.

3. Fertilization. Distant and contact interaction of germ cells. Zygote formation.

4. Cleavage. Chronology of the process. The structure and localization of the embryo during this period.

5. Blastula formation. Embryoblast and trophoblast, their significance

6. Implantation. Phases.

7. Gastrulation. Formation of germ layers and notochord.

8. Differentiation of ectoderm. Neurulation.

9. Differentiation of the mesoderm, its derivatives.

10. Differentiation of endoderm, its derivatives.

11. Formation and derivatives of mesenchyme.

12. Critical periods of development.

6. General material and methodological support of the lecture:

- classrooms;

- equipment;

- equipment;

- illustrative materials.

List of recommended literature .

The main one:

1.Lutsyk O.D., Tchaikovsky Y.B. Histology, cytology, embryology Vinnytsia, New Book, 2018.
2.Barinov E.F., Tchaikovsky Y.B. General histology and embryology of internal organs: textbook.Kyiv: Medicine; 2013
3.Wojciech Pawlina. Histology: textbook and atlas. WSV: Medicine, 2021.

Additional:

1.Histology and embryology of internal organs: textbook / E.F. Barinov, Y.B. Tchaikovsky, O.M. Sulaeva et al.
2.Cytology of human organs and tissues edited by L.S.Bolgova. Kyiv: Book-plus, 2018, p.288

Addition

Theme: "The basics of general and comparative embryology."

Embryology is the study of developmental process of embryo from the moment of fertilization until the moment of birth.

Medical embryology includes studies of molecular, cellular, and structural factors contributing to the formation of an organism; metabolic and functional characteristics of placental barrier (system mother-placenta-fetus); and causes of birth defects formation.

The principal aims of embryology

1. Investigation of various endogenous and exogenous factors and the role of microenvironment in development and functioning of gametes.

2. Investigation of mechanisms that control reproductive function and provide maintenance of homeostasis in human embryo.

3. Investigation of critical periods in human embryogenesis.

4. Cultivation of oocytes, embryos and their subsequent implantation in the endometrium of uterus.

5. Investigation of sources and mechanisms of tissues development.

Studying of embryology is impossible without having basic knowledge of comparative embryology, hence evolutionary the embryonic development of all mammals could be characterized by the similar principal stages, sequence and consistent patterns. For correct comprehension of the process of human individual development it is necessary to carry out analysis and compare the principal stages of human development with those of other animals.

It was estimated that the principal stages and consistent patterns of embryogenesis were established during the process of evolutional development of the mammals. At the same time some stages of human embryonic development are analogous to those of lower organized chordate animals; hence the process of human embryonic

development is a result of long-term evolution and it partially reflects the features of development of other animals.

The idea of correlation between individual and historical (evolutional) development was proposed at the beginning of the XIX century by the eminent scientists K.Berr and F. Muller, who came to conclusion that a large group of animals at the early stages of development reveal much more common features than individual differences.

The quintessence of this idea is the Haeckel-Muller law (or Recapitulation theory), which proclaims that in developing from embryo to adult, animal go through stages resembling successive stages of evolution of their remote ancestors ("**ontogenesis recapitulates phylogenesis"**).

ONTOGENESIS

***Ontogenesis*-** is a process of individual development of an organism from the moment of fertilization until death.

Periods of ontogenesis

I Prenatal – period of intrauterine development (duration – 280 days);

a) initial period (early embryo) – first week

b) embryonic period (embryo) – 2^{nd}-8^{th} week, formation of primary cavity, organogenesis and appearance of heart beating on 21^{st} day

c) fetal (until birth) – placentation, differentiation of tissues.

II Postnatal – period of development after the birth;

early postembryonic

subsequent development, maturation, ageing and death.

Initial period include the following stages:

zygote – beginning of the DNA synthesis;

cleavage – beginning of synthesis of the all types of RNA;

morula – the cells are totipotential;

blastocyst - loss of totipotency; the cells are determined to formation of embryonic and extraembryonic structures;

gastrula – appearance of the germ layers and stem cells.

Ontogenesis is always preceded by progenesis hence the formation of new organism is impossible without formation and maturation of male and female gametes.

PROGENESIS

Progenesis – the process of formation, development and maturation of male and female gametes.

Gametes, unlike somatic cells, contain haploid number of chromosomes. All chromosomes of gametes are autosomes except the one which is referred to as sex gonosome.

Male gametes could contain X or Y-sex chromosome.

Female gametes could contain only X-chromosome.

The mature gametes are incapable to proliferation and characterized by low level of metabolism.

Male reproductive cells

Male gametes – spermatozoa are about 70 μm in size and capable of active movement (30-50mm per second in human). In human it is formed several thousand million spermatozoa.

♦*Spermatogenesis* – the process of formation and maturation of spermatozoa.

The structure of spermatozoa

The spermatozoon is composed of two principal parts: 1) head; 2) tail.

The head of spermatozoon contains dense nucleus with haploid number of chromosomes (22 autosomes and 1 sex chromosome). Depending on what kind of sex chromosome they possess, the spermatozoa are divided into two types:

androspem – carry Y-chromosome,

gynosperm – carry X-chromosome.

♦ The nucleus is rich in nucleoproteins and nucleohistones. The anterior wall of nucleus is covered by a vesicle called acrosome. The acrosome is a derivative of Golgi complex.

The acrosome contains a complex of enzymes, among which the most important are hyaloronidase and proteases (trypsin), which are crucial for dissolving ovum's coats.

Externally the head is surrounded by a plasma membrane.

The tail (flagellum) is composed of:

connecting piece, which contains **two centrioles** (proximal and distal). The axial filament (axoneme) extends from the distal centriole.

midpiece, which contain two central microtubules and nine pairs of peripheral microtubules spirally surrounded by several mitochondria (mitochondrial sheath);

tail piece contains axial filament, which resembles cilia;

end piece, which contains solitary contractive filaments.

The tail of spermatozoon, like its head, is surrounded by a plasma membrane.

The functions of spermatozoa

1. Fertilization of the ovum. By means of its tail the spermatozoa is capable to move in distinct direction determined by the specific substances which are produced by an ovum – *gynogamones.*

2. React on the chemical stimuli – *chemotaxis.*

3. Can move in opposite direction to the flow of fluid – *rheotaxis*.

4. In optimal conditions can remain their capacity to fertilization during 36-88 hours.

5. The favorable condition for spermatozoa is slightly alkaline environment.

Female reproductive cells

Female gametes – ova (oocytes) are developed in ovaries. In human there are produced several hundreds oocytes during the whole life.

The ovum is spherical cell, whose size can reach up to several cm. The characteristic features of ovum are big amount of cytoplasm and presence of yolk. The ovum, unlike spermatozoon, is not capable of movement.

Classification of ova

Depending on the amount of yolk the ova are divided into the following types:

1. Alecithal ova have no yolk in cytoplasm;

2. Oligolecithal ova have small amount of yolk in cytoplasm

a) primary oligolecithal – in primitive chordate, which are characterized by quick development via the stage of larva;

b) **secondary oligolecithal** – in mammals (placental) and **human**.

3. Mesolecithal ova contain moderate amount of yolk (amphibians).

4. Polylecithal ova contain enormous amount of yolk. (birds, reptiles, fishes).

Depending on the distribution of yolk the ova are classified into the following types:

1. Isolecithal – the yolk is uniformly distributed through the cytoplasm. Such distribution is usually characteristic for oligolecithal ova.

2. Centrolecithal - yolk is concentrated in the center of ovum's cytoplasm.

3. Teleolecithal - are polylecithal ova, where the yolk is concentrated in one hemisphere (vegetal pole) and organelles remain in another hemisphere (animal pole).

The structure of ovum

The ovum of placental mammals is relatively small (50-150 μm). It is surrounded by zona pellucida and a layer of follicular cells, which provide its nutrition. The ovum is composed of coats, cytoplasm and nucleus.

♦ Coats – all ova are surrounded by the cytolemma (oolemma or primary coat), most of them also possess the secondary coat – a carbohydrate-protein coat, and some types of ova are covered by the tertiary coat – eggshell.

♦ Cytoplasm (ooplasm) contains nutritive material – yolk. Besides this the ooplasm stores a range of proteins: histones, ribosomal structural proteins, tubulin etc.

♦ Among other organelles, the rough ER exhibits strong development. The number of mitochondria is moderate. At the periphery of cytoplasm the Golgi complex and small cortical granules containing glycosaminoglycans are situated.

♦ Yolk – is a type of inclusion which appears as granules or larger globes and plates. The yolk is composed of phospholipids, proteins and carbohydrates. The structural unit of yolk is a complex of lipovitelin (lipoprotein) and phosvitin (phosphoprotein).

The ovum is characterized by cell polarity. The more yolk it contains the more conspicuous is its cell polarity. The pole of cytoplasm which contains yolk is called vegetal, and the pole which contains organelles and nucleus – animal.

♦ Nucleus possesses haploid number of chromosomes. Intensive synthetic processes (RNA, DNA synthesis) take place at the period of growth.

EMBRYOGENESIS

Embryogenesis – a period of intrauterine development of humans and animals which begins at the moment of fertilization, includes formation and development of all tissues, organs and system of fetus, and ends with a birth of child.

The embryonic development is phasic and accompanied by gradual quantitative and qualitative changes. The process of embryogenesis includes the following phases:

fertilization;

cleavage and formation of blastula;

gastrulation and differentiation of germ layers;

histogenesis (differentiation of tissues);

organogenesis (differentiation of organs);

formation of systems of organs.

***Fertilization* –** is the process, by which male and female gamete fuse, which results in restoration of the diploid number of chromosomes and formation of unicellular embryo - **zygote**.

Fertilization is preceded by *insemination* – introduction of sperm into female reproductive tract in case of internal fertilization, or into the environment where the ovum is situated in case of external fertilization.

In human the fertilization normally takes occurs in the ampullary region of the uterine tube.

Spermatozoa are not able to fertilize the oocytes immediately upon arrival in the female genital tract, but must undergo capacitation and acrosome reaction to acquire this capability.

• Capacitation is a period of activation in the female reproductive that in human lasts approximately 7 hours. Much of this activation occurs in the uterine tube and involves epithelial interactions between the sperm and the mucosal surface of the tube. A significant role in this process is played by progesterone (the hormone of corpus luteum of ovary). Only capacitated sperm can undergo acrosome reaction.

• Acrosome reaction occurs after binding to zona pellucida of the oocyte and is induced by zona proteins. This reaction culminates in the release of enzymes needed to penetrate the zona pellucida, including acrosin- and trypsin-like substances.

• The phases of fertilization include:

1. Distant interaction is performed by several non-specific factors which facilitate the "meeting" of reproductive cells. Special chemical substances (gamones) are discharged by both spermatozoa and ovum. The female gamones are called gynogamones, the male gamones – androgamones. Gynogamones type I – are low-molecular non-protein substances which are believed to attract spermatozoa. Gynogamones type II – are species-specific proteins that cause gluing of spermatozoa in case of their reaction with complementary androgamone type II. Androgamones type I – being antagonists of gynogamones type I they depress sperm motility.

2. Contact interaction and penetration into the ovum is performed by mean of the acrosome. The enzymes required for penetration of corona radiata (hyaloronidase, trypsin) are released from the acrosome and destroy cell contacts between follicular cells (acrosome reaction). This phenomenon called denudation of the oocyte results in total dissolution of zona pellucida. The plasma membranes of

ovum and spermatozoon fuse. The enzymes released from the acrosome dissolve the corona radiata and break down glycosaminoglycans of the zona pellucida. The separated follicular cells form conglomerate which follows the ovum while it moves via the uterine tube. The movement of fertilized ovum is provided by the peristaltic contraction and synchronic movements of cilia of the mucosa of the uterine tube.

3. Penetration of the ovum. Both the head and the tail of the spermatozoon enter the cytoplasm of oocyte. As a result of the release of cortical oocyte granules, which contain lysosomal enzymes, the oocyte membrane becomes impenetrable for other spermatozoa and the zona pellucida alters its structure and composition to prevent sperm penetration (cortical reaction). This reaction prevents polyspermy (penetration of more than one spermatozoon into the oocyte). After the penetration the head of spermatozoon makes a 180° degree turn; its nucleus becomes swollen and forms *male pronucleus*. The ovum's nucleus forms *female pronucleus*. Male and female pronuclei eventually come into close contact and lose their nuclear envelopes. The fusion of male and female pronuclei initiates the spiralization of chromosomes and formation of metaphase plate. A nucleus formed by two preexisting pronuclei is called **synkaryon**. The spermatozoon delivers centriole, which is essential for mitotic division of zygote, to the oocyte. In this way the zygote containing both maternal and paternal genes is formed.

At the same time the redistribution of cytoplasmic material of zygote and subsequent division of its cytoplasm into two zones (zone with high concentration of yolk granules and zone with high concentration of pigment granules) occurs. This phenomenon is called **ooplasmic segregation**. During further development each zone of the cytoplasm gives rise to distinct part of the organism. Such zones are called **presumptive zones**.

***Cleavage* –** is a series of mitotic divisions of zygote, which results in its transformation into multicellular organism called blastocyst. As the protein synthesis is inhibited, the cells, known as blastomeres, become smaller with each cleavage division. Due to the absence of the G_1- period of interphase, the size of an embryo does not exceed that of the zygote. The cleavage lasts from 1^{st} to 6^{th} day of pregnancy.

The type of cleavage differs among different animals. It is determined by amount and distribution of yolk within an ovum.

Types of cleavage

Depending on the type of ovum, the following types of cleavage are distinguished:

1. Total equal cleavage is characteristic for primary oligolecithal, isolecithal ova (amphioxus).

2. Total unequal cleavage is characteristic for mesolecithal ova; hence the mitotic divisions of vegetal pole occur not so fast as that of the animal pole.

3. Partial or meroblastic cleavage is characteristic for teleolecithal ova. In such case only the apical part of ovum undergoes mitotic divisions (birds).

4. **Total asynchronous unequal cleavage** or holoblastic is characteristic for secondary oligolecithal isolecithal ova (mammals, **human**).

Approximately three days after fertilization the divisions of cells of an embryo result in formation of 16-cells morula. **Morula –** is a compacted aggregation of blastomeres which resembles mulberry.

Inner cells of the morula constitute the inner cell mass, and surrounding cells compose the outer cell mass. The inner cell mass gives rise to tissue of embryo proper, and the outer cell mass forms the trophoblast, which later contributes to the placenta.

About the time the morula enters the uterine cavity, fluid begins to penetrate through the zona pellucida into the intercellular spaces of the inner cell mass, which results in formation of cavity – blastocele. At this time the embryo is **blastocyst**. Cells of the inner cell mass, now called the **embryoblast**, are at one pole, and those of the outer cell mass, or **trophoblast**, flatten and form the epithelial wall of the blastocyst **(blastoderm)**. The zona pellucida has disappeared, allowing implantation to begin.

Types of blastula

Coeloblastula forms as a result of total equal cleavage. The blastoderm is formed of a single layer of cells. The blastocele is centric.(Amphioxus)

Amphiblastula is formed as a result of total unequal cleavage. The blastoderm is multi-layered. The blastocele is eccentric. (Amphibians)

Discoblastula is formed as a result of partial meroblastic cleavage. The blastocele is small and situated below the blastoderm. (Birds, reptiles).

***Gastrulation* –** a period of embryogenesis that includes differentiation of the germ layers: ectoderm (outer layer), endoderm (inner layer), and mesoderm (middle layer).

Types of gastrulation

The process of gastrulation could be carried out in four main ways:

Migration – movement of part of blastomeres from the wall to the center of an embryo and formation of endoderm.

Invagination – inward of the wall of blastula into its center.

Epiboly – spread of an outside cell layer (where the mitosis is faster) to envelope a deeper layer (where the mitosis is relatively slow). It happens when the blastomeres of vegetal pole contain high amount of yolk (in amphibians).

Delamination – is a process accompanied by tangential splitting of the wall of blastula, which results in formation of two germ layers – primary ectoderm (outer) and primary endoderm (inner). Such type of gastrulation is characteristic for birds and mammals.

The types of gastrulation depend on preceded phases of development and amount of yolk in ovum. The vertebrates are characterized by combination of two or three types of gastrulation.

In the human the gastrulation lasts from 7^{th} to 17^{th} day of embryogenesis and includes 2 phases:

I phase (7-14^{th} day) involves formation of inner (endoderm) and outer (ectoderm) germ layers. As a result of *delamination* the layer of cells that faces the blastocyst cavity splits out from the primitive node, thereby forming the primary endoderm (hypoblast). At the same time the cells of the primitive node which lie under the hypoblast undergo *cavitation* (due to the cumulation of liquid a cavity is formed in the center of the nodule; the cells which surround this cavity obtain epithelium-like shape – the amniotic vesicle is formed).

The opposite edges of the primary endoderm turn down, fuse together and form the yolk vesicle. The adjacent parts of both vesicles (amniotic and yolk) form the embryonic disc, which gives rise to the body of an embryo.

Simultaneously with the formation of amniotic and yolk vesicles, beginning from the 8^{th} day of development, occurs the differentiation of *extraembryonic*

mesoderm, which gives rise to chorion and amniotic stalk (the basis of the future umbilical cord).

II phase lasts from 15^{th} to 17^{th} day of embryonic development and involves formation of the embryonic mesoderm. This process is realized migration of the cells of primary ectoderm in the space between two germ layers.

The space between germ layers is filled with the embryonic connective tissue – mesenchyme.

The mesenchymal cells migrate from mesoderm, endoderm and ectoderm. That is why two types of mesenchyme are distinguished:

endomesenchyme – originates from the endo- and mesoderm;

ectomesenchyme – originates from the ectoderm.

These two types of mesenchyme are morphologically indistinguishable, but they give rise to different structures:

- endomesenchyme – to the tissues of internal environment;

- ectomesenchyme – to auditory bones, the connective tssues of head.

The cell migration from the primitive node results in formation of axial chord of an embryo – chorda. At the end of the second week the hematopoietic cords and germs of primary blood vessels appear in the yolk sac.

The finger-like process – allantois, grows inwards the amniotic stalk of the intestinal endoderm. Blood vessels of the yolk sac grow inwards the wall of allantois and chorionic villi, which are supplied with maternal blood. Allantochorion, which is formed as a result of these processes, provides nutrition and gas exchange of fetus at this stage of development.

HISTO- and ORGANOGENESIS

Histo-organogenesis – is the process that involves differentiation and formation of tissue, organs and systems of organs of the fetus through several sequential stages: induction, determination, cell reproduction, migration, growth of cells, intercellular interactions, and cell death.

Induction – the process by which cells and tissues in embryo direct the development of adjacent cells and tissues. An example of induction is the development of the eye lens from epidermis under influence of the eye cup, which grows toward the skin from the brain. As the eye cup comes into contact with any

neighbouring epidermis, it transforms that particular region into a lens. The exact nature of the stimulus for lens induction is not known, although ribonucleic acid (RNA) has been implicated as a messenger.

Determination – is progressive restriction in developmental potential of the embryonic cells via blocking of particular components of genome.

Determination is a foundation of process of differentiation. Differentiation – is a process through which cells change to a more specialized type.

Cell reproduction – is the process by which cells divide to form new cells.

The process of renewal and restoration of biological object is called regeneration. There are distinguished three types of regeneration:

physiological – continuously occurs in healthy organism (renewal of blood, epithelial cell etc.);

reparative – occurs after injuries and trauma (healing of the wound);

pathological – normally does not occur; such type of regeneration is characteristic for cells of malignant tumors.

Migration – is the massive translation of cells from one location to another, which results in formation of tissues and organs.

Growth of cells – is a series of processes, which include development and organization of cells from the moment of their division until next division.

Intercellular interactions perform the leading role in differentiation of embryonic germ layers. For example, it was estimated that for development and existence of epithelium it is essential to be supported by connective tissue.

Cell death – is an unaltered process of termination of all its functions and interaction with external environment.

ODESA NATIONAL MEDICAL UNIVERSITY

DEPARTMENT OF HISTOLOGY, CYTOLOGY AND EMBRYOLOGY

METHODICAL RECOMMENDATION OF LECTURES

for dentistry faculty

Theme: “The concept of tissue. Epithelial tissue.”

Approved on the methodical conference of department

«____»_____ 20___., protocol №_____

Head of Department, doc._____ Tiron O.I.

Approved on the methodical conference of department

«____»_____ 20___., protocol №_____

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«____»_____ 20___., protocol №_____

Head of Department, doc._____ Tiron O.I.

Theme: “The concept of tissue. Epithelial tissue.”-2h.

1.Relevance of the topic

Epithelial tissues or epithelium cover the surface of the body, mucous membranes and serous membranes of internal organs, and also create most of the glands. In this regard, the integumentary and glandular epithelium are distinguished. The integumentary epithelium occupies a borderline place in the body, separating the internal environment from the external, and at the same time participating in the exchange of substances between the body and the environment, carrying out the functions of absorption and excretion of metabolic products.

In addition, the integumentary epithelium performs an important protective function, protecting the tissues that lie beneath it from a variety of chemical, mechanical, infectious and other influences. Finally, the epithelium, which covers the internal organs that are located in the body cavities, creates conditions for their movement.
The glandular epithelium performs a secretory function, synthesizes and secretes ecretions that are involved in various processes that occur in the body. The epithelium always functions as an one layer, it has a high regenerative capacity.A common primary feature of epithelial tissues is polarity, which follows from their borderline position in the body. For the property of polarity in cells, two parts are distinguished: the apical apex and the basal. Knowledge of the characteristic morphological features of epithelial tissues in normal conditions will help to understand the essence of many pathological processes, correctly diagnose and analyze the results of the disease.

2. Purpose of the lecture

2.1. Learning

To give an idea of the morphofunctional and histological features of epithelial tissues, and the specificity of epithelial tissues.

2.2. Educational

To form students' professional significance of the topic. Discuss deontology issues

3. Plan and organizational structure of the lecture.

Lecture stages	Contents of the lecture stages	Aim	Lecture equipment	Time management
Preparatory stage	Relevance of the topic and goal setting.	I	Tables. Slides. Dummies.	3 min.
	Definition of embryology as a science	II		3 min.
The main stage	The concept of tissue	III		8 min.
	Morpho-functional characteristics of simple squamos epithelium	III		12 min.
	Structure and function of simple cuboidal epithelium	III		12 min.
	Structure and function of pseudostratified epithelium	III		12 min.
	Structure and function of stratified epithelium	III		30 min.
The final stage	Summary of the lecture. General conclusions.			5 min.
	Self-study assignments			5 min.

4. Topic content

application

5. Materials for activating students during the lecture.

1) Definition of the concept of tissue. General characteristics of tissues.

2) Classification of tissues.

3) Sources of tissue development.

4) Epithelial tissue. General characteristics.

5) Morphological classification of epithelial tissues.

6) Phylogenetic classification of epithelial tissues.

7) Characteristics of the endothelium.

8) Characteristics of the mesothelium.

9) Characteristics of simple cuboidal epithelium.

10) Characteristics of a single-layer prismatic (cylindrical) epithelium.

11) Characteristics of pseudo-stratified epithelium

6. General material and methodological support of the lecture.

1.Tables:

- Types of epithelium

-Classification of epithelial tissues

2.Slides according to the list of tables

3 Dummies

List of recommended literature .

The main one:

1.Lutsyk O.D., Tchaikovsky Y.B. Histology, cytology, embryology Vinnytsia, New Book, 2018.
2.Barinov E.F., Tchaikovsky Y.B. General histology and embryology of internal organs: textbook.Kyiv: Medicine; 2013
3.Wojciech Pawlina. Histology: textbook and atlas. WSV: Medicine, 2021.

Additional:

1.Histology and embryology of internal organs: textbook / E.F. Barinov, Y.B. Tchaikovsky, O.M. Sulaeva et al.
2.Cytology of human organs and tissues edited by L.S.Bolgova. Kyiv: Book-

plus, 2018, p.288

Addition

Theme: "The concept of tissue. Epithelial tissue."

Epithelial tissue makes covering for body surfaces, lines body cavities and constitutes glands.

The characteristic feature of this tissue is that it is composed only of cells, named epithelial cells, and it is almost devoid of extracellular matrix.

The epithelial cells are connected to each other via different types of cell-to-cell junctions and form a solid layer that lies on the basal lamina. Under the microscope the basal lamina appears as homogenous plate of 1μm in thickness.

The basal lamina separates epithelium from underlying loose connective tissue.

The epithelial cells are characterized by cell polarity. It means that each epithelial cell has two cell domains – apical domain facing the external environment, and basal domain lying on the basal lamina. The apical and the basal domain are different in their structure:

The basal domain contains nucleus and main organelles;

The apical domain may contain microvilli, brush border, cilia or flagella.

Epithelial tissue has a high capacity of both physiological and reparative regeneration due to its immediate contact with the external environment. The regeneration occurs due to the presence of stem cells, which are specific for each type of epithelium.

CLASSIFICATION OF EPITHELIA

Nowadays, there are two classifications of epithelia, which are based on its origin (phylogenetic classification) or its structure (morphological classification).

According to phylogenetic classification, we distinguish six types of epithelium:

1) **Skin epithelium** (epidermal) arises from ectoderm; structure: stratified and pseudostratified epithelium; localization: skin, oral cavity, esophagus, cornea, vagina.

2) **Intestinal epithelium** (enterodermal) arises from entoderm; structure: simple columnar epithelium; localization: stomach, small and large intestine; function: absorption.

3) **Kidney epithelium** (nephrodermal) arises from mesoderm; structure: simple cuboidal or columnar epithelium; localization: kidney tubules;

Function: reabsorption of primary urine.

4) **Coelomic epithelium** arises from splanchnotomes of mesoderm; structure: simple squamos epithelium; function: delimiting and secretion.

5) **Ependymoglial epithelium** arises from neural tube; structure: simple epithelium; function: lines fluid-containing cavities of CNS;

6) **Angiodermal epithelium** (endothelium) arises from mesenchyme; structure: simple squamos epithelium; localization: lines blood and lymphatic vessels heart; function: protection, absorption.

MORPHOLOGICAL CLASSIFICATION

This classification is based on structural and functional characteristics of different types of epithelia. According to this classification we distinguish two types of epithelia: covering epithelia and glandular epithelia.

Covering epithelia, in its turn, is subdivided into

1.Simple epithelia:

a)

- squamos;
- cuboidal;
- columnar;

2.Stratified epithelia:

a) keratinized;

squamos;

b) non-keratinized:

- squamos;

b) pseudostratified
- columnar

- cuboidal;
- columnar;

c) transitional.

STRUCTURE OF DIFFERENT TYPES OF EPITHELIA

I Simple squamos epithelium (endothelium and mesothelium)

Endothelium lines blood and lymphatic vessels, and also heart chambers. It represents a singular layer of squamos (flattened) cells – endothelial cells, which rest on the basal lamina.

*Endothelial cells are polygonal cells with irregular borders; may possess 2-3 nuclei. Endothelial cells are relatively poor in organelles and contain pinocytotic vesicles in their cytoplasm.

♦ Function: transendothelial transport of oxygen, carbon dioxide and other substances; also participates in regulation of blood flow.

* Mesothelial cells are flattened, polygonal cells with irregular borders; may contain 2-3 nuclei. The apical domain of mesothelial cells possesses solitary microvilli.

♦ Function: secretion and absorption of serous liquid, prevents friction of inner organs.

II Simple cuboidal epithelium covers a part of the renal tubules (proximal and distal), excretory ducts of glands, small bronchi. The epithelial cells have equal height and width. The epithelial cells of proximal renal tubules possess brush border and basal striations. The basal striations appear because of high concentration of mitochondria in the basal domain of the cell.

♦ Function: reabsorption of substances from primary urine into the blood.

III Simple columnar epithelium are of three types:

1) *epithelium with a brush border* lines intestine, gallbladder.

2) *ciliated epithelium* lines oviducts; the cells possess cilia on their apical domain, which moves an egg towards the uterus.

3) *glandular epithelium* lines stomach; contains cells that are capable of production of mucous secretion and that's why were named glandular cells. Along this these cells, the glandular epithelium contains endocrine cells, which regulate the activity of digestive tract.

IV Pseudostratified epithelium lines respiratory tract and some parts of reproductive system.

This epithelium includes four types of cells:

ciliated cells;

long and short basal cells;

goblet cells;

endocrine cells

♦ Basal cells are considered to be cambial (stem cells), which are capable of regeneration and differentiation into ciliated and goblet cells.

Basal cells are wedge-shaped, their wide basal surface lies on the basal lamina, while their sharp apical surface inserts between the ciliated cells and does not achieve the surface of epithelium. .

♦ Ciliated cells are also wedge-shaped cells, their narrow basal surface lies on the basal lamina, while their wide apical surface, which possesses cilia, achieves the surface of epithelium.

♦ Goblet cells, hence their name, are goblet-shaped cells, which produce mucous secretion on the epithelial surface.

♦ Endocrine cells (their basal domain possesses granules) produce biologically active substances – hormones.

Pseudostratified epithelium is a type of simple epithelium; hence all epithelial cells lie on the basal lamina. Due to the different shapes of the cell, the nuclei are located at different levels, which makes this epithelium appear as stratified one.

V. Stratified squamos non-keratinized epithelium

Localization: cornea, oral cavity, esophagus, vagina, anal part of rectum.

This epithelium is composed of three layers of cells:

Stratum basale is composed of columnar epithelial cells, which lie immediately on the basal lamina. The cells of this include stem cell, capable of mitotic division; that's why is layer is also named cambial layer.

Stratum spinosum consists of polygonal epithelial cells that possess projections inserted between the apical portions of the underlying basal cells. These cells form several layers and possess projections that resemble spines.

Stratum superficiale is the outermost layer consisting of flattened cells.

VI. Stratified squamos keratinized epithelium covers the skin and is named **epidermis**.

The epidermis includes 5 layers, where occurs the transformation of epithelial cells into anucleate squamos cells filled with keratin protein. This process is called keratinization.

1) **Stratum basale** , also called stratum germinativum, is represented the single layer of cells, which rest on the basal lamina. It contains the stem cells from which new cells, the keratinocytes, arise by mitotic division. As new keratinocytes arise in this layer by mitotic division, they move into the next layer, thus beginning their process of upward migration. Besides the stem cells and keratinocytes, the stratum basale contains melanocytes, Merkel's cells, and Langerhans' cells.

The keratinocytes have a cuboidal or low columnar shape, basophilic cytoplasm and oval, rich in chromatin nucleus. Their cytoplasm contains keratine intermediate filaments and organelles; they also may contain various amounts of melanin.

The melanocytes – are pigment cells, which form processes branching towards the epidermal surface. On histological specimens the melanocytes are revealed by the silver impregnation method. The melanocytes synthesize melanin; their cytoplasm does not contain tonofibrils, but it is rich in ribosomes and melanosomes.

The Langenharns' cells are the type of macrophages, provide the immune defense. They are dendritic-appearing cells with cytoplasm containing Birbeck granules, which have an appearance of tennis racket. Langerhans' cells encounter and process antigens entering through the skin.

2) Stratum spinosum is formed by 5-10 layers of polygonal keratinocytes. Their cytoplasm contains tonofibrils, which take part in formatiom of desmosomes. The

basal cells and cells of inner layers of stratum spinosum form the cambial zone of epidermis.

3) Stratum granulosum is formed by 3-4 layers of cells. At this layer filaggrin, a protein aggregating the keratin tonofilaments, is synthesized within the keratinocytes. As a result of aggregation of the keratin tonofilaments, the cytoplasm of keratinocytes stores the basophilic granules of keratohyaline. Involucrin and keratolinin form a protein layer under the plasmolemme, protecting it from action of hydrolytic enzymes of keratosomes and lysosomes, which are activated by the Langenharns' cells. The appearance of keratohyaline granules is an indicative of the beginning of keratinization process.

4) Stratum lucidum is formed by 3-4 layers of squamos cells, within whose cytoplasm the nucleus and organelles are completely disrupted; the keratohyaline granules fuse into the refractile mass, which consists of aggregated keratin fibrils and amorphous matrix.

5) Stratum corneum of scores of layers of annucleate squamos cells largely filled with keratin filaments. Filaggrin provides the further aggregation of intermediate filaments within the keratinocytes. The keratinocytes store the air vesicles; the light cavity is appears at the site of nucleus. The intercellular lipid barrier and the keratinocytes provide impenetrability of the epidermis. The keratinocytes of stratum corneum are eventually sloughed off at the skin surface. The mechanism of desquamation is controlled by keratinosomes – the modificated lysosomes, which dissolve desmosomes and provide the separation of cornified cells from each other.

The stratum corneum is the layer that varies most in thickness, being thickest in thick skin. The thickness of this layer constitutes the principal difference between the epidermis of thick and thin skin.

The interrelated processes of differentiation and keratinization of keratinocytes constantly occur in the epidermis. These processes provide regular renewal of stratum corneum, which is characterized by mechanical and chemical resistance, high hydrolytic capability, poor heat conduction, and impenetrability for bacteria and their toxins.

VII. Transitional epithelium lines the urinary passages – renal pelvis, urethers, urinary bladder, and urethra. The epithelium begins in the minor calyces as two cell layers and increases to an apparent four to five layers in the ureter and as many as six or more layers in the empty bladder. However when the bladder is distended, as few as three layers are seen. This change reflects the ability of the cells to accommodate to

distension.

Transitional epithelium consists of three layers of cells:

Basal layer consists of small rounded dark cells.

Transitional layer is composed of polygonal cells.

Superficial layer contains large dome-shaped cells, which possess 2-3 nuclei.

GLANDULAR EPITHELIUM. GLANDS.

Glandular epithelium consists of glandular cells that produce and discharge specific secretions on the surface of skin, mucous membranes, within the cavities of the inner organs (exocrine glands); or directly into the blood or lymph (endocrine glands).

The cytoplasm of glandular (secretory) cells exhibits numerous secretory inclusions and strongly developed rough Endoplasmic reticulum.

The glandular epithelium composes glands, which are subdivided into two big groups on the basis of the way the release secretion:

Exocrine glands release their secretion on the surface of epithelium. All exocrine glands are composed of two parts: secretory portion (acinus); excretory ducts	Endocrine glands do not possess excretory ducts and release thaeir secretion directly into the blood or lymph.

Besides this, glands are classified on the basis of their structure, type of secretion, and location in respect to the epithelial layer.

On the basis of location in respect to the epithelial layer, all glands are subdivided into:

Endoepithelial glands – do not exceed the borders of the epithelial layer. In the human, the only example of such glands is goblet cell, which is referred to as

unicellular endoepithelial gland. The goblet cells are found within the epithelium of respiratory tract and intestine.

Exoepithelial glands are situated within the connective tissue that underlies the epithelial layer; they are connected with epithelial layers through the excretory duct. The exoepithelial glands are multicellular. Depending on the number of excretory ducts they are subdivided into **simple glands**, which possess only one excretory duct, and **compound glands**, which possess to or more excretory ducts.

Simple glands, depending on the number of secretory portions, are subdivided into two types:

Branched glands – possess two and more secretory portions;

Non-branched glands – possess only one secretory portion.

Compound glands are always branched, as they possess several excretory ducts that end with several secretory portions.

- On the basis of the shape of secretory portion, glands are classified into:

tubular;

alveolar;

tubulo-alveolar.

Tubular – the shape of secretory portion is tube-like;

Alveolar- the shape of secretory portion is sac-like.

- On the basis of the mode of secretion, the glands are subdivided into:

merocrine;

apocrine;

holocrine.

Merocrine glands – the cell releases its secretion by exocytosis. The destruction of the secretory cell after discharge of secretion **does not** take place at all. Most glands release their product in this way.

Apocrine glands- the apical portions of cells are pinched off and lost during the secretory process. This results in a secretory product that contains a variety of molecular components including those of the membrane. (mammary glands).

Holocrine glands – the secretory breaks apart, the contents of the cell become the secretory product. (sebaceous glands).

Depending on the chemical composition of secreted product, the glands are subdivided into: serous, mucous, mixed (sero-mucous), sebaceous, and sweat glands.

Structure of glandular cells

The shape of glandular cells varies significantly and might change depending on the phase of secretion. Such cells usually possess quite large nucleus with rough surface.

The glandular cells that produce protein (serous) secretion contain strongly developed rough ER.

The glandular cells producing non-protein secretions (lipids, steroids) contain strongly developed smooth ER.

All types of secretory cells are characterized by presence of well developed Golgi complex, where transport vesicles are formed, and numerous mitochondria. The cytoplasm contains a big amount of inclusions. The glandular cells are also characterized by cell polarity.

PHASES OF SECRETION

Secretion represents the process, when the cell produces and releases some synthesized products.

The process of secretion includes 4 phases:

Absorption;

Synthesis and storage;

Release;

Restoration.

Absorption : the glandular cells absorb various substances, which are essential for synthesis of secretion (water, salts, ions, amino acids, monosaccharides, fatty acids), from blood and lymph.

Synthesis and storage: in the ER the absorbed substances are used for the synthesis of secretion (protein secretion – rough ER, non-protein secretion – smooth ER). The produced products are transported to Golgi complex, where they are modified, stored, and packed into transport vesicles.

Release: the secretory vesicles are released out of the cell by apocrine, holocrine or merocrine mode of secretion.

Restoration: the secretory cells return to their initial condition.

Usually these phases occur sequentially, constituting the secretory cycle, but sometimes they can occur simultaneously, which is characteristic for the spontaneous secretion.

ODESA NATIONAL MEDICAL UNIVERSITY

DEPARTMENT OF HISTOLOGY, CYTOLOGY AND EMBRYOLOGY

METHODICAL RECOMMENDATION OF LECTURES

for dentistry faculty

THEME: «The Blood.»

Approved on the methodical conference of department

«____»_____ 20___., protocol №_____

Head of Department, doc._____ Tiron O.I.

Approved on the methodical conference of department

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Head of Department, doc._____ Tiron O.I.

Topic: “The Blood.”-2h.

1. Relevance of the topic

Blood is a crucial component of the human well-being, it performs transport and trophic functions, which consist of the transfer substances that the body receives with food, metabolic products, hormones, and other biologically active substances. Blood takes part in the delivery of oxygen from the lungs to other organs and the removal of carbon dioxide, performing the respiratory function. Together with the nervous and endocrine systems, blood takes part in maintaining homeostasis - the constancy of the internal environment of the body. The protective function is to provide cellular and humoral immunity.

Blood and lymph are special types of tissues of mesenchymal origin that form the internal environment of the body. They have a liquid consistency and consist of two main components: plasma (intercellular substance) and shaped elements (erythrocytes, leukocytes, and platelets). Blood cells are free cells of connective tissue since they are not connected either with each other or with cells of any other type.

Moreover, unlike most other connective tissue cells, they are not fixed in a certain position by the intercellular substance. Knowledge of the morphology of blood is necessary not only for hematologists but also for doctors of any profession since blood is one of the tissues that quickly respond to abnormalities in the physiological state of tissues. In a healthy person, blood corpuscles are in certain quantitative ratios, which are usually called a hemogram. Differentiated counting of leukocytes (leukocyte formula) is an important for characterizing the state of the organism. The study of the percentage composition of blood corpuscles and their tinctorial features is widely used in the clinical practice of doctors of all specialties.

2. Purpose of the lecture

2.1. Learning

To acquaint students with the concept of "Tissues of the internal environment", with the morphology and histophysiology of blood and lymph, hemogram leukocyte formula.

2.2. Educational

To form students' professional significance of the topic. Discuss the issue of deontology.

3. Plan and organizational structure of the lecture.

Lecture stages	Contents of the lecture stages	Aim	Lecture equipment	Time management
Preparatory stage	Relevance by those and goal setting	I	Tables. Slides. Dummies.	3min.
	The concept of the blood system	II		3 min.
The main stage	Blood plasma	III		12 min.
	Morphological and functional characteristics of erythrocytes	III		10 min.
	Ultramicroscopic structure of the erythrocyte membrane	III		12 min.
	Morphofunctional characteristics of leukocytes	III		20 min.
	General characteristic of hematopoiesis	III		20 min.
The final stage	Summary of the lecture. General conclusions			5 min.
	Self-study assignments			5 min.

4. Content by those

Addition

5. Materials for activating students during the lecture.

1) Blood. General morphological and functional characteristics of blood.

2) Blood plasma. Blood plasma components.

3) Characteristics of blood plasma proteins.

4) Erythrocytes. Structure. Functions.

5) Leukocytes. Classification of leukocytes.

6) The structure of neutrophilic granulocytes. Function.

7) The structure of oxyphilic (eosinophilic) granulocytes. Function.

8) Lymphocytes. Features of the structure. Function.

9) Monocyte, structure, function. 10) Platelets, structure, function.

11) Lymph, components. Characteristic. Function.

12) Hemogram. Leukocyte formula.

13) Hematopoiesis. General characteristics of the stem cell.

6. General material and methodological support of the lecture.

Tables:

1. Human blood (smear)

2. Mesenchyme

3. Hemogram

4. Leukocyte formula

Slides:

1. Various forms of erythrocytes

2. Eosonophilic leukocyte

3. Basophilicleukocyte

4. Monocyte

5. Lymphocyte

List of recommended literature .

The main one:

1.Lutsyk O.D., Tchaikovsky Y.B. Histology, cytology, embryology Vinnytsia, New Book, 2018.
2.Barinov E.F., Tchaikovsky Y.B. General histology and embryology of internal organs: textbook.Kyiv: Medicine; 2013
3.Wojciech Pawlina. Histology: textbook and atlas. WSV: Medicine, 2021.

Additional:

1.Histology and embryology of internal organs: textbook / E.F. Barinov, Y.B. Tchaikovsky, O.M. Sulaeva et al.
2.Cytology of human organs and tissues edited by L.S.Bolgova. Kyiv: Book-plus, 2018, p.288

Theme: "The Blood." *Addition*

Blood is a fluid tissue that circulates through the cardiovascular system. It constitutes approximately 5-9% of the total body mass (5-5,5litres).

Development: blood arises from mesenchyme. All blood cells arise from one common *pluripotential blood stem cell*. The further differentiation of the blood stem cell is determined by several factors:

microenvironment (reticular tissue of hematopoietic organs);

hemopoietins.

The population of blood cells is a constantly renewed system, where the mature (definitive) cells, after their death, are substituted by the newly-formed cells. The formation of new blood cells and destruction of the old ones are in physiological equilibrium, that's why the quantitative and qualitative composition of blood remains the same.

♦ Blood consists of cells and its derivatives and a protein rich fluid called plasma.

Blood cells and their derivatives include:

erythrocytes, also called red blood cells (RBCs);

leukocytes, also known as white blood cells (WBCs);

thrombocytes, also termed as platelets.

The relative volume of cells and plasma in whole blood is approximately **45% to 55%** respectively. This ratio is called **hematocrit**.

Functions of blood

1. Transport
2. Immune defense
3. Maintenance of homeostasis
4. Trophic
5. Respiratory

Transport and trophic functions: delivery of nutrients and other substances directly or indirectly to cells.

Respiratory function: delivering of oxygen from lungs to tissue and removing of carbon dioxide.

Immune defense: transport of humoral agents and cells of the immune system that protect the body from pathogenic agents (microorganisms or cancer cells).

Maintenance of homeostasis: acts as buffer and participates in coagulation.

Plasma

Blood plasma is the liquid extracellular material that impairs fluid properties to blood. The blood plasma represents a colloid system which is composed of water (90-93%), organic (proteins: albumins, globulins and fibrinogen, and other organic substances - about 7%) and non-organic material (3%). The total concentration of mineral components constitute 0, 9% of the total plasma volume. The pH of the blood plasma is 7,36.

Plasma proteins:

1. Albumins (4%); functions: binds and transport hormones, metabolites and drugs; maintain osmotic blood pressure.

2.Globulins (1,1-3,1%); The globulins are of three types:

a) α - globulins;

b) β - globulins;

b) γ **- globulins** – are referred to as **antibodies**;

3. *Fibrinogen (0,2-0,4%)* is soluble in water, but in a series of cascade reactions with other clotting factors it is transformed into the insoluble protein fibrin. Due to this property, the fibrinogen is responsible for blood clotting and preventing of blood loss in case of damaging of the blood vessel. The blood plasma without fibrinogen is named **blood serum**.

Forming elements of blood

The blood cells and their derivates are traditionally referred to as forming elements of blood.

Erythrocytes (red blood cells) are immobile anucleate post-cellular structures devoid of nucleus and typical organelles. The main function of erythrocytes is to bind and transport oxygen and carbon dioxide. They carry out this function due to the specific iron-containing protein – **hemoglobin** (Hb).

Besides this, erythrocytes also provide transport of amino acids, antibodies, toxins and medicines by absorbing them on their plasma membrane.

The number of erythrocytes varies in males and females, and changes with ageing.

The number of erythrocytes per 1L of blood:

In males - $3,9 \times 10^{12}$ - $5,5 \times 10^{12}$;

In females - $3,7 \times 10^{12}$ - $4,9 \times 10^{12}$;

In newborns - $6,0 \times 10^{12}$ - $9,0 \times 10^{12}$;

In elderly people - up to $6,0 \times 10^{12}$.

Shape and structure

The major part of erythrocytes has a shape of biconcave discs. Such erythrocytes are called *discocytes*.

The discocytes account for 80% of total number of erythrocytes.

The electron microscope examinations revealed the erythrocytes of other shapes:

planocytes – flattened erythrocytes;

stomatocytes – domed-shaped erythrocytes;

saddle-shaped erythrocytes;

spherocytes- sphere-shaped erythrocytes;

echinocytes – spinous erythrocytes.

Echinoctytes and spherocytes are the old forms of erythrocytes.

The phenomenon of shape diversity of erythrocytes is named physiological poikilocytosis. Normally the percentage of abnormally shaped erythrocytes does not exceed 20% of total erythrocytes number.

If this percentage is higher, such condition, named pathological poikilocytosis, requires treatment.

♦ The shape of erythrocyte is maintained due to the structure of its plasma membrane, which contains specific structural proteins like *β - sialoglycoprotein, spectrin, and ankyrin within* the **cortical layer**.

♦ In the human the diameter of erythrocyte is 7,1 - 7,9 μm; the edge thickness is 2,0 – 2,5 μm, the central thickness is 0,8-1 μm.

The depression in the center of erythrocyte, named physiological excavation, maximizes the cell's surface area, which is an important attribute in gas exchange.

Normally 75% of circulating erythrocytes are of 7,1 - 7,9 μm in diameter (physiological anisocytosis). Besides them, two other forms of erythrocytes are found in blood – macrocytes and microcytes.

Macrocytes(12,5%) – are more than 8,0 μm in diameter.

Microcytes (10,5%) – are less than 6,0 μm in diameter.

The phenomenon when macrocytes and microcytes account form more than 25% of total number of erythrocytes is named pathological anisocytosis. The general surface area of erythrocyte constitute 125 μm.

♦Plasma membrane of erythrocyte is approximately 20 nm thick. The outer surface of the plasma membrane contains *phospholipids, sialic acid, antigenic oligosaccharides, and adsorbed proteins*.

The inner surface of the erythrocyte plasma membrane contains glycolytic enzymes, Na+ K+, ATP-ases, glycoproteins, hemoglobin.

Being semi-permeable, the erythrocyte's plasma membrane provides active transmembrane transport of ions of Na, K, O_2 и CO_2 , and other substances.

♦ Cytoplasmic matrix possesses numerous hemoglobin-containing granules. It consists of water (60%) and dry residue (40%). Hemoglobin constitutes 95% of the dry residue.

Hemoglobin is a complex protein which consists of four polypeptide chains of globin, and iron-containing heme group. It can bind oxygen (O_2) – oxyhemoglobin, or carbon dioxide (CO_2) – carbohemoglobin, thereby performing the respiratory function. The complex of hemoglobin with carbon monoxide (CO) is more stable than those with oxygen and carbon dioxide. The affinity between hemoglobin and carbon monoxide is approximately 300 times higher than the affinity between hemoglobin and oxygen so hemoglobin binds to carbon monoxide in preference to oxygen. So, carbon monoxide prevents hemoglobin from carrying oxygen to tissues, thereby causing death.

In the human the following types of hemoglobin can be distinguished:

HbA – prevalent in adults, accounts for 98% of total hemoglobin;

HbF – the principal form of hemoglobin in fetus. In adults accounts for 2%. Its capacity of binding oxygen is much higher that that of the HbA that enables HbF to provide tissues of the fetus with oxygen in conditions of mixed blood circulation. HbF production falls dramatically after the birth.

Mutations in genes encoding globin chains can cause disorders in hemoglobin production. Hence erythrocytes are devoid of mitochondria, the main way they produce energy is glycolysis – anaerobic oxidation of glucose followed by production of ATP and NADP.

The life span of erythrocyte is 120 days. Every day approximately 200 million erythrocytes are destroyed in the spleen. This destruction is accompanied with breakdown of hemoglobin into protein **globin** and iron-containing **heme**

group. The released iron is used for hemoglobin synthesis in new erythrocytes. The globin is used for formation of bile acids in the liver.

Physiologically, along with the mature erythrocytes, in the blood are found 1-5% of young erythrocytes with lower concentration of hemoglobin – reticulocytes. Reticulocytes are stained with both basic and acidic dyes (polychromatic). Their cytoplasm reveals rests of mitochondria and endoplasmic reticulum which contain RNA.

Thrombocytes are anucleate fragments of cytoplasm that was separated from the giant cells of the red bone marrow – **megakaryocytes**.

*Size – 2-3 μm

* Number - 180 - 320 x 10^9 per 1L of blood

Structure

Thrombocyte consists of:

1) Hyalomere is the basis of thrombocyte;

2) Granulomere includes granules that form aggregations in the central or peripheral part of the cytoplasm.

Two types of granules are distinguished in thrombocyte:

1) dense, dark α-granules;

2) serotonin granules (δ-granules);

3) lysosomes and microperoxisomes (λ-granules).

- Granulomere contains also contains granules of glycogen and mitochondria.

- Hyalomere contains circularly arranged bundles of 10-15 microtubules that maintain the cytoskeleton of thrombocyte, and actin and myosin filaments.

Thrombocytes possess numerous processes of different size and thickness that take part in their aggregation and formation of thrombus.

The Romanovsky-Giemza staining reveals **5 types** of thrombocytes:

young thrombocytes with basophilic hyalomere and solitary azurophilic granules;

mature thrombocytes with slightly acidic hyalomere and numerous azurophilic granules;

old thrombocytes – dark, bluish-purple with dark-purple granules;

degenerating thrombocytes – with grayish- blue hyalomere and bluish-purple granules;

giant thrombocytes – their size is 2-3 times than usual one, possess pinkish-purple hyalomere and purple granules.

The life span of thrombocytes is 5-8 days.

Продолжительность жизни тромбоцита 5-8 дней.

♦ Function: take part in blood clotting. Thrombocytes discharge enzyme thromboplastin that catalyses transformation of soluble fibrinogen into insoluble fibrin. Aggregated thrombocytes also serve as a frame for the thrombus.

Leukocytes

Leukocytes are white, globe-shaped blood cells that possess nucleus and all organelles. Leukocytes can leave the blood stream and carry out their functions in connective tissue.

In adults the number of white blood cells per 1L is $3{,}8 \times 10^9$- 9×10^9. Increase of total number of leukocytes in blood is called leukocytosis; decrease of total number of leukocytes in blood is referred to as leucopenia.

Classification

All leukocytes are classified into two general groups. The basis of this division is the presence or absence of prominent specific granules in the cytoplasm.

1. Leukocytes containing specific granules are classified as **granulocytes.**

2. Leukocytes that lack specific granules are classified as **agranulocytes.**

On the basis of granules' staining the **granulocytes** are subdivided into:

1) neutrophils;

2) eosinophils;

3) basophils.

The agranulocytes are of two types: lymphocytes and monocytes.

Granulocytes

I *Neutrophils*

♦ Neutrophils account for 65-70% of total leukocytes number. They measure 7-9 μm in fresh blood and 10-12 μm in blood smear.

♦ The cytoplasm of neutrophils contains granules. Each cell cam possess from 50 to 200 granules. Not whole cytoplasm is occupied by granules; a thin peripheral layer of cytoplasm is devoid of granules, as it contains the elements of cytoskeleton. This layer provides the amoebic movements of the cell by formation of pseudopodia.

♦ Neutrophils possess two types of granules:

1) azurophilic (primary);

2) neutrophilic (secondary) - specific;

Azurophilic granules arise in early granulopoiesis and are named primary granules. They are less numerous than specific granules (10-20% of total amount of granules). Each granule is rounded or oval-shaped and measures 0,4-0,8 μm in diameter. These granules are the lysosomes of neutrophil and contain typical **acid hydrolases.**

Neutrophilic granules (specific) are named secondary as they increase in number with maturation of the cell. In mature neutrophil they account for 80-90% of total amount of granules. Neutrophilic granules are ellipsoidal, they measure 0,2-0,4μm. They contain acidic phosphatase, basic cationic proteins, lactoferrins, lysozymes, amino peptidases, and complement activators.

♦ The cytoplasm of neutrophils possesses poorly developed organelles, small amount of mitochondria, sometimes reduced elements of Endoplasmic reticulum can be found. It also usually contains glycogen and lipid inclusions. The Romanovsky-Giemza stain gives the granules both pink and purple color.

♦ The nuclei of neutrophils contain dense chromatin. Wide regions of heterochromatin are located chiefly at the periphery of the nucleus; regions of

euchromatin are located primarily at the center of the nucleus. In woman, the Barr body (the condensed, single, inactive X-chromosome) forms a drumstick-shaped appendage on one of the nuclear lobes. Neutrophils possess multilobal nuclei, which are variable in shape; thus, they are also called polymorphonuclear neutrophils.

Mature neutrophils possess two to four lobes of nuclear material joined by thinner nuclear strands. These neutrophils are referred to as **segmented neutrophils**. They account for 49-72% of total number of leukocytes.

Band neutrophils are immature cells accounting for 1-6% of total number of leukocytes. These neutrophils possess S-shaped or horseshoe-shaped nucleus.

Metamyelocytes (young neutrophils) are characterized by bean-shaped nucleus and account only for 0-0,5% of total number of leukocytes.

Neutrophils are motile cells that can leave the bloodstream and migrate to the site of inflammation in the connective tissue. They are capable of **phagocytosis.**

Neutrophils also produce chalones – specific substances that inhibit the DNA synthesis in granulocytes and regulate the processes of proliferation and differentiation of leukocytes. The life span of neutrophils is about 8 days; they circulate in the bloodstream for 8-12 hours, after that they migrate in the connective tissue and perform their functions.

II *Eosinophils*

♦ The diameter if eosinophil in the fresh blood is 9-10 μm; in the blood smear – 12-14 μm. They account for 1-5% of total number of leukocytes.

♦ The cytoplasm contains two types of granules:

Specific granules are oval or polygonal in shape, measuring about 0,5-1,5μm. Specific granules of eosinophils exhibit intense acidophilia due to the containing of **major basic protein that is rich in arginin**. Specific granules also contain histaminase, arylsulfatase and collagenase.

Azurophilic granules are lysosomes. They contain variety of the usual lysosomal acid hydrolases and other hydrolytic enzymes which function is destruction of parasites and hydrolysis of antigen-antibody complexes.

♦Three types of eosinophils are distinguished

a) segmented;

b) band eosinophils;

c) young eosinophils.

The nuclei of segmented eosinophils usually consist of two lobes joined by thin strands. Band and young eosinophils are rarely found in blood; they resemble neutrophils of the same stages of maturation. The nuclei of eosinophils contain predominantly heterochromatin, the nucleoli are not distinguishable. Eosinophils are less motile than neutrophils.

Functions. Eosinophils take part in defensive reactions against foreign proteins, and allergic reactions. They are capable of phagocytosis and breakdown of histamine by the enzyme histaminase. The number of eosinophils in blood increases in case of parasites invasion and allergic reactions. The capacity of phagocytosis in eosinophils is lower than that of neutrophils.

III. Basophils measure 9μm in diameter in the fresh blood and 11-12 μm in the blood smear. They account for 0,5-1% of total number of leukocytes.

♦ Cytoplasm contains large, rounded or polygonal, basophilic granules with diameter of 0,5-1,2 μm.

The granules are characterized by metachromasia due to the containing of acidic glycosaminoglycan – **heparin**.

Metachromasia is an ability to change the initial color of dye. Besides heparin, the granules also contain **histamine.**

The density of granules can be different that reflects different degree of maturity and functional conditions. Besides specific granules, basophils also contain primary azurophilic granules that represent lysosomes. The cytoplasm possesses all general-purpose organelles.

♦ The lobules of the nuclei of basophils are not very conspicuous. The nuclei of basophils are stained less intensively than those of neutrophils and eosinophils.

♦ Functions of basophils are determined by their capacity of metabolism of histamine and heparin. They take part in regulation of blood clotting (heparin is anticoagulant) and permeability of blood vessels (histamine). They also take part in immunological reactions, especially allergic reactions. Due to the presence of receptors to antibodies on their plasma membrane, they can react on antigen-

antibody complexes by discharging of histamine. Histamine, by increasing of permeability of blood vessels, causes the symptoms of allergic reaction (itch, redness, and edema). Besides these, histamine causes spasm of smooth muscles of the small bronchi, and is involved in pathogenesis of the bronchial asthma. Basophils also produce eosinophils-chemotaxis factor. Eosinophils take part in inactivation of histamine, thereby stopping allergic reactions. Basophils are practically incapable of phagocytosis.

Agranulocytes

Lymphocytes account for 19-37% of total number of leukocytes. Their size varies significantly from 4,5 to 10 μm. That's why three types of lymphocytes are distinguished on the basis of their size:

a) small – 4,5-6,0 μm in diameter;

b) medium – 7-10 μm in diameter;

c) large – more than 10 μm in diameter.

Lymphocytes are characterized by intensively stained, rounded or bean-shaped nucleus and relatively small amount of basophilic cytoplasm. The cytoplasm of lymphocytes contains small amount of azurophilic granules (lysosomes).

The electron microscope examination revealed four types of lymphocytes in adults:

1) small light lymphocytes;

2) small dark lymphocytes;

3) medium lymphocytes;

4) plasma cell (lymphoplasmocytes).

Small light lymphocytes measure about 7 μm in diameter. The nucleus occupies more space than the surrounding cytoplasm. The nucleus is rounded; heterochromatin is concentrated at the periphery of the nucleus.

The cytoplasm contains relatively few ribosomes and polysomes, lysosomes, poorly developed Golgi complex, mitochondria, but numerous vacuoles and vesicular bodies. The organelles are concentrated near the nucleus. Small light lymphocytes account for 70-75% of total number of lymphocytes.

Small dark lymphocytes measure of 6-7 μm in diameter and account for 12-13% of total number of lymphocytes. The nucleus occupies even more space than that of

small light lymphocytes. The chromatin appears dense; the nucleolus is relatively big.

A thin layer of dense dark cytoplasm surrounds nucleus, contains numerous ribosomes, a few mitochondria. Other organelles are found rarely.

Medium lymphocytes measure of about 10 μm in diameter and account for 10-12% of total number of lymphocytes. They possess bean-shaped nucleus with visible finger-like projections of nuclear envelope. The chromatin is less condensed, the regions with heterochromatin are revealed only near the nuclear envelope; the nucleolus is well distinguished.

The cytoplasm contains elongated canaliculi of endoplasmic reticulum, free ribosomes and polysomes. The centrosome and Golgi complex are usually situated near the site of invagination of the nuclear envelope. Lysosomes and mitochondria are not numerous.

Plasma cells are characterized by canaliculi of the rough ER that concentrically surround the nucleus. They account only for 1-2% of total number of lymphocytes.

Three functionally distinct types of lymphocytes are present in the human body:

T-lymphocytes;

B-lumphocytes;

NK – cells.

T-lymphocytes (thymus-dependent) arise from the blood stem cell in the red bone marrow and provide reactions of cell-mediated immunity and regulation of humoral immunity.

The life span of T-lymphocytes can last for several (even several decades) years. They account for 80% of total number of lymphocytes.

Three types of T-lymphocytes have been identified:

1. Cytotoxic T-killer cells;

2. T-cells that regulate humoral imminity:

- T-helper cells;

- T-suppressor cells.

T-killer cells are effector cells of the cell-mediated immunity. They are responsible for rejection of allografts and elimination of tumor cells.

T-helper cells initiate and encourage the production of antibodies by B-lymphocytes.

T-suppressor cells inhibit the production of antibodies by B-lymphocytes. They act via production of specific soluble substances – **lymphokines**, which is initiated by action of antigens.

T-memory cells keep the information about previously circulating antigens.

B-lymphocytes arise from the blood stem cell in the red bone marrow. No distinctive morphological differences were revealed between T- and B-lymphocytes. B-lymphocytes possess stronger developed rough ER, whilst T-lymphocytes possess more lysosomes. T-lymphocytes are relatively smaller; possess smaller nucleus with more heterochromatin.

The plasma membrane of B-lymphocytes contains various receptors to different antigens.

♦ Function: provide humoral immunity by producing antibodies (immunoglobulins).

The definitive form of B-lymphocyte is plasma cell.

NK (natural killer) cells are programmed during their development to kill certain virus-infected cells and some types of tumor cells. They also secrete an antiviral agent, interferon.

Monocytes measure 9-12 μm in fresh blood and 18-20 μm in blood smear. Monocytes are the part of the macrophagic system of the body. The cells of the macrophagic system arise from the precursors of monocytes of the red bone marrow, circulate with the bloodstream for 36-104 hours and then migrate into the connective tissue and maturate there.

♦ The cytoplasm is less basophilic than that of lymphocytes. The Romanovsky-Giemza staining gives it light-blue color. The peripheral part of the cytoplasm is densely stained, as it contains numerous fine azurophilic granules (lysosomes). Monocyte possesses finger-like projections, phagocytic vacuoles, pinocytotic vesicles, short canaliculi of the rough ER and small mitochondria.

♦ The nuclei of monocytes are variable in shape: bean-shaped, horseshoe-shaped, lobulated, with diverse projections or invagination etc. The nuclei can possess one or more nucleoli. The chromatin is scattered through the nucleus.

Monocytes account for 3-11% of total number of leukocytes.

Functions: As it leaves the bloodstream, monocyte differentiate into macrophage and carry out its specific functions.

Lymph is a yellowish fluid consisting predominantly of proteins that circulates through the lymphatic vessels. It is composed of lymph plasma and forming elements.

The lymph plasma composition is similar to that of the blood plasma, but contains fewer proteins. It contains more albumins than globulins. Most of the proteins are enzymes, like diastase, lipase, and glycolytic enzymes. It also contains neutral fats, simple sugars, NaCl, Na_2CO_3, and complexes containing Mg, Ca and Fe.

Forming elements include predominantly lymphocytes (98%), and also monocytes.

Three types of lymph are distinguished:

Peripheral lymph – flows from tissues to lymph nodes;

Transitional lymph – outflows from lymph nodes;

Central lymph – the lymph of the thoracic duct and the right lymphatic duct.

Lymph is formed in lymphatic capillaries of tissues and organs under the influence of different factors that include osmotic and hydrostatic pressure.

ODESA NATIONAL MEDICAL UNIVERSITY

DEPARTMENT OF HISTOLOGY, CYTOLOGY AND EMBRYOLOGY

METHODICAL RECOMMENDATION OF LECTURES

for dentistry faculty

THEME: «Tissues of internal environment. Connective tissue proper.»

Approved on the methodical conference of department

«____»_____ 20___., protocol №_____

Head of Department, doc._____ Tiron O.I.

Approved on the methodical conference of department

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«____»_____ 20___., protocol №_____

Head of Department, doc._____ Tiron O.I.

Theme: «Tissues of internal environment. Connective tissue proper.»-2h.

1. Relevance of the topic

Connective tissues are an absolute integral system that as such is isolated from the embryonic rudiments in the form of a mesenchyme before all other tissues. Despite the structural diversity, this group of tissues is stored throughout life, and is a tissue of the internal environment.

Knowledge of the structure and function of different types of connective tissues, which are part of most organs, form the stroma and accompany blood vessels, is necessary for understanding the basic vital processes of a healthy organism, because connective tissue is actively involved in metabolic processes, in maintaining homeostasis and organ architectonics. As a tissue of the internal environment, it contains a large number of immunocompetent cells and is involved in the body's immune defense.

2. Purpose of the lecture

2.1. Learning

To familiarize students with the classification of connective tissues, structure, histophysiology of cells and intercellular substance, fibrous connective tissues, peculiarities of histophysiology of connective tissues with special properties.

2.2. Educational

To form students' professional significance of the topic. Discuss the issue of deontology

3. Plan and organizational structure of the lecture.

Lecture stages	Contents of the lecture stages	Aim	Lectureequipment	Time management
Preparatory stage	Relevance by those and goal setting	I	Tables. Slides. Dummies.	3 min.
	Connective tissue concept	II		3 min.
The main stage	Connective tissue proper	III		10 min.
	Connective tissue cells	III		10 min.
	Intercellular substance of connective tissue	III		17 min.
	Fibrous component of connective tissue	III		17 min.
	Connective tissue with special properties	III		20 min.
The final stage	Summary of the lecture. General conclusions			5 min.
	Self-study assignment			5 min.

4. Topic content

addition

5. Materials for activating students during the lecture.

1)Morphofunctinal characteristic of loose connective tissue cells

2) Intercellular substance and characteristics of the constituent components.

3) Morphological and functional characteristics of collagen fibers.

4) Levels of collagen fiber organization. Collagen types.

5) Elastic fibers. Structure, chemical components, functional characteristics.

6)Reticular fibers. Structure, functional significance.
7)Chemical components, functional features and origin of the main amorphous component.

8) Morphofunctional characteristics of various types of dense fibrous connective tissue.

8) Tendon. Structure, function.

9) Fibrous membranes. Structure, function.

10) Dense irregular fibrous connective tissue, structure, function.

6. General material and methodological support of the lecture.

Tables:

1.Loose connective tissue

2.Connective tissue cells

3.Collagen fiber

4 White and brown adipose tissue

Slides:

1. Mast cells

2.Macrophages

3.Pigment cells

4.Plasma cells

Dummies:

1) collagenfibers

List of recommended literature .

The main one:

1.Lutsyk O.D., Tchaikovsky Y.B. Histology, cytology, embryology Vinnytsia, New Book, 2018.
2.Barinov E.F., Tchaikovsky Y.B. General histology and embryology of internal organs: textbook.Kyiv: Medicine; 2013
3.Wojciech Pawlina. Histology: textbook and atlas. WSV: Medicine, 2021.

Additional:

1.Histology and embryology of internal organs: textbook / E.F. Barinov, Y.B. Tchaikovsky, O.M. Sulaeva et al.
2.Cytology of human organs and tissues edited by L.S.Bolgova. Kyiv: Book-plus, 2018, p.288

Addition

Theme: "Tissues of internal environment. Connective tissue proper."

Tissues of internal environment include blood, lymph and all types of connective tissue. Despite of a significant difference between each other, all these tissue can be referred to the one group because of their common origin, structure and functions.

♦ Origin: all of the tissues of internal environment are derived from mesenchyme.

Mesenchyme is an embryonic connective tissue. The mesenchyme structurally resembles a network, since the stellate-shaped or spindle-shaped mesenchymal cells contact with one another by their processes. Spaces between the cells are occupied by extracellular matrix. Density of the extracellular depends on intensity of metabolism. The mesenchyme gives rise to blood, lymph and all types of connectives tissues.

The structural and functional characteristics vary in different kinds of connective tissue and depend on the physical and chemical properties of the extracellular matrix.

Classification of tissues of internal environment

All tissues of internal environment are divided into two main groups:

Fluid tissues. 2. Connective tissues

Fluid tissues include two types of tissues:

blood;

lymph.

Connective tissues are divided into the following types:

Connective tissue proper;

Skeletal connective tissue.

Connective tissue proper, in its turn, is divided into:

fibrous connective tissue;

connective tissue with special properties;

* Depending on the amount of fibers, the fibrous connective can be:

1) loose;

2) dense.

Loose fibrous connective tissue consists predominantly of cells and ground substance.

Dense fibrous connective tissue contains a great amount of fibers and, on the basis of their arrangement, is subdivided into:

reguar;

irregular.

Dense regular connective tissue – the fibers are arranged parallel to one another.

Dense irregular connective tissue – the fibers are randomly arranged, forming a network.

* Connective tissues with special properties include the following:

1. Reticular

2. Adipose

3. Pigment

4.Mucous

* Skeletal connective tissues include:

1. Cartilage

2. Bone tissue

Connective tissues are the tissue of internal environment which are characterized by wide range of cells and strong development of the extracellular matrix.

The physical properties and chemical composition of the extracellular matrix determines the functions and features of each type of connective tissue.

Functions of connective tissues

Mechanical and supporting: form capsule and stroma of the inner organs;

Protective: mechanical protection (fascia, bones, cartilage), provide cell-mediated and humoral immunity by phagocytosis and production of antibodies;

Participates in healing of wounds, regeneration and reactions of adaptation to changing conditions of external environment.

Nutritive: provides nutrition for surrounding tissues, regulates metabolism and maintenance of homeostasis.

Classification

All connective tissues are subdivided into:

Connective tissue proper (fibrous connective tissue);

Skeletal connective tissue (cartilage, bone).

Depending on the amount of fibers, the fibrous connective tissue is subdivided into

loose connective tissue;

dense connective tissue.

Loose connective tissue contains more cells and ground (amorphous) substance.

Dense connective tissue is composed predominantly of fibers and, depending on their organisation , is subdivided into:

dense **regular** connective tissue;

dense **irregular** connective tissue

In dense regular connective tissue the fibers are laid down parallel to one another.

In dense irregular connective tissue the fibers are laid down in different directions to each other, forming a network.

* The types of connective tissues with special properties are:

1. Reticular tissue;

2. Adipose tissue;

3. Pigment tissue;

4. Mucous tissue.

LOOSE CONNECTIVE TISSUE

Loose connective tissue is composed of cells and extracellular matrix. It is found in all tissues and organs, as it accompanies blood and lymphatic vessels.

Cells of connective tissue

Fibroblasts are the most numerous group of cells, capable of production of fibrillar and globular proteins (collagen, elastin), glycosamonoglycans (sulfated and non-sulfated), proteoglycans, glycoproteins, which are then released in the extracellular matrix.

In emryogenesis the fibroblasts arise from the mesenchymal cells, after the birth – from stem cells.

The histogenetic lineage (differon) of fibroblasts includes:

stem cells → semi-stem cells-precursors→ young (immature) fibroblats→ mature firoblasts (functioning) → fibrocytes (definitive cells), and also myofibroblasts and fibroclasts.

Young fibroblasts are of 20-25 μm in size. The young fibroblast possesses rounded nucleus with small nucleolus, and basophilic karyoplasm, rich in RNA. The cytoplasm contains numerous ribosomes. Endoplasmic reticulum and Golgi complex are poorly developed. The cell **does not** possess distinctive cytoplasmic processes. These fibroblasts are characterized by very low level of protein synthesis and secretion. They are capable of mitotic division.

Mature fibroblasts – in the specimen their size can account for 40-50μm. The nucleus is oval, contains 1-2 large nucleoli. The cytoplasm contains well developed rough ER, which at some sites even contacts with the plasma membrane. The Golgi complex, which appears as tubules and cisterns, is distributed throughout the cell. The cortical layer of cytoplasm contains microfilaments of 5-6nm thick that are composed of actin- and myosin-like proteins. These microtubules enable the fibroblasts to movement. Active synthesis

of components of the extracellular matrix (collagen and elastic proteins, glycosaminoglycans, and proteoglycans) occurs within the fibroblasts.

In usual conditions, the fibroblasts reveal weak motility and low phagocytic activity. Their motility is activated in case of binding to the supporting fibrillar structures (fibrin, connective tissue fibers) with a help of fibronectin –glycoprotein which is responsible for adhesion of cells to extracellular matrix.

Fibrocytes are definitive forms of fibroblasts. Shape: spindle-shaped with prominent wing-like (pterygoid) processes. The cytoplasm contains small amount of organelles, vacuoles, lipids, and glycogen. In these cells the synthesis of collagen and other substances is dramatically reduced.

Myofibroblasts are the cells functionally related to the smooth muscle cells, but, unlike the smooth muscle cells, their cytoplasm possesses strongly developed rough ER. These cells are especially numerous and active at the sites of healing of wounds and in the uterus during pregnancy.

Fibroclasts are the cells of fibroblast differon, which are characterized by extremely high phagocytic and hydrolytic activity. They contain numerous lysosomes. The fibroclasts participate in dissolving of the extracellular matrix at the period of involution of an organ.

Macrophages are the cells of hematogenic origin, which are capable of active phagocytosis. The macrophages of two types are distinguished: fixed macrophages and wandering macrophages.

Size: 10-15μm.

Shape: rounded, elongated, polygonal.

The nucleus is smaller than that of the fibroblasts, but it is denser, as it contains more heterochromatin.

The cytoplasm is basophilic, heterogeneous, contains numerous lysosomes, phagosomes, pinocytotic vesicles, rough ER, Golgi complex, mitochondria.

The plasma membrane forms both deep folds and long projections, which helps these cells to uptake foreign particles. Because of the presence of receptors to cancer cells, erythrocytes, T-and B-lymphocytes, and immunoglobulins on the surface of their plasma membrane, the macrophages actively participate in immune reactions.

Functions: phagocytosis, synthesis and secretion of biologically active substances (interferon, lysosyme, pyrogens, prostheses, acidic hydrolases). The important role is performed by mediators- monokines: interleukin –I, which activates the DNA synthesis in lymphocytes; factors, stimulating the production of antibodies by B-lymphocytes; factors, stimulating the differentiation of T- and B-lymphocytes; factors, activating T-helper cells and cytolytic factors.

Development: the macrophages arise from the stem cell of blood (red bone marrow).

Macrophage system is a powerful defensive system, participating in both general and local defensive reactions. The macrophage system is regulated by local mechanisms and by nerve and endocrine system as well.

The macrophage system includes all cells which are capable of uptake and breakdown of foreign particles, old or dead cells, bacteria etc:

macrophages (histiocytes) of loose connective tissue;

stellate cells of sinusoidal capillaries of liver (Kupffer's cells);

fixed and wandering macrophages of hemopoietic organs;

lung macrophages (dust cells);

macrophages of inflammatory exudates;

osteoclasts;

foreign-body giant cells;

glial macrophages of the nerve tissue.

All named cells are capable of phagocytosis, possess receptors to immunoglobulins on the surface of their plasma membrane, and arise from monocyte-precursors of the red bone marrow or monocytes of the blood.

Besides of their capacity of phagocytosis, fibroblasts, reticulocytes, endothelial cells, and neutrophils are not included in the macrophage system.

Plasma cells

Size: 7-10μm.

Shape: rounded or oval.

The nucleus is not big, located eccentrically. It contains condensed chromatin, which gives the nucleus the characteristic pattern of **"spoke wheel"**.

The cytoplasm is basophilic, contains well developed rough ER and numerous ribosomes. The nucleus is surrounded by a light area of cytoplasm – perinuclear zone. In the perinuclear zone the centrioles surrounded by the cisterns Golgi complex are found.

Functions: synthesis of immunoglobulins (antibodies), thereby providing specific humoral immunity.

The plasma cells arise from B-lymphocytes of blood.

Tissue basophils (mast cells)

Size: 4-14μm in width, up to 22μm in length.

Shape: variable (rounded, oval, irregular, polygonal); may possess short wide processes that enable them to amoeboid movements.

The nuclei are relatively small, contain densely packed chromatin. The cytoplasm exhibits numerous mitochondria, small amounts of smooth and rough ER, well developed Golgi complex. There are also found membrane-bounded granules of 0,2-0,8μm. These granules contain heparin (30%) and histamine (10%). The matrix of the granules is composed of proteins (chimase) and heparin, which from a stable network that bounds histamine via ionic bonds. The granules also contain chondroitin sulfate, hyaluronic acid, and, in some animals, serotonin.

Functions: regulate local homeostasis of connective tissue, participate in regulation of blood clotting, increase permeability of bood-tissue barriers, and participate in inflammatory and allergic reactions.

Adipocytes (fat cells). The diameter of fat cell can account for 120μm. Shape: spherical. Almost all inner volume of adipocyte is filled with a droplet of neutral flat (triglycerides). The cytoplasm and organelles form a thin layer that surrounds the fat droplet. Organelles are situated near the elongated nucleus and include both types of endoplasmic reticulum, Golgi complex, mitochondria.

Functions: depositing of fat, thermoregulation, maintenance of water balance.

Pigment cells possess short processes of varying shape. The cytoplasm is filled with pigment – melanin. Pigment cells arise from crests of neural tube.

Adventitial cells are low-specialized cells which accompany blood vessels. Shape: flattened or spindle-shaped. Nucleus – oval. Cytoplasm – slightly basophilic, the organelles are underdeveloped. Adventitial cells can give rise to fibroblasts, fibroclasts, myofibroblasts, and adipose cells.

FIBRILLAR STRUCTURES

Collagen fibers in loose connective tissue are laid in different directions and appear as wavy, spirally twisted rounded or flattened strands of 1-10μm thick. They form bundles of 150 μm thick.

Levels of organization of collagen fiber

The collagen molecules are built of three polypeptide chains (α-chains) of pre-collagen which twist in spiral within the cell. This is the first, molecular, level of organization.

The second, supramolecular, level of organization is represented by aggregated and cross-linked via hydrogen bonds molecules of collagen – protofibrils. A bundle of linked protofibrils compose microfibrils.

The third, fibrillar, level of organization – glycosaminoglycans and glycoproteins surround bundles of microfibrils, thereby forming fibrils. The fibrils exhibit cross-striations due to the arrangement of amino acids in secondary cross links.

Several fibrils aggregated together compose collagen fiber – the fourth level of organization.

12 types of collagen exist:

I type of collagen – connective tissue of skin, bones, cornea, sclera, arteries;

II type – hyaline and fibrocartilage, corpus vitreous;

III type – skin derma of fetus, wall of large blood vessels, reticular fibers;

IV type – basal lamina, capsule of lens;

V type – near the cells which produce it;

VI- VII type – is named microfibrillar;

VIII- XII type – endothelium, cartilage, corpus virtues.

Elastic fibers

Elastic fibers endow connective tissue with flexibility and elasticity. Shape of the fibers is rounded or flattened.

Structure

The main structural component of elastic fiber is globular protein – elastin, which is produced by fibroblasts. The molecules of elastin appear as globules with a diameter of 2,8 nm – the first, molecular, level of organization. In the extracellular matrix they are connected in chain of 3-3,5 nm thick, which is called elastin protofibril – the second level of organization. Protofibrils surrounded by glycoproteins from 8-10nm wide microfibrils – the third level of organization. Elastic fiber (the fourth level of organization) represents cylinder, which center is filled with amorphous component and surrounded by microfilaments.

Mature elastic fibers contain 90% of elastin and 10% of microfilaments.

Reticular fibers

Reticular fibers are the type of collagen fibers, as they are built type III collagen. They contain an increased number of carbohydrates, which are produced by reticular cells and form a three-dimensional network – reticulum.

Ground substance of extracellular matrix

Ground substance of extracellular matrix accounts for 20% of total body mass and represents jelly-like hydrophilic mass with changing density and chemical composition. The ground substance is mainly produced by fibroblasts.

Chemical composition: water, proteins, polysaccharides, mineral substances. Polysaccharides are represented by glycosaminoglycans which are of two types:

sulfated – heparin sulfate, chondroitin sulfate, dermatan sulfate etc.

non-sulfated – hyaluronic acid.

The amount of ground substance varies in different types of tissues.

Functions : regulation of water metabolism, ion balance, cell adhesion etc.

DENSE CONNECTIVE TISSUE

Dense irregular connective tissue is characterized by abundant fibers and few cells. Dense irregular connective tissue contains mostly collagen fibers. Cells are sparse and are typically of a single type, the fibroblast. This tissue also contains relatively little ground substance. Because of its high proportion of collagen fibers, dense irregular connective tissue provides significant strength.Typically, the fibers are arranged in bundles oriented in various directions (thus, the term

irregular) that can withstand stresses on organs or structures.

Skin contains a thick layer of dense irregular connective tissue called the reticular ayer (or deep layer) of the dermis. The reticular layer provides

resistance to stretching forces from different directions.

Dense regular connective tissue is characterized by ordered and densely packed arrays of fibers and cells. Dense regular connective tissue is the main functional component of tendons, ligaments, and aponeuroses. As in dense irregular connective tissue, the fibers of dense regular connective tissue are the prominent feature, and there is little

ground substance. However, in dense regular connective tissue, the fibers are arranged in parallel array and are densely packed to provide

maximum strength. The cells that produce and maintain the fibers are packed and aligned between fiber bundles.

• **Tendons** are cordlike structures that attach muscle to bone. They consist of parallel bundles of collagen fibers. Situated between these bundles are rows of fibroblasts called tendinocytes.In H&E–stained cross sections of tendon, the tendinocytes appear stellate. The substance of the tendon is surrounded by a thin connective tissue capsule, the epitendineum, in which the collagen fibers are not nearly as orderly. Typically, the tendon is subdivided into fascicles by endotendineum, a connective tissue extension of the epitendineum. It contains the small

blood vessels and nerves of the tendon.

• **Ligaments,** like tendons, consist of fibers and fibroblasts arranged in parallel. The fibers of ligaments, however, are less regularly arranged than those of tendons. Ligaments join bone to bone, which in some locations, such as in the spinal column, requires some elasticity.

• **Aponeuroses** resemble broad, flattened tendons. Instead of fibers lying in parallel arrays, the fibers of aponeuroses are arranged in multiple layers. The bundles of collagen fibers in one layer tend to be arranged at a right angle to those in the neighboring layers. The fibers within each of the layers are arranged in regular arrays; thus, aponeurosis is a dense regular connective tissue.

CONNECTIVE TISSUES WITH SPECIAL PROPERTIES

These types of connective tissues are characterized by predomination of particular cell types, which determine the name of the tissue.

Reticular tissue is a type of connective tissue which forms stroma of hemopoietic organs and microenvironment for developing blood cells.

Structure: it is composed of reticular cells and reticular fibers. Reticular cells and reticular fibers, anastomosing with each other via cell processes, form an interconnected network. Fibers and cells form a loose reticulum, hence the name of the tissue.

Reticular fibers by their chemical composition resemble collagen fibers, but they are less thick and anastomosing. Reticular fibers are revealed after a silver impregnation, that's why they are also called argirophilic fibers.

There are distinguished proper reticular fibers and pre-collagen fibers.

Proper reticular fibers – definitive, are composed of III type collagen.

Pre-collagen fibers – are precursors, immature type of collagen fibers.

Reticular fibers contain more sulfur, lipids and carbohydrates than the pro-collagen ones.

Reticular cells are subdivided into:

a) reticular fibroblast-like cells;

b) phagocytic cells (arise from monocytes);

c) low-differentiated (immature) cells.

Adipose tissue is an aggregation of fat cells (adipocytes). Two types of adipose tissue are distinguished:

white adipose tissue;

brown adipose tissue

White adipose tissue is situated under the skin, especially in area of abdominal wall, buttocks, and hips, where it constitutes hypoderm; and also in omentum, mesentery and retroperitoneal area.

Structure: white adipose tissue is composed of fat cells (adipocytes) which contain one single fat drop. Fat cells are closely attached to each other and form lobules of different shapes and sizes. Tiny spaces between adipocytes are occupied by fibroblasts, lymphoid elements, tissue basophils, and also thin collagen fibers lying in different directions.

The lobules are separated from each other by layers of loose connective tissue.

Brown adipose tissue is found in newborns and some animals in the area of neck, shoulder blades and other.

Fat cells of brown adipose tissue contain numerous small fat inclusions within the cytoplasm. They have a brown color due to the presence of iron-containing pigments – cytochroms of mitochondria. Here are found much more mitochondria than in fat cells of white adipose tissue. That's why the oxidative capacity of fat cells of brown adipose tissue is approximately 20 times higher than that of fat cells of white adipose tissue.

Mucous tissue is found only in umbilical cord of fetus (Wharton's jelly). It consists of mucocytes (fibroblast-like cells), loose network of collagen fibers (appear only in third trimester of pregnancy), and jelly-like ground substance rich in hyaluronic acid.

Function: protection of umbilical vessels from clamping.

Pigment tissue contains a lot of pigment cells- melanocytes.

It is found in iris of the eye, skin of nipples of mammary gland, scrotum, anus, birthmarks.

ODESA NATIONAL MEDICAL UNIVERSITY

DEPARTMENT OF HISTOLOGY, CYTOLOGY AND EMBRYOLOGY

METHODICAL RECOMMENDATION OF LECTURES

for medical faculty

THEME: «The Skeletal tissues.»

Approved on the methodical conference of department

«____»_____ 20___., protocol №_____

Head of Department, doc._____ Tiron O.I.

Approved on the methodical conference of department

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Approved on the methodical conference of department

«____»_____ 20___., protocol №_____

Head of Department, doc._____ Tiron O.I.

Theme: «The Skeletal tissues.» -2h.

1. Relevance of the topic

Cartilage and bone tissue are combined with the term "skeletal". Cartilage tissue plays a form-forming role in the process of embryogenesis, and then a supporting function in children and adults. Bone tissue together with cartilaginous tissue carries the main mechanical support of the body. The properties of these tissues (elasticity, elasticity, hardness, etc.) are associated with the structural features of their intercellular substance, which can be changed under the influence of thyroid and parathyroid hormones, functional loads, etc. A comprehensive study of histogenesis, histophysiology, and regeneration of skeletal tissues are of great importance for doctors, especially traumatologists.

2. Purpose of the lecture

2.1. Learning purpose

To acquaint students with the structure, histophysiology, and development of cartilage,bone tissue, direct and indirect osteogenesis of bone tissue.

2.2. Educational purpose

To form students of the professional significance of the topic. Discuss the issue of deontology

3. Plan and organizational structure of the lecture.

Lecture stages	Contents of the lecture stages	Aim in levels	Lecture equipment	Time management
Preparatory stage	Relevance by those and goal setting	I	Tables. Slides. Dummies.	3 min.
	The concept of cartilage and bone	II		3 min.

	tissue			
The main stage	Varieties of cartilage tissue	III		7 min.
	Cartilage histogenesis	III		7 min.
	Bone tissue, structure, varieties, functions	III		20 min
	Direct osteohistogenesis	III		20 min.
	Indirect osteohistogenesis	III		20 min.
The final stage	Summary of the lecture. General conclusions			5 min.
	Self-study assignment			5 min.

4. Topic content

Addition

5. Materials for activating students during the lecture.

1) General morphological and functional characteristics of cartilage tissue. Classification.

2) Cellular elements and their characteristics.

3) Intercellular substance. Structure. Features of the chemical components.

4) Structural organization of hyaline cartilage. Localization.

5) Elastic cartilage. Structural features. Localization.

6) Fibrous cartilage Structural features. Localization.

7) The main stages of chondrohistogenesis.

8) The structure and function of the perichondrium.

9) Cartilage growth. Their regeneration and age-related changes.

10) Classification of bone tissue.

11) Function, origin and structure of bone tissue cells - osteoblasts, osteocytes, osteoclasts.

12) The intercellular substance of bone tissue; structure and features of the chemical components.

13) The structure of reticulofibrous bone tissue.

14) Morphofunctional characteristics of lamellar bone tissue.

15) The histological structure of the tubular bone.

16) Function and structure of the periosteum (periosteum and endosteum).

17) Growth, regeneration and age-related changes in bone tissue.

6. General material and methodological support of the lecture.

Tables:

1.Reticulofibrous bone tissue

2.Lamellar bone tissue

3.Bone cells

4.Direct osteohistogenesis

5.Indirect osteohistogenesis

6. Cartilage

7. Chondrogistogenesis

Slides:

1.Osteoblasts

2.Osteoclasts

3.Osteone

Dummies:

1) Tubular bone

List of recommended literature .

The main one:

1.Lutsyk O.D., Tchaikovsky Y.B. Histology, cytology, embryology Vinnytsia, New Book, 2018.
2.Barinov E.F., Tchaikovsky Y.B. General histology and embryology of internal organs: textbook.Kyiv: Medicine; 2013
3.Wojciech Pawlina. Histology: textbook and atlas. WSV: Medicine, 2021.

Additional:

1.Histology and embryology of internal organs: textbook / E.F. Barinov, Y.B. Tchaikovsky, O.M. Sulaeva et al.
2.Cytology of human organs and tissues edited by L.S.Bolgova. Kyiv: Book-plus, 2018, p.288

Addition

Theme: "The Skeletal tissues."

Skeletal connective tissues include cartilage and bone tissue, which take part in regulation of water-salt balance, carry out supporting, protective and mechanical functions.

CARTILAGE

Cartilage is avascular connective tissue that is found in several organs of the respiratory system and intervertebral discs. Cartilage consists of cells (chondrocytes) and extensive extracellular matrix.

Cartilage is composed of 75% of water, 10-15% of organic component, and 4-7% of inorganic salts. Collagen constitutes 50-70% of dry mass of cartilage.

Classification of cartilage

Three types of cartilage are distinguished on the basis of structural and functional characteristics of their extracellular matrix:

1. Hyaline cartilage;

2. Elastic cartilage;

3. Fibrocartilage.

♦ Functions: the cartilage is well adapted o bear weight, especially in joints; it is a key tissue in the development of fetal skeleton.

Chondrogenesis

Chondrogenesis is a process of cartilage development. It takes place in the embryonic period and in the postembryonic period in case of regeneration.

Embryonic chondrogenesis

The cartilage arises from mesenchyme – embryonic connective tissue. The chondrogenesis includes three stages:

- *First stage* – **formation of chondrogenic islet.** The process cartilage development begins with the aggregation of chondroprogenitor mesenchymal cells to form a mass of rounded closely apposed cells. Such aggregations are called chondrogenic islets. The chondroprogenitor cells lose their cytoplasmic processes, their nucleus becomes rounded. These changes result in the cell becoming a chondroblasts, which will give rise to a cartilage by producing its matrix. Numerous free ribosomes and rough ER appear in the cytoplasm of chondroblasts.

- *Second stage* – **formation of primary cartilage.** The chondroblasts start to produce extracellular matrix containing fibrillar proteins (collagen of the III type), which results in their differentiation into the primary chondrocytes. The newly formed extracellular matrix exhibits distinctive oxyphyllia.

- *Third stage* – **differentiation of cartilage.** In this stage the primary chondrocytes differentiate into secondary chondrocytes and obtain capacity of synthesis of sulfated glycosaminoglycans (chondroitin sulfate), which form complexes with the collagen proteins (proteoglycans).

The mesenchyme surrounding the developing cartilage gives rise to perichondrium that consists of the outer fibrous and the inner cellular (cambial) layers.

- Cartilage is capable of two types of growth :appositional and interstitial.

- *Appositional growth*, the process that forms new cartilage at the surface of an existing cartilage. The cells of the inner (cambial) layer of perichondrium differentiate into chondroblasts and chondrocytes, which produce extracellular matrix. The chondroblasts progressively move apart while they produce matrix. When they are completely surrounded by a matrix material they produce, they become chondrocytes.

- *Interstitial growth*, the process which forms new cartilage within an existing cartilage mass. The chondrocytes lying within their lacunae retain their ability to divide, that's why the daughter cell occupies the same lacuna as the maternal cell

does. Such types of grows takes place in the embryonic development of cartilage and in case of its regeneration.

Physiological regeneration of cartilage is provided by the activity of chondrocytes. The chondrocytes produce chondromucoid, collagen and elastin.

With continued secretion of the cartilage matrix moves the cells away from their source of nutrition – perichondrium. Due to the lack of nutrition the chondrocytes, finally, lose their ability to divide; some of them even dye.

Cells of cartilage

Chondroblasts are young cells that are capable of proliferation and synthesis of the cartilage extracellular matrix.

Shape: polygonal, flattened.

Origin: arise from chondroprogenitor cells that, in their turn, arise from the mesenchymal stem cells. Stem cells, chondroprogenitor cells, chondroblasts and chondrocytes form one common differon.

Cytoplasm possesses strongly developed ER (both rough and smooth), Golgi complex, and a big amount of RNA. The cytoplasm of chondroblast exhibits basophilia.

In the process of development the chondroblasts become chondrocytes. The chondroblasts are responsible for the appositional growth of cartilage.

Chondrocytes are the main cells of cartilage.

Shape: oval, rounded or polygonal.

Localization: within the cavities of cartilage matrix (lacunae). Isogenous group – the group of chondrocytes situated in one common lacuna. The chondrocytes of one isogenous group arise as a result of division of one maternal cell. There distinguished three types of chondrocytes in one isogenous group:

Ist type of chondrocytes predominates in young developing cartilage. These chondrocytes are capable of **mitotic division**, which allows considering them as the source of reproduction of the isogenous groups. These cells are characterized by a high nuclear-cytoplasmic index. Their cytoplasm contains numerous vacuoles, well-developed Golgi complex, mitochondria and free ribosomes.

IInd type of chondrocytes is characterized by a decreased nuclear-cytoplasmic index, less active DNA synthesis; but increased RNA synthesis, strongly

developed Golgi complex that is responsible for **synthesis and secretion** of glycosaminoglycans and proteoglycans into the extracellular matrix.

IIIrd type of chondrocytes is characterized by a low nuclear-cytoplasmic index, strong development and regular arrangement of rough ER. The cells of this type retain ability to produce and secrete proteins, but their capacity of synthesis of glycosaminoglycans decreases dramatically.

Extracellular matrix of cartilage is composed of organic material: proteins (predominantly collagen of II type), lipids, glycosaminoglycans and proteoglycans. Cartilage has the highest concentration of proteoglycans.

The fibers orientation within the cartilage matrix is determined by the direction of the lines of force.

The extracellular matrix that surrounds the lacuna is more intensively basophilic and is referred to as **territorial matrix**.

Hyaline cartilage

Localization: the wall of trachea, bronchi, sites of junctions of ribs to sternum, articular surfaces, and epiphyseal plates.

Structure: Externally the hyaline cartilage is covered by perichondrium.

The perichondrium consists of two layers: 1) outer fibrous layer; 2) inner cellular layer.

The outer fibrous layer is formed by dense irregular connective tissue with a network of blood vessels;

The inner cellular layer is predominantly composed of cells – *chondroprogenitor cells and chondroblasts*.

Immediately under the perichondrium the young spindle-shaped chondrocytes are situated. The long axis of these young chondrocytes lies along the long axis of the cartilage itself.

The chondrocytes found in deeper layers of cartilage become oval or rounded in shape and form the isogenous groups. The young chondrocytes and the isogenous

groups are surrounded by the extracellular matrix containing high concentrations of chondromucoid and collagen fibers (II type of collagen).

• However not all kinds of hyaline cartilage have the same structure. The hyaline cartilage of articular surfaces (articular cartilage) is not covered by perichondrium. The articular cartilage is composed of three poorly distinguished zones: 1) outer zone; 2) medium zone; 3) deep zone.

The outer zone contains young immature cells.

The medium zone possesses large oval or rounded cells which form columns. The columns are directed perpendicularly to the articular surface.

The deep zone is composed of calcified cartilage; only here the blood vessels are found.

Elastic cartilage

Localization: external ear, external acoustic meatus, auditory tube, epiglottis.

Structure: In general, the structure of the elastic cartilage is similar to that of the hyaline cartilage. It is covered by perichondrium. The cells lay in lacunae and form isogenous groups.

Unlike hyaline cartilage, the extracellular matrix of elastic cartilage possesses **elastic fibers** along with collagen fibers.

Anastomosing with each other, the elastic fibers form a dense branching network and continue with the fibers of the perichondrium.

Besides this, elastic cartilage contains less lipids, glycogen and chondroitin sulfate than hyaline cartilage. Unlike hyaline cartilage, which calcifies with ageing, the matrix of elastic cartilage does not calcify during the ageing process.

Fibrocartilage

Localization: intervertebral discs, slightly movable joints, certain places where tendons attach to bones.

Structure: the extracellular matrix consists of parallel bundles of collagen fibers, which continue with the fibers of hyaline cartilage. The chondrocytes of elastic cartilage form rows. There is no surrounding perichondrium in fibrocartilage.

Extracellular matrix of fibrocartilage is characterized by presence of both type I and type II collagen fibers.

BONE TISSUE

Bone tissue is a specialized form of connective tissue that is characterized by a highly mineralized extracellular matrix.

Bone tissue is composed of cells (osteoblasts, osteocytes and osteoclats) and extracellular matrix (osseomucoid). The extracellular matrix consists of 70% of inorganic substances, principally calcium phosphate. Organic component is represented by proteins and lipids, which constitute bone matrix. Such combination of organic and inorganic components produces an extremely hard tissue capable of providing mechanical support.

Functions

support – due to its hardness and strength bone tissue provides mechanical support and movements of body;

protection – bone tissue protects entire organs from injuries;

storage site for calcium and phosphate.

Classification

Two types of bone tissue are distinguished depending on their structure and physical properties:

Woven bone

Lamellar bone

Woven bone (immatute) is characterized by irregular interlacing arrangement of ossein fibers (collagen type I), which are surrounded by calcified osseomucoid. Osteocytes lie in lacunae within osteomucoid between bundles of collagen fibers. Such type of bone is characteristic for skeleton of a developing fetus; in adults areas of woven bone are common in the alveolar sockets, sutures of skull and where tendons insert into bones.

Lamellar bone (mature) is characterized by a strictly parallel arrangement of bundles of collagen fibers and formation of bone lamellae.

According to the orientation of bone lamellae it is distinguished two types of lamellar bone: 1) compact bone; 2) spongy bone.

Compact bone (dense) is characterized by the absence of cavities. The diaphyses of long bones are built from this type of bone.

Spongy bone (cancellous) is characterized by the bone lamellae forming a meshwork of thin anastomosing spicules – trabeculae. The spaces within the bone meshwork are occupied by bone marrow. Spongy bone forms flat bones and epiphyses of long bones.

Development of bone

Mesenchyme is a source of development of bone tissue. During the embryonic development of bone the formation of two cell differons takes place.

The first cell differon – osteoprogenitor cell, osteoblast, osteocyte.

The second cell differon – hematogenic cells: stem cell of blood, common myeloid progenitor, granulocyte/monocyte progenitor, osteoclast precursor, osteoclast.

It is distinguished an embryonic and post-embryonic formation of bone.

The embryonic formation of bone (osteohistogenesis) is classified as direct (intramembranous ossification) and indirect (endochondral ossification).

Direct osteohistogenesis – development of bone directly from

mesenchyme.

Indirect osteohistogenesis – a cartilage model serves as a

precursor of future bone.

The post-embryonic bone formation takes place in case of regeneration of bone or ectopic osteohistogenesis.

Embryonic osteohistogenesis

Direct (intramembranous ossification) is characteristic for

development of woven bone during formation of flat bones of skull and occurs during first month of embryonic development. It is characterized by formation of primary membrane osteoid bone, which is then impregnated with salts of Calcium and Phosphorus.

Intramembranous osiffication includes four stages:

Formation of osteogenic island;

Osteoid stage;

Calcification of extracellular matrix, formation of woven bone;

Formation of secondary spongy bone.

1)Formation of osteogenic island. The focal proliferation and aggregation of mesenchymal cells starts at the sites where future bone is destined to form. It results in formation of osteogenic island, which then penetrated by blood vessels.

2) Osteoid stage. The cells of osteogenic islands differentiate into osteoblasts, which start to produce the organic bone matrix (osteoid) - oxyphilic extracellular matrix with collagen fibers. As the matrix is produced and the amount of collagen fibers increases, the osteoblasts within bone matrix become separated from one another, but they still remain connected to each other by their thin cytoplasmic processes. The components of bone matrix also include mucoproteins that harden the collagen fibers in a dense mass. When the osteoblasts become embedded into the bone matrix they differentiate into osteocytes. Then more of the surrounding mesenchymal cells proliferate, differentiate into osteoblasts and add more matrix. This process is called **appositional growth of bone**.

3) Calcification of the extracellular bone matrix. The osteoblasts produce enzyme called phosphatase that brakes down the glycerophosphate taken from blood into sugar and phosphoric acid. Phosphoric acid reacts with calcium salts contained in ground substance and collagen fibers of the bone matrix, thereby forming the hydroxyapatite crystals. The important role in bone matrix calcification is carried out by the matrix vesicles with diameter of 1μm which contain active alkaline

phosphatase and pyruvate phosphatase. The significant role in the process of calcification also belongs to the osteonectin – the glycoprotein that binds calcium and phosphorus salts to collagen.

The result of calcification is formation of bone spicules or trabeculae which anastomose with one another and form a wide network. The space between the spicules is occupied by loose connective tissue with blood vessels.

By the finishing of osteogenesis numerous osteoprogenitor cells and fibers appear around the future bone. A portion of connective tissue immediately surrounding the bone spicules is transformed into the periosteum that provides nutrition and regeneration of bone. Such bone, formed at early stages of embryonic development, is called woven or membrane or primary spongy bone.

Formation of secondary spongy bone (lamellar). This stage is

accompanied by destruction of particular portions of primary bone and its penetration by blood vessels. This process, both in embryonic and postembryonic periods, involves osteoclasts.

The mesenchyme surrounding blood vessels differentiate into new osteoblasts which produce bone lamellae. The collagen fibers in each lamella are laid down parallel to one another, but in different direction to adjacent lamella. Due to that the blood vessel becomes surrounded by concentric bone cylinders insert in one another (primary osteon), the formation of woven bone stops and it is substituted by the lamellar bone.

At the side of periosteum and endosteum there are formed the outer and inner circumferential bone lamellae which surround the whole mass of the bone.

By the described mechanism the formation of flat bones occurs. Formed in the embryonic period the bone is remodeled (the old osteons are destroyed and the new ones are formed) during the whole future life.

Indirect osteogenesis

Indirect osteogenesis includes 4 stages:

Formation of hyaline cartilage model.

Perichondral ossification.

Endochondral ossification.

Epiphyseal ossification.

Formation of hyaline cartilage model occurs at the 2nd month of the embryonic development. It also begins with proliferation and aggregation of mesenchymal cells at the site of the future bone. The mesenchymal cells differentiate into chondroblasts and the hyaline cartilage model with the general shape of the future bone is formed. The cartilage model is covered by perichondrium. Once established, the cartilage model grows by interstitial and appositional growth.
Perichondral ossification.

The process of bone formation is initiated at the diaphyseal region of cartilage model. The perichondreal cells in the midregion of diaphysis of cartilage model differentiate into osteoblasts and form there the intramembranous (woven) bone. This cuff of bone around the cartilage model is called bony collar**.** The bony collar alters the nutrition of cartilage resulting in dystrophic changes in the midregion of cartilage model. The chondrocytes enlarge; their surrounding cartilage matrix is resorbed. With the death of chondrocytes much of the matrix breaks down and neighboring lacunae become confluent, producing a large cavity.

The unchanged distal portions of diaphysis continue growing. The chondrocytes located at the boundary of epiphysis and diaphysis are arranged in columns oriented in the same direction with the long axis of future bone.

It must be mentioned that the chondrocytes in column undergo two opposite processes simultaneously:

proliferation and growth in distal regions of diaphysis;

dystrophy (hypertrophy) and death in the midregion of diaphysis.

The hypertrophic chondrocytes begin to synthesize alkaline phosphatase that is responsible for calcification of cartilage matrix, resulting in its basophilic staining and fragility. With the expanding of blood vessels and appearance of osteoblasts perichondrium is transformed into periosteum. Blood vessels with surrounding mesenchyme, osteoprogenitor cells and osteoclasts grow through the thin diaphyseal bony collar and vascularize the calcified cartilage. Osteoclasts discharge the hydrolytic enzymes that destroy the calcified cartilage matrix. The cavities appeared after the destruction of cartilage are now occupied by osteoblasts, which form here the bone tissue.

Endochondral ossification is the process of bone formation within the cartilage model (diaphyseal ossification center).

Due to the activity of osteoclasts the endochondral bone is destroyed and the large cavities appear. These cavities are the future site of red bone marrow location. The hemopoietic stem cells gain access here via the blood vessels and give rise to the red bone narrow including all the blood cell lineages.

At the same time the periosteum gives rise two new and new bone lamellae, which expand in length and with forming a dense bone. The concentric bone lamellae are formed around blood vessels forming the primary osteons.

Epiphyseal ossification is the process of formation of ossification centers in epiphysis. It is preceded by differentiation and hypertrophy of chondrocytes and calcification of cartilage matrix.

Between the epiphyseal and the diaphyseal ossification it is formed the epiphyseal plate, which consists of 3 zones:

zone of reverse cartilage;

zone of columnar cartilage (proliferation);

zone of hypertrophy.

When the epiphyseal and diaphyseal ossification centers become confluent the bone growth stops. In human it happens at the age of 20-25 years.

Cells of bone tissue

The bone tissue contains three types of cells:

osteocytes;

osteoblasts;

osteoclasts.

Osteocytes are predominant definitive cells of bone tissue, which have lost their capacity of division.

Shape: elongated, possess processes;

Size: 15×45 μm;

Nucleus: relatively compact, round;

Cytoplasm: less basophilic, poorly developed organelles.

Localization: occupies bone lacuna, which conforms to the shape of the cell.

Osteoblasts are differentiated bone-forming cells that secrete bone matrix.

Shape: cuboidal, pyramidal, or polygonal;

Size: 15-20 μm

Nucleus: round or oval in shape, eccentrically located, may contain one or more nucleoli.

Cytoplasm: markedly basophilic, exhibits well-developed rough Endoplasmic reticulum, mitochondria, Golgi complex, big amount of RNA.

Osteoclasts are derived from the hemopoietic progenitor cells; they are responsible for bone and cartilage resorption.

Shape: irregular, rounded;

Size: up to 90 μm;

Nucleus: from 3 to several decades;

Cytoplasm: markedly acidophilic, contains numerous lysosomes and mitochondria.

At the site of adhesion to the resorbed bone the osteoclast exhibits two distinct zones:

ruffled border;

clear zone (sealing zone).

Ruffled border is the part of the cell in direct contact with bone. It contains numerous deep plasma membrane infoldings forming microvillous-like structures that increase the surface area for the exocytosis of hydrolytic enzymes.

Clear zone is a ring-like perimeter of cytoplasm adjacent to the ruffled border that demarcates the area of bone which is being resorbed. It contains actin microfilaments, but lacks other organelles.

The peripheral cytoplasm of the osteoclast contains numerous small vesicles and vacuoles, mitochondria, and lysosomes; rough ER is poorly developed. It is suggested that osteoclasts discharge CO_2, whilst the enzyme carboanhydrase uses it produce the acid H_2CO_3 that dissolves Calcium salts and destroys the organic matrix of bone. As a result of osteoclast activity the lacuna is formed at the site of its attachment to a bone.

Extracellular matrix of bone tissue

The extracellular matrix of bone tissue consists of ground substance impregnated with inorganic salts, and bundles of collagen fibers.

The ground substance contains small amounts of chondroitin sulfuric acid and large amounts of citric acid that binds calcium to the organic bone matrix. The ground substance of bone tissue also contains regularly arranged hydroxyapatite crystals and amorphous Calcium phosphate. Bone tissue contains more than 30 microelements (Cu, Sr, Zn, Mg, Ba etc.)

The collagen fibers form bundles. They are built of the type I collagen. In the primary (woven) bone the collagen fibers are randomly scattered, whilst in the mature (lamellar) bone they are regularly arranged.

The structure of long (tubular) bones

The long bones are predominantly composed of the lamellar bone tissue (except tubercles).

Anatomically the long bone consists of central part – diaphysis and peripheral endings – epiphyses.

The diaphysis of the long bone is composed of three layers:

periosteum;

osteonal layer;

endosteum.

Periosteum consists of the outer fibrous layer formed of collagen fibers, and the inner cellular layer containing osteoprogenitor cells and osteoblasts. The periosteum provides nutrition, appositional growth and regeneration of the bone.

Osteonal layer (the bone proper) is separated from the periosteum by outer circumferential laminae and from endosteum by inner circumferential laminae.

The outer circumferential lamellae do not form close rings around the diaphysis; they are overlapped by succeeding lamellae. **Perforating canals (Volkmann's canals)** are channels in lamellar bone which perforate periosteum and outer circumferential lamellae to reach the osteonal canal. Besides this, perforating collagen fibers (Sharpey's fibers) also enter bone tissue through the periosteum.

The inner circumferential lamellae are distinguished only at the sites where the compact bone immediately bounds with the marrow cavity. If the compact bone continues with the spongy bone, the inner circumferential lamellae continue with the spongy bone lamellae.

Osteonal layer. The osteonal layer is composed of cylindrical units called **osteons or Haversian systems.** The osteon, as a ***structural unit of compact bone***, is a bony tube with a diameter of 20-300 μm.

Each osteon consists of 5-20 concentric lamellae of bone matrix which surround the central (Haversian) canal that contains vascular and nerve supply. The lacunae with osteocytes are located within the bone lamellae. The processes of osteocytes lying in canaliculi anastomose with each other via gap junctions. The system of canaliculi opens to the osteonal canal, thereby serving for passage of substances between the osteocytes and blood vessels.

The collagen fibers in the concentric lamellae in an osteon are laid down parallel to one another in any given lamella but in different directions in adjacent lamellae. This arrangement imparts great strength to the osteon.

Between the osteons are remnants of previous concentric lamellae called **interstitial lamellae**.

* **Endosteum** is a lining tissue of bone facing the marrow cavity. It is composed of fibrous connective tissue containing osteoblasts and osteoclasts.

* **Bone epiphysis** is composed of spongy bone. Externally it is covered by periosteum. Under the periosteum are the layer of circumferential lamellae and osteonal layer. In the depth of epiphysis the bone lamellae form a network of trabeculae. The spaces between these trabeculae are filled with reticular tissue and hemopoietic cells.

Growth of long bones

The growth of long bones in length is provided by the presence of the epiphyseal cartilaginous plate, within which the two opposite processes occur simultaneously:

destruction of the epiphyseal cartilage;

continuous proliferation of the cartilage cells and formation of the new cartilage.

Three zones are distinguished in the epiphyseal cartilage:

zone of reverse cartilage;

zone of proliferation (zone of columnar cells);

zone of hypertrophy.

* Zone of reverse cartilage consists of the isogenous groups of chondrocytes, which exhibit no active proliferation or cartlage matrix production. This zone connects the cartilaginous plate with the bone. Between the bone and the cartilage are blood capillaries.

* Zone of proliferation consists of cartilage cells which undergo division and organize into columns.

* Zone of hypertrophy contains greatly enlarge (hypertrophic) cartilage cells. The hypertrophied cells begin to degenerate and the cartilage matrix becomes calcified. The calcified cartilage situated nearest the diaphysis is in direct contact with the connective tissue of the bone marrow cavity. In this region, small blood vessels and accompanying connective tissue invade the space previously occupied by the dying chondrocytes. The invading blood vessels are the source of osteoprogenitor cells, which will differentiate into bone-producing cells (osteoblasts).

When an individual achieves maximal growth, proliferation of new cartilage within the epiphyseal plate terminates. The cartilage that has already been produced in the epiphyseal plate continues to undergo changes that lead to the formation of new bone until there is, finally, no remaining cartilage. At this point the epiphyseal and diaphyseal marrow cavities become confluent. The elimination of the epiphyseal plate is called **epiphyseal closure**.

The growth of bone in width is provided by the proliferation of the osteogenic layer of periosteum.

Immature (woven) bone

Immature bone is the major bone type in developing fetus. In adults it is found in the alveolar sockets of the oral cavity and where tendons insert into bone.

The collagen fibers form dense interlacing fibers.

The matrix of immature bone has more ground substance than does of the matrix of mature bone. The osteocytes lying in lacunae tend to be randomly arranged.

Periosteum forms the external covering of immature (woven) bone.

Mature (lamellar) bone

Lamellar bone consists of the bone lamellae, which are composes of osteocytes and mineralized ground substance with collagen fibers.

ODESA NATIONAL MEDICAL UNIVERSITY

DEPARTMENT OF HISTOLOGY, CYTOLOGY AND EMBRYOLOGY

METHODICAL RECOMMENDATION OF LECTURES

for dentistry faculty

THEME: “Specialized tissue. Muscle tissue.”

Approved on the methodical conference of department

«____»_____ 20___., protocol №_____

Head of Department, doc._____ Tiron O.I.

Approved on the methodical conference of department

«____»_____ 20___., protocol №_____

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«____»_____ 20___., protocol №_____

Head of Department, doc._____ Tiron O.I.

Theme: "Specialized tissue. Muscle tissue."-2h.

1. Relevance of the topic:

Muscle tissues are a group of tissues that have different origins and structures, but are united according to a functional feature - contractility. The entire group is characterized by an elongated shape of their structural components and the presence of specialized structures - myofibrils. Muscle elements can be unstated and striated. Accordingly, distinguish between smooth and striated muscle tissue.

Various forms of body movement and its functions are associated with muscle tissues: body movement in space, heart contractions, and blood flow through the vessels, movement of food masses in the intestines, urination, childbirth, and others. Besides, muscle tissue stores energy material. In case of violation of the structure and functions of muscle tissue, serious diseases occur. This makes a detailed study of muscle tissue necessary for future doctors. Besides, for more than 100 years, researchers of various profiles have been concerned about the problems of myogenesis and muscle regeneration.

2. Purpose of the lecture

2.1. Learning

To acquaint students with the classification, structure, histophysiology, physiological and reparative regeneration of muscle tissues.

2.2. Educational

To form students' professional significance of the topic. Discuss the issue of deontology.

3. Plan and organizational structure of the lecture.

Lecture stages	Contents of the lecture stages	Aim	Lecture equipment	Time distribution
Preparatory stage	Relevance of the topic and goal setting	I	Tables. Slides. Dummies.	3 min.
	General morphological and functional characteristics of muscle tissue	II		3 min.
The main stage	Unstriated muscle tissue of mesenchymal origin	III		10 min.
	Myocyte. Organization of the contractile apparatus.	III		10 min.
	Striated muscle tissue	III		17 min.
	Muscle fiber structure	III		17 min.
	Muscle as an organ. Cardiac muscle tissue	III		20 min.
The final stage	Summary of the lecture. General conclusions			5 min.
	Self-study assignment			5 min.

4. Topic content

Addition

5. Materials for activating students during the lecture.

1. Sources of muscle tissue development.

2. Features of the structure and function of smooth muscle tissue myocytes.

3. Skeletal muscle tissue, localization, functional features.

4. Muscle fiber as a structural unit of skeletal muscle tissue.

5. The structure of the myofibril. Sarcomere.

6. The structure and function of myosatelytocytes.

7. Sarcoplasmic reticulum. T-systems.

8. Histophysiology of contraction.

9. Tipi muscle fibers.

10. The structure of the muscle of the yak organ.

11.Morphofunctional characteristics of the heart muscle. Contractile cardiomyocyte.

12. Features of the structure of atrial myocytes.

13. Conducting cardiomyocytes, types, structural features.

14. Way store generate different types of muscle tissue.

6. General material and methodical support of the lecture

Tables:

1. Striated skeletal muscle tissue.

2.Smooth muscle tissue

3.Cardiac muscle tissue

Slides:

1.myosatelytocytes

1.histogenesis of skeletal muscle tissue

2.myocardium

Dummies:

1.fiber of cross-braided skeletal tissue

List of recommended literature .

The main one:

1.Lutsyk O.D., Tchaikovsky Y.B. Histology, cytology, embryology Vinnytsia, New Book, 2018.
2.Barinov E.F., Tchaikovsky Y.B. General histology and embryology of internal organs: textbook.Kyiv: Medicine; 2013
3.Wojciech Pawlina. Histology: textbook and atlas. WSV: Medicine, 2021.

Additional:

1.Histology and embryology of internal organs: textbook / E.F. Barinov, Y.B. Tchaikovsky, O.M. Sulaeva et al.
2.Cytology of human organs and tissues edited by L.S.Bolgova. Kyiv: Book-plus, 2018, p.288

Theme: "Specialized tissue. Muscle tissue." *Addition*

Muscle tissue (textus muscularis) is a specialized tissue, whose structural elements are capable of contraction, which is accompanied by changes in the membrane potential. Contraction, as a process of change of shape of the contractile elements, occurs due to the interaction between actin and myosin filaments with the participation of Calcium ions and other structural proteins.

Sources of development

Five different sources of development can give rise to the muscle tissue. Depending on its origin muscle tissue is classified into five different histogenetic types:

1) somatic type – originates from myotomes of mesoderm (skeletal muscle)

2) coelomic type – originates from ventral mesoderm (cardiac muscle)

3) visceral type – originates from mesenchyme (smooth muscle of inner organs)

4) neural type – originates from the neural tube (smooth muscle of the iris)

5) epidermal type – originates from skin ectoderm (myoepithelial cells of sweat, mammary, salivary and lachrymal gland)

Morphofunctional classification of the muscles

1. Smooth muscle, in which the cells do not exhibit cross-striations.

2. Striated muscle, in which the fibers exhibit cross-striations due to the arrangement of the actin and myosin myofilaments.

THE SMOOTH MUSCLE

The smooth muscle of mesenchymal origin

Histogenesis. The stem cells and the cells-precursors of the smooth muscle cells are suggested to be related to the cells-precursors of the connective tissue fibroblasts. Like the fibroblast, the smooth muscle cells of mesenchymal origin produce glycosaminoglycans and collagen.

Localization – the wall of the hollow organs (alimentary tract, respiratory tract, urinary tract, reproductive tract, blood and lymphatic vessels), the capsule of spleen and lymph nodes.

Structural and functional unit – **smooth muscle cell**.

The smooth muscle is fusiform cell, which could be from 20 to 500 μm in length and from 5-8 μm in diameter. In the uterus, endocardium, aorta, urine bladder are found the smooth muscle cells which possess processes. During the contraction the smooth muscle cell becomes round or even spiral.

The plasmalemma of the smooth muscle cells forms numerous invaginations – pinocytic vesicles and **caveolae**, through which the Calcium ions enter the

cytoplasm. The cytoplasm is acidophilic. The general-function organelles are concentrated at each end of the nucleus. There could be found inclusions of lipids, carbohydrates and pigments. The well developed **general-function organelles** of the smooth muscle cells are smooth Endoplasmic reticulum and mitochondria.

The specialized organelles are represented by the actin and myosin myofilaments.

The actin (thin) myofilaments form the three-dimensional network within the cytoplasm of the smooth muscle cell. The sites of attachment of the actin myofilaments to the cytoplasm are called **dense bodies**. These structures are distributed throughout the cytoplasm and are composed of the protein α- actinin. The actin myofilaments are more numerous than the myosin. Besides the contractile protein actin, the thin filaments are composed of the structural proteins – tropomyosin, caldesmon, calponin.

The myosin (thick) filaments are longitudinally arranged within the cytoplasm of the smooth muscle cell. During the contraction the actin filaments are pulled over the entire length of the myosin filaments. The process of the smooth muscle contraction is initiated by the phosphorylation of the myosin, which depends on concentration of the Calcium ions. The regulation of Calcium concentration is provided by the special protein – **calmodulin**. The complex of Calcium and calmodulin activates the enzyme that phosphorylates the myosin. Only the phosphorylated myosin is capable to interaction with the actin.

Due to the molecular interactions with the myosin, the actin filaments slide towards each other and, being attached to the plasmalemma, change the shape of the smooth muscle cell.

Each smooth muscle cell is surrounded by a basal lamina, which contains holes. Due to these holes the gap junctions – **nexus** are formed between two adjacent smooth muscle cells. The smooth muscle cells are surrounded by thin collagen, elastic and reticular fibers which form the reticular network – **endomysium.** The groups of 10-12 smooth muscle cells are surrounded by a connective layer containing blood vessels and nerve fibers.

The smooth muscle of epidermal origin

The myoepithelial cells of this tissue originate from the skin ectoderm.

Localization – sweat, salivary, mammary, lachrymal glands. Having the same precursors as the secretory epithelial cells of the named glands, the myoepithelial cells immediately adjoin the secretory cells and have a common basal lamina.

Shape – stellate or basket-like. The myoepithelial possess cytoplasmic processes, which surround the secretory portions of the glands and **stimulate the discharge of secretion**. The contractile apparatus of the myoepithelial cells is organized similarly to that of the smooth muscle cells of mesenchymal origin.

The nucleus and organelles are situated in the center of the cell cytoplasm.

The ***regeneration of the myoepithelial cells is possible*** due to the low-differentiated cells of the epidermal origin.

The smooth muscle of neural origin

The smooth muscle cells of neural origin originate from the neural tube.

Localization – constitute two muscles of the iris – m.sphincter pupillae and m.dilatator pupillae (iris dilator muscle, iris sphincter muscle).

The smooth muscle tissue as a part of organs

The smooth muscle cells are collected in bundles, which are separated by thin layers of the loose connective tissue (perimysium). Such bundles form the whole muscle, which is covered by thicker layer of the connective tissue (epimysium). The connective tissue layers contain blood vessels, nerve fibers, which supply and innervate the smooth muscle cells.

Localization – the walls of the hollow organs (respiratory system, alimentary canal, reproductive system, blood vessels).

STRIATED MUSCLES

T he cardiac muscle tissue

Histogenesis. The source of development of this tissue is the *myoepicardial plate* (symmetric areas of the visceral layer of splanchnotome). The most cells of the myoepicardial plate give rise to the cardiac muscle cells, whilst the rest of the cells undergo differentiation into the mesothelial cells of the epicardium).

There are distinguished three types of the cardiac muscle cells:

contractile

conducting

secretory

The structure of the contractile cardiac muscle cells

Shape – elongated, cylindrical

Size – 100-150 μm.

The contractile cardiac muscle cells adjoin each other, thereby forming chains which compose so-called functional fibers of 10-20 μm in length.

The specialized cell-to-cell attachment of the cardiac muscle cells is called ***intercalated disc***. Some cardiac muscle cells in a "fiber" may join two or more cells through intercalated disc, thereby forming a branched fiber.

The lateral surface of the cardiac muscle cells is covered with basal lamina.

*Nucleus (*may be 2) is oval in shape, occupies the central portion of cytoplasm. In most cases nuclei of the smooth muscle cells are polyploid.

Cytoplasm contains general-function organelles including Golgi complex, centrosome, poorly developed rough ER, lysosomes. A highly developed **smooth ER** forms anastomosing **tubules of the L-systems**. Besides these, the cytoplasm exhibits inclusions of glycogen, lipids and **myoglobin**. There are also found numerous mitochondria, which from chains surrounding the specialized organelles – **myofibrils**.

The structure of myofibrils

The myofibrils are composed of regularly arranged actin and myosin filaments, which represent the contractile proteins. For structuring of the actin and myosin filaments there are present the specialized structures – *telophragm (Z-line) and mesophragm (M-line).*

♦ Telophragm is a network of protein molecules, which are attached to the plasmalemma. On a longitudinal section of the cardiac muscle cell the

telophragms appear as about 100 nm thick lines, which were named Z-lines. A portion of the myofibril located between two Z-lines is called **sarcomere**.

♦ In the middle of sarcomere it is located the mesophragm (M-line). The myosin (thick) filaments are restricted to the central portion of sarcomere (M-line). The actin (thin) filaments are attached to the Z-line. Each myosin filament is accompanied by six actin filaments.

A segment of the sarcomere, where are found only myosin filaments is called H-band (light zone). The segment of sarcomere, where both actin and myosin filaments are found is called A-band.

Two neighboring segments of two adjoining sarcomeres, separated by the Z-line and containing only actin filaments compose the I-band.

Such names of the bands were given because of the different light refraction. In polarizing microscopy the A-bands are birefringent (alter polarized light in two planes). Being doubly refractive, the *A*-bands are dark *(anisotropic)*. The *I*-bands are monorefringent (do not alter the plane of polarized light) and called *isotropic*.

The myofibrils are surrounded by mitochondria and smooth ER. The mitochondria are quite large and form a dense three-dimensional network around at the area of I-band.

At the level of telophragm the plasmalemma of the cardiac muscle cell forms deep invaginations named transverse tubules (T-tubules). The T-tubules in the cardiac muscle include not only the invagination of the plasmalemma, but also the invagination of the basal lamina. The T-tubules provide fast conduction of the action potential to each myofibril, thereby providing the synchronous contraction. Along the myofibrils there are found cisterns of the smooth ER, which anastomose with each other and approach the T-tubules.

As previously noted, the intercalated disc is the attachment site between cardiac muscle cells. The intercalated disc includes several types of cell-to-cell contacts: interdigitations, adhering junctions, desmosomes and gap junctions (nexus). The transverse component of intercalated disc is represented by adhering junctions and desmosomes. The adhering junction serves as the site at which the actin filaments from the neighboring cardiac muscle cell anchor. The desmosome helps prevent the cells from pulling apart under the strength of contraction.

Gap junctions (nexus) constitute the lateral component of the intercalated disc. Gap junctions provide ionic continuity between adjacent cardiac muscle cells, thus allowing informational macromolecules to pass from cell to cell.

The structure of conducting cardiac muscle cells

Size – are significantly larger than the contractile cells (100 μm in length, 50 μm in width).

Cytoplasm contains the all general-function organelles. The mitochondria are evenly distributed through the cytoplasm.

Myofibrils are not numerous and concentrated at the periphery of the cytoplasm.

Plasmalemma does not form T-tubules.

The conducting cardiac muscle cells are connected via intercalated discs, but they are more primitively organized that those of the contractile cardiac muscle cells.

The conducting cardiac muscle cells are organized into nodes and include the following types:

Pacemaker cells (SA node) –generate nerve impulse;

Transitional cells (AV node);

Cells of the bundle of His and Purkinje fibers.

The conducting cardiac muscle cells initiate, regulate and coordinate the heartbeat by conducting impulses to the contractile cardiac muscle cells.

The regeneration of the cardiac muscle is believed to be impossible because of lack of the stem and progenitor cells.

The molecular mechanisms of muscle contraction

When the muscle is relaxed the Calcium ions are deposited in the tubules of its smooth ER. The action potential spreads through the plasmalemma and T-tubules and initiates releasing of the Calcium ions. The Calcium ions interact with the special regulatory proteins of the myofibrils – *troponin and tropomyosin*. The troponin and tropomyosin surround the actin filament and mask the myosin-binding site on the actin molecule. The interaction with Calcium ions makes the troponin and tropomyosin molecules open the myosin-binding sites on the actin molecule, which initiates the movement of actin filaments along the myosin filaments. As a result of such movement of the actin filaments (as they are attached to the Z-lines), the sarcomere shortens. When a muscle contracts, each sarcomere shortens and becomes thicker, but the myofilaments remain the same length.

The process of muscle contraction requires energy of the ATP. The heads of myosin are capable of binding the ATP molecules and, oppositely, breaking down the ATP.

SKELETAL MUSCLE

The skeletal muscle tissue originates from cells of myotomes of the dorsal **mesoderm**. The skeletal muscle progenitors differentiate into types of cells.

Myoblasts which fuse together and form a multinucleated syncytium – myotubes. The myotubes undergo further differentiation into the myosymplasts.

Satellite cells, which do not fuse with other myoblasts.

The structure of muscle fiber

Muscle fiber is the structural and functional unit of the skeletal muscle tissue. The muscle fiber is composed of myosymplast, satellite cells and basal lamina.

When viewed in a cross section, the mature multinucleated muscle fiber reveals a polygonal shape with a diameter of 10-150 μm. The length of each muscle fiber is the same as the length of the whole muscle.

Sarcolemma ("sarcos"-meat) of muscle fiber consists of two layers. The inner layer is the plasma membrane of myosymplast. The outer layer is represented by a basal lamina with reticular and thin collagen fibers woven into it.

Myosymplast is covered by a plasma membrane, which forms T-tubules through that the action potential is conducted.

The myosymplast may possess up to several thousands nuclei. The nuclei are situated below the plasma membrane; they are elongated, contain nucleoli and small amounts of heterochromatin.

The cytoplasm of myosymplast was named sarcoplasm. The sarcoplasm contains three groups of well-organized structures:

general-function organelles;

specialized organelles – **myofibrils**;

inclusions – lipids, carbohydrates, pigment.

♦ The general-function organelles surround nucleus. The mitochondria are large and numerous. The rough endoplasmic reticulum (rER) is poorly developed. The smooth ER is extremely well developed and here it was named ***sarcoplasmic reticulum***. The sarcoplasmic reticulum represents the system of tubules and flattened cisterns which surround the myofibrils. It forms a collar-like structure around the sarcomere. The terminal cisterna of the sarcoplasmic reticulum forms L-tubule which serves as reservoir for Ca^{2+}.

Between two neighboring L-tubules there is located one transverse tubule (T-tubule). The T-tubule in the skeletal muscle is an invagination of plasma membrane of myosymplast. Also located around the myofibrils are large number of mitochondria and glycogen granules, both of which are involved in providing the energy necessary for contraction.

♦ The myofibrils are located along the muscle fiber; they are 1-2 μm thick and extend the full length of the muscle fiber.

The structure of myofibril

Myofibrils are composed of bundles of myofilaments. Cross-striations are seen in preparations of striated muscle examined with a phase contrast or polarizing microscope as alternating light and dark bands. These bands are termed the **I-band** (isotropic) and the **A-band** (anisotropic).

In H&E- stained preparation the A-bands are more intensively stained than the I-bands. In the center of each A-band there is a thin dark line called telophragm or **Z-line**. In the center of each A-band there is a less dense light region named **H-band**. Furthermore, the H-band is bisected by a narrow dense line called **M-line** (mesophragm).

The structural and functional unit of myofibril is **sarcomere**. Sarcomere is the region of myofibril bounded by two Z-lines (telophragms). The length of each sarcomere is 2-3nm.

Sarcomere is the basic contractile unit of striated muscle. The sarcomere is composed of ***actin (thin) and myosin (thick) myofilaments***. The arrangement of thick and thin filaments gives rise to the density differences which produce the cross-striations of the myofibril.

~ The actin (thin) filaments attach to the Z-line, compose the I-band and extend into the A-band the edge of the H-band. The thin filaments are

composed of the contractile protein actin and structural proteins troponin and tropomyosin. They are approximately 5nm in diameter and 1 μm in length.

~ The thick (myosin) filaments are found only in the A-band. They are composed of the contractile protein myosin. The thick filaments are 1,5 μm long and 10-12 nm in diameter.

Each myosin filament is accompanied by two actin filament.

Satellite cells

Satellite cells are interposed between the plasma membrane of myosymplast and external basal lamina. The plasma membrane of the satellite cells attaches to that of the myosymplast. Each satellite cell has a single nucleus with a dense chromatin network. Their cytoplasm contains evenly distributed mitochondria and ER. The Golgi complex and centrosome surround the nucleus. The specialized contractile organelles are absent in the satellite cells.

THE TYPES OF SKELETAL MUSCLE FIBERS

The free types of skeletal muscle are **red muscle fibers** (type I), **intermediate muscle fibers** (type IIa), and **white muscle fibers** (type IIb).

Three types of the fibers are found in any given skeletal muscle; their proportion depends on the functional role of the muscle.

Red muscle fibers appear red in fresh specimens because of large amounts of myoglobin and cytochrom complexes. They are characterized by slow myosin ATPase reaction velocity. These fibers are slow-twitched and fatigue-resistant.

Intermediate muscle fibers. Besides high myosin content and numerous mitochondria the intermediate fibers also contain large amounts of glycogen and are capable of anaerobic glycolysis. Such fibers are both quite fast-twitched and fatigue-resistant.

White muscle fibers appear light pink in fresh specimens and contain less myoglobin and fewer mitochondria than two other types of muscle fibers. They have a low level of oxidative enzymes, but exhibit high anaerobic enzyme activity and store a considerable amount of glycogen. The white muscle fibers are fast-twitched and fatigue-prone.

THE SKELETAL MUSCLE AS AN ORGAN

A skeletal muscle consists of striated muscle fibers held together by connective tissue.

The individual muscle fiber is surrounded by a delicate layer of connective tissue called **endomysium.** Reticular and collagen fibers of the endomysium interweave with fibers of the sarcolemma.

Perimysium is a thicker connective tissue layer that surrounds a group of fibers to form a bundle.

Epimysium is the sheath of dense connective tissue that surrounds the whole muscle. The major vascular and nerve supply of the muscle penetrates the epimysium.

ODESA NATIONAL MEDICAL UNIVERSITY

DEPARTMENT OF HISTOLOGY, CYTOLOGY AND EMBRYOLOGY

METHODICAL RECOMMENDATION OF LECTURES

for dentistry faculty

THEME: «Nervous tissue.»

Approved on the methodical conference of department

«____»_____ 20___., protocol №_____

Head of Department, doc._____ Tiron O.I.

Approved on the methodical conference of department

«____»_____ 20___., protocol №_____

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Head of Department, doc._____ Tiron O.I.

Theme: “Nervous tissue.”-2h.

1. Relevance of the topic

The nervous system in all higher animals and humans is a rather complex and have a complex histological structure. Nervous tissue is the main structural element of the nervous system, which regulates the activity of tissues and organs, their interaction and connection with the environment, correlation of function, integration and adaptation of the organism. Nerve tissue provides the perception of irritation and the transmission of nerve impulses.

Nerve tissue consists of nerve cells (neurocytes, neurons), nerve fibers and neuroglia cells associated with them. Together, these structural elements constitute the only morphological and functional basis of all organs of the nervous system. Knowledge of the histology of the nervous tissue creates the basis for understanding the structure and function of the nervous system, is the beginning

for mastering the relevant sections of biomedical and clinical disciplines. Modern understanding of the degeneration and regeneration of nerve fibers in the composition of the peripheral nerve is important for surgeons of various profiles, especially neurosurgeons and traumatologists.

2. Purpose of the lecture

2.1. Learning

To acquaint students with the classification, structure, histophysiology, physiological and reparative regeneration of nerve tissues.

2.2. Educational

To form students' professional significance of the topic. Discuss the issue of deontology.

3. Plan and organizational structure of the lecture.

Lecture stages	Contents of the lecture stages	Aim	Lecture equipment	Распределение времени
Preparation stage	Relevance of the topic and goal setting.	I	Tables. Slides. Dummies	3 min.
	General morphofunctional characteristics of the nervous tissue.	II		3 min.
The main stage	Neuroglia. General characteristics, classification.	III		10 min.
	Nerve fibers. Classification. Myelinated and non-myelinated nerve fibers.	III		10 min.
	Nerve endings. Receptors and effectors, classification, structure	III		18 min

	Synapses. Classification, structure. The transmission of the nerve impulse at the synapse.	III		18 min
	Morphological substrate of receptor activity (cells) of the system.	III		18 min.
The final stage	Summary of the lecture. General conclusions.			5 min.
	Self-study assignment			5 min.

4. Topic content

addition

5. Materials for activating students during the lecture.

1.Nerve fibers. Classification. Functions.

2.The structure of myelin-free nerve fibers. Features of the conduction of a nerve impulse.

3.The structure of myelinated nerve fibers. Features of the conduction of a nerve impulse.

4.Morphology of the processes of myelinated nerve fibers.

5.Stages of regeneration of nerve fibers after damage.

6.Nerve endings. Classification.

7.Sensitive nerve endings. Functions. Classification, structure.

8. Features of the structure of the little body of Vater-Pacini, Meissner, Merkel's disk, neuromuscular spindle.

9. Effector nerve endings. Functions and structure of the motor ending.

10. Synapses. Functions. Classification, structure.

11. Principles of the structural organization of chemical and electrical synapses.

12. The structure of the peripheral nerve.

6. General material and methodological support of the lecture.

Tables:

1.Nerve cells

2.Neuroglia

3.Myelinic and nonmyelinated nerve fibers

4 synapses

5.Receptor nerve endings

Slides:

1neurofibrilli

2.Astrocytes

3.Ependymocytes

Dummies:

1 Neuron

2.Myelin nerve fiber

3.Myelin-freenervefiber

List of recommended literature .

The main one:

1.Lutsyk O.D., Tchaikovsky Y.B. Histology, cytology, embryology Vinnytsia, New Book, 2018.
2.Barinov E.F., Tchaikovsky Y.B. General histology and embryology of internal organs: textbook.Kyiv: Medicine; 2013
3.Wojciech Pawlina. Histology: textbook and atlas. WSV: Medicine, 2021.

Additional:

1.Histology and embryology of internal organs: textbook / E.F. Barinov, Y.B. Tchaikovsky, O.M. Sulaeva et al.
2.Cytology of human organs and tissues edited by L.S.Bolgova. Kyiv: Book-plus, 2018, p.288

Theme: "Nervous tissue." *Addition*

Nervous tissue (textus nervosus) is one of the four principal tissues of the body. It provides regulation of activities of organs and tissues and their interaction with external environment. It is composed of nerve cells (neurons) and supporting cells (neuroglia).

Histogenesis

Nerve tissue is derived from a dorsal thickening of **ectoderm** – neural plate. Neural plate is sequentially transformed into neural groove and then into neural tube. Neural tube is separated from overlying epidermal ectoderm. A part of cells is included neither in the epidermal ectoderm nor in the neural tube and remains located between them as a loose aggregation of cells – neural crest. The cells of neural crest start to migrate in both lateral and ventral directions, thereby forming the nuclei of cranial nerves, neurons of spinal and autonomic ganglia, neurolemmocytes (neuroglia), pigment cells.

The thickenings of ectoderm at the sides of head (neural placodes) give a rise to ganglia of the V, VII, IX and X pairs of cranial nerves, as a result of cell migration from neural placode.

At the early stages of embryogenesis the neural tube is referred to as pseudostratified neural epithelium formed by ventricular and neuroepithelial cells.

Ventricular cells are cylindrical in shape and connected with each other via gap junctions; they possess apical processes, which reach the lumen of neural tube. The basal portions of these cells adjoin the subpial limiting membrane. The cyclic migration of nuclei is characteristic for the ventricular cells: the nuclei of premitotic cells lie deep, during prophase they approach the surface, karyokinesis takes place near the ventricular surface, and the nuclei of daughter cells again return into the depth.

The proliferative activity of ventricular cells constantly decreases during embryonic development, and it completely disappears after the birth.

Morphologically similar ventricular cells undergo differentiation into different types of cells of mature nerve tissue. A part of them gives a rise to neurons, another part – to glial cells (ependymal cells, astrocytes and oligodendrocytes).

In that parts of brain where the histogenesis is especially intensive the ventricular cells lose cylindrical shape and capacity for migration of nuclei, but remain high

proliferative activity. Such cells are referred to as subventricular and neurogerminative (cambial) cells. Further they give a rise some types of neurons and glial cells. Subventricular and extraventricular cells exist during some time after birth.

NEURONS. CLASSIFICATION. STRUCTURE.

Nerve cell (neuron) is morphological and functional unit of nerve tissue. Depending on their morphological and functional features neurons of different parts of nervous system vary from each other.

Two classifications of neurons exist: a) morphological; b) functional.

Morphological classification

According to this classification neurons are classified on the basis of the number of processes extending from the cell body:

Unipolar – have only one process, an axon. In human body such neurons are not revealed. Only the neuroblasts are referred to as unipolar neurons.

Bipolar – have two processes: axon and dendrite. These neurons are rare and associated with organs of special senses; they are found within the retina of the eye and the ganglia of the vestibulocochlear nerve of the ear.

Pseudounipolar – have one process that divides close to the cell body into two branches. In human nervous system such neurons are found within spinal ganglia.

Multipolar – have numerous processes, one of them is an axon, the all others are dendrites. The most of neurons of human body are the multipolar ones.

Functional classification

Depending on their function, neurons are classified into the following:

1. Sensory neurons (receptive or afferent);

2. Interneurons (intercalated or associative);

3. Motor neurons (efferent).

Sensory neurons generate nerve impulse under the influence of external or internal stimuli.

Interneurons form a communicating and integrating network between sensory and motor neurons.

Motor neurons transmit impulses to tissues of effector organ (skeletal muscle, smooth muscle, glands).

Structure of neurons

♦ Neurons show variation in size, from 4-6 μm in granular layer of cerebellar cortex to 130 μm – giant pyramidal cells in cerebral cortex (Betz cells). Neurons consist of cell body (perikaryon) and processes.

♦ Although neurons demonstrate great variation in shape, presence of processes is the characteristic feature for all of them. Given that the neurons' processes provide transmission of nerve impulse from one part of the body to another, their length varies from several micrometers to 1,5 meters. The neurons' processes are of two types: axon and dendrites. Neurons have only one axon, usually the longest process (up to 1,5m) extending from the cell, which transmits impulses away from the cell body. Most of neurons usually have many dendrites, shorter branching processes which transmit impulses from the periphery towards perikaryon.

♦ Nucleus of neuron is round and usually centrally located. The nucleus is euchromatic, containing 1 or sometimes 2-3 prominent nucleoli. Most neurons possess only one nucleus, multinucleated neurons are very rare and found only among ganglia of autonomic nervous system. For example in prostatic gland and cervix of uterus the neurons possessing up to 15 nuclei are found.

♦ Cytoplasm contains the following organized structures:

special organelles;

general-function organelles;

inclusions – carbohydrates (glycogen), pigments (melanin, lipofuscin), several secretions (in neurosecretory cells).

Special organelles of neurons are *Nissl substance* and *neurofibrils.*

Nissl (chromatophilic) substance corresponds to a rough endoplasmic reticulum (rER). When the nerve tissue is stained with aniline dyes, the Nissl substance is revealed in cytoplasm of neuron as an aggregation of basophilic granules of various sizes (Nissl bodies). It occupies perikaryones and dendrites, and is absent within axons and in the area of cell body, which the axon extend from (axonal hillock). The Nissl bodies reveal a high content of ribonucleoproteins. Under the electron microscope examination it was revealed that each Nissl body corresponds to a stack of rER. The degree of the Nissl bodies' arrangement varies among different types of neurons. They are the most regularly arranged in neurons of spinal ganglia. In motor neurons of spinal cord the granules of the Nissl substance are large and surround the nucleus. In sensory neurons of spinal ganglia the Nissl substance appears as a powdered granularity. The Nissl substance is considered to be an indicator of neuron's functional activity.

Because the synthetic activity of the neuron is concentrated in the nerve cell body, the continuous movement of cytoplasm is required to convey enzymes essential for synthesis of neurotransmitters from perikaryon to axon terminals. Such type of transport is called *slow axonal transport*, which occurs at the speed of 1-3 mm per day.

The *fast axonal transport* (5-10 mm per 1 hour) is possible in two directions: from the nerve cell body to the axon terminal *(anterograde)* and to the nerve cell body from the axon terminal *(retrograde).* Through the *fast anterograde transport* the membrane-limited organelles and low-molecular-weight proteins are carried to the axon terminal. While the *fast retrograde transport* serves for carrying the same materials as well as other molecules endocytosed by axon terminal to nerve cell body.

Dendritic transport (3mm per 1 hour) appears to have the same characteristic for the dendrites as axonal transport does for the axon, provides transport of enzymes (for example acetylcholinesterase, which breaks down the neurotransmitter acetylcholine).

Neurofibrils are revealed in the nerve tissue when it is impregnated with silver. Neurofibrils appear as thin filaments of 0,3-0,5μm in diameter, in the perikaryon they form a dense meshwork, while in axon and dendrites they have parallel arrangement. When observed with electron microscope the neurofibrils are estimated to be composed of bundles of the neurofilaments of 6-10nm in diameter and the neurotubules of 20-30nm in diameter. The neurotubules and neurofilaments are referred to as the cytoskeleton of the neuron.

General-function organelles of neurons

The Golgi apparatus of the neuron has a usual ultrastructure.

The centriole of the neuron is situated between the nucleus and the dendrites.

The mitochondria are found in the perikaryon as well as in the axons and dendrites, at the nerve terminals they are especially numerous.

The neurons also reveal numerous lysosomes and ribosomes within their cytoplasm.

Neurosecretory cells are neurons, which are specialized predominantly in synthesis and secretion of biologically active substances. The secretions of theses neurons are referred to as neuroregulators taking part in interaction between nervous and endocrine system.

Such neurosecretory cells are found in hypothalamus. They have several morphological characteristics:

they are large neurons;

the Nissl substance is located at the periphery of the cell body;

in the cytoplasm of the axons and dendrites the secretory granules containing proteins and sometimes lipids and polysaccharides are found;

contain irregular-shaped nuclei, which is the sign of high anabolic activity.

SUPPORTING CELLS OF THE NERVE TISSUE:

THE NEUROGLIA

Neuroglia forms the environment that surrounds neurons and carries out supportive, delimiting, protective and trophic functions.

Such morphological peculiarities of capillaries of the nerve tissue as continuous endothelial lining and thick dense basal lamina provide the selectivity of exchange between the nerve tissue and blood. Besides this the glial cells (predominantly astrocytes) stretch their processes from blood capillaries to neurons, thereby delimiting neurons from immediate attachment to the wall of blood vessels. The endothelium and basal lamina of blood capillaries and the astrocytes together form the **blood-brain barrier.**

Neuroglia includes cells which belong to two different histogenetic lineages:

Macroglia (glial cells);

Microglia (glial macrophages).

Macroglia

The cells of macroglia include 1) ependymal cells, 2) astrocytes,

3) oligodendrocytes.

Ependymal cells form the epithelium-like lining of the fluid-filled cavities of CNS (central canal of the spinal cord, ventricles of the brain).

Ependymal cells are the first glial cells which are differentiated from the glioblats of the neural tube. On the internal surface of neural tube their elongated cell bodies from the epithelium-like lining, carrying out the delimiting and supportive functions. The ependymal cells facing the lumen of the neural tube possess up to 40 cilia on their apical surface. These cilia are considered to facilitate the movement of cerebrospinal liquor. From the basal portion of the ependymal cells the long processes extend, then branch along the whole neural tube and form its supportive apparatus. These processes are involved in formation of *superficial glial limiting membrane*, which separates the content of the neural tube from other tissues.

After the birth the ependymal cells gradually lose their cilia; the cilia remain only in some parts of the CNS (aqueduct of cerebrum).

At the area of posterior comissure the ependymal cells carry out the secretory function forming the “subcomissural organ”, which discharge the secretion which is suggested to take part in regulation of water balance.

The ependymal cells which cover choroid plexus of the brain ventricles are cuboidal in shape, in newborns they possess cilia, which are reduced later. The basal cell surface exhibits numerous infoldings of cytoplasm with large mitochondria, lipid and pigment inclusions.

Astrocytes are the largest of the neuroglial cells. They are stellate in shape and possess numerous widely branched processes.

Two kinds of astrocytes are identified:

protoplasmic;

fibrous.

Protoplasmic astrocytes

- Localization – gray matter.
- Size – 15-25 μm, possess short but widely branching processes.
- Nucleus – large, oval, light.
- Cytoplasm – contains small amount of rER cisterns, free ribosomes and microtubules, rich in mitochondria.
- Function – delimiting and trophic.

Fibrous astrocytes

- Localization – white matter.
- Size – up to 20 μm, possess 20-40 long and relatively straight processes. These processes, which are referred to as glial fibers, form a dense network – supporting apparatus of the brain. Attaching to the blood vessels and to the brain surface, the astrocytes’ processes by their terminal dilatations form the perivascular glial limiting membranes.
- Cytoplasm – under the electronic microscope examination appears light; contains not numerous lysosomes and elements of rough ER; is filled with numerous fibrils of 8-9 nm in diameter, which form bundles and extend into the processes.

♦ Nucleus – large, light; the nuclear envelope sometimes forms deep folds; the karyoplasm is characterized by homogenous electronic density.

♦ Function – supporting and isolation of neurons from external influences.

Oligodendrocytes are the most numerous and polymorphic group of the glial cells responsible for the synthesis of myelin in the CNS.

♦ Localization – surround the nerve cell bodies in the central and peripheral nervous system, are found as a part of sheaths of nerve fibers and nerve endings.

♦ Size – very small.

♦ Shape – different parts of the nervous system are characterized by different shapes of the oligodendrocytes. The cell bodies of oligodendrocytes give a rise to short slightly branched cell processes.

♦ Cytoplasm – its density is approximately the same as that of the neurons' one; doesn't contain neurofilaments.

♦ Function – carry out the trophic function by taking part in metabolism of the neurons. Provide formation of the sheaths around both myelinated and unmyelinated nerve fibers (in such case are called **neurolemmocytes or Schwann cells**). Take part in maintenance of the water-salt balance, regeneration and degeneration of the nerve fibers.

Microglia

Microglia is an aggregation of small cells possessing 2-3 processes, which contain short secondary and tertiary branches. These cells are capable to amoebic movements.

The nuclei are elongated or triangular in shape; are rich in chromatin.

In case of irritation of microglial cellsthey change their shape, pull their processes into and become round-shaped. Recently the microglial cells were proved to be able to produce proteins – immunoglobulins (antibodies). This all indicates on the fact that the microglial cells belong to the macrophage system.

NERVE FIBERS. CLASSIFICATION. STRUCTURE

Nerve fibers are represented by the nerve cells' processes covered with sheaths. Depending on the structure of the sheath the nerve fibers are divided into two main groups:

Myelinated.

Unmyelinated.

Both of them include nerve cell's processes, which is located in the center and called axial cylinder, and sheath formed by the oligodendrocytes (neurolemmocytes or Schwann cells).

Myelinated nerve fibers consist of the *axial cylinder, myelin sheath, neurolemma and basal lamina.*

- Diameter in cross section – 1-20 μm.
- Localization – Central nervous system, peripheral nervous system.

The axial cylinder is referred to as the nerve cell's process (axon or dendrite). The axial cylinder consists of neuroplasm covered by a membrane – axolemma.

Neuroplasm is the cytoplasm of the nerve cell which contains longitudinally oriented neurofilaments and neurotubules. The neuroplasm possesses mitochondria, which are densely concentrated near the nodes of Ranvier.

Axolemma is the continuation of the plasmalemma of neuron. Axolemma provides conduction of the nerve impulse. The speed of the nerve impulse conduction via thick myelinated nerve fiber varies from 5 to 120 m/s.

Myelin sheath is a tube from 0,3 to 20 μm thick which covers the axial cylinder throughout all its length. The axonal hillock and the terminal arborizations of axon are not covered by myelin. The myelin sheath is also absent at nodes of Ranvier. The node of Ranvier is represents the junction between two adjacent oligodendrocytes (Schwann cells). The part of nerve fiber between two sequential nodes of Ranvier is called internodal segment. The length of internodal segments varies from several micrometers to several millimeters. The size of the node of Ranvier is 0,25 – 1 μm.

Hence the myelin is composed of about 80% lipids it is intensively stained by the osmic acid into dark brown color. In this case the whole nerve fiber appears as

homogenous cylinder, which reveals light lines, located on a distance from each other – myelin incisures (Schmidt-Lanterman clefts).

During formation of the myelin nerve fiber the axial cylinder initially lies in a groove on the surface of the oligodendrocyte, thereby forming a deep fold. This double fold of the plasmalemma of oligodendrocyte is called mesaxon. Myelin sheath formation is initiated when the Schwann cell mesaxon surrounds the axon. A sheetlike extension of the mesaxon then wraps around the axon in a spiraling motion. Under the electron microscope examination each whorl of mesaxon appears as a light area about 8-12 nm in depth, which corresponds to the lipid bilayers of two layers of plasmalemma of the oligodendrocyte. The myelin incisures (Schmidt-Lanterman clefts) correspond to those sites where the whorls of mesaxon are moved apart by the cytoplasm of oligodendrocyte (Schwann cell).

Numerous oligodendrocytes participate in formation of one nerve fiber. They contact with each other at the sites of the nodes of Ranvier. One internodal segment corresponds to one oligodendrocyte.

On a longitudinal section near the node of Ranvier the area where the whorls of mesaxon successively contact with the axial cylinder are visible. The sites of attachment of the innermost whorls of mesaxon are the furthermost from the node, while the all subsequent whorls gradually approach it. This is because of stratification of the mesaxon which takes place during the growth of the axial cylinder and the oligodendrocytes; that's why the first layers of mesaxon are shorter than the subsequent ones. The edges of two adjacent Schwann cells form annulate processes of 50 nm in diameter at the site of the node of Ranvier.

Neurolemma – is peripheral portion of the nerve fiber, which contains the nuclei and cytoplasm of the oligodendrocytes.

Basal lamina forms the external covering of myelinated nerve fiber. It is associated with the longitudinally oriented dense cords of collagen fibrils, which don't interrupt at the nodes of Ranvier.

Unmyelinated nerve fibers

Unmyelinated nerve fibers are predominantly found in the autonomic nervous system.

♦ The diameter of fibers is 1-4 μm. They are significantly thinner than the myelinated fibers.

The unmyelinated nerve fibers are composed of the axial cylinder, neurolemma and basal lamina.

The neurolemma consists of the densely aggregated neurolemmocytes (oligodendrocytes), which form cords. These cords exhibit oval nuclei, which are located on a distance from each other.

The axial cylinder represents the nerve cell process. It invaginates into the plasmalemma of the neurolemmocyte; thereby the neurolemmocyte encloses the axial cylinder like a muff. The plasmalemmae of neurolemmocytes surround the axial cylinders and occlude forming deep folds.

Occluded at the area of the fold, the sites of plasmalemma of neurolemmocyte form double membrane called mesaxon. Hence the plasmalemmae of the neurolemmocytes are extremely thin, it is impossible to view the cells' boundaries and mesaxon. That's why the neurolemma appears as continuous cord of the cytoplasm, which covers the axial cylinder.

The nerve fibers of the inner organs usually contain not only one, but several (10-20) axial cylinders in the cord of the neurolemmocytes. Such unmyelinated nerve fibers are called the fibers of cable type.

Externally the unmyelinated nerve fiber is covered by basal lamina.

The speed of nerve impulse conduction in unmyelinated nerve fiber (1-2 m/s) is much lower than in the myelinated one (120 m/s). This is explained by the fact that in unmyelinated nerve fiber the wave of depolarization continuously spreads along the all length of the plasmalemma of the nerve fiber. In myelinated nerve fibers the conduction of nerve impulse is described as "jumping" from node to node. This process is called salutatory conduction. The myelin sheath around the fibers does not conduct the nerve impulse, the electric impulse can only occur at the node of Ranvier, where the plasmalemma lacks a myelin sheath.

REGENERATION OF THE NERVE CELLS AND NERVE FIBERS

The nerve cells (neurons) form constant (non-dividing) cell population. The neurons are capable only to intracellular physiological regeneration, which is represented by continuous rebuilding of structural proteins of their cytoplasm.

However the nerve cells' processes and peripheral nerves, in case of their alteration, reveal regenerative capacity. Initially they undergo degeneration. At this stage, which lasts approximately 24 hours, the acute activation of neurolemmocytes (oligodendrocytes) is observed. Their cytoplasm exhibit the increased number of free ribosomes, polysomes and developing endoplasmic reticulum. The myelin sheath is no more revealed as separated structure. The following 3-4 days are characterized by the intensive proliferation and enlargement of the neurolemmocytes. At the end of a second week the myelin sheaths and some portions of the axial cylinders are resorbed. The resorption is performed by the connective tissue macrophages as well as by the cells of microglia.

The axial cylinders form clavate expansions (growth cones) at their terminals. These growth cones help the axial cylinder to grow into the neurolemmocytes of the peripheral portion of the nerve. The speed of such growth is approximately 1-4mm per day. Renewal of the myelin sheath and terminal structures takes place a little bit later.

NERVE ENDINGS

Absolutely all nerve fibers posses their terminal apparatus which is called nerve ending.

Classification of nerve endings

Depending on their functional role the nerve endings are divided into three principal groups:

1. Effector: 2. Receptive 3.Terminal

a) motor; (affector or sensory)

b) secretory.

Effector nerve endings

Motor nerve endings are represented by the terminal apparatus of axons of the somatic and autonomic nervous systems. The nerve impulse via these nerve endings is transmitted to the tissues of working (effector organ).

The motor nerve endings in the skeletal muscles are called neuromuscular endings. The neuromuscular endings are the terminals of axons of the motor neurons of anterior horns of the spinal cord. The neuromuscular ending includes the following components:

terminal branches of the axial cylinder of the nerve fiber;

specialized site of the muscle fiber.

As the nerve fiber approaches the muscle fiber, it looses the myelin sheath and penetrates the muscle fiber involving its plasmalemma. The plasmalemma of the axonal terminal branches is separated from the plasmalemma of the muscle fiber by a cleft of approximately 50 nm wide. This gap is called synaptic cleft.

At the site of contact the plasmalemma of the muscle fiber forms numerous folds which are referred to as secondary synaptic clefts.

The terminal branches of the nerve fiber in neuromuscular synapse are rich in mitochondria and presynaptic vesicles filled with the neurotransmitter – acetylcholine.

The muscle fiber at the site of contact with the nerve ending doesn't exhibit typical striation and is characterized by an abundance of mitochondria and aggregation of round and oval nuclei. The sarcoplasm together with mitochondria and nuclei forms the postsynaptic part of synapse.

In case of excitation the acetylcholine is released from the vesicles and transported through the presynaptic membrane to the synaptic cleft. Then the neurotransmitter binds to its specific receptor on the postsynaptic membrane, which leads to the depolarization (excitation) of the postsynaptic membrane.

The postsynaptic membrane of the neuromuscular ending contains the enzyme called acetylcholinesterase. This enzyme breaks down the molecule of acetylcholine and limits the time of its action.

The motor nerve endings in the smooth muscle have much more primitive structure. The thin bundles of axons or their terminals penetrate the spaces between the smooth muscle cells and form expansions (varices), which contain cholinergic and adrenergic presynaptic vesicles.

Secretory nerve endings are terminal expansions of the axons which contain presynaptic vesicles usually filled with acetylcholine.

Receptive nerve endings are scattered throughout all over the body and percept various stimuli from external environment as well as from inner organs.

~Exteroceptors percept stimuli from external environment.

~Interoceptors percept stimuli from inner organs and tissues of the body.

Proprioceptors are referred to as a type of interoceptors. They represent the sensory nerve endings in muscles and tendons which are involved in regulation of movements and muscle tone.

Depending on nature of the percepted stimulus all sensory nerve endings are classified as mechanoreceptors, baroreceptors, chemoreceptors, thermoreceptors, nociceptors etc.

Based on their structure the sensory nerve endings are divided into **free** and **non-free**. Free nerve endings are represented **only** by the terminal branches of the axial cylinder, while non-free nerve endings retain all components of the nerve fiber (branches of the axial cylinder, myelin sheath, glial cells).

- Non-free nerve endings could be enclosed in connective tissue capsule, in such case they are referred to as ***encapsulated.***

- Non-free nerve endings which are not enclosed in a capsule are called ***non-encapsulated***.

The sensory nerve endings of epithelial, connective and muscle tissues are characterized by the several distinctive features.

The epithelial tissues are endowed with *free* nerve endings. As they approach the epithelial layer, the myelinated nerve fibers loose the myelin sheaths and their axial cylinders penetrate and branch between the epithelial cells.

The free receptors of epidermis perform the function of perception of temperature and pain stimuli. Network of free dermal nerve endings also surround most hair follicles and attach to their outer root sheath. They are particularly sensitive to hair movements and serve as mechanoreceptors.

The stratified epithelium owes nerve endings which include not only nerve terminals but also modified epithelial cells – ***tactile epithelial cells of Merkel***, which serve as mechanoreceptors. These cells are distinguished from other

epithelial cells by the light cytoplasm, flattened nucleus and presence of osmiophilic granules, which are 65-180 nm in diameter.

The basal domain of the Merkel cell together with adjoining nerve endings form receptive terminal structures – ***Merkel discs***.

Connective tissue also posses wide range of receptive nerve endings, which are divided into ***non-free encapsulated, non-free non-encapsulated and neurotendinous spindles***.

Despite their variability, the encapsulated receptors of connective tissue are always composed of branching axial cylinder and glial cells which are surrounded by a connective tissue capsule.

The encapsulated nerve endings of connective tissue include ***Pacinian corpuscles, Golgi-Mazzoni bodies, Meissner's corpuscles and end-bulbs of Krause***.

♦ **Pacinian corpuscles** are large ovoid structures of 0,5x2mm in size.

They are composed of a myelinated nerve ending surrounded by a capsule structure. The nerve enters the capsule at one pole with its myelin sheath intact. The myelin is retained for one or two nodes and is then lost. The unmyelinated portion of the axon extends toward the opposite pole from which it entered, and its length is covered by a series of tightly packed, flattened Schwann cell lamellae that form the inner core of the corpuscle. The remainder or bulk of the capsule, the outer core, is formed by a series of concentric lamellae. Pacinian corpuscles respond to **pressure and vibration**. They are found in the deeper dermis and hypodermis (especially in the fingertips), in connective tissue in general, and in association with joints, periosteum, and internal organs.

♦ **Golgi-Mazzoni bodies** are smaller than Pacinian corpuscles; possess thinner capsule and relatively large inner core. They are found in skin, serous and mucous tunics of inner organs. Golgi-Mazzoni bodies serve as **baroreceptors**.

♦ **Meissner's corpuscles** are oval structures that measure about 50-100 μm. They are composed of oligodendrocytes oriented perpendicularly to the long axis of the corpuscle. As it penetrates the corpuscle, the nerve fiber looses its myelin sheath and branches into several terminals which contact with the glial cells. A thin connective tissue capsule is predominantly composed of collagen fibers.

Meissner's corpuscles are found in the papillary layer of hairless skin. They serve as **touch** receptors which are particularly responsive to low-frequency stimuli.

♦ **End-bulbs of Krause**. Entering the capsule the nerve fiber looses myelin sheath, and then ends as a bulb-like expansion and branches, thereby forming a network of unmyelinated nerve fibers. The capsule is extremely thin. End-bulbs of Krause are found in connective tissue of tongue and external genitalia. They perform the role of **mechanoreceptors**.

♦ **Neuro-tendon spindles** (**Golgi tendon organ**) are formed by the myelinated nerve fibers of 15 μm in diameter. As they approach the collagen fibers of tendon, the nerve fibers lose their myelin sheath, give numerous branches and surround the tendon bundles.

♦ **Ruffini corpuscles** have the similar structure. They are found in deep layers of the derma and the hypoderm; are the most numerous within the skin of feet.

The Golgi tendon organs and the Ruffini corpuscles serve as mechanoreceptors.

Neuromuscular spindles

The neuromuscular spindle is composed of 10-12 thin and short striated muscle fibers, surrounded by a connective tissue capsule. Such fibers are called **intrafusal**. At their endings these muscle fibers possess actin and myosin filaments which do contract. The receptive part of the intrafusal muscle fiber is represented by the central **non**-contractive part.

There are two types of intrafusal muscle fibers:

nuclear bag fibers;

nuclear chain fibers.

The neuromuscular spindle contains 1-3 nuclear bag fibers, which possess numerous nuclei in their central dilated part.

And there are 3-7 nuclear chain fibers. They are two times thinner and two times shorter than the nuclear bag fibers. The nuclei in the nuclear chain fibers are found along the whole receptive zone.

Externally the connective tissue capsule is surrounded by the striated muscles, which form the outer capsule. Such muscles are called extrafusal.

The intrafusal muscle fibers are innervated by the two types of afferent nerve fibers: a) primary; b) secondary.

♦ The primary nerve fibers are of 17μm in diameter; they form the annulospiral nerve endings on the nuclear bag fibers as well as on the nuclear chain fibers.

♦ The secondary nerve endings are of 8μm in diameter; they form the flower-spray endings on the both sides of the annulospiral nerve endings. Both of these nerve endings react on the change in length of the muscle fibers.

INTERNEURON SYNAPSES

The synapse is composed of three parts: presynaptic part, postsynaptic part and synaptic cleft.

There are distinguished two types of synapses according to the type of transmission of the nerve impulse:

chemical;

electrical.

Depending on their localization the synapses are divided into:

Axosomatic – between the axon of one neuron and the nerve cell body (perikaryon) of another one.

Axodendritic – between the axon and the dendrite.

Axoaxonic – between the axon of one neuron and the axon of another one. Such synapses inhibit the nerve impulse transmission.

The structure of chemical synapse

The presynaptic part is formed by the extended terminal branch of the axon that transmits the nerve impulse. It is covered by the presynaptic membrane; contains numerous mitochondria and presynaptic vesicles, containing neurotransmitter – acetylcholine (cholinergic synapses), noradrenalin (adrenergic synapses). The

function of neurotransmitter could be performed by various biologically active substances: dopamine, glycine, gamma aminobyturic acid (GABA), glutamine acid, substance P, serotonin, histamine etc. Dopamine, glycine, gamma aminobyturic acid (GABA) are inhibitory neurotransmitters.

The synaptic cleft is 20-30 nm wide and filled with the tissue liquor. The neurotransmitter is released here from the vesicles of the presynaptic part.

The postsynaptic part is covered by the postsynaptic membrane, which contains receptors to the neurotransmitter.

THE REFLEX ARCH

The reflex arch is represented by a chain of neurons, connected with each other via synapses, which provide the conduction of the nerve impulse from the receptor (sensory neuron) to the motor (effector) nerve ending on a working organ.

The most primitive reflex arch consists of 2 neurons – the sensory and the motor one. In most cases there are several interneurons (associative) between them.

ODESA NATIONAL MEDICAL UNIVERSITY

DEPARTMENT OF HISTOLOGY, CYTOLOGY AND EMBRYOLOGY

METHODICAL RECOMMENDATION OF LECTURES

for dentistry faculty

THEME: «Nervous system.»

Approved on the methodical conference of department

«____»_____ 20___., protocol №_____

Head of Department, doc._____ Tiron O.I.

Approved on the methodical conference of department

«____»_____ 20___., protocol №_____

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Head of Department, doc._____ Tiron O.I.

Topic: "Nervous system" -2 h.

1. Relevance of the topic.

The central nervous system is a set of nerve formations of the spinal cord and the main brain, which provides the perception, processing, transmission, storage and recreation of information for the purpose of adequate interaction of the body to environmental changes, the organization of the optimal functioning of organs, their systems and the body as a whole.

Each structure of the central nervous system has morphological and functional specifics. But next to this, all these systems have a number of common properties and functions to which they belong - neuronal structure, synaptic connection between neurons, the creation of local connections of neurons that implement a specific function, the multiplicity of direct and feedback connections between structures. The nervous system is extremely plastic and dynamic. The study of the compensatory and adaptive processes of the nervous system to its different functional states and disorders acquires important theoretical and practical significance.

The possibility of a directed influence on the regulation of disorders of structural and functional relations in the nerve centers and systems of the brain is becoming more and more real. But this requires knowledge of the structural and molecular mechanisms of brain activity.

2. Objectives of the lecture:

a) learning:

- analysis of the structural organization of the nervous centers of the central nervous system;
- modern ideas about the morphofunctional organization of the nervous system;
- interpretation of interrelationships between structural centers of the nervous system, assessment of their functional state, interpretation of age-related changes, mechanisms of regeneration, adaptation to the action of various factors.
- acquaint students with the structure of somatic and autonomic reflex archs.

b) educational:

- to bring to the students the importance of studying the structural and molecular mechanisms of brain activity, its importance in the process of its formation as a doctor;
- to acquaint students with the general properties and functions to which they belong
- neural structure, synaptic connection between neurons, the creation of local connections of neurons that implement a specific function, the multiplicity of direct and feedback connections between structures, to determine their significance for practical medicine;
- to form students' professional significance of the topic. Discuss the issue of deontology.

3. Plan and organizational structure of the lecture.

№№	The main stages of the lecture and their content	Objectives in levels of abstraction	Lecture type. Lecture equipment	Time management
1	2	3	4	5
I. 1. 2. II III.	*Preparatory stage.* Determination of the learning goal. Providing positive motivation. *The main stage* Teaching lecture material according to the plan: 1. Morpho-functional characteristics of different parts of the central nervous system. 2. Structural and molecular mechanisms of brain activity. 3. Reflex arch. 4.The concept of brain modules *The final stage.* Summary of the lecture. General conclusions. Lecturer's answer to possible questions. Self-study assignment.	I. Descriptive. II. Analytico - synthetic, high quality.	Tables. Slides. In accordance with the publication "Guidelines for the planning, preparation and analysis of lectures." References, questions, institutions .	5% 85-95% 5%

4. Content of the lecture material:

- structural and logical scheme of content by those;
- text of the lecture (attached)

5. Materials for activating students during the lecture:

1) Morphological and functional classification of neurons.

2) Neuroglia: localization, functions.

3) Hydrocephalus is a decrease in the absorption of cerebrospinal fluid or a blockade of its outflow from the ventricles of the brain, which causes an increase in intracranial pressure. Congenital hydrocephalus leads to an increase in the chairman, accompanied by impaired brain activity and muscle weakness. Many neurological symptoms develop in adults.

4) Tumors of the nervous system. Virtually all cells in the nervous system can give rise to tumors. Glial cells form gliomas, immature nerve cells produce medulloblastomas, and Schwann cells produce schwanomas. Since neurons in adults do not divide, they do not form tumors.

Questions:

1. Morphofunctional characteristics of the spinal cord.

2. Cytoarchitectonics of the cerebral cortex. Morphological and functional characteristics of neurons. Granular and agranular types of cerebral cortex.

3. Myeloarchitectonics of the cerebral cortex.

4. General plan of the structure and function of the cerebellum. Cytoarchitectonics of the cerebellar cortex. Cerebellar neuroglia.

5. The cortex of the cerebral hemispheres: the concept of brain modules.

6. The blood-brain barrier, structure, meaning.

6. General material and methodological support of the lecture:

- classrooms;
- equipment;
- equipment;
- illustrative materials.

List of recommended literature .

The main one:

1.Lutsyk O.D., Tchaikovsky Y.B. Histology, cytology, embryology Vinnytsia, New Book, 2018.
2.Barinov E.F., Tchaikovsky Y.B. General histology and embryology of internal organs: textbook.Kyiv: Medicine; 2013
3.Wojciech Pawlina. Histology: textbook and atlas. WSV: Medicine, 2021.

Additional:

1.Histology and embryology of internal organs: textbook / E.F. Barinov, Y.B. Tchaikovsky, O.M. Sulaeva et al.
2.Cytology of human organs and tissues edited by L.S.Bolgova. Kyiv: Book-plus, 2018, p.288

Theme: "Nervous system" *Addition*

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

There are two classifications of organs of the nervous system:

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

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

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

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

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

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

There are distinguished the following types of extrapyramidal neurons:

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

7. fusiform neurons with long horizontal axons.
   This classification was based on the number, morphology and the type of branching of nerve cell processes.

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

There are distinguished six layers of the cerebral cortex:

1. molecular layer;

2. outer granular layer;

3. outer pyramidal layer;

4. inner granular layer;

5. ganglionic (inner pyramidal) layer;

6. multiform layer.

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

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

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

The inner granular layer is formed by small stellate neurons.

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

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

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

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

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

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

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

The inhibitory neurons of the module are the neurons with axonal brush, axo-axonal neurons, basket neurons and neurons with double bouquet of dendrites.

The axons of pyramidal cells contact with three modules within the same hemisphere and two modules of the opposite hemisphere.

The cerebral cortex contains about 3 millions modules.

Among the nerve fibers of the cerebral cortex the following types are distinguished:

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

Within the cerebral cortex the nerve cell processes are arranged in tangential bundles, so-called stripes, located between the layers of nerve cell bodies. The

arrangement of nerve fibers in layers is called *myeloarchitectonics*. There are distinguished the following layers of nerve fibers:

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

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

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

The cerebellar cortex consists of three layers:

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

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

The generation of impulse in the axons of basket cells exerts inhibitory influence on the pyriform neurons (Purkinje cells).

The stellate neurons of the molecular layer are divided into the small and the large.

The processes of small stellate neurons contact with the dendrites of pyriform cells of the Purkinje cell layer.

The large stellate neurons have long and extensively branched dendrites and axons. The axons of large stellate neurons connect with the dendrites of Purkinje cells; some of them take part in formation of the baskets of cerebellum.

The neurons of the molecular layer are interneurons, which conduct inhibitory nerve impulses to the Purkinje cells.

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

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

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

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

The afferent impulses are conducted to neurons of cerebellar cortex through the **mossy and climbing fibers.** The mossy fibers pass as a part of olivocerebellar and pontocerebellar tracts. Through the granule cells the mossy fibers conduct excitatory nerve impulses to the Purkinje cells.

The climbing fibers enter the cerebellar cortex as a part of vestibulocerebellar tract.

Then the climbing fibers pass through the granule layer and conduct excitatory impulses immediately to the Purkinje cells. Degeneration of the Purkinje cells leads to cerebellar dysfunction.

The excitatory nerve impulses, conducted to cerebellum through the mossy fibers are realized by the granule cells and glomerules of cerebellum. The inhibition is provided by the basket cells of the molecular and granule layers. The stellate neurons with long axon provide the connection between different areas of

cerebellar cortex. The stellate neurons with short axon are situated near the Purkinje cell layer. Their branched dendrites form synapses with the axons of granule cells; their axons pass into the granular layer to the glomerules of cerebellum and form synapses with terminal branches of the dendrites of granule cells above their synapses with the mossy fibers. This means that excitation of stellate neurons can block the nerve impulses conducted through the mossy fibers.

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

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

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

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

The anterior median fissure and dorsal septum divide the spinal cord into two symmetric parts. The gray matter forms projections, which are called horns. There are distinguished anterior (ventral) horns, lateral horns and posterior (dorsal horns).

The posterior (dorsal) roots enter the posterior horns, from the anterior horns the anterior (ventral) roots extend. The spinal canal is located in the center of gray matter.

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

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

- radicular neurons;
- fascicular neurons;
- interneurons.

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

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

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

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

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

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

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

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

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

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

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

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

the spinal cord. The neurons of spinal ganglia are surrounded by the layer of glial cells, which are termed mantle cells or satellite cells.

ODESA NATIONAL MEDICAL UNIVERSITY

DEPARTMENT OF HISTOLOGY, CYTOLOGY AND EMBRYOLOGY

METHODICAL RECOMMENDATION OF LECTURES

for dentistry faculty

THEME: «Sensory organs.»

Approved on the methodical conference of department

«____»_____ 20___., protocol №_____

Head of Department, doc._____ Tiron O.I.

Approved on the methodical conference of department

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Theme: "Sensory organs." – 2h.

1. Relevance by those.

The sensory organs are receptors for environmental stimuli; they play a special role in recognizing the world. Functionally, the sensory organs are closely related to the activity of the nervous system and are the peripheral parts of the analyzers. All sensory organs provide the perception of stimuli from the external environment, the transformation of the energy of stimulation into a nerve impulse and their conduction to the center of the higher analyzer (cortical-subcortical centers). Knowledge of the characteristic morphological and histological parameters of the sensory organs normally helps to understand the essence of many pathological processes, correctly diagnose and predict the result of the treatment of the disease, which is primarily necessary for doctors - ophthalmologists, neuropathologists, etc.

2. Objectives of the lecture:

a) learning:

- analysis of the structural organization of the sensory organs;
- modern ideas about the morphofunctional organization of the sensory organs;
- interpretation of the relationship between the structural and functional apparatuses of the organ of vision;
- assessment of the functional state of the eyeball, interpretation of age-related changes, regeneration mechanisms, adaptation to the action of various factors.
- to acquaint the ice-cold with the structure of the receptor and auxiliary apparatus of the eye.
- morphofunctional characteristics of the organ of hearing and equilibrium
- morphofunctional characteristics of the organ taste and smell

b) educational:

- to bring to the students the importance of studying the structural and molecular mechanisms of the activity of the organ of vision, hearing, equilibrium, smell, taste, its importance in the process of forming a future doctor;
- to familiarize students with the morphological and functional features of the organs of vision and smell, to determine their importance for practical medicine;
- to form students' professional significance of the topic. Discuss the issue of deontology.

3. Plan and organizational structure of the lecture.

№№	The main stages of the lecture and their content	Objectives in levels of abstraction	Lecture type. Lecture equipment	Time management
1	2	3	4	5
I.	*Preparatory stage.*		Tables.	5%

			Slides.	
1. 2.	Determination of the learning goal. Providing positive motivation.			
II	*The main stage* Teaching lecture material according to the plan: 1. Morpho-functional characteristics of the organ of vision. 2. Structural and molecular mechanisms of the eyeball activity. 3. Functional apparatus of the eye. 4. Auxiliary apparatus of the eye. 5. Morphofunctional characteristics of the organs of smell and taste. 6. Morpho-functional characteristics of the organs of hearing and balance.	I. Descriptive. II. Analytical - synthetic, high quality.	In accordance with the publication "Guidelines for the planning, preparation and analysis of lectures."	85-95%
III.	*The final stage.* Summary of the lecture. General conclusions. Lecturer's answer to possible questions. Self-study assignment.		List of literature, question, task.	5%

4. Content of the lecture material:

- structural and logical scheme of the content of the topic;

- the text of the lecture. (attached)

5. Materials for activating students during the lecture:

1) Glaucoma - an increase in intraocular pressure as a result of a violation of the outflow of water moisture from the drainage channels.

2) With age, the elasticity of the lens decreases, causing a violation of accommodation when looking at closely spaced objects. This is a normal aging process - presbyopia, which correlates with glasses.

3) Cataract - the opacity of the lens, which occurs as a result of excessive exposure to the UV ray. In diabetes mellitus, the development of cataracts occurs as a result of an increase in blood glucose levels.

Questions:

1.General plan of the structure of the eyeball: membranes, their derivatives.

2.The concept of the functional apparatus of the eye.

3.Morpho-functional characteristics of the structural components of the dioptric apparatus of the eye: cornea, lens, vitreous body.

4.Morpho-functional characteristics of the structural components of the eye accommodation apparatus: iris, ciliary body.

5.The receptor apparatus of the eye. The visual part of the retina. The histological structure of the retina

6. Pigment epithelium of the retina, structure, functional significance.

7. Retinal neurons, topography, interaction.

8. Ultrastructural features of the structure of neurosensory cells. Photoreception mechanisms.

9. Auxiliary apparatus of the eye.

10. Morphofunctional characteristics of the structural components of the organs of smell and taste.

11. Morphofunctional characteristics of the structural components of the organs of hearing and equilibrium.

6. General material and methodological support of the lecture:

- classrooms;

- equipment;

- equipment;

- illustrative materials.

List of recommended literature .

The main one:

1.Lutsyk O.D., Tchaikovsky Y.B. Histology, cytology, embryology Vinnytsia, New Book, 2018.
2.Barinov E.F., Tchaikovsky Y.B. General histology and embryology of internal organs: textbook.Kyiv: Medicine; 2013
3.Wojciech Pawlina. Histology: textbook and atlas. WSV: Medicine, 2021.

Additional:

1.Histology and embryology of internal organs: textbook / E.F. Barinov, Y.B. Tchaikovsky, O.M. Sulaeva et al.
2.Cytology of human organs and tissues edited by L.S.Bolgova. Kyiv: Book-plus, 2018, p.288

Theme: «Sensory organs.» *Addition*

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

Each analyzer consists of three parts:

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

The types of receptors according to the nature of irritation:

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

Classification of sensory organs

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

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

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

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

ORGAN OF VISION

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

The eyeball consists of three layers or coats:

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

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

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

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

Sclera is formed by dense regular connective tissue containing bundles of collagen fibers, between which fibroblasts and occasional elastic fibers are found.

The sclera is divided into three rather ill-defined layers:

- the episcleral layer (episclera), the external layer, is the loose connective tissue adjacent to the periorbital fat.

- the substantia propria (sclera proper, also called Tenon's capsule), is the investing fascia of the eye and is composed of a dense network of thick collagen fibers.

- the suprachoroid lamina (lamina fusca), the inner aspect of the sclera, is located adjacent to the choroid and contains thinner collagen fibers and elastic fibers as well as fibroblasts, melanocytes, macrophages, and other connective tissue cells.

The sclera is covered by conjunctiva.

The dioptric apparatus of the eye

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

1. corneal epithelium;
2. anterior basement membrane (Bowman's membrane);
3. corneal stroma;

4. posterior basement membrane (Descemet's membrane);
5. corneal endothelium (posterior epithelium).

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

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

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

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

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

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

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

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

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

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

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

The vascular coat (uvea) consists of four layers:

1. suprachoroid lamina is located adjacent to the sclera. It is formed by loose connective tissue, containing numerous elastic fibers, fibroblasts and pigment cells (melanocytes);

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

Accommodative apparatus

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

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

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

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

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

Iris is a derivate of the uvea. It arises from the anterior border of the ciliary body

and is attached to the sclera about 2 mm posterior to the corneoscleral junction; it is a border between anterior and posterior chambers of the eye. The pupil is the central aperture of the iris. The iris consists of five layers:

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

sphincter pupillae muscle is located near the papillary margin of the iris, the dilatator pupillae muscle – near the cilliary margin of the iris;
4. inner limiting layer has the same structure as the outer limiting layer;
5. posterior pigment epithelium is continuation of the epithelium of retina; it covers the ciliary body and processes too.

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

Receptive apparatus of the eye

Retina consists of ten layers:

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

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

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

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

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

The rod and cone photoreceptors consist of the outer and the inner segments, connected together via the connecting cilium. The outer segment of the rod is

cylindrical in shape and contains numerous closed membranous discs. These membranous discs contain the visual pigment – **rhodopsin**, which is composed of the protein opsin and the vitamin A aldehyde – A-retinal.

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

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

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

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

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

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

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

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

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

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

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

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

The fovea appears as a small depression located at the posterior pole of the optical axis of the eye. Its central region is known as foveola. Except for the photoreceptor layer, most of the layers of the retina are markedly reduced or absent in this region. Here the photoreceptor is composed entirely of cones (approximately 4,000) that are longer and more slender and rodlike than they are elsewhere. In this area, the retina is specialized for discrimination of details and color vision. The macula lutea is the area surrounding the fovea, approximately

5.5 mm in diameter. It is yellowish because of the presence of yellow pigment (xanthophyll). The macula lutea contains approximately 17,000 cones and gains rods at its periphery. Here the retinal cells and their processes, especially the ganglion cells, are heaped up on the sides of the fovea so that light may pass unimpeded to this most sensitive area of the retina.

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

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

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

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

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

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

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

ORGAN OF HEARING AND BALANCE

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

The external ear consists of:

1. auricle;
2. external acoustic meatus;

3. tympanic membrane.

The auricle consists of elastic cartilage covered with a skin.

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

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

The middle ear consists of:

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

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

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

The auditory ossicles

- maleus;
- incus;
- stapes;

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

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

The inner ear is located within the petrous part of the temporal bone. It consists of two labyrinthine compartments, one contained within the other. The bony labyrinth is a complex system of interconnected cavities and canals. The membranous labyrinth lies within the bony labyrinth and consists of a complex system of small sacs and tubules that also form a continuous space enclosed within a wall of epithelium and connective tissue. The perilymphatic space lies between the wall of the bony labyrinth and the wall of the membranous labyrinth. It is filled with fluid – the perilymph. The space within the membranous labyrinth also contains fluid – the endolymph. The perilymph and the endolymph are different in chemical composition. The membranous labyrinth is composed of two divisions: cochlear labyrinth and vestibular labyrinth. The vestibular labyrinth contains semicircular ducts, the utricle and the saccule.

The bony labyrinth consists of three connected spaces:

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

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

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

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

The membranous labyrinth is also consists of three parts:

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

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

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

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

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

The scala media is the cochlear duct itself. The scala vestibuli and scala tympani are the perilymph-containing spaces above and below, respectively, the scala media. The scala vestibuli and scala tympani communicate with each other at the apex of the cochlea through a small channel called **helicotrema**.

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

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

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

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

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

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

The types of supporting cells are the following:

1. pillar cells, inner and outer;

2. phalangeal cells (Deiters cells), inner and outer;

3. limiting cells (Hensen's cells), outer;

4. supporting cells (Claudius cells), outer.

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

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

portion of the hair cell completely and send apical processes toward the endolymphatic space.

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

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

The sensory hair cells are divided into:

- inner hair cells;
- outer hair cells.

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

The inner hair cells are jug-shaped cells with expanded basal portion, which form a single row of cells. The apical potrion of these cells contains approximately 30-

60 large specialized microvili – stereocilia. The stereocilia pass through the cuticle covering the apical surface of the hair cell.

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

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

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

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

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

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

The hair cells are divided into two types:

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

The apical portion of these cells is covered with cuticle, from which about 60-80 immovable cilia – the stereocilia and the one mobile cilium – the kinocilium arise. The kinocilium is always located diametrically to the bundle of stereocilia. If the kinocilium moves towards the stereocilia, the hair cell undergoes excitation; if the movement is in opposite direction, the hair cell is inhibited. The macula of saccule contains 18 thousands sensory cells; the macula of utricle – 33 thousands.

The supporting cells rest on the basal lamina between the sensory cells. The supporting cells contain large dark oval nuclei, numerous mitochondria. On the apical portion numerous microvili are found.

The epithelial surface is covered with jelly-like otolithic membrane containing inclusions, so-called otoliths, which consist of crystals of potassium carbonate. The otolithic membrane is a product of secretion of the supporting cells.

The macula of the utricle – is a receptor of linear accelerations and gravitation; the macula of the saccule – is a receptor of gravitation and vibration.

During the movement of head the otolithic membrane, like a flat stone, draws the cilia of sensory cells, leading to the generation of nerve impulses.

Ampullary crests look like a transverse folds into the ampule of semicircular duct, which is covered by the hair cells and the sensory cells. The apical portion of these cells is covered with gelatinous dome, which have an appearance of bell without lumen. The ampullar crests are the receptors of angular accelerations. During movement of the head or fast rotation of the body the movement of endolymph makes the dome easily change its postion, thereby stimulating the hair cells.

OLFACTORY ORGAN

The olfactory organ is a chemoreceptor. It perceives the molecules of odorous substances. Phylogenetically it is the oldest type of perception. The peripheral part of olfactory analyzer is located at the olafactory region of nasal cavity. The olfactory region is located on part of the dome of each nasal cavity and, to a variable extent, the contiguous lateral and medial nasal walls. Mucosa of the olfactory region appears yellowish.

The olafactory analyzer consists of three parts:

- peripheral part – the olfactory region of the nasal cavity;

- conductive part – olfactory bulb;

- central part – olfactory center in cerebral cortex.

Structure. The olfactory region is lined with specialized olfactory mucosa. In humans, the total surface area of the olfactory mucosa is only about 10 cm2. The olfactory epithelium consists of olfactory receptor cells, supporting cells, and basal cells. The olfactory epithelium is distinguished from the underlying lamina propria by the basal lamina. The surface of olfactory region facing the nasal cavity is covered with mucus.

Receptor cells are located between supporting cells. The receptor cells have long central process – axon and short peripheral process – dendrite. Their cell bodies are located in the middle of thickness of the olfactory epithelium; they contain light nuclei with one or two nucleoli and well-developed rough ER. The distal ends of dendritic processes dilate and form knob-like structures called the olfactory vesicles. A number of long, thin cilia (10 to 23) arise from the olfactory vesicle and extend radially in a plane parallel to the epithelial surface. The cilia of ofactory vesicles contain longitudinally oriented fibrils: 9 pairs of peripheric fibrils and 2 pairs of fibrils extended from the basal bodies. The cytoplasm of dendritic processes contains microtubules elongated along its long axis and mitochondria.

The olfactory cilia act like antenna for the molecules of odorous substances.

The dendritic processes of the receptor cells can contract under the action of odorous substances. The basal domain of the cell gives rise to an unmyelinated axonal process that leaves the epithelial compartment. Collections of axons from olfactory receptor cells do not come together as a single nerve, but instead they are

grouped into bundles that pass through a thin cribriform plate of the ethmoid bone, course through the dura and arachnoid matters, and finally are surrounded by pia matter, entering the olfactory bulb of the brain.

Supporting cells form multinuclear epithelial layer, within which the receptor cells are located. The apical portion of supporting cells contains numerous microvili. These cells reveal the signs of apocrine secretion and characterized by an intensive metabolism. Their cytoplasm contains mitochondria, ER, Golgi apparatus, granules, vacuoles and yellowish brown pigment, which causes the yellow color of the olfactory mucosa.

Basal cells rest on the basal lamina and form projection, which surround the bundles of axons of the receptor cells. These cells form cambial layer for renewal of cells of the olfactory mucosa.

Epithelium of the vomeronasal organ consists of the respiratory and receptor regions. The structure of receptor part is almost similar to that of the olfactory region. The main difference is that the olfactory vesicles of vomeronasal organ contain on their apical surfaces not cilia, but immobile microvili. The main function of vomeronasal organ is the regulation of sexual behavior.

The underlying loose connective of the olfactory region contains the acini of tuboalveolar (Bowman's) glands, which consist of secretory and myoepithelial cells. The secretion of these glands dissolves odorous substances, which interact with receptor cells. It causes the change of membrane potential, which is transmitted through the chain of neurons to the central part of olfactory analyzer.

ORGAN OF TASTE

The peripheral part of taste analyzer carries out the function of chemoreceptor. It is represented by an aggregation of taste buds located within the stratified epithelium of tongue papillae.

Structure. In histologic sections, taste buds appear as oval, pale-staining bodies that extend through the thickness of the epithelium. Three principal cell types are found in taste buds: neuroepithelial (sensory cells), supporting cells and basal (cambial) cells. A small opening onto the epithelial surface at the apex of the taste bud is called the taste pore, which leads to a small depression – taste fovea.

The neuroepithelial cells are spindle-like cells, whose cytoplasm contains smooth ER and mitochondria. The apical portion of these cells contains about 30-50 microvili, called taste brads. By these microvili the sensory cells perceive the stimuli. The molecules of food adsorb on the active centers of membranes of the

microvilli. They selectively react on the substances with different tastes. The basal portions of receptor cells form synapses with afferent nerve fibers. The excitation is transmitted to the dendrites of sensory neurons.

The supporting cells – are various-shaped cells with large nuclei and well-developed organelles. They surround and isolate the sensory cells and nerve fibers at the basal portion of the taste bud. They also carry out secretory function by discharging secretion into the taste fovea. The supporting cells posses microvili on their apical surfaces, and do not form synapses with nerve fibers.

The basal cells rest on the basal lamina and, unlike sensory and supporting cells, do not reach the epithelial surface. Theses cells are small, contain small amounts of cytoplasm and organelles. They are considered to be the source of regeneration of sensory and supporting cells.

ODESA NATIONAL MEDICAL UNIVERSITY

DEPARTMENT OF HISTOLOGY, CYTOLOGY AND EMBRYOLOGY

METHODICAL RECOMMENDATION OF LECTURES

for dentistry faculty

THEME: «Cardiovascular system. Organs of hematopoiesis and immune defense.»

Approved on the methodical conference of department

«____»_____ 20___., protocol №_____

Head of Department, doc._____ Tiron O.I.

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Head of Department, doc._____ Tiron O.I.

Theme: «Cardiovascular system. Organs of hematopoiesis and immune defense.»-2h.

1. Relevance of the topic.

The cardiovascular system meets the current needs of organs and tissues in blood circulation. In this case, the level of systemic circulation is determined by the activity of the heart, vascular tone and blood condition, disorders or changes that can lead to circulatory failure. The cardiovascular system consists of the heart and blood vessels: arteries, microvasculature and veins, the elements of which are located in all tissues and organs. Each section of the circulatory system has its own structural features, which depend on the location and hemodynamic conditions of the vessels.

In violation of the structure and function of different parts of the cardiovascular system, serious diseases occur: heart defects, myocardial infarctions, atherosclerosis, hypertension, etc. Despite the fact that in recent years there has been a tendency towards a decrease in mortality rates from cardiovascular diseases, they rank first among the causes of disability and death. All this makes it necessary to study the cardiovascular system in detail for future doctors of any profession, especially therapists and cardiologists.

The organs of hematopoiesis and immune defense include the red bone marrow, thymus, lymph nodes, spleen. In addition to the main function - reproduction and differentiation of blood cells, these organs deposit blood and lymph, filter it, enrich it with new cells. Violation of hematopoiesis and the formation of immune functions of the cells of the blood system leads to a number of serious diseases. Yes, the two most dangerous pathological conditions - AIDS and neoplasm - are directly related to damage to the organs of the immune system.The lack of effective methods of treatment indicates the complexity of the processes of immune defense and the close interaction of all hematopoietic organs.

Diagnosis of many diseases is based on the histological examination of bone marrow punctates, lymph nodes, therefore, knowledge of the normal structure of these organs, their cellular composition is necessary for a hematologist, immunologist, allergist, etc. At the same time, the concept of the structure and participation of hematopoietic organs in protective the reaction of the body is necessary for a doctor of any profession.

1. Objectives of the lecture:

a) learning:

- analysis of the structural organization of the organs of the cardiovascular system;

- modern ideas about the morphofunctional organization of the organs of the cardiovascular system;

- interpretation of the relationship between structural and functional parts of the cardiovascular system;

- assessment of the functional state of the organs of the cardiovascular system, mechanisms of adaptation to the action of various factors.
- to acquaint students with the structure of the walls of vessels of different types in relation to hemodynamic conditions;

- modern ideas about the morphofunctional organization of the organs of hematopoiesis and immune defense;
- interpretation of the relationship between the structural and functional parts of the hematopoietic organs.

b) educational:
- to educate students on the importance of studying the structural and molecular mechanisms of the activity of the organs of the cardiovascular system, their importance in the process of forming a future doctor;

- to acquaint students with the morphological and functional features of the organs of the cardiovascular system, to determine their importance for practical medicine;

- to bring to the students the importance of studying the structural and molecular mechanisms of the activity of the organs of hematopoiesis and immune defense, their importance in the process of forming a future doctor;
- to familiarize students with the morphological and functional features of the organs of hematopoiesis and immune defense, to determine their importance for practical medicine;
- to form students' professional significance of the topic. Discuss the issue of deontology.

3. Plan and organizational structure of the lecture.

№№	The main stages of the lecture and their content	Objectives in levels of abstraction	Lecture type. Lecture equipment	Time management
1	2	3	4	5
I. 1. 2.	*Preparatory stage.* Determination of the learning goal. Providing positive		Tables. Slides.	5%

	motivation			
II	*The main stage* Teaching lecture material according to the plan: 1. Morphofunctional characteristics of the organs of the cardiovascular system. 2. Relationship of structural features of the walls of different vessels with hemodynamic conditions. 3. Structural and molecular mechanisms of the activity of the organs of hematopoiesis and immune defense. 4.Histophysiology of the regulatory influence of the hematopoietic organs and immune defense on the vital activity of the organism.	I. Descriptive. II. Analytical - synthetic, quality.	In accordance with the publication "Guidelines for the planning, preparation and analysis of lectures." List of literature, question, task.	85-95%
III.	*Conclusions stage.* Summary of the lecture. General conclusions. Lecturer's answer to possible questions. Self-study assignment .			5%

4. Content of the lecture material:

- structural and logical scheme of the content of the topic;
- text of the lecture. (attached)

5 Materials for activating students during the lecture:
1) Since each lymph node collects lymph from a separate part of the body, malignant tumor cells often reach the lymph nodes and further through the external lymphatic vessels, as well as blood vessels spread to the second parts of the body. Infection and antigenic stimulation often causes swollen lymph nodes.
2) The spleen, although it performs many important functions in the human body, is not a vital organ. In some situations, a splenectomy is necessary. In this case, the functions of the spleen are taken over by other organs (for example, the liver). A person who has a splenectomy may have an increased risk of developing infections.
3) Diseases of the immune system are divided into three types:
- allergic reactions,
- immunodeficiency.
- autoimmune diseases.

Questions:
1. The concept of the immune system and its tissue components. Classification and characterization of immunocytes and their interaction in the reactions of humoral and cellular
2. Morphofunctional characteristics of the organs of hematopoiesis and immune defense.
3.Cardiovascular system. Morphological and functional characteristics. Classification of vessels. The relationship of hemodynamic conditions with the structure of blood vessels.
4. Heart. General plan of the structure of the wall. Endocardium. Myocardium. Morphofunctional characteristics of contractile and leading cardiomyocytes.
5. Vessels of the hemomicrocirculatory bed. Morphological and functional characteristics of its links. Arterio-venular anastomoses. Classification, structure of different types of anastomoses, their functions.

6. General material and methodological support of the lecture:
- classrooms;
- equipment;
- equipment;
- illustrative materials.

List of recommended literature .

The main one:

1.Lutsyk O.D., Tchaikovsky Y.B. Histology, cytology, embryology Vinnytsia, New Book, 2018.
2.Barinov E.F., Tchaikovsky Y.B. General histology and embryology of internal organs: textbook.Kyiv: Medicine; 2013
3.Wojciech Pawlina. Histology: textbook and atlas. WSV: Medicine, 2021.

Additional:

1.Histology and embryology of internal organs: textbook / E.F. Barinov, Y.B. Tchaikovsky, O.M. Sulaeva et al.
2.Cytology of human organs and tissues edited by L.S.Bolgova. Kyiv: Book-plus, 2018, p.288

Addition

Theme: "Cardiovascular system. Organs of hematopoiesis and immune defense."

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

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

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

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

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

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

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

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

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

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

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

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

Tunica intima consists of three layers:

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

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

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

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

Tunica externa (adventitia) consists of two layers:

- external – is formed by loose connective tissue

- internal - contains separated bundles of the smooth muscle cells

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

Muscular arteries consist of three layers:

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

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

The vessels of microvascular bed

As the diameter of arteries decreases, all the tunics of their wall become thinner. Arteries gradually turn into arterioles, which the microvascular bed starts with. The exchange of water, ions, micro- and macromolecules between blood and tissues occurs through the wall of the vessels of microvascular bed. This process of exchange between blood, lymph and tissues is called **microcirculation**. The interstitial and intraorganic homeostases depend on the process of microcirculation. Microvascular bed consists of arterioles, associated capillary network, and postcapillary venules.

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

presence of perforations in the internal elastic membrane and in the basal lamina of endothelium.

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

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

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

The wall of capillaries consists of three layers:

- internal layer consists of endothelial cells, which lie on the basal lamina

- middle layer consists of pericytes connected by the basal lamina

- external layer consists of adventitial cells and thin collagen fibers drowned in ground substance

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

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

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

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

Classification of capillaries

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

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

Two types of AVA are distinguished:

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

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

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

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

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

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

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

Venules. Three types of venules are distinguished:

- postcapillary
- colligens
- muscular

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

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

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

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

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

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

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

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

1) Amuscular veins
2) Muscular veins

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

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

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

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

Veins with high development of muscular elements. These veins are characterized by high development of muscle cells in all three tunics. In tunica interna and externa they are longitudinally arranged, in tunica media – circularly.

The characteristic feature of these veins is the presence of valves. This category includes veins of lower part of the body and lower limbs.

Valves – are pocket-like folds of tunica interna opened towards the heart. They prevent retrograde movement of blood because of gravity. The valve is formed by loose connective tissue and in some cases small amount of smooth muscle cells.

Great saphenous vein (v. cava inferior) is structurally different from other veins. Tunica interna and media are low-developed. Tunica externa is 6-7 times thicker than tunica externa and media together and contains a lot of longitudinally arranged bundles of smooth muscle cells. The valves are absent in great saphenous vein, their function is provided by the folds of tunica externa.

According to the size veins are classified into small, medium and large.

Lymphatic vessels

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

Classification. Lymphatic vessels include:

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

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

Two types of lymphatic vessels are distinguished: muscular and amascular.

Medium and big lymphatic vessels contain three well-developed layers (tunica interna, media and externa). Tunica interna forms numerous folds – the valves. The dilatated areas between adjacent valves are called lymphangions. Tunica media is

more conspicuous in the vessels of lower limbs. Before lymph is returned to the blood, it passes through lymph nodes, where it is exposed to the cells of the immune system. The characteristic feature of the wall of large lymphatic vessels (thoracic duct and right lymphatic duct) is high-developed tunica externa, which is 3-4 times thicker than tunica interna and media together. In tunica externa are located longitudinally arranged bundles of the smooth muscle cells. It is located up to nine semilunar valves in thoracic duct.

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

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

- endocardium
- myocardium
- epicardium

Endocardium consists of four layers:

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

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

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

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

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

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

Epicardium and pericardium. The outer covering of the heart or epicardium is also known as the visceral layer of serous pericardium. Epicardium consists of the thin layer of connective tissue covered with mesothelium.

There is a space between the epicardium and pericardium containing a minimal amount of serous fluid, which act as a lubricant.

Organs of hematopoiesis and immune defense.

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

The central organs are:

- red bone marrow;
- thymus.

The functions of the central organs of hematopoiesis are:

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

The peripheral organs are:

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

The functions of the peripheral organs of hematopoiesis are:

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

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

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

There are distinguished the following parts in red bone marrow:

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

Rough stroma is formed by the endosteum of spongy bone trabeculae and supports the gentle stroma.

Gentle stroma – is the reticular connective tissue that serve as a framework for the developing blood cells.

Parenchyma consists of the blood cells on the different stages of development (hematopoietic stem cells, progenitor stem cells, lineage-restricted progenitor cells of erythrocytes, trombocytes, granulocytes, monocytes and lymphocytes).

The most intensive division and maturation of the blood cells occurs near the endosteum. The red bone marrow is highly vascularized and contains numerous fenestrated (sinusoidal) capillaries, which provide the passage of the mature blood cells into the bloodstream.

Hematopoietic cells are arranged in nests or “islands”. Each island contains the cells of the one blood cell lineage. Each island in which erythrocytes develop contains a macrophage. Since the developing erythrocytes need the iron ions for the formation of hemoglobin molecule, they surround the macrophage, which stores the iron. The macrophages serve as “breadwinners” for the erythroblasts, enriching them in iron. Immature erythroid cells are surrounded by the glycoproteins. As the erythroid cells mature, the amount of glycoproteins decreases. At the same time the mobility of the cells increases and they pass into the bloodstream.

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

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

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

In the age of 12-18 years, the red bone marrow of the long bones diaphyses is substituted to the inactive **yellow bone marrow**. Yellow bone marrow consists of adipocytes, which contain the pigment lipochrome. Although normally yellow bone marrow doesn't provide hematopoietic function, in case of severe loss of blood or some pathologic states it can revert to the red bone marrow by repopulation the yellow bone marrow by circulating stem cells.

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

Thymus – is the central organ of lymphocytopoiesis and immunogenesis.

The functions of thymus are:

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

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

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

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

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

There are distinguished two portions in the thymus parenchyma:

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

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

- small and medium lymphocytes;

- macrophages and their subtype – dendritic cells;

- epithelioreticulocytes;

- T-lymphoblasts.

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

The precursors of T-lymphocytes are delivered to thymus from the red bone marrow. Here under the action of thymosin, which is produced by the epithelioreticulocytes, T-lymphocytes undergo cell division and some of them are phagocyted by the macrophages. It is considered that T-lymphocytes of thymic cortex migrate into the bloodstream, without getting to the thymic medulla. With the bloodstream T-lymphocytes are delivered to the peripheral organs of lymphopoiesis – lymph nodes and spleen, where they are differentiated into subpopulations. However not all the lymphocytes formed in thymus pass into the bloodstream, but only those that have passed the **T- cell education"** and obtained the receptors to the specific antigens. T-lymphocytes, which have the receptors to their own antigen as a rule die in thymus.

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

The following components constitute the blood-thymus barrier:

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

The thymic medulla is formed by:

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

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

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

There four phases in the age involution of thymus:

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

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

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

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

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

The lymph nodes include:

- rough stroma (capsule and trabeculae);

- gentle stroma (reticular connective tissue);

- parenchyma (T- and B-lymphocytes, macrophages, dendritic cells).

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

In the lymph node the following portions are distinguished:

- cortex;

- paracortex (deep cortex);

- medulla.

The cortex is formed by lymphatic nodules (follicles) – concentrations of B-lymphoblasts, macrophages and dendritic cells. They have an ability to fix the antigen-antibody complexes on their surfaces. The contact with the dendritic cells stimulates the B-lymphocytes to produce antibodies. The framework of the nodule is formed by the reticular connective tissue. The follicles are surrounded by the

reticuloendothelial cells. Structurally reticuloendothelial cells are the reticular cells, but they provide the function of endothelial cells as they line the sinuses of the lymph nodes. Among reticuloendotheliocytes the numerous fixed macrophages (the coastal cells) are revealed.

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

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

The paracortex is located between the cortex and medulla of the lymph node.

This region contains numerous T-lymphocytes and macrophages and is called **thymusdependent.** Macrophages in the paracortex are represented as interdigitative cells, which have lost their ability to phagocytosis. These cells secrete the biologically active substances, which stimulate the proliferation of T-lymphocytes. In the paracortex the proliferation of T-lymphocytes, their blast transformation and differentiation into the effector cells (T-killers, helpers etc) occurs.

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

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

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

There four types of lymphatic sinuses:

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

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

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

The functions of the spleen:

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

There are distinguished the following portions in the spleen:

- rough stroma (connective tissue capsule and trabeculae);

- gentle stroma (reticular tissue);

- parenchyma (lymphocytes, plasma cells, macrophages, erythrocytes, dendritic and interdigitative cells, destroyed erythrocytes and platelets).

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

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

In the spleen parenchyma are distinguished:

- the white pulp;

- the red pulp.

The white pulp is formed by lymphocytes, plasma cells, macrophages, dendritic and interdigitative cells and the cells that are located within the reticular tissue meshwork. These cells are arranged in circular cell clusters, which are called

lymphatic follicles (nodules) or splenic corpuscles. The follicles are surrounded by the capsule, which is formed by the reticuloendothelial cells.

In the lymphatic follicle the four zones are distinguished:

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

The light germinal center of lymphatic follicles contains:

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

Periarterial zone contains:

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

The dark mantle zone is formed by densely packed:

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

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

- B-lymphocytes
- T-lymphocytes
- macrophages

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

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

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

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

Blood supply of the spleen

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

METHODICAL RECOMMENDATION OF LECTURES

for dentistry faculty

THEME: «Endocrine system.»

Approved on the methodical conference of department

«____»_____ 20___., protocol №_____

Head of Department, doc._____ Tiron O.I.

Approved on the methodical conference of department

«____»_____ 20___., protocol №_____

Head of Department, doc._____ Tiron O.I.

Approved on the methodical conference of department

«____»_____ 20___., protocol №_____

Head of Department, doc._____ Tiron O.I.

Theme: «Endocrine system.»-2h.

1. Relevance of the topic.

One of the most significant results of phylogenesis is considered to be the formation of perfect mechanisms of neuroendocrine regulation of the most important functions - adaptation, reproduction, etc.

Complex subordinate relations between the nervous and endocrine systems provide for both direct and reverse regulatory influence of endocrine gland hormones on

different systems of the body. The organs of the endocrine system fold the afferent link of the regulatory system, which is designed to maintain homeostasis in the body. Changes in the functional activity of these organs are accompanied by a restructuring of their structure, and, conversely, violations of the structure of the organs pulls an imbalance of the corresponding hormones.
Knowledge of what is acquired by this section is necessary for understanding the morphological manifestations of hormonal regulation disorders. Today there is not a single branch of clinical medicine where hormonal drugs are not used, and in many critical conditions their timely application keeps the patient alive. Any doctor in his practice constantly encounters endocrine pathology of varying severity.
Therefore, a deep and perfect study of the histophysiology and structure of the organs of the endocrine system in clinical practice will help earlier diagnosis and treatment of diseases, the more progress in the field of scientific research has made it possible to reconsider the issue of pathogenesis and treatment of many endocrine diseases.

2. Objectives of the lecture:

a) learning:

- analysis of the structural organization of the organs of the endocrine system;
- modern ideas about the morphofunctional organization of the organs of the endocrine system;
- interpretation of the relationship between the structural and functional parts of the nervous and endocrine systems;
- assessment of the functional state of the organs of the central and peripheral endocrine system, interpretation of control, age-old changes, mechanisms of adaptation to the action of various factors.
- to familiarize with the structure of the organs of the endocrine system; - single hormone-producing cells (APUD cells - systems)

b) educational:

- to bring to the students the importance of studying the structural and molecular mechanisms of the activity of the organ of endocrine system, its importance in the process of forming a future doctor;
- to acquaint students with the morphological and functional features of the organs of endocrine system, to determine their importance for practical medicine;
- to form students' professional significance of the topic. Discuss the issue of deontology.

3. Plan and organizational structure of the lecture.

№№	The main stages of the lecture and their content	Objectives in levels of abstraction	Lecture type. Lecture equipment	Time management
1	2	3	4	5

I. 1. 2.	*Preparatory stage.* Defining the learning goal Providing positive motivation.		Tables. Slides.	5%
II	*The main stage* Teaching lecture material according to the plan: 1. Morpho-functional characteristics of the organs of the endocrine system. 2. Structural and molecular mechanisms of the endocrine system organs. 3. Histophysiology of the regulatory influence of the endocrine system on the vital activity of the body. 4. Morphofunctional connections of the nervous and endocrine systems ..	I. Descriptive II. Analytical - synthetic, high quality.	In accordance with the publication "Guidelines for the planning, preparation and analysis of lectures."	85-95%
III.	*The final stage.* Summary of the lecture. General conclusions. Lecturer's answer to possible questions. Self-study assignment.		List of literature, question, task.	5%

4. Content of the lecture material:

- structural and logical scheme of the content of the topic;
- text of the lecture. (attached)

5. Materials for activating students during the lecture:

1) Disruption of the hypothalamus, which destroy the neurosecretory cells that produce ADH, causes diabetes insipidus, a disease in which the kidneys' ability to concentrate urine is impaired (polyuremia).
2) Tumors of the pituitary gland usually turn out to be adenomas, that is, of a benign nature. The clinical diagnosis of these tumors is confirmed using immunocytochemical methods.
3) Hypothyroidism (decreased production of TSH) in children can cause cretinism, which is accompanied by a halt in physical and mental development.
4) Hyperthyroidism can be caused by a variety of diseases of the thyroid gland, of which the most common Graves' disease (Bazet's disease), which is accompanied by exophthalmos, weight loss, nervousness, asthenia, and a fast heartbeat.

Questions:
1. Classification of the endocrine glands. The concept of target cells and hormone receptors.
2. Classification of the endocrine glands. Characteristics of single hormone-producing cells.
3.Hypothalamus. The neurosecretory nuclei of the hypothalamus, features of the structure and function of neurosecretory cells. Hypothalamic adenohypophyseal and hypothalamic pituitary systems.
4.Pituitary gland. Development, structure, blood supply, histophysiology of the adeno- and neurohypophysis. The connection of the pituitary gland with the hypothalamus.
5. Epiphysis. Sources of development. Structure. Secretory functions.
6. Thyroid gland. Development, structure, histophysiology, functional significance. Age-related changes.
7. Parathyroid gland. Development, structure and functional significance. Age-related changes.
8. Adrenal glands. Sources of development. Structure, histophysiology of the cortex and medulla.
9. Connection of the adrenal glands with the pituitary gland and the central nervous system. Age-related changes.
10. Single hormone-producing cells (APUD cells - systems): localization, structure, functions.

6. General material and methodological support of the lecture:

- classrooms;
- equipment;
- equipment;
- illustrative materials

List of recommended literature .

The main one:

1.Lutsyk O.D., Tchaikovsky Y.B. Histology, cytology, embryology Vinnytsia, New Book, 2018.
2.Barinov E.F., Tchaikovsky Y.B. General histology and embryology of internal organs: textbook.Kyiv: Medicine; 2013
3.Wojciech Pawlina. Histology: textbook and atlas. WSV: Medicine, 2021.

Additional:

1.Histology and embryology of internal organs: textbook / E.F. Barinov, Y.B. Tchaikovsky, O.M. Sulaeva et al.
2.Cytology of human organs and tissues edited by L.S.Bolgova. Kyiv: Book-plus, 2018, p.288

Theme: «Endocrine system.» *Addition*

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

inhibit the main functions of the body: metabolic processes, somatic growth and reproductive functions.

Hormones are chemically divided into three classes:

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

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

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

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

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

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

Розрізняють чотири групи елементів ендокринної системи.

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

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

Central endocrine organs

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

For convenience hypothalamus is divided into three parts:

- anterior hypothalamus
- middle hypothalamus
- posterior hypothalamus

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

Two pairs of nuclei are located in the anterior hypothalamus:

- supraoptic nucleus
- paraventricular nucleus

The neurosecretory cells of supraoptic nucleus produce hormone **Vasopressin**. Biological action of Vasopressin results to the increasing of blood pressure by promoting the contraction of the smooth muscle in small arteries and arterioles. Another biological effect of Vasopressin is reduction of urine excretion by the facilitation of resorption of water from the distal tubules and collecting ducts of the kidney. That's why the second name of this hormone is **antidiuretic hormone (ADH)**. Supraoptic nuclei are formed by the large cholinergic neurosecretory cells that contain secretory granules in perikaryones and cell processes. Axons of these cells pass through the median eminence and pituitary stalk to the posterior pituitary, where they end near the blood capillaries, forming dilatations called **Herring bodies**.

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

Hormones through the axons of neurosecretory cells enter the posterior pituitary, where they pass into the bloodstream through the axovasal synapses. The central part of these nuclei is formed by large cholinergic neurosecretory cells, while the peripheral part consists of small adrenergic neurosecretory cells. Axons of these cells enter posterior pituitary (neurohypophysis). The nuclei of hypothalamus are formed by the large or small multipolar neurons that contain

well-developed granular EPR, Golgi apparatus. These organelles provide synthesis and secretion of hormones. Specific granules, containing biologically active substances are revealed in the cytoplasm of all neurosecretory cells.

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

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

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

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

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

Hypophysis-dependent endocrine organs are:

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

Non-endocrine cells regulated by hypophysis are:

- lactocytes of mammary gland;
- melanocytes;
- adipocytes;

- chondrocytes;
- spermatogoniums of testis etc.

The pituitary gland has two functional components:

• Anterior lobe **(adenohypophysis)**, the glandular epithelial tissue

• Posterior lobe **(neurohypophysis),** the neural secretory tissue.

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

• Pars distalis

• Pars intermedia

• Pars tuberalis

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

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

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

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

- chromophilic
- chromofobe

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

Among chromophilic endocrinocytes three types of cells are distinguished:

- basophilic
- acidophilic
- corticotropes (intermediate cells).

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

- **gonadotropes**, these cells produce **follicle-stimulating hormone (FSH)**, which stimulates spermatogenesis in testis in males and follicular cells of ovaries in females and **luteinizing hormone (LH)**, whose function is the stimulation of development of corpus luteum in females and stimulation of Leydig cell production of testosterone in males. Gonadotropes are characterized by peripherically located nucleus and centrally located macula (well-developed Golgi complex). The cytoplasm contains a lot of secretory vesicles, which are 200-250 nm in diameter, a lot of mitochondria and well-developed rough EPR. In case of the lack of sex hormones in the body the cells of anterior lobe of pituitary gland increase the production of gonadotrophic hormones acoording to the principle of negative feedback. Due to this gonadotropes undergo hypertrophy; the cytoplasm of some cells becomes occupied by a large vacuole (in the area of macula) that displaces the nucleus to the periphery. Such transformed gonadotropes are called castration cells.
- **thyrotropes** produce **thyroid-stimulating hormone (TSH)** that regulates the activity of thyroid gland. These large polygonal cells contain very small secretory vesicles (80-150 nm).

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

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

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

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

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

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

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

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

Pars tuberalis is an extension of the anterior lobe along the stalklike infundibulum. It is formed by the cords of cuboidal epithelial cells with basophilic cytoplasm. Some cells of tuberal cords contain basophilic granules in their cytoplasm. The function of the cells of pars tuberalis is still unclear.

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

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

- neurosecretory (pinealocytes)
- gliocytes (astroglial cells)

Pinealocytes are the chief cells of pineal gland located mostly in the center of the lobules. They are large polygonal cells with branched processes. The expanded, clublike endings of the processes are associated with the blood capillaries. The

cytoplasm contains well-developed smooth and rough EPR, Golgi complex, mitochondria and lysosomes.

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

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

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

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

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

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

In humans pineal gland reaches the maximal development to the age of 5-6 years, after this, in spite of continuing functioning, it undergoes age involution. A part of pinealocytes undergo atrophy, while the stroma expands. Derived from the precipitation of salts, the calcified concretions appear in the stoma of pineal gland. These concretions are called brain sand.

Peripheral endocrine organs

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

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

to polypeptide chain (globulin). The apical surfaces of the follicular cells are in contact with the colloid, and the basal surfaces rest on a typical basal lamina.

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

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

Synthesis of thyroid hormones involves two phases:

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

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

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

Another type of cells of thyroid gland is **parafollicular cells (C-cells)**. They are located in the periphery of the follicular epithelium and lie within the follicle basal lamina. These cells have no exposure to the follicle lumen. Parafollicular cells are large irregular in shape with numerous secretory vesicles in the cytoplasm. The characteristic feature of parafollicular cells is their ability to reduce the heavy

metal oxides that's why they are argyrophilic. The cytoplasm contains well-developed rough EPR and Golgi apparatus.

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

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

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

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

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

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

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

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

Adrenal cortex is divided into three zones on the basis of morphological and functional features:

- zona glomerulosa
- zona fasciculata
- zona reticularis

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

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

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

Zona reticularis. The cells of the zona reticularis are noticeably smaller than those of the zona fasciculata. These polygonal cells are arranged in anastomosing cords, which under the microscope remain reticulum. The cells of the zona reticularis decrease in size and become cuboidal, rounded or irregular in shape. The cells have relatively few lipid inclusions. The mitochondria are characterized by the **tubular cristae**. Endocrinocytes of the zona reticularis secrete **weak sex steroid hormones** – dehydroepiandrosterone (hormone, similar to testosterone), and small amounts of female sex hormones (estrogen and progesterone).

Between the three main zones of adrenal cortex the clusters of low-differentiated cells are revealed. These cells are the source of physiological regeneration of adrenal cortex. The first layer of such cells is located between the connective tissue capsule and the zona glomerulosa. The second germinative layer, called sudanophobe zone, is located between the zona glomerulosa and the zona fasciculata. Between the zona reticularis and adrenal medulla the **X-zone** is located. X-zone consists of the rests of embryonic adrenal cortex.

Adrenal medulla is separated from the adrenal cortex by the discontinuous layer of loose connective tissue. The adrenal medulla is formed by the large rounded or polygonal cells. The cells of adrenal medulla are divided into two groups on the basis of their products of secretion:

- epinephrocytes
- norepinephrocytes

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

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

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

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

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

ODESA NATIONAL MEDICAL UNIVERSITY

DEPARTMENT OF HISTOLOGY, CYTOLOGY AND EMBRYOLOGY

METHODICAL RECOMMENDATION OF LECTURES

for dentistry faculty

THEME: «Urinary system.»

Approved on the methodical conference of department

«____»_____ 20___., protocol №_____

Head of Department, doc._____ Tiron O.I.

Approved on the methodical conference of department

«____»_____ 20___., protocol №_____

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Head of Department, doc._____ Tiron O.I.

Theme: «Urinary system.»-2h.

1. **Relevance of the topic.**

The urinary system plays an important role in maintaining homeostasis in the human body. In the process of life, slags are formed in the body, 80% of which are excreted due to the urinary activity of the kidneys. In addition, the kidneys are involved in the regulation of the volume and composition of extracellular fluid, blood pressure, ion exchange, maintenance of the acid-base state, and stimulation of erythropoiesis.

In this regard, it becomes clear why edema, a state of uremia, and renal coma appear when the kidneys function is impaired, in which the products of nitrogen metabolism rapidly accumulate in the body and a sharp suppression of all functions occurs. Therefore, knowledge of the structural foundations of the functioning of the kidney is necessary to understand the normal and pathological physiology of

the organ, and is also the starting point and the choice of adequate diagnostic and therapeutic tactics during the treatment of patients with nephrological pathology.

2. Objectives of the lecture:

a) learning:

- analysis of the structural organization of the organs of the urinary system;
- modern ideas about the morphofunctional organization of the organs of the urinary system;
- interpretation of the relationship between the structural and functional parts of the organs of the urinary system;
- assessment of the functional state of the urinary system organs, the interpretation of age-related changes, mechanisms of adaptation to the action of various factors.

b) educational:

- to bring to the students the importance of studying the structural and functional features of the activity of the organs of the urinary system, their importance in the process of forming a future doctor;
- to interpret the histophysiology of urine formation, structural features of the countercurrent-multiplying apparatus, to determine their significance for practical medicine;
- to form students' professional significance of the topic. Discuss the issue of deontology.

3. Plan and organizational structure of the lecture.

№№	The main stages of the lecture and their content	Objectives in levels of abstraction	Lecture type. Lecture equipment	Time management
1	2	3	4	5
I. 1. 2. II	*Preparatory stage.* Determination of the learning goal. Providing positive motivation. *The main stage* Teaching lecture material according to the plan: 1. Morpho-functional	 I. Descriptive. II. Analytical - synthetic, high quality.	Tables. Slides.	5% 85-95%

	characteristics of the organs of the urinary system 2. Nephron - as a structural and functional unit of the kidney. Heterogeneity of the nephron. 3. Topography and differential diagnostics of different parts of the nephron, collecting tubules, their histophysiology. 4. Histophysiology of urine formation. Countercurrent multiplier apparatus. 5. Endocrine apparatus of the kidneys.		In accordance with the publication "Guidelines for the planning, preparation and analysis of lectures." List of literature, question, task.	
III.	*The final stage.* Summary of the lecture. General conclusions. Lecturer's answer to possible questions. Self-study assignment			5%

4. Content of the lecture material:
- structural and logical scheme of the topic content;
- lecture text

5. Materials for activating students during the lecture:

1) Proteinuria - the content of protein in the urine, as a result of damage to the glomerular filter of the nephron. This occurs in diabetes mellitus and glomerulonephritis.

2) Lack of aldosterone in animals with removed adrenal glands causes Addison's disease, in humans it causes sodium loss in the urine.

Questions:

1. The urinary system, its morphological and functional characteristics.
2. Kidneys. Sources and main stages of development. The structure and features of the blood supply.
3. The structure and functional significance of the nephron.
4. The mechanism of urine formation.
5. Counter-current multiplier. The mechanisms of dilution and concentration of urine.
6. Endocrine apparatus of the kidney. Structure and function.
7. Urinary tract. Development. Structure and functional significance.

6. General material and methodological support of the lecture:
- classrooms;
- equipment;
- equipment;
- illustrative materials.

List of recommended literature .

The main one:

1.Lutsyk O.D., Tchaikovsky Y.B. Histology, cytology, embryology Vinnytsia, New Book, 2018.
2.Barinov E.F., Tchaikovsky Y.B. General histology and embryology of internal organs: textbook.Kyiv: Medicine; 2013
3.Wojciech Pawlina. Histology: textbook and atlas. WSV: Medicine, 2021.

Additional:

1.Histology and embryology of internal organs: textbook / E.F. Barinov, Y.B. Tchaikovsky, O.M. Sulaeva et al.
2.Cytology of human organs and tissues edited by L.S.Bolgova. Kyiv: Book-plus, 2018, p.288

Theme: «Urinary system.» *Addition*

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

The kidney is an organ, which continuously produce the urine. It is the main organ, which remove certain waste products of metabolism from the body. The

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

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

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

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

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

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

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

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

Nephron consists of the following parts:

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

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

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

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

Among cortical nephrons there are distinguished two types: the short ones and the intermediate ones. The short cortical nephrons have their renal corpuscles located in the outer part of the cortex; they have short loops of Henle located within the cortex. The intermediate nephrons have their loops of Henle extending in the outer part of the cortex (80%).

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

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

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

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

- endothelium of the glomerular capillaries, which posseses numerous fenestrations of about 70 to 90 nm in diameter, and lies on the inner surface of the basement membrane;
- the glomerular basement membrane is the joint product of the endothelium and cells of the visceral layer of Bowman's capsule. It consists of three layers: two of them (the lamina rara externa and the lamina rara interna) are electron-lucent layers; the middle layer is the electron-dense one (lamina densa) containing a microfibrillar meshwork with a mesh diameter of about 7nm;

- visceral layer of Bowman's capsule is formed by large (about 30mcm) polygonal epithelial cells called **podocytes**. The basal portions of podocytes extend processes, cytotrabeculae, around the capillaries and develop numerous secondary processes called foot pedicles or cytopodia. The expanded bases of the foot pedicles contact with the basement membrane.

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

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

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

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

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

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

acidophilic and heterogeneous due to the presence of various inclusions (urates, lipids, pigments etc), pinocytotic vesicles and lysosomes.

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

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

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

The distal straight tubule has a diameter of 30 mcm, its epithelium is similar to the epithelium of the distal convoluted tubule. The cuboidal epithelial cells lie on

the basal lamina. The distal segment cells do not reveal the brush border. Their basal portions contain deep folds of cytolemme, where the large elongate mitochondria are located.

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

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

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

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

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

The juxtaglomerular apparatus consists of the following components:

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

The juxtaglomerular cells are located mainly under the endothelial in the wall of the afferent arteriole and least in the efferent arteriole. These cells are oval-shaped; their cytoplasm contains the granules of rennin, which they secrete into the blood. Renin catalyzes the formation of angiotensin, which causes the constriction of blood vessels, thereby increasing the blood pressure. Besides this, rennin stimulates the production of aldosteron by the adrenal cortex.

The macula densa – is an area of distal segment of nephron located between the afferent and the afferent arteriole. Epithelial cells of macula densa, unlike other

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

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

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

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

Blood supply. Each kidney receives a large branch from the abdominal aorta, called the renal artery. The renal artery branches within the renal sinus and sends interlobar arteries into the substance of the kidney. These arteries travel between

the pyramids as far as the cortex and then turn to follow an arched course along the base of the pyramid between the medulla and the cortex. Thus, these interlobar arteries are designated arcuate arteries. Interlobular arteries branch from the arcuate arteries and ascend through the cortex toward the capsule. As they traverse the cortex toward the capsule, the interlobular arteries give off branches, the afferent arterioles, one to each glomerulus. Afferent arterioles give rise to the capillaries that form the glomerulus. This capillary network is called primary capillary network or rete mirabile, because here the capillaries are located between two arterioles. These capillaries merge into the efferent arteriole. Leaving the renal corpuscle, the efferent arteriole again branches into the capillary network, which

surrounds the renal tubules, called secondary or peritubular capillary network. Its functions – are trophic of nephron and taking part in the reabsorption phase of urine formation. From the peritubular capillary network the venous system of renal circulation begins. Generally, venous flow in the kidney follows a reverse course to arterial flow, with the veins running in parallel with the corresponding arteries. Peritubular capillaries near the kidney surface and capillaries of the capsule drain into stellate veins, which in turn drain into interlobular veins , interlobar veins, and the renal vein. Such system of blood circulation is true only for cortical nephrons and is called cortical circulation. Its characteristic features are associated with the process of urine formation, in which the cortical nephrons are involved.

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

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

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

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

Due to the presence of submucosa, the mucosa of ureter and urinary bladder form deep folds, which enable these organs to stretch and expand the lumen of ureter, which is important during the passage of urine calculus. On a cross-section the lumen of ureter reveals star-like shape. The submucosa in lower parts of ureter contains small tuboalveolar glands, structurally resembling glands of the prostatic gland. The muscularis form two layers in the upper parts of ureter and two layers

in its lower parts. It consists of the smooth muscle bundles, which spirally encircle the ureter; these bundles are the continuation of the muscularis of renal pelvis and continue with the muscularis of urinary bladder. Only in the area, where the ureter opens into the urinary bladder the smooth muscle bundles have only longitudinal direction, which provides the opening of ureteral ostium independently on the condition of the smooth muscles of urinary bladder.

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

The muscularis of renal calyces and renal pelvis consists of two layers of the smooth muscle – the inner longitudinal and the outer circular, however near the pyramidal papillae only the circular layer is found; its contraction compress the papilla and causes the discharge of urine. The muscularis of urinary bladder consists of three layers: the outer and inner longitudinal and the middle circular layer. In the area of trigone there is only one muscular layer. These muscular layer consists of two parts:

1. Muscles, which combine the muscular structures of both ureters

2. Muscle-sphincter of trigonum, which opens the urethral ostium. It consists of two layer: the outer layer of striated muscle and the inner layer of smooth muscle.

METHODICAL RECOMMENDATION OF LECTURES

for dentistry faculty

THEME: «Male reproductive system. Female reproductive system.»

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Approved on the methodical conference of department

«____»_____ 20___., protocol №_____

Head of Department, doc._____ Tiron O.I.

Approved on the methodical conference of department

«____»_____ 20___., protocol №_____

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«____»_____ 20___., protocol №_____

Head of Department, doc._____ Tiron O.I.

Theme: "Male reproductive system. Female reproductive system." -2h.

1. **Relevance of the topic.**

The male reproductive system performs two interrelated functions - the formation of male germ cells and the secretion of male sex hormones, which ensures the storage of the biological species, the formation of secondary sexual characteristics, and the sexual characteristics of the behavior of the individual. Dysregulation and structural and functional state of the testes leads to the development of male infertility.Diseases of the male reproductive system are the subject of an

independent science - andrology, which is rapidly developing in our time. Understanding of the peculiarities of the development and structure of the organs of the male reproductive system will make it possible to find out their histophysiology, to understand the reasons for the occurrence of possible defects in the development of the reproductive system, spermatogenesis disorders, to find out the etiology and pathogenesis of incendiary, dystrophic, tumor diseases of the organs of this system, as well as changes in homeostasis in the body that occurs under such conditions.

All this knowledge is necessary for future doctors to understand correctly the processes of pathophysiology, to successfully diagnose and treat patients with different pathologies.

Consideration of the basic patterns of development, structure and histophysiology of the organs of the female reproductive system is necessary to understand the possibility of their pathology. In addition to the generative function, the ovaries produce female sex hormones, which ensure the functioning of not only the genital tract, but also affect the state of the nervous, cardiovascular systems, and the musculoskeletal system of the female body.

Rhythmic fluctuations in the secretion of ovarian hormones predetermine, in turn, the corresponding structural and functional changes in hormone-dependent organs. Knowledge of micro- and ultramicroscopy of the structure of the structural elements of the ovary will enable students to understand the histophysiology of the organ, and in further courses of study, the course of the processes that develop in it in the case of pathology of gametogenesis, disruption of the growth and maturation of follicles, ovulation, endocrine function of the ovary, which is necessary conditions of an objective analysis of the pathogenesis of diseases of the female reproductive system.
Obstetric and gynecological practice is based on knowledge of the basic laws of the structural and functional organization and regulation of the organs of the female reproductive system. The cyclical nature of the implementation of generative and endocrine functions is used in clinical diagnostics to assess the hormonal status of the female body, to search for structural and functional determinants of reproductive disorders that may be associated with infertility, the development of ectopic pregnancy, inflammatory and nonplastic processes and bleeding.

2. Objectives of the lecture:
a) learning:

- analysis of the structural organization of the organs of the male reproductive system;
- modern ideas about the morphofunctional organization of the organs of the male reproductive system; - interpretation of the relationship between the structural and functional parts of the organs of the male reproductive system;
- assessment of the functional state of the organs of the male reproductive system, interpretation of age-related changes, mechanisms of adaptation to the action of various factors.
- to acquaint students with the structure of the organs of the male reproductive system
- analysis of the structural organization of the organs of the female reproductive system;
- modern ideas about the morphofunctional organization of the organs of the female reproductive system;
- interpretation of the relationship between the structural and functional parts of the organs of the female reproductive system;
- assessment of the functional state of the organs of the female reproductive system, the interpretation of age-related changes, mechanisms of adaptation to the action of various factors.
- to acquaint students with the structure of the organs of the female reproductive system

b) educational:
- to bring to the students the importance of studying the structural and functional features of the activity of the organs of the male reproductive system, their importance in practical medicine.
- to interpret the morphofunctional features of organs and disorders of the male reproductive system, to determine their significance for practical medicine;
- to form students' professional significance of the topic. Discuss the issue of deontology.
- to bring to the students the importance of studying the structural and functional features of the activity of the organs of the female reproductive system for the interpretation of pathological processes in them with diseases, are studied at further stages of study;
- to interpret the morpho-functional features of organs and disorders of the female reproductive system, to determine their significance for practical medicine;
- to form students' professional significance of the topic. Discuss the issue of deontology. Plan and organizational structure of the lecture.

3. Plan and organizational structure of the lecture.

№№	The main stages of the lecture and their content	Objectives in levels of abstraction	Lecture type. Lecture equipment	Time management

1	2	3	4	5
I. 1. 2. II	*Preparatory stage* Determination of the learning goal. Providing positive motivation. *The main stage* Teaching lecture material according to the plan: 1.Morphofunctional characteristics of the organs of the male reproductive system 2. Testes. The structure and histophysiology of the convoluted seminiferous tubules. 3. Stages of spermatogenesis, their essence and physiological meaning. Hemato-testicular barrier. 4. Regulation of the endocrine and generative function of the testes. 5. Seed bearing paths. Additional glands 6. Morphofunctional characteristics of the organs of the female reproductive system 7. The ovary. Structure and histophysiology. 8. Stages of ovogenesis, their essence and physiological meaning. 9. Regulation of the endocrine and generative function of	I. Descriptive. II. Analytical - synthetic, high quality.	Tables. Slides. In accordance with the publication "Guidelines for the planning, preparation and analysis of lectures." List of literature, question, task.	5% 85-95%

	the ovaries. The final stage.			5%
III.	*The final stage.* Summary of the lecture. General conclusions. Lecturer's answer to possible questions. Self-study assignment.			

4. Content of the lecture material:
- structural and logical scheme of the topic content;
- lecture text

5. Materials for activating students during the lecture:
1) Cryptorchidism - a violation of the displacement of the testicles into the scrotum is associated with their presence at a temperature of 37 ° C, which suppresses spermatogenesis.
2) Benign prostatic hypertrophy occurs in 50% of men over 50 years old and in 95% of men over 70 years old. It is caused by a violation of the patency of the urinary tract, which is manifested by clinical symptoms in only 5-10% of cases. Malignant tumors of the prostate are the second most common cancer in men and the third leading cause of cancer death.

Questions:
1. Morphofunctional characteristics of the organs of the male reproductive system. Structure. Embryonic and postembryonic histogenesis. Functions. Spermatogenesis and its regulation.
2. The structure and histophysiology of the convoluted seminiferous tubules. The concept of the blood-testicular barrier.
3. The vas deferens and auxiliary glands of the male reproductive system. The epididymis. Seminal vesicles. Prostate. Structure, functions. Age-related changes.
4. General plan of the structure of the female genital organs.
5. The ovary. Tissue composition. Cortex and medulla. Folliculogenesis. Ovulation. Atresia.
6. Ovogenesis, stage characteristics.
7. Fallopian tubes. Structure and function.
8. Uterus. Structure, cyclical changes.
9. Ovarian-menstrual cycle. The role of the hypothalamic-pituitary-testicular system.
10. Cervix. Cytodiagnostics of the cervical epithelium.
11. Vagina. Features of the structure of the mucous membrane.

12. Age-related changes and the possibility of regeneration of the structural elements of the genital tract.

6. General material and methodological support of the lecture:
- classrooms;
- equipment;
- equipment;
- illustrative materials.

List of recommended literature .

The main one:

1.Lutsyk O.D., Tchaikovsky Y.B. Histology, cytology, embryology Vinnytsia, New Book, 2018.
2.Barinov E.F., Tchaikovsky Y.B. General histology and embryology of internal organs: textbook.Kyiv: Medicine; 2013
3.Wojciech Pawlina. Histology: textbook and atlas. WSV: Medicine, 2021.

Additional:

1.Histology and embryology of internal organs: textbook / E.F. Barinov, Y.B. Tchaikovsky, O.M. Sulaeva et al.
2.Cytology of human organs and tissues edited by L.S.Bolgova. Kyiv: Book-plus, 2018, p.288

Addition

Theme: «Male reproductive system. Female reproductive system.»

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

Testis. The functions of the testes are:

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

Each testis is surrounded by an unusually thick dense connective tissue capsule called **tunica albuginea**. Along the posterior surface of testis the tunica albuginea

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

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

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

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

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

The myoid layer consists of the contractive, so-called “myoid” cells, containing the actin filaments. The myoid cells provide the rhythmical contraction of the seminiferous tubule wall.

The fibrous layer consists of two portions:

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

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

The basal, myoid and fibrous layers together with the endothelial cells of blood capillaries form the **blood-testis barrier.** The blood-testis barrier prevents the

passage of toxic agents into the seminiferous tubules.

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

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

The seminiferous epithelium is composed of two basic cell populations:

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

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

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

1. the outer basal
2. the inner adluminal

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

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

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

1. spermatogonia
2. primary spermatocytes

3. secondary spermatocytes
4. spermatids
5. spermatozoa

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

Spermatogenesis consists of four phases:

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

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

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

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

The phase of maturation begins when the primary spermatocytes enter the metaphase of the first meiotic division. After crossingover is complete, the homologous chromosomes separate and move to the opposite poles of the meiotic spindle. Thus, the tetrads, which have been modified by crossing-over, separate and become dyads again. The two chromatids of each original chromosome (although modified by crossing-over) remain together. The cells derived from the first meiotic division are called **secondary spermatocytes.** These cells immediately enter the prophase of the second meiotic division without

synthesizing new DNA. Each secondary spermatocyte has a reduced number of chromosomes to (1n), which is represented by 22 autosomes and an X or a Y chromosome. Each of these chromosomes consists of two sister chromatids.

The secondary spermatocyte has the (2d), diploid amount of DNA. During metaphase of the second meiotic division, the chromosomes line up at the metaphase plate, and the sister chromatids separate and move to opposite poles of the spindle. As the second meiotic division is completed and the nuclear membranes re-form, two haploid **spermatids**, each containing 23 single-stranded chromosomes (1n) and the (1d) amount of DNA, are formed from each secondary spermatocyte.

This means that as result of meiotic division each spermatogonium gives a rise to four spermatids.

The phase of differentiation. In this phase the spermatids are remodeled and differentiate into the mature sperm. The elements of Golgi apparatus are transformed into acrosome. Acrosome is the special structure, which provides the penetration of spermatozoa into the oocyte. The microtubules and centriole take part in the formation of flagellum. Flagellum – is the special organelle used for locomotion. The proximal part of flagellum is surrounded by mitochondria. The excesses of cytoplasm are phagocyted by Sertoli cells. Sertoli cells secrete the fluid which helps the mature sperm to move towards the distal part of the seminiferous tubule. The process of differentiation of the spermatids into the mature sperm lasts approximately 75 days.

The exccurent ducts system begins with the **straight tubules** of testes, which are the immediate continuation of the seminiferous ducts.

The wall of the straight ducts, as the wall of other portions of the exccurent ducts system, consists of three layers:

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

The mucosa of the straight tubules is lined with simple columnar epithelium, which can reveal secretory activity.

The straight tubules become continuous with the **rete testis**. The tubules of the rete testis are covered with simple cuboidal or simple squamos epithelium. Epithelial layer of tubules of the rete testis contains macrophages, which phagocyte defective spermatozoa.

The muscularis is formed by the circular layer of the smooth muscle.

The adventitia is formed by loose connective tissue.

Efferent ductules in number of 15-20 empty into the **duct of the epididymis**. The efferent ductules are lined with pseudostratified columnar epithelium, that contains ciliated tall columnar cells and basal cells.

In the lumen of the ducts of the epididymis the differentiation of spermatozoa finishes. Under the influence of androgens this epithelium produces protein substances, which regulate the "packing" of the polysaccharides and enzymes into the acrosome. Besides this, the secretion of epithelial cells rarefies sperm. The lumen of the duct of the epididymis is the reservoir of spermatozoa.

The wall of the duct of the epididymis consists of three layers:

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

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

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

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

The adventitia is formed by loose connective tissue.

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

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

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

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

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

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

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

The wall of the ejaculatory duct consists of three layers:

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

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

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

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

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

The wall of the urethra consists of three layers:

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

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

The pseudostratified epithelium of the spongy urethra contains numerous goblet cells and occasional endocrine cells. The lamina propria, containing numerous blood vessels and small mucous glands, lies under the epithelium.

The submucosa is formed by loose connective tissue, containing venous plexus.

The muscularis of the urethra is formed by bundles of the smooth muscle; it is the most developed in the prostatic segment and becomes thinner towards the spongy segment.

Accessory sex glands

Seminal vesicles – are paired sex glands, the excretory ducts of which combine with the ampulla of the ductus deferens to form the ejaculatory duct.

The secretion of the seminal vesicles contains fructose – a monosaccharide used by the spermatozoa to maintain their metabolism. Besides this, the products of secretion of the seminal vesicles dilute sperm, thereby providing alkaline environment, which increases motility of the spermatozoa.

The wall of the seminal vesicles consists of three layers:

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

The mucosa is lined with simple columnar epithelium, forms numerous folds. The lamina propria of mucosa is rich in elastic fibers and contains acini of mucus-secreting alveolar glands.

The muscularis is formed by bundles of the smooth muscle, which are arranged in two layers: the inner circular and the outer longitudinal.

The adventitia of the seminal vesicles is formed by dense connective tissue, containing numerous elastic fibers.

Prostate gland is the large accessory sex gland, which surrounds the upper (prostatic) segment of urethra. The excretory ducts of the prostatic gland empty into the urethra.

The prostate gland provides both the endocrine and the exocrine functions. The endocrine part of the prostate gland secretes biologically active substances, which affect on the production of male sex hormones and the process of spermatogenesis, stimulate the growth of nerves and the smooth muscle contraction etc.

The prostate gland is under the influence of testosterone; in case of castration, it undergoes atrophy.

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

The prostate gland – is the lobular gland, covered by a thin connective tissue capsule. The parenchyma of the prostate gland is formed by separate glands

located in the mucosal layer of the organ. The excretory ducts of these glands empty into the prostatic segment of urethra. The glands, surrounding the urethra, are divided into three groups: the central, the peripheral and the transitional.

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

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

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

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

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

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

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

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

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

Penis – is the intromittent organ, which provides the ejaculation of sperm into the female genital tract and serves to urination. It consists of two dorsal masses of erectile tissue, the corpora cavernosa, and a ventral mass of erectile tissue, the corpus spongiosum. In the corpus spongiosum the spongy part of urethra is embedded. Erection of the penis involves the filling of the vascular spaces of the corpora cavernosa and corpus spongiosum. Penis is covered by the tunica albuginea. The tunica albuginea consists of the connective tissue, containing

numerous venous anastomoses. The balanus is covered with skin, containing sebaceous glands. The arteries of penis are called **helicine arteries**. These arteries dilate during erection to increase the blood flow to the penis.

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

Female reproductive system.

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

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

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

The ovarian structure in adult women

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

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

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

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

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

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

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

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

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

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

The fluid secreted by the granulosa cells is called **liquor folliculi** and contains the female sex hormone – estrogen. As the follicle grows, stromal cells surrounding it form a sheath of connective tissue cells, known as the theca folliculi. Futher the numerous blood vessels penetrate the **theca folliculi** and it differentiates into two layers – the theca interna and the theca externa. The theca interna contains

interstitial cells surrounded by branched capillaries. The theca externa is the outer layer of dense connective tissue.

The secondary follicles still contain the **primary** oocyte.

Despite enlargement of the follicle due to the cumulation of the liquor folliculi, the oocyte doesn't increase in size. The secondary follicles start their development in puberty.

Mature follicle – is the follicle prepared to ovulation. The corona radiata composed of cumulus cells that send penetrating microvilli throughout the zona pellucida to communicate via gap junctions with microvilli of the oocyte.Through these processes the nutrients come to the oocyte from the follicle cells, which produce lipoproteins of yolk. Graafian follicle, has a diameter of 10 mm or more. Because of its large size, it extends through the full thickness of the ovarian cortex and causes a bulge on the surface of the ovary.

A surge in the release of follicle-stimulating hormone is induced in the adenohypophysis approximately 24 hours before ovulation. Triggered by this surge, the first meiotic division of the primary oocyte resumes, resulting in the formation of the **secondary oocyte** and the first polar body.

The further growth of the Graafian follicle causes the rupture of its wall and release of the oocyte.

The process of transformation of primary follicles into the mature follicles is called the follicle growth. The follicle growth is controlled by the gonadotrope hormones of adenohypophysis – follicle-stimulating hormone and small amounts of luteinizing hormone. The initial stages of the follicle growth do not depend on gonadotropin stimulation.

Normally, only one follicle completes maturation in each cycle and ruptures to release its secondary oocyte.

The optimal conditions of the follicle growth are provided by the blood-follicular barier, which consists of endothelial cells of capillaries of the theca, endothelial basal lamina, interstitial elements of theca, basal lamina of the follicle epithelium, the follicle cells and the zona pellucida.

Ovulation – is the process by which a secondary oocyte, surrounded by the cells of corona radiata is released from the mature follicle. The oocyte firmly adheres to the fimbriae of the utrine tube and is actively transported by ciliated epithelium, preventing its passage into the peritoneal cavity. At this time the oocyte is arrested

in the metaphase of the first meiotic division. The ovulation is mediated by the luteinizing hormone of hypophysis.

Thecocytes (interstitial cells) and stratum granulosum produce estrogen hormones (estradiol, estron and estriol). Estrogen provides the development of sexual characteristics (enlargement of pelvis; development of mammary glands, uterus, epoophorons; woman pattern of hair distribution; beginning of menstruation) and controls the first phase of menstrual cycle (regeneration and proliferation phases).

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

The development of corpus luteum consists of four stages:

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

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

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

The blossom of corpus luteum. The luteal cells start to produce progesterone. Progesterone controls the phase of secretion of menstrual cycle, prepare the endometrium for the implantation of developing zygote. Progesterone is essential for supporting the pregnancy during first 3-4 month. If fertilization and

implantation do not occur, the corpus luteum remains active for 12-14 days. In this case it is called **the corpus luteum of menstruation**.

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

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

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

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

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

1. proliferation
2. growth
3. maturation

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

The period of growth starts from the 3rd month of intrauterine development. In this period the primary oocyte of primary follicle grows to the primary oocyte of mature follicle. The oocyte increases in size, becomes surrounded by the follicle cells. The oocyte stays in the meiotic resting phase called the **dictyotene**. Girls are born with the primary oocytes. The primary oocytes remain arrested in dictyotene for 12 to 50 years.

In puberty oocytes undergo the following, so-called "big growth". The oocyte increases in size, cumulates yolk. The zona pellucida and corona radiata are formed and surround the oocyte. The zona pellucida consists of glycoprotein complexes. Microvilli of the follicular cells pass through the zona pellucida and adhere to the oocyte surface. Above the zona pellucida the cells of corona radiata and cumulus oophoron are located.

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

The meiosis II occurs **only in case of fertilization** and again results in the formation of two cells: the first one – is the mature **haploid** oocyte; the second one – is the second polar body.

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

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

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

The muscularis consists of two layers of the smooth muscle: inner circular and outer longitudinal.

The serosa consists of loose connective tissue covered by mesothelium.

Each uterine tube could be divided into four anatomical parts:

- **The infundibulum** is the funnel-shaped segment of the tube adjacent to the ovary. The proximal end communicates with the ampulla. Fringed extensions, or fimbriae, extend from the mouth of the infundibulum toward the ovary. In the moment of ovulation the fimbriae increase in volume and sweep the oocyte. The ciliated cells lining and peristaltic contraction of the uterine tube provide the transport of the oocyte along it.

- **The ampulla** is the longest segment of the tube, constituting about two thirds of the total length, and is the site of fertilization.

- **The isthmus** is the narrow, medial segment of the uterine tube adjacent to the uterus.

- **The uterine or intramural part**, measuring about 1 cm in length, lies within the uterine wall and opens into the cavity of the uterus.

The functions of the uterine tubes are:

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

Uterus – is the muscular organ which serves for the development of fetus.

The wall of the uterus consists of three layers:

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

The **endometrium** is the most dynamic layer of the uterus, since it undergoes the hormone-induced changes during the menstrual cycle. The endometrium consists of two layers: **basal layer** (stratum basale) and **functional layer** (stratum functionale). The functional layer proliferates and degenerates during the menstrual cycle. The endometrium is covered by simple columnar epithelium with underlying lamina propria. The lamina propria contains the **uterine glands**. The mouths of the uterine glands are surrounded by ciliated cells.

The uterine glands extend through the whole thickness of the endometrium and even reach the surficial layers of myometrium. They are simple tubular glands.

The lamina propria is formed by loose connective tissue. Some connective tissue cells of the lamina propria diffentiate into the **decidual cells.** The decidual cells are the large rounded cells, containing inclusions of glycogen and lipoproteins in their cytoplasm. The number of decidual cells increases during the placenta formation in pregnancy.

The myomterium is formed by the smooth muscle cells, containing processes. The myometrium consists of three layers:

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

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

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

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

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

The vaginal wall consists of the three layers:

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

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

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

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

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

The adventitia is formed by loose connective tissue.

The external genitalia (vulva) unclude:

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

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

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

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

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

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

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

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

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

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

portions of the spiral arteries. This layer is the basal layer. The epithelial cells of basal portions of the uterine glands migrate to cover the denuded endometrial surface.

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

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

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

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

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

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

1. the outer compact zone, containing decidual cells;

2. the inner spongy zone, containing enlarged glands.

All the changes, occurring at the secretory phase prepare the endometrium for the implantation of the fertilized oocyte. This phase is regulated by progesterone. Progesterone is produced by the corpus luteum, which develops from the rests of an ovulated follicle under the influence of pituitary luteinizing hormone. Progesterone maintains the edematous endometrium and prevents it from desquamation. If pregnancy doesn’t occur, the corpus luteum dies. The decline of

the progesterone level causes the start of the menstrual period. With the absence of progesterone, the follicle growth and production of estrogen starts. Estrogen stimulates the regeneration and proliferation of the functional layer and the cycle repeats.

ODESA NATIONAL MEDICAL UNIVERSITY

DEPARTMENT OF HISTOLOGY, CYTOLOGY AND EMBRYOLOGY

METHODICAL RECOMMENDATION OF LECTURES

for dentistry faculty

THEME: «Human embryogenesis.»

Approved on the methodical conference of department

«____»_____ 20___., protocol №_____

Head of Department, doc._____ Tiron O.I.

Approved on the methodical conference of department

«____»_____ 20___., protocol №_____

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Head of Department, doc._____ Tiron O.I.

Theme: «Human embryogenesis.»

1. **Relevance of the topic.**

Recently, embryology has come into ever closer contact with two biological disciplines: cytology and genetics. The study of the basics of embryonic

development is important for understanding the sources and mechanisms of formation of tissues (histogenesis) and organs (organogenesis) of a person.

The most important section of embryology for medical practice is human embryology, which covers both the study of pathological abnormalities during development and the occurrence of congenital anomalies and defects (teratology).

The study of human embryonic development makes it possible to establish the characteristics of the development of the human embryo. Knowledge of the processes of fertilization, cleavage, implantation, gastrulation, as well as the developmental features of the placenta, extraembryonic membranes and organs of the embryo is necessary for the future doctor for the rational prevention of fetal anomalies and malformations.

It makes it possible to think over and evaluate the entire cycle of biological phenomena accompanying pregnancy, to prevent the consequences of the adverse effects of environmental factors and everyday life. The rational management of pregnant women, the management of childbirth, the implementation of many therapeutic and preventive measures in obstetrics, pediatrics and gynecology is impossible without a deep knowledge of embryology.

2. Objectives of the lecture:

a) learning:

- analysis of the main stages of human embryogenesis;
- modern ideas about the morpho-functional organization of provisional organs;
- interpretation of the relationship between the structural and functional parts of the fetal organs;
- assessment of the functional state of the organs of the female body during pregnancy, interpretation of the mechanisms of adaptation to the action of various factors.
- to acquaint students with the structure of the organs of the female reproductive system.

b) educational:

- to bring to the students the importance of studying the structural and functional features of human embryogenesis for the interpretation of pathological processes during pregnancy, are studied at the subsequent stages of training;
- to interpret the morphological and functional features of organs and disorders of the stages of human development, to determine their significance for practical medicine;
- to form students' professional significance of the topic. Discuss the issues of deontology.

3. Plan and organizational structure of the lecture.

№№	The main stages of the lecture and their content	Objectives in levels of abstraction	Lecture type. Lecture equipment	Time management
1	2	3	4	5
I. 1. 2. II	*Preparatory stage.* Determination of the learning goal. Providing positive motivation. *The main stage* Presentation of the lecture material according to the plan: 1. Morpho-functional characteristics of the stages of human	 I. Descriptive. II. Analytical - synthetic, high quality.	Tables. Slides. In accordance with the	5% 85-95%

	embryogenesis. 2. Provisional human organs. Development. Structure. Functions. 3.Histophysiology of the hemotoplacental barrier. 4. System mother placenta-fetus. 5. Critical periods of human embryogenesis.		publication "Guidelines for the planning, preparation and analysis of lectures."	
III.	*The final stage.* Summary of the lecture. General conclusions. Lecturer's answer to possible questions. Self-study assignments.		List of literature, question, task.	5%

4. Content of the lecture material:

- structural and logical scheme of the content of the topic;
- the text of the lecture. (Provided)

5. Materials for activating students during the lecture:

1) One fetus usually develops in a woman's uterus, however, in about 1% of pregnancies, multiple twin fetuses develop and are born. Identical twins develop from a single fertilized cell. It occurs rather at the blastocyst stage as a result of the division of the embryoblast into two symmetrical parts.Some embryologists believe that symmetrical separation of the embryo is possible during gastrulation - at the stage of development of the embryonic shield. Identical twins share a common placenta, a common or separate amniotic membrane, always of the same

sex. Fraternal twins occur when two or more eggs are fertilized at the same time. Each has its own placenta, amnion and develops independently. They can be of the same gender or different.

2) In medical practice, the procedure of artificial (in vitro) fertilization is now widely used to treat male and female infertility. The first child conceived outside the mother's body - Louise Brown - was born in 1976. In Great Britain. Her godparents were the English embryologists Edwards and Stentow.

3) In connection with the development of modern reproductive technologies, a new medical and legal concept has appeared - surrogacy. Ovocytes are obtained from a woman; using the sperm of the husband or donor, in vitro fertilization is performed; an embryo at the stage of 18-32 blastomeres is implanted into the uterus of another woman who will carry the fetus until the moment of birth. When carrying out in vitro fertilization, it is possible to choose the sex of the unborn child: one blastomere is removed from the obtained several blastocysts, analyzing the chromosome sets of these cells, the presence of the X or Y-sex chromosome is established, blastocysts with the desired chromosome set are inserted into the uterus.

4) Embryological knowledge is necessary for future doctors for the rational prevention of fetal anomalies and malformations, as well as for the prevention of adverse effects of environmental factors and everyday life during pregnancy.

Questions:

1. Fertilization. Distant and contact interaction of germ cells. Zygote formation.
2. Crushing. Chronology of the process. The structure and localization of the embryo during this period.
3. Blastula formation. Embryoblast and trophoblast, their significance
4. Implantation. Phases.
5. Gastrulation. Formation of germ layers and notochord.
6. Differentiation of ectoderm. Neurulation.

7. Differentiation of the mesoderm, its derivatives.

8. Differentiation of endoderm, its derivatives.

9. Formation and derivatives of mesenchyme.

10. Critical periods of development.

11. Provisional organs: development, structure, functions.

12. System mother placenta-fetus.

6. General material and methodological support of the lecture:

- classrooms;

- equipment;

- equipment;

- illustrative materials.

List of recommended literature .

The main one:

1.Lutsyk O.D., Tchaikovsky Y.B. Histology, cytology, embryology Vinnytsia, New Book, 2018.
2.Barinov E.F., Tchaikovsky Y.B. General histology and embryology of internal organs: textbook.Kyiv: Medicine; 2013
3.Wojciech Pawlina. Histology: textbook and atlas. WSV: Medicine, 2021.

Additional:

1.Histology and embryology of internal organs: textbook / E.F. Barinov, Y.B. Tchaikovsky, O.M. Sulaeva et al.
2.Cytology of human organs and tissues edited by L.S.Bolgova. Kyiv: Book-plus, 2018, p.288

Theme: «Human embryogenesis.» *Addition*

Embryology is the study of developmental process of embryo from the moment of fertilization until the moment of birth.

Medical embryology includes studies of molecular, cellular, and structural factors contributing to the formation of an organism; metabolic and functional characteristics of placental barrier (system mother-placenta-fetus); and causes of birth defects formation.

The principal aims of embryology

1. Investigation of various endogenous and exogenous factors and the role of microenvironment in development and functioning of gametes.

2. Investigation of mechanisms that control reproductive function and provide maintenance of homeostasis in human embryo.

3. Investigation of critical periods in human embryogenesis.

4. Cultivation of oocytes, embryos and their subsequent implantation in the endometrium of uterus.

5. Investigation of sources and mechanisms of tissues development.

Studying of embryology is impossible without having basic knowledge of comparative embryology, hence evolutionary the embryonic development of all mammals could be characterized by the similar principal stages, sequence and consistent patterns. For correct comprehension of the process of human individual development it is necessary to carry out analysis and compare the principal stages of human development with those of other animals.

It was estimated that the principal stages and consistent patterns of embryogenesis were established during the process of evolutional development of the mammals. At the same time some stages of human embryonic development are analogous to those of lower organized chordate animals; hence the process of human embryonic development is a result of long-term evolution and it partially reflects the features of development of other animals.

The idea of correlation between individual and historical (evolutional) development was proposed at the beginning of the XIX century by the eminent scientists K.Berr and F. Muller, who came to conclusion that a large group of animals at the early stages of development reveal much more common features than individual differences.

The quintessence of this idea is the Haeckel-Muller law (or Recapitulation theory), which proclaims that in developing from embryo to adult, animal go through stages resembling successive stages of evolution of their remote ancestors ("**ontogenesis recapitulates phylogenesis"**).

ONTOGENESIS

***Ontogenesis*-** is a process of individual development of an organism from the moment of fertilization until death.

Periods of ontogenesis

I Prenatal – period of intrauterine development (duration – 280 days);

a) initial period (early embryo) – first week

b) embryonic period (embryo) – 2^{nd}-8^{th} week, formation of primary cavity, organogenesis and appearance of heart beating on 21^{st} day

c) fetal (until birth) – placentation, differentiation of tissues.

II Postnatal – period of development after the birth;

a) early postembryonic
b) subsequent development, maturation, ageing and death.

Initial period include the following stages:

1) zygote – beginning of the DNA synthesis;
2) cleavage – beginning of synthesis of the all types of RNA;
3) morula – the cells are totipotential;
4) blastocyst - loss of totipotency; the cells are determined to formation of embryonic and extraembryonic structures;
5) gastrula – appearance of the germ layers and stem cells.

Ontogenesis is always preceded by progenesis hence the formation of new organism is impossible without formation and maturation of male and female gametes.

PROGENESIS

Progenesis – the process of formation, development and maturation of male and female gametes.

Gametes, unlike somatic cells, contain haploid number of chromosomes. All chromosomes of gametes are autosomes except the one which is referred to as sex gonosome.

Male gametes could contain X or Y-sex chromosome.

Female gametes could contain only X-chromosome.

The mature gametes are incapable to proliferation and characterized by low level of metabolism.

Male reproductive cells

Male gametes – spermatozoa are about 70 μm in size and capable of active movement (30-50mm per second in human). In human it is formed several thousand million spermatozoa.

♦*Spermatogenesis* – the process of formation and maturation of spermatozoa.

The structure of spermatozoa

The spermatozoon is composed of two principal parts: 1) head; 2) tail.

The head of spermatozoon contains dense nucleus with haploid number of chromosomes (22 autosomes and 1 sex chromosome). Depending on what kind of sex chromosome they possess, the spermatozoa are divided into two types:

1) androspem – carry Y-chromosome,
2) gynosperm – carry X-chromosome.

♦ The nucleus is rich in nucleoproteins and nucleohistones. The anterior wall of nucleus is covered by a vesicle called acrosome. The acrosome is a derivative of Golgi complex.

The acrosome contains a complex of enzymes, among which the most important are hyaloronidase and proteases (trypsin), which are crucial for dissolving ovum's coats.

Externally the head is surrounded by a plasma membrane.

The tail (flagellum) is composed of:

a) connecting piece, which contains **two centrioles** (proximal and distal). The axial filament (axoneme) extends from the distal centriole.
b) midpiece, which contain two central microtubules and nine pairs of peripheral microtubules spirally surrounded by several mitochondria (mitochondrial sheath);
c) tail piece contains axial filament, which resembles cilia;
d) end piece, which contains solitary contractive filaments.

The tail of spermatozoon, like its head, is surrounded by a plasma membrane.

The functions of spermatozoa

1. Fertilization of the ovum. By means of its tail the spermatozoa is capable to move in distinct direction determined by the specific substances which are produced by an ovum – *gynogamones.*

2. React on the chemical stimuli – *chemotaxis.*

3. Can move in opposite direction to the flow of fluid – *rheotaxis*.

4. In optimal conditions can remain their capacity to fertilization during 36-88 hours.

5. The favorable condition for spermatozoa is slightly alkaline environment.

Female reproductive cells

Female gametes – ova (oocytes) are developed in ovaries. In human there are produced several hundreds oocytes during the whole life.

The ovum is spherical cell, whose size can reach up to several cm. The characteristic features of ovum are big amount of cytoplasm and presence of yolk. The ovum, unlike spermatozoon, is not capable of movement.

Classification of ova

Depending on the amount of yolk the ova are divided into the following types:

1. Alecithal ova have no yolk in cytoplasm;

2. Oligolecithal ova have small amount of yolk in cytoplasm

a) primary oligolecithal – in primitive chordate, which are characterized by quick development via the stage of larva;

b) **secondary oligolecithal** – in mammals (placental) and **human**.

3. Mesolecithal ova contain moderate amount of yolk (amphibians).

4. Polylecithal ova contain enormous amount of yolk. (birds, reptiles, fishes).

Depending on the distribution of yolk the ova are classified into the following types:

1. Isolecithal – the yolk is uniformly distributed through the cytoplasm. Such distribution is usually characteristic for oligolecithal ova.

2. Centrolecithal - yolk is concentrated in the center of ovum's cytoplasm.

3. Teleolecithal - are polylecithal ova, where the yolk is concentrated in one hemisphere (vegetal pole) and organelles remain in another hemisphere (animal pole).

The structure of ovum

The ovum of placental mammals is relatively small (50-150 μm). It is surrounded by zona pellucida and a layer of follicular cells, which provide its nutrition. The ovum is composed of coats, cytoplasm and nucleus.

♦ Coats – all ova are surrounded by the cytolemma (oolemma or primary coat), most of them also possess the secondary coat – a carbohydrate-protein coat, and some types of ova are covered by the tertiary coat – eggshell.

♦ Cytoplasm (ooplasm) contains nutritive material – yolk. Besides this the ooplasm stores a range of proteins: histones, ribosomal structural proteins, tubulin etc.

♦ Among other organelles, the rough ER exhibits strong development. The number of mitochondria is moderate. At the periphery of cytoplasm the Golgi complex and small cortical granules containing glycosaminoglycans are situated.

♦ Yolk – is a type of inclusion which appears as granules or larger globes and plates. The yolk is composed of phospholipids, proteins and carbohydrates. The structural unit of yolk is a complex of lipovitelin (lipoprotein) and phosvitin (phosphoprotein).

The ovum is characterized by cell polarity. The more yolk it contains the more conspicuous is its cell polarity. The pole of cytoplasm which contains yolk is called vegetal, and the pole which contains organelles and nucleus – animal.

♦ Nucleus possesses haploid number of chromosomes. Intensive synthetic processes (RNA, DNA synthesis) take place at the period of growth.

EMBRYOGENESIS

Embryogenesis – a period of intrauterine development of humans and animals which begins at the moment of fertilization, includes formation and development of all tissues, organs and system of fetus, and ends with a birth of child.

The embryonic development is phasic and accompanied by gradual quantitative and qualitative changes. The process of embryogenesis includes the following phases:

1) fertilization;
2) cleavage and formation of blastula;
3) gastrulation and differentiation of germ layers;
4) histogenesis (differentiation of tissues);
5) organogenesis (differentiation of organs);
6) formation of systems of organs.

***Fertilization* –** is the process, by which male and female gamete fuse, which results in restoration of the diploid number of chromosomes and formation of unicellular embryo - **zygote**.

Fertilization is preceded by *insemination* – introduction of sperm into female reproductive tract in case of internal fertilization, or into the environment where the ovum is situated in case of external fertilization.

In human the fertilization normally takes occurs in the ampullary region of the uterine tube.

Spermatozoa are not able to fertilize the oocytes immediately upon arrival in the female genital tract, but must undergo capacitation and acrosome reaction to acquire this capability.

• Capacitation is a period of activation in the female reproductive that in human lasts approximately 7 hours. Much of this activation occurs in the uterine tube and involves epithelial interactions between the sperm and the mucosal surface of the tube. A significant role in this process is played by progesterone (the hormone of corpus luteum of ovary). Only capacitated sperm can undergo acrosome reaction.

• Acrosome reaction occurs after binding to zona pellucida of the oocyte and is induced by zona proteins. This reaction culminates in the release of enzymes needed to penetrate the zona pellucida, including acrosin- and trypsin-like substances.

• The phases of fertilization include:

1. Distant interaction is performed by several non-specific factors which facilitate the "meeting" of reproductive cells. Special chemical substances (gamones) are discharged by both spermatozoa and ovum. The female gamones are called gynogamones, the male gamones – androgamones. Gynogamones type I – are low-molecular non-protein substances which are believed to attract spermatozoa. Gynogamones type II – are species-specific proteins that cause gluing of spermatozoa in case of their reaction with complementary androgamone type II. Androgamones type I – being antagonists of gynogamones type I they depress sperm motility.

2. Contact interaction and penetration into the ovum is performed by mean of the acrosome. The enzymes required for penetration of corona radiata (hyaloronidase, trypsin) are released from the acrosome and destroy cell contacts between follicular cells (acrosome reaction). This phenomenon called denudation

of the oocyte results in total dissolution of zona pellucida. The plasma membranes of ovum and spermatozoon fuse. The enzymes released from the acrosome dissolve the corona radiata and break down glycosaminoglycans of the zona pellucida. The separated follicular cells form conglomerate which follows the ovum while it moves via the uterine tube. The movement of fertilized ovum is provided by the peristaltic contraction and synchronic movements of cilia of the mucosa of the uterine tube.

3. Penetration of the ovum. Both the head and the tail of the spermatozoon enter the cytoplasm of oocyte. As a result of the release of cortical oocyte granules, which contain lysosomal enzymes, the oocyte membrane becomes impenetrable for other spermatozoa and the zona pellucida alters its structure and composition to prevent sperm penetration (cortical reaction). This reaction prevents polyspermy (penetration of more than one spermatozoon into the oocyte). After the penetration the head of spermatozoon makes a 180° degree turn; its nucleus becomes swollen and forms *male pronucleus*. The ovum's nucleus forms *female pronucleus*. Male and female pronuclei eventually come into close contact and lose their nuclear envelopes. The fusion of male and female pronuclei initiates the spiralization of chromosomes and formation of metaphase plate. A nucleus formed by two preexisting pronuclei is called **synkaryon**. The spermatozoon delivers centriole, which is essential for mitotic division of zygote, to the oocyte. In this way the zygote containing both maternal and paternal genes is formed.

At the same time the redistribution of cytoplasmic material of zygote and subsequent division of its cytoplasm into two zones (zone with high concentration of yolk granules and zone with high concentration of pigment granules) occurs. This phenomenon is called **ooplasmic segregation**. During further development each zone of the cytoplasm gives rise to distinct part of the organism. Such zones are called **presumptive zones**.

Cleavage **–** is a series of mitotic divisions of zygote, which results in its transformation into multicellular organism called blastocyst. As the protein synthesis is inhibited, the cells, known as blastomeres, become smaller with each cleavage division. Due to the absence of the G_1- period of interphase, the size of an embryo does not exceed that of the zygote. The cleavage lasts from 1^{st} to 6^{th} day of pregnancy.

The type of cleavage differs among different animals. It is determined by amount and distribution of yolk within an ovum.

Types of cleavage

Depending on the type of ovum, the following types of cleavage are distinguished:

1. Total equal cleavage is characteristic for primary oligolecithal, isolecithal ova (amphioxus).

2. Total unequal cleavage is characteristic for mesolecithal ova; hence the mitotic divisions of vegetal pole occur not so fast as that of the animal pole.

3. Partial or meroblastic cleavage is characteristic for teleolecithal ova. In such case only the apical part of ovum undergoes mitotic divisions (birds).

4. **Total asynchronous unequal cleavage** or holoblastic is characteristic for secondary oligolecithal isolecithal ova (mammals, **human**).

Approximately three days after fertilization the divisions of cells of an embryo result in formation of 16-cells morula. **Morula –** is a compacted aggregation of blastomeres which resembles mulberry.

Inner cells of the morula constitute the inner cell mass, and surrounding cells compose the outer cell mass. The inner cell mass gives rise to tissue of embryo proper, and the outer cell mass forms the trophoblast, which later contributes to the placenta.

About the time the morula enters the uterine cavity, fluid begins to penetrate through the zona pellucida into the intercellular spaces of the inner cell mass, which results in formation of cavity – blastocele. At this time the embryo is **blastocyst**. Cells of the inner cell mass, now called the **embryoblast**, are at one pole, and those of the outer cell mass, or **trophoblast**, flatten and form the epithelial wall of the blastocyst **(blastoderm)**. The zona pellucida has disappeared, allowing implantation to begin.

Types of blastula

1. Coeloblastula forms as a result of total equal cleavage. The blastoderm is formed of a single layer of cells. The blastocele is centric.(Amphioxus)
2. Amphiblastula is formed as a result of total unequal cleavage. The blastoderm is multi-layered. The blastocele is eccentric. (Amphibians)
3. Discoblastula is formed as a result of partial meroblastic cleavage. The blastocele is small and situated below the blastoderm. (Birds, reptiles).

***Gastrulation* –** a period of embryogenesis that includes differentiation of the germ layers: ectoderm (outer layer), endoderm (inner layer), and mesoderm (middle layer).

Types of gastrulation

The process of gastrulation could be carried out in four main ways:

1. Migration – movement of part of blastomeres from the wall to the center of an embryo and formation of endoderm.
2. Invagination – inward of the wall of blastula into its center.
3. Epiboly – spread of an outside cell layer (where the mitosis is faster) to envelope a deeper layer (where the mitosis is relatively slow). It happens when the blastomeres of vegetal pole contain high amount of yolk (in amphibians).
4. Delamination – is a process accompanied by tangential splitting of the wall of blastula, which results in formation of two germ layers – primary ectoderm (outer) and primary endoderm (inner). Such type of gastrulation is characteristic for birds and mammals.

The types of gastrulation depend on preceded phases of development and amount of yolk in ovum. The vertebrates are characterized by combination of two or three types of gastrulation.

In the human the gastrulation lasts from 7^{th} to 17^{th} day of embryogenesis and includes 2 phases:

I phase ($7\text{-}14^{th}$ day) involves formation of inner (endoderm) and outer (ectoderm) germ layers. As a result of *delamination* the layer of cells that faces the blastocyst cavity splits out from the primitive node, thereby forming the primary endoderm (hypoblast). At the same time the cells of the primitive node which lie under the hypoblast undergo *cavitation* (due to the cumulation of liquid a cavity is formed in the center of the nodule; the cells which surround this cavity obtain epithelium-like shape – the amniotic vesicle is formed).

The opposite edges of the primary endoderm turn down, fuse together and form the yolk vesicle. The adjacent parts of both vesicles (amniotic and yolk) form the embryonic disc, which gives rise to the body of an embryo.

Simultaneously with the formation of amniotic and yolk vesicles, beginning from the 8^{th} day of development, occurs the differentiation of *extraembryonic mesoderm*, which gives rise to chorion and amniotic stalk (the basis of the future umbilical cord).

II phase lasts from 15th to 17th day of embryonic development and involves formation of the embryonic mesoderm. This process is realized migration of the cells of primary ectoderm in the space between two germ layers.

The space between germ layers is filled with the embryonic connective tissue – mesenchyme.

The mesenchymal cells migrate from mesoderm, endoderm and ectoderm. That is why two types of mesenchyme are distinguished:

a) endomesenchyme – originates from the endo- and mesoderm;
b) ectomesenchyme – originates from the ectoderm.

These two types of mesenchyme are morphologically indistinguishable, but they give rise to different structures:

- endomesenchyme – to the tissues of internal environment;

- ectomesenchyme – to auditory bones, the connective tssues of head.

The cell migration from the primitive node results in formation of axial chord of an embryo – chorda. At the end of the second week the hematopoietic cords and germs of primary blood vessels appear in the yolk sac.

The finger-like process – allantois, grows inwards the amniotic stalk of the intestinal endoderm. Blood vessels of the yolk sac grow inwards the wall of allantois and chorionic villi, which are supplied with maternal blood. Allantochorion, which is formed as a result of these processes, provides nutrition and gas exchange of fetus at this stage of development.

HISTO- and ORGANOGENESIS

Histo-organogenesis – is the process that involves differentiation and formation of tissue, organs and systems of organs of the fetus through several sequential stages: induction, determination, cell reproduction, migration, growth of cells, intercellular interactions, and cell death.

Induction – the process by which cells and tissues in embryo direct the development of adjacent cells and tissues. An example of induction is the development of the eye lens from epidermis under influence of the eye cup, which grows toward the skin from the brain. As the eye cup comes into contact with any neighbouring epidermis, it transforms that particular region into a lens. The exact nature of the stimulus for lens induction is not known, although ribonucleic acid (RNA) has been implicated as a messenger.

***Determination* –** is progressive restriction in developmental potential of the embryonic cells via blocking of particular components of genome.

Determination is a foundation of process of differentiation. Differentiation – is a process through which cells change to a more specialized type.

***Cell reproduction* –** is the process by which cells divide to form new cells.

The process of renewal and restoration of biological object is called regeneration. There are distinguished three types of regeneration:

1) physiological – continuously occurs in healthy organism (renewal of blood, epithelial cell etc.);
2) reparative – occurs after injuries and trauma (healing of the wound);
3) pathological – normally does not occur; such type of regeneration is characteristic for cells of malignant tumors.

***Migration* –** is the massive translation of cells from one location to another, which results in formation of tissues and organs.

Growth of cells – is a series of processes, which include development and organization of cells from the moment of their division until next division.

Intercellular interactions perform the leading role in differentiation of embryonic germ layers. For example, it was estimated that for development and existence of epithelium it is essential to be supported by connective tissue.

Cell death – is an unaltered process of termination of all its functions and interaction with external environment.

PROVISIONAL ORGANS

***Provisional organs* –** are temporary organs, which are developed during embryogenesis, they are referred to as extraembryonic organs, which growth and development of an embryo.

The provisional organs include: 1) yolk sac; 2) amniotic sac; 3) serous coat; 4) allantois; 5) chorion; 6) placenta.

Yolk sac appears as a vesicle connected with the intestinal tube. Internally the wall of the yolk sac is lined with epithelium, externally – it is formed by connective tissue.

The formation of yolk sac is initiated at the stage of early gastrula, when there are distinguished the embryonic (intestinal) endoderm and the peripherally located extraembryonic yolk endoderm. The yolk sac maintains its connection with the intestinal tube via connecting stalk.

♦Functions: a) trophic; b) hematopoietic (7-8 weeks).

Amniotic sac – is a thin but tough transparent pair of membranes that hold a developing embryo. It takes part in secretion of amniotic fluid. The amniotic sac consists of two parts*: amniotic part* facing an embryo (fetus) and external part – *serosa*.

The amniotic sac originates from ectoderm and parietal layer of mesoderm, which firstly from amniotic folds growing towards the dorsal surface of an embryo. These folds surround an embryo and fuse, so the ectoderm and adjacent parietal mesoderm fuse with the analogous layers of the opposite side. Two layers of the folds give rise to two coats – *amniotic* (fluid-secreting) and *serous* (external).

The fluid secreted by the ectoderm of the amniotic coat contains proteins and carbohydrates; it acts as shock absorber and protects fetus from mechanical trauma.

♦ Functions: shock absorption; allows fetus to move freely.

Serous coat develops simultaneously with the amniotic coat. Hence it helps to supply an embryo with oxygen, it is considered to be a provisional respiratory organ. **It is not present in the human**.

Allantois begins its development in caudal region of an embryo proper as a projection of ventral wall of dorsal intestine, which is formed by endoderm and visceral mesoderm. The proximal part of allantois is situated along the yolk stalk; while the distal one invades the gap between the amniotic and serous coats. Allantois carries out the functions of excretion and gas exchange: the oxygen is delivered to an embryo via blood vessels which originate from the mesoderm of allantois; at the same time the waste products are excreted into allantois.

Recently it was estimated that at the early stages of the ontogenesis allantois performs the analogous function to the Bursa of Fabricius, i.e. acts as main organ of B-lymphocytopoiesis. Allantois undergoes reduction after second month of the embryogenesis.

Chorion originates from the trophoblast and extraembryonic mesoderm. The trophoblast is primarily represented by a coat with primary villi, via which the connection with maternal organism is established. At the 2-3rd week of development the extraembryonic mesoderm appears, grow towards the trophoblast; and together they form the *secondary (epitheliomesenchymal) villi*. After this the trophoblast transforms into chorion.

Invading the mucosa of the uterus chorion takes part in formation in formation of placenta.

Placenta – is an organ that connects the developing fetus to the maternal organism.

♦ The development of placenta begins at the 3rd week, when the secondary epitheliomesenchymal villi are penetrated by blood vessels and transform into the *tertiary villi*. At the 6-8th weeks of development the differentiation of macrophages, fibroblasts and collagen fibers around the blood vessels takes place. The formation of collagen fibers in the chorionic villi is accompanied by the intensification of proteolytic activity of the trophoblastic epithelium (cytotrophoblast) and its derivate (syncytiotrophoblast).

The development of placenta initiates destruction of the uterine mucosa; and the histotrophic type of nutrition is substituted by the hematotrophic one. It means that now the chorionic villi are supplied with maternal blood discharged into lacunae from the disrupted vessels of the endometrium.

Placenta is composed of two parts: 1) maternal; 2) fetal.

Maternal part of placenta is formed by the area of uterine mucosa, which is invaded by the chorionic villi (**decidua basalis or placentalis**). The remainder of the decidua, which is free from the chorionic villi, is called **decidua parietalis.** Also, there is **decidua capsularis**, which grows over the embryo on the luminal side, enclosing it into the endometrium and surrounding the embryo together with the decidua basalis.

Fetal part of placenta is the chorionic portion of placenta, containing the fetal blood vessels. There are distinguished two types of chorion:

a) chorion frondosum
b) smooth chorion (leave)

The villi of the chorion frondosum grow inwards the endometrium of the decidua basalis.

The smooth chorion is a place of contact of the trophoblast with the decidua capsularis.

The most intensive development of placenta occurs from 3rd to 6th week of the embryogenesis.

The placentas of mammals are divided into four types according to their structure:

1) epitheliochorial; 2) desmochorial; 3) endotheliochrial; 4) hemochorial.
The **human placenta** is referred to as the **discoid desmochorial** one.

The structural and functional unit of placenta is called **cotyledon.** Each cotyledon represents the branches of the one *anchoring villium*.

The human placenta consists of about 200 cotyledons that are separated from each other by connective tissue septa, through which the arteries carrying oxygenated blood pass to the lacunae of the placenta. The blood outflow from the placenta occurs via the lacunar veins, which open into the lacunae. The wall of lacuna is composed of the endometrial connective tissue, covered by the amorphous substance – fibrinoid of Rohr.

The part of decidual membrane located between the chorion frondosum and the smooth chorion intimately grows together with the last one and forms the **chorionic plate**, which prevents the entrance of blood to the uterine lumen.

The placental barrier is composed of structures that separate the maternal and the fetal blood. It is composed of

1) epithelial cell and basal membrane of blood capillaries of the chorionic villi;
2) a layer of connective surrounding the blood capillaries; it is rich in macrophages and fibroblasts;
3) basal membrane of the chorionic villi;
4) syncytiotrophoblast;
5) fibrinoid of Langhans

Functions of placenta: 1. trophic; 2. excretory; 3. depositing; 4. endocrine; 5. respiratory; 6. defensive.

Umbilical cord – is a cord that contains blood vessels, which provide blood circulation between the fetus and placenta (two umbilical arteries and one umbilical vein) surrounded by a **mucous connective tissue** (Warton's jelly). It also contains the rests of yolk stalk and allantois. The mucous connective tissue contains great amount of the hyaluronic acid, which provides the turgor of the umbilical cord. There were revealed the tissue basophiles and the cells of Kaschenko-Gobfauer (protect the fetus from intrauterine infections) among the cells of the umbilical cord.

THE CRITICAL PERIODS OF DEVELOPMENT

The critical periods of embryogenesis – are the periods when the developing reproductive cells (progenesis) or the embryo (embryogenesis) are the most susceptible to the unfavorable factors.

Such periods are:

1) in progenesis – ovogenesis and spermatogenesis;
2) in embryogenesis – fertilization, implantation (6-8 day), placentation, gastrulation (3,8 week); period of intensive development of the brain (15-20 week); period of formation of the main systems of organs (20-24 week); parturition.
3) in postnatal ontogenesis – period of a newborn (until 1 year); period of sexual maturation (11-16 years).

ODESA NATIONAL MEDICAL UNIVERSITY

DEPARTMENT OF HISTOLOGY, CYTOLOGY AND EMBRYOLOGY

METHODICAL RECOMMENDATION OF LECTURES

for dentistry faculty

THEME: «Organs of oral cavity.»

Approved on the methodical conference of department

«____»_____ 20___., protocol №_____

Head of Department, doc._____ Tiron O.I.

Approved on the methodical conference of department

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Head of Department, doc._____ Tiron O.I.

Theme: «Organs of the oral cavity.»-2h.

1. Relevance of the topic.

In the digestive system, due to the peculiarities of its development, structure and functions are divided into three sections: front, middle and back. The oral cavity is the initial section of the digestive tract. The presence of its own microflora and the constant supply of microorganisms from the external environment, the action of temperature, acid-base factors, trauma to the mucous membrane with solid food can lead to the development of an inflammatory process, erosions and ulcers, tumors, and the like. To diagnose various diseases, a study of smears-prints of the mucous membrane is carried out.

The study of the structure of the organs of the oral cavity is the basis for understanding the patterns of morphological changes in the case of the development of pathological processes. Mechanical processing of food in the anterior part of the digestive tube depends on the condition of the dental-jaw apparatus. The teeth are involved in articulation, they are an important anatomical element of the face. Experienced dentists, based on the condition of the teeth, can conclude about the functioning of the digestive tract and systems for regulating homeostasis, the content of Ca 2+, the change in the acid-base state both in the oral cavity and in the body.

The oral cavity is the initial section of the digestive tract. The presence of its own microflora and the constant supply of microorganisms from the external environment, the effect of temperature, acid-base factors can lead to the development of an inflammatory process, caries, periodontal disease, and the like. To diagnose various diseases, a dental examination is carried out. Knowledge of the patterns of development and the general plan of the structure of the teeth, microscopic and ultramicroscopy of the structure of tooth tissues, the possibilities and mechanisms of their regeneration is important for understanding the formation

of defects in the development of the dental-jaw apparatus, the interpretation of cause-and-effect relationships in various pathological processes in the oral cavity.

2. Objectives of the lecture:

a) learning:

- analysis of the structural organization of the oral cavity organs;
- modern ideas about the morphofunctional organization of the oral cavity organs;
- interpretation of the relationship between the structural and functional parts of the organs of the oral cavity;
- assessment of the functional state of the oral cavity organs, interpretation of age-related changes, mechanisms of adaptation to the action of various factors.
- to acquaint students with the structure of the mucous membrane of different types in relation to localization and functions;
- analysis of the structural organization of the teeth;
- modern ideas about the morphofunctional organization of tooth tissues;
- interpretation of the relationship between the structural and functional parts of the teeth;
- assessment of the functional state of tooth tissues, interpretation of age-related changes, mechanisms of adaptation to the action of various factors.
- to acquaint students with the structure of tooth tissues in relation to localization and functions;

b) educational:

- to bring to the students the importance of studying the structural and functional features of teeth, their importance in the process of forming a future doctor;
- to interpret the histophysiology of tooth tissues, structural features in different zones to assess the functional state., to determine their significance for practical medicine;
- to form students' professional significance of the topic. Discuss the issue of deontology.
- to bring to the students the importance of studying the structural and functional features of the activity of the organs of the oral cavity, their importance in the process of forming a future doctor;
- to interpret the histophysiology of the oral mucosa, structural features in different zones to assess the functional state., to determine their significance for practical medicine;
- to form students' professional significance of the topic. Discuss the issue of deontology.

3. Plan and organizational structure of the lecture.

№№	The main stages of the lecture and their content	Objectives in levels of abstraction	Lecture type. Lecture equipment	Time management

1	2	3	4	5
I. 1. 2.	*Preparatory stage.* Determination of the learning goal. Providing positive motivation.		Tables. Slides.	5%
II	*The main stage* Teaching lecture material according to the plan: 1. Morpho-functional characteristics of the oral cavity organs. 2. Ligaments of structural features of different zones of the mucous membrane of the organs of the oral cavity according to localization and functions. 3. Histophysiology of the regulatory influence of the organs of the oral cavity on the vital activity of the organism. 4. Morphofunctional connections of the oral cavity organs with other organs of the digestive tract. The final stage.	I. Descriptive. II. Analytical - synthetic, high quality.	In accordance with the publication "Guidelines for the planning, preparation and analysis of lectures." List of literature, question, task.	85-95%
III.	*Summary of the lecture.* General conclusions. Lecturer's answer to possible questions. Self-study assignment.			5%

4. Content of the lecture material:
- structural and logical scheme of the content of the topic;
- the text of the lecture. (attached)

5. Materials for activating students during the lecture:
1) The metabolic activity of cement is lower than that of bones, because it does not have its own blood vessels. This feature allows the movement of teeth using orthodontic appliances, does not cause resorption of the tooth root.
2) The development of dental caries is based on the ability of enamel to dissolve at acidic pH values, while some of its crystals transmit pain sensitivity - the only type of sensitivity in teeth.
3) The metabolic activity of cement is lower than that of bones, because it does not have its own blood vessels. This feature allows the movement of teeth using orthodontic appliances, does not cause resorption of the tooth root.

Questions:

1. General plan of the structure of the tooth. Innervation and blood supply.

2. Morphological features of the structure of primary and permanent teeth.

3. Morphological and functional characteristics of tooth tissues. Physicochemical properties, microscopic structure.

4. Tooth-gingival connection: components, their structure, significance in health and disease. Paradont.

5. Morphological and functional characteristics of the stages of tooth development:

- laying of dental germs;

- formation and differentiation of dental germs;

- histogenesis of the tooth.

6. Alimentary canal. General plan of the structure of the wall. Innervation and vascularization.
7. Morphological features of the structure of the mucous membrane of various organs of the oral cavity.
8. Morphofunctional characteristics of the oral cavity organs.
9. Language. Development. General plan of the building. Features of the structure of the mucous membrane on different surfaces.
10. General plan of the structural organization of the teeth.

6. General material and methodological support of the lecture:
- classrooms;
- equipment;
- illustrative materials.

List of recommended literature .

The main one:

1.Lutsyk O.D., Tchaikovsky Y.B. Histology, cytology, embryology Vinnytsia, New Book, 2018.
2.Barinov E.F., Tchaikovsky Y.B. General histology and embryology of internal organs: textbook.Kyiv: Medicine; 2013
3.Wojciech Pawlina. Histology: textbook and atlas. WSV: Medicine, 2021.

Additional:

1.Histology and embryology of internal organs: textbook / E.F. Barinov, Y.B. Tchaikovsky, O.M. Sulaeva et al.
2.Cytology of human organs and tissues edited by L.S.Bolgova. Kyiv: Book-plus, 2018, p.288

Theme: "Organs of oral cavity." *Addition*

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

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

The mucosa lining the oral cavity has the following features:

- lined with stratified squamos epithelium
- the absence or poor development of muscularis mucosae
- the absence of submucosa in some areas
- high vascularization

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

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

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

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

The mucous part of the lip is lined with mucosa. The epithelium of the mucosa is stratified squamos non-keratinized. The lamina propria is formed by dense connective tissue, has short irregular papillae and contains blood vessels and

excretory ducts of the lip salivary glands. The submucosa is formed by loose connective tissue, which consists of strands of densely grouped collagen fibers and contains fat and small mixed salivary glands between these strands. According to their structure the minor salivary glands of the lip are the compound tubulo-alveolar ones. The muscularis mucosae is absent that's why the submucosa connects the lamina propria directly to the thin fascia of the muscles.

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

- maxillary
- intermediate
- mandibular

The muscularis mucosae is absent in the buccal mucosa.

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

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

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

The hard palate. The mucosa of the hard palate is tightly fixed to the

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

Palatine rugae (transverse palatine ridges)

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

ODESA NATIONAL MEDICAL UNIVERSITY

DEPARTMENT OF HISTOLOGY, CYTOLOGY AND EMBRYOLOGY

METHODICAL RECOMMENDATION OF LECTURES

for dentistry faculty

THEME: «Structure and development of teeth.»

Approved on the methodical conference of department

«____»_____ 20___., protocol №_____

Head of Department, doc._____ Tiron O.I.

Approved on the methodical conference of department

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«____»_____ 20___., protocol №_____

Head of Department, doc._____ Tiron O.I.

Theme: «Structure and development of teeth.»-2h.

1. Relevance of the topic.

The study of the structure of the organs of the oral cavity is the basis for understanding the patterns of morphological changes in the case of the development of pathological processes. Mechanical processing of food in the anterior part of the digestive tube depends on the condition of the dental-jaw apparatus. The teeth are involved in articulation, they are an important anatomical element of the face. Experienced dentists, based on the condition of the teeth, can conclude about the functioning of the digestive tract and systems for regulating homeostasis, the content of Ca 2+, the change in the acid-base state both in the oral cavity and in the body.

The oral cavity is the initial section of the digestive tract. The presence of its own microflora and the constant supply of microorganisms from the external environment, the effect of temperature, acid-base factors can lead to the development of an inflammatory process, caries, periodontal disease, and the like. To diagnose various diseases, a dental examination is carried out. Knowledge of the patterns of development and the general plan of the structure of the teeth, microscopic and ultramicroscopy of the structure of tooth tissues, the possibilities and mechanisms of their regeneration is important for understanding the formation of defects in the development of the dental-jaw apparatus, the interpretation of cause-and-effect relationships in various pathological processes in the oral cavity.

2. Objectives of the lecture:

a) learning:

- analysis of the structural organization of the teeth;
- modern ideas about the morphofunctional organization of tooth tissues;
- interpretation of the relationship between the structural and functional parts of the teeth;
- assessment of the functional state of tooth tissues, interpretation of age-related changes, mechanisms of adaptation to the action of various factors.
- to acquaint students with the structure of tooth tissues in relation to localization and functions;

b) educational:

- to bring to the students the importance of studying the structural and functional features of teeth, their importance in the process of forming a future doctor;
- to interpret the histophysiology of tooth tissues, structural features in different zones to assess the functional state., to determine their significance for practical medicine;
- to form students' professional significance of the topic. Discuss the issue of deontology.

3. Plan and organizational structure of the lecture.

№№	The main stages of the lecture and their content	Objectives in levels of abstraction	Lecture type. Lecture equipment	Time management
1	2	3	4	5
I. 1. 2. II	*Preparatory stage.* Determination of the learning goal. Providing positive motivation. *The main stage* Teaching lecture material according to the plan: 1.Morphological and functional characteristics of tooth tissues. 2. Relationship of structural features of different tooth structures according to localization and functions. 3. Histophysiology of the stages of tooth development: the formation of tooth germs, differentiation of tooth germs, histogenesis of tooth tissues. 4. Teething theory.	I. Descriptive. II. Analytical - synthetic, high quality.	Tables. Slides. In accordance with the publication "Guidelines for the planning, preparation and analysis of lectures." List of literature, question, task.	5% 85-95%

III.	*Summary of the lecture.* General conclusions. Lecturer's answer to possible questions. Self-study assignment.			5%

4. Content of the lecture material:
- structural and logical scheme of the content of the topic;
- the text of the lecture. (attached)

5. Materials for activating students during the lecture:
1) The metabolic activity of cement is lower than that of bones, because it does not have its own blood vessels. This feature allows the movement of teeth using orthodontic appliances, does not cause resorption of the tooth root.
2) The development of dental caries is based on the ability of enamel to dissolve at acidic pH values, while some of its crystals transmit pain sensitivity - the only type of sensitivity in teeth.
3) The metabolic activity of cement is lower than that of bones, because it does not have its own blood vessels. This feature allows the movement of teeth using orthodontic appliances, does not cause resorption of the tooth root.

Questions:

1. General plan of the structure of the tooth. Innervation and blood supply.

2. Morphological features of the structure of primary and permanent teeth.

3. Morphological and functional characteristics of tooth tissues. Physicochemical properties, microscopic structure.

4. Tooth-gingival connection: components, their structure, significance in health and disease. Paradont.

5. Morphological and functional characteristics of the stages of tooth development:

- laying of dental germs;

- formation and differentiation of dental germs;

- histogenesis of the tooth.

6. General plan of the structural organization of the teeth.

6. General material and methodological support of the lecture:
- classrooms;
- equipment;

- illustrative materials.

List of recommended literature .

The main one:

1.Lutsyk O.D., Tchaikovsky Y.B. Histology, cytology, embryology Vinnytsia, New Book, 2018.
2.Barinov E.F., Tchaikovsky Y.B. General histology and embryology of internal organs: textbook.Kyiv: Medicine; 2013
3.Wojciech Pawlina. Histology: textbook and atlas. WSV: Medicine, 2021.

Additional:

1.Histology and embryology of internal organs: textbook / E.F. Barinov, Y.B. Tchaikovsky, O.M. Sulaeva et al.
2.Cytology of human organs and tissues edited by L.S.Bolgova. Kyiv: Book-plus, 2018, p.288

Theme: "Structure and development of teeth." *Addition*

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

The hard tissues of the tooth are:

- enamel
- dentin
- cementum

The soft tissues are:

- pulp
- periodontium (surrounds the tooth)

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

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

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

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

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

Dentin – is the calcified living material that forms the crown, the neck and the root of the tooth. Dentin consists of 70-72% of inorganic material (predominantly hydroxyapatite and small amounts of calcium fluoride, calcium hydrocarbonate, magnesium and sodium). The organic material constitutes about 28-30% of dentin mass and is represented mostly by the I type of collagen, mucopolysaccharides and lipids. Dentin consists of dentinal tubules grounded into the calcified amorphous substance. Within the dentinal tubules the processes of specialized cells - odontoblasts (Tom's fibers) are situated. The Tom's fibers provide the nutrition of the hard tissues of the tooth and supply it with mineral salts. Dentinal tubules extend from the pulp cavity and end perpendicular to dentinoenamel or dentinocementum junction. Dentinal tubules are grounded into the amorphous substance, which consists of the collagen fibers and cementing material. On the basis of the collagen fibers arrangement there are distinguished two layers of dentin: mantle dentin and circumpulpal dentin. **Mantle** dentin is the outermost layer of dentin characterized by the **radial** direction of collagen fibers (von Korff's fibers). **Circumpulpal** dentin is charactezied by the **tangential** direction of collagen fibers (von Ebner's fibers).

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

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

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

The cells of cementum, like the cells of bone tissue), lie in small cavities (lacunae) and connect to the source of nutrition by their processes. But, unlike the bone tissue, cementum doesn't contain blood vessels. The nutrition of cementum is

provided by diffusion through the periodontal vessels. Acellular cementum doesn't contain cells and cell processes. It consists only of collagen embedded in ground substance.

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

The pulp contains three layers:

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

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

Odontoblats – are the pear-shaped cells, located in the peripheral (odontogenic) layer of the pulp. The narrow apical domain of odontoblast gives a rise to the long branched process, which pass into the entire thickness of dentine through the dentinal tubule. Some of these processes even reach the enamel. Nucleus is located at the basal domain of odontoblast. Odontoblasts are characterized by basophilic cytoplasm, well-developed rough EPR, mitochondria and Golgi complex. Odontoblasts produce collagen, by which the collagen fibers of dentine are formed and alkaline phosphatase, which regulates the process of dentin calcification. In erupted tooth dentinoblasts supply dentine and enamel with nutrients and mineral salts and provide the regeneration of dentin.

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

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

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

TOOTH DEVELOPMENT

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

The process of tooth development consists of three stages:

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

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

1. inner enamel epithelium attached to the dental papilla – simple columnar epithelium formed by ameloblasts. Ameloblasts are the enamel-secreting cells;
2. outer enamel epithelium separates enamel organ from dental sac. The cells of this layer don't leave any derivates.
3. pulp of enamel organ or stellate reticulum is located between the outer and inner enamel epithelium. It is formed by the star-shaped cells that obtain their shape due to the water being drawn into the enamel organ from dental papilla. The pulp of enamel organ takes part in formation of the pellicula of enamel.

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

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

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

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ODESA NATIONAL MEDICAL UNIVERSITY

DEPARTMENT OF HISTOLOGY, CYTOLOGY AND EMBRYOLOGY

METHODICAL RECOMMENDATION OF LECTURES

for dentistry faculty

THEME: «Digestive system. Esophagus. Stomach. Intestine. »

Approved on the methodical conference of department

«____»_____ 20___., protocol №_____

Head of Department, doc._____ Tiron O.I.

Approved on the methodical conference of department

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Head of Department, doc._____ Tiron O.I.

Theme: «Digestive system. Esophagus. Stomach. Intestine. »-2h.

1. **Relevance of the topic.**

Diseases of the digestive system are the most common, and dyspeptic symptoms are familiar to almost everyone. These disorders are based on morphological and functional changes in the organs of the digestive tract. This led to the relevance of the use of endoscopic research methods in gastroenterology and surgery, which make it possible to verify the diagnosis, determine the effectiveness of treatment, and the like.

The correct and complete interpretation of the endoscopic picture significantly depends on the doctor's understanding of the general morphofunctional organization of the digestive tract organs, the tissue composition and functions of their membranes, and relief features. Knowledge of the structure of the mucous membrane, which determines the leading functions of organs, the principles of digestion in them, the peculiarities of functioning and regulation, the cellular basis

of regeneration, is the basis for understanding the causes and mechanisms of the development of pathological processes in the digestive system.Almost 70% of people suffer from stomach problems. The structural and functional features of the gastric mucosa are the basis for the clinical types of gastric secretion, which determine the causes and mechanisms of development of gastritis, peptic ulcer, tumors, and the like.

2. Objectives of the lecture:

a) *training:*

- analysis of the structural organization of the digestive system;
- modern ideas about the morphofunctional organization of the gastrointestinal tract;
- interpretation of the relationship between the structural and functional parts of the digestive system;
- assessment of the functional state of the digestive system organs, interpretation of age-related changes, mechanisms of adaptation to the action of various factors.
- to acquaint students with the structure of the mucous membrane of different parts of the gastrointestinal tract in relation to localization and functions;

b) educational:

- to bring to the students the importance of studying the structural and functional features of the activity of the organs of the digestive system, their importance in the process of forming a future doctor;
- to interpret the histophysiology of the mucous membrane, structural features in different zones to assess the functional state., to determine their significance for practical medicine;
- to form students' professional significance of the topic. Discuss the issue of deontology.

3. Plan and organizational structure of the lecture.

№№	The main stages of the lecture and their content	Objectives in levels of abstraction	Lecture type. Lecture equipment	Time management
1	2	3	4	5
I. 1. 2. II	*Preparatory stage.* Determination of the learning goal. Providing positive motivation. *The main stage*		Tables. Slides.	5% 85-95%

	Teaching lecture material according to the plan: 1. Morphofunctional characteristics of the organs of the gastrointestinal tract. 2. Relationship of structural features of the mucous membrane of different parts of the digestive system according to localization and functions. 3. Histophysiology of the absorption mechanism. 4.Morphofunctional connections of organs digestive system.	I. Descriptive. II. Analytical - synthetic, high quality.	In accordance with the publication "Guidelines for the planning, preparation and analysis of lectures."	
III.	*Conclusion stage.* Summary of the lecture. General conclusions. Lecturer's answer to possible questions. Self-study assignment.		List of literature, question, task.	5%

4. Content of the lecture material:
- structural and logical scheme of the topic content;
- the text of the lecture.

5. Materials for activating students during the lecture .:
1) Gastroesophageal reflux disease is an inferiority of the barriers in the gastroesophageal junction, which is caused by a decrease in the tone of the lower esophageal sphincter or a hiatal hernia.
2) Peptic ulcer disease occurs as a result of the destruction of the epithelium of the mucous membrane by various factors. Any imbalance between the actions of the aggressive factors of the dads' defense can lead to pathological changes. 3) Dysfunction of the parietal cells of the stomach's own glands causes gastritis, as well as malignant anemias.

4) Appendicitis - inflammation of the appendix.
5) Approximately 90-95% of malignant tumors of the digestive system develop from epithelial cells of the intestine and stomach. Malignant tumors of the colon develop exclusively from the glandular epithelium (adenocarcinoma).

Questions:
1. Alimentary canal. General plan of the structure of the wall. Pharynx and esophagus. Its structure and function.
2. The esophagus. The structure of the walls of the esophagus.
3. Glands of the esophagus: localization, structure, functions.
4. Stomach. General plan of the building.
5.Mucous membrane of the stomach: layers, tissue composition.
6. Glands of the fundus and body of the stomach: structure, cellular composition.
7. Morphofunctional characteristics of gastric exocrinocytes: main, parietal, mucocytes.
8. Small intestine. Development. General morphological and functional characteristics. Histophysiology of the crypt-villus system.
9. The large intestine. General morphological and functional characteristics. Sources of development. Structure, regeneration, age-related changes.
10. The alimentary canal. General plan of the structure of the wall. Morphology. 11. The mucous membrane of the small intestine. The fabric composition of the layers. Varieties of epithelial cells, their structure and function.
12. Relief. Crypt-villus system. Histophysiology of digestion. 13. The large intestine. Wall structure. Histophysiology. The appendix. 14.General plan of the structure of the intestinal wall. Functions of the thin and thick sections.
15.Features of the structure of the duodenum, jejunum and ileum.
16. Rectum, departments, their morphofunctional features.
17. Regeneration of the epithelium of the small and large intestine. Age-related changes.

6. General material and methodological support of the lecture:
- classrooms;
- equipment;
- equipment;
- illustrative materials.

List of recommended literature .

The main one:

1.Lutsyk O.D., Tchaikovsky Y.B. Histology, cytology, embryology Vinnytsia, New Book, 2018.
2.Barinov E.F., Tchaikovsky Y.B. General histology and embryology of internal

organs: textbook.Kyiv: Medicine; 2013
3.Wojciech Pawlina. Histology: textbook and atlas. WSV: Medicine, 2021.
Additional:

1.Histology and embryology of internal organs: textbook / E.F. Barinov, Y.B. Tchaikovsky, O.M. Sulaeva et al.
2.Cytology of human organs and tissues edited by L.S.Bolgova. Kyiv: Book-plus, 2018, p.288

Theme: "Digestive system. Esophagus. Stomach. Intestine." *Addition*

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

The mucosa consists of three layers: epithelium, lamina propria and muscularis mucosae. The epithelium of esophagus is stratified squamos non-keratinized. The lamina propria is formed by loose connective tissue. At the level of cricoid cartilage and in the terminal portion of esophagus the **lamina propria** contains secretory acini of **esophageal cardiac glands**. These simple branched

glands produce mucous. Their acini are formed by cuboidal and columnar mucous cells. Besides mucous cells the acini of esophageal cardiac glands contain endocrine cells and solitary parietal cells, which produce H+ ions. The ducts of these glands are lined with columnar epithelium.

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

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

The submucosa is formed by dense irregular connective tissue that contains the acini of esophageal glands proper. Esophageal glands proper are compound branched tubulo-alveolar glands, which produce mucous. The small ducts of these glands are covered with simple low columnar epithelium, the large ducts – by stratified squamos epithelium, in which ciliated cells sometimes occur. The esophageal glands proper are the most concentrated in the upper half of esophagus.

Mucous secreted by cardiac glands of esophagus and esophageal glands proper lubricates the lumen and facilitates the passage of the food. On cross section of esophagus, the lumen in its is normally collapsed state has a branched appearance because of longitudinal folds. When a bolus of food passes through the esophagus, the lumen expands without mucosal injury.

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

STOMACH

Stomach provides the several important functions in human body. The main function of stomach is providing conditions for breaking down of food bolus by its gastric secretions. The enzymes of gastric juice – pepsin and chemosin break down the proteins and lipids. These enzymes are active only in acidic environment. Besides the activation of gastric enzymes, the acidic environment causes the death of pathogenic microorganisms, which can enter the gastrointestinal tract with food.

The absorption of water, salts, monosaccharides and alcohols occurs through the wall of stomach. Through the wall of stomach to the lumen of gastrointestinal tract the excretion of ammonium, urea and alcohol occurs. The endocrine function of stomach is represented by the production of biologically active substances – gastrin, serotonin, motilin, enteroglycon, which regulate the secretion of gastric glands, motility of stomach and intestine. The mucosa of stomach produces the internal antianemic factor, which is necessary for absorption of vitamin B12. The mechanical function of stomach is performed by mixing of the food with gastric juice.

The wall of stomach consists of four layers: mucosa, submucosa, muscularis externa and serosa.

Mucosa of stomach forms rugae, mammilated areas and gastric pits (foveolae).

Gastric **rugae** are the folds formed by mucosa and submucosa.

Mammilated areas are the bulging irregular areas of the stomach surface, which are bounded by grooves of the mucosa. The origin of mammilated areas is explained by that the gastric glands form aggregations, which are separated from each other by connective tissue. The superficial veins of connective tissue are visible through the mucous as reddish lines. These reddish lines are the boundaries of mammilated areas.

Gastric pits – are the invaginations of epithelium into the lamina propria. They are revealed all over the surface of stomach.

The mucosa of stomach consists of three layers: epithelium, lamina propria and muscularis mucosae. Epithelium lining mucosa is simple columnar glandular epithelium. On the apical surface of epithelial cells microvilli are revealed. The apical domain of epithelial cells contains granules filled with mucous secretion.

The secreted mucous covers the surface of mucosa and protects it from self-digestion by gastric juice. The basal domain contains nucleus and Golgi apparatus.

The epithelium near the gastric pits contains low-differentiated epithelial cells, which undergo division and substitute old and dead epithelial cells of mucosa.

The lamina propria is formed by loose connective tissue, containing gastric glands. **Lamina propria** also contains the aggregations of lymphocytes arranged in lymphatic nodules or diffuse lymphatic tissue.

The gastric glands (fundic glands) are simple, branched, tubular glands. Each fundic gland is composed of five types of cells:

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

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

The glands of stomach have different structure in the different parts of stomach. There are distinguished three types of glands in stomach: fundal (gastric), pyloric and cardiac glands. The gastric (fundal) glands are the most numerous and present throughout the entire gastric mucosa except for the relatively small regions occupied by cardiac and pyloric glands.

The gastric (fundal) glands contain five main types of cells:

Chief cells are located predominantly in the deeper part of the fundic glands. The apical portion of cytoplasm owns secretory vesicles, containing digestive enzyme precursors. The apical surface of chief cells is covered with microvilli. The basal portion contains nucleus, rough endoplasmic reticulum and Golgi complex. In H&E sections the cytoplasm of chief cells appears basophilic. The secretions of chief cell are **pepsinogen and chemosin**. Pepsinogen is an inactive proenzyme. On contact with the acid gastric juice, pepsinogen is converted to pepsin, a proteolytic enzyme. Chemosin breaks down the proteins of milk; it is produced predominantly in children.

Parietal cells produce **H+ and Cl- ions**, from which hydrochloric acid is formed. Hydrochloric acid provides the acidic environment in stomach. Parietal cells are

found in the neck of the fundic glands, among the mucous neck cells, and in the deeper part of the gland. They are large, irregular- shaped cells, sometimes binucleate. When examined with the electron microscope, parietal cells are seen to have an extensive intracellular canalicular system that communicates with the lumen of the gland. Numerous mitochondria supply the high levels of energy necessary for acid secretion. Parietal cells take part in the production of inner antianemic factor.

Mucous neck cells are localized at the neck region of the gland and line its excretory ducts. They are cuboidal or columnar in shape. The basal portion of cytoplasm contains nucleus, the apical – mucinogen granules.

Undifferentiated adult stem cells (accessory mucous cells) are the source of regeneration of all cells of gastric glands.

Enteroendocrine cells are found between the chief cells at every level of the fundic gland. They are the constituting part of diffuse neuroendocrine system (DNES) or APUD-system.

On the basis of type of produced biologically active substances there distinguished several types of enteroendocrine cells of stomach: EC-, ECL-, G-, P-, D-, A- and X-cells. These cells regulate synthesis and secretion of gastric juice, motility and blood supply of stomach and other organs of digestive system.

EC (enterochromaffine)-cells – produce **serotonin and melatonin**, which stimulate the secretion of digestive enzymes, mucous secretion and motility of stomach. Melatonin regulates the fotoperiodicity of digestive system functioning.

ECL (enterochromaffine-like)-cells – produce **histamine**, which regulates the activity of parietal cells.

G-cells – produce **gastrin**, which stimulates the secretion of pepsinogen by chief cells and the secretion of hydrochloric acid by parietal cells.

P-cells – produce **bombesin**, which stimulates the secretion of hydrochloric acid and pancreatic juice, and stimulates contraction of the smooth muscle of gallbladder.

D-cells – produce **somatostatin**, which acts directly on the acid-producing parietal cells to reduce acid secretion. Somatostatin can also indirectly decrease stomach acid production by preventing the release of gastrin, secretin and histamine.

D1-cells – produce **vasoactive interstitial peptide** (VIP), which induces the relaxation of smooth muscle of arteries, decreases blood pressure and stimulates the secretion of pancreatic enzymes.

A-cells – produce **glucagon**, which causes the liver cells to convert glycogen into glucose.

Submucosa is formed by dense irregular connective tissue containing numerous elastic fibers.

Muscularis externa consists of three layers of smooth muscle: an outer longitudinal layer, a middle circular layer, and an inner oblique layer. Between the muscle layers myenteric (Auerbach's) nerve plexus is located.

Serosa is formed by connective tissue lined with mesothelium.

Cardiac and pyloric glands are simple, branched, tubular glands.

Pyloric glands are located in the pyloric antrum (the part of the stomach between the fundus and the pylorus). They differ from the fundic glands in that they are much more branched, their lumen is relatively wide, they almost don't contain parietal cells.

Cardiac glands are limited to a narrow region of the stomach (the cardia) that surrounds the esophageal orifice. They are composed mainly of mucus-secreting cells, with occasional interspersed enteroendocrine cells. The short excretory ducts of cardiac glands are lined with columnar epithelium, containing cells with elongated nuclei. The duct segment is the site at which the surface mucous cells and the gland cells are produced.

INTESTINE

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

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

- duodenum;
- jejunum
- ileum.

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

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

The wall of the small intestine consists of four layers:

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

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

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

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

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

Enterocytes are the most numerous cells of the epithelium of villi. They are the tall columnar cells, measuring about 25 mcm. Each enterocyte possesses several thousands closely packed microvilli, located on its apical surface. Microvilli

increase the apical surface area as much as 600 times. Microvilli are recognized in the light microscope as forming a **striated border** on the luminal surface. They are about 1 mcm high and 0,1 mcm in diameter.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Large intestine – is the part of alimentary canal that provides the formation and movement of fecal masses. In the lumen of large intestine the metabolic products,

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

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

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

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

The lamina propria contains numerous lymphatic follicles, which can form solitary lymphatic follicles or distort the regular spacing of the intestinal glands and extend into the submucosa. The aggregations of diffuse leukocytes and lymphatic follicles in the alimentary canal are considered to be the analog of the Bursa Fabricii of birds, which provides the maturation and immune activation of B-lymphocytes.

The most numerous lymphatic follicles are revealed in the wall of vermiform appendix. The wall of the appendix is covered with simple columnar epithelium, which is not rich in goblet cells. Paneth cells and enteroendocrine cells are revealed in the epithelium of the appendix. The great bulk of serotonin and melatonin is secreted by the enteroendocrine cells of the appendix.

Because of the poor development of the muscularis mucosae, the lamina propria merges with submucosa. The lamina propria contains and the submucosa numerous large lymphatic follicles, which merge together. The vermiform appendix performs the function of immune defense.

The muscularis mucosae consists of two layers: the inner circular layer and the outer longitudinal.

The submucosa is formed by dense irregular connective tissue, containing aggregations of adipocytes and numerous lymphatic follicles.

The muscularis externa contains two layers: inner circular and outer longitudinal. Between them the layer of loose connective tissue is located.

The muscular layer of colon is not continuous and forms teniae coli. **Teniae coli** represent three narrowed, thickened,equally spaced bands of the outer longitudinal layer of the muscularis externa.

The most portion of the large intestine is covered with serosa, except the caudal part covered with adventitia.

Rectum and anal canal. The rectum is divided into two parts: the upper pelvic part and the lower anal part. The upper part is distinguished from the rest of the large

intestine by the presence of folds called **transverse rectal folds**.

The mucosa of the pelvic part is lined with simple cuboidal epithelium forming deep crypts.

The anal part is divided into three

zones according to the character of the epithelial lining:

- columnar zone is covered with stratified columnar epithelium;

- transitional zone is covered with stratified squamous non-keratinized epithelium -- cutaneous zone, which is found in the lower third of the anal canal. This zone is lined with stratified squamous epithelium that is continuous with that of the perianal skin.

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

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

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

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

The muscularis consists of two layers: the inner circular and the outer longitudinal. It forms two sphincters, which play an important role in act of

defecation. The inner anal sphincter if formed by the inner layer of the muscularis externa; the outer anal sphincter is formed by the striated muscle. The upper part of rectum is covered with serosa; the anal part – with adventitia.

ODESA NATIONAL MEDICAL UNIVERSITY

DEPARTMENT OF HISTOLOGY, CYTOLOGY AND EMBRYOLOGY

METHODICAL RECOMMENDATION OF LECTURES

for dentistry faculty

THEME: «Digestive system. Liver. Pancreas. Salivary glands.»

Approved on the methodical conference of department

«____»_____ 20___., protocol №_____

Head of Department, doc._____ Tiron O.I.

Approved on the methodical conference of department

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Theme: «Digestive system. Liver. Pancreas. Salivary glands.»

1. Relevance of the topic.

The liver is a vital organ that combines the functions of not only the digestive gland, but also an important regulator of the body's metabolic processes. Knowledge of the histophysiology of the liver will contribute to the understanding of causal relationships in the development of diseases such as hepatitis, cirrhosis, neoplasia and metastatic organ lesions, pathology of the biliary tract, and the like. The doctor's competence in assessing the results of morphological examination of the liver biopsy material will make it possible to individualize the patient's treatment regimen.

The pancreas is associated with the digestive tube, participates in digestion, as well as in the regulation of metabolic processes in the body. A decrease in the function of the pancreas is accompanied not only by a violation of the cavity and parietal digestion, but also by a change in the mechanisms of regulation of blood

glucose levels. Activation of enzymes inside the organ can cause a destructive process with severe pain. Knowledge of the histophysiology of the pancreas will help the doctor analyze cause-and-effect relationships in case of indigestion, metabolism and the state of the digestive system.

2. Objectives of the lecture:

a) learning:

- analysis of the structural organization of large digestive glands;
- modern ideas about the morphofunctional organization of large digestive glands
- interpretation of the relationship between the structural and functional parts of the digestive system, the liver, pancreas and salivary glands;
- assessment of the functional state of the large digestive glands, interpretation of age-related changes, mechanisms of adaptation to the action of various factors.
- to acquaint students with the structure of the liver, pancreas and salivary glands .;

b) educational:

- to educate students on the importance of studying the structural and functional features of the activity of the organs of the digestive system, their importance in the process of forming a future doctor;
- to interpret the histophysiology of the large digestive glands, structural features for assessing the functional state., to determine their significance for practical medicine;
- to form students' professional significance of the topic. Discuss the issue of deontology.

3. Plan and organizational structure of the lecture.

№ №	The main stages of the lecture and their content	Objectives in levels of abstraction	Lecture type. Lecture equipment	Time management
1	2	3	4	5
I. 1. 2.	*Preparatory stage* Determination of the learning goal. Providing positive motivation.		Tables. Slides.	5%

II	*The main stage* Teaching lecture material according to the plan: 1.Morphofunctional characteristics of large digestive glands 2. Communication of large digestive glands with different parts of the digestive system according to localization and functions. 3. Microscopic and ultramicroscopy of the structure of hepatocytes, morphological manifestations of changes in functional activity. 4. Histophysiology of the endo- and exocrine part of the pancreatic parenchyma. 5. Morpho-functional connections of the digestive system organs. 6. Morphofunctional characteristic of salivary glands.	I. Descriptive. II. Analytical - synthetic, high quality.	In accordance with the publication "Guidelines for the planning, preparation and analysis of lectures." List of literature, question, task.	85-95%
III.	*The final stage.* Summary of the lecture. General conclusions. Lecturer's answer to possible questions. Self-study assignment.			5%

4. Content of the lecture material:

- structural and logical scheme of the topic content;
- the text of the lecture.

5. Materials for activating students during the lecture:

1) In chronic liver diseases, Ito cells are activated by factors that produce hepatocytes and Kupffer cells and take on the characteristics of myofibroblasts, which play a large role in the development of fibrosis, which can lead to liver cirrhosis.

2) One of the most serious causes of jaundice in infants is the underdevelopment of the aggregate EPS in hepatocytes (neonatal hyperbilirubinemia).

3) The occurrence of various forms of hepatitis is associated with a violation of the intercellular contacts of the biliary surfaces of hepatocytes.

4) Disruption of the balance of hormones that decree cells of the pancreatic islets (A- and B-insulocytes) causes a serious illness - diabetes mellitus.

Questions:

1. Liver. General morphological and functional characteristics. The structure of hepatocytes, perisinusoid lipocytes and the walls of sinusoids.
2. Liver. General morphological and functional characteristics. Sources of development. The structure of the classic hepatic lobule. The concept of the portal lobe and acinus.
3. The blood supply system of the liver.
4. Pancreas. Development. General plan of the building. Histophysiology, regeneration, age-related changes.
5. Pancreas. Development, general plan of the structure. Exocrine and endocrine parts, its structure and functions.
6. Age-related changes, features of innervation and regeneration.

6. General material and methodological support of the lecture:

- classrooms;
- equipment;
- equipment;
- illustrative materials

List of recommended literature .

The main one:

1.Lutsyk O.D., Tchaikovsky Y.B. Histology, cytology, embryology Vinnytsia, New Book, 2018.

2.Barinov E.F., Tchaikovsky Y.B. General histology and embryology of internal organs: textbook.Kyiv: Medicine; 2013

3.Wojciech Pawlina. Histology: textbook and atlas. WSV: Medicine, 2021.

Additional:

1.Histology and embryology of internal organs: textbook / E.F. Barinov, Y.B. Tchaikovsky, O.M. Sulaeva et al.
2.Cytology of human organs and tissues edited by L.S.Bolgova. Kyiv: Book-plus, 2018, p.288

Theme: "Digestive system. Liver. Pancreas. Salivary glands." *Addition*

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

- detoxication of waste products (formation of urea from the toxic nitrous products of protein metabolism);
- inactivation of hormones, biogenic amines and a number of drug substances;
- taking part in defense reactions;
- synthesis of glycogen, which is the source of maintenance of constant glucose level in blood;
- synthesis of blood plasma proteins: albumins, fibrinogen, prothrombin etc;
- production of bile, which is necessary for emulsification of lipids;

- playing a significant role in metabolism of cholesterol and iron;
- storage of fat-soluble vitamins (A,D,E etc.);
- hemopoietic function in embryonic period.

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

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

The portal vein collects blood from all unpaired organs of abdominal cavity and carries it to the liver. The portal blood carried to the liver is largely depleted of oxygen and contains nutrients and toxic material adsorbed in the intestine, blood cells and breakdown products of cells from the spleen, endocrine secretions of pancreas. The hepatic artery carries oxygenated arterial blood to the liver. These two large blood vessels branch into the smaller ones: lobular (vv. seu aa. lobulares), segmental (vv. seu aa. segmentales), interlobular (vv. seu aa. interlobulares), perilobular (vv. seu aa. perilobulares) veins and arteries. They are accompanied by bile ducts and together constitute the portal triad. The lymphatic vessels are located near the portal triad. The interlobular arteries and veins travel along the lateral faces of the lobule; the perilobular arteries and veins branch off from the interlobular and encircle the lobules at different levels. The interlobular and perilobular veins have poorly developed muscular layer, but in the areas of furcation the aggregations of muscular elements, which form sphincters are found. The corresponding interlobular and perilobular arteries are referred to muscular type of arteries. From the perilobular arteries and veins the blood capillaries arise. At the periphery of the lobule the arterial and venous capillaries fuse together and form the sinusoid capillaries, through which blood flows in direction from the periphery to the center of hepatic lobule. The sinusoid capillaries are

approximately 30 mcm in diameter and characterized by discontinuous basal lamina. They travel in radial direction between the plates of liver cells – hepatic laminae, and drain into the central vein located in the center of hepatic lobule.

With the central vein the system of blood outflow from hepatic lobules begins.

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

The hepatic lobules consist of hepatic laminae and sinusoid blood capillaries.

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

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

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

According to the classic conception, the hepatic lobules are formed by hepatic laminae and intralobular sinusoid capillaries. The hepatic laminae consist of two rows of hepatocytes – epithelial cells of liver, which are arranged in radial

direction. Between the hepatocytes the blood and bile capillaries run in the same direction, from periphery to center. The bile capillaries do not posses their proper wall. The wall of bile capillaries is formed by the plasmolemme, so-called biliary surface, of two adjacent hepatocytes. The lumen of bile capillary is separated from the intercellular space due to the presence of tight junctions (zonulae occludens) between the hepatocytes. That's why in normal conditions the bile does not enter the intercellular space and further into the blood. The biliary surface of hepatocytes contains microvili projecting into the lumen of bile capillaries.

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

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

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

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

The liver acinus. The liver acinus is the structural unit that provides the best correlation between blood perfusion, metabolic activity, and liver pathology. The liver acinus is lozenge shaped and represents the smallest functional unit of the hepatic parenchyma. The short axis of the acinus is defined by the terminal branches of the portal triad that lie along the border between two classic lobules.

The long axis of the acinus is a line drawn between the two central veins closest to the short axis. Therefore, in a two-dimensional view the liver acinus occupies parts

of adjacent classic lobules. This concept allows a description of the exocrine secretory function of the liver comparable to that of the portal lobule.

The liver cells or h**epatocytes**. Hepatocytes are polyhedral cells, about 20-25mcm in diameter. These cells usually posses two or more round nuclei, which contain small amounts of heterochromatin; sometimes large polyploidic nuclei occur. The cytoplasm remains basophilic and acidophilic, contains all types of general organelles and various inclusions. The rough ER synthesizes blood plasma proteins and enzymes for inactivation of harmful substances, drugs and hormones. The smooth ER is involved in glycogen synthesis, the Golgi apparatus – in bile secretion, the peroxysomes – in metabolism of fatty acids. Hepatocytes posses numerous mitochondria and are lack of lysosomes. The main inclusions of hepatocytes are glycogen, lipids, iron and vitamins.

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

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

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

The adventitia is formed by loose connective tissue.

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

The mucosa forms numerous folds. It is lined with simple columnar epithelium with the striated border. The lamina propria containing numerous

elastic fibers underlies the epithelium. At the neck of gallbladder it contains mucus-secreting tubo-alveolar glands.

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

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

PANCREAS

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

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

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

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

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

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

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

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

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

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

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

The interlobular ducts lie in the connective tissue septa between the lobules. They drain into the common pancreatic duct, which runs within the thickness of gland,

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

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

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

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

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

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

A-cells constitute approximately 20-25% of the whole mass of insulocytes. They occupy predominantly peripheral parts of the islets. A-granules are resistant to alcohol, but are soluble in water. By an acidic fuchsine they are stained in bright-red color. The size of granules is about 230nm. The granules of A-cells contain glucagon. Glucagon is an indirect antagonist of insuline. It stimulates the breakdown of glycogen to glucose, thereby increasing the glucose level in blood.

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

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

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

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

SALIVARY GLANDS

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

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

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

Saliva moistens the food, prepares it for swallowing, and helps in speech articulation. Due to the presence of enzymes saliva provides the initial digestion of the food. Saliva has an antibacterial effect due to the presence of leukocytes and lysozyme.

Besides the exocrine function salivary glands provide the endocrine function too. Hormones secreted by salivary glands include parotin, insulin-like factor, nerve growth factor, epithelial growth factor, lethal factor etc.

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

Secretory acini of parotid gland produce only serous secretion. They consist of conical serous cells (serocytes) and myoepithelial cells. Serous cells have small apical portion facing the lumen of acinus, where acidophilic secretory vesicles are revealed. The wide basal portion contains nucleus. In the spaces between serous cells the intercellular secretory canaliculi are located. At first the secretion of serous cells enters the intercellular canaliculi and after that passes into the lumen of acinus. The lumen of intercellular canaliculi is about 1 mcm in diameter.

Myoepithelial cells form the second layer of cells of secretory acinus. They are also called stellate cells, because of their star-like shape. They embrace the acinar secretory cells like a basket. Myoepithelial cells are always located between basal

lamina and the basal plasma membrane of epithelial cell. The contraction of myoepithelial cells causes the moving of secretory products towards the excretory ducts.

Salivary ducts

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

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

Interlobular ducts are lined with two-layer epithelium which gradually transforms into the stratified one. Interlobular ducts are surrounded by small amounts of connective tissue.

Excretory ducts of the parotid gland are lined with stratified cuboidal epithelium. As the ducts approach the oral epithelium, stratified squamous epithelium may be present. The excretory duct of parotid gland enters the oral cavity opposite the second upper molar tooth.

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

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

The structure of serous acini is similar to that of parotid gland. Mixed acini are larger than the serous ones and consist of two types of cells – serous and mucous.

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

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

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

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

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

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

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

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

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

Mucous acini are formed by typical mucous cells.

Myoepithelial cells surround all types of secretory acini.

Intercalated ducts are almost not defined in sublingual gland.

Striated ducts are poorly developed and very short. They are lined with columnar or cuboidal epithelium with basal striation.

Iterlobullar and excretory ducts have the same structure as that in submandibular gland. Excretory duct of submandibular gland empties into the submandibular duct as well as directly onto the floor of the mouth. As the duct approaches the oral epithelium, stratified squamous epithelium may line its lumen.

METHODICAL RECOMMENDATION OF LECTURES

for dentistry faculty

THEME: «Respiratory system.»

Approved on the methodical conference of department

«____»_____ 20___., protocol №_____

Head of Department, doc._____ Tiron O.I.

Approved on the methodical conference of department

«____»_____ 20___., protocol №_____

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«____»_____ 20___., protocol №_____

Head of Department, doc._____ Tiron O.I.

Theme: "Respiratory system." -2h.

1. Relevance of the topic.

Respiratory pathology occupies one of the leading places in the structure of human morbidity. The reason for this is the deterioration of the ecological situation in large countries. Respiratory organs provide air intake, humidification, purification, warming, gas exchange in the lungs makes it possible to maintain an optimal level of redox processes in cells, tissues and organs.

Knowledge of the morphological substrate that implements gas exchange and other functions of the respiratory system creates the prerequisites for a correct understanding of the physiology of respiration; the formation of ideas about the structural features at different age periods is a theoretical basis for differential diagnosis and choice of treatment for patients with pathology of the respiratory

system. Deep and complete laboratory and clinical studies of patients, which are necessary for diagnosis (sputum analysis, bronchoscopy, tomography, etc.), are possible only after thorough preparation for this section of histology.

2. Objectives of the lecture:

a) learning:

- analysis of the structural organization of the respiratory system;
- modern ideas about the morphofunctional organization of the respiratory system;
- interpretation of the relationship between the structural and functional parts of the respiratory system;
- differentiation of the structural elements of the airways;
- assessment of functional features to determine the presence, localization and nature of pathomorphological and pathophysiological changes in the respiratory system, as well as related disorders in the body;

b) educational:

- to bring to the students the importance of studying the structural and functional features of the activity of the respiratory system, their importance in the process of forming a future doctor;
- to interpret the histophysiology of the airways and the respiratory department, structural features for assessing the functional state., to determine their importance for practical medicine;
- to form students' professional significance of the topic. Discuss the issue of deontology.

3. Plan and organizational structure of the lecture.

№№	The main stages of the lecture and their content	Objectives in levels of abstraction	Lecture type. Lecture equipment	Time management
1	2	3	4	5
I. 1. 2. II	*Preparatory stage.* Determination of the learning goal. Providing positive motivation. *Basic stage* Teaching lecture material according to the plan: 1. Morpho-functional characteristics of parts of the respiratory system 2. Bronchial tree. Features of the	 I. Descriptive. II. Analytical - synthetic, high quality.	Tables. Slides. In accordance with the publication	5% 85-95%

	structure of the bronchi of different caliber. 3. Microscopic and ultramicroscopic structure of the epithelium of the mucous membrane of the airways, manifestations of changes in functional activity. 4. Histophysiology of gas exchange in the lungs.		"Guidelines for the planning, preparation and analysis of lectures."	
III.	*Conclusions stage.* Summary of the lecture. General conclusions. Lecturer's answer to possible questions. Self-study assignment		List of literature, question, task.	5%

4. Content of the lecture material:

- structural and logical scheme of the topic content;
- the text of the lecture.

5. Materials for activating students during the lecture:

1) Infant Respiratory Failure Syndrome is a life threatening disorder associated with impaired lung function resulting from surfactant deficiency.

2) The increased resistance of the airways in asthma is predetermined by the contraction of the smooth muscle tissue of the bronchioles.

Questions:
1. Respiratory system. Morphological and functional characteristics. Respiratory and non-respiratory functions, airways. The structure and function of the inner surface of the nasal cavity.

2. Respiratory system. Morphological and functional characteristics. Airways. Sources of development. The structure and function of the trachea and bronchi of various sizes.
3. Lungs. Morphological and functional characteristics. Sources of development. The structure of the respiratory department. Aerogematic barrier. Features of the blood supply. Age-related changes. 4. The structure and histophysiology of the lung acinus.

6. General material and methodological support of the lecture:
- classrooms;
- equipment;
- equipment;
- illustrative materials.

List of recommended literature .

The main one:

1.Lutsyk O.D., Tchaikovsky Y.B. Histology, cytology, embryology Vinnytsia, New Book, 2018.
2.Barinov E.F., Tchaikovsky Y.B. General histology and embryology of internal organs: textbook.Kyiv: Medicine; 2013
3.Wojciech Pawlina. Histology: textbook and atlas. WSV: Medicine, 2021.

Additional:

1.Histology and embryology of internal organs: textbook / E.F. Barinov, Y.B. Tchaikovsky, O.M. Sulaeva et al.
2.Cytology of human organs and tissues edited by L.S.Bolgova. Kyiv: Book-plus, 2018, p.288

Theme: "Respiratory system." *Addition*

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

phonation, smell sensation and immune defense.

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

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

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

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

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

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

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

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

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

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

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

The adventitia of larynx is formed by loose connective tissue.

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

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

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

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

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

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

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

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

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

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

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

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

The bronchial tree. At the level of T5 (fifth thoracic vertebra) the trachea divides into two main bronchi (right and left), which extend to the right and left lung respectively. On entering the hilum of the lung, each main bronchus divides into the lobar bronchi. The lobar bronchi are in turn divided into segmental bronchi, subsegmental bronchi, small bronchi, and terminal bronchioles. According to their diameter and structure, all named bronchi are classified into main, large, medium, small bronchi and terminal bronchioles.

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

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

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

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

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

The adventitia is formed by loose connective tissue.

The medium bronchi are from 2 to 5mm in diameter. Compared with the large bronchi, the epithelium of medium bronchi consists of less tall epithelial cells; but it still remains ciliated, pseudostratified columnar epithelium containing goblet cells. The lamina propria contains more elastic fibers. Within the submucosa the

mixed sero-mucous glands are found. In the fibrocartilaginous layer the hyaline cartilage is represented as small “islands”. As the cartilaginous islands become smaller, the hyaline cartilage is substituted into the elastic one.

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

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

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

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

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

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

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

The respiratory portions of the lung are the sites of gas exchange between blood and alveolar air. The pulmonary acinus begins with the respiratory bronchiole, which arises immediately from the terminal bronchiole. The respiratory

bronchioles are lined with simple cuboidal epithelium, within which the ciliated cells occasionally occur. The muscularis mucosae wears and breaks up into separated, circularly arranged bundles of the smooth muscle. The loose connective tissue of adventitia continues with the interstitial connective tissue.

The respiratory bronchiole is in turn divided into respiratory bronchioles of the

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

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

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

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

The respiratory alveolar cells are extremely thin squamos cells, which lie most of the surface of the alveoli. They contain short cytoplasmic projections on their apical surface, which increases the contact area between alveolar epithelium and air. The cytoplasm of the respiratory alveolar cells contains pynocytic vesicles and small mitochondria. The nuclear-free portions of respiratory alveolar cells adjoin the nuclear-free portions of endothelial cells of capillaries. In such areas the basal lamina of capillary endothelium is closely attached to the basal lamina of respiratory alveolar cells. A thin layer of surfactant, a type I epithelial cell and its basal lamina, and a capillary endothelial cell and its basal lamina are the components of the thinnest air-blood barrier. Often, these two basal laminae are fused. Connective tissue cells and fibers that may be present between the two basal laminae widen the air–blood barrier.

The secretory alveolar cells lie on the common basal lamina with the respiratory alveolar cells. These cells are cuboidal in shape; their cytoplasm contains well-developed Golgi apparatus, ER. Their apical cytoplasm is filled with granules that

are resolved with the TEM as stacks of parallel membrane lamellae, the lamellar bodies. They are rich in a mixture of phospholipids, neutral lipids, and proteins,

that is secreted by exocytosis to form an alveolar lining, surface-active agent called surfactant.

The surfactant consists of three phases:

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

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

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

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

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