

**MINISTRY OF HEALTH OF UKRAINE
HIGHER STATE EDUCATIONAL ESTABLISHMENT OF
UKRAINE
«UKRAINIAN MEDICAL STOMATOLOGICAL
ACADEMY»
Department of histology, cytology and embryology**

***HISTOLOGY, CYTOLOGY AND
EMBRYOLOGY
Special histology and embryology***

**METHODICAL INSTRUCTIONS
for the students
MEDICAL FACULTY**

MODULE 2

**“A P P R O V E D”
at the meeting of the Department
of Histology, Cytology and Embryology
Protocol № 1 by 30 August 2017**

<i>Subject</i>	<i>Histology, cytology and embryology</i>
<i>Modul №2</i>	<i>Histology, cytology and embryology</i>
<i>Submodul №3</i>	<i>Special histology</i>
<i>Topic 1</i>	NERVOUS SYSTEM. SPINAL CORD. SPINAL GANGLION. PERIPHERAL NERVES

Hours: 2

1. The topic basis: the topic “**NERVOUS SYSTEM. SPINAL CORD. SPINAL GANGLION. PERIPHERAL NERVES**” is very important for future doctors in their professional activity, positively influences the students in their attitude to the future profession, forms professional skills and experience as well as taking as a principle the knowledge of the subject learnt.

2. The aims of the training course:

- 1) To have general knowledge of the topic studied.
- 2) To understand, to remember and to use the knowledge received.
- 3) To learn the classification, structure and functions of the different histological methods.
- 4) To form the professional experience by reviewing, training and authorizing it.
- 5) To be able to carry out laboratory and experimental work.

3. Materials for the before – class work self – preparation work:

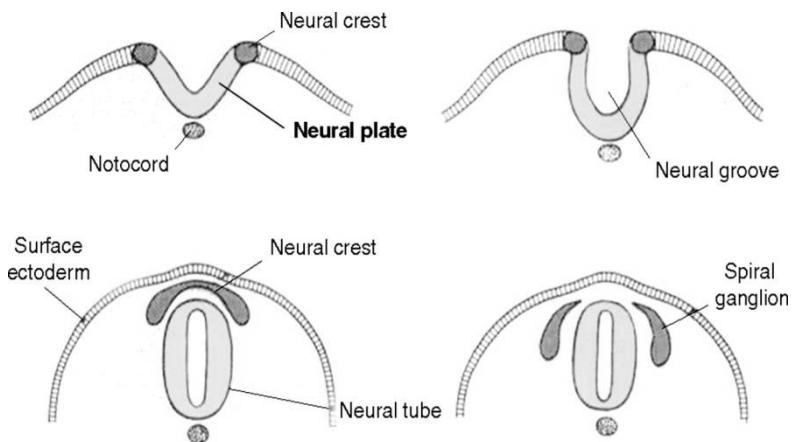
3.1 Basic knowledge, experience, skills necessary for studying the topic in connection with other subjects:

	To know	To be able to
Med. Biology	the structure of the cells and tissues	work with a light microscope
Med. Physics	the structure of the light and electron microscopes	work with a light microscope
Organic Chemistry	the chemical content of the cell	Speak of the topic

The contents of the topic:

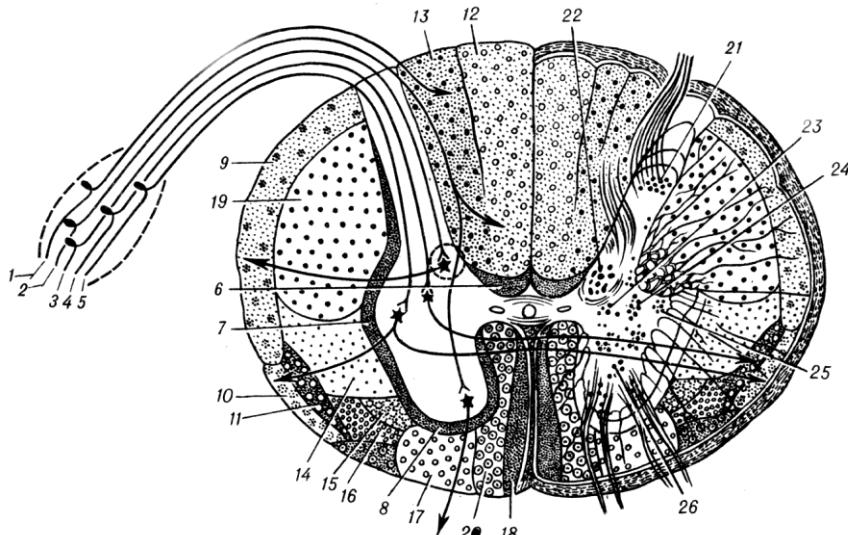
Neural and other cell derivatives of neural tube and crest

- **Neural Tube**
 - *CNS*: Neurons, Astrocytes, Oligodendrocytes, Ependymal cells, Special central glia
- **Neural Crest**
 - *PNS*: Sensory- & autonomic-ganglion neurons, Adrenal neurons, Satellite cells, Schwann cells, Enteric glia
 - *Others*: Chromaffin cells, C-cells, Melanocytes, some Cardiac (outflow tract) & Carotid-body cells
- **Neural Crest in Mesectoderm**
 - *Anterior Cranial Skeletal Tissues*: Osteoblasts, Chondroblasts
 - *Dental Tissues*: Odontoblasts, Cementoblasts, Ligament fibroblasts
 - *Head Muscles & Connective Tissues*: Smooth & skeletal muscle cells, Fibroblasts, Adipocytes, Meningeal cells.



Spinal cord

1. Enclosed in CT *meninges* with pia extending in at the *ventral fissure* with the anterior spinal artery.
2. The ependyma-lined *central canal* lies centrally.
3. Surrounding the canal in a butterfly shape is grey matter (grey to the naked eye when fresh and unstained).
4. *Horns* of grey matter partly separate three columns of white matter: dorsal (posterior), lateral, and ventral (anterior) columns.



5. *White matter* is composed of nerve fibres, many thickly *myelinated*, running mainly up or down the cord. Generally, fibres projecting to or from a particular brain region run together in a *tract*.
6. *Grey matter* has groups of multipolar nerve cell bodies, nerve fibres entering and leaving the grey matter, and preterminal fibre branches (poorly myelinated, hence the grey colour in the fresh, unstained cord).
7. Glial cells and blood vessels are in both white and grey matter. Grey matter is more vascular. The oligodendrocyte is the principal glial cell of white matter.
8. Roots of nerve fibres enter the cord on the dorsal sides; other roots leave on the ventral sides.
9. *Substantia gelatinosa* lies at the extreme margin of the dorsal horn of grey matter.
10. The *multipolar neurons* include: motoneurons, whose axons pass out of the cord to join peripheral nerves and serve skeletal muscles; and short-axon interneuron/Renshaw cells.

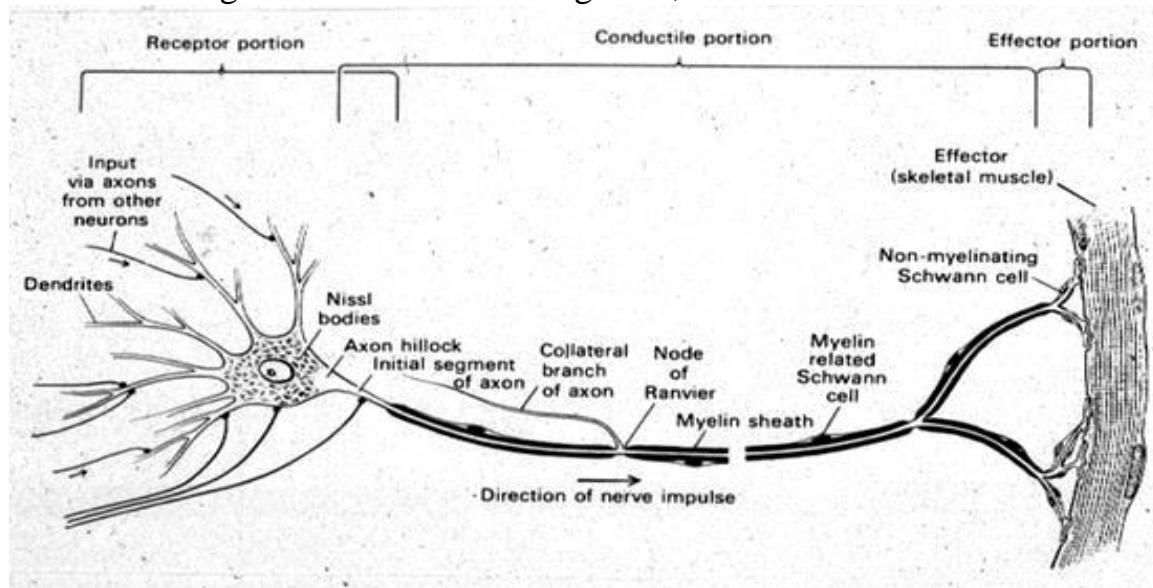
Brain stem

- Resembles the spinal cord in having nerve cell bodies grouped in nuclei and nerve fibres in tracts.
- Some *special nuclei* of the brain stem and hypothalamus are:
 - The *reticular formation* is an extensive system of groups of neurons serving many vital tasks, but whose nuclear organization is hard to discern.
 - Neurons of the *substantia nigra* contain melanin pigment and dopamine.
 - Certain hypothalamic nuclei have *neurosecretory* neurons.

Peripheral Nervous System Peripheral Nerve

Nerves fibres present may be:

1. centripetal *sensory* fibres,
2. centrifugal *motor* fibres to skeletal muscle,
3. centrifugal *autonomic* fibres to glands, and smooth muscles.

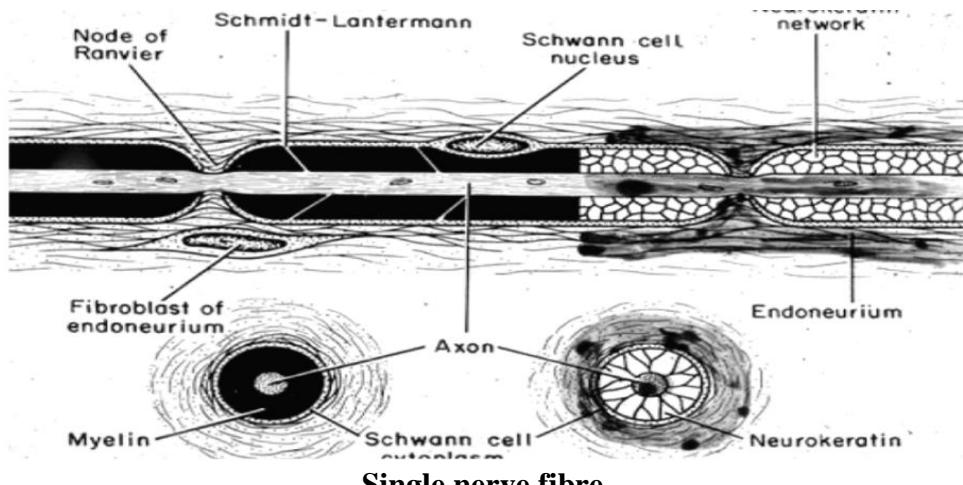


Connective tissue wrappings

1. *Epineurium* around the whole nerve trunk with blood and lymphatic vessels (vasa nervorum), collagen and fibroblasts, and fat cells.
2. *Perineurium* around each fasciculus of nerve fibres: the site of the blood-nerve barrier. Perineurial cells are tightly attached.
3. *Endoneurium* around each individual myelinated nerve fibre, but separated from its Schwann cells by a basal lamina.

Cross-section of nerve in LM shows:

1. Close-to-round shape with no lumen; CT coat and divisions.
2. Nuclei of Schwann cells, fibroblasts and a few capillaries.
3. Axons and some remnant of myelin (so-called neurokeratin) around them (with H & E staining); or brownish-black rings (myelin with an unstained axon within each) (osmium tetroxide treatment).
4. The eosin of H & E shows the collagen of epi- and perineurium, which remain very pale yellow with osmium. Osmium tetroxide will, however, show intensely black the fat in the adipocytes, usually present in epineurium.

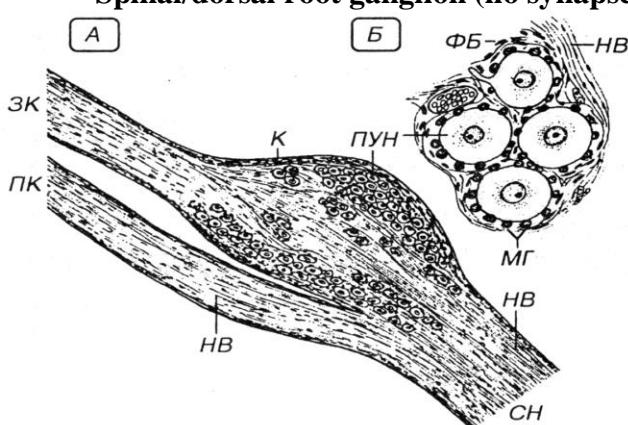


Single nerve fibre

Single fibres that have branched off from nerves to pass to and enter some kind of *end-organ* remain unseen unless special techniques are used, although the CT capsule and supporting cells of the end-organ are usually discernible with HE staining. The fibre-revealing techniques are EM, silver impregnation, or histochemical ones for cholinesterase, neuropeptides, and catecholamines.

Ganglia

Spinal/dorsal root ganglion (no synapse involved)



- Has a collagenous connective tissue investment.
- Many *bundles* of thick, myelinated, nerve fibres separate *groups* of large, round-bodied nerve cells.
- Each neuron has a thin CT capsule like an endoneurium.
- Between capsule and neuron is a layer of small *satellite cells* of a glial nature.
- Neuron* has only one process (not a dendrite) branching into two near to the soma. The thinner axon runs centrally via a dorsal root into the spinal cord, the thicker runs peripherally to a nervous receptor.

3.3. Literature recommended

Main Sources:

- L.C. Junqueira, J. Carneiro - "Basic histology" – 11 edition - 2005.
- A.S. Pacurar, J.W. Bigbee – "Digital histology" – Virginia - 2004.
- "Color Atlas of basic histology" – R.Berns – 2006.
- Sadler T.V. – "Medical embryology" Montana – 1999.
- Ronald W., Dudek Ph.D. – "Embryology" 2 edition – 1998.
- Inderbir Singh Textbook of Human Histology.- Jaypee. India. - 1997.

Additional ones:

- Methodical Instructions.

3.4 How to work with the literature recommended:

Main tasks	Recommendations
To review the material	To use the material studied
To learn the material	To use the material on pages
To read and compose the plan	To learn the new material and be ready to write a summary
To answer the questions	
To do the test on the material	To be ready to give an answer to the following:
To be ready to answer the topic	

3.5. Self-control material:

A. Questions to be answered:

1. Nervous system. General morfo-functional characteristic.
2. Sources of development.
3. Peripheral nervous system.
4. A nerve. A constitution and regeneration of the nerves.
5. Spinal ganglia. Morfo-functional characteristic. Cellular structure.
6. Spinal cord, morfo-functional characteristic. A constitution of the grey and white matter. Cellular structure.
7. Sensing and motoring paths of a spinal cord as parts of reflex arcs.

B. Test tasks to be done: Tests are applied

4. Self-preparation in the classroom.

1) Listen to the information. 2) Work with the tables and a Light microscope. 3) Ask about the problems that haven't been found in the information given. 4) To sketch in the album the investigated preparations.

5. Self-preparation work at home.

1) Review the material learnt in the classroom. 2) Compose the plan of your answer. 3) Answer the questions to this topic. 4) Do the test given above.

6. The subject of the research work.

“Spinal cord's diseases”

“Regeneration of the cutting nerves”

<i>Subject</i>	<i>Histology, cytology and embryology</i>
<i>Modul №2</i>	<i>Histology, cytology and embryology</i>
<i>Submodul №3</i>	<i>Special histology</i>
<i>Topic 2</i>	CEREBRAL CORTEX. CEREBELLUM

Hours: 2

1. The topic basis: the topic “CEREBRAL CORTEX. CEREBELLUM” is very important for future doctors in their professional activity, positively influences the students in their attitude to the future profession, forms professional skills and experience as well as taking as a principle the knowledge of the subject learnt.

2. The aims of the training course:

- 1) To have general knowledge of the topic studied.
- 2) To understand, to remember and to use the knowledge received.
- 3) To learn the classification, structure and functions of the different histological methods.
- 4) To form the professional experience by reviewing, training and authorizing it.
- 5) To be able to carry out laboratory and experimental work.

3. Materials for the before – class work self – preparation work:

3.1 Basic knowledge, experience, skills necessary for studying the topic in connection with other subjects:

	To know	To be able to
Med. Biology	the structure of the cells and tissues	work with a light microscope
Med. Physics	the structure of the light and electron microscopes	work with a light microscope
Organic Chemistry	the chemical content of the cell	Speak of the topic

The contents of the topic:

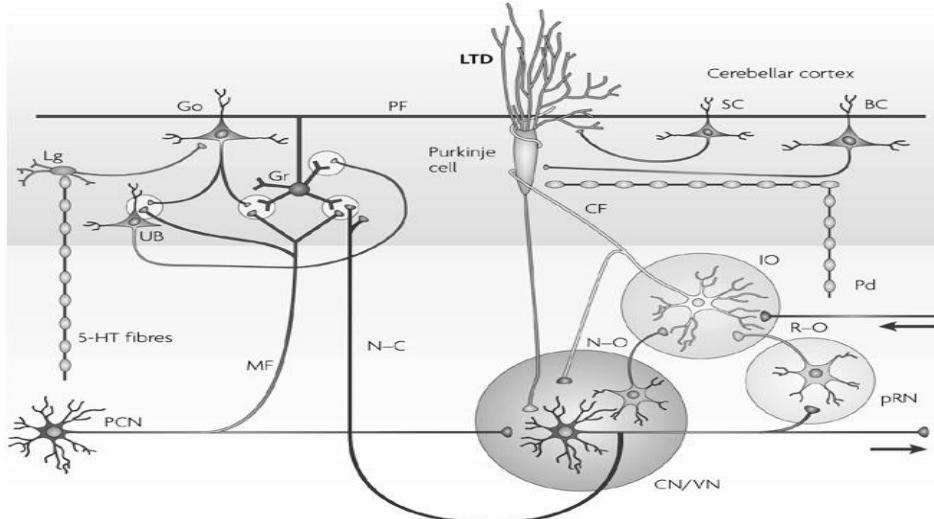
The brain, spinal cord and optic nerves are enclosed in vascular connective tissue sheaths - the *meninges* - and protected by bone. From the inner meninges, the leptomeninges, blood vessels pass into the substance of the brain to vascularize it extensively and to supply the CSF-forming *choroid plexus*. CSF dilutes and carries away metabolites and excess neurotransmitters, and drains to form a cushion around the brain.

CNS elements

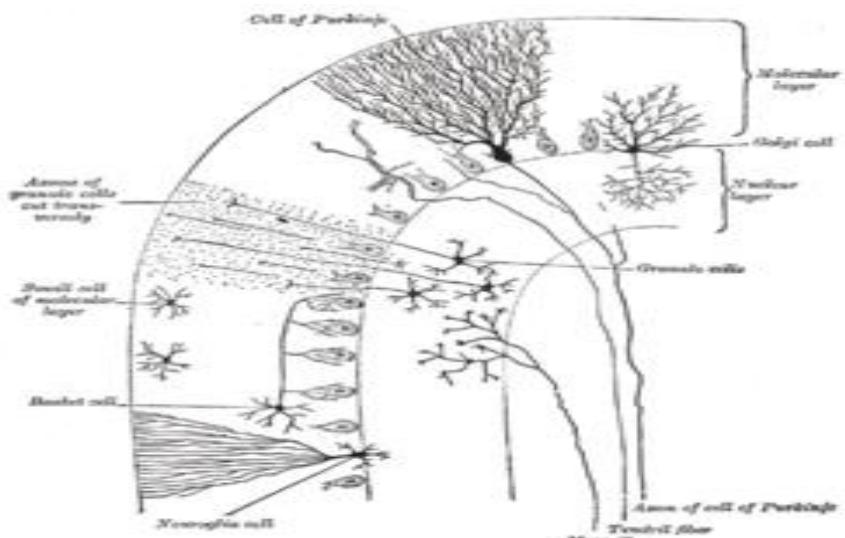
The two cells specific to neural tissues are the *neuron/nerve cell* and the *glia cell*, for the latter of which several varieties exist. Some of the glial cells are used to form a layer - *glia limitans* - separating neurons from the numerous blood vessels and the enclosing pia matter.

Special Features of Brain Regions

Cerebellar and cerebral cortices



Microcircuitry of the cerebellum. (+): excitatory; (-): inhibitory; MF: Mossy fiber; DCN: Deep cerebellar nuclei; IO: Inferior olive; CF: Climbing fiber; GC: Granule cell; PF: Parallel fiber; PC: Purkinje cell; GgC: Golgi cell; SC: Stellate cell; BC: Basket cell



Transverse section of a cerebellar folium, showing principle cell types and connections

Two types of neuron play dominant roles in the cerebellar circuit: Purkinje cells and granule cells. Three types of axons also play dominant roles: mossy fibers and climbing fibers (which enter the cerebellum from outside), and parallel fibers (which are the axons of granule cells). Functionally, there are two main pathways through the cerebellar circuit, originating from mossy fibers and climbing fibers, both terminating in the deep cerebellar nuclei.

Mossy fibers project directly to the deep nuclei, but also give rise to the pathway: mossy fiber → granule cells → parallel fibers → Purkinje cells → deep nuclei. Climbing fibers project to Purkinje cells and also send collaterals directly to the deep nuclei. The mossy fiber and climbing fiber inputs each carry fiber-specific information; the cerebellum also receives dopaminergic, serotonergic, noradrenergic, and cholinergic inputs that presumably perform global modulation.

The cerebellar cortex is divided into three layers. At the bottom lies the thick granular layer, densely packed with granule cells, along with much smaller numbers of

interneurons, mainly Golgi cells. In the middle lies the Purkinje layer, a narrow zone that contains only the cell bodies of Purkinje cells. At the top lies the molecular layer, which contains the flattened dendritic trees of Purkinje cells, along with the huge array of parallel fibers penetrating the Purkinje cell dendritic trees at right angles. This outermost layer of the cerebellar cortex also contains two types of inhibitory interneurons, stellate cells and basket cells. Both stellate and basket cells form GABAergic synapses onto Purkinje cell dendrites.

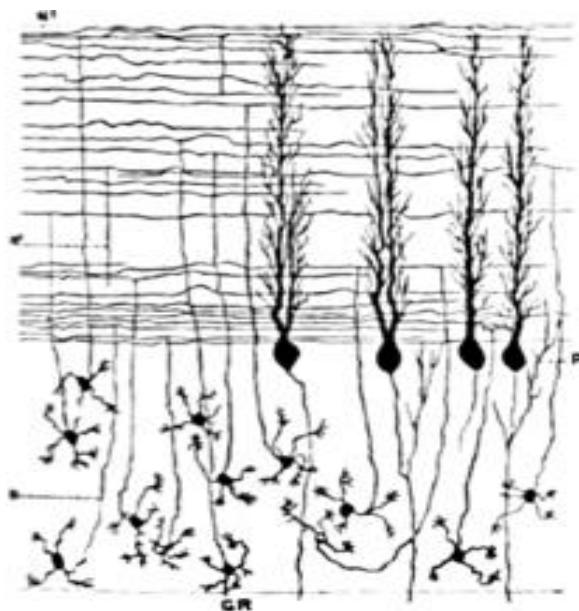
Purkinje cells

Purkinje cells are among the most distinctive neurons in the brain, and also among the earliest types to be recognized—they were first described by the Czech anatomist Jan Evangelista Purkyně in 1837. They are distinguished by the shape of the dendritic tree: the dendrites branch very profusely, but are severely flattened in a plane perpendicular to the cerebellar folds. Thus, the dendrites of a Purkinje cell form a dense planar net, through which parallel fibers pass at right angles. The dendrites are covered with dendritic spines, each of which receives synaptic input from a parallel fiber. Purkinje cells receive more synaptic inputs than any other type of cell in the brain—estimates of the number of spines on a single human Purkinje cell run as high as 200,000. The large, spherical cell bodies of Purkinje cells are packed into a narrow layer (one cell thick) of the cerebellar cortex, called the Purkinje layer. After emitting collaterals that innervate nearby parts of the cortex, their axons travel into the deep cerebellar nuclei, where they make on the order of 1,000 contacts each with several types of nuclear cells, all within a small domain. Purkinje cells use GABA as their neurotransmitter, and therefore exert inhibitory effects on their targets.

Drawing of a Purkinje cell from cat cerebellum

Purkinje cells form the heart of the cerebellar circuit, and their large size and distinctive activity patterns have made it relatively easy to study their response patterns in behaving animals using extracellular recording techniques. Purkinje cells normally emit action potentials at a high rate even in the absence of synaptic input. In awake, behaving animals, mean rates averaging around 40 Hz are typical. The spike trains show a mixture of what are called simple and complex spikes. A simple spike is a single action potential followed by a refractory period of about 10 msec; a complex spike is a stereotyped sequence of action potentials with very short inter-spike intervals and declining amplitudes. Physiological studies have shown that complex spikes (which occur at baseline rates around 1 Hz and never at rates much higher than 10 Hz) are reliably associated with climbing fiber activation, while simple spikes are produced by a combination of baseline activity and parallel fiber input. Complex spikes are often followed by a pause of several hundred msec during which simple spike activity is suppressed.

Granule cells



Cerebellar granule cells, in contrast to Purkinje cells, are among the smallest neurons in the brain. They are also easily the most numerous neurons in the brain: in humans, estimates of their total number average around 50 billion, which means that about 3/4 of the brain's neurons are cerebellar granule cells. Their cell bodies are packed into a thick layer at the bottom of the cerebellar cortex. A granule cell emits only four to five dendrites, each of which ends in an enlargement called a dendritic claw. These enlargements are sites of excitatory input from mossy fibers and inhibitory input from Golgi cells.

Granule cells, parallel fibers, and Purkinje cells with flattened dendritic trees

The thin, unmyelinated axons of granule cells rise vertically to the upper (molecular) layer of the cortex, where they split in two, with each branch traveling horizontally to form a parallel fiber; the splitting of the vertical branch into two horizontal branches gives rise to a distinctive "T" shape. A parallel fiber runs for an average of 3 mm in each direction from the split, for a total length of about 6 mm (about 1/10 of the total width of the cortical layer). As they run along, the parallel fibers pass through the dendritic trees of Purkinje cells, contacting one of every 3–5 that they pass, making a total of 80–100 synaptic connections with Purkinje cell dendritic spines. Granule cells use glutamate as their neurotransmitter, and therefore exert excitatory effects on their targets.

Granule cells receive all of their input from mossy fibers, but outnumber them 200 to 1 (in humans). Thus, the information in the granule cell population activity state is the same as the information in the mossy fibers, but recoded in a much more expansive way. Because granule cells are so small and so densely packed, it has been very difficult to record their spike activity in behaving animals, so there is little data to use as a basis of theorizing. The most popular concept of their function was proposed by David Marr, who suggested that they could encode combinations of mossy fiber inputs. The idea is that with each granule cell receiving input from only 4–5 mossy fibers, a granule cell would not respond if only a single one of its inputs was active, but would respond if more than one were active. This combinatorial coding scheme would potentially allow the cerebellum to make much finer distinctions between input patterns than the mossy fibers alone would permit.

Mossy fibers

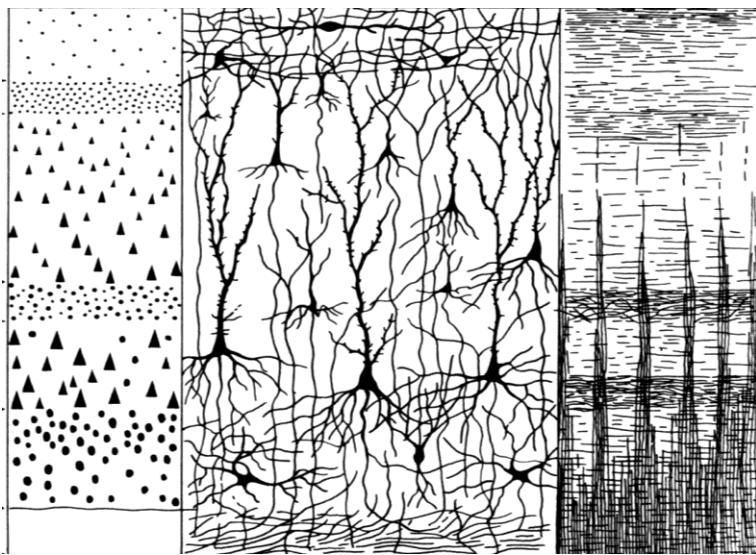
Mossy fibers enter the granular layer from their points of origin, many arising from the pontine nuclei, others from the spinal cord, vestibular nuclei, etc. In the human cerebellum, the total number of mossy fibers has been estimated at about 200 million.[4] These fibers form excitatory synapses with the granule cells and the cells

of the deep cerebellar nuclei. Within the granular layer, a mossy fiber generates a series of enlargements called rosettes. The contacts between mossy fibers and granule cell dendrites take place within structures called glomeruli. Each glomerulus has a mossy fiber rosette at its center, and up to 20 granule cell dendritic claws contacting it. Terminals from Golgi cells infiltrate the structure and make inhibitory synapses onto the granule cell dendrites. The entire assemblage is surrounded by a sheath of glial cells.[4] Each mossy fiber sends collateral branches to several cerebellar folia, generating a total of 20–30 rosettes; thus a single mossy fiber makes contact with an estimated 400–600 granule cells.[4]

Climbing fibers

Purkinje cells also receive input from the inferior olfactory nucleus (IO) on the contralateral side of the brainstem, via climbing fibers. Although the IO lies in the medulla oblongata, and receives input from the spinal cord, brainstem, and cerebral cortex, its output goes entirely to the cerebellum. A climbing fiber gives off collaterals to the deep cerebellar nuclei before entering the cerebellar cortex, where it splits into about 10 terminal branches, each of which innervates a single Purkinje cell. In striking contrast to the 100,000-plus inputs from parallel fibers, each Purkinje cell receives input from exactly one climbing fiber; but this single fiber "climbs" the dendrites of the Purkinje cell, winding around them and making a total of up to 300 synapses as it goes. The net input is so strong that a single action potential from a climbing fiber is capable of producing an extended complex spike in the Purkinje cell: a burst of several spikes in a row, with diminishing amplitude, followed by a pause during which activity is suppressed. The climbing fiber synapses cover the cell body and proximal dendrites; this zone is devoid of parallel fiber inputs.

Climbing fibers fire at low rates, but a single climbing fiber action potential induces a burst of several action potentials in a target Purkinje cell (a complex spike). The contrast between parallel fiber and climbing fiber inputs to Purkinje cells (over 100,000 of one type versus exactly one of the other type) is perhaps the most provocative feature of cerebellar anatomy, and has motivated much of the theorizing. In fact, the function of climbing fibers is the most controversial topic concerning the cerebellum. There are two schools of thought, one following Marr and Albus in holding that climbing fiber input serves primarily as a teaching signal, the other holding that its function is to shape cerebellar output directly. Both views have been defended in great length in numerous publications. In the words of one review, "In trying to synthesize the various hypotheses on the function of the climbing fibers, one has the sense of looking at a drawing by Escher. Each point of view seems to account for a certain collection of findings, but when one attempts to put the different views together, a coherent picture of what the climbing fibers are doing does not appear. For the majority of researchers, the climbing fibers signal errors in motor performance, either in the usual manner of discharge frequency modulation or as a single announcement of an 'unexpected event'. For other investigators, the message lies in the degree of ensemble synchrony and rhythmicity among a population of climbing fibers."



Cerebral neocortex: 1

Molecular layer. Layers 2, 3, 4, 5, 6 with varying proportions of stellate, fusiform and small, medium, and large pyramidal cells (white matter).

The number of layers to be clearly seen depends on the particular area of the cerebral cortex and the criteria of the investigator. Thus Cajal worked with an 8-layered scheme, whereas Brodmann adopted 6 - today's choice. Even so, in the motor region only 5 are to be easily made out

Divisions of the cerebral cortex

- *Anatomical*, based on the lobes, and the pattern of sulci and gyri.
- *Functional*, founded on functional specializations revealed by extirpation, clinical lesions, stimulation of certain regions, on gross and microrecording of the neurons' electrical activity, or PET-detected patterns of glucose use, in response to specific stimuli, e.g., visual.
 - *Histological*, based on cell- or cytoarchitecture, and fibroarchitecture. Histologically defined areas often coincide with functional areas. A conservative view of the histological parcellation of the cortex is now taken, that commonly adopts the numbering used by Brodmann, but does not acknowledge all his subdivisions in the frontal, parietal and temporal association areas.
 - *Projection* areas demonstrated by histological studies of degeneration or transport to be connected with particular brainstem nuclei.

Meninges

1. *Dura mater* - (pachymeninx) - dense fibrous CT; osteoblastic outside (skull), or mesothelial facing the epidural space (spine); specialized layer of dural fibroblasts* attaches dura to arachnoid.
2. *Arachnoid complex* - apposed to the dura is a layer of well attached cells, several cells thick; between this layer and the pia are open subarachnoid spaces, crossed by trabeculae of collagen, clad in other arachnoid cells, and supporting the vessels.
3. *Pia mater* - thin cellular, vascular and collagenous layer, adherent to the BL of the nervous tissue.

(Arachnoid and pia comprise the *leptomeninges*.)

The idea that the arachnoid was merely a membrane led to the mistaken notion that it had to be separated from the dura by a 'sub-dural space'. Such a space only arises by a forcible cleaving between the fibroblasts of the inner dura, as occurs in 'sub-dural' haematomas.

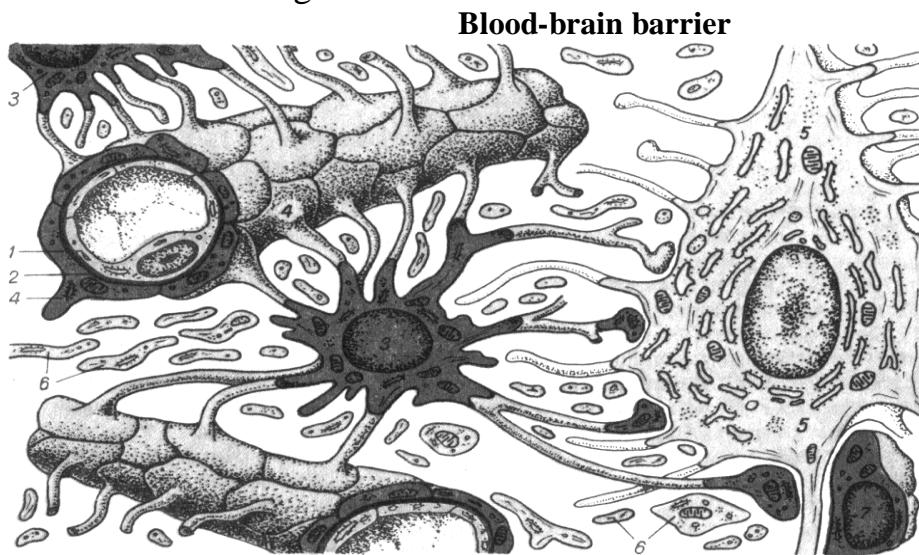
Ependyma and choroid plexus

Ependymal epithelium lining the ventricular cavities and canals of the CNS is simple, columnar or cuboidal. In regions of each ventricle, tufts of blood vessels (mainly fenestrated capillaries) project out from the pia, and are covered by a loose CT coat, then a layer of cuboidal *ependymal cells* on a BL. This choroid plexus forms *cerebrospinal fluid* (CSF) secreted into the ventricles.

These plexus ependymal cells have ion pumps, deep basal infoldings, and luminal microvilli.

Cerebrospinal fluid's return to blood

The *subarachnoid space*, which dilates into chambers, cisterns, fills with CSF spilled out of the ventricular system via the *foramina of Lushka and Magendie* in the fourth ventricle. Some CSF may come out of the brain tissue via spaces between blood vessels and the pia. CSF returns to the *dural sinus blood* through the thin walls of the *arachnoid villi* and granulations.



The blood capillaries serving the brain tissue have a characteristic structure of *unfenestrated endothelial cells* held together by *tight/occluding junctions* on a thick basal lamina, whose outer surface is enclosed by glial cell processes (astrocytes' pedicles). The endothelium has *few transcytotic vesicles* and is very selective in what it transports. In most regions of the brain the endothelium blocks the passage of most materials from the blood into the neural tissue, and a *blood-brain barrier* (BBB) is said to exist for such substances.

3.3. Literature recommended

Main Sources:

1. L.C. Junqueira, J. Carneiro - “Basic histology” – 11 edition - 2005.
2. A.S. Pacurar, J.W. Bigbee – “Digital histology” – Virginia - 2004.
3. “Color Atlas of basic histology” – R.Berns – 2006.
4. Sadler T.V. – “Medical embryology” Montana – 1999.
5. Ronald W., Dudek Ph.D. – “Embryology” 2 edition – 1998.
6. Inderbir Singh Textbook of Human Histology.- Jaypee. India. - 1997.
7. Ten Cate A.R. Oral Histology.- St.Louis, Baltimore, Toronto.- 1995.
8. William A., Beresford M.A. Cytology and Histology.- Anatomy department, West Virginia University, USA.- 1992.
9. K.E. Jonson - “Histology and cell biology” – 2 edition – Washington – 1991.

Additional ones:

1. Methodical Instructions.

3.4 How to work with the literature recommended:

Main tasks	Recommendations
To review the material	To use the material studied
To learn the material	To use the material on pages
To read and compose the plan	To learn the new material and be ready to write a summary
To answer the questions	To be ready to give an answer to the following:
To do the test on the material	
To be ready to answer the topic	

3.5. Self-control material:**A. *Questions to be answered:***

1. General morfo-functional characteristic of large hemispheres.
2. Cytoarchitectonic. Myeloarchitectonic.
3. Neuronic organization of a cortex of large hemispheres.
4. Cerebellum. Constitution and functional characteristic.
5. A neuronic structure of the cerebellum cortex.

B. *Test tasks to be done: Tests are applied***4. Self-preparation in the classroom.**

- 1) Listen to the information.
- 2) Work with the tables and a Light microscope.
- 3) Ask about the problems that haven't been found in the information given.
- 4) To sketch in the album the investigated preparations.

5. Self-preparation work at home.

- 1) Review the material learnt in the classroom.
- 2) Compose the plan of your answer.
- 3) Answer the questions to this topic.
- 4) Do the test given above.

6. The subject of the research work.

“Age changes of the cerebral cortex.”

<i>Subject</i>	<i>Histology, cytology and embryology</i>
<i>Modul №1</i>	<i>Histology, cytology and embryology</i>
<i>Submodul №3</i>	<i>Special histology</i>
<i>Topic 3</i>	VEGETATIVE NERVOUS SYSTEM.

Hours: 2

1. The topic basis: the topic “**VEGETATIVE NERVOUS SYSTEM**” is very important for future doctors in their professional activity, positively influences the students in their attitude to the future profession, forms professional skills and experience as well as taking as a principle the knowledge of the subject learnt.

2. The aims of the training course:

- 1) To have general knowledge of the topic studied.
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- 3) To learn the classification, structure and functions of the different histological methods.
- 4) To form the professional experience by reviewing, training and authorizing it.
- 5) To be able to carry out laboratory and experimental work.

3. Materials for the before – class work self – preparation work:

3.1 Basic knowledge, experience, skills necessary for studying the topic in connection with other subjects:

	To know	To be able to
Med. Biology	the structure of the cells and tissues	work with a light microscope
Med. Physics	the structure of the light and electron microscopes	work with a light microscope
Organic Chemistry	the chemical content of the cell	Speak of the topic

The contents of the topic:

The autonomic nervous system (ANS or visceral nervous system) is the part of the peripheral nervous system that acts as a control system functioning largely below the level of consciousness, and controls visceral functions. The ANS affects heart rate, digestion, respiration rate, salivation, perspiration, diameter of the pupils, micturition (urination), and sexual arousal. Whereas most of its actions are involuntary, some, such as breathing, work in tandem with the conscious mind.

It is classically divided into two subsystems: the parasympathetic nervous system and sympathetic nervous system. Relatively recently, a third subsystem of neurons that have been named 'non-adrenergic and non-cholinergic' neurons (because they use nitric oxide as a neurotransmitter) have been described and found to be integral in autonomic function, particularly in the gut and the lungs.

With regard to function, the ANS is usually divided into sensory (afferent) and motor (efferent) subsystems. Within these systems, however, there are inhibitory and excitatory synapses between neurones.

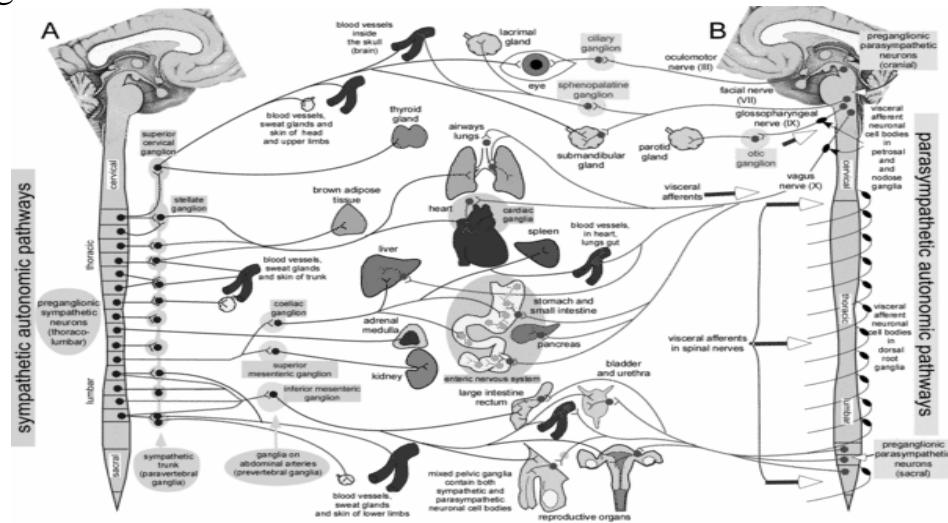
The enteric nervous system is sometimes considered part of the autonomic nervous system, and sometimes considered an independent system.

The sympathetic nervous trunk consists of sympathetic ganglia running directly adjacent to the spinal column. The adrenal medulla can be considered a sympathetic

ganglion; although separate from the main trunk, the sympathetic fibers run through the sympathetic trunk before synapsing in the adrenal medulla. The parasympathetic division consists of a sacral and cranial part. In the cranium the PSN originate from cranial nerves CN III (oculomotor nerve), CN VII (facial nerve), CN IX (glossopharyngeal nerve) and CN X (vagus nerve). In the sacral region of the body the PSN is derived from spinal nerves S2, S3 and S4, commonly referred to as the pelvic splanchnics. The reflex arcs of the ANS comprise a sensory (afferent) arm, and a motor (efferent or effector) arm. Only the latter is shown in the illustration.

Sensory neurons

The sensory arm is made of “primary visceral sensory neurons” found in the peripheral nervous system (PNS), in “cranial sensory ganglia”: the geniculate, petrosal and nodose ganglia, appended respectively to cranial nerves VII, IX and X. These sensory neurons monitor the levels of carbon dioxide, oxygen and sugar in the blood, arterial pressure and the chemical composition of the stomach and gut content. (They also convey the sense of taste, a conscious perception). Blood oxygen and carbon dioxide are in fact directly sensed by the carotid body, a small collection of chemosensors at the bifurcation of the carotid artery, innervated by the petrosal (IXth) ganglion.



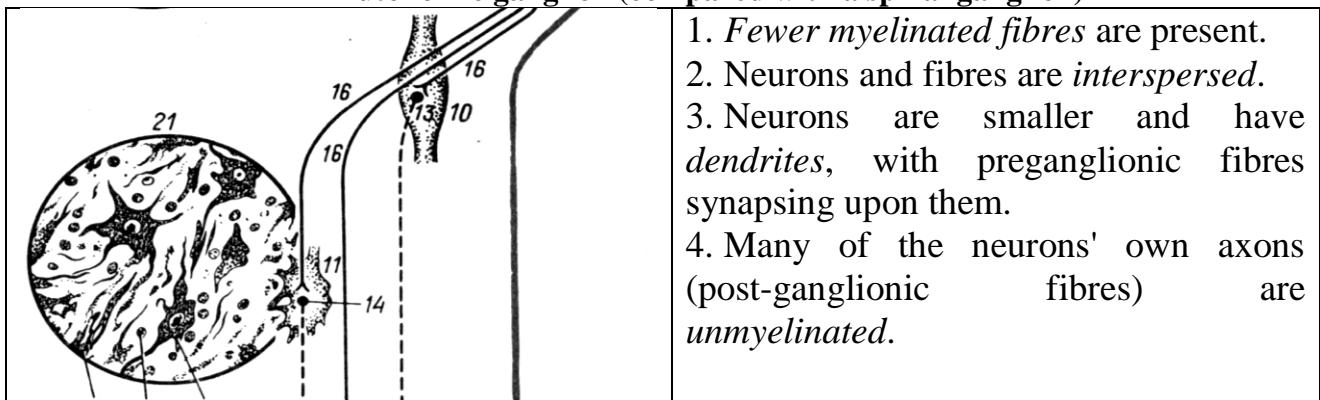
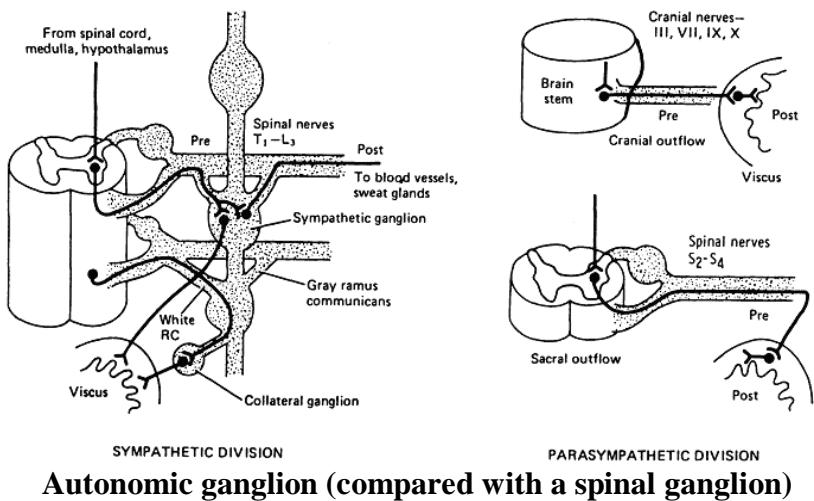
Motor neurons

Motor neurons of the ANS are also located in ganglia of the PNS, called “autonomic ganglia”. They belong to three categories with different effects on their target organs: sympathetic, parasympathetic and enteric.

Sympathetic ganglia are located in two sympathetic chains close to the spinal cord: the prevertebral and pre-aortic chains. Parasympathetic ganglia, in contrast, are located in close proximity to the target organ: the submandibular ganglion close to salivary glands, paracardiac ganglia close to the heart etc... Enteric ganglia, which as their name implies innervate the digestive tube, are located inside its walls and collectively contain as many neurons as the entire spinal cord, including local sensory neurons, motor neurons and interneurons. It is the only truly autonomous part of the ANS and the digestive tube can function surprisingly well even in isolation. For that reason the enteric nervous system has been called “the second brain”.

The activity of autonomic ganglionic neurons is modulated by “preganglionic neurons” (also called improperly but classically "visceral motoneurons") located in

the central nervous system. Preganglionic sympathetic neurons are in the spinal cord, at thoraco-lumbar levels. Preganglionic parasympathetic neurons are in the medulla oblongata (forming visceral motor nuclei: the dorsal motor nucleus of the vagus nerve (dmnX), the nucleus ambiguus, and salivatory nuclei) and in the sacral spinal cord. Enteric neurons are also modulated by input from the CNS, from preganglionic neurons located, like parasympathetic ones, in the medulla oblongata (in the dmnX). The feedback from the sensory to the motor arm of visceral reflex pathways is provided by direct or indirect connections between the nucleus of the solitary tract and visceral motoneurons.



In a cross-sectional view, several unmyelinated fibres share one Schwann cell, lying in many deep invaginations of its membrane. In the gut, enteric glia take the place of Schwann cells.

3.3. Literature recommended

Main Sources:

1. L.C. Junqueira, J. Carneiro - “Basic histology” – 11 edition - 2005.
2. A.S. Pacurar, J.W. Bigbee – “Digital histology” – Virginia - 2004.
3. Sadler T.V. – “Medical embryology” Montana – 1999.
4. Ronald W., Dudek Ph.D. – “Embryology” 2 edition – 1998.
5. Inderbir Singh Textbook of Human Histology.- Jaypee. India. - 1997.
6. K.E. Jonson - “Histology and cell biology” – 2 edition – Washington – 1991.

Additional ones:

1. Methodical Instructions.

3.4 How to work with the literature recommended:

Main tasks	Recommendations
To review the material	To use the material studied

To learn the material To read and compose the plan To answer the questions To do the test on the material To be ready to answer the topic	To use the material on pages To learn the new material and be ready to write a summary To be ready to give an answer to the following:
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3.5. Self-control material:

A. *Questions to be answered:*

1. Vegetative nervous system. Morfo-functional characteristic, departments.
2. Constitution of extra- and intramural ganglions.
3. Nucleuses of central departments of the vegetative nervous system.

B. *Test tasks to be done: Tests are applied*

4. Self-preparation in the classroom.

- 1) Listen to the information.
- 2) Work with the tables and a Light microscope.
- 3) Ask about the problems that haven't been found in the information given.
- 4) To sketch in the album the investigated preparations.

5. Self-preparation work at home.

- 1) Review the material learnt in the classroom.
- 2) Compose the plan of your answer.
- 3) Answer the questions to this topic.
- 4) Do the test given above.

<i>Subject</i>	<i>Histology, cytology and embryology</i>
<i>Modul №2</i>	<i>Histology, cytology and embryology</i>
<i>Submodul №3</i>	<i>Special histology</i>
<i>Topic 4</i>	SENSE ORGANS. EYES.

Hours: 2

1. The topic basis: the topic “SENSE ORGANS. EYES.” is very important for future doctors in their professional activity, positively influences the students in their attitude to the future profession, forms professional skills and experience as well as taking as a principle the knowledge of the subject learnt.

2. The aims of the training course:

- 1) To have general knowledge of the topic studied.
- 2) To understand, to remember and to use the knowledge received.
- 3) To learn the classification, structure and functions of the different histological methods.
- 4) To form the professional experience by reviewing, training and authorizing it.
- 5) To be able to carry out laboratory and experimental work.

3. Materials for the before – class work self – preparation work:

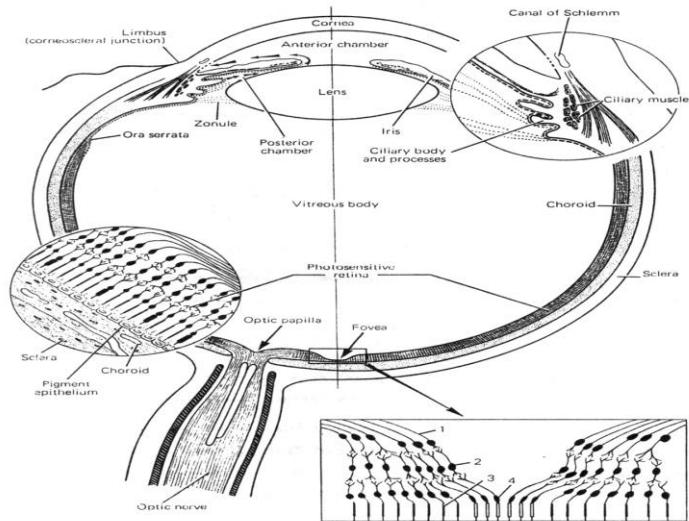
3.1 Basic knowledge, experience, skills necessary for studying the topic in connection with other subjects:

	To know	To be able to
Med. Biology	the structure of the cells and tissues	work with a light microscope
Med. Physics	the structure of the light and electron microscopes	work with a light microscope
Organic Chemistry	the chemical content of the cell	Speak of the topic

The contents of the topic:

The eyeball is one of a pair of roughly spherical, rigid structures sensitive to precise light stimuli and movable in coordination with its fellow. The camera performs a similar task, and the camera and the eye have in common:

1. a rigid supporting structure,
2. a light-excluding lining,
3. a moveable control or stop for the light allowed to enter,
4. a lens to focus that light on
5. a light-sensitive sheet, and
6. protective devices.



Before the histology is considered the overall anatomy should be briefly reviewed. Then the various structures will be taken in order as they are met on the light path. After that the accessory structures or adnexa will be dealt with, to lead to a final classification of all the structures along functional lines.

Cornea

1. *Stratified squamous epithelium* roughly five cells thick. Cells are held together by desmosomes, and supported on
2. *Bowman's membrane*: collagen fibrils in an amorphous matrix, viewed as a limiting condensation of the wide
3. *Corneal stroma*: orderly lamellae of collagen fibrils of uniform diameter, and keratocytes/fibroblasts with plenty of chondroitin and keratan sulphates; no blood vessels or lymphatics; takes up to 90 per cent of the corneal thickness.
4. *Descemet's membrane*: thick, distinct basal lamina with collagen fibrils in orderly array.
5. *Endothelium*: single layer of pavement/squamous cells, working to control the water content of the cornea.

Corneal functions: refraction, transparency, protection, and sensitivity (from intraepithelial free axons) for protective reflexes.

Anterior chamber

Limited by the posterior surface of the cornea and anterior surfaces of the iris and lens. It is filled to turgor with *aqueous humour* resembling serum, but very low in protein, and produced in the posterior chamber. To define this, some structures off the optical axis must be discussed.

Angle of the iris/anterior-chamber angle

Limbus forms the boundary between the cornea and the sclera which, although collagenous, is not transparent because of the disorder of its collagen fibres, its deficiency of sulphated ground substances, and its greater water content than the cornea.

Where Descemet's membrane terminates is a corneo-scleral *trabecular meshwork/pectinate ligament* enclosing the *spaces of Fontana*. These drain the aqueous humour towards *Schlemm's canal*, from which it passes to the episcleral or aqueous veins for venous return. The meshwork lies in the drainage angle between the sclera and the scleral spur.

Iris

1. Rings the *pupil* and controls, by dilation or constriction, the light entering and the depth of focus.
2. *Stroma*: loose vascular CT with a variable proportion of pigment cells/melanophores.
3. Posterior surface is covered by a *pigmented cuboidal epithelium* forming the inner layer of the *iridial retina*.
4. *Sphincter smooth muscle* near the pupillary margin receives para-sympathetic fibres, eliciting a contraction in response to increased light intensity.
5. *Dilator muscle* is a less substantial myoepithelial structure lying peripherally and posteriorly as the outer layer of the iridial retina, with fibres oriented radially and under sympathetic autonomic control.

Lens

1. Is a biconvex, elastic, transparent, protein structure with: thick 'elastic' glycoprotein outer *capsule* tending to give it a round form, under which lies an inner layer of *cuboidal epithelial cells* which peel off, elongate and insinuate themselves into the inner substance as *lens fibres* at the lens bow, thereby adding to lens *crystallins* - the main lens proteins.
2. The lens is held out of the rounder shape of its own inclination by its attaching *zonule/suspensory ligament* running to the smooth muscle ciliary body, which is itself firmly attached to the CT sclera. Lens nutrition is indirect by the aqueous humour.

Ciliary body

1. *Circular smooth muscle* (Müller's muscle): innervated by para-sympathetic fibres from the ciliary ganglion to contract, reducing tension in the zonule thus allowing the lens to become rounder and accommodate to near vision.
2. Radial and meridional muscle fibres (Brücke's muscle): function and innervation are uncertain.
3. Covered by a double layer of cuboidal epithelial cells (*ciliary retina*), with the outer ones heavily pigmented.
4. Gives off a number of projections, *ciliary processes*, covered by the two-layered epithelium and enclosing fenestrated blood capillaries, which produce the aqueous humour in a manner similar to the production of CSF by the choroid plexus.

Posterior chamber

1. Is limited by the posterior surface of the iris, the zonule and parts of the lens and ciliary body;
2. from the last of which comes the *aqueous humour* that fills it and passes out via the pupil to the anterior chamber.

Here the three *tunics* of the wall - sclera, uvea, retina - are most clearly recognized.

Vitreous body

1. Viscid and transparent fluid which, although mainly water, contains proteoglycans, hyaluronic acid, and collagen.
2. It fills the space bounded by the lens, zonule, pars plana and neural retina.
3. The *hyaloid canal* extends anteroposteriorly through it.

Neural retina

1. Curved membrane terminating its receptor function as an irregular line at the *ora serrata/ora terminalis*.

2. Contains a *pigment cell layer*, light-sensitive *photoreceptors*, and *nerve cells* arranged in layers to partially integrate the nervous information and transmit it out of the eye to the brain.

3. In most regions of the retina, light has to pass through the inner structures to reach the outer ones that are actually photosensitive.

4. *Retinal layers* in brief:

- Pigment-cell layer
- Photoreceptors
- External limiting membrane
- Outer nuclear layer
- Outer plexiform layer
- Inner nuclear layer
- Inner plexiform layer
- Ganglion cell layer
- Nerve-fibre layer
- Inner limiting membrane

When looking at slides of the posterior eye, resist the temptation to view the neural retina as an epithelium facing a lumen. The reference point for 'inner' and 'outer' is the unseen *vitreous*, not the BL on which the pigment cells sit.

Retinal layers details:

• *Pigmented epithelium*, simple cuboidal, lying on Bruch's wide membrane of basal laminae reinforced by collagen and elastic fibrils. Pigment cells absorb light, and destroy the used-up tips of the rods.

• *Photoreceptors*

- An *outer segment* of stacked, infolded cell membrane, incorporating the light-sensitive chemical, is connected via a cilium-like neck to
- an *inner segment* with mitochondria, Golgi body and ER for the continual replacement of outer segment materials.
- Then comes a dilation with the nucleus, and further inward the cell narrows to become an inner fibre before synapsing with the dendrites of bipolar nerve cells.
- The nerve and photoreceptor cells are separated by processes of the special glial cells, *Müller cells*.
- Photoreceptors are classified by shape as: (a) *rods* (*rhodopsin* as the visual pigment and converging neural connections give them high sensitivity, but poor acuity and no colour discrimination); or (b) *cones* (varieties of *iodopsin* and less convergence in connections provide for colour vision and fine acuity).

• *External limiting 'membrane'* is formed of outer terminal processes of Müller cells and lies at the level of the photoreceptors' inner segments, to which the Müller cells tightly attach by junctional complexes.

• *Outer nuclear layer* - nuclei of photoreceptors.

• *Outer plexiform layer* - synapsing processes: photoreceptors' spherules or pedicles with bipolar neuron dendrites.

• *Inner nuclear layer* - nuclei and bodies of *bipolar neurons*; Müller cells, horizontal neurons and amacrine cells.

- *Inner plexiform layer* - axons of bipolar neurons synapsing with dendrites of ganglion neurons.
- *Ganglion cell layer* - somas of ganglion neurons, whose axons pass over the internal surface of the retina as the
 - *nerve fibre layer* to converge on the *optic papilla*, where they pass out unmyelinated through the eye's other two coats to form the optic nerve.
- *Inner limiting membrane* - a basal lamina separates the inner processes of Müller cells from the vitreous.

Retinal modifications

1. *Macula lutea* with *fovea centralis* - on the visual axis is a yellow-ringed depression, from which the inner layers have been displaced to a peripheral hump so that: (a) the light can fall directly on the photoreceptors, that (b) are all tightly packed cones with straight-through neural connexions, for high acuity.
2. *Optic papilla/nerve head*, where optic nerve fibres leave the eye (no receptors, therefore a *blind spot*), and where retinal blood vessels leave and enter for widespread retinal distribution.

The condition of these vessels is a crucial part of the ophthalmoscopic examination.

3. *Optic nerve* - the ganglion cells' fibres acquire myelin sheaths, then run centrally with accompanying glial cells and a meningeal sheath as a CNS tract. The retinal artery and vein run centrally in the intraorbital section of the nerve.

Choroid

Posterior part of the *uvea* - the eyeball's middle tunic - acts as a light-dense, nutritive backing for the retina with:

1. *Bruch's membrane* supporting the retina.
2. *Choriocapillaris* - a plexus of large capillaries.
3. *Choroid* and outermost epichoroid/suprachoroid - highly vascular, loose stroma of collagen and elastic fibres, fibroblasts and pigmented melanophores. (The pigment is static inside mammalian melanophores, which are thus unlike those of lower vertebrates.)

Sclera

Dense, tough outer tunic of collagenous fibrous tissue. It has some regional variations:

1. At the *lamina cribrosa*, where its fibres interweave with bundles of optic nerve fibres leaving the eye.
2. At the *limbus*, where it is more vascular, related to Schlemm's canal and the ciliary body.
3. Near to the limbus are the *insertions* for the oculomotor skeletal muscles moving the eye.
4. Throughout, its innermost layer (*lamina fusca*) also has melanophores and elastic fibres.

Accessory Structures (Adnexa)

Eyelids protect and lubricate the eye's anterior surface.

1. Fine skin with a loose dermis faces outward.
2. Palpebral *conjunctiva* (stratified columnar epithelium with goblet cells on a lamina propria) faces inward.
3. Orbicularis oculi skeletal *muscles* (served by VIIth nerve) close lids.

4. *Levator palpebrae* muscle raises the upper lids.
5. *Tarsal plates* of dense CT have imbedded in them
6. *Meibomian seaceous glands* to make protective secretions.
7. *Eyelash* hair follicles are separated by the
8. sweat glands of Moll and seaceous glands of Zeiss.

Conjunctiva

1. *Palpebral conjunctiva* lines the eyelids, and *bulbar* covers the eyeball's sclera, with the *fornices* as the angle of reflection.
2. *Stratified columnar epithelium* has goblet and Langerhans cells, with many lymphocytes in the loose lamina propria.
3. Epithelium changes at the limbus (to corneal) and at the lid margin (to skin). Conjunctival epithelium is a *source of cells* to repair damaged corneal epithelium.
4. Plica semilunaris is a small conjunctival fold in the medial margin of the eye above the *caruncle*, with its sebaceous glands.

Lachrymal glands

1. In upper, lateral orbit, opening via ducts to the conjunctiva.
2. Compound, tubulo-acinar, serous gland with many myoepithelial cells. Mucous cells also are present.
3. Tears drain through the lachrymal punctum via lachrymal canaliculi into the lachrymal sac. Then they pass via the nasolachrymal duct to the lateral side of the inferior meatus of the nose.
4. Tear fluid is chemically complex. Tears have water, salts, glycoproteins, and bactericidal factors, e.g., lysozyme.

Other orbital structures

1. Tenon's CT capsule.
2. Extraocular skeletal muscles (fine-fibred).
3. Adipose tissue.
4. Ciliary ganglion.

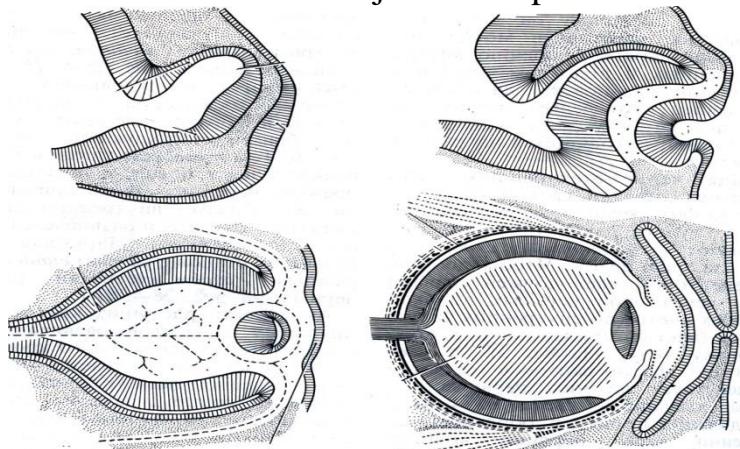
Functional Classification of the Eye and Adnexa

1. *Optical refractive agents*: cornea, lens, aqueous humour, and vitreous humour; form a small, inverted, real image.
2. *Receptor and neural tissues*: retina and optic nerve.
3. *Sustaining and light-excluding tissue*: vascular uvea comprising the pigmented choroid coat, ciliary body and iris.
4. *Form- and rigidity-endowing tissues*: cornea, sclera and intraocular fluid.
5. *Oculomotor system*: sclera and three pairs of muscles.
6. *Protective tissues*: lids, conjunctiva, cornea, lachrymal, Meibomian and other glands, and the orbital bone.

Development of the Eye

1. *Forebrain* grows out as the hollow *optic vesicle*, whose proximal part constricts to become an *optic stalk*, later the optic nerve.
2. Superficial *ectoderm* over the optic vesicle thickens, then separates to become the *lens vesicle*.

3. Meanwhile, the anterior wall of the optic vesicle *invaginates* into the posterior producing a *two-layered cup* that becomes the retina with its posterior pigment epithelium.
4. *Mesectoderm* gives the corneal stroma, uvea and sclera.
5. *Ectoderm* provides the corneal and conjunctival epithelia.



3.3. Literature recommended

Main Sources:

1. L.C. Junqueira, J. Carneiro - "Basic histology" – 11 edition - 2005.
2. A.S. Pacurar, J.W. Bigbee – "Digital histology" – Virginia - 2004.
3. "Color Atlas of basic histology" – R.Berns – 2006.
4. Sadler T.V. – "Medical embryology" Montana – 1999.
5. Ronald W., Dudek Ph.D. – "Embryology" 2 edition – 1998.
6. Inderbir Singh Textbook of Human Histology.- Jaypee. India. - 1997.
7. Ten Cate A.R. Oral Histology.- St.Louis, Baltimore, Toronto.- 1995.
8. William A., Beresford M.A. Cytology and Histology.- Anatomy department, West Virginia University, USA.- 1992.
9. K.E. Jonson - "Histology and cell biology" – 2 edition – Washington – 1991.

Additional ones:

1. Methodical Instructions.

3.4 How to work with the literature recommended:

Main tasks	Recommendations
To review the material	To use the material studied
To learn the material	To use the material on pages
To read and compose the plan	To learn the new material and be ready to write a summary
To answer the questions	To be ready to give an answer to the following:
To do the test on the material	
To be ready to answer the topic	

3.5. Self-control material:

A. Questions to be answered:

1. Analyzers. Their value for the human organism.
2. Sense organs as peripheral departments of analyzers.
3. Sense organs. General morfo-functional characteristic.
4. Classification of sense organs.
5. Optical organ. A general plan of a constitution.

6. The eyeball's shells and apparatus.
7. Optical organ. Characteristic of the retina.

B. Test tasks to be done: Tests are applied

4. Self-preparation in the classroom.

- 1) Listen to the information.
- 2) Work with the tables and a Light microscope.
- 3) Ask about the problems that haven't been found in the information given.
- 4) To sketch in the album the investigated preparations.

5. Self-preparation work at home.

- 1) Review the material learnt in the classroom.
- 2) Compose the plan of your answer.
- 3) Answer the questions to this topic.
- 4) Do the test given above.

6. The subject of the research work.

“Adaptive changes of a retina”

<i>Subject</i>	<i>Histology, cytology and embryology</i>
<i>Modul №2</i>	<i>Histology, cytology and embryology</i>
<i>Submodul №3</i>	<i>Special histology</i>
<i>Topic 5</i>	AUDITORY AND VESTIBULAR ORGANS.

Hours: 2

1. The topic basis: the topic “AUDITORY AND VESTIBULAR ORGANS.” is very important for future doctors in their professional activity, positively influences the students in their attitude to the future profession, forms professional skills and experience as well as taking as a principle the knowledge of the subject learnt.

2. The aims of the training course:

- 1) To have general knowledge of the topic studied.
- 2) To understand, to remember and to use the knowledge received.
- 3) To learn the classification, structure and functions of the different histological methods.
- 4) To form the professional experience by reviewing, training and authorizing it.
- 5) To be able to carry out laboratory and experimental work.

3. Materials for the before – class work self – preparation work:

3.1 Basic knowledge, experience, skills necessary for studying the topic in connection with other subjects:

	To know	To be able to
Med. Biology	the structure of the cells and tissues	work with a light microscope
Med. Physics	the structure of the light and electron microscopes	work with a light microscope
Organic Chemistry	the chemical content of the cell	Speak of the topic

The contents of the topic:

Organs - *cochlea* and *vestibular apparatus* - sensitive respectively to air vibrations (*sound*), and movement of the head and its position relative to the gravitational field (*balance*), are combined in the *inner ear* within communicating spaces - the *bony labyrinth* - of the temporal bone.

Actually the receptors are enclosed in membranous tubes forming a *membranous labyrinth* that lies within, but does not fill the bony labyrinth.

The two separate systems contain different fluids. The membranous labyrinth is filled with *endolymph* and is a closed system, although it extends a *ductus endolymphaticus* through the bone to end blindly by the brain as an *intradural sac* involved in metabolic functions. This sac can be drained surgically to relieve damaging excess endolymphatic pressure - *endolymphatic hydrops*.

The space between the tubules of the membranous labyrinth and the bone is occupied by *perilymph*, which is in communication via the *aqueductus cochleae* and

aqueductus vestibularis with the meninges and with the *CSF* of the brain's *subarachnoid space*.

The fluid in the bony labyrinth can interact with the middle ear (and indirectly with the external environment) by means of two soft areas in its bony walls:

The *oval window/fenestra ovalis* occupied by the moveable stapes bone acting as a plunger.

The *round window/fenestra rotunda* covered with fibrous tissue and epithelium, and moving passively as a pressure release for pressures generated within the fluid system by movement at the oval window.

The stimulus in the environment that causes movement of the oval window and pressure changes in the fluids is *movement of air/sound*, allowed a little way into the head via the external ear.

The fluids of the labyrinth are also subject to the *gravitational force* and that accompanying *movement of the head*.

Divisions of the Ear

External ear

1. *Auricle*: core of elastic cartilage; lobule of adipose tissue; skin-covered.
2. *External auditory meatus*: lined with skin and stratified squamous epithelium; has ceruminous (modified apocrine sweat) and sebaceous glands; supported by cartilage and, further in, by bone.
3. *Tympanic membrane/eardrum*: inner limit of the external ear, core of atypical collagen with thin epidermis externally, and a mostly simple squamous epithelium internally; the manubrium of the malleus bone inserts into the collagen. Elastin is present in the flaccid region.

Middle ear

1. Epithelium-lined, air-filled, bony spaces of the *tympanic cavity*.
2. Communicates with the nasopharynx via the *Eustachian/auditory/pharyngotympanic tube*, allowing equalization of air pressures on either side of the tympanic membrane. The mucosa of the tube and middle ear has several kinds of cell, and defensive systems.
3. *Auditory ossicles* articulate with one another - *malleus, incus* and *stapes*. The malleus is vibrated by air moving the tympanic membrane. This movement is then transmitted via the incus to the stapes with its foot held in the *oval window* by the annular ligament.
4. Elastic membrane of the *round window* transforms the fluid pressures generated in the inner ear into other forms of energy, thus acting as a pressure-release.
5. *Fine skeletal muscles*, stapedius and tensor tympani, inserting into the stapes and malleus are protective, and influence sound discrimination. Fine *nerves* pass to them.

Inner ear

The outer and middle ear thus have an *exteroceptor* function, transmitting air vibrations (20-20000 cycles per second is the perceptible range) to the perilymph fluid in the bone of the inner ear. Although the resulting pressure changes involve all perilymph, the receptors sensitive to the changes are localized in only one part of the labyrinth, the *cochlea*, and lie in the inner endolymph-filled system. Elsewhere in this

inner system lie the *intero-* or *proprioceptors* for balance and movement, located in the *vestibular apparatus*.

Vestibular Apparatus

1. **Bony vestibule** houses the membranous *utricle* and *saccule*.
2. The vestibule extends into three semicircular tubes or canals distributed in three planes perpendicular to one another and containing the membranous *semicircular ducts*/canals, each swelling out at one end into an *ampulla*.
3. Movement of endolymph within the connecting membranous chambers stimulates receptors in *maculae* and *cristae* - modified, small, neuroepithelial areas of the lining membrane.

- **Macula**, flat with:

1. *Basal lamina* penetrated by
2. *nerve fibres* from bipolar neurons of Scarpa's vestibular ganglion passing to synapse with
3. *sensory hair cells*, of two types, with their companion
4. *sustentacular cells*, making a pseudostratified neuroepithelium.
5. The 25 µm-long *hairs* (long microvilli and one cilium per cell) of the hair cells project into
6. the gelatinous *otolithic membrane*, in which are imbedded
7. small crystalline *otoconia/otoliths* (weights subject to gravity).

- **Crista** - rounded, *crest-like prominence* similar to a macula in its components, but the gelatinous mass is called the cupola, and is without otoliths. The crista detects the start and end of movement in the plane of its duct.

4. *Utricle* (with a macula) is oriented in the plane of the base of the skull, and the *saccule* (macula) in the sagittal plane. Both are responsive to gravity and linear acceleration, thus giving information on how the head is positioned.
5. *Ampulla* (with a crista) oriented in each of the horizontal, sagittal and transverse planes; responsive to movement of the head in the plane of that canal, thus furnishing information on the rate of angular acceleration.
6. The insensitive remainder of the vestibular membranous labyrinth is lined by a simple squamous epithelium on CT, which is supported by collagen and fibroblasts passing to the periosteum of the bony labyrinth, except on the side it fastens to the bony wall.

Cochlea

Structures and elements

The tube - the cochlear duct - containing the cochlear endolymph is not surrounded by perilymph, but has it on two of its triangular sides. Thus, three chambers are contained within the *bony cochlea* which spirals for 2 1/2 turns around an axis of spongy bone, the *modiolus*. The spiralling unit comprises:

1. *Scala vestibuli* with perilymph and mesothelium-lined.
2. *Reissner's membrane* (*membrana vestibularis*), thin;
3. *Cochlear duct/scala media* with K⁺-rich endolymph made in the *stria vascularis*; epithelium-lined, and containing the *Organ of Corti* (the actual receptor) on the

4. *basilar membrane*, stretched from the tympanic lip of the bony spiral lamina to the spiral ligament.

5. *Scala tympani* with perilymph and mesothelium-lined, separated by bone from the scala vestibuli adjacent in the spiral.

6. Scalae vestibuli and tympani connect by a *helicotrema* at the apex of the cochlea, whilst the cochlear duct ends blindly as the *caecum cupulare*.

The cochlear duct at its base communicates with the saccule via the *ductus reuniens*.

Organ of Corti

1. Rests on the tympanic lip and *basilar membrane*.

2. Internal border cells and *internal hair cells* (receptive).

3. *Internal pillar cells* lean outwards towards inwardly leaning *external pillar cells*, thereby enclosing an inner *tunnel*.

4. *Phalangeal cells/Dieter's supporting cells* support *external hair cells*, more contractile than receptive (50-100 hairs per cell); in three rows; damaged by loud sounds, streptomycin, cisplatin, etc. *Hairs* (stereocilia of graded lengths) of outer cells go through a *reticular plate* to attach to the overlying *tectorial membrane* - a gelatinous body attached at the vestibular lip to the CT limbus spiralis.

5. *Nerve fibres* derived from bipolar neurons of the *spiral ganglion/ganglion of Corti* in the bony spiral lamina, passing through the bone, serve the inner and outer hair cells.

(*Centrifugal* fibres also run from the brain stem to the outer hair cells, to improve sensitivity.)

6. The centripetal fibres of Scarpa's vestibular and Corti's cochlear ganglia join to form the *auditory/VIIth cranial nerve*.

Organ of Corti's transducer function

Inner *Hair cells* convert into neuronal discharges fluid pressure changes, transmitted through the basilar membrane to the cochlear endolymph, from the perilymph of the scala tympani. These changes originated at the oval window in response to vibration of the auditory ossicles caused by air moving the tympanic drum.

Discrimination of pitch (sound frequency) is based on different cochlear regions responding preferentially to particular tones, with high frequency received at the basal cochlea and lower ones apically where the basilar membrane is broader.

Fluids and gelatinous bodies

Although these are lost or grossly distorted in the histological processing, they are very important. The fluids transmit forces, and provide a metabolic pathway and favourable ionic environment for the receptor and other cells of the membranous labyrinth. In life, the gelatinous cupola and tectorial and otolithic membranes are large, filling or almost filling their respective membranous chambers.

3.3. Literature recommended

Main Sources:

1. L.C. Junqueira, J. Carneiro - "Basic histology" – 11 edition - 2005.
2. A.S. Pacurar, J.W. Bigbee – "Digital histology" – Virginia - 2004.
3. "Color Atlas of basic histology" – R.Berns – 2006.
4. Sadler T.V. – "Medical embryology" Montana – 1999.
5. Ronald W., Dudek Ph.D. – "Embryology" 2 edition – 1998.

6. Inderbir Singh Textbook of Human Histology.- Jaypee. India. - 1997.
7. Ten Cate A.R. Oral Histology.- St.Louis, Baltimore, Toronto.- 1995.
8. William A., Beresford M.A. Cytology and Histology.- Anatomy department, West Virginia University, USA.- 1992.
9. K.E. Jonson - “Histology and cell biology” – 2 edition – Washington – 1991.

Additional ones:

1. Methodical Instructions.

3.4 How to work with the literature recommended:

Main tasks	Recommendations
To review the material	To use the material studied
To learn the material	To use the material on pages
To read and compose the plan	To learn the new material and be ready to write a summary
To answer the questions	To be ready to give an answer to the following:
To do the test on the material	
To be ready to answer the topic	

3.5. Self-control material:

A. Questions to be answered:

1. Auditory organ. Morfo-functional characteristic.
2. Constitution, cytophysiology of receptor cells of the Corti organ.
3. Vestibular organ. A constitution, function. The characteristic of receptor cells.
4. General principles of the constitution function of acoustical cristaes and acoustical macules, difference in their constitution and functions.

B. Test tasks to be done: Tests are applied

4. Self-preparation in the classroom.

- 1) Listen to the information.
- 2) Work with the tables and a Light microscope.
- 3) Ask about the problems that haven't been found in the information given.
- 4) To sketch in the album the investigated preparations.

5. Self-preparation work at home.

- 1) Review the material learnt in the classroom.
- 2) Compose the plan of your answer.
- 3) Answer the questions to this topic.
- 4) Do the test given above.

6. The subject of the research work.

<i>Subject</i>	<i>Histology, cytology and embryology</i>
<i>Modul №2</i>	<i>Histology, cytology and embryology</i>
<i>Submodul №3</i>	<i>Special histology</i>
<i>Topic 6</i>	SENSE ORGANS. TASTE ORGAN. ORGAN OLFATORIA

Hours: 2

1. The topic basis: the topic “SENSE ORGANS. TASTE ORGAN. ORGAN OLFATORIA” is very important for future doctors in their professional activity, positively influences the students in their attitude to the future profession, forms professional skills and experience as well as taking as a principle the knowledge of the subject learnt.

2. The aims of the training course:

- 1) To have general knowledge of the topic studied.
- 2) To understand, to remember and to use the knowledge received.
- 3) To learn the classification, structure and functions of the different histological methods.
- 4) To form the professional experience by reviewing, training and authorizing it.
- 5) To be able to carry out laboratory and experimental work.

3. Materials for the before – class work self – preparation work:

3.1 Basic knowledge, experience, skills necessary for studying the topic in connection with other subjects:

	To know	To be able to
Med. Biology	the structure of the cells and tissues	work with a light microscope
Med. Physics	the structure of the light and electron microscopes	work with a light microscope
Organic Chemistry	the chemical content of the cell	Speak of the topic

The contents of the topic:

Olfactory Mucosa of nasal cavity

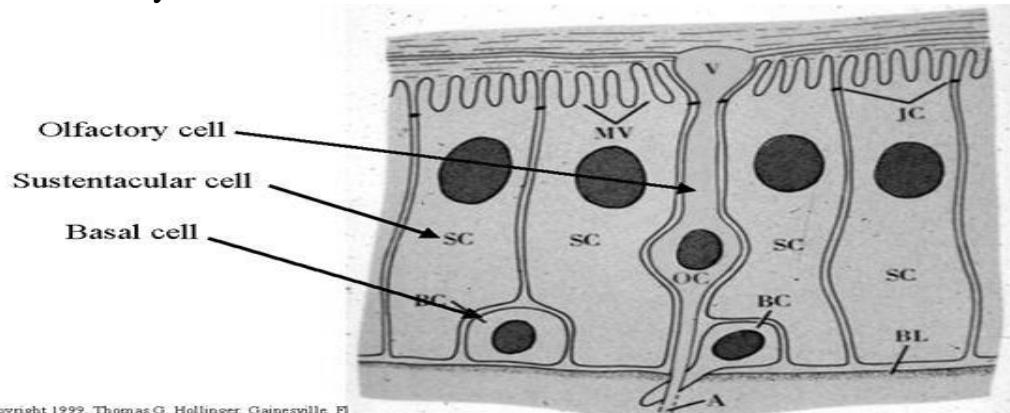
- Three cell kinds are in the pseudostratified, columnar *neuro-epithelium*:
- *Bipolar sensory cell*, with an axon going directly through the ethmoid bone to the olfactory bulb and, at the apical end, several, long, cilium-like processes (olfactory hairs) extending into the surface coat of mucus and lipid.
- *Sustentacular cell* has pigment in its apical cytoplasm and is equipped with microvilli.
- *Basal cells* to divide and replace sustentacular and sensory cells.

- All cell types rest on a BL penetrated by axons that become grouped as *unmyelinated nerves* in the lamina propria.
- *Bowman's compound serous glands* also contribute secretion to the surface. Unlike other serous cells, they have much smooth ER.

This is yellow in colour, in contrast to the pink colour of the respiratory mucosa. It consists of a lining epithelium and a lamina propria.

The olfactory epithelium is pseudostratified. It is much thicker than the epithelium lining the respiratory mucosa (about 100 µm). It does not have a basement membrane. Within the epithelium there is a superficial zone of clear cytoplasm below which there are several rows of nuclei. Using special methods three types of cells can be recognized in the epithelium.

(1) The olfactory cells are modified neurons. Each cell has a central part containing a rounded nucleus. Two processes, distal and proximal, arise from this central part. The distal process (representing the dendrite) passes towards the surface of the olfactory epithelium. It ends in a thickening (called the rod or knob) from which a number of non-motile olfactory cilia arise and project into a layer of fluid covering the epithelium. The proximal process represents the axon. It passes into the subjacent connective tissue where it forms one fibre of the olfactory nerve. The nuclei of olfactory cells lie at various levels in the basal two-thirds of the epithelium.



In vertebrates olfactory cells are unique in being the only neurons that have cell bodies located in an epithelium.

Olfactory cells are believed to have a short life. Dead olfactory cells are replaced by new cells produced by division of basal cells. This is the only example of regeneration of neurons in mammals.

(2) The sustentacular cells support the olfactory cells. Their nuclei are oval, and lie near the free surface of the epithelium. The free surface of each cell bears numerous microvilli (embedded in overlying mucus). The cytoplasm contains yellow pigment (lipofuscin) which gives olfactory mucosa its yellow colour. In addition to their supporting function sustentacular cells may be phagocytic, and the pigment in them may represent remnants of phagocytosed olfactory cells.

(3) The basal cells lie deep in the epithelium and do not reach the luminal surface. They divide to form new olfactory cells to replace those that die. Some basal cells have a supporting function.

The lamina propria, lying deep to the olfactory epithelium consists of connective tissue within which blood capillaries, lymphatic capillaries and olfactory

nerve bundles are present. It also contains serous glands (of Bowman) the secretions of which constantly 'wash' the surface of the olfactory epithelium. This fluid may help in transferring smell carrying substances from air to receptors on olfactory cells. The fluid may also offer protection against bacteria.

Taste Buds

- Barrel-shaped; lying within the stratified squamous epithelium of the tongue's circumvallate and fungiform papillae
- At the apex towards the opening of the *taste pore*, project processes of two fusiform cell kinds: (i) thin, dark *neuro-epithelial* cells, and (ii) paler vesicular '*sustentacular*' cells.
- Both have long microvilli (hair processes), and both have axons terminating on them from the facial and glossopharyngeal nerves. (Taste buds in the pharynx and epiglottis are served by the vagus nerve.)
- *Von Ebner's glands* in the lamina propria send a *serous* secretion into the trench around the vallate papilla, in whose walls the taste buds lie.

Taste buds are present in relation to circumvallate papillae, to fungiform papillae, and to leaf-like folds of mucosa (*folia linguae*) present on the posterolateral part of the tongue. Taste buds are also present on the soft palate, the epiglottis, the palatoglossal arches, and the posterior wall of the oropharynx.

Each taste bud is a piriform structure made up of modified epithelial cells. It extends through the entire thickness of the epithelium. Each bud has a small cavity that opens to the surface through a gustatory pore. The cavity is filled by a material rich in polysaccharides.

The cells present in taste buds are elongated and are vertically orientated; those towards the periphery being curved like crescents. Each cell has a central broader part containing the nucleus, and tapering ends. The cells are of two basic types. Some of them are receptor cells or gustatory cells. Endings of afferent nerves end in relation to them. Other cells perform a supporting function.

It is by no means easy to distinguish between receptor and supporter cells, the essential difference being the presence of innervation. Early observers using the light microscope found hairs at the tips of some cells and concluded that these were the receptor cells. However, this has not been confirmed by EM studies. The latter have shown that the 'hair' seen with the light microscope are microvilli which are more common on supporting cells rather than receptors. Two types of receptor cells can be distinguished on the basis of the vacuoles present in them.

Supporting cells are probably of three types. Some of them that lie at the periphery of the taste bud form a sheath for it. Those near the centre of the bud are truly supporting. They probably secrete a material that fills the cavity at the apex of the taste bud. Microvilli are often present at the tips of these cells. A third variety of supporting cell is seen in the basal part of the bud. These basal cells multiply and produce new supporting and receptor cells to replace those that are worn out. This may be correlated with the fact that cells of taste buds have a short life and are continuously being replaced.

It has been held that taste buds in different parts of the tongue may respond best to particular modalities of taste. It is now known that the same taste bud can

respond to different types of taste (sweet, sour, salt and bitter) and that taste is a complicated sensation depending upon the overall pattern of responses from taste buds all over the tongue.

3.3. Literature recommended

Main Sources:

1. L.C. Junqueira, J. Carneiro - "Basic histology" – 11 edition - 2005.
2. A.S. Pacurar, J.W. Bigbee – "Digital histology" – Virginia - 2004.
3. "Color Atlas of basic histology" – R.Berns – 2006.
4. Sadler T.V. – "Medical embryology" Montana – 1999.
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6. William A., Beresford M.A. Cytology and Histology.- Anatomy department, West Virginia University, USA.- 1992.
7. K.E. Jonson - "Histology and cell biology" – 2 edition – Washington – 1991.

Additional ones:

1. Methodical Instructions.

3.4 How to work with the literature recommended:

Main tasks	Recommendations
To review the material	To use the material studied
To learn the material	To use the material on pages
To read and compose the plan	To learn the new material and be ready to write a summary
To answer the questions	To be ready to give an answer to the following:
To do the test on the material	
To be ready to answer the topic	

3.5. Self-control material:

A. Questions to be answered:

1. Organ olfactoria. Constitution, development, cytophysiology of receptor cells.
2. Taste organ. A constitution, function.
3. Cytophysiological characteristic of taste bulbs.

B. Test tasks to be done: Tests are applied

4. Self-preparation in the classroom.

- 1) Listen to the information.
- 2) Work with the tables and a Light microscope.
- 3) Ask about the problems that haven't been found in the information given.
- 4) To sketch in the album the investigated preparations.

5. Self-preparation work at home.

- 1) Review the material learnt in the classroom.
- 2) Compose the plan of your answer.
- 3) Answer the questions to this topic.
- 4) Do the test given above.

6. The subject of the research work.

<i>Subject</i>	<i>Histology, cytology and embryology</i>
<i>Modul №2</i>	<i>Histology, cytology and embryology</i>
<i>Submodul №3</i>	<i>Special histology</i>
<i>Topic 7</i>	SKIN. SKIN GLANDS. HAIR AND NAILS

Hours: 2

1. The topic basis: the topic “**SKIN. SKIN GLANDS. HAIR AND NAILS**” is very important for future doctors in their professional activity, positively influences the students in their attitude to the future profession, forms professional skills and experience as well as taking as a principle the knowledge of the subject learnt.

2. The aims of the training course:

- 1) To have general knowledge of the topic studied.
- 2) To understand, to remember and to use the knowledge received.
- 3) To learn the classification, structure and functions of the different histological methods.
- 4) To form the professional experience by reviewing, training and authorizing it.
- 5) To be able to carry out laboratory and experimental work.

3. Materials for the before – class work self – preparation work:

3.1 Basic knowledge, experience, skills necessary for studying the topic in connection with other subjects:

	To know	To be able to
Med. Biology	the structure of the cells and tissues	work with a light microscope
Med. Physics	the structure of the light and electron microscopes	work with a light microscope
Organic Chemistry	the chemical content of the cell	Speak of the topic

The contents of the topic:

Skin, integument covers the body and serves many functions. It consists of a thick, protective, cornified, stratified squamous epithelium (*epidermis*), on a firm, dense CT lamina propria (*dermis*), adipose tissue (*hypodermis*) and has special *appendages*, hair and nails, and *accessory glands*, sweat, sebaceous, ceruminous, and mammary glands.

Skin Functions

1. *Protection* against water, bacteria, sunlight, mechanical forces, dehydration, cold, etc.

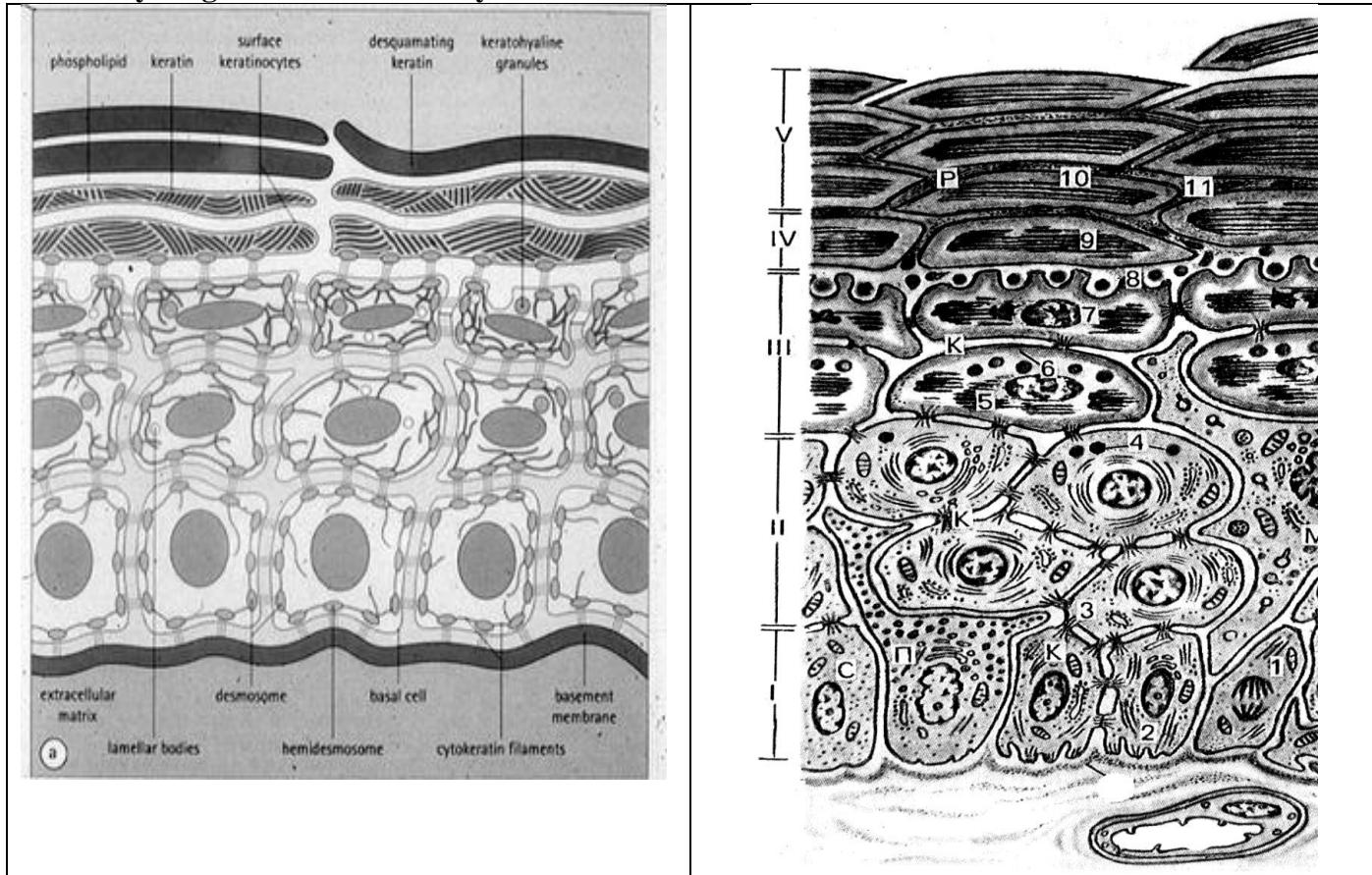
2. *Retaining body fluids*, i.e., protection against dehydration.
3. *Temperature regulation* by: (a) varying peripheral blood flow, (b) sweating, (c) hair elevation, and (d) insulation by adipose tissue under the skin. (Note that heavy sweating defeats 2 above.)
4. *Food storage* and fat metabolism in the subcutaneous hypodermis.
5. *Vitamin D formation* by the action of ultraviolet light.
6. *Sensory appreciation* of the environment by nervous receptors.
7. *Friction surface* for motor tasks involving grasping, rubbing, scratching, etc.
8. *Display and communication*: social, sexual, and diagnostic. Many diseases distinctively affect the skin and its hair and nails.

Epidermis (epithelium)

Layers

1. *Stratum corneum* of keratinized cells (outermost).
2. *Stratum lucidum*, a thin pale layer of keratin seen when the stratum corneum is very thick.
3. *Stratum granulosum* of cells with basophilic granules.
4. *Stratum spinosum* of prickle epithelial cells.
5. *Stratum germinativum*, bordering on the BL.

Cytological details of the layers



1. *Stratum germinativum/basale*

Keratinocyte precursor cells, cuboidal or columnar in form, lie on a BL.

Cells project down many small basal processes.

The whole underside of the epithelium is indented by CT *dermal papillae* for effective attachment, nutrition, and sensation.

Cells proliferate to replace lost surface cells.

2. *Stratum spinosum*

- *Keratinocytes*/prickle cells

Principal cell kind; ectodermal in origin; move upwards in the layer and continue to proliferate, despite the many desmosomes holding them together (which, with processing shrinkage, lead to the cells' spiny, *prickly* appearance).

Cytoplasm is rich in keratin filaments, bundled into *tonofilaments* and increasing in number towards the keratin layer, and formed from prekeratin monomers.

- *Melanocytes*

- Ectodermal; but migrated neural crest cells.
- Constitute 1 in 4 to 1 in 10 of basal epithelial cells.
- Deficient in tonofilaments and desmosomes.

▪ Synthesize *melanin* and transfer it via their long dendritic *processes* to neighbouring *keratinocytes*.

▪ EM shows that the Golgi apparatus participates in forming the *melanosome granules*.

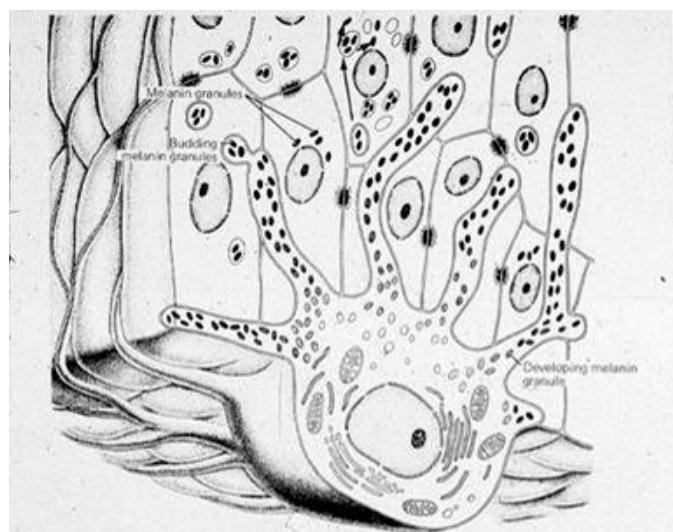
▪ Melanin is formed from tyrosine by the enzyme tyrosinase. Cells with melanin-forming ability can be revealed in a section by treating it with dihydroxyphenylalanine (*DOPA*), which is oxidized to melanin.

▪ *Albinos* have an inborn error of metabolism, making them unable to synthesize melanin in the skin and eye.

▪ *UV light* causes greater melanin formation and a thickening of the keratin layer. *Pituitary* and *adrenal hormones* also increase pigmentation, which is a useful sign for diagnosis.

○ *Langerhans cells* are poorly phagocytic, marrow-derived, specialized macrophages, with long dendrites. They are antigen-presenting cells, accessory to T-cell immunity.

○ *Merkel cells* are sensory cells with vesicles and a polylobulated nucleus. They attach to disc-shaped endings of some of the axons that penetrate the epithelium.



3. *Strata granulosum and corneum*.

- Stratum granulosum cells form a *kerato-hyaline matrix* from their basophil granules, binding together *packed tonofilaments* within the cells to convert the cells to *soft keratin*. Other organelles and the nucleus vanish, while the plasmalemma thickens and toughens, to build a cornified envelope.
- Flattened, dead, keratinized, surface cells desquamate.
- Only with EM is keratin seen to be *cellular*. In the usual HE preparation it is eosinophilic, and often splits and breaks.
- Epidermis is thrown up into ridges - *cristae cutis* - on the palmar and plantar surfaces of the hands and feet: the basis of finger and palm prints.
- At the top of the ridges, *spiralling holes* open through the keratin to let out the sweat.
- *Keratin layer* may be very thick, for instance on the soles and palms. Such thick skin is hairless, and lacks sebaceous glands.

- *Filaggrin* is the protein of keratohyaline granules, and aggregates 'keratinocyte' *keratins Nos. 5/14*. These acidic-basic combinations of keratins (numbered indirectly according to Mr) are characteristic for particular classes of epithelia, e.g., simple versus squamous, and help in interpreting pathological changes. The protein of the cornified cell envelope is *involucrin*. Ceramide and other lipids surround the envelope to boost the barrier function.

Dermis (Corium)

Divided into layers: *papillary*, fine-textured CT adjacent to the epidermis, and deeper *reticular* layer.

Reticular layer is *thick collagenous CT* of a variable thickness, not always related to that of the overlying epidermis.

Elastic fibres of the dermis give skin its elasticity, but cause wounds to gape. Ruptured dermis often heals as a white line visible through the epidermis, e.g., a mother's stretch marks.

Has the usual *cell* of CT - fibroblasts, macrophages and other defensive cells, and sometimes pigment-bearing chromatophores/dermal melanocytes.

Smooth muscle of arrectores pilorum, nipples and scrotal dartos, and skeletal muscle in the scalp and face, are attached in the dermis.

Blood vessels are derived from arterial plexuses: a deep cutaneous plexus/rete, and a subpapillary plexus sending capillary loops up into dermal papillae. Lymphatics accompany blood vessels. *Blood flow* is varied greatly by shunts through glomi (coiled arteriovenous anastomoses), and by the constriction or relaxation of arterioles.

Nervous receptors, with sensory *nerve fibres* are present and autonomic nerve fibres:

- *vasomotor* to vascular smooth muscle,
- *pilomotor* to hair arrector muscles,
- *sudomotor* to sweat glands.

Hair follicles and glands lie mostly in the dermis.

Hypodermis

Hypodermis consists of the adipose tissue lobules and areolar connective tissue.

Glands of the skin

Sweat Glands (Glandulae sudoriparae)

Single coiled tubules, lined by simple cuboidal light and dark cells; distributed over the body except for the lips, glans penis and inner prepuce.

Secretory part lies in the lower dermis, or subcutaneously in the hypodermis/superficial fascia. One tubule is cut through many times in one section.

The *secretion*, mainly water and electrolytes plus some lipids, is led to the epidermis through a *duct*, lined by stratified cuboidal epithelium, then through the living/Malpighian layer and a spiralling hole in the keratin. The gland's chloride channel is one that is impaired in cystic fibrosis.

Myoepithelial cells are seen within the basal lamina of the secretory tubule. Their contraction is under autonomic control.

The *larger variety* of gland seen in the axillary, perianal and perigenital regions is termed *apocrine*, in contrast to the eccrine glands in the majority. Apocrine glands become active with pubertal development of the ambosexual hair, and may be related to animal's scent glands.

The *ceruminous glands* of the external auditory meatus seem to be enlarged sweat glands, producing a secretion of pigmented lipids.

Sebaceous Glands

Pear-shaped, simple, branched alveolar, with large cells, usually looking *vacuolated* because their fatty content is dissolved out.

Several glands are clustered with often no apparent lumen by the side of a hair follicle, into which they discharge the secretion - *sebum*. Their short duct is lined by stratified squamous epithelium.

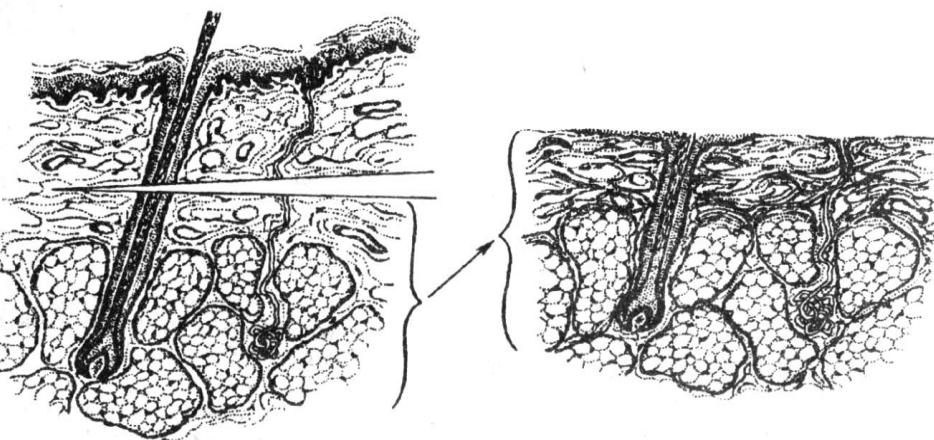
Sebum, formed in a *holocrine* manner by the total breakdown of the cells, may lubricate the hair shaft, protect the skin from drying and moisture, and be bacteriostatic.

Lie independently of hairs on the labia minora, glans penis, in the oral mucosa by the red margin of the lips, and as the Meibomian glands of the eyelid. They are absent from the palms and soles.

HAIR

Varieties and sites

1. Lanugo - fine, fetal, hairy covering, shed at birth.
2. Replaced by the *vellus* - fine body hairs.
3. Scalp, eyebrow and eyelash hairs are thicker.
4. Ambosexual hair - pubic and axillary.
5. Masculine hair - face (beard), chest and extremities.



Hair development

Hair is a *hard keratin* derivative of the epithelium of a *hair follicle*.

In development, an *epithelial bud* grows down from the young epidermis; a vascular *CT dermal papilla* invaginates the bud; in the bud a *germinal matrix* develops, forming the special keratin; and *side buds* form sebaceous glands.

Hair shaft comprises:

Medulla, as the central core of soft keratin and sometimes air spaces. The medulla may be absent.

Cortex of closely packed, elongated, hard-keratinized cells, formed without any intermediary kerato-hyaline granules developing. Melanin and other pigments may be incorporated in the cells during keratinization.

Cuticle - outermost coat of shingled/imbricated cells, with their free edges projecting upwards.

Hair follicle

Outer CT *sheath* and inner basal lamina (hyaline membrane).

Vascular papilla lies directly under the synthesizing epithelial area, responsible for the upward growth of the hair and its inner root sheath.

External root sheath is a continuation of the epidermal living layer, expanding to form the basal *hair bulb*.

Internal root sheath forms a cuticle layer from which the other cuticle, on the hair, can separate at the level of entry of the sebaceous gland's duct. Internal root sheath thus comprises: innermost cuticle cells, Huxley's layer of cells with trichohyaline granules, Henle's single, outer layer of clear cells.

Epidermal *germinal matrix*, above the papilla, forms the hair's cuticle, cortex and medulla. NB - the appearance of cross-sections varies with the level in the hair follicle at which they are taken.

Arrector pili of smooth muscle fastens the lower hair bulb's CT sheath to the upper dermis nearby.

Epithelial replacement and hair growth are cyclical, not constant activities. The hair stops growing, via a relatively short *catagen* period of regression or involution, to enter a long non-growing *telogen* phase of being a club hair, which eventually falls out. It is replaced during an *anagen/growth* phase by a new hair from the reactivated deep region of the follicle.

Pilomotor activity

Hairs are raised from their relaxed, inclined attitude by contraction of their arrectores pilorum muscles in response to cold, so that more *insulating air* is trapped near to the skin. Hairs also 'stand up' in fear and other emotional reactions.

NAIL

The horny *plate* of hard beta keratin is synthesized by the proximal, germinal, part of the *nail bed*.

The *nail bed* comprises the living layers of the epidermis, ridged longitudinally, and lacking glands and follicles. Part of its germinal region is seen by the naked eye as the *lunule*, the pale half-moon area just distal to the *eponychium* - an extension of the stratum corneum of the dorsal skin.

3.3. Literature recommended

Main Sources:

1. L.C. Junqueira, J. Carneiro - "Basic histology" – 11 edition - 2005.
2. A.S. Pacurar, J.W. Bigbee – "Digital histology" – Virginia - 2004.
3. Sadler T.V. – "Medical embryology" Montana – 1999.
4. Ronald W., Dudek Ph.D. – "Embryology" 2 edition – 1998.
5. Inderbir Singh Textbook of Human Histology.- Jaypee. India. - 1997.
6. Ten Cate A.R. Oral Histology.- St.Louis, Baltimore, Toronto.- 1995.
7. William A., Beresford M.A. Cytology and Histology.- Anatomy department, West Virginia University, USA.- 1992.
8. K.E. Jonson - "Histology and cell biology" – 2 edition – Washington – 1991.

Additional ones:

1. Methodical Instructions.

3.4 How to work with the literature recommended:

Main tasks	Recommendations
To review the material	To use the material studied
To learn the material	To use the material on pages
To read and compose the plan	To learn the new material and be ready to write a summary
To answer the questions	To be ready to give an answer to the following:
To do the test on the material	
To be ready to answer the topic	

3.5. Self-control material:

A. Questions to be answered:

1. What skin functions do you know?
2. Describe the epidermis (epithelium).
3. What layers of the skin epithelium do you know?
4. Describe cytological details of the *strata granulosum and corneum*.
5. Describe the structure of the dermis.
6. Describe cytological details and functions of the hypodermis.
7. What are the structure and functions of the sweat glands?
8. What are the structure and functions of the sebaceous glands?
9. What are the structure and functions of the hair?
10. What are the structure and functions of the nail?

B. Test tasks to be done: Tests are applied

4. Self-preparation in the classroom.

- 1) Listen to the information.

- 2) Work with the tables and a Light microscope.
- 3) Ask about the problems that haven't been found in the information given.
- 4) To sketch in the album the investigated preparations.

5. Self-preparation work at home.

- 1) Review the material learnt in the classroom.
- 2) Compose the plan of your answer.
- 3) Answer the questions to this topic.
- 4) Do the test given above.

6. The subject of the research work.

	<i>Histology, cytology and embryology</i>
<i>Modul №2</i>	<i>Histology, cytology and embryology</i>
<i>Submodul №3</i>	<i>Special histology</i>
<i>Topic 8</i>	CIRCULATORY SYSTEM. HEART.

Hours: 2

1. The topic basis: the topic “CIRCULATORY SYSTEM. HEART” is very important for future doctors in their professional activity, positively influences the students in their attitude to the future profession, forms professional skills and experience as well as taking as a principle the knowledge of the subject learnt.

2. The aims of the training course:

- 1) To have general knowledge of the topic studied.
- 2) To understand, to remember and to use the knowledge received.
- 3) To learn the classification, structure and functions of the different histological methods.
- 4) To form the professional experience by reviewing, training and authorizing it.
- 5) To be able to carry out laboratory and experimental work.

3. Materials for the before – class work self – preparation work:

3.1 Basic knowledge, experience, skills necessary for studying the topic in connection with other subjects:

	To know	To be able to
Med. Biology	the structure of the cells and tissues	work with a light microscope
Med. Physics	the structure of the light and electron microscopes	work with a light microscope

The contents of the topic:

The cardiovascular system consists of the heart and of blood vessels. The blood vessels that take blood from the heart to various tissues are called arteries. The smallest arteries are called arterioles. Arterioles open into a network of capillaries that pervade the tissues. Exchanges of various substances between the blood and the tissues take place through the wall of capillaries. In some situations capillaries are replaced by slightly different vessels called sinusoids. Blood from capillaries (or from sinusoids) is collected by small veinules which join to form veins. The veins return blood to the heart.

General Functions and Aspects of the Circulatory System

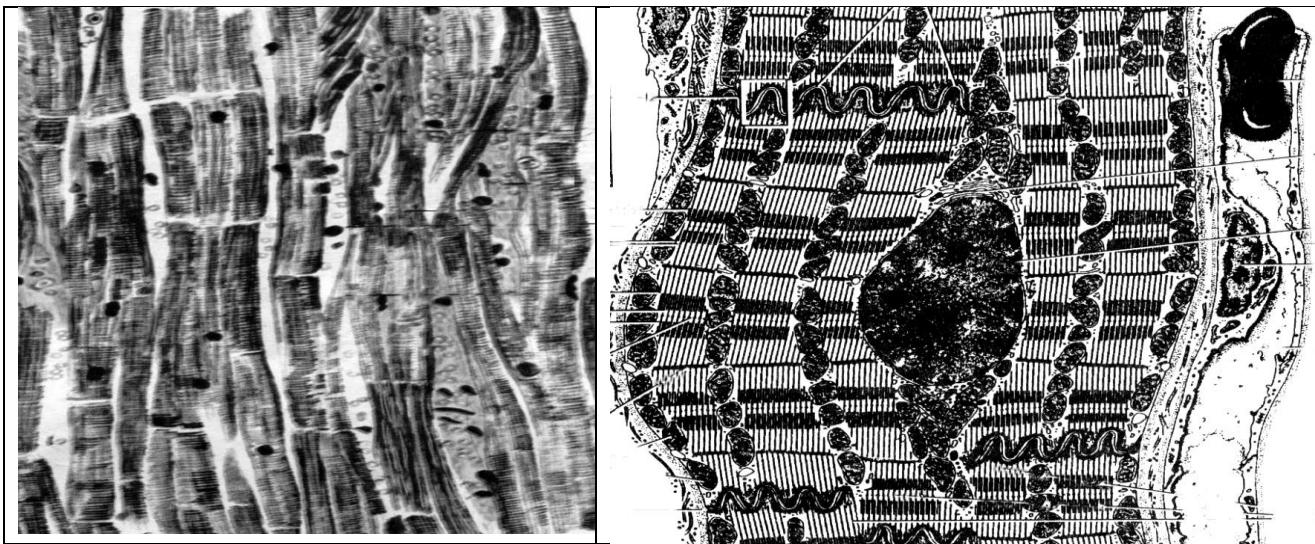
1. *Closed* system of tubes, through which blood is forced by the pumping action of the four-chambered, contractile heart.
2. Tubular walls are *permeable* so that exchange of materials can take place between the system of small blood vessels and their environment - cells, or tissue spaces.
3. *Lymphatic system* collects fluid and colloids and crystalloids from the tissue spaces and returns them to the bloodstream.
4. There is a *balance* whereby materials are lost, e.g., from kidneys, lungs, skin, and replenished by the intake of foodstuffs, air and water.

Heart

Thick-walled, hollow, muscular pumping, and endocrine, organ.

Heart wall's three layers

1. *Endocardium* (innermost)
 - o Lined by endothelium on a basal lamina.
 - o Subendothelial layer of collagenous and elastic fibres, fibroblasts and some smooth muscle cells.
 - o Subendocardial layer of CT with blood and lymphatic vessels, nerve fibres, and Purkinje fibres of the heart's conducting system. A layer worth calling a subendocardium is not everywhere present.
2. *Myocardium*
 - o Cardiac muscle fibres bundled and wound in spiralling sheets, thickest in the left ventricle, thinnest in the atria.
 - o Blood vessels and lymphatics and fine CT.
3. *Epicardium* (visceral pericardium) and subepicardium
 - o Outer mesothelial sheet and BL on
 - o loose subepicardial CT of fat cells and collagen fibres with
 - o blood vessels (coronary), lymphatics and nerves to the heart nodes.
4. *Pericardium (parietal)* CT membrane of fibres supporting a mesothelium. This faces the epicardium across the *pericardial cavity* containing a small amount of lubricating fluid.



Cardiac skeleton of dense fibrous CT, with a tendency to turn into fibrocartilage.

Cardiac muscle is a type of involuntary striated muscle found in the walls and histologic foundation of the heart, specifically the myocardium. Cardiac muscle is one of three major types of muscle, the others being skeletal and smooth muscle. The cells that comprise cardiac muscle are called cardiomyocytes and are sometimes seen as an intermediate between other types of muscle in terms of appearance, structure, metabolism, excitation-coupling and mechanism of contraction. Cardiac muscle shares similarities with skeletal muscle with regard to its striated appearance and contraction, with both differing significantly from smooth muscle cells. In addition, cardiac muscle cells, like skeletal muscle cells, are multinuclear whereas smooth muscle cells are mononuclear.

Coordinated contraction of cardiac muscle cells in the heart propel blood forward from the atria and ventricles to the blood vessels of the circulatory system. Cardiac muscle cells, like all tissues in the body, rely on an ample blood supply to deliver oxygen and nutrients and to remove waste products such as carbon dioxide. The coronary arteries fulfill this function

Striation

Cardiac muscle exhibits cross striations formed by alternating segments of thick and thin protein filaments. Like skeletal muscle, the primary structural proteins of cardiac muscle are actin and myosin. The actin filaments are thin causing the lighter appearance of the I bands in striated muscle, while the myosin filament is thicker lending a darker appearance to the alternating A bands as observed with electron microscopy. However, in contrast to skeletal muscle, cardiac muscle cells may be branched instead of linear and longitudinal.

T-Tubules

Another histological difference between cardiac muscle and skeletal muscle is that the T-tubules in cardiac muscle are larger, broader and run along the Z-Discs. There are fewer T-tubules in comparison with skeletal muscle. Additionally, cardiac muscle forms dyads instead of the triads formed between the T-tubules and the sarcoplasmic reticulum in skeletal muscle. T-tubules play critical role in excitation-contraction

coupling (ECC). Recently, the action potentials of T-tubules were recorded optically by Guixue Bu et al.

Intercalated discs

Main article: intercalated disc

Intercalated discs (IDs) are complex adhering structures which connect single cardiac myocytes to an electrochemical syncytium (in contrast to the skeletal muscle, which becomes a multicellular syncytium during mammalian embryonic development) and are mainly responsible for force transmission during muscle contraction. Intercalated discs also support the rapid spread of action potentials and the synchronized contraction of the myocardium. IDs are described to consist of three different types of cell-cell junctions: the actin filament anchoring adherens junctions (fascia adherens), the intermediate filament anchoring desmosomes (macula adherens) and gap junctions. Gap junctions are responsible for electrochemical and metabolic coupling. They allow action potentials to spread between cardiac cells by permitting the passage of ions between cells, producing depolarization of the heart muscle. However, novel molecular biological and comprehensive studies unequivocally showed that IDs consist for the most part of mixed type adhering junctions named area composita (pl. areae compositae) representing an amalgamation of typical desmosomal and fascia adhaerens proteins (in contrast to various epithelia)[citation needed]. The authors discuss the high importance of these findings for the understanding of inherited cardiomyopathies (such as Arrhythmogenic Right Ventricular Cardiomyopathy, ARVC).

Under light microscopy, intercalated discs appear as thin, typically dark-staining lines dividing adjacent cardiac muscle cells. The intercalated discs run perpendicular to the direction of muscle fibers. Under electron microscopy, an intercalated disc's path appears more complex. At low magnification, this may appear as a convoluted electron dense structure overlying the location of the obscured Z-line. At high magnification, the intercalated disc's path appears even more convoluted, with both longitudinal and transverse areas appearing in longitudinal section.

Role of calcium in contraction

In contrast to skeletal muscle, cardiac muscle requires extracellular calcium ions for contraction to occur. Like skeletal muscle, the initiation and upshoot of the action potential in ventricular muscle cells is derived from the entry of sodium ions across the sarcolemma in a regenerative process. However, an inward flux of extracellular calcium ions through L-type calcium channels sustains the depolarization of cardiac muscle cells for a longer duration. The reason for the calcium dependence is due to the mechanism of calcium-induced calcium release (CICR) from the sarcoplasmic reticulum that must occur under normal excitation-contraction (EC) coupling to cause contraction. Once the intracellular concentration of calcium increases, calcium ions bind to the protein troponin, which initiates contraction by allowing the contractile proteins, myosin and actin to associate through cross-bridge formation. Cardiac muscle is intermediate between smooth muscle, which has an unorganized sarcoplasmic reticulum and derives its calcium from both the extracellular fluid and intracellular stores, and skeletal muscle, which is only activated by calcium stored in the sarcoplasmic reticulum.

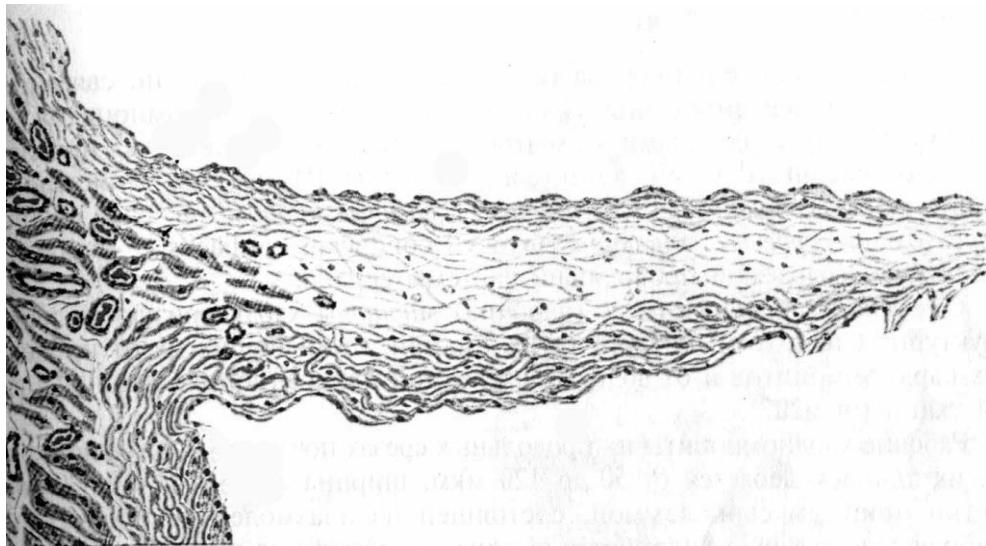
Regeneration of heart muscle cells

Until recently, it was commonly believed that cardiac muscle cells could not be regenerated. However, a study reported in the April 3, 2009 issue of *Science* contradicts that belief. Olaf Bergmann and his colleagues at the Karolinska Institute in Stockholm tested samples of heart muscle from people born before 1955 when nuclear bomb testing caused elevated levels of radioactive carbon 14 in the Earth's atmosphere. They found that samples from people born before 1955 did have elevated carbon 14 in their heart muscle cell DNA, indicating that the cells had divided after the person's birth. By using DNA samples from many hearts, the researchers estimated that a 20-year-old renews about 1% of heart muscle cells per year and about 45 percent of the heart muscle cells of a 50-year-old were generated after he or she was born.

Heart valves

1. Atrio-ventricular valves

- Leaflets are covered with endothelium on a core of dense CT fused to the supporting annulus.
- Cords of CT (chordae tendineae) connect the valve to the papillary muscles in the ventricular wall.



Semi-lunar valves

- Deploy three leaflets.
- Thinner than the atrio-ventricular valves.
- Lack chordae tendineae.
- Fibrous core enlarges to the nodule of Arantius at the free margin.

Impulse-conducting system

(coordinates myocardial contractions)

1. *Sino-atrial node* of thin, modified, cardiac muscle fibres, influenced by parasympathetic (ganglionic neurons are found in the heart) and sympathetic autonomic nerve fibres, initiates contraction (*pacemaker*).
2. Contraction spreads through the *atrial myocardium* to the *atrio-ventricular node* (Tawara's) consisting of a tangled plexus of modified cardiac fibres in the medial wall of the right atrium.

3. These fibres enlarge into Purkinje fibres and continue through the septal CT as the *bundle of His*, which then branches.

4. *Purkinje fibres* are rich in sarcoplasm and glycogen, but poor in myofilaments. They lack T-tubules, and are connected by intermediary transitional cells with ordinary myocardial fibres, whose contraction they can thus evoke in many regions of the ventricles.

5. In ungulates, Purkinje fibres are very large, pale and easily recognized: in man, the system is less obvious.

5. Endocrine role of heart

Atrial myocytes synthesize *atrial natriuretic factor* (ANF), which relaxes blood vessels and increases the excretion of sodium and water by the kidney. ANF is thus a partial counterweight to the renin-angiotensin system.

3.3. Literature recommended

Main Sources:

1. L.C. Junqueira, J. Carneiro - "Basic histology" – 11 edition - 2005.
2. A.S. Pacurar, J.W. Bigbee – "Digital histology" – Virginia - 2004.
3. "Color Atlas of basic histology" – R.Berns – 2006.
4. Sadler T.V. – "Medical embryology" Montana – 1999.
5. Ronald W., Dudek Ph.D. – "Embryology" 2 edition – 1998.
6. Inderbir Singh Textbook of Human Histology.- Jaypee. India. - 1997.
7. Ten Cate A.R. Oral Histology.- St.Louis, Baltimore, Toronto.- 1995.
8. William A., Beresford M.A. Cytology and Histology.- Anatomy department, West Virginia University, USA.- 1992.
9. K.E. Jonson - "Histology and cell biology" – 2 edition – Washington – 1991.

Additional ones:

1. Methodical Instructions.

3.4 How to work with the literature recommended:

Main tasks	Recommendations
To review the material	To use the material studied
To learn the material	To use the material on pages
To read and compose the plan	To learn the new material and be ready to write a summary
To answer the questions	To be ready to give an answer to the following:
To do the test on the material	
To be ready to answer the topic	

3.5. Self-control material:

A. Questions to be answered:

1. What parts are contain the cardiovascular system?
2. What general functions of the cardiovascular system do you know?
3. Describe heart wall's layers.
4. Describe the structure of the heart valves.
5. What components of the heat impulse-conducting system do you know?
6. What is the endocrine role of heart?

B. Test tasks to be done: Tests are applied

4. Self-preparation in the classroom.

- 1) Listen to the information.

- 2) Work with the tables and a Light microscope.
- 3) Ask about the problems that haven't been found in the information given.
- 4) To sketch in the album the investigated preparations.

5. Self-preparation work at home.

- 1) Review the material learnt in the classroom.
- 2) Compose the plan of your answer.
- 3) Answer the questions to this topic.
- 4) Do the test given above.

6. The subject of the research work.

“Comparative morphological characteristic of the atrial ventricular cardiomyocytes”
 “Opportunities of the cardiac muscle’s regeneration”

<i>Subject</i>	<i>Histology, cytology and embryology</i>
<i>Modul №2</i>	<i>Histology, cytology and embryology</i>
<i>Submodul №3</i>	<i>Special histology</i>
Topic 9	CIRCULATORY SYSTEM. ARTERIES AND VIENS

Hours: 2

1. The topic basis: the topic “CIRCULATORY SYSTEM. ARTERIES AND VIENS” is very important for future doctors in their professional activity, positively influences the students in their attitude to the future profession, forms professional skills and experience as well as taking as a principle the knowledge of the subject learnt.

2. The aims of the training course:

- 1) To have general knowledge of the topic studied.
- 2) To understand, to remember and to use the knowledge received.
- 3) To learn the classification, structure and functions of the different histological methods.
- 4) To form the professional experience by reviewing, training and authorizing it.
- 5) To be able to carry out laboratory and experimental work.

3. Materials for the before – class work self – preparation work:

3.1 Basic knowledge, experience, skills necessary for studying the topic in connection with other subjects:

	To know	To be able to
Med. Biology	the structure of the cells and tissues	work with a light microscope
Med. Physics	the structure of the light and	work with a light

	electron microscopes	microscope
Organic Chemistry	the chemical content of the cell	Speak of the topic

The contents of the topic:

Vessel Development

1. Blood and lymphatic vessels form initially as simple endothelial tubes developed from mesenchymal cells - *angioblasts*.
2. Larger vessels and systems start *independently* of one another.
3. Their tunics with muscle and CT are added from mesenchymal condensations around the endothelium.
4. Capillaries of the adult can multiply or *regenerate* by extending cords of endothelial cells, which arrange themselves into a tubule. Cords can fuse with one another to build an anastomosing network.
5. Various cytokines promote or inhibit *angiogenesis*, e.g., vascular endothelial growth factor (VEGF).

Morphology in relation to physical factors in various vessels of the system

1. *Large elastic or conducting arteries* - collagen fibres and elastic laminae predominate for strength, and elastic distensibility provides for elastic recoil during diastole thus damping the pulsatile flow resulting from the intermittent contractions of the heart. Endothelium provides a smooth lining to facilitate flow and prevent clotting.
2. *Muscular distributing arteries* - lumens of a controllable size are narrowed by smooth muscular contraction to direct blood flow appropriately for the needs of various regions; mainly muscular media, strong CT adventitia with vasa vasorum, and autonomic nerve fibres to the muscle; elastic tissue limits distension of the lumen, and acts with the muscle.
3. *Arterioles* - smooth muscle provides for a great reduction, by vasoconstriction, of the blood flow to a region; they maintain an adequate arterial pressure, but reduce blood pressure to an acceptable level for:
4. *Capillaries* - pressure is low so can be thin-walled to permit exchange of gases, minerals, carbohydrates and small molecules + water by:
 - diffusion or carrier-mediated transport through and between endothelial cells;
 - active transcytotic transport through endothelial cells; then passage through the basal lamina.

The wall serves to keep back in the capillary most of the colloidal proteins of the plasma; the presence of these then encourages the return of fluids at the venous end of the capillary.

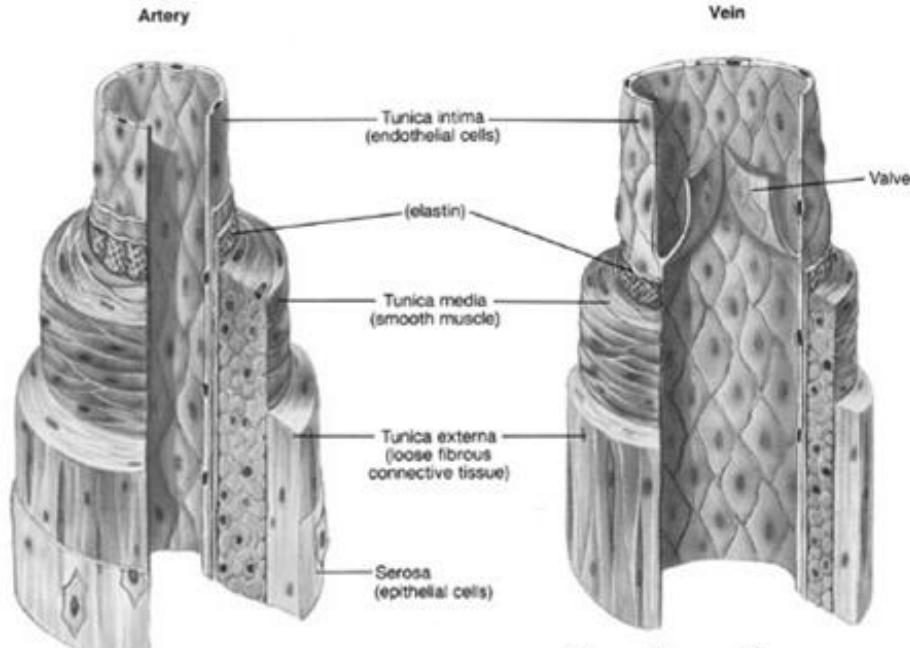
5. *Veins* - low, even pressure so have large lumens, thin collagenous walls, and valves to prevent backflow; larger veins acquire some muscle, circular and longitudinal, in the media and adventitia. In general, elastic is not needed for recoil, for variations in pressure between diastole and systole are insignificant, but the vena cava has significant numbers of elastic fibres.

Arteries

Have three main layers composed of several tissues:

- *Tunica intima*
 - Endothelial lining on a BL
 - Subendothelial CT

- Internal elastic lamina (fenestrated)
 - *Tunica media*
 - Smooth muscle cells (tightly spiralling or 'circular')
 - Sparse reticular and elastic fibres
 - *Tunica adventitia*
 - External elastic lamina (interrupted)
 - Collagenous and elastic CT (mostly longitudinal)
1. *Arterioles*, less than 0.5 mm wide, have (a),(c),(d),(e) and (g) of the above.
2. Small and medium-sized arteries (muscular/distributing) have all elements.
3. Large arteries (*elastic/conducting*) differ significantly:
- *Tunica intima*
 - Endothelium on a BL
 - Subendothelial CT
 - Innermost fenestrated elastic lamina
 - *Tunica media*
 - Many fenestrated elastic laminae interspersed with smooth muscle cells and collagen fibres
 - *Tunica adventitia*
 - Collagenous CT with vessels and nerves
- The larger arteries and veins have nutrient vessels and nerves (of vessels) in the adventitia - *vasa vasorum* and *nervi vasorum*.



Elastic and Muscular Arteries

On the basis of the kind of tissue that predominates in the tunica media, arteries are often divided into elastic arteries and muscular arteries. Elastic arteries include the aorta and the large arteries supplying the head and neck (carotids) and limbs (subclavian, axillary, iliac). The remaining arteries are muscular.

Although the arteries carry blood to peripheral tissues, elastic and muscular

arteries play differing additional roles. When the left ventricle of the heart contracts and blood enters the large elastic arteries with considerable force, these arteries distend significantly. They are able to do so because of much elastic tissue in their walls. During diastole (i.e., relaxation of the left ventricle) the walls of the arteries come back to their original size because of the elastic recoil of their walls. This recoil acts as an additional force that pushes the blood into smaller arteries. It is because of this fact that blood flows continuously through arteries (but with fluctuation of pressure during systole and diastole). In contrast a muscular artery has the ability to alter the size of its lumen by contraction or relaxation of smooth muscle in its wall. Muscular arteries can, therefore, regulate the amount of blood flowing into the regions supplied by them.

Difference between Elastic and Muscular Arteries

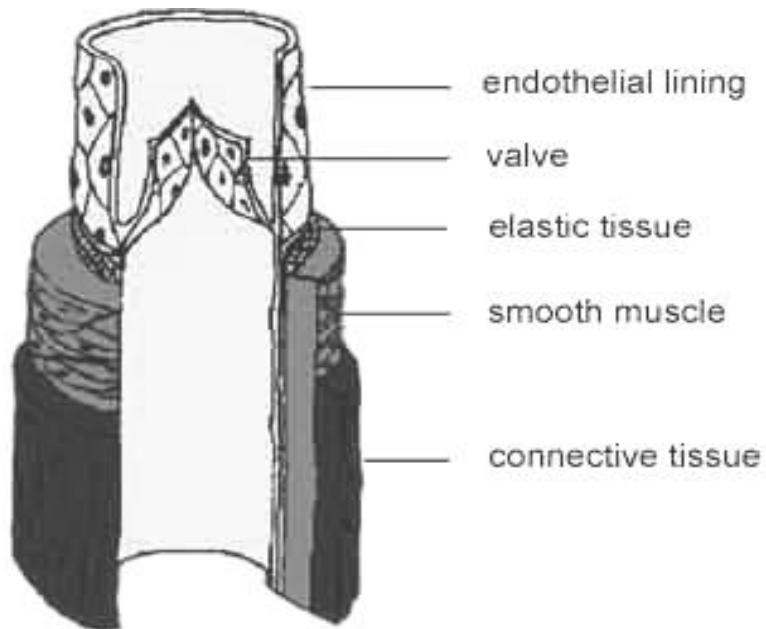
The main difference in structure of elastic and muscular arteries is in the constitution of the tunica media. In elastic arteries the media is made up mainly of elastic tissue. The elastic tissue is in the form of a series of concentric membranes that are frequently fenestrated. Between the elastic membranes there is some loose connective tissue. Some smooth muscle cells may be present. On the contrary in muscular arteries the media is made up mainly of smooth muscle. This muscle is arranged circularly. Between groups of muscle fibres some connective tissue is present this may contain some elastic fibres.

Longitudinally arranged muscle is present in the arteries that undergo repeated stretching or bending. Examples of such arteries are the coronary, carotid, axillary and palmar arteries.

The transition from elastic to muscular arteries is not abrupt. In proceeding distally along the artery there is a gradual reduction in elastic fibres and increase in smooth muscle content in the media.

There is not much difference in the intima of elastic and muscular arteries, except that the subendothelial connective tissue contains more elastic fibres in the former. In elastic arteries the internal elastic lamina is not distinct from the media as it has the same structure as the elastic membranes of the media. It stands out distinctly from the muscular media of smaller arteries.

The adventitia also does not show significant differences in elastic and muscular arteries. It is relatively thin in large arteries, in which a greater proportion of elastic fibres are present. These fibres merge with the external elastic lamina.



VEINS

1. *Venules* have an endothelial lining, BL and a collagenous outer sheath. The wall is thin enough to permit transport through it. White blood cells can squeeze between endothelial cells (*transmigration/ diapedesis*) and escape into the tissues. Lymphocytes may migrate actually through the cytoplasm of the endothelial cell. Pericytes are numerous.
2. *Small veins* acquire an additional thin media of smooth muscle and a thicker adventitia of collagen and elastic fibres.
3. No distinct elastic laminae are seen, but sparse elastic networks are found throughout the wall.
4. Many veins have *valves* - leaf-like projections of the intima, usually in a bicuspid form.
5. *Large veins* (e.g., vena cava) have bundled longitudinal smooth muscle in the CT adventitia and intima, whilst the media is thin or absent.

The basic structure of veins is similar to that of arteries. The tunica intima, media and adventitia can be distinguished especially in large veins. The structure of veins differs from that of arteries in the following respects.

1. The wall of a vein is distinctly thinner than that of an artery having the same sized lumen.
2. The tunica media contains a much larger quantity of collagen than in arteries. The amount of elastic tissue or of muscle is much less.
3. Because of the differences mentioned above, the wall of a vein is easily compressed. After death veins are usually collapsed. In contrast arteries retain their potency.
4. In arteries the tunica media is usually thicker than the adventitia. In contrast the adventitia of veins is thicker than the media (especially in large veins). In some large veins (e.g., the inferior vena cava) the adventitia contains a considerable amount of elastic and muscle fibres which run in a predominantly longitudinal direction. These fibres facilitate elongation and shortening of the vena cava with respiration. This is also facilitated by the fact that collagen fibres in the adventitia

form a meshwork that spirals around the vessel.

5. A clear distinction between the tunica intima, media and adventitia cannot be made out in small veins as all these layers consist predominantly of fibrous tissue. Muscle is conspicuous by its complete absence in venous spaces of erectile tissue, in vein of cancellous bone, dural venous sinuses, retinal veins, and placental veins.

VALVES OF VEINS

Most veins contain valves that allow the flow of blood towards the heart, but prevent its regurgitation in the opposite direction. Typically each valve is made up of two semilunar cusps. Each cusp is a fold of endothelium within which there is some connective tissue that is rich in elastic fibres. Valves are absent in very small veins; in veins within the cranial cavity, or within the vertebral canal; in the venae cavae; and in some other veins.

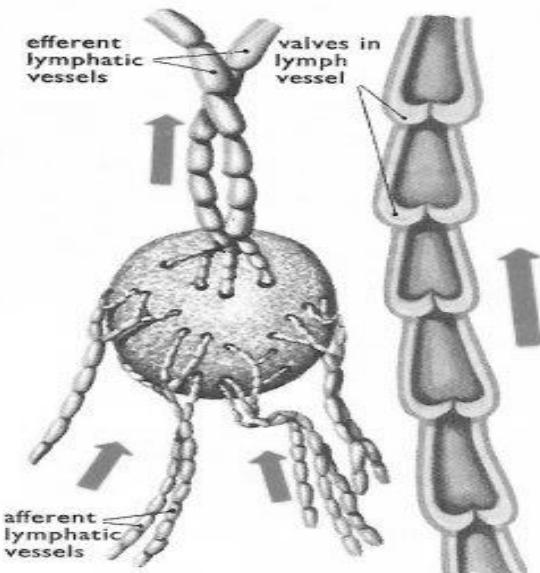
Comparison between a vein and its companion artery

<i>Artery</i>	<i>Vein</i>
(a) Shape less deformed	(a) Flattened
(b) Thick wall	(b) Thin wall
(c) Intima crinkled	(c) Intima smooth
(d) Three distinct layers (media prominent)	(d) Layering indistinct (media weak)

EXCEPTIONAL VASCULAR STRUCTURES

1. *Cerebral, retinal and osseous veins* have no valves and no media. Veins in general are very variable in their structure.
2. *Cerebral arteries* are thin walled and have no external elastic layer.
3. *Umbilical vein* is very muscular; and the umbilical arteries have little elastic, and a media with distinct longitudinal and circular muscle layers.
4. *Arterial intimal cushions* are present in arteries to erectile tissue, kidneys, etc.
5. Some vessels have a high protruding endothelium, e.g., fetal stem arteries.

LYMPHATIC VESSELS



1. Lymphatic capillaries

1. Network of blindly ending or anastomosing tubes, 5-50 µm wide.
2. The wall is made of an *endothelial tube*, with a discontinuous basal lamina and fine anchoring fibrils.
3. The wall permits the capillary to collect water, solutes and macromolecules from the tissue spaces.
4. Capillaries (i.e., a *lymphatic drainage*) are absent from the CNS, bone marrow, eye, and parts of the spleen.

2. Collecting vessels

1. Lymph passes from capillaries into larger *lymphatic vessels* with very thin walls of endothelium, basal lamina and collagen, and numerous valves.
2. Lymph is led to small protective ovoid bodies - *lymph nodes* - through whose tissues it must filter before going further.
3. Lymph collects in the *thoracic duct* before entering the circulating blood at the left innominate vein; the right lymphatic duct also collects lymph for return to the bloodstream.
4. *Thoracic duct*
 - o *Intima* of endothelium, BL, CT, some longitudinal smooth muscle and an elastic lamina.
 - o Thick *media* of mixed longitudinal and circular smooth muscle.
 - o Thin *adventitia* of collagen and a little longitudinal smooth muscle, vasa vasorum and nerve fibres.
 - o A *valve* is at the venous exit.

3. Lymph

1. Adds to the blood proteins leaked from blood capillaries, new and recirculated lymphocytes, and antibodies, fat droplets (chylomicrons), etc.
2. Fat is collected from the gut in blind lymphatic capillaries lying centrally in intestinal villi. The fat-whitened lymph (chyle) gives these vessels a milky colour, hence their name *lacteal*.

4. Oedema and its causes

Oedema is an excessive accumulation of tissue fluid, involving mainly the extracellular space (except in CNS), and making the tissue swollen and puffy. It is caused by:

1. *Venous obstruction*, e.g., from cardiac incompetence, which
 - o raises intracapillary hydrostatic pressure, thus forcing more fluid into the tissues;
 - o reduces the volume of blood collected from the capillaries.
2. *Injured capillary walls*, e.g., from heat, become permeable permitting greater egress of fluid, solutes and colloids.
3. Resulting *reduction in intracapillary colloid* at the venous end of the blood capillary lessens the *osmotic attraction* for tissue fluid to come back into the capillary.
4. *Lowering of systemic plasma colloids* (proteins), from
 - o proteinuria (excretion of protein in the urine),
 - o protein starvation, or exudation from burnt skin surfaces, will likewise reduce the osmotic return of extracellular fluid to capillary blood.

5. *Obstruction of lymphatic vessels* receiving the lymph drained from tissue fluid by lymph capillaries, for instance, blockage by metastatic cancer cells. The tropical filaria parasites often block the lymphatics of their host causing gross swelling (elephantiasis) of affected extremities.

3.3. Literature recommended

Main Sources:

1. L.C. Junqueira, J. Carneiro - “Basic histology” – 11 edition - 2005.
2. A.S. Pacurar, J.W. Bigbee – “Digital histology” – Virginia - 2004.
3. “Color Atlas of basic histology” – R.Berns – 2006.
4. Sadler T.V. – “Medical embryology” Montana – 1999.
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6. William A., Beresford M.A. Cytology and Histology.- Anatomy department, West Virginia University, USA.- 1992.
7. K.E. Jonson - “Histology and cell biology” – 2 edition – Washington – 1991.

Additional ones:

1. Methodical Instructions.

3.4 How to work with the literature recommended:

Main tasks	Recommendations
To review the material	To use the material studied
To learn the material	To use the material on pages
To read and compose the plan	To learn the new material and be ready to write a summary
To answer the questions	To be ready to give an answer to the following:
To do the test on the material	
To be ready to answer the topic	

3.5. Self-control material:

A. Questions to be answered:

1. From what tissues vessel develop?
2. Describe morphology in relation to physical factors in various vessels.
3. What are the arteries?
4. What differences between elastic and muscular arteries?
5. What are the veins?
6. Describe comparisons between a vein and its companion artery.
7. What exceptional vascular structures do you know?
8. What do you know about lymphatic vessels?
9. What about oedema and its causes?

B. Test tasks to be done: Tests are applied

4. Self-preparation in the classroom.

- 1) Listen to the information.
- 2) Work with the tables and a Light microscope.
- 3) Ask about the problems that haven't been found in the information given.
- 4) To sketch in the album the investigated preparations.

5. Self-preparation work at home.

- 1) Review the material learnt in the classroom.
- 2) Compose the plan of your answer.
- 3) Answer the questions to this topic.
- 4) Do the test given above.

6. The subject of the research work.

<i>Subject</i>	<i>Histology, cytology and embryology</i>
<i>Modul №2</i>	<i>Histology, cytology and embryology</i>
<i>Submodul №3</i>	<i>Special histology</i>
Topic 10	CIRCULATORY SYSTEM. MICROVASCULATION

Hours: 2

1. The topic basis: the topic “CIRCULATORY SYSTEM. MICROVASCULATION” is very important for future doctors in their professional activity, positively influences the students in their attitude to the future profession, forms professional skills and experience as well as taking as a principle the knowledge of the subject learnt.

2. The aims of the training course:

- 1) To have general knowledge of the topic studied.
- 2) To understand, to remember and to use the knowledge received.

- 3) To learn the classification, structure and functions of the different histological methods.
- 4) To form the professional experience by reviewing, training and authorizing it.
- 5) To be able to carry out laboratory and experimental work.

3. Materials for the before – class work self – preparation work:

3.1 Basic knowledge, experience, skills necessary for studying the topic in connection with other subjects:

	To know	To be able to
Med. Biology	the structure of the cells and tissues	work with a light microscope
Med. Physics	the structure of the light and electron microscopes	work with a light microscope
Organic Chemistry	the chemical content of the cell	Speak of the topic

The contents of the topic:

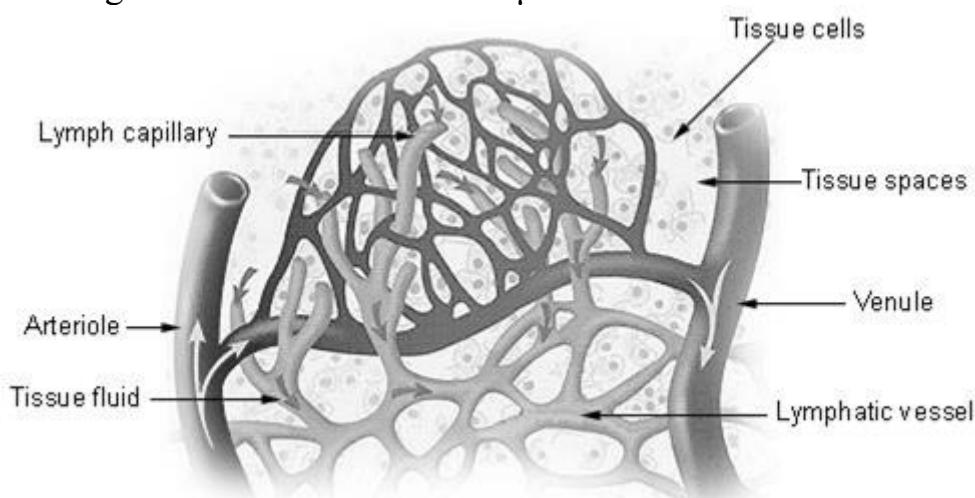
MICROVASCULATION

(Microcirculatory rate) contain arterioles, capillaries, venules and arteriovenules anastomoses.

ARTERIOLES

When traced distally, muscular arteries progressively decrease in calibre till they have a diameter of about 100 µm. They then become continuous with arterioles. The larger or muscular arterioles are 100 to 50 µm in diameter. Arterioles less than 50 nm in diameter are called terminal arterioles. Muscular arterioles can be distinguished from true arteries by their small diameter, and by the fact that they do not have an internal elastic lamina. They have a few layers of smooth muscle in their media. Terminal arterioles can be distinguished from muscular arterioles as follows.

As stated above they have a diameter less than 50 µm, the smallest terminal arterioles having a diameter as small as 12 µm.



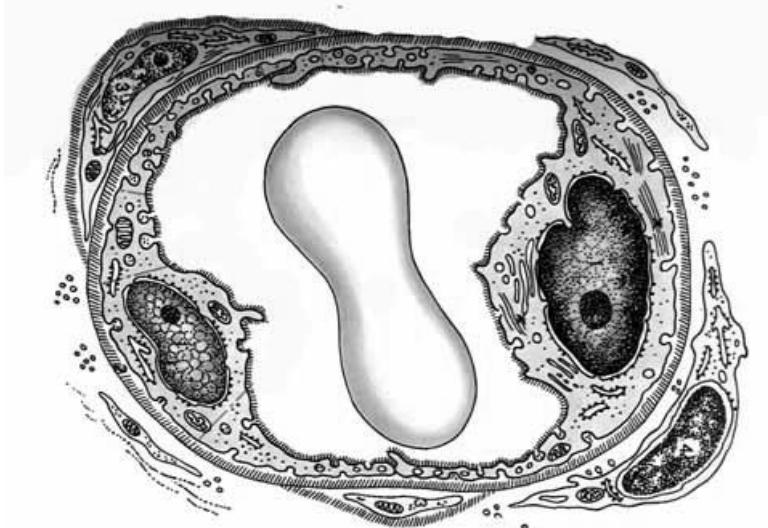
They have only a thin layer of muscle in their walls.

They give off lateral branches (called meta-arterioles) to the capillary bed.

The initial segment of each lateral branch is surrounded by a few smooth muscle cells. These muscles constitute the precapillary sphincter. The adventitia of arterioles is formed by a thin network of collagen fibres.

BLOOD CAPILLARIES

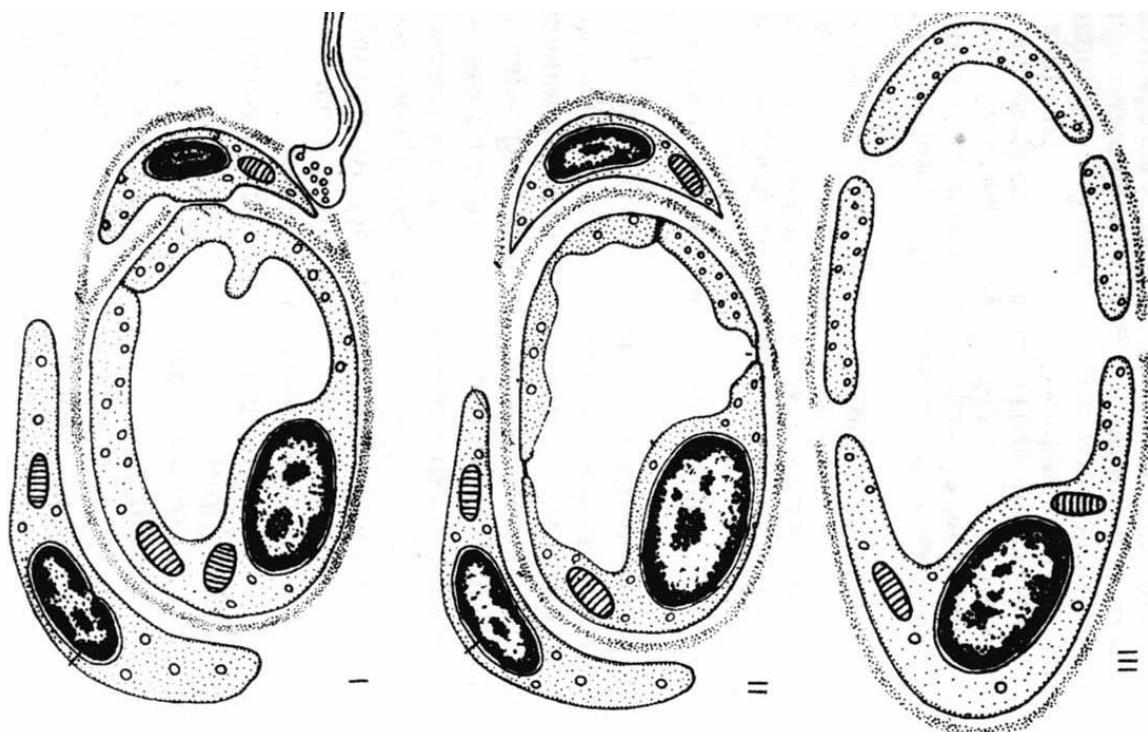
Very numerous, anastomosing, delicate tubes of diameter 7-9 μm .



Total cross-sectional area of the *capillary bed* is very great, thus blood flows slowly under low pressure.

Wall is made up of curved, thin, plate-like *endothelial cells* lying on a BL and oriented with the tube's long axis.

Type I unfenestrated capillaries have complete endothelial cells, e.g., in muscle and skin: type II capillaries have endothelial cells with *fenestrations/pores* through them (not between them), e.g., in kidney and choroid plexus. Type III capillaries have wide irregular lumens and a continuous, but fenestrated, *non-phagocytic* lining; are the usual smallest vessel in endocrine tissue.



1. Endothelial cells have serrated margins where they *attach* by glycocalyx and gap junctions to each other, and by occluding junctions where more of a barrier is

needed, e.g., in the brain. Continuous capillaries have no gaps between the endothelial cells, in contrast to *discontinuous* capillaries.

2. *Transport* is controlled by the cells, with diffusion and facilitated transport for small molecules, and through the BL, and transcytotic vesicles or passage through the pores for larger materials.

3. Some capillaries have the occasional pericapillary cell imbedded with the BL - *pericyte* - of unknown (perhaps contractile) function.

Show transitions at both ends: to *arterioles* (by acquiring smooth muscle cells), or *venules* (by widening and taking on more collagen fibrils).

Endothelial cells secrete vasoconstrictor, vasodilator, and mitotic agents, and their own BL; they interact with blood, leucocytes and platelets, vary their permeability, and proliferate. Despite their lack of presence in routine light microscopy, they keep very busy, and are specialised for each organ that they serve.

Selectins are molecules expressed on the endothelial cells of small vessels, and on white blood cells. They bond intermittently with the sugars of a glycoprotein on the corresponding cell to cause the WBC *to roll* to a stop attached to the endothelium, before squeezing through the vessel wall into the connective tissues for defence. Sometimes the selectin is on endothelium, the ligand on the WBC, at other times the reverse achieves a similar result.

von Willebrand factor (vWF) also has a dual distribution, being present in Weibel-Palade granules of endothelial cells and alpha granules of platelets. Vascular injury releases vWF from endothelium to cause platelet activation, aggregation, binding to subendothelial collagen, and blood clotting - processes of *haemostasis*.

VENULES

The smallest veins, into which capillaries drain, are called venules. They are 20-30 μm in diameter. Their walls consist of endothelium, basal lamina, and a thin adventitia consisting of longitudinally running collagen fibres. Flattened or branching cells called pericytes may be present outside the basal laminae of small venules (called post-capillary venules), while some muscle may be present in larger vessels (muscular venules).

Functionally, venules have to be distinguished from true veins. The walls of venules (especially those of post-capillary venules) have considerable permeability and exchanges between blood and surrounding tissues can take place through them. In particular venules are the sites at which lymphocytes and other cells may pass out of (or into) the blood stream.

MECHANISMS CONTROLLING BLOOD FLOW THROUGH THE CAPILLARY BED

The requirements of blood flow through a tissue may vary considerably at different times. For example, a muscle needs much more blood when engaged in active contraction, than when relaxed. Blood flow through intestinal villi needs to be greatest when there is food to be absorbed. The mechanisms that adjust blood flow through capillaries are considered below.

Blood supply to relatively large areas of tissue is controlled by contraction or relaxation of smooth muscle in the walls of muscular arteries and arterioles. Control of supply to smaller areas is effected through arteriovenous anastomoses, precapillary

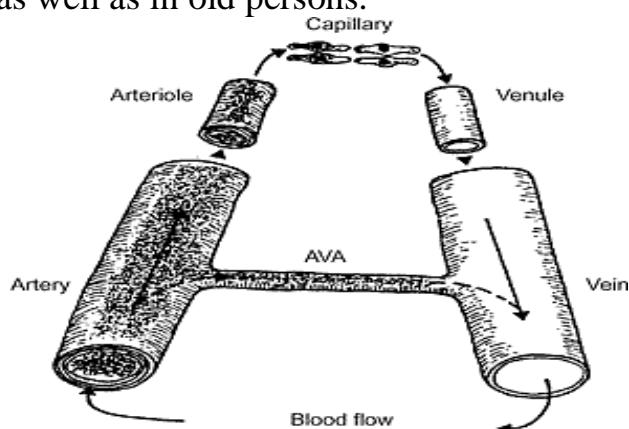
sphincters, and thoroughfare channels as described below.

ARTERIOVENOUS ANASTOMOSES

In many parts of the body small arteries and veins are connected by direct channels that constitute arteriovenous anastomoses. These channels may be straight or coiled. Their walls have a thick muscular coat which is richly supplied with sympathetic nerves. When the anastomoses are patent blood is short circuited from the artery to the vein so that very little blood passes through the capillary bed. However, when the muscle in the wall of the anastomosing channel contracts its lumen is occluded so that all blood now passes through the capillaries. Arteriovenous anastomoses are found in the skin especially in that of the nose, lips and external ear; and in the mucous membrane of the alimentary canal and nose. They are also seen in the tongue, in the thyroid, in sympathetic ganglia, and in the erectile tissues of sex organs.

Arteriovenous anastomoses in the skin help in regulating body temperature, by increasing blood flow through capillaries in warm weather; and decreasing it in cold weather to prevent heat loss.

Arteriovenous anastomoses are few and inefficient in the newborn. In old age again, arteriovenous anastomoses of the skin decrease considerably in number. These observations are to be correlated with the fact that temperature regulation is not efficient in the newborn as well as in old persons.



PRECAPILLARY SPHINCTERS & THOROUGHFARE CHANNELS

Arteriovenous anastomoses described above control blood flow through relatively large segments of the capillary bed. Much smaller segments can be individually controlled as follows.

We have seen that capillaries arise as side branches of terminal arterioles; and that the initial segment of each such branch is surrounded by a few smooth muscle cells that constitute a precapillary sphincter. Blood flow through any part of the capillary bed can be controlled by the precapillary sphincter.

In many situations arterioles and venules are connected (apart from capillaries) by some channels that resemble capillaries, but have a larger calibre. These channels run a relatively direct course between the arteriole and venule. Isolated smooth muscle fibres may be present on their walls. These are called thoroughfare channels. At times when most of the precapillary sphincters in the region are contracted (restricting flow through capillaries), blood is short circuited from arteriole to venule through the thoroughfare channels. A thoroughfare channel and the capillaries

associated with it are sometimes referred to as a microcirculatory unit.

EXCEPTIONS TO THE VASCULAR PATTERN OF ARTERIES, ARTERIOLES, CAPILLARY BED, VENULES, VEINS, HEART

1. *Arteriovenous anastomoses* - bypassing the bed (e.g., in the skin and gut) with thick muscle to close the bypass.

2. *Arterial anastomoses*, e.g., circle of Willis to the brain.

3. In the periphery, arteries and veins run together with nerves bound in CT as a *neurovascular bundle*. In the brain, arterial and venous distributions are separate.

4. *Vasa vasorum* are blood vessels serving the adventitia and media of larger arteries and veins.

5. *Portal systems* exist to the liver and pituitary gland, where venous blood drained from one organ is fed as a supply to the sinusoids or capillaries of another.

6. *Sinusoids* may take the place of a capillary bed. Thus, for instance, sinusoidal capillaries permit blood to pass slowly by and influence chemosensitive epithelioid cells in the *carotid body/glomus caroticum*.

7. *Venous sinuses* are endothelium-lined CT spaces where blood can collect for purposes other than metabolic exchange, thus, as part of the venous collecting system, e.g, coronary and dural sinuses, and in erectile tissue. (Caution: sinus is also a term for the pocket behind a venous valve - a site causing problems, when veins are grafted to substitute for arteries.)

3.3. Literature recommended

Main Sources:

1. L.C. Junqueira, J. Carneiro - “Basic histology” – 11 edition - 2005.
2. A.S. Pacurar, J.W. Bigbee – “Digital histology” – Virginia - 2004.
3. “Color Atlas of basic histology” – R.Berns – 2006.
4. Sadler T.V. – “Medical embryology” Montana – 1999.
5. Ronald W., Dudek Ph.D. –“Embryology” 2 edition – 1998.
6. Inderbir Singh Textbook of Human Histology.- Jaypee. India. - 1997.
7. Ten Cate A.R. Oral Histology.- St.Louis, Baltimore, Toronto.- 1995.
8. William A., Beresford M.A. Cytology and Histology.- Anatomy department, West Virginia University, USA.- 1992.
9. K.E. Jonson - “Histology and cell biology” – 2 edition – Washington – 1991.

Additional ones:

1. Methodical Instructions.

3.4 How to work with the literature recommended:

Main tasks	Recommendations
To review the material	To use the material studied
To learn the material	To use the material on pages
To read and compose the plan	To learn the new material and be ready to write a summary
To answer the questions	To be ready to give an answer to the following:
To do the test on the material	
To be ready to answer the topic	

3.5. Self-control material:

A. Questions to be answered:

1. What components of the microcirculatory rate do you know?

2. What about arterioles do you know?
3. Describe types of blood capillaries.
4. What about venules do you know?
5. What are the mechanisms controlling blood flow through the capillary bed?
6. Give the characteristic of the arteriovenous anastomoses.

B. Test tasks to be done: Tests are applied

4. Self-preparation in the classroom.

- 1) Listen to the information.
- 2) Work with the tables and a Light microscope.
- 3) Ask about the problems that haven't been found in the information given.
- 4) To sketch in the album the investigated preparations.

5. Self-preparation work at home.

- 1) Review the material learnt in the classroom.
- 2) Compose the plan of your answer.
- 3) Answer the questions to this topic.
- 4) Do the test given above.

6. The subject of the research work.

<i>Subject</i>	<i>Histology, cytology and embryology</i>
<i>Modul №2</i>	<i>Histology, cytology and embryology</i>
<i>Submodul №3</i>	<i>Special histology</i>
<i>Topic 11</i>	HAEMOCYTOPOIESIS. BONE MARROW

Hours: 2

1. The topic basis: the topic “**HAEMOCYTOPOIESIS. BONE MARROW**” is very important for future doctors in their professional activity, positively influences the students in their attitude to the future profession, forms professional skills and experience as well as taking as a principle the knowledge of the subject learnt.

2. The aims of the training course:

- 1) To have general knowledge of the topic studied.
- 2) To understand, to remember and to use the knowledge received.
- 3) To learn the classification, structure and functions of the different histological methods.
- 4) To form the professional experience by reviewing, training and authorizing it.
- 5) To be able to carry out laboratory and experimental work.

3. Materials for the before – class work self – preparation work:

3.1 Basic knowledge, experience, skills necessary for studying the topic in connection with other subjects:

	To know	To be able to
Med. Biology	the structure of the cells and tissues	work with a light microscope
Med. Physics	the structure of the light and electron microscopes	work with a light microscope

The contents of the topic:**Haemocytopoiesis**

Continuous formation of the cells, corpuscles, and platelets of the blood is necessary to keep their numbers relatively constant as they wear out or are lost from the body. The formation is called *haemocytopoiesis* or *haemopoiesis* for short.

Divisions of Haemopoiesis

1. *Myelopoiesis* - formation of granular leucocytes (granulopoiesis), monocytes (monopoiesis), erythrocytes (erythropoiesis), and platelets (thrombopoiesis).
2. *Lymphopoiesis* - formation of lymphocytes and plasma cells. (Plasma cells are not normally seen in the blood.)

Sites of Myelopoiesis

1. *Embryonic*: mesenchyme gives rise to:

- blood islands in the yolk sac;
- fetal liver haemopoietic tissue;
- bone marrow in cavities of the developing bones;
- marrow in the spleen and lymph nodes.

2. *Adult*

- Red/myeloid marrow remains mostly in the axial skeleton - skull diploë, ribs, sternum, parts of the vertebrae and pelvis.
- Ectopic/extramedullary myelopoiesis may be seen in adults, usually in disease, e.g., fibrosis of marrow, and at the sites of myelopoiesis in the fetus.

Theoretical Considerations of Haemopoiesis

1. Granular leucocytes and RBCs are specialized *end products* in being unable to divide, and living for only a few weeks. Since their numbers in the blood stay constant, new cells must be forming from less specialized ones.
2. Bone marrow, stained as for a blood smear, has cells, construed from their granularity, eosinophilia, nuclear morphology, etc, as members of developmental sequences, apparently starting with a large, undistinguished weakly basophil, primitive cell, and ending as one of the clear-cut specialized kinds.
3. If all the primitive marrow cells multiplied and then turned into blood cells, when the blood cells were spent, no primitive ones would exist to replace them. Thus, the primitive cells must act as stem cells able to divide, and with two possible fates: some *to stay* as primitive stem cells, others *to differentiate* into special forms.
4. Since there are several specialized blood cells, are there separate, but histologically indistinguishable, stem cells: one for each blood cell type? - The *polyphyletic theory* of committed progenitors for each lineage. Yes, but the *monophyletic* theory also survives, because rare multipotent/pluripotent stem cells exist, and can replenish the restricted stem cells, e.g., those for erythropoiesis.
5. CFU-S denotes the pluripotent cell in mouse, and forms the basis for naming progenitor cells in humans. *Colony-forming unit - spleen/CFU-S* was the cell that could give rise to an island/colony of complete haemopoiesis in the spleen of the mouse, after splenic and other sites of haemopoiesis had been totally destroyed by irradiation. Where, then, did the rescuing cell come from to form the colony? The

CFU-S was obtained from infant mice and injected just after the irradiation. (A convenient human source for equivalent stem cells is blood from the umbilical cord.)

6. All cell divisions and differentiations need controlling growth factors (cytokines), not only to maintain the stem cell population, but to persuade some of them to fill precisely the ranks of the various blood cells.

7. After a stem cell becomes a *committed precursor/progenitor* for a certain cell line, a period elapses when histology, without immunostaining, cannot identify the line. Later, perceptible morphological changes make the cell a recognizable precursor, say a proerythroblast. Thereafter, the development of the cell is divided into named stages, each based on a significant change in appearance from the previous stage.

The potential for confusion exists, since workers have differed in the number of stages chosen, e.g., omitting pre-stages, and their names for a given cell type, e.g., rubriblast/normoblast for erythroblast.

8. The ability of the few stem cells to divide does not preclude proliferation by committed precursors, and by cells at later, recognizable, stages of development, for continued *amplification* of cell numbers.

Changes in Developing Blood Cells

1. Erythrocytes

1. Large, weakly basophilic *pro-erythroblast* increases the free ribosomes in its cytoplasm to become a *basophil erythroblast*.
2. Cell size decreases, and organelles are lost.
3. *Nucleus*, initially large and pale, with nucleoli, gets smaller and stains more darkly.
4. *Cytoplasm* acquires *haemoglobin* at the expense of ribosomal ribonucleoprotein (RNP) - thus its staining affinity changes from basophilia to acidophilia; the mixed-hued halfway stage is the *polychromic/polychromatophil erythroblast*.
5. Small cell, with orange cytoplasm and a round dark nucleus, is the *orthochromic erythroblast/normoblast*.
6. Nucleus, in a little cytoplasm, is *extruded* for phagocytosis.
7. *Reticulocyte/polychromatophil erythrocyte* is an RBC that is released into the blood still with RNP in its cytoplasm. Supravital staining with brilliant cresyl blue causes this material to clump as a blue network (reticulum) in around 2 per cent of the RBCs of normal blood.

2. Granulocyte

1. *Myeloblast/granuloblast* develops into a
2. *promyelocyte* beginning to acquire non-specific azurophil granules in the cytoplasm, and with its nucleus getting smaller and darker.
3. Myelocyte starts to have granules *specific* for one of the three kinds of granulocyte in their staining affinity.
4. Nucleus elongates and indents, and chromatin becomes coarser, giving the *metamyelocyte* (now unable to divide).
5. More granules form and the nucleus starts segmenting - *band/juvenile granulocyte*, which becomes the mature granulocyte.

3. Platelets

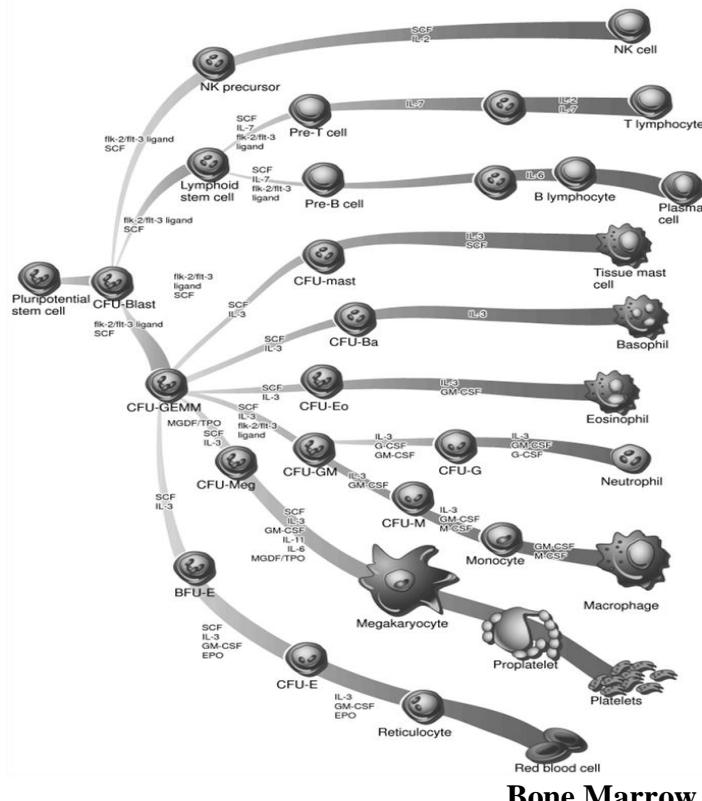
1. *Haemocytoblast* enlarges to become a *megakaryoblast*.
2. The nucleus experiences several rounds of DNA replication, but each time with reassembly of a single nuclear envelope and no segregation into separate nuclei. Thus

the nucleus takes on a distinctive *lumpy, polyplloid* form. (The single, large, lumpy nucleus is the criterion for distinguishing megakaryocytes from nearby osteoclasts in bone sections.)

3. Fine cytoplasmic azurophil granules accumulate as the cell becomes a very large granular *megakaryocyte*.
4. Many paired membranes of smooth ER (*demarcation membranes*) appear and contribute plasmalemma to the formation of
5. *pseudopodia*, which are extended into the lumen of a sinusoid, where they cast off in the blood as *platelets*.
6. Megakaryocyte cytoplasm might also serve as a transcellular migration pathway for some new leucocytes passing from the marrow into the blood.

4. Agranular leucocytes

1. In developing, they do not become so strikingly different from their stem cells as do granulocytes and RBCs.
2. Monocytes form from monoblast/pre-monocyte precursors in bone marrow.
3. Lymphocytes develop from lymphoblasts in bone marrow and lymphoid organs.
4. Some circulating lymphocytes appropriately stimulated can also become lymphoblasts.



Bone Marrow

1. The naked-eye appearance of fresh, unstained marrow may be *red* from many developing RBCs, or *yellow* from mainly fat cells.
2. Red marrow has many elements:
 - o *Blood sinusoids* are lined by *endothelial cells* on an incomplete BL. *Collagen fibrils* (reticular fibres) support these, and
 - o *adventitial stromal/reticular cells*, similar to fibroblasts, but extending processes between, and greatly influencing, the haemopoietic cells.

- *Macrophages* cleanse blood, and detect and destroy worn-out RBCs and other elements. The iron recovered is stored, combined with protein as ferritin granules, before release to the labile pool and reuse.
 - *Blood cells* develop extravascularly, are stored, then released through the sinusoidal wall into the circulation.
 - *Megakaryocytes* form and release platelets.
 - *Fat cells* are present, large and empty of fat in embedded sections.
 - *Bone surface cells* act as an enclosing sac for the marrow.
3. *Microscopic methods for marrow* include sections, and smears of aspirated sternal marrow stained with a blood stain.

3.3. Literature recommended

Main Sources:

1. L.C. Junqueira, J. Carneiro - “Basic histology” – 11 edition - 2005.
2. A.S. Pacurar, J.W. Bigbee – “Digital histology” – Virginia - 2004.
3. “Color Atlas of basic histology” – R.Berns – 2006.
4. Ronald W., Dudek Ph.D. –“Embryology” 2 edition – 1998.
5. Inderbir Singh Textbook of Human Histology.- Jaypee. India. - 1997.
6. William A., Beresford M.A. Cytology and Histology.- Anatomy department, West Virginia University, USA.- 1992.

Additional ones:

1. Methodical Instructions.

3.4 How to work with the literature recommended:

Main tasks	Recommendations
To review the material	To use the material studied
To learn the material	To use the material on pages
To read and compose the plan	To learn the new material and be ready to write a summary
To answer the questions	
To do the test on the material	To be ready to give an answer to the following:
To be ready to answer the topic	

3.5. Self-control material:

A. Questions to be answered:

1. What is the haemocytogenesis?
2. What studies of the divisions of haemopoiesis do you know?
3. What are the sites of myelopoiesis in embryo?
4. What are the sites of myelopoiesis in adult?
5. Describe the changes in developing red blood cells.
6. Describe the changes in developing granulocyte.
7. Describe the changes in developing platelets.
8. Describe the changes in developing agranular leucocytes.
9. Describe the structure of the bone marrow.

B. Test tasks to be done: Tests are applied

4. Self-preparation in the classroom.

- 1) Listen to the information. 2) Work with the tables and a Light microscope. 3) Ask about the problems that haven't been found in the information given. 4) To sketch in the album the investigated preparations.

5. Self-preparation work at home.

- 1) Review the material learnt in the classroom.
- 2) Compose the plan of your answer.
- 3) Answer the questions to this topic.
- 4) Do the test given above.

6. The subject of the research work.

“Modern theories of the haemopoiesis”
“Stem cells in the medicine”

<i>Subject</i>	<i>Histology, cytology and embryology</i>
<i>Modul №2</i>	<i>Histology, cytology and embryology</i>
<i>Submodul №3</i>	<i>Special histology</i>
<i>Topic 12</i>	THYMUS. PALATINE TONSILS

Hours: 2

1. The topic basis: the topic “**THYMUS. PALATINE TONSILS**” is very important for future doctors in their professional activity, positively influences the students in their attitude to the future profession, forms professional skills and experience as well as taking as a principle the knowledge of the subject learnt.

2. The aims of the training course:

- 1) To have general knowledge of the topic studied.
- 2) To understand, to remember and to use the knowledge received.
- 3) To learn the classification, structure and functions of the different histological methods.
- 4) To form the professional experience by reviewing, training and authorizing it.
- 5) To be able to carry out laboratory and experimental work.

3. Materials for the before – class work self – preparation work:

3.1 Basic knowledge, experience, skills necessary for studying the topic in connection with other subjects:

	To know	To be able to
Med. Biology	the structure of the cells and tissues	work with a light microscope
Med. Physics	the structure of the light and electron microscopes	work with a light microscope
Organic Chemistry	the chemical content of the cell	Speak of the topic

The contents of the topic:

Lymphoid cells mediating the immune response - lymphocytes, plasma cells, dendritic cells (APCs) and macrophages - occur:

(a) pathologically, at any site of chronic infection;

(b) regularly in the lamina propria of tracts exposed to antigens - respiratory, GI and genito-urinary, and the ocular conjunctiva; lymphocytes also migrate into the epithelia;

(c) in dedicated secondary lymphoid organs - spleen and lymph nodes.

Lymphocyte and APC traffic Lymphocytes circulate between tissue sites and blood and lymph flows; and APCs, such as the Langherhans cell, travel to nodes as the lymph-borne dendritic antigen-presenting cell - the *veiled cell*. Lymphocytes travel locally in a lamina propria of a mucosa.

The lymphoid cells are densely packed in rounded *nodules/follicles* in parts of the spleen and nodes. Aggregates of nodules occur in the *tonsils*, *appendix* and ileal *Peyer's patches* of the GI tract; whereas *solitary nodules* may exist anywhere in the mucosae of all 'open' tracts.

Wherever nodules may be found, close by are lymphoid cells dispersed more *diffusely*.

Most nodules have paler central regions - *germinal centres*, but these are not essential for cell proliferation. Germinal centres recruit virgin B cells, and follicular dendritic cells then present them with antigen. The B cells progressively refine their response to the antigen, in terms of Ig class, affinity, cell numbers, and whether to be plasma cells or memory cells.

The *primary lymphoid organs* - thymus and fetal bone marrow - store, release and confer competence on the lymphocytes that populate the secondary organs and CTs, but do not participate directly in defence.

Lymphocytes migrate in the blood and lymphatic flows for:

(a) the initial *colonization* of spleen, etc;

(b) a constant vigilant patrol by *recirculation* around the body, as memory or naïve cells;

(c) the *propagation* of an active immune response, as activated cells.

The *secondary lymphoid organs* provide:

(a) APCs/reticular cells and macrophages to activate lymphocytes;

(b) many lymphocytes to respond to a major antigenic challenge coming via the blood (spleen) or lymph (nodes);

(c) lymphocytes to propagate the immune response further, say, to recruit other nodes;

(d) a cleansing action by macrophages to remove from blood and lymph undesirable materials.

THYMUS

The thymus is an organ that not usually seen in dissection hall cadavers (because of atrophy in old people, and because of rapid autolysis after death). The organ is also not accessible for clinical examination (as it lies deep to the manubrium sterni). It is well developed between birth and puberty, but thereafter undergoes gradual involution. However, the thymus is now believed to produce T-lymphocytes throughout life.

The thymus consists of right and left lobes that are joined together by fibrous tissue. Each lobe has a connective tissue capsule. Connective tissue septa passing inwards from the capsule incompletely subdivide the lobe into a large number of lobules.

Each lobule is about 2 mm in diameter. It has an outer cortex and an inner medulla. Both the cortex and medulla contain cells of two distinct lineages as described below. The medulla of adjoining lobules is continuous.

Epithelial Cells

Embryologically these cells are derived from endoderm lining the third pharyngeal pouch. (It is possible that some of them may be of ectodermal origin). The cells lose all contact with the pharyngeal wall. In the fetus their epithelial origin is obvious. Later they become flattened and may branch. The cells join to form sheets that cover the internal surface of the capsule, the surfaces of the septa, and the surfaces of blood vessels. The epithelial cells lying deeper in the lobule develop processes that join similar processes of other cells, to form a reticulum. It may be noted that this reticulum is cellular, and has no similarity to the reticulum formed by reticular fibres (and associated fibroblasts) in lymph nodes and spleen. Epithelial cells of the thymus are not phagocytic.

It has been suggested that the sheets of epithelial cells present deep to the capsule, around septa, and around blood vessels form an effective blood-thymus barrier that prevents antigens (present in blood) from reaching lymphocytes present in the thymus.

On the basis of structural differences several types of epitheliocytes are recognized. Type 1 epitheliocytes line the inner aspect of the capsule, the septa and blood vessels. These are the cells forming the partial haemothymic barrier mentioned above. Type 2 and type 3 cells are present in the outer and inner parts of the cortex respectively. Type 4 cells lie in the deepest parts of the cortex, and also in the medulla. Type 5 cells are present around corpuscles of Hassall.

Lymphocytes (Thymocytes)

In the cortex of each lobule of the thymus the reticulum formed by epithelial cells is densely packed with lymphocytes. Stem cells formed in bone marrow focal to the thymus. Here they come to lie in the superficial part of the cortex, and divide repeatedly to form small lymphocytes. Lymphatic nodules are not present in the normal thymus.

The medulla of each Lobule also contains lymphocytes, but these are less densely packed than in the cortex. As a result the epithelial reticulum is more obvious in the medulla than in the cortex. As thymocytes divide they pass deeper into the cortex and into the medulla. Ultimately, they leave the thymus by passing into blood vessels and lymphatics.

Macrophages

Apart from epithelial cells and lymphocytes the thymus contains a fair number of macrophages (belonging to the mononuclear phagocyte system). They are present subjacent to the capsule, at the cortico-medullary junction, and in the medulla. The subcapsular macrophages are highly phagocytic. Deeper lying macrophages are dendritic cells.

Corpuscles of Hassall

These are small rounded structures present in the medulla of the thymus. Each corpuscle has a central core formed by epithelial cells that have undergone degeneration. These cells ultimately form a pink staining hyaline mass. Around this mass there is a wall formed by concentrically arranged epithelial cells. These cells also stain bright pink with haematoxylin and eosin. The central mass of the corpuscle may also contain degenerating macrophages. The functional significance of the corpuscles of Hassall is not understood.

Thymic finer structure

1. *Cells* are:
 - packed *lymphocytes* (thymocytes), less densely packed in the medulla, making it paler, supported by
 - stellate *epithelio-reticular cells* of endodermal origin, not phagocytic, and with their processes attached by desmosomes;
 - pale *interdigitating dendritic/reticulum cells* in the medulla;
 - a few *macrophages* in cortex and medulla;
 - some *myoid cells*, resembling dystrophic skeletal muscle fibres;
2. *Absent* are afferent lymphatics, germinal centres, and significant numbers of reticular fibres.
3. Epithelio-reticular cells form concentrically lamellated, rounded, keratinizing, eosinophilic bodies - *thymic/Hassall's corpuscles* - in the older medulla.
4. Blood capillaries have intact basal laminae, few fenestrations in the endothelium, and an outside sheath of epithelio-reticular cells: all comprising the basis for a *barrier* hindering cells, e.g., B cells, and perhaps blood-borne antigens, from reaching the thymic cortical lymphocytes.

Thymic function

1. Neonatal removal of the thymus causes the secondary lymphoid organs - nodes, spleen, tonsils, etc - to develop only partially and be unable to respond to many antigens.
2. Before birth, the thymus - a primary lymphoid organ - receives stem cells from the marrow that proliferate and undergo selection and maturation (by interacting with epithelial reticular cells and APC reticular cells), before *seeding out* via the blood to populate the secondary organs with T or thymus-dependent *immunologically competent lymphocytes*.

Self-reactive lymphocytes are selected against, die, and are phagocytosed, while the surviving T lymphocytes migrate from subcapsular cortex towards the medulla.

3. At puberty the thymus starts a slow *involution* and replacement by adipose tissue, accelerated by severe stresses.
4. Despite the involution, the adult thymus maintains a low level of T-cell development from immature precursors that have not yet rearranged their TCR genes.

The Palatine Tonsils

Each palatine tonsil (right or left) consists of diffuse lymphoid tissue in which lymphatic nodules are present. The lymphoid tissue is covered by stratified squamous epithelium continuous with that of the mouth and pharynx. This epithelium extends into the substance of the tonsil in the form of several tonsillar crypts. Numerous

mucous glands open into the crypts. The lumen of a crypt usually contains some lymphocytes that have travelled into it through the epithelium. Desquamated epithelial cells and bacteria are also frequently present in the lumen of the crypt.

The palatine tonsils are often infected (tonsillitis) leading to sore throat. Frequent infections can lead to considerable enlargement of the tonsils especially in children. Such enlarged tonsils may become a focus of infection and their surgical removal (tonsillectomy) may then become necessary.

The Pharyngeal Tonsil

This is a mass of lymphoid tissue present on the posterior wall of the nasopharynx, in the midline. It is covered by epithelium. In children the pharyngeal tonsil may hypertrophy and is then referred to as the adenoids. The resulting swelling may be a cause of obstruction to normal breathing. The child tends to breathe through the mouth, and this may in turn lead to other abnormalities.

3.3. Literature recommended

Main Sources:

1. L.C. Junqueira, J. Carneiro - "Basic histology" – 11 edition - 2005.
2. A.S. Pacurar, J.W. Bigbee – "Digital histology" – Virginia - 2004.
3. Sadler T.V. – "Medical embryology" Montana – 1999.
4. Ronald W., Dudek Ph.D. – "Embryology" 2 edition – 1998.
5. Inderbir Singh Textbook of Human Histology.- Jaypee. India. - 1997.

Additional ones:

1. Methodical Instructions.

3.4 How to work with the literature recommended:

Main tasks	Recommendations
To review the material	To use the material studied
To learn the material	To use the material on pages
To read and compose the plan	To learn the new material and be ready to write a summary
To answer the questions	To be ready to give an answer to the following:
To do the test on the material	
To be ready to answer the topic	

3.5. Self-control material:

A. Questions to be answered:

1. Give the main characteristic of the lymphoid tissue.
2. Describe the structure of the thymus.
3. What are the functions of the thymus epithelial cells?
4. Give the characteristic of the lymphocytes (thymocytes).
5. What functions of the macrophages in the thymus?
6. What functions of the corpuscles of Hassall?
7. What are the thymic functions?
8. Describe the structure of the palatine tonsils.
9. Describe the structure of the pharyngeal tonsil.

B. Test tasks to be done: Tests are applied

4. Self-preparation in the classroom.

- 1) Listen to the information.
- 2) Work with the tables and a Light microscope.

- 3) Ask about the problems that haven't been found in the information given.
- 4) To sketch in the album the investigated preparations.

5. Self-preparation work at home.

- 1) Review the material learnt in the classroom.
- 2) Compose the plan of your answer.
- 3) Answer the questions to this topic.
- 4) Do the test given above.

6. The subject of the research work.

“Accidental involution of the thymus, its biological value”

<i>Subject</i>	<i>Histology, cytology and embryology</i>
<i>Modul №2</i>	<i>Histology, cytology and embryology</i>
<i>Submodul №3</i>	<i>Special histology</i>
<i>Topic 13</i>	SPLEEN. LYMPH-NODES

Hours: 2

1. The topic basis: the topic “**SPLEEN. LYMPH-NODES**” is very important for future doctors in their professional activity, positively influences the students in their attitude to the future profession, forms professional skills and experience as well as taking as a principle the knowledge of the subject learnt.

2. The aims of the training course:

- 1) To have general knowledge of the topic studied.
- 2) To understand, to remember and to use the knowledge received.
- 3) To learn the classification, structure and functions of the different histological methods.
- 4) To form the professional experience by reviewing, training and authorizing it.
- 5) To be able to carry out laboratory and experimental work.

3. Materials for the before – class work self – preparation work:

3.1 Basic knowledge, experience, skills necessary for studying the topic in connection with other subjects:

	To know	To be able to
Med. Biology	the structure of the cells and tissues	work with a light microscope
Med. Physics	the structure of the light and electron microscopes	work with a light microscope

The contents of the topic:**Lymph Nodes**

Nodes are small bodies placed at intervals along the lymphatic vessels, and structured so that the lymph has to pass through them. *Afferent lymphatics* bring lymph from a *drainage area*. The node is responsible for combating intruders and confining infection to that area, by sending out antibodies and cells via *efferent lymphatics*.

Each lymph node consists of a connective tissue framework; and of numerous lymphocytes, and other cells, that fill the interstices of the network. The entire node is bean-shaped, the concavity constituting a hilum through which blood vessels enter and leave the node. Several lymph vessels enter the node on its convex aspect. Usually, a single lymph vessel leaves the node through its hilum.

When a section through a lymph node is examined (at low magnification) it is seen that the node has an outer zone which contains densely packed lymphocytes, and therefore stains darkly: this part is the cortex. The cortex does not extend into the hilum. Surrounded by the cortex, there is a lighter staining one in which lymphocytes are fewer: this area is the medulla.

Within the cortex there are several rounded areas that are called lymphatic follicles or lymphatic nodules. Each nodule has a paler staining germinal centre surrounded by a zone of densely packed lymphocytes.

Within the medulla, the lymphocytes are arranged in the form of branching and anastomosing cords.

We will now consider some of these constituents in greater detail.

The Connective Tissue Framework

The lymph node is covered by a capsule consisting mainly of collagen fibres. Some elastic fibres and some smooth muscle may be present. A number of septa for trabeculae extend into the node from the capsule and divide the node into lobules. The hilum is occupied by a mass of dense fibrous tissue.

The remaining space within the node is filled by a delicate network of reticular fibres. Associated with the network there are reticular cells that have traditionally been regarded as macrophages. However, it is now believed that they are fibroblasts and do not have phagocytic properties.

Lymph-node structure

1. A CT capsule, with some smooth muscle, sends in thin CT trabeculae, supporting a network of *reticular fibres*, and *reticular cells* of fibroblastic and the accessory dendritic kinds.

2. A denser outer *cortex* and a looser, inner *medulla* are present.

3. Efferent lymphatics leave at a *hilus*: the point of entry for blood vessels, serving a mostly cortical microvasculature.

4. *Afferent lymphatics* open through the capsule at several places to feed a system of 'sinus' channels running so: *subcapsular/marginal sinus* --> *cortical/intermediate sinuses* --> *medullary sinuses* --> efferent lymphatics.

Sinuses are lined by reticular cells, accompanied by macrophages.

5. Denser masses of lymphoid tissue, extensive and *follicular/nodular* in the cortex, and continuing into the medulla as widely spaced *medullary cords*, have packed cells: lymphocytes, lymphoblasts and antigen- trapping dendritic reticular cells with processes. Lymphoblasts/centroblasts occur in the paler germinal centres of the cortical follicles. The follicular zone contains B lymphocytes separated by follicular dendritic cells (FDCs).

6. The deeper lying *paracortical region* has mostly *T lymphocytes*, and dendritic APCs wrapping so intimately around lymphocytes that they received the name *interdigitating reticular cells* (IPCs).

Lymph-node functions

1. Mechanical *filtration* of lymph in the sinuses, trapping, for instance, soot carbon particles. Tumour cells are not so easily stopped.

2. *Phagocytosis* of materials in lymph by macrophages along the sinuses or lodged across them. The materials taken up include antigens, e.g., on bacteria. APCs and MØs process antigens for lymphocyte activation.

3. *Proliferation* of sensitized lymphocytes to become lymphoblasts, large, with little GER, but many ribosomes, stainable with pyronin. These lymphoblasts are the source of:

- *plasma cells*, and hence humoral antibodies, or
- *cytolytic lymphocytes*, which set out for their distant target - antigen in the drainage area - in the sinus lymph.

4. *Recirculation* of mature lymphocytes from venule blood to sinus lymph by migration through the cuboidal endothelium of the venules (*high-endothelial venules* - HEVs).

Mucoso-Lymphoid Organs

1. Aggregates of nodules occur in the *tonsils*, *appendix* and ileal *Peyer's patches* of the GI tract; whereas *solitary nodules* may exist anywhere in the mucosae of all tubular systems open to the outside.

2. Wherever nodules may be found, close by are lymphoid cells dispersed more *diffusely*.

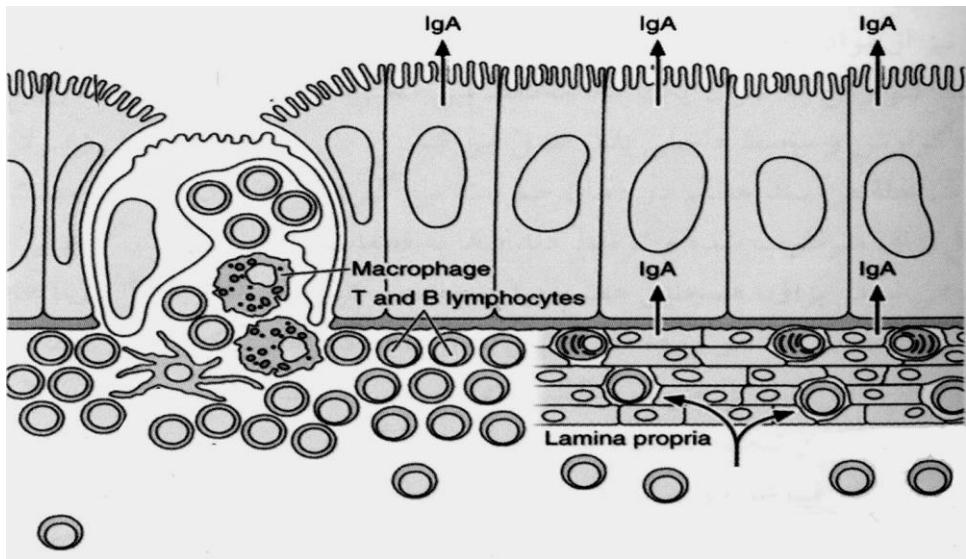
3. The gut- and bronchus-associated diffuse lymphoid tissues (*GALT*, *BALT*) are notable. MALT (mucosa-associated lymphoid tissue) usually refers to the unorganized lymphoid tissue of the gut.

4. Having an epithelium between the microorganisms and the connective tissue, where most of the lymphoid cells reside, poses problems:

- Over the nodules, special low columnar epithelial cells - *M cells* - develop in order to pass antigens to the underlying antigen-presenting cells in the lamina propria. The APC and lymphocytes sometimes lie in a pocket in the M cell. ('M' for microfolds on the M cell surface.)

- The antibodies subsequently made by the plasma cells are immunoglobulins of a kind that the typical epithelial cells can take up basally, and *secrete* apically into the lumen needing protection.

- It is also necessary for certain types of lymphocytes to enter the epithelium.



SPLEEN

Lies in the upper left of the abdomen, but there may also be small accessory spleens. It receives blood from the splenic artery for a treatment similar to that given the lymph by the node.

Splenic functions

Until birth, the spleen takes part in *myelopoiesis*, as do lymph nodes.

1. *White pulp* serves for:
 - recirculation of lymphocytes;
 - formation of new lymphocytes and plasma cells for immune responses to blood-borne antigens, met first at the marginal zone.
2. *Red pulp* provides:
 - *blood cleansing* by the sequestration and phagocytic destruction by macrophages of unfit blood cells and platelets, and bacteria;
 - *metabolic breakdown* of RBCs so that their iron can be reused;
 - a place to accumulate *platelets*;
 - sites by the marginal zone for *plasma cells* after antigenic stimulation, analogous to the cords and medulla of the active lymph node.

SPLENIC STRUCTURE

1. Thick fibro-elastic CT *capsule* has some myofibroblasts and a covering mesothelium.
2. Internally, thick CT *trabeculae* bear branches of the splenic artery and veins, entering and leaving at the hilum.
3. To the naked eye, most of the freshly cut organ is *red pulp* with white spots - *white pulp*.
4. *Red pulp* consists of a loose reticular tissue infiltrated with blood cells, and arranged in the so-called *cords* of Billroth around *sinusoidal* channels/sinuses - a Swiss-cheese situation of red-pulp cheese and sinusoidal holes.

The outermost white pulp, abutting the red pulp, is a boundary zone - the *marginal zone*, not to be confused with the *mantle zone* of densely packed mature lymphocytes around germinal centres.

(A mantle zone is not usually symmetrical; it is concentrated to one side of its germinal centre.)

5. *Cord tissue* has dendritic and fibroblastic reticular cells, and collagen fibrils supporting macrophages, and white and red blood cells.

6. *Sinusoids/sinuses* are lined by non-phagocytic endothelial/littoral cells, separated by slits and oriented longitudinally on a fenestrated BL. Blood cells thus can pass from sinusoid to cord and back, and cordal macrophages can extend pseudopodia into the sinusoidal lumen.

7. *White pulp* is a *dense lymphoid tissue* ensheathing branches of the arteries, once they have left the trabeculae. The sheath (PALS) dilates into follicles/nodules, some with germinal centres.

8. Lymphocytes are predominantly B in the nodules, and T in the periarterial lymphoid sheath (PALS). To match, reticular antigen-presenting cells are follicular/dendritic in the B-zone, interdigitating (IDCs) in the T-zone.

However, PALS and nodules/follicles work together, in that, the outer PALS is where B lymphocytes are initially selected for population-expansion in the nodules.

Connective Tissue Basis

The spleen is the largest lymphoid organ of the body. Except at the hilum, the surface of the spleen is covered by a layer of peritoneum (referred to as the serous coat). Deep to the serous layer the organ is covered by a capsule. Trabeculae arising from the capsule extend into the substance of the spleen. As they do so the trabeculae divide into smaller divisions which form a network. The capsule and trabeculae are made up of fibrous tissue in which elastic fibres are abundant. In some animals they contain much smooth muscle, but this is not a prominent feature of the human spleen.

The spaces between the trabeculae are pervaded by a network formed by reticular fibres embedded in an amorphous matrix. Fibroblasts (reticular cells) and macrophages are also present in relation to the reticulum. The interstices of the reticulum are pervaded by lymphocytes, blood vessels and blood cells, and by macrophages. To understand further details of the arrangement of these tissues it is necessary to first consider some aspects of the circulation through the spleen.

Circulation through the Spleen

1. Fed by the splenic artery, a *trabecular artery* branches out away from the CT as a *central artery* (arteriole) of the white-pulp lymphoid sheath, which it supplies by small branches. The artery is not central in the nodules.

2. The arteriolar branches of the central artery turn towards the red pulp, as several very straight branches - *penicilli/pulp arterioles*.

3. The vessels become smaller, and some have discontinuities in the BL, and gain a sheath of macrophages - *sheathed capillaries* - before the *terminal capillaries* open into a cord (Open Circulation Theory) or a sinusoid (Closed/Fast Circulation). Probably both kinds of termination exist.

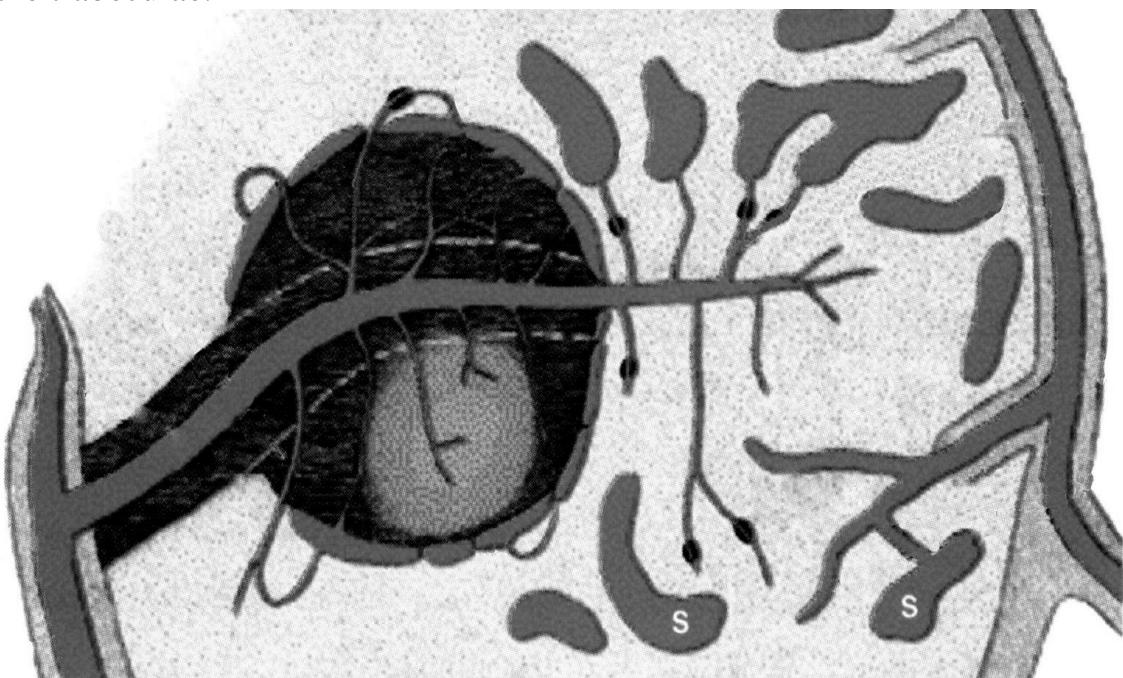
4. *Sinusoids* and *cords* both contain blood.

5. *Pulp venules* collect the blood and carry it to *trabecular veins* for return to the hilum, and exit via the *splenic vein*.

Note that the spleen displays substantial *species differences*: the dog spleen has very muscular trabeculae; rodent spleens have a significant marginal sinus, along the white-red border; MØ-sheathed capillaries are not prominent in man, and lie in a perifollicular zone of red pulp, special to man.

On reaching the hilum of the spleen the splenic artery divides into about five branches that enter the organ independently. Each branch divides and subdivides as it travels through the trabecular network. Arterioles arising from this network leave the trabeculae to pass into the inter-trabecular spaces. For some distance each arteriole is surrounded by a dense sheath of lymphocytes. These lymphocytes constitute the white pulp of the spleen. The arteriole then divides into a number of straight vessels that are called penicilli. Each of the penicilli shows a localized thickening of its wall that is called an ellipsoid. The ellipsoid consists of concentric lamellae formed by aggregation of fibroblasts and macrophages. The lumen of each penicillus is much narrowed at the ellipsoid.

The exact behaviour of the parts of penicilli distal to the ellipsoid is controversial. The usual description is that the vessel dilates to form an ampulla the walls of which become continuous with the reticular framework. As a result blood flows into the reticular spaces coming into direct contact with cells there. The part of splenic tissue which is infiltrated with blood in this way is called the red pulp. The circulation in the spleen is thus an 'open' one in contrast to the 'closed' circulation in other organs. Blood from these spaces is collected by wide sinusoids which drain into veins in the trabeculae.



The concept of an open splenic circulation is not accepted by all authorities. Some believe that the arterial vessels open directly into sinusoids. However, it is accepted that the vessel walls here do allow passage of blood cells into surrounding spaces.

The sinusoids of the spleen are lined by a somewhat modified endothelium. The endothelial cells here are elongated and are shaped like bananas. They are referred to as stave cells. With the EM a system of ultramicroscopic fibrils is seen to be present in their cytoplasm. The fibrils may help to alter the shape of the endothelial cells thus opening or closing gaps between adjoining cells.

The White pulp

We have seen that the white pulp is made up of lymphocytes that surround

arterioles. As a result it is in the form of cord-like aggregations of lymphocytes that follow the branching pattern of the arterioles. The cords appear to be circular in transverse section. At places the cords are thicker than elsewhere and contain lymphatic nodules similar to those seen in lymph nodes. These nodules are called Malpighian bodies. Each nodule has a germinal centre and a surrounding cuff of densely packed lymphocytes. The nodules are easily distinguished from those of lymph nodes because of the presence of an arteriole in each of them. The arteriole is placed eccentrically at the margin of the germinal centre (between it and the surrounding cuff of densely packed cells). More than one arteriole may be present in relation to one germinal centre.

The functional significance of the white pulp is similar to that of cortical tissue of lymph nodes. Lymphatic nodules of the white pulp are aggregations of B-lymphocytes, while the remaining white pulp is made up of T-lymphocytes. The germinal centres are areas where B-lymphocytes are dividing. The reticular framework is denser around the periphery of the white pulp than elsewhere, and this area is referred to as the marginal zone.

The Red Pulp

The red pulp is permeated by the sinusoids already described. The intervals between the sinusoids are filled by B-lymphocytes as well as T-lymphocytes, macrophages, and blood cells. These cells appear to be arranged as cords (splenic cords, of Billroth). The cords form a network.

Lymph Vessels of the Spleen

Traditionally, it has been held that in the spleen lymph vessels are confined to the capsule and trabeculae. Recent studies have shown, however, that they are present in all parts of the spleen. Lymphocytes produced in the spleen reach the blood stream mainly through the lymph vessels.

3.3. Literature recommended

Main Sources:

1. L.C. Junqueira, J. Carneiro - "Basic histology" – 11 edition - 2005.
2. A.S. Pacurar, J.W. Bigbee – "Digital histology" – Virginia - 2004.
3. "Color Atlas of basic histology" – R.Berns – 2006.
4. Sadler T.V. – "Medical embryology" Montana – 1999.
5. Ronald W., Dudek Ph.D. – "Embryology" 2 edition – 1998.
6. Inderbir Singh Textbook of Human Histology.- Jaypee. India. - 1997.
7. Ten Cate A.R. Oral Histology.- St.Louis, Baltimore, Toronto.- 1995.
8. William A., Beresford M.A. Cytology and Histology.- Anatomy department, West Virginia University, USA.- 1992.
9. K.E. Jonson - "Histology and cell biology" – 2 edition – Washington – 1991.

Additional ones:

1. Methodical Instructions.

3.4 How to work with the literature recommended:

Main tasks	Recommendations
To review the material	To use the material studied
To learn the material	To use the material on pages
To read and compose the plan	To learn the new material and be

To answer the questions To do the test on the material To be ready to answer the topic	ready to write a summary To be ready to give an answer to the following:
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3.5. Self-control material:

A. *Questions to be answered:*

1. What are the functions of the lymph nodes?
2. What is the lymph-node structure?
3. What are the elements of its connective tissue framework?
4. What are the parenchymal elements of the lymph-node?
5. What are the mucoso-lymphoid organs?
6. What are the splenic functions do you know?
7. Describe the splenic structure.
8. Describe the connective tissue basis of the spleen.
9. Describe the circulation through the spleen.
10. Describe the elements of white pulp.
11. Describe the elements of red pulp.
12. Describe the lymph vessels of the spleen.

B. *Test tasks to be done: Tests are applied*

4. Self-preparation in the classroom.

- 1) Listen to the information.
- 2) Work with the tables and a Light microscope.
- 3) Ask about the problems that haven't been found in the information given.
- 4) To sketch in the album the investigated preparations.

5. Self-preparation work at home.

- 1) Review the material learnt in the classroom.
- 2) Compose the plan of your answer.
- 3) Answer the questions to this topic.
- 4) Do the test given above.

6. The subject of the research work.

“Elimination of the old erythrocytes in the spleen”

“Participation of the lymph nodes in the inflammatory processes”

<i>Subject</i>	<i>Histology, cytology and embryology</i>
<i>Modul №2</i>	<i>Histology, cytology and embryology</i>
<i>Submodul №3</i>	<i>Special histology</i>
<i>Topic 14</i>	IMMUNITY SYSTEM

Hours: 2

1. The topic basis: the topic “**IMMUNITY SYSTEM**” is very important for future doctors in their professional activity, positively influences the students in their attitude to the future profession, forms professional skills and experience as well as taking as a principle the knowledge of the subject learnt.

2. The aims of the training course:

- 1) To have general knowledge of the topic studied.
- 2) To understand, to remember and to use the knowledge received.
- 3) To learn the classification, structure and functions of the different histological methods.
- 4) To form the professional experience by reviewing, training and authorizing it.
- 5) To be able to carry out laboratory and experimental work.

3. Materials for the before – class work self – preparation work:

3.1 Basic knowledge, experience, skills necessary for studying the topic in connection with other subjects:

	To know	To be able to
Med. Biology	the structure of the cells and tissues	work with a light microscope
Med. Physics	the structure of the light and electron microscopes	work with a light microscope
Organic Chemistry	the chemical content of the cell	Speak of the topic

The contents of the topic:

Precise targeting is made possible by the prior proliferation of billions of B & T lymphocytes, accompanied by the generation of diversity in the antibody or TCR. The diversity is immense, covering all the possible molecular forms that might show up and injure one. Controlled mutation and rejoining of DNA (V & J regions) of the Ab or TCR genes produce the variety.

The initially crude targeting of the innate or primitive system is refined and made more effective by the evolutionarily more recent lymphocyte-based immune system, which, in its turn, receives directions from the innate system.

The specific immune takes days to get going after a new antigenic encounter, because of the need to recruit cells and greatly amplify their number.

1. A multicellular organism has to contend with *three related problems*:

- some of its cells have short lives and their remains must be disposed of;
 - foreign non-living matter may enter, e.g., dust and grit, and has to be eliminated or made harmless;
 - foreign living matter may gain entrance, carrying the additional hazard that the intruder may poison or proliferate and overwhelm its host.
2. The *macrophage system* can recognize and phagocytose decrepit and dead cells, and cell debris, and tries to cope with inert foreign matter. Material that cannot be digested can be held in cells, or surrounded by giant cells enclosed in a collagenous capsule.

In the lungs, the collagenous fibrosis impedes elasticity and is harmful.

The macrophage system, in dealing with foreign living intruders, tries routine phagocytosis, but it also calls upon several kinds of defensive cell working together to combat the intruder and its harmful products, toxins, and its various strategies, e.g., encystment, viral commandeering of host cells, mimicry of self materials, etc.

3. Against living things the defence has to be prompt, coordinated and successful, but also selective enough to cause little harm to the tissues of the host. The selectivity and coordination call for special cells to recognise the intruder for what it is - a *foreign/non-self* entity. The macrophages and other antigen-presenting cells recognize the foreign nature of such materials of living organisms as their surface proteins and carbohydrates. After phagocytosis, fragments of the foreign materials are *presented* as antigens, to which *lymphocytes* respond with specifically targeted immune responses - cell-mediated and humoral.

4. Immunologically competent cells - *T & B lymphocytes* and *plasma cells* - show an *exquisite specificity* to an individual kind of alien body, e.g., polio virus rather than smallpox, in binding themselves (by the *T-cell receptor*), or in their humoral product - *immunoglobulins/ antibodies*.

The accessory cells of the immune system do not have this specificity, but their activities are guided and enhanced by lymphocytes and antibodies, and they in turn contribute, by presenting antigen, under *histocompatibility restriction*, to the specificity of the lymphocytes' responses. An important aspect of this restriction is that the immune system does not attack one's own cells and materials.

5. *Sources of antigen*, actual or potential, are:

- viruses and microorganisms;
- venoms;
- inspired particles, e.g., fungi, pollen, dander;
- foods;

- semen;
- the embryo;
- transplanted tissues, e.g., skin;
- altered autologous (own) cells, e.g., tumour products
- some medicaments, e.g., penicillin.

1. Plasma cells (immunologically competent)

1. Develop from B lymphocytes via a transitional cell involved in rearranging its immunoglobulin genes for expression, first for the cell-surface, then for secretion.
2. Synthesize and release specific *humoral antibodies* (immunoglobulins), after engagement with the presented antigens, and stimulations from helper T lymphocytes.

	<p>3. Immunoglobulins:</p> <ul style="list-style-type: none"> ○ bind and inactive the antigenic bodies; ○ neutralize toxins; ○ enhance phagocytosis; ○ trigger the activation of special blood proteins - <i>complement factors</i> - which amplify the immune response.
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4. Complement also binds to the antigen, potentiating the action of the bound antibody, and itself has lytic, signalling, and other effects. The three-part entity - antigen, antibody and complement - is an *immune complex*.

2. Lymphocytes (competent)

1. Start as stem cells of fetal haemopoietic tissue, but fall into two classes differing in where they were conditioned for distinct tasks.

-B lymphocytes develop in the bone marrow from stock originating perhaps in the fetal liver, then populate germinal centres, and can proliferate and differentiate to become the sessile (non-moving) antibody-forming *plasma cells*;

-T lymphocytes originate in marrow, develop and survive elimination in the thymus, are more mobile, and play many roles.

2. Both B and T lymphocytes seed out to populate the *secondary lymphoid organs*: spleen, nodes, and major mucosal lymphoid structures, and some lymphocytes then circulate. (Thymus, bone marrow, and fetal liver are primary lymphoid organs.)

3. Roles of the T lymphocyte

- By gene rearrangement and selective expression, to offer a very broad range of T-cell receptors (one specific TCR per clone) for the diverse antigens that might be met.
- Patrolling the body as a *naïve* or virgin lymphocyte able to be stimulated by a new antigen taken up by macrophages or dendritic cells.
- For some antigens, T lymphocytes *help* the humoral response of B lymphocytes.
- Less often, they have a *suppressor* action on the B cell's response.
- For certain antigens, e.g., virally-infected cells or foreign transplanted tissue, the stimulated lymphocyte proliferates, sending its progeny via the circulation as *cytolytic/cytotoxic lymphocytes* (CTLs) to attack the target cells at close range - the *cell-mediated response*.

Cytolytic lymphocytes release substances that:

- lyse the target cells or organisms, e.g., *perforin*, which inserts uncontrollable pores into the target cell's membrane;
- trigger apoptosis, after entering via the pores.
- as *cytokines*, attract other leucocytes to the site of antigen,
- activate naive lymphocytes and cause their proliferation,
- enhance leucocytes' phagocytic activity;
- and trigger the release of histamine by basophils.

4. *Natural killer/NK cells* are marrow-derived lymphocytes that act early and independently of antigen presentation to attack tumour cells and infected cells, using membrane-damaging perforin and other agents.

5. Lymphocytes are classified by the reaction of certain of their surface glycoproteins to monoclonal antibodies. Thus, inducer/helpers are CD4+; cytolytic lymphocytes are CD8+; natural killer cells are CD3-, CD16+, CD56+; B lymphocytes are CD19+, etc. CD means *Cluster-of-Differentiation* antigens, and stems from the patterns of response of differentiating leucocytes to a great variety of monoclonal antibodies. It turns out that many kinds of cell aside from leucocytes express one or more of the antigens that the CD antibodies mark. These antigens only incidentally help characterize cells (e.g., marrow stem cells are CD34+), since they are working molecules - in adhesion and signalling, as enzymes, protective agents, etc.

6. Some T and B cells, having participated in an immune response to a certain antigen, patrol the body as long-lived *memory cells* ready to initiate an early and stronger secondary response, should the same antigen intrude again - the basis of *vaccination*.

7. The distinction between self- and non-self-recognition, and the acquisition of memory by lymphocytes, may be confounded by presentation of the antigen in high doses, by unusual routes, or in immaturity just after birth. The confused lymphocytes that result remember to *tolerate* an antigen, to which they should react. This tolerance is believed to be a by product of a normal mechanism, whereby all normal cells are telling circulating T lymphocytes, with receptors for the normal cells' materials, not to react, but to die.

3. Dendritic antigen-presenting cells (APCs) and Macrophages (accessory)

1. APCs and macrophages/Øs concentrate some antigenic fragments on their surface, presenting them in a form more potent for stimulating lymphocytes.

2. What is presented on the surface is a small peptide, derived by degradation from the antigen, bound to a *histocompatibility protein* (MHC class I or II depending on whether the antigen is of intracellular (self) or foreign/exogenous origin). Intracellular antigens presented in this way include materials that viruses have forced the cell to make.

A non-sequitur: antigen-presentation is not limited to MØs and antigen-presenting cells. For example, B lymphocytes present antigen to T lymphocytes.

3. Once activated by a particular antigen, lymphocytes and macrophages exchange cytokine messages to:

- *recruit* more macrophages from the circulating monocytes;

- *inhibit* macrophage migration to keep macrophages at hand;
- *activate* macrophages to attack more vigorously the antigen by which the lymphocyte is activated, e.g., tuberculosis bacilli.

(These cytokines convey simple 'doggy' orders: Come! Stay! Attack!)

1. Macrophages *phagocytose* toxins and cells killed by other immune actions, and make cytokine factors, e.g., chemotactic for neutrophils.
2. Macrophages and other phagocytes liberate destructive enzymes and oxygen metabolites to lyse cells. They also digest matrix, e.g., by MØ elastase, so that they themselves may move more freely. Enzymes may also be regurgitated in phagocytosis, or be spilled after death of the cell.

To reduce the damage to surrounding tissues, extra-cellular degradative enzymes normally are neutralized by *protease inhibitors* in the plasma and tissues, such as *alpha 1-antitrypsin*.

3. '*Tingible-body*' macrophages are in germinal centres. Their darkly stained (tingible) inclusion material is nuclear debris of apoptotic B lymphocytes that were selected against for not improving their affinity for antigen fast enough.

4. Granular leucocytes

1. *Neutrophils* respond in strength to certain bacterial and fungal infections, avidly ingesting, say, streptococci, dying, and often accumulating to become pus.
2. Neutrophils and eosinophils are attracted to immune complexes which they phagocytose, but the materials that they use to attack microbes and parasites also damage tissues, e.g., airway epithelium in allergies.

5. Mast cells

1. One kind of immunoglobulin (Ig) is already bound to their surface. Antigen entering the tissue bridges these *IgE* molecules, triggering the release of
2. *Histamine*, which dilates vessels, increases their permeability and facilitates the exit of granular leucocytes, monocytes, antibodies, etc.
3. *Heparin* may hold histamine and other factors ready for discharge; if released itself, it might, as a polyanion, bind and neutralize toxins. Among the many other mediators are bradykinin and factors attracting granulocytes - *chemokines*.
4. The mast cell's reaction is an *immediate hypersensitive* one: the basis of allergies. An anaphylactic hypersensitive response in the airway lining is life-threatening, by overconstricting smooth muscle, and other effects.

Transplantation

Of the many intriguing manifestations of immunity, such as *anaphylaxis*, *autoimmunity*, *graft rejection*, *graft-versus-host reaction*, and *immunodeficiency syndromes*, only autoimmunity and transplantation will be considered further.

Transplantation has wide use in the experimental approaches.

1. Most tissues can be grafted *autologously* to another site in the same individual, where they will live, if they can soon gain a new blood supply by revascularization by, or anastomosis with, the vessels of the host bed.
2. Transplants between two individuals will *take* - not be rejected - if they are *isogenic/syngeneic*, and thus have identical tissue proteins synthesized according to the same DNA, e.g., in identical twins, or animals of the same sex whose forebears have been many times inbred.
3. Transplants between genetically different individuals can be:
 - *allogeneic/homologous* between members of the same species;

- *xenogeneic*/heterologous between members of different species or orders.
- The grafted tissue is antigenic and evokes the delayed T cell-mediated immune response.
4. An allogeneic graft made to a *neonatal host* can induce a permanent tolerance for that graft and subsequent grafts of the same tissue. The host, now composed of tissues differing genetically, has been made a *chimaera*.
5. Certain sites for allogeneic grafts slow down or prevent the antigen from draining to lymphoid tissue and eliciting an immune response. Such *immunologically privileged* sites are the cornea and brain.
6. Immunity depends on the proliferation and synthesis by cells. To help a graft to take, the response could be inhibited for a while by provoking apoptosis in the competent cells, or hindering their proliferation, with *irradiation* with X-rays, or with *cytotoxic drugs* or *glucocorticoids*. Transplant surgeons can also use agents, e.g., *cyclosporin*, to block the activation of T cells.

Autoimmunity

Sometimes the mechanisms of restraint against attacking one's own materials go awry. Clinically significant *autoimmune targets* include: gastric parietal cells, renal mesangial cells, pancreatic beta cells, thyroid follicular cells, skeletal muscle, myelin components, and basement membranes.

3.3. Literature recommended

Main Sources:

1. L.C. Junqueira, J. Carneiro - "Basic histology" – 11 edition - 2005.
2. A.S. Pacurar, J.W. Bigbee – "Digital histology" – Virginia - 2004.
3. "Color Atlas of basic histology" – R.Berns – 2006.
4. Sadler T.V. – "Medical embryology" Montana – 1999.
5. Inderbir Singh Textbook of Human Histology.- Jaypee. India. - 1997.
6. William A., Beresford M.A. Cytology and Histology.- Anatomy department, West Virginia University, USA.- 1992.
7. K.E. Jonson - "Histology and cell biology" – 2 edition – Washington – 1991.

Additional ones:

1. Methodical Instructions.

3.4 How to work with the literature recommended:

Main tasks	Recommendations
To review the material	To use the material studied
To learn the material	To use the material on pages
To read and compose the plan	To learn the new material and be ready to write a summary
To answer the questions	To be ready to give an answer to the following:
To do the test on the material	
To be ready to answer the topic	

3.5. Self-control material:

A. Questions to be answered:

1. Describe the specific immune tasks.
2. What are the defensive cells of the immunity system?
3. What functions of the plasma cells do you know?
4. Give the characteristic of the immunoglobulins.
5. What functions of the lymphocytes do you know?
6. What about dendritic antigen-presenting cells (APCs) do you know?
7. What about macrophages do you know?

8. What functions of the granular leucocytes do you know?
9. What functions of the Mast cells do you know?
10. Describe the problems of the transplantation.
11. What do you know about autoimmunity diseases?

B. Test tasks to be done: Tests are applied

4. Self-preparation in the classroom.

- 1) Listen to the information.
- 2) Work with the tables and a Light microscope.
- 3) Ask about the problems that haven't been found in the information given.
- 4) To sketch in the album the investigated preparations.

5. Self-preparation work at home.

- 1) Review the material learnt in the classroom.
- 2) Compose the plan of your answer.
- 3) Answer the questions to this topic.
- 4) Do the test given above.

6. The subject of the research work.

“Modern representations to the cellular immunity response”

“Morphological features of the immunocytes”

“Cellular interactions in the immunity response”

<i>Subject</i>	<i>Histology, cytology and embryology</i>
<i>Modul №2</i>	<i>Histology, cytology and embryology</i>
<i>Submodul №3</i>	<i>Special histology</i>
<i>Topic 15</i>	ENDOCRINE SYSTEM. HYPOTHALAMUS. PINEAL

Hours: 2

1. The topic basis: the topic “**ENDOCRINE SYSTEM. HYPOTHALAMUS. PINEAL GLAND**” is very important for future doctors in their professional activity, positively influences the students in their attitude to the future profession, forms professional skills and experience as well as taking as a principle the knowledge of the subject learnt.

2. The aims of the training course:

- 1) To have general knowledge of the topic studied.
- 2) To understand, to remember and to use the knowledge received.
- 3) To learn the classification, structure and functions of the different histological methods.
- 4) To form the professional experience by reviewing, training and authorizing it.
- 5) To be able to carry out laboratory and experimental work.

3. Materials for the before – class work self – preparation work:

3.1 Basic knowledge, experience, skills necessary for studying the topic in connection with other subjects:

	To know	To be able to
Med. Biology	the structure of the cells and tissues	work with a light microscope
Med. Physics	the structure of the light and electron microscopes	work with a light microscope

The contents of the topic:

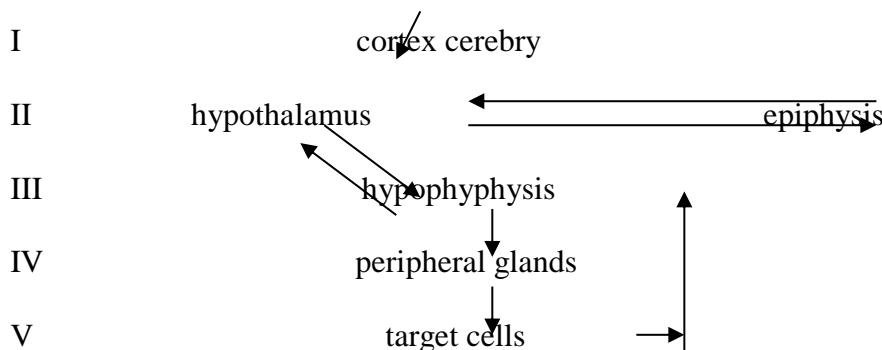
Endocrine tissue is made up essentially of cells that produce secretions which are poured directly into blood. It follows that endocrine cells must lie in close apposition to blood capillaries or to sinusoids. The secretions of endocrine cells are called hormones. Hormones travel through blood to target cells whose functioning they may influence profoundly. Some hormones act only on one organ or on one type of cell, while other hormones may have widespread effects. Along with the autonomic nervous system the endocrine organs coordinate and control the metabolic activities and the internal environment of the body.

Some organs are entirely endocrine in function. They are referred to as endocrine glands (or ductless glands). Those traditionally included under this heading are the hypophysis cerebri (or pituitary), the thyroid gland, the parathyroid glands, and the suprarenal (or adrenal) glands. Recent work suggests that the pineal gland should also be included in this group.

Groups of endocrine cells may be present in organs that have other functions. Several examples of such tissue have been described in previous chapters. They include the islets of the pancreas, the interstitial cells of the testes, and the follicles and corpora lutea of the ovaries. Hormones are also produced by some cells in the kidney, the thymus, and the placenta. Some authors describe the liver as being partly an endocrine gland.

Isolated endocrine cells may be distributed in the epithelial lining of an organ. Such cells are seen most typically in the gut. Similar cells are also present in the epithelium of the respiratory passages. Recent studies have shown that cells in many other locations in the body produce amines that have endocrine functions. Many of these amines also act as neurotransmitters or as neuromodulators. These widely distributed cells are grouped together as the neuroendocrine system or the APUD cell system.

In the endocrine system there are **two main parts**: central and peripheral. Central part contains hypothalamus, epiphysis and hypophyphysis. Peripheral part contain of the peripheral endocrine glands, groups of endocrine cells in the organs and APUD cells.



The secretion of hormones by adenohypophysis takes place under higher control of neurons in the hypothalamus, notably those in the median eminence and in the infundibular nucleus. The axons of these neurons end in relation to capillaries in the median eminence and in the upper part of the infundibulum. Different neurons produce specific releasing factors (or releasing hormones) for each hormone of the

adenohypophysis.

These factors are released into the capillaries mentioned above. Portal vessels arising from the capillaries carry these factors to the pars anterior of the hypophysis. Here they stimulate the release of appropriate hormones. Some factors inhibit the release of hormones. The synthesis and discharge of releasing factors by the neurons concerned is under nervous control. As these neurons serve as intermediaries between nervous impulses and hormone secretion they have been referred to as neuroendocrine transducers. Some cells called tanycytes, present in ependyma, may transport releasing factors from neurons into the CSF, or from CSF to blood capillaries. They may thus play a role in control of the adenohypophysis.

Recent studies indicate that circulation in relation to the hypophysis cerebri may be more complex than presumed earlier. Some points of interest are as follows.

The entire neurohypophysis (from the median eminence to the pars posterior) is permeated by a continuous network of capillaries in which blood may flow in either direction. The capillaries provide a route through which hormones released in the pars posterior can travel back to the hypothalamus, and into CSF.

Some veins draining the pars posterior pass into the adenohypophysis. Secretions by the adenohypophysis may thus be controlled not only from the median eminence, but by the entire neurohypophysis.

Blood flow in veins connecting the pars anterior and pars posterior may be reversible providing a feed back from adenohypophysis to the neurohypophysis.

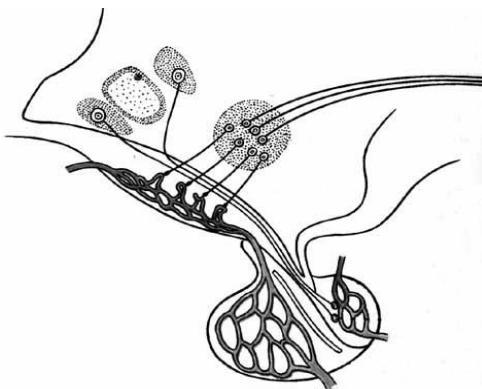
These are potent chemical substances travelling via the bloodstream from one cell to another. They work in conjunction with the nervous system to control the *homeostasis* of the body, and *to anticipate* future events such as birth, lactation, fighting or fleeing.

The hormone reaches many cells but, except for hormones affecting growth and some general metabolic processes, only certain *target* or end-organ cells respond. The *response* is often a start or increase in a cell's activity, e.g., contraction, release of a secretion, growth by proliferation (hyperplasia) or by an increase in size (hypertrophy). However, a hormone may sometimes *inhibit* a cell's activity, e.g., calcitonin inhibits osteoclasts' resorption of bone.

The hormone may stimulate its target cell either by binding with a *membrane receptor* in the plasmalemma that starts a *signal transduction* sequence, say, to alter the level of a second, internal, messenger, within the cell, e.g., cyclic AMP or GMP; or by penetrating the cell membrane and binding with a cytoplasmic receptor. Once inside the cell the bound hormone itself, the second messenger, or downstream effectors such as Ca^{2+} , can trigger the release of secretion, an increase in nucleus-controlled synthesis, a contraction, or some other useful task.

In its usual concentrations, a hormone's action is called *physiological*. *Pharmacological* effects are seen when abnormally high quantities are injected.

Pathological effects are observed when: too little or too much hormone is present; the target organ is insensitive to the hormone; or the hormone molecule is defective.



Cytology of Hormone Secretion

1. Hormones are formed in:
 - o pure endocrine glands, e.g., thyroid;
 - o mixed exocrine and endocrine glands, e.g., pancreas and testis;
 - o some of the cells in organs having other functions, e.g., placenta, kidney, GI tract.
2. The hormone is a *product* synthesized and released by glandular cells, mostly epithelial, but some are modified neurons or muscle cells.
3. Cells have *organelles* associated with synthesis, e.g., granular or smooth ER, Golgi complex, and may store the hormone or prohormone as membrane-bound *inclusion* granules. *Lysosomes* may be used to destroy excess hormone. Actin filaments are used to discharge the granules by *exocytosis*. The chemical nature of the hormone is reflected in the cytology, e.g., steroid cells store the lipid precursor, but not the hormone, and have much smooth ER.
4. The secretory granules may *stain selectively* because of the chemical nature of the hormone, e.g., glycoprotein with the PAS reaction, and have a distinctive *size, shape and density* in EM.
5. The stored hormone can be demonstrated in its cell by *immunostaining*, using an antibody that binds specifically with that hormone, coupled with a visually demonstrable tag, e.g., a fluorescent compound (for LM) or a peroxidase (for EM and LM).
6. Catecholamines can be seen with *fluorescence microscopy* after treatment with an aldehyde. The mRNA for the hormone or its precursor, or for enzymes necessary to its synthesis, can be seen by using *in situ hybridization*.
7. The stimulus for the release of hormone, and the synthesis of more hormone, may be:
 - o *nervous* by synaptic action, e.g., adrenal medulla;
 - o *another hormone*, e.g., TSH for thyroid follicular cells; or
 - o the blood level of a non-hormonal *chemical*, e.g., Ca^{2+} for parathyroid chief cells.
8. To facilitate the blood-endocrine cell interactions, cords and small clusters of endocrine cells are supported by *reticular fibres*, close to numerous wide capillaries (*sinusoidal capillaries*), lined by fenestrated but non-phagocytic endothelial cells.

APUD Neuroendocrine and Peptide Systems

In the 1970s, the focus was on the amine metabolism that gave a unifying aspect to rather perplexing cells, scattered in many organs, which had been noticed and considered on an individual basis as clear (empty looking), or having granules reacting with silver salts. It turned out that most of these cell types made and released non-cytokine peptide mediators, to act locally or at a distance. The peptide story has now overwhelmed the amine or APUD idea, because these peptide factors are many, and are made and used for signalling in every part of the body, including the brain. The basis of the APUD classification is outlined below, because it helps explain aspects of pathology.

Within some endocrine glands, chemoreceptors, the brain, and dispersed in epithelia, are cells that form amine compounds. After an Amine Precursor has been taken up, the cell decarboxylates it to form serotonin (5-HT) from 5-hydroxytryptophane, or a catecholamine from dihydroxyphenylalanine (hence APUD).

Noticing that many of these cells secrete polypeptide hormones, Professor Pearse proposed a far-flung 'APUD' neuroendocrine system, secreting peptide mediators. The amines and peptides function variously as neurotransmitters, hormones, and modulators of neural action. Some vary their role by site. Some cells come from neural crest; for others, their origin is disputed.

Established APUD members

Peripheral

- *Pancreatic islet cells* -> insulin, glucagon, somatostatin, PP and VIP
- *Thyroid C cells* -> calcitonin
- *Parathyroid chief cells* -> parathormone
- *Gastrointestinal endocrine cells* -> gastrin, secretin, pancreozymin/cholecystokinin, glucagon, motilin, somatostatin, and many other active peptides. (Cells have a designating letter, if the hormone is known).

- Other endocrine/neuroendocrine cells in respiratory and genito-urinary tract epithelia hold granules, reacting with silver salts in the argyrophilic and argentaffin ways of the GI-tract endocrine cells, and produce a variety of peptides, e.g., vasoactive intestinal polypeptide/VIP.

Central

- Pituitary
 - *somatotrophs* -> growth hormone (GH)
 - *mammatrophs* -> prolactin (PRL/MTH)
 - *corticotrophs* -> adrenocorticotrophic hormone (ACTH)
 - *melanotrophs* -> melanocyte-stimulating hormone (MSH)
- *Hypothalamic large neurosecretory cells* -> oxytocin, vasopressin
- *Hypothalamic small neurosecretory cells* -> releasing factors/hormones, e.g., LH.RF; and somatostatin (SRIF) inhibiting GH release from pituitary somatotrophs.
- *Pinealocytes* -> melatonin

APUD members with an uncertain peptide role

The peptide substance normally formed, if any, has not yet been identified, or its role is unclear.

1. *Carotid-body type I cell* and similar cells in the aortic and other chemoreceptive bodies contain norepinephrine and/or dopamine.

2. *Chromaffin-system cells*, in the adrenal medulla and abdominal paraganglia, contain catecholamines and enkephalins.

(The GI tract cells of 2.4 above, despite their old 'enterochromaffin' name do not form catecholamines.)

3. *Melanocytes* of skin, and dermal and ocular CT cells using amines to form melanin, come from the neural crest.

Neuroendocrine cells

The granular cells of the GI tract, airway, and genitourinary system produce a variety of peptide factors, some acting locally in a paracrine mode, others maybe having more distant effects. A common denominator is the presence along with the peptide(s) of certain materials in the dense-cored granules, e.g., *chromogranin A* or B, which provide markers for histopathologists seeking to find these relatively rare and dispersed cells.

PINEAL GLAND/EPIPHYSIS CEREBRI

The pineal gland (or pineal body) is a small piriform structure present in relation to the posterior wall of the third ventricle of the brain. It is also called the epiphysis cerebri. The pineal has for long been regarded as a vestigeal organ of no functional importance. However, it is now known to be an endocrine gland of great importance.

These masses constitute the corpora arenacea or brain sand. The organ is covered by connective tissue (representing the piamater) from which septa pass into its interior.

The organ is made up mainly of cells called pinealocytes. Each cell has a polyhedral body containing a spherical oval or irregular nucleus. The cell body gives off long processes with expanded terminal buds that end in relation to the wall of capillaries, or in relation to the ependyma of the third ventricle. The cell bodies of pinealocytes contain both granular and agranular endoplasmic reticulum, a well developed Golgi complex, and many mitochondria. An organelle of unusual structure made up of groups of microfibrils and perforated lamellae may be present (canalicate lamellar bodies). The processes of pinealocytes contain numerous mitochondria. Apart from other organelles the terminal buds contain vesicles in which there are monamines and polypeptide hormones. The neurotransmitter gamma-amino-butyric acid is also present.

The pinealocytes are separated from one another by neuroglial cells that resemble astrocytes in structure (5%). The nerve fibres present in the pineal are sympathetic (adrenergic, unmyelinated). Release of pineal secretions appears to require sympathetic stimulation. The pinealocytes produce a number of hormones (chemically indolamines or polypeptides). These hormones have an important regulating influence (chiefly inhibitory) on many other endocrine organs. The organs influenced include the adenohypophysis, the neurohypophysis, the thyroid, the parathyroids, the adrenal cortex and medulla, the gonads, and the pancreatic islets. The hormones of the pineal body reach the hypophysis both through the blood and through the CSF. Pineal hormones may also influence the adenohypophysis by inhibiting production of releasing factors.

The best known hormone of the pineal gland is the aminoacid melatonin. Large concentrations of melatonin are present in the pineal gland. Considerable amounts of 5-hydroxytryptamine (serotonin), which is a precursor of melatonin, are also present. The presence of related enzymes has been demonstrated.

The synthesis and discharge of melatonin is remarkably influenced by exposure of the animal to light, the pineal gland being most active in darkness. The neurological pathways concerned involve the hypothalamus and the sympathetic nerves. Because of

this light mediated response, the pineal gland may act as a kind of biological clock which may produce circadian rhythms (variations following a 24 hour cycle) in various parameters.

It has been suggested that the suprachiasmatic nucleus of the hypothalamus plays an important role in the cycle activity of the pineal gland. This nucleus receives fibres from the retina. In turn it projects to the segmental reticular nuclei (located in the brainstem). Reticulospinal fibres arising in these nuclei influence the sympathetic preganglionic neurons located in the first thoracic segment of the spinal cord. Axons of these neurons reach the superior cervical ganglion and supply the pineal gland.

3.3. Literature recommended

Main Sources:

1. L.C. Junqueira, J. Carneiro - "Basic histology" – 11 edition - 2005.
2. A.S. Pacurar, J.W. Bigbee – "Digital histology" – Virginia - 2004.

Additional ones:

1. Methodical Instructions.

3.4 How to work with the literature recommended:

Main tasks	Recommendations
To review the material	To use the material studied
To learn the material	To use the material on pages
To read and compose the plan	To learn the new material and be ready to write a summary
To answer the questions	To be ready to give an answer to the following:
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To be ready to answer the topic	

3.5. Self-control material:

A. Questions to be answered:

B. Test tasks to be done: Tests are applied

4. Self-preparation in the classroom.

1) Listen to the information. 2) Work with the tables and a Light microscope. 3) Ask about the problems that haven't been found in the information given. 4) To sketch in the album the investigated preparations.

5. Self-preparation work at home.

1) Review the material learnt in the classroom. 2) Compose the plan of your answer. 3) Answer the questions to this topic. 4) Do the test given above.

<i>Subject</i>	<i>Histology, cytology and embryology</i>
<i>Modul №2</i>	<i>Histology, cytology and embryology</i>
<i>Submodul №3</i>	<i>Special histology</i>
<i>Topic 16</i>	<u>ENDOCRINE SYSTEM. HYPOPHYSIS.</u>

Hours: 2

1. The topic basis: the topic “**ENDOCRINE SYSTEM. HYPOPHYSIS**” is very important for future doctors in their professional activity, positively influences the students in their attitude to the future profession, forms professional skills and experience as well as taking as a principle the knowledge of the subject learnt.

2. The aims of the training course:

- 1) To have general knowledge of the topic studied.
- 2) To understand, to remember and to use the knowledge received.
- 3) To learn the classification, structure and functions of the different histological methods.
- 4) To form the professional experience by reviewing, training and authorizing it.
- 5) To be able to carry out laboratory and experimental work.

3. Materials for the before – class work self – preparation work:

3.1 Basic knowledge, experience, skills necessary for studying the topic in connection with other subjects:

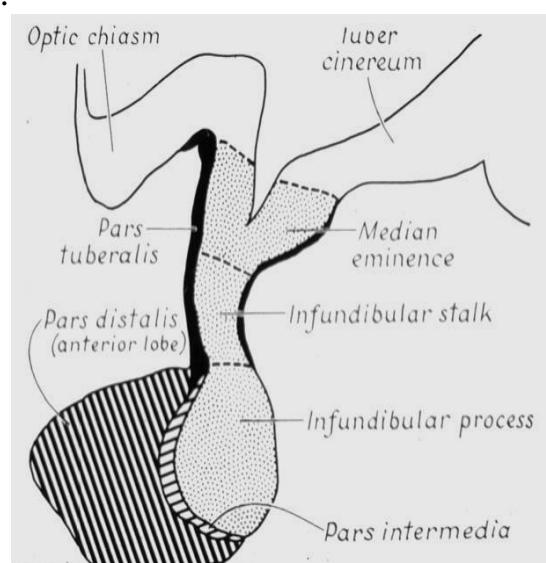
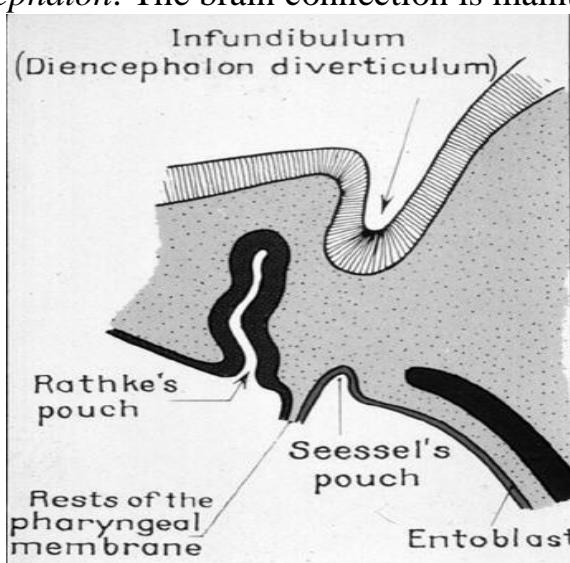
	To know	To be able to
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Med. Biology	the structure of the cells and tissues	work with a light microscope
Med. Physics	the structure of the light and electron microscopes	work with a light microscope
Organic Chemistry	the chemical content of the cell	Speak of the topic

The contents of the topic:

General morphology and development

1. Linked by a *stalk* to the base of the brain, and lies surrounded by dural membrane (capsule) in the bony *sella turcica*.
2. *Embryological origins*
 - Adenohypophysis develops from the ectodermal *Rathke's pouch* above the oral cavity.
 - Rostral wall of Rathke's pouch becomes the anterior lobe; caudal wall gives the intermediate lobe; the cleft between the intermediate and anterior lobes occludes to a line of cysts; and the dorsolateral corners of the pouch give the pars tuberalis.
 - Neurohypophysis comes as a downgrowth of the *floor of the diencephalon*. The brain connection is maintained.



Adenohypophysis

1. *Pars tuberalis* - wrapped around the neural stalk are cords of basophilic cells containing gonadotrophic hormones.
2. *Pars intermedia* - rudimentary in man; variable in width; several colloid-filled cysts; glandular cells - chromophobe or basophil; basophilic cells may extend into the neural lobe; function - unknown in man, but in fish and amphibia the melanocyte stimulating hormone (MSH) formed varies skin pigmentation.
3. *Pars distalis*
 - Thick, branching *cords* and *plates* of cells, supported on basal laminae and reticular fibres. Between the cords run wide *sinusoidal capillaries* of fenestrated endothelial cells on their own BLs.
 - Classical division of the cells was into *acidophils* (40 per cent), *basophils* (10 per cent), and *chromophobes* (50 per cent).

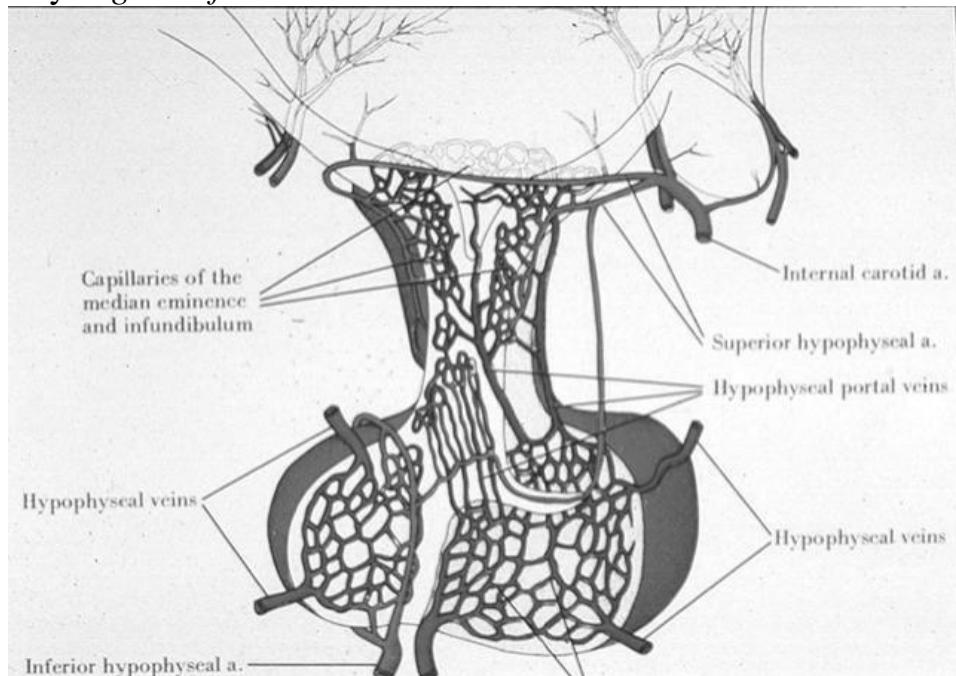
- *Chromophobes* are sparsely granular, small, pale, and often clustered together. They are thought to be less active forms of the five secretory, granular, chromophil cell kinds.

- *Chromophils* can be distinguished by various stains, since some form peptide hormones, others glycoproteins; by EM, from the size, density and shape of the granules; and by immunostaining, for LM and EM.

- **ACIDOPHILS**, *Somatotroph* - makes growth hormone (GH)/somatotrophin (STH); stained by orange-G *Lactotroph/Mammotroph* - makes prolactin/mammotrophin (MTH); stained by erythrosin

- **BASOPHILS**, staining also with PAS and aniline blue *Thyrotroph* gives thyrotrophic hormone (TSH/TH) *Gonadotroph* gives luteinizing hormone (LH) and follicle-stimulating hormone (FSH)/interstitial cell-stimulating hormone (ICSH) *Corticotroph* makes adrenocorticotrophin (ACTH), and related hormones, e.g., MSH, by cleaving proopiomelanocortin appropriately

- Hypothalamic regulation of the adenohypophysis is via the *hypothalamo-hypophyseal portal circulation*, and for gonadotrophins, ACTH, and TSH, functions by *negative feedback* thus:



1. *Hypothalamic neurons* are specialized to be sensitive to a blood deficiency of the target gland's hormone, e.g. thyroxine.

2. From the sensitive neuron's terminal, a neurosecretory, chemical peptide *releasing factor*, e.g. TH-RH/TH-RF, passes into blood *capillaries* of the median eminence, whence it drains down via the *portal circulation* to the pars distalis.

3. The releasing factor passes out of the blood to activate the appropriate *chromophil cell*, which produces more *trophic hormone*, e.g., TH.

4. The trophic hormone passing in the blood to the *target gland*, thyroid, promotes an increased output of *target gland hormone*, thyroxine, whose raised blood level then reduces the activity of the sensitive hypothalamic neurons, i.e., the system uses a *negative feedback*.

This simplification ignores the *inhibitory* factors, such as hypothalamic somatostatin preventing the release of growth hormone.

- The hypothalamus thus acts as an endocrine organ.

Neurohypophysis

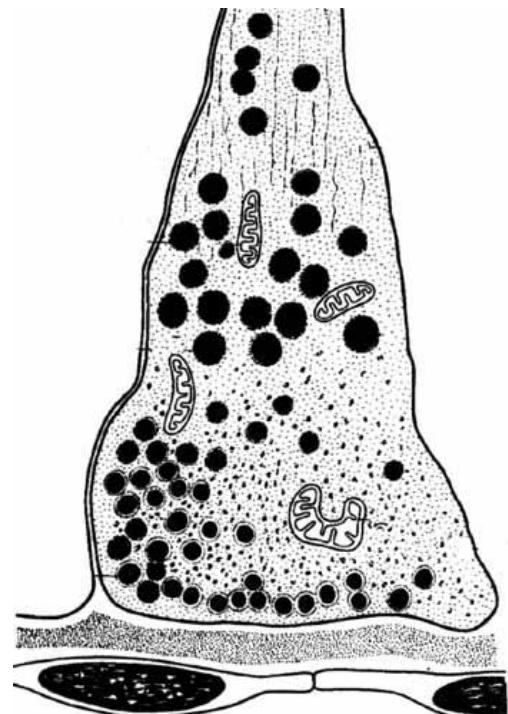
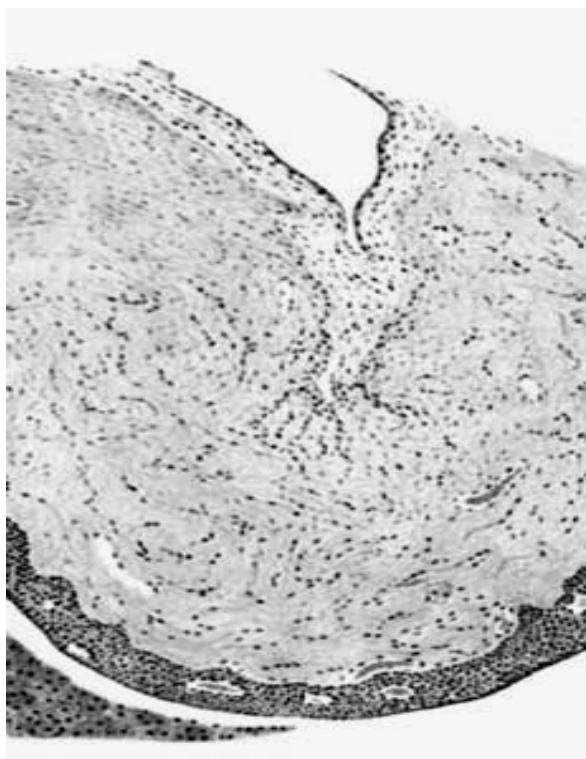
May be viewed as a downward extension of the hypothalamus, allowing for hormone storage and a complete breach of the blood-brain barrier for hormone release.

Its structure follows:

1. The *neural stalk* and *posterior lobe* consist of the unmyelinated axons (grouped as the hypothalamo-hypophyseal tract) of neurosecretory neurons of the hypothalamic *supraoptic* and *paraventricular nuclei*.

2. The *neurosecretion* collects, and dilates some axons and their terminals into *Herring bodies*. Gomori staining or EM shows the presence of granules in these axons, but not in the *pituicytes* - a neuroglial kind of cell.

3. The secretion collects in terminals arranged as a palisade around blood vessels. Its *release* may involve electrical discharge in the axon and chemical factors in the 'synaptic' vesicles also present.



4. Two polypeptide hormones in the secretion are:

- *oxytocin/pitocin*: makes mammary gland myoepithelial cells and uterine smooth muscle contract;

- *vasopressin/pitressin/antidiuretic hormone (ADH)*: makes the kidney collecting tubule permeable to water, and influences vascular and gut smooth muscle.

5. The neural lobe has a direct arterial supply from the inferior hypophyseal arteries to its fenestrated capillaries.

3.3. Literature recommended

Main Sources:

1. L.C. Junqueira, J. Carneiro - “Basic histology” – 11 edition - 2005.
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6. Inderbir Singh Textbook of Human Histology.- Jaypee. India. - 1997.
7. Ten Cate A.R. Oral Histology.- St.Louis, Baltimore, Toronto.- 1995.
8. William A., Beresford M.A. Cytology and Histology.- Anatomy department, West Virginia University, USA.- 1992.
9. K.E. Jonson - “Histology and cell biology” – 2 edition – Washington – 1991.

Additional ones:

1. Methodical Instructions.

3.4 How to work with the literature recommended:

Main tasks	Recommendations
To review the material	To use the material studied
To learn the material	To use the material on pages
To read and compose the plan	To learn the new material and be ready to write a summary
To answer the questions	To be ready to give an answer to the following:
To do the test on the material	
To be ready to answer the topic	

3.5. Self-control material:

A. Questions to be answered:

1. What is the hypophysis?
2. From what sources the hypophysis develops?
3. Give characteristic of the adenohypophysis function?
4. Describe the structure of the pars tuberalis.
5. Describe the structure of the pars intermedia.
6. Describe the structure of the pars distalis
7. What is the hypothalamic regulation of the adenohypophysis?
8. Describe the structure of the neurohypophysis.
9. What arterial supply the neural lobe has?
- 10.What is the structure of the pineal gland?

B. Test tasks to be done: Tests are applied

4. Self-preparation in the classroom.

- 1) Listen to the information.
- 2) Work with the tables and a Light microscope.
- 3) Ask about the problems that haven't been found in the information given.
- 4) To sketch in the album the investigated preparations.

5. Self-preparation work at home.

- 1) Review the material learnt in the classroom.
- 2) Compose the plan of your answer.
- 3) Answer the questions to this topic.
- 4) Do the test given above.

6. The subject of the research work.

<i>Subject</i>	<i>Histology, cytology and embryology</i>
<i>Modul №2</i>	<i>Histology, cytology and embryology</i>
<i>Submodul №3</i>	<i>Special histology</i>
Topic 17	THYROID GLAD. PARATHYROID GLANDS

Hours: 2

1. The topic basis: the topic “**THYROID GLAD. PARATHYROID GLANDS**” is very important for future doctors in their professional activity, positively influences the students in their attitude to the future profession, forms professional skills and experience as well as taking as a principle the knowledge of the subject learnt.

2. The aims of the training course:

- 1) To have general knowledge of the topic studied.
- 2) To understand, to remember and to use the knowledge received.
- 3) To learn the classification, structure and functions of the different histological methods.
- 4) To form the professional experience by reviewing, training and authorizing it.
- 5) To be able to carry out laboratory and experimental work.

3. Materials for the before – class work self – preparation work:

3.1 Basic knowledge, experience, skills necessary for studying the topic in connection with other subjects:

	To know	To be able to
Med. Biology	the structure of the cells and tissues	work with a light microscope
Med. Physics	the structure of the light and electron microscopes	work with a light microscope
Organic Chemistry	the chemical content of the cell	Speak of the topic

The contents of the topic:

THYROID GLAND

1. Develops from an endodermal down growth at the base of the tongue. The thyroglossal duct, connecting it with its point of origin, later disappears. Two lateral lobes, an isthmus (and sometimes a pyramidal lobe) are established.

2. The inner, true, CT *capsule* sends in septa to partially enclose lobules.

3. In the lobules are rounded or elongated bodies - *follicles*, in a loose stroma of CT, with many blood vessels.

Thyroid follicle

1. In man, they vary between 0.02 and 0.9 mm in diameter. A gland has several million follicles.

2. Filled with viscous fluid - *thyroid colloid* - variably acidophil or basophil, and often shrunken and showing knife chatters.

3. Lined by basophilic cuboidal *follicular cells*, varying in height as a simple epithelium on a *basal lamina*, outside which is an extensive plexus of blood capillaries, and reticular fibres and fibroblasts.

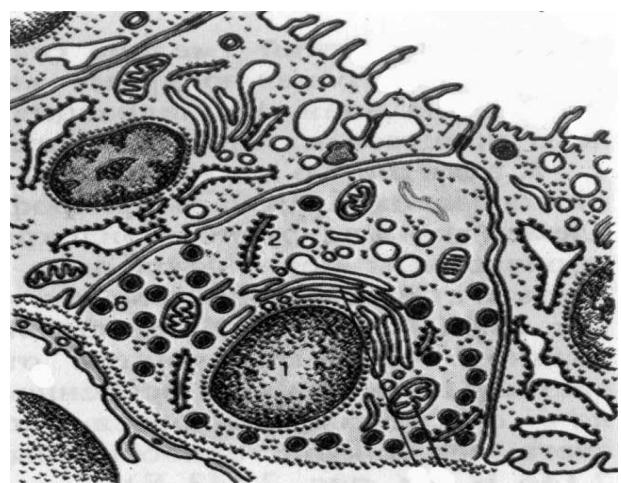
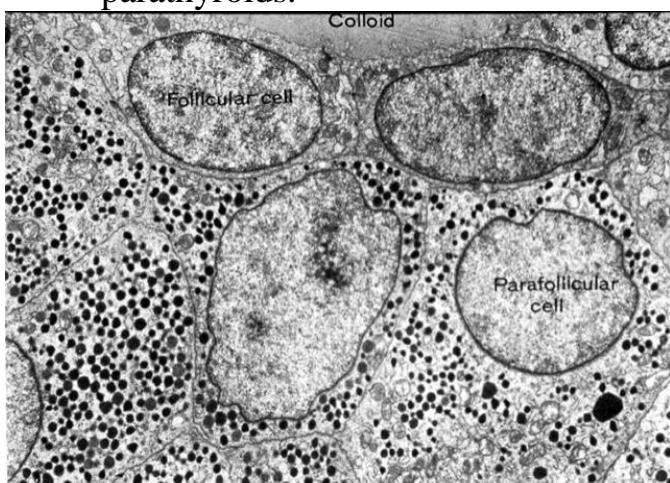
4. *Follicular cells* are polarized with respect to the follicle lumen; the nucleus is central, the Golgi complex supranuclear; EM shows plenty of granular ER, some luminal microvilli, endocytotic vesicles, and lysosomes.

5. Between the follicular cells and the BL, and sometimes outside the BL, lie occasional *C cells* (clear/parafollicular cells), having no direct access to the lumen, and no colloid droplets, but with small argyrophil, secretory granules.

Thyroid histophysiology

1. C Cells

- Are APUD cells of neural crest origin, and produce the polypeptide *calcitonin* for the reduction of high plasma Ca^{2+} and phosphate levels.
- Although diffuse, in sum they form a gland antagonistic to the action of the parathyroids.



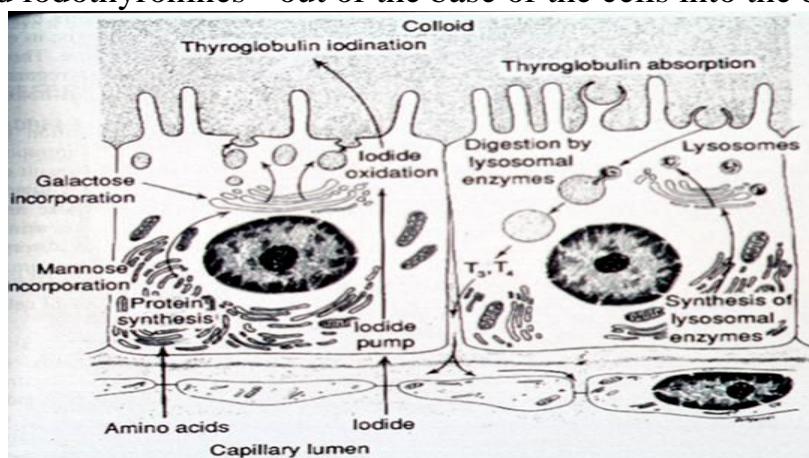
2. Follicular cells

-Are stimulated by pituitary *thyrotrophic hormone* (TSH) to produce and release two iodinated amino-acid hormones - *tetraiodo-thyronine* (*thyroxine/T4*) and *3,5,3'-triiodo-L-thyronine(T3)*, which are stored in the colloid, as component amino acids of the glycoprotein - *thyroglobulin*.

-The hormones accelerate general and specific metabolic processes of the body.

-Electron radioautography has shown the sites in the sequence of hormone production by the follicular cells:

- Iodide concentration - basal part of the follicular cell.
- Iodide oxidation - throughout the cell.
- Synthesis of thyroglobulin - basal cell, granular ER, Golgi body, by vesicle to the lumen.
- In the luminal thyroglobulin, tyrosine residues are iodinated, and then pairs condense.
- Cellular retrieval of thyroglobulin from colloid storage - cell's apical region by endocytosis.
- Transport to lysosomes, where cathepsins degrade the large modified molecule.
- Release of freed iodothyronines - out of the base of the cells into the blood.



PARATHYROID GLANDS

General morphology

1. Derived embryologically from the 3rd and 4th *pharyngeal grooves*.
2. Adherent to the true capsule of the thyroid.
3. Each of the four or more rounded or ovoid bodies has a fine CT capsule and delicate, incomplete septa.
4. These septa carry vessels, nerves and many fat cells.

Histophysiology

1. Supported on fine reticular fibres are many fenestrated blood capillaries and sheets and cords of
 2. *glandular cells*:
- (a) *Chief cells*: small, 7-10 μm diameter; some dark, some light: contain glycogen, a Golgi complex, lipofuscin pigment, and argyrophil secretory granules; form occasional small follicles.
 - (b) *Oxyphil cells*; larger, acidophilic, and often occur in clumps; cytoplasm is packed with mitochondria; no secretory granules; serve no known role. More oxyphil cells are seen in older individuals.
 - *Functions*
 - Secretory granules of chief cells are the polypeptide hormone, *parathormone/PTH*, released in response to low blood Ca^{2+} , and acting on osteoclasts and macrophages to increase *bone resorption*.

- In the kidney, PTH: promotes the tubular reabsorption of *calcium*, and the 1, activation of *vitamin D*; and inhibits the renal tubular reabsorption of *phosphate* - a phosphaturic action.
- Unlike most other endocrine glands, no specific pituitary trophic hormone is involved in its control.

3.3. Literature recommended

Main Sources:

1. L.C. Junqueira, J. Carneiro - “Basic histology” – 11 edition - 2005.
2. A.S. Pacurar, J.W. Bigbee – “Digital histology” – Virginia - 2004.
3. “Color Atlas of basic histology” – R.Berns – 2006.
4. Sadler T.V. – “Medical embryology” Montana – 1999.
5. Inderbir Singh Textbook of Human Histology.- Jaypee. India. - 1997.

Additional ones:

1. Methodical Instructions.

3.4 How to work with the literature recommended:

Main tasks	Recommendations
To review the material	To use the material studied
To learn the material	To use the material on pages
To read and compose the plan	To learn the new material and be ready
To answer the questions	to write a summary
To do the test on the material	To be ready to give an answer to the
To be ready to answer the topic	following:

3.5. Self-control material:

A. Questions to be answered:

1. What is the general morphology of the thyroid gland?
2. Describe the structure of the thyroid follicle.
3. What are the C-cells of the thyroid gland?
4. Give the morphological characteristic of the follicular cells.
5. Describe secretory stages of the thyrocyte.
6. What is the parathyroid gland?
7. Describe histophysiology of the glandular cells.

B. Test tasks to be done: Tests are applied

4. Self-preparation in the classroom.

- 1) Listen to the information.
- 2) Work with the tables and a Light microscope.
- 3) Ask about the problems that haven't been found in the information given.
- 4) To sketch in the album the investigated preparations.

5. Self-preparation work at home.

- 1) Review the material learnt in the classroom.
- 2) Compose the plan of your answer.
- 3) Answer the questions to this topic.
- 4) Do the test given above.

6. The subject of the research work.

“Features of the thyroid gland's secretion”

“Modern representation about supporting of the calcium homeostasis”

<i>Subject</i>	<i>Histology, cytology and embryology</i>
<i>Modul №2</i>	<i>Histology, cytology and embryology</i>
<i>Submodul №3</i>	<i>Special histology</i>
<i>Topic 18</i>	SUPRARENAL GLAND.

Hours: 2

1. The topic basis: the topic “SUPRARENAL GLAND” is very important for future doctors in their professional activity, positively influences the students in their attitude to the future profession, forms professional skills and experience as well as taking as a principle the knowledge of the subject learnt.

2. The aims of the training course:

- 1) To have general knowledge of the topic studied.
- 2) To understand, to remember and to use the knowledge received.
- 3) To learn the classification, structure and functions of the different histological methods.
- 4) To form the professional experience by reviewing, training and authorizing it.
- 5) To be able to carry out laboratory and experimental work.

3. Materials for the before – class work self – preparation work:

3.1 Basic knowledge, experience, skills necessary for studying the topic in connection with other subjects:

	To know	To be able to
Med. Biology	the structure of the cells and tissues	work with a light microscope
Med. Physics	the structure of the light and electron microscopes	work with a light microscope
Organic Chemistry	the chemical content of the cell	Speak of the topic

The contents of the topic:

General morphology and development

1. Elongated glands of cocked-hat or crescentic shape.
2. Composite of *medullary* and *cortical tissues*, linked by blood supply, but embryologically and functionally distinct.

3. *Mesodermal* cells of coelomic mesothelium differentiate into: inner, provisional or *fetal cortex* (involutes at birth); and *outer, permanent cortex*.

4. *Neural crest* ectodermal cells migrate: to coeliac ganglion; and then some go beyond to invade the cortical tissue and form the *medulla*.

5. Mature adrenal has a thick CT *capsule*, bringing arteries to serve radial capillaries draining down towards the venules and *central vein* of the medulla. Arterioles also penetrate the cortex to serve a medullary capillary bed.

6. The *medulla* is a long, thin strip of basophilic cells, which can be made outstanding by the *chromaffin reaction* - a darkening produced by dichromate ions.

7. The supporting element throughout is the *reticular fibre*.

Cortex

1. Polyhedral glandular cells, in cords usually two cells wide, run roughly radially, along with sinusoidal capillaries.

2. *Three layers* are visible:

- *Zona glomerulosa* - under the capsule, rounded balls or groups of columnar cells with dark nuclei.

- *Zona fasciculata* - long, straight cords of large cells, swollen with lipid droplets.

- *Zona reticularis* - network made up of cells, small and often lipid-free; lies nearest to the medulla.

3. Lipid droplets (Sudanophilic and osmiophilic) contain cholesterol and cholesterol esters, used in conjunction with the Golgi body, smooth ER and special mitochondria, to produce two kinds of *steroid hormones*: *mineralo-* and *gluco-corticoids*.

- *Aldosterone* (mineralo-corticoid) helps control water and electrolyte balance, e.g., by promoting renal Na⁺ reabsorption, and having repercussions on blood pressure; secreted in the *Z. glomerulosa*, and released in response to angiotensin II.

- *Cortisol* (gluco-corticoid) helps control carbohydrate metabolism, e.g., facilitates protein catabolism and gluconeogenesis (thus interfering with processes requiring a high rate of protein synthesis, such as wound repair and antibody responses): formed in *Z. fasciculata* and *reticularis* in response to pituitary ACTH, itself released under hypothalamic control; glucocorticoids affect the cells and ground substances of connective tissues.

- Other glucocorticoids, and significant amounts of sex hormones, in *Z. Fasciculata* and *reticularis*.

Medulla

1. *Two cell kinds*:

- *Sparse ganglion nerve cells*, probably serving vascular smooth muscle in arterioles and the central vein.

- *Chromaffin cells*: large, granular, and arranged around venules, with their other pole by blood capillaries.

2. Release is controlled by a direct, 'preganglionic', *sympathetic innervation*, terminating synaptically on the glandular cells.

3. The hormones released are:
 - o *Norepinephrine* (transmitter substance for sympathetic, postganglionic fibres).
 - o *Epinephrine* (increases cell respiration, cardiac output, and glucose mobilization, for the great muscular effort needed in fighting or fleeing).

4. The hormones are stored in characteristic membrane-bound granules, visible in EM. The granules form in relation to the Golgi body, but a dense GER is not required. They also contain enkephalins and chromogranin.

5. Both principal hormones are *catecholamines*, which can be converted by oxidizing agents, e.g., dichromate or ferric salts, to brown-coloured polymers - adrenochromes: this is the *chromaffin reaction*.

3.3. Literature recommended

Main Sources:

1. L.C. Junqueira, J. Carneiro - "Basic histology" – 11 edition - 2005.
2. A.S. Pacurar, J.W. Bigbee – "Digital histology" – Virginia - 2004.
3. "Color Atlas of basic histology" – R.Berns – 2006.
4. Sadler T.V. – "Medical embryology" Montana – 1999.
5. Ronald W., Dudek Ph.D. – "Embryology" 2 edition – 1998.
6. Inderbir Singh Textbook of Human Histology.- Jaypee. India. - 1997.
7. Ten Cate A.R. Oral Histology.- St.Louis, Baltimore, Toronto.- 1995.
8. William A., Beresford M.A. Cytology and Histology.- Anatomy department, West Virginia University, USA.- 1992.
9. K.E. Jonson - "Histology and cell biology" – 2 edition – Washington – 1991.

Additional ones:

1. Methodical Instructions.

3.4 How to work with the literature recommended:

Main tasks	Recommendations
To review the material	To use the material studied
To learn the material	To use the material on pages
To read and compose the plan	To learn the new material and be ready to write a summary
To answer the questions	To be ready to give an answer to the following:
To do the test on the material	
To be ready to answer the topic	

3.5. Self-control material:

A. Questions to be answered:

1. Describe general morphology of the suprarenal gland.
2. Describe development of the suprarenal gland.
3. Give main characteristic of the suprarenal glands cortex.
4. What are the target cells to the cortex hormones?
5. Describe general morphology of the suprarenal gland medulla.
6. What endocrine cells are there in the kidneys?

B. Test tasks to be done: Tests are applied

4. Self-preparation in the classroom.

- 1) Listen to the information.
- 2) Work with the tables and a Light microscope.
- 3) Ask about the problems that haven't been found in the information given.

4) To sketch in the album the investigated preparations.

5. Self-preparation work at home.

- 1) Review the material learnt in the classroom.
- 2) Compose the plan of your answer.
- 3) Answer the questions to this topic.
- 4) Do the test given above.

6. The subject of the research work.

“Development of the suprarenal gland”

“Role of the steroids in the endocrine regulation of the organism’s functions”

<i>Subject</i>	<i>Histology, cytology and embryology</i>
<i>Modul №2</i>	<i>Histology, cytology and embryology</i>
<i>Submodul №3</i>	<i>Special histology</i>
<i>Topic 19</i>	CONTROL TESTS 3

Hours: 2

1. The topic basis: the topic “**CONTROL TESTS 3**” is very important for future doctors in their professional activity, positively influences the students in their attitude to the future profession, forms professional skills and experience as well as taking as a principle the knowledge of the subject learnt.

2. The aims of the training course:

- 1) To have general knowledge of the topic studied.
- 2) To understand, to remember and to use the knowledge received.
- 3) To learn the classification, structure and functions of the different histological methods.
- 4) To form the professional experience by reviewing, training and authorizing it.
- 5) To be able to carry out laboratory and experimental work.

3. Materials for the before – class work self – preparation work:

3.1 Basic knowledge, experience, skills necessary for studying the topic in connection with other subjects:

	To know	To be able to
Med. Biology	the structure of the cells and tissues	work with a light microscope
Med. Physics	the structure of the light and electron microscopes	work with a light microscope
Organic Chemistry	the chemical content of the cell	Speak of the topic

The contents of the topic:

3.3. Literature recommended

Main Sources:

1. L.C. Junqueira, J. Carneiro - “Basic histology” – 11 edition - 2005.

2. A.S. Pacurar, J.W. Bigbee – “Digital histology” – Virginia - 2004.
3. “Color Atlas of basic histology” – R.Berns – 2006.
4. Sadler T.V. – “Medical embryology” Montana – 1999.
5. Ronald W., Dudek Ph.D. –“Embryology” 2 edition – 1998.
6. Inderbir Singh Textbook of Human Histology.- Jaypee. India. - 1997.
7. Ten Cate A.R. Oral Histology.- St.Louis, Baltimore, Toronto.- 1995.
8. William A., Beresford M.A. Cytology and Histology.- Anatomy department, West Virginia University, USA.- 1992.
9. K.E. Jonson - “Histology and cell biology” – 2 edition – Washington – 1991.

Additional ones:

1. Methodical Instructions.

3.4 How to work with the literature recommended:

Main tasks	Recommendations
To review the material	To use the material studied
To learn the material	To use the material on pages
To read and compose the plan	To learn the new material and be ready to write a summary
To answer the questions	To be ready to give an answer to the following:
To do the test on the material	
To be ready to answer the topic	

3.5. Self-control material:

A. Questions to be answered:

1. Nervous system. General morfo-functional characteristic. Sources of development.
2. Peripheral nervous system. A nerve. A constitution and regeneration of the nerves.
3. Spinal ganglia. Morfo-functional characteristic. Cellular structure.
4. Spinal cord, morfo-functional characteristic. A constitution of the grey and white matter. Cellular structure. Sensing and motoring paths of a spinal cord as parts of reflex arcs.
5. Shaft of the brain. Grey and white matter. Principles of organization of ascending conduction paths. Myelencephalon. Nucleuses. A reticular formation, its constitution, function.
6. General morfo-functional characteristic of large hemispheres. Cytoarchitectonic. Myeloarchitectonic.
7. Neuronic organization of a cortex of large hemispheres. Age changes of the cerebral cortex.
8. Cerebellum. Constitution and functional characteristic. A neuronic structure of the cerebellum cortex.
9. Vegetative nervous system. Morfo-functional characteristic, departments. Constitution of extra- and intramural ganglia. Nucleuses of central departments of the vegetative nervous system.
10. Analyzers. Their value for the human organism. Sense organs as peripheral departments of analyzers.
11. Sense organs. General morfo-functional characteristic. Classification of sense organs.

12. Organ olfactoria. Constitution, development, cytophysiology of receptor cells.
13. Optical organ. A general plan of a constitution of the eyeball's shells and apparatuses.
14. Optical organ. Characteristic of the retina. Adaptive changes of a retina.
15. Taste organ. A constitution, function. Cytophysiological characteristic of taste bulbs.
16. Auditory organ. Morfo-functional characteristic. Constitution, cytophysiology of receptor cells of the Corti organ.
17. Vestibular organ. A constitution, function. The characteristic of receptor cells. General principles of the constitution function of acoustical cristaes and acoustical macules, difference in their constitution and functions.
18. Give the characteristic of the endocrine system.
19. What parts of the endocrine system do you know?
20. What are the functions of the endocrine system?
21. What is the axo-vasal synaps?
22. What types of hormones do you know?
23. What is the APUD-system?
24. What are the neuroendocrine cells of the hypothalamus?
25. From what sources the hypophysis develops?
26. Give characteristic of the adenohypophysis function?
27. Describe the cytostructure of the adenohypophysis.
28. What is the hypothalamic regulation of the adenohypophysis?
29. Describe the structure of the neurohypophysis.
30. What arterial supply the neural lobe has?
31. What is the structure of the pineal gland?
32. What is the general morphology of the thyroid gland?
33. Describe the structure of the thyroid follicle.
34. What are the C-cells of the thyroid gland?
35. Describe secretory stages of the thyrocyte.
36. What is the parathyroid gland?
37. Describe general morphology of the suprarenal gland.
38. Describe development of the suprarenal gland.
39. Give main characteristic of the suprarenal glands cortex.
40. What are the target cells to the cortex hormones?
41. Describe general morphology of the suprarenal gland medulla.
42. What parts are containing the cardiovascular system?
43. What general functions of the cardiovascular system do you know?
44. Describe heart wall's layers.
45. What components of the heat impulse-conducting system do you know?
46. What is the endocrine role of heart?
47. Describe morphology in relation to physical factors in various vessels.
48. What are the arteries?
49. What differences between elastic and muscular arteries?
50. What are the veins?
51. What do you know about lymphatic vessels?

- 52.What components of the microcirculatory rate do you know?
- 53.What about arterioles do you know?
- 54.Describe types of blood capillaries.
- 55.What about venules do you know?
- 56.Give the characteristic of the arteriovenous anastomoses.
- 57.What is the haemocytopoiesis?
- 58.What studies of the divisions of haemopoiesis do you know?
- 59.What are the sites of myelopoiesis in embryo?
- 60.What are the sites of myelopoiesis in adult?
- 61.Describe the changes in developing red blood cells.
- 62.Describe the changes in developing granulocyte.
- 63.Describe the changes in developing platelets.
- 64.Describe the changes in developing agranular leucocytes.
- 65.Describe the structure of the bone marrow.
- 66.Give the main characteristic of the lymphoid tissue.
- 67.Describe the structure of the thymus.
- 68.What are the functions of the thymus epithelial cells?
- 69.Give the characteristic of the lymphocytes (thymocytes).
- 70.What functions of the macrophages in the thymus?
- 71.What functions of the corpuscles of Hassall?
- 72.What are the thymic functions?
- 73.Describe the structure of the palatine tonsils.
- 74.What are the functions of the lymph nodes?
- 75.What is the lymph-node structure?
- 76.What are the parenchymal elements of the lymph-node?
- 77.What are the mucoso-lymphoid organs?
- 78.What are the splenic functions do you know?
- 79.Describe the splenic structure.
- 80.Describe the connective tissue basis of the spleen.
- 81.Describe the circulation through the spleen.
- 82.Describe the elements of white pulp.
- 83.Describe the elements of red pulp.
- 84.Describe the specific immune tasks.
- 85.What are the defensive cells of the immunity system?
- 86.What functions of the plasma cells do you know?
- 87.Give the characteristic of the immunoglobulins.
- 88.What functions of the lymphocytes do you know?
- 89.What about dendritic antigen-presenting cells (APCs) do you know?
- 90.What about macrophages do you know?
- 91.What functions of the granular leucocytes do you know?
- 92.What functions of the mast cells do you know?
- 93.What do you know about autoimmunity diseases?

<i>Subject</i>	<i>Histology, cytology and embryology</i>
<i>Modul №2</i>	<i>Histology, cytology and embryology</i>
<i>Submodul №4</i>	<i>Special histology</i>
<i>Topic 20</i>	DIGESTIVE SYSTEM. ORGANS OF ORAL CAVITY

Hours: 2

1. The topic basis: the topic “**DIGESTIVE SYSTEM. ORGANS OF ORAL CAVITY**” is very important for future doctors in their professional activity, positively influences the students in their attitude to the future profession, forms professional skills and experience as well as taking as a principle the knowledge of the subject learnt.

2. The aims of the training course:

- 1) To have general knowledge of the topic studied.
- 2) To understand, to remember and to use the knowledge received.
- 3) To learn the classification, structure and functions of the different histological methods.
- 4) To form the professional experience by reviewing, training and authorizing it.
- 5) To be able to carry out laboratory and experimental work.

3. Materials for the before – class work self – preparation work:

3.1 Basic knowledge, experience, skills necessary for studying the topic in connection with other subjects:

	To know	To be able to
Med. Biology	the structure of the cells and tissues	work with a light microscope
Med. Physics	the structure of the light and electron microscopes	work with a light microscope
Organic Chemistry	the chemical content of the cell	Speak of the topic

3.2 The contents of the topic:

ORAL CAVITY. WALLS OF THE ORAL CAVITY

The term mucous membrane is used to describe the moist lining of the body cavities that communicate with the exterior. In the oral cavity this lining is called the oral mucous membrane or oral mucosa. At the lips the oral mucosa is continuous with the skin a dry covering layer with a structure that resembles the oral lining in some respects at the pharynx it is continuous with the moist mucosa lining the rest of the intestine. Thus the oral mucosa is situated anatomically between skin and intestinal mucosa and shows some of the properties of each.

The skin, the oral mucosa and the intestinal lining each consist of two separate tissue components, a covering epithelium and an underlying connective tissue. Because these two tissues together perform a common function, the oral mucosa, like the skin and the intestinal lining, should be considered an organ. The major functional adaptations of the oral mucosa are the results of evolutionary changes in the species that have taken place over a long period of time. Although small and usually reversible changes in structure may be seen in response to function or use during the lifetime of an individual, such changes are not heritable.

The oral mucosa serves several functions. The major one is the protection it provides the deeper tissues of the oral cavity. Among its other functions, the oral

mucosa is a sensory organ, and the site of some glandular activity, chiefly minor salivary glands and occasionally some sebaceous glands.

FUNCTIONS OF ORAL MUCOSA

The oral mucosa serves several functions. The major one is the protection it provides the deeper tissues of the oral cavity. Among its other functions, the oral mucosa is a sensory organ, and the site of some glandular activity, chiefly minor salivary glands and occasionally some sebaceous glands.

Protection

As a surface lining, the oral mucosa separates and protects deeper tissues and organs in the oral region from the environment of the oral cavity. The normal activities of seizing food (prehension), biting it, and chewing it expose the oral soft tissues to mechanical forces such as compression, stretching, and shearing and to surface abrasion from hard particles in the diet. The oral mucosa shows a number of adaptations of both the epithelium and the connective tissue to withstand these insults. Furthermore, there is normally a resident population of microorganisms within the oral cavity that would cause infection if they gained access to the tissues. Many of these organisms also produce substances that have a toxic effect on tissues. The epithelium of the oral mucosa acts as the major barrier to these threats.

Sensation

The sensory function of the oral mucosa is important because it provides considerable information about events in the oral cavity whereas the lips and tongue can also perceive stimuli outside the mouth. In the mouth there are receptors that respond to temperature touch, and pain, as well as the taste buds, which are not found anywhere else in the body. Certain receptors in the oral mucosa probably respond to the taste of water and signal the satisfaction of thirst. Reflexes such as swallowing, gagging, retching and salivation are also initiated by receptors in the oral mucosa.

Thermal regulation

In some animals such as the dog, considerable body heat is dissipated through the oral mucosa by panting thus the mucosa plays a part in the regulation of body temperature for such animals. Human oral mucosa however, probably plays little part in the regulation of body temperature, because there are no obvious specializations of the blood vessels for controlling heat transfer.

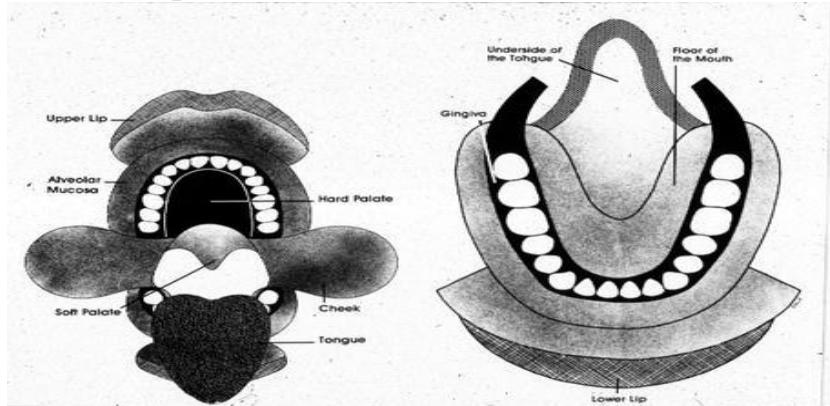
Secretion

The major secretion associated with oral mucosa is the saliva, produced by the salivary glands which contribute to the maintenance of a moist surface. The major salivary glands are situated far from the mucosa and their secretions pass through the mucosa via long ducts, however, many minor salivary glands are associated with the oral mucosa.

ORGANIZATION OF ORAL MUCOSA

The oral cavity consists of two parts, an outer vestibule bounded by the lips and cheeks, and the oral cavity proper that is separated from the vestibule by the alveolus bearing the teeth and gingiva. The superior border of the oral cavity proper is formed by the hard and soft palates, whereas the floor of the mouth and base of the tongue form the inferior border. Posteriorly, the oral cavity is bound by the pillars of the palate and the tonsils. The oral mucosa shows considerable structural variation in

different regions of the oral cavity, but three main types of mucosa can be recognized. These are identified according to their primary function as masticatory mucosa, lining mucosa, and specialized mucosa.



The oral mucosa varies considerably in its firmness and texture. The lining mucosa of the lips and cheeks, for example, is soft and pliable, whereas the gingiva and hard palate are covered by a firm, immobile layer. These differences have important clinical implications when it comes to giving local injections of anesthetics or taking biopsies of oral mucosa. Fluid can be easily introduced into loose lining mucosa but injection into a masticatory mucosa is difficult and painful. On the other hand, lining mucosa gapes when incised and may require suturing, masticatory mucosa does not.

REGION		MUCOSA	SUBMUCOSA
	Covering epithelium	Lamina propria	
Lining mucosa			
Soft palate	Thin (150 nm) nonkeratinized stratified squamous epithelium, taste buds present	Thick with numerous short papillae, elastic fibres forming an elastic lamina, highly vascular with well-developed capillary network	Diffuse tissue containing numerous minor salivary glands
Ventral surface of tongue	Thin, nonkeratinized, stratified squamous epithelium	Thin with numerous short papillae and some elastic fibres, a few minor salivary glands, capillary network in subpapillary layer, reticular layer relatively avascular	Thin and irregular, may contain fat and small vessels, where absent the mucosa is bound to the connective tissue surrounding the tongue musculature
Floor of mouth	Very thin (100 nm) nonkeratinized, stratified squamous epithelium	Short papillae, some elastic fibres, extensive vascular supply with short anastomosing capillary loops	Loose fibrous connective tissue containing fat and minor salivary glands
Alveolar mucosa	Thin, nonkeratinized, stratified squamous epithelium	Short papillae, connective tissue containing many elastic fibres, capillary loops close to the surface supplied by vessels running superficially to the periosteum	Loose connective tissue, containing thick elastic fibres attaching it to periosteum of alveolar process, minor salivary glands
Labial and buccal mucosa	Very thick (500 nm) nonkeratinized, stratified squamous epithelium	Long, slender papillae, dense fibrous connective tissue containing collagen and some elastic fibres, rich vascular supply giving off anastomosing capillary loops into papillae	Mucosa firmly attached to underlying muscle by collagen and elastin, dense collagenous connective tissue with fat, minor salivary glands, sometimes sebaceous glands

Lips vermillion border	Thin, orthokeratinized, stratified squamous epithelium	Numerous narrow papillae, capillary loops close to surface in papillary layer	Mucosa firmly attached to underlying muscle, some sebaceous glands in vermillion border, minor salivary gland and fat in intermediate zone
Lips intermediate zone	Thin parakeratinized, stratified squamous epithelium	Long irregular papillae, elastic and collagen fibres in connective tissue	
Masticatory mucosa			
Gingiva	Thick (250 µm), orthokeratinized or para keratinized, stratified squamous epithelium often showing stippled surface	Long, narrow papillae, dense collagenous connective tissue, not highly vascular but long capillary loops with numerous anastomoses	No distinct layer, mucosa firmly attached by collagen fibres to cementum and periosteum of alveolar process ("mucoperiosteum")
Hard palate	Thick, orthokeratinized (often parakeratinized in parts), stratified squamous epithelium thrown into transverse palatine ridges (rugae)	Long papillae, thick dense collagenous tissue, especially under rugae, moderate vascular supply with short capillary loops	Dense collagenous connective tissue attaching mucosa to periosteum ("mucoperiosteum"), fat and minor salivary glands are packed into the connective tissue in regions where mucosa overlays lateral palatine neurovascular bundles
Specialized mucosa			
Dorsal surface of tongue	Thick, keratinized and nonkeratinized, stratified squamous epithelium forming three types of lingual papillae, some bearing taste buds	Long papillae, minor salivary glands in posterior portion, rich innervation especially near taste buds, capillary plexus in papillary layer, large vessels lying deeper	No distinct layer, mucosa is bound to the connective tissue surrounding the musculature of the tongue

Lip

In the area of lips there is a gradual transition of a skin cover, located on the external surface of lip, in the of oral cavity mucosa. A transitional rea is a red border of lips. In lip composition there are 3 departments: 1) dermic; 2) transitional or intermediate; 3) mucous. Basis of lip is made by transversal-striped muscular tissue. A **skin** department of a lip has a structure of skin. It is covered by epidermis – compound squamous keratinized flat cornification epithelium which consists of 5 layers: *basal, spinal, granular, brilliant and squamous*. The high connective tissue papillae of derma jut out into an epithelium. Derma is formed by two layers: papillary (loose fibred connecting tissue) and reticular (dense connective tissue). In this department there are sebaseous and sweat glands, hair. The **intermediate** department of lip, or red border, consists of two areas: external (smooth) and internal (villiferous). Epithelium of external area is squamous keratinized. In an external area the squamous layer of epithelium is thinner, than in a skin department, with no hairs and sweat-glands. Absence of salivary glands in this area results in drying up of its surface. Sebaseous-glands are presented, excretory ducts are opened directly on the surface of epithelium. At corking sebaseous-gland ducts become noticeable and take form of yellow-white color granules, which are translucent through an epithelium. Loose connective tissue of own plate juts out into an epithelium as papillae. Blood in the

capillaries of papillae is translucent through the layer of epithelium, betraying the intermediate department of lip of a red color. The high sensitiveness of lips is provided by the presence in the mucous membrane of many nervous endins. In the internal area of red border an epithelium becomes in 3-4 times thicker, it is deprived of squamous layer. In this area there is a transition of compound keratinized epithelium in nonkeratinized. Epitheliocytes are increased in sizes, sebaseous-glands are absent. At new-born the epithelium of internal area of transitional department forms epithelial growings (tillies hairs), which serve as adaptation for suction. With age epithelial hair are smoothed out. A **mucous** department is covered by the thick layer of compound squamous nonkeratinized epithelium. Papillae situated below, in the red border of lips in an own plate, jut out into an epithelium, comprising 3/4 of its thickness. The bunches of collagen fibres which pass to the intramuscular layers of connective tissue are located in a submucosa. It provides the smoothness of mucous surface of lip and hinders a creasy. This membrane contains the accumulations of adipose cells and secretory departments of mucous and mixed salivary glands, the bringing out ducts of which are opened to vestibular part of oral cavity. There are arterial and venous anastomoses in a submucous membrane.

Cheek.

Cheeks are muscular formations which form the lateral wall of oral cavity. From outside cheek is covered by skin, and from within - by a mucous membrane. In a mucous part cheeks consist of 3 areas: 1) upper overhead - maxillary; 2) lower - mandibular; 3) middle - intermediate, which is located on the line of teeth. Mucous membrane of maxillary and mandibular areas of cheek has a structure which looks like the structure of mucous department of lip. A surface is covered by a thick layer of nonkeratinized epithelium. An own plate forms low, rarely located papillae which deepen in an epithelium on 1/4 of it's thicknesses. Papillae have a conical, sharp or finger-like shape. Collagen fibers are well developed in connective tissue of own plate. A submucosa is well expressed, contains plenty of salivary glands which are located at the muscle of cheek quite often. The largest salivary glands lie in the area of cheek-teeth. There are accumulations of adipose cells. The intermediate area of cheek is mucosa. It occupies the area within the airways about 10 mm, which extends from the corner angle of mouth to the branch of lower jaw and has a number of structural features. An epithelium on the line of teeth has a tendency of keratinization ("white line"). The own plate forms high connective tissue papillae which jut out into an epithelium. Bunches of collagen fibers are located in a submucosa. Salivary glands are absent, but often there are enough sebaseous glands. In embryogenesis and during first-year of the child's life there are epithelial "fibers", in the epithelium of mucosa of intermediate area or filies similar to those which are found in the internal area of red border of lips. It goes to explain that cheeks appear in embryo due to accretion of upper and lower edges of lips. An intermediate area of cheek, as well as intermediate department of lip, is the area of contact of skin and mucosa of oral cavity. The muscles of a cheek are formed of striated muscle tissue. At new-born and children of early age there is a layer of adipose tissue between a skin and muscles of cheek which hinders involvement of cheeks during suction.

Gum. Gum is the area of oral mucosa, which cover the alveolar processes of jaws and surrounds teeth. There are 3 parts in the gum: fixed (alveolar), free (marginal) and gingival interdental papillae. The fixed part of gums densely accretes with the periosteum of alveolar processes of jaws. Free part of gums (free edge) freely belongs to the surface of the teeth, moving away from it by forming a narrow crack - gingival furrow. Gingival interdental papillae are areas of gums that have three-cornered form, located in intervals between nearby teeth (Fig.3). From the inside gums pass to the mucous membrane in the area of hard palate or bottom of oral cavity. The mucous membrane of alveolar sprouts, which is presented by multi-compound nonkeratinized epithelium and own plate, has the red colour due to the blood vessels which are translucent through an epithelium. Gums which are covered by keratinized epithelium have a mat tint. In an epithelium there are melanocytes, producing melanin. The accumulation of melanin in epitheliocytes provides pigmentation of gums. The own plate of mucosa is presented with papillary and reticular layers. Connective tissue of papillae which deeply jut out into the epithelium of gums contains plenty of blood vessels and nervous endings. In area of gingival furrow papillae are smoothed out. Dense irregular connective tissue with the thick bunches of collagen fibers forms the reticular layer of mucosa. Bunches of collagen fibers are fixed by gums to the periosteum of alveolar proc.(fixed part of gum) and bind gums to cement of tooth (gingival fibers of periodontal copula). The muscle plate of mucosa, submucosa and glands are absent in gums. Due to the quiescent mechanical work which gums are exposed to, a mucosa has certain features in a structure. Gums on 90% are covered by keratinized epithelium which loses a squamous layer in area of gingival furrow. The highest speed of proliferation proceeding in an epithelium in an oral cavity is exactly in the epithelium of gums. Epithelial attachment of gums plays an important role in defence of tissues, circumferential teeth, from penetration of infection and other harmful factors, and also takes part in fixing of tooth in an alveolus. Gums are well blood supplied and innervated. The own plate has encapsulated and unincapsulated nervous endings.

Hard palate.

A hard palate consists of bone basis, which is covered by mucosa. Palate is a septum, dividing an oral and nasal cavity. The mucosa of hard palate relates to the masticatory type, it densely accretes with a periosteum, therefore is immobile. It is accepted to select 4 areas: 1) **adipose**, occupies one third of hard palate; 2) **glandular**, occupies back two thirds of hard palate; 3) **area of palatal guy-sutures** (medial area), located on the middle line of hard palate; 4) **marginal** area, directly adjoining to the teeth. A mucosa is thin in sutural area and is most developed in the back departments of hard palate. Epithelium of palate is multi-layered flat cornification. An own plate is presented by connective tissue, which contains a number of thick bunches of collagen fibers and forms finger-like papillae, jutting out into an epithelium on 2/3 of its thicknesses. A mucosa in a adipose area forms folds, at right angles outgoing from palatal guy-sutures (Fig.9). They are most expressed at fetus and considerably smoothed out after birth. A submucosa differs by the structure in the different departments of hard palate. In the front department of palate a submucosa contains the accumulations of adipose tissue, in the back one is plenty of salivary glands.

According to it they select adipose glandular and ferrous areas. In sutural area, and also in the place of passing to the alveolar processes (marginal area), a submucosa is absent, own plate densely fastened with a periosteum. That is why the suture marginal area is called fibrotic. The submucosa of adipose and glandular zones of hard palate is pierced by the thick bunches of dense fibred connective tissue, which attach an own plate to the periosteum of palatal bones. A mucosa in these departments of hard palate is motionlessly fixed to the bones. There are the round accumulations of epithelial cells in the own plate of mucosa membrane in the sutural area (epithelial pearls). They are tailings of epithelium which is bricked up in connective tissue at accretion of palatal processes in an embryonic period.

Soft palate. Uvula.

The soft palate separate the oral cavity from a gullet. Basis of soft palate is made of the thick bunches of striated muscle fibers and connective tissue. During swallowing a soft palate is pulled up and back, closing, thus, closing the entrance into nasopharynxes. We distinguish: 1) front (oral or oral-pharyngeal surface) 2)Uvula; 3) back (nasal or epipharyngeal) surface . A **frontal** (oral) surface is covered by a multi-layered flat nonkeratinized epithelium in which taste buds are sometimes presented. The own plate of mucosa forms high enough papillae which deeply jut out into an epithelium, contains numerous blood vessels. There is the well developed layer of elastic fibers on the border of own plate of mucosa and submucosa. Muscle plate is absent. A submucosa contains plenty of salivary glands, producing a mucous secret. The removing ducts of these glands are opened on the oral surface of soft palate. Striated muscle fibers crutch form and anastomoses. The accumulations of adipose tissue are located in a submucosa. A **back** (nasal) surface, turned to nasopharynxes, is covered with a one layer (simple) muco-ciliary epithelium, characteristic for respiratory tracts. The end -pieces of the mixed or mucous salivary glands and lymphatic nodes are located in the own plate of mucosa. A submucosa absents on the back surface of soft palate. **Uvula.** Both surfaces of uvula in adults are covered by a multi-layered flat nonkeratinized epithelium. At new-born the back surface of uvula is covered by multi-row muco-ciliary which in future is substituted with multi-layered flat uncornification.

Bottom of oral cavity.

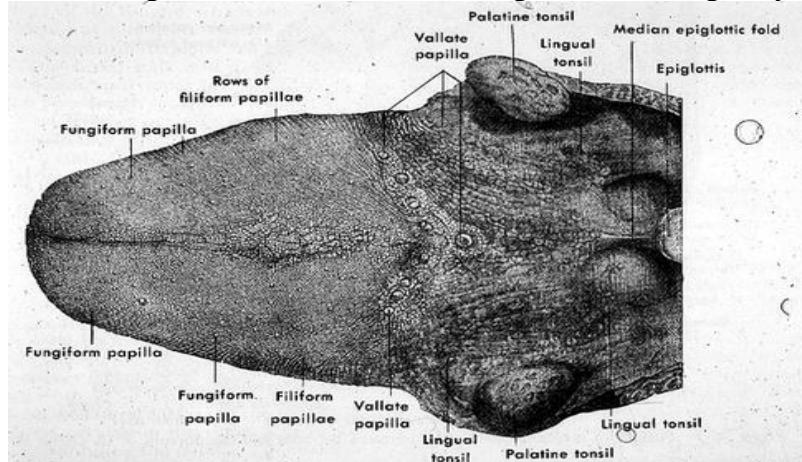
The mucosa of oral cavity's bottom is limited by gums and passes to (ventral) the hypoglossis. It is mobile, easily going to the folds and yields to a stretch. A multi-layered flat nonkeratinized epithelium covers a mucosa. An own plate is formed by loose connective tissue, which has a negligible quantity of fibers, forms rare low papillae and contains plenty of blood and lymphatic vessels. A submucosa is well expressed and presented loose connective and adipose tissues, contains small salivary glands.

TONGUE

The tongue lies on the floor of the oral cavity. It has a dorsal surface which is free; and a ventral surface that is free anteriorly, but is attached to the floor of the oral cavity posteriorly. The dorsal and ventral surfaces become continuous at the lateral margins, and at the tip (or apex) of the tongue.

Near its posterior end the dorsum of the tongue is marked by a V-shaped

groove called the sulcus terminalis. The apex of the V points backwards and is marked by a depression called the foramen caecum. The limbs of the sulcus terminalis run forwards and laterally. The sulcus terminalis divides the tongue into a larger (2/3) anterior, or oral, part; and a smaller (1/3) posterior, or pharyngeal, part.



The substance of the tongue is made up chiefly of skeletal muscle supported by connective tissue. The muscle is arranged in bundles that run in vertical, transverse and longitudinal directions. The substance of the tongue is divided into right and left halves by a connective tissue septum.

The surface of the tongue is covered by mucous membrane lined by stratified squamous epithelium. The epithelium is supported on a layer of connective tissue.

On the undersurface of the tongue the mucous membrane resembles that lining the rest of the oral cavity, and the epithelium is not keratinized.

The mucous membrane covering the dorsum of the tongue is different over the anterior and posterior parts. Over the part laying in front of the sulcus terminalis the mucosa bears numerous projections or papillae. Each papilla consists of a lining of epithelium and a core of connective tissue. The epithelium over the papillae is partly keratinized.

The papillae are of various types as follows.

Circumvallate Papillae

Adjacent and anterior to the sulcus terminalis are 8 to 12 circumvallate ("walled") papillae, which are large papillae, each surrounded by a deep circular groove into which open the ducts of minor salivary glands, known as the glands of von Ebner. These papillae have a connective tissue core which is covered on the superior surface with a keratinized epithelium. The epithelium covering the lateral walls is nonkeratinized and contains taste buds.

Foliate Papillae

Foliate ("leaf-like") papillae are sometimes present on the lateral margins of the posterior part of the tongue, although they are more frequently seen in mammals other than humans. These papillae consist of 4 to 11 parallel ridges that alternate with deep grooves in the mucosa, and a few taste buds are present in the epithelium of the lateral walls of the ridges.

Fungiform Papillae

The anterior portion of the tongue bears the fungiform ("fungus-like") and filiform ("hair-like") papillae. Single fungiform papillae are scattered between the

numerous filiform papillae at the tip of the tongue. They are smooth, round structures, which appear red because of the highly vascular connective tissue core visible through a thin, nonkeratinized covering epithelium. Taste buds are normally present in the epithelium on the superior surface.

Filiform papillae

Filiform papillae cover the entire anterior part of the tongue and consist of cone-shaped structures in which a core of connective tissue is covered by a keratinized epithelium. They form a tough abrasive surface that is involved in compressing and breaking food when the tongue is apposed to the hard palate. In this way, the dorsal mucosa of the tongue functions as a masticatory mucosa. The tongue is highly extensible and changes in its shape are accommodated by the regions of nonkeratinized flexible epithelium between the filiform papillae.

These elevations are produced by collections of lymphoid tissue present deep to the epithelium. These collections of lymphoid tissue collectively form the lingual tonsil.

Numerous **mucous and serous glands** are present in the connective tissue deep to the epithelium of the tongue. Mucous glands are most numerous in the pharyngeal part, in relation to the masses of lymphoid tissue. They open into recesses of mucosa that dip into the masses of lymphoid tissue. The serous glands are present mainly in relation to circumvallate papillae, and open into the furrows surrounding the papillae. Serous glands also open in the vicinity of other taste buds. It is believed that the secretions of these glands dissolve the substance to be tasted and spread it over the taste bud; and wash it away after it has been tasted.

The largest glands in the tongue are present on the ventral aspect of the apex. They contain both mucous and serous acini and are referred to as the anterior lingual glands.

Taste Buds

Taste buds are present in relation to circumvallate papillae, to fungiform papillae, and to leaf-like folds of mucosa (*folia linguae*) present on the posterolateral part of the tongue. Taste buds are also present on the soft palate the epiglottis, the palatoglossal arches, and the posterior wall of the oropharynx.

Each taste bud is a piriform structure made up of modified epithelial cells. It extends through the entire thickness of the epithelium. Each bud has a small cavity that opens to the surface through a gustatory pore. The cavity is filled by a material rich in polysaccharides.

The mucosa of the dorsal surface of the tongue is unlike that anywhere else in the oral cavity because, although covered by what is functionally a masticatory mucosa, it is also a highly extensible lining, and in addition has different types of lingual papillae. Some of these have a mechanical function, whereas others bear taste buds and therefore have a sensory function.

3.3. Literature recommended

Main Sources:

- 10.L.C. Junqueira, J. Carneiro - “Basic histology” – 11 edition - 2005.
- 11.A.S. Pacurar, J.W. Bigbee – “Digital histology” – Virginia - 2004.
- 12.“Color Atlas of basic histology” – R.Berns – 2006.

13. Sadler T.V. – “Medical embryology” Montana – 1999.
14. Ronald W., Dudek Ph.D. – “Embryology” 2 edition – 1998.
15. Ten Cate A.R. Oral Histology.- St.Louis, Baltimore, Toronto.- 1995.
16. William A., Beresford M.A. Cytology and Histology.- Anatomy department, West Virginia University, USA.- 1992.
17. K.E. Jonson - “Histology and cell biology” – 2 edition – Washington – 1991.

Additional ones:

1. Methodical Instructions.

3.4 How to work with the literature recommended:

Main tasks	Recommendations
To review the material	To use the material studied
To learn the material	To use the material on pages
To read and compose the plan	To learn the new material and be ready to write a summary
To answer the questions	To be ready to give an answer to the following:
To do the test on the material	
To be ready to answer the topic	

3.5. Self-control material:

A. Questions to be answered:

7. Describe general morphology of the digestive system.
8. General characteristic of the oral mucosa.
9. Lip. Describe the structure and functions.
10. Describe the structure and functions of cheek.
11. What is the structure of gum?
12. Describe the structure and functions of yard and soft palates.
13. Describe development and structure of tongue.

B. Test tasks to be done: Tests are applied

4. Self-preparation in the classroom.

- 1) Listen to the information.
- 2) Work with the tables and a Light microscope.
- 3) Ask about the problems that haven't been found in the information given.
- 4) To sketch in the album the investigated preparations.

5. Self-preparation work at home.

- 1) Review the material learnt in the classroom.
- 2) Compose the plan of your answer.
- 3) Answer the questions to this topic.
- 4) Do the test given above.

6. The subject of the research work.

“Development of oral cavity and organs of digestive system”

<i>Subject</i>	<i>Histology, cytology and embryology</i>
<i>Modul №2</i>	<i>Histology, cytology and embryology</i>
<i>Submodul №4</i>	<i>Special histology</i>
<i>Topic 21</i>	TOOTH STRUCTURE

Hours: 2

1. The topic basis: the topic “**TOOTH STRUCTURE**” is very important for future doctors in their professional activity, positively influences the students in their attitude to the future profession, forms professional skills and experience as well as taking as a principle the knowledge of the subject learnt.

2. The aims of the training course:

- 1) To have general knowledge of the topic studied.
- 2) To understand, to remember and to use the knowledge received.
- 3) To learn the classification, structure and functions of the different histological methods.
- 4) To form the professional experience by reviewing, training and authorizing it.
- 5) To be able to carry out laboratory and experimental work.

3. Materials for the before – class work self – preparation work:

3.1 Basic knowledge, experience, skills necessary for studying the topic in connection with other subjects:

	To know	To be able to
Med. Biology	the structure of the cells and tissues	work with a light microscope
Med. Physics	the structure of the light and electron microscopes	work with a light microscope
Organic Chemistry	the chemical content of the cell	Speak of the topic

3.2 The contents of the topic:

Histologically teeth consist of hard parts (enamel, dentine, cement) and soft part (pulp, periodont).

Enamel

Enamel (enamelum, substantia adamantia) covers the anatomical crown of the tooth at the most developed part of its apex. Thickness of layer of enamel is maximal in area of masticatory tubercles of the permanent teeth and is evened 2,3-3,5 mm. On the lateral surfaces of the permanent teeth it makes 1-1,3 mm, the thinnest layer of enamel covers the neck of tooth - 0,01 mm. Enamel is the most durable tissue of tooth and human body. It consists of mineral salts (96-97%): phosphate of calcium (90%), fluoride of calcium (4%), limeolith (4%) and other matters. The crystalline phosphate of calcium (known as hydroxiapatite) feels like dissolution acids, that can result in the carious damage of enamel. Organic part occupies 1,2%, proteins-glycoproteins which form the matrix of enamel. Water, related to the crystals and organic components and in the free state, takes 3,8 %. Enamel has the white or slightly yellow color, and protects the dentine and endodontium from the action of external factors. Enamel on hardness is equal to mild steel. Enamel has most durability on the cutting surfaces of tooth. The closeness of enamel goes down from the surface of crown to the dentinal-enamel border and forms cutting edges to the

neck. Under enamel there is a layer of more resilient dentine which makes enamel labial and allows it to resist the action of the considerable mechanical loadings. Enamel prisms stick together by an interprismatic substance which is less calcified, than prism. They appear as a result of activity of cells of enameloblasts (ameloblasts, adamantoblasts). Deep layer of enamel (near a dentinal-enamel border) and superficial - does not contain enamel prisms. Parallel the surfaces of tooth's crown on longitudinal microsections are noticeable fawn tangential lines (**lines of Retcius**). Their appearance is bound to periodicity of enamelogenesis, different zonal calcifiedness of enamel prisms and origin of lines of force during mastication. Lines of Retcius are smaller calcified areas of enamel. Appearance of plenty of such lines is explained by the varied disorders in enameloformation, related to violations of feed and exchange of substances of child. Some of these lines arise up under act of endured diseases or violations of diet in early child's age. The line of Retcius, which dissociates prenatal enamel from postnatal, is considerably selected. It arises up as a result of dyspoiesis enamel in the period of adaptation of new-born child to the new terms of feed. In the places of output of lines of Retcius there are furrows on the surface of enamel. The areas of enamel between furrows shape rollers are 2-4 mcm high, which have the name **of pericimates**. Sometimes pericimates are poorly expressed or quite absent, that most characteristically for canines. On the transversal microsections of tooth there are not identified enough calcified areas enamels which are named enamel bunch and enamel plates. **Enamel bunches** are located on the border of enamel and dentine. They got the name due to likeness with bunches of grass. **Enamel plates** pierce all of layer of enamel. Plates and bunches become the place of penetration in the tooth to infection and development of caries more frequent than all. In an enamel **there are enamel spindles**, being retortlike widenings on the ends of dentinal tubules, contain terminals processes of dentinoblast (Toms), penetrable in an enamel from a dentine. Most frequently they meet in the areas of masticatory tubercles of molar and premolar. The fibers of Toms grow in the layer of enamel-formating cells from the beginning of enamelogenesis and are gradually bricked up in it. Dentino-enamel border has the winding scalloped kind often, that is instrumental in strong connection of enamel and dentine.

Enamel is covered by a thin **cuticle** which appears at eruption and is worn away at mastication. There select 2 types of cuticle: primary (internal), presented with glycoproteins which are the last secretory products of enameloblasts and their tailings; second (external) – formed tailings of reduced epithelium of enamel organ. Above the cuticle of tooth **pellicula** is located. It is presented by the skim of glycoproteins of saliva and protects enamel from dissolution in a sour environment, and also takes part in development of pathological processes. After the mechanical cleaning of teeth pellicula recommences through a few hours. Microorganisms can populate pellicula, and in 1 day a dental plaque develops on enamel. Speed of its development depends on the features of microflora, character of feed and properties of saliva. Mineralization of dental plaque results in forming of dental calculus which continues increasing in sizes due to an accumulation on its surface of bacteria. Age-dependent changes in enamel show up diminishing of thickness of its layer due to elimination. With age there is maintenance of calcium, fluorine, phosphorus, zinc in

enamel increased, and waters – diminishes, that results in the decline of its permeability.

Dentine.

A dentine (dentinum) makes the basis of tooth in area of crown, neck and root and determines it shape. Together with predentine it forms the wall of pulp chamber. On the morphofunctional signs a dentine looks like roughly fibrous bone tissue, but differs from it by the greater hardness and absence of cells, sometimes it is defined as the specialized bone tissue. A dentine is characterized by certain elasticity and flexibility and protects more strong enamel from damages at mechanical influences on a tooth.

Cells which form a dentine are after its (borders) limits - in the peripheral layer of pulp. A dentine is a calcified tissue considerable hardness of which is explained by high maintenance in it of mineral salts - to 72%. Inorganic substances are presented by hydroxyapatites and additions of fluoride of calcium, calcspar, magnesium and sodium.

Organic substances (mainly collagen of the II type) are 18% and about 10% is water which is adsorbed on the surface minerals or is in intervals between crystals. Dentine has a yellow color and quite often is translucent through the skim of enamel, giving it the proper tint. If there are any diseases of endodontium or at it is absent a dentine darkens, that is why the clinical crown of such teeth is darker, than crown of healthy teeth. A dentine is built from a calcified intercellular substance, pierced tubes (to the tubules) which provide the tropism of dentine. Dentinal tubes go in radial direction from the internal surface of dentine to external one, diameter of which diminishes from pulp to the dentino-enamel border. Due to the presence of dentinal tubes, a dentine is characterized by high permeability that has a substantial clinical value for providing of rapid reaction of pulp on the damage of dentine. On a border with enamel and cement of tube they branch and anastomoses between itself. Dentinal tubes have sizes of approximately 2,5 mcm in a diameter near pulp, 1,2 mcm in central part of dentine and 900 nm near a dentinal-enamel border. In a crown dentine there are about 20.000 tubes on a square millimetre near enamel and 45.000 on a square millimetre near pulp. There are processes of dentinoblasts (odontoblasts) in dentinal tubules – cells which are located in a pulp and tissue liquid, in nervous fibers pass some from them. These processes are named as the **Toms'**, processes function of them consists in the nutrition of dentine and providing its mineral substances. Dentinal processes which penetrate through enamel spindles from a dentine in enamel take part in the nutrition of enamel. Dentinal tubes make a dentine permeable, providing the development of caries. Researches show that dentinal tubes contain the greater amount of microorganisms, than dentine between them. Medications and chemical substances in the varied dental materials also can spread through a dentine and result in the damage of pulp. Periodontoblastic space (between the processes of dentinoblasts and wall of dentinal tube) is filled with a dentinal liquid which on protein composition is similar on plasma and contains a fibronectin and glycoproteins. Dentine that surrounds every dentinal tube and forms it's wall is called peritubular. Space between tubes is filled by intertubular dentine, containing on 40% less mineral substances as compared to peritubular. The intercellular

substance of dentine is presented by collagen fibrils and amorphous substance (glycoproteins). There are distinguished two layers of dentine: external cloak, in which collagen fibers go radially (**fibers of Korf**) and internal nearpulp, in which fibers are located tangentially (**fibers of Ebner**) bed perpendicular to tube. Such location of fibers of stipulated considerable durability of its tissue. Parallel to the fibers of Ebner **the growth lines of Owen** appear in a dentine, which are responsible for the periods of rest in activity of dentinoblasts. A dark line, separating a dentine (formed before and after birth of child), is visible in the dentine of some teeth (milk and first permanent native). Normally collagen fibers are not mineralized. The complexes of crystals of hydroxyapatite in the amorphous substance of dentine form spherical mineralized structures – globules which did not unite in homogeneous mass in the period of formation of dentine, they are especially widespread in human teeth at the deficit of vitamin D. Between them are the areas of uncalcified dentine - **interglobular dentine** are disposed. The large areas of interglobular dentine form wrong rhombuses or semiarcs that can be seen in the crown of the tooth. Small accumulations of interglobular dentine are in a root on a border with cement, where they lie densely to each other as grains of black and form the grainy layer of Toms. Dentinal tubules pass through a interglobular dentine, not changing direction. Between a dentine and dentinoblasts there is a strip of uncalcified dentine - predentin. Predentin consists of collagen fibers and amorphous substance. It is the area of permanent growth of dentine, that is performed during all the life of human, has a thickness about 10-47 μm . Predentin is characterized by the well expressed sensitiveness. That means, that the origin of pain in teeth a certain role is played by the changes of hydrodynamic terms in dentinal tubules, information about which is passed through the dentinoblasts processes on the nervous elements of pulp. A dentine which appears in the period of odontogenesis is named **primary**. Dentinoblasts produce it at a speed of 4-8 μm a day. Periodicity of activation and deceleration of its process shows up a presence in the dentine of growing lines. Formation of dentine is not halted after eruption. Such dentine is named **the second** (regular) and differs from primary by the less organized placing of dentin tubules, numerous accumulations of interglobular dentine and less degree of mineralization. The second dentine appears in the already formed tooth after its eruption considerably slower primary; speed of its laying goes down with age. As a result of laying of the second dentine the form of pulp chamber changes and the volume of it diminishes. **The tertiary** (reparative, irregular, and substitutable) appears as an responsibility for the action of irritating factors. The products of it considerably increase at local inflammatory reactions, which arise up as a result of caries, enhanceable elimination of enamel, preparing of cavity of tooth et cetera .Thus laying of tertiary (substitutable) dentine takes place in the area of pulp which is responsible for the damaged area of tooth. Dentinoblasts formed locally react on irritation. A tertiary dentine is characterized by weak mineralization and wrong motion or absence of dental tubes. Laying of such dentine begins in 30 days after preparation of tooth. In a pulp there are structures from the second dentine - “**denticles**”. They appear at metabolic disturbances, at local inflammatory processes. Close-walls and free denticles are distinguished depending on localization. The first lie near the wall of

pulp chamber, second - freely in pulp. A tertiary dentine which appears at caries hinders penetration of infection lie in pulp. In the teeth of elderly people, and also at a slowly developing sapodontia, mineral salts are put aside not only in the intercellular substance of dentine but also round processes in dentinal tubules.

Cement.

Cement (cementum) is a calcified tissue of tooth, which covers a dentine in area of tooth's anatomical root. The thickness of cement is maximal at the apex of root, and minimum - in the area of neck of tooth, where cement partly covers the enamel. There are about 30% organic substances (mainly collagen) and 70% inorganic - mainly salts of phosphate and calc spar in cement. On a structure cement looks like bone tissue. However, it does not feel like permanent alteration and does not contain blood vessels. In cement the fibers of periodontium are fastened, therefore it is a component part of supporting apparatus of tooth. There are cellularless and cellular cement. **Cellularless** (primary) cement appears firstly, from the beginning of odontogenesis. It does not contain cells, consists of calcified intercellular substance: collagen fibers, located in various directions and basic substance. Cellularless cement is on the lateral surfaces of roots and in (upper part of tooth). The thickness of it is increased in direction from a cement-enamel border to the apex of tooth. Lines which are responsible for the periodicity of its laying lie parallel to the surface of root in primary cement. **Cellular** (secondary) cement is localized in lower third of root on its apex and in the places of forks of roots (branching) of multirooted teeth. Cellular cement appears after an odontogenesis it is disposed on the surface of cellularless cement, and if the last absents, adjoin directly to the dentine. Cellular cement consists of cells (cementocytes and cementoblasts) and calcified intercellular substance. **Cementocytes** are in the cavities of cement (lacunas) and on a structure alike as osteocytes (cells of bone tissue). They have a polygonal shape, large nucleus and developed organelles. The numerous processes of cementocytes are disposed in tubules, and are united with tight contacts. While laying the new layers of cement, cementocytes are removed from the source of nutrition (vessels of periodontium) and perish. **Cementoblasts** are active cells with the well developed synthetic apparatus. Disposed on the surface of cement, they provide the rhythmic laying of its new layers. At forming of cellular less cement of cementoblasts they are moved aside from the cement (formed by them) and are bricked up in it. In the intercellular substance of cellular cement there are distinguished such structures as fibers, synthesized the cells of cement ("own"), going parallel surfaces of root, and also fibers of periodontal copula ("external"), oriented perpendicular to the surface of tooth's root. As a result of the permanent laying of cement in area of root's apex there is its lengthening. Shortening of crown of the tooth is made due to its compensation at its elimination. The nutrition of cement is carried out diffusely from the blood vessels of periodontium. An important role in it belongs to the system of tubule which walks away from bone lacunes. Circulation of liquid in hard parts of tooth is carried out due to pressure of blood in the vessels of pulp and periodontium. From some data, there are anastomoses between the processes of cementocytes and dentinal tubule. Due to it there is the additional system of dentine in the case of

violations bloodsupply of pulp (at inflammation, pulp extraction, closing of the ducts of root et cetera).

Pulp

The secondary cement takes part in adaptation of tooth supporting apparatus to the changing loadings, and also in reparative processes (at paradontoses, disorders of tooth root and at resorbtion of its surface). The permanent compensatory lying of cement is provided by the maintainance of general length of tooth. The surplus lying of cement is named **hypercementosis**; it can be diffuse, generalized and local. At chronic infectious diseases there is the diffuse laying of cement on all of surface of root of tooth that can result in accretion of root with the wall of bone alveolar. At surplus formation of cement there is generalized hypercementosis in all of teeth. Local hypercementosis shows up forming of different form of structures from cement in the lateral or interroot spaces of tooth, sometimes reason of their origin are cementicles. They are development with a diameter of 0,1-0,5 mm which are formed by cementoblasts. Cementicles can be increased in sizes and come close to each other. Pulp (pulpa) fills the tooth cavity in area of crown and root canals. It is presented by loose connective tissue, rich on cells and intercellular substance. Pulp contains plenty of vessels and nerves. Due to a presence of dentinoblasts in it, pulp takes part in formation of dentine and its trophics, performs protective, sensory and reparative functions. There are three layers in pulp: peripheral, intermediate and central. Immature collagen fibers and dentinoblasts lie in the **peripheral** layer of pulp. Cells have prolate or pear-like shape, for which plenty synthetic organelles of (Goldgy complex, granular endoplasmic reticulum) and long process on the apical surface. Such substances are secreted through the last structure: collagen of the II type, glycoproteins, phosphoproteins, proteoglycans and phosphoranes, which are needed for formation of predentin. Long processes of dentinoblasts, which are disposed in dentinal tubules, deliver mineral salts to dentine and enamel. Histochemical researches had shown a presence of alkaline phosphatase, calcium, phosphorus and potassium in these cells. In addition, in the dentinoblasts' processes acetylcholinesterase was found which plays an important role in the conducting of nervous impulse. In crown pulp dentinoblasts have a pear-shape or prismatic shape, in a root – fusiform. The more functionally and more active dentinoblasts have a greater height. The **intermediate** layer of pulp contains immature collagen fibers and cells-predecessors of dentinoblasts. In its composition there are distinguished 2 areas: external and internal. An external area is named cell-free (layer of Veyl), contains blood vessels, net of nervous fibers, collagen and reticular fibers. An internal (cellular) area contains numerous cells: Predentinoblasts, fibroblasts, little differentiated cells, and also of the circulatory system capillaries and nervous fibers. A **central** layer is presented by loose connective tissue with plenty of cells (adventitial, macrophages, fibroblasts), fibers (argyrophilic and collagen). Elastic fibers are absent in pulp. Blood and lymphatic vessels, bunches of nervous fibers are disposed in a central layer. In root pulp, unlike crown one bunch of collagen fibers prevail above cellular elements. On the structure it is similar to the dense connective tissue of periodontium which it contacts with in area of root's apex. Through apical of foramen duct arteries and nerves get to pulp. An important role

belongs to pulp in providing of tooth trophic, at its delete development, growth and regeneration of tooth, is violated. A plastic function (formation of dentine), protective (participating is in immune and inflammatory reactions), is inherent pulp, reparative and sensory. A pulpless tooth is shortlived.

Age-dependent changes in an pulp show up diminishing of the amount of cells, decrease of synthetic activity of dentinoblasts. The amount of collagen fibers is considerably increased, there is worsening of blood supply of pulp, there are regressive changes of tooth's nervous apparatus.

The volume of pulp chamber diminishes due to the permanent laying of the second dentine. With age frequency of calcified structures (denticles) is increased, majority of them appears in root pulp. **Periodontium**.

Periodontium (periodontum) is dense fibred connective tissue. With the help of periodontium the tooth is fixed in a alveolar bone, and also amortizes pressure, arising up at mastication. The thick bunches of collagen fibers in the different areas of periodontal space have different direction. In its upper departments they are strained almost horizontally, lateral - obliquely, near the apex of root bunches of fibers decussate. They fixed one end to cement, and other – to the alveolar bone. In the wall of alveolus the collagen bunches of periodontium are intertwined in the sharp fibers of bone tissue. Part of fibers, passing above the comb of alveolus, connects between itself nearby teeth. In intervals between bunches of dense connective tissue there are layers of loose connective tissue with blood and lymphatic vessels. The basic source of blood supply of periodontium is upper- and lower-alveolar arteries. Arteriolae which provide periodontal blood go out from medullar spaces of interroot and interdental parts of alveolar processes.

From periapical part the branches of dental artery pass toward gums. Capillaries of dental and supraperiostal arteries form interlacing round the root of tooth. Periodontium participates in eruption, providing of nutrition of cement, regulates the mechanisms of structural-functional changes of teeth and supporting apparatus, performs a protective function.

Due to vast innervation, periodont performs a sensory function. Nervous completions are presented nanoreceptors (by pain) and mechanoreceptors. Adaptation of periodontal (copula) to the action of the masticatory loadings is provided its permanent alteration. In periodont constantly there is substituting for fibroblasts and proceeding in a collagen. Violation of its synthesis causes the change of the state of periodontium. The necessary condition of normal collagenogenesis is a presence of vitamin C, speed of proceeding goes down with age. Penetration of infection - a chronic inflammatory process – periodontitis, which results in destruction of not only periodontium but also all of supporting apparatus of tooth, develops in periodont (cement, wall of dental alveolus, gum).

Alveolar processes. Parts of upper and lower jaws, which walk away from their bodies, named alveolar processes. Separate small holes of alveolar processes are dental teethridges, contain teeth. Every alveolus has an external wall (cheek or labial) and internal (mouth). Depth of alveolus is a few less than the length of tooth's root. In an alveolar tere are an alveolar bone (wall of dental alveolus) and supporting alveolar bone

(Fig.36) an alveolar bone is presented by a bone plate which surrounds the root of tooth and is the place of attachment of fibers of periodontium (formed plate bone tissue).

3.3. Literature recommended

Main Sources:

6. L.C. Junqueira, J. Carneiro - “Basic histology” – 11 edition - 2005.
7. A.S. Pacurar, J.W. Bigbee – “Digital histology” – Virginia - 2004.
8. Sadler T.V. – “Medical embryology” Montana – 1999.
9. Inderbir Singh Textbook of Human Histology.- Jaypee. India. - 1997.
10. Ten Cate A.R. Oral Histology.- St.Louis, Baltimore, Toronto.- 1995.

Additional ones:

1. Methodical Instructions.

3.4 How to work with the literature recommended:

Main tasks	Recommendations
To review the material	To use the material studied
To learn the material	To use the material on pages
To read and compose the plan	To learn the new material and be ready to write a summary
To answer the questions	To be ready to give an answer to the following:
To do the test on the material	
To be ready to answer the topic	

3.5. Self-control material:

A. Questions to be answered:

1. General plan of the tooth constitution.
2. Enamel. Its microscopic characteristic.
3. Dentinum. Its microscopic and ultramicroscopic characteristic, physicochemical properties.
4. Morfo-functional characteristic of cementum and its physicochemical properties.
5. Pulp. Structure of peripheral and central pulp.
6. Tooth supporting structures. Periodontium.

B. Test tasks to be done: Tests are applied

4. Self-preparation in the classroom.

- 1) Listen to the information.
- 2) Work with the tables and a Light microscope.
- 3) Ask about the problems that haven't been found in the information given.
- 4) To sketch in the album the investigated preparations.

5. Self-preparation work at home.

- 1) Review the material learnt in the classroom.
- 2) Compose the plan of your answer.
- 3) Answer the questions to this topic.
- 4) Do the test given above.

<i>Subject</i>	<i>Histology, cytology and embryology</i>
<i>Modul №2</i>	<i>Histology, cytology and embryology</i>
<i>Submodul №4</i>	<i>Special histology</i>
<i>Topic 22</i>	TOOTH DEVELOPMENT

Hours: 2

1. The topic basis: the topic “**TOOTH DEVELOPMENT**” is very important for future doctors in their professional activity, positively influences the students in their attitude to the future profession, forms professional skills and experience as well as taking as a principle the knowledge of the subject learnt.

2. The aims of the training course:

- 1) To have general knowledge of the topic studied.
- 2) To understand, to remember and to use the knowledge received.
- 3) To learn the classification, structure and functions of the different histological methods.
- 4) To form the professional experience by reviewing, training and authorizing it.
- 5) To be able to carry out laboratory and experimental work.

3. Materials for the before – class work self – preparation work:

3.1 Basic knowledge, experience, skills necessary for studying the topic in connection with other subjects:

	To know	To be able to
Med. Biology	the structure of the cells and tissues	work with a light microscope
Med. Physics	the structure of the light and electron microscopes	work with a light microscope
Organic Chemistry	the chemical content of the cell	Speak of the topic

3.2 The contents of the topic:

A face and jaws of a child are smaller than in the adult, and that is why can contain many small teeth which make a temporal or primary dental row. When growth of human takes place there is a considerable increase in size of jaws, there is a necessity to have teeth larger in sizes and their greater amount. As teeth can not rise with age, they become in 6-7 years inadequate to the sizes of jaws and are replaced by the permanent or second tooth. Development in the man of two generations of teeth is related to adaptation of sizes and amount of teeth to the sizes of jaws. Teeth are derivative mucous membrane of oral cavity of embryo. A multi-layered flat epithelium takes part in formation of enamel organs which give beginning of enamel. A mesenchyma takes part in formation of dentine, pulp, and cement and circumferential tooth hard and soft tissues (parodontium). Consequently, only enamel has an ectodermal origin, and other dental tissues – mesenchymal. They select three stages of development of tooth: 1) foundation and formation of dental rudiments; 2) embryonization of dental rudiments; 3) histogenesis of tissues of tooth. The first two stages relate to early, the third - to later periods.

The first stage of development (foundation and formation of dental rudiments) begins with the separation of oral cavity and formation of vestibular. At the end of the second month of embryogenesis a cheek-lip plate which grows in a mesenchyma

moves away from the epithelium of oral cavity. A crack appears in its plate that testifies to the isolation of cavity of mouth from vestibule. From the bottom of vestibule in area of one-root teeth grows the second epithelial thrusting out of a billow which a dental plate is formed from. An independent dental plate develops in the area of foundation of multirooted teeth. From the edge of dental plates grow the retort-shaped thrusting - tooth, or enamel dispersers (buds). Their amount is equal to the number of future baby teeth - for 10 on every jaw. In every disperser of enamel on the 10th week of embryonic development a mesenchyma begins to grow in (dental papilla). A disperser becomes look like a two-steps bowl - tooth, or enamel organ. To the end of 3th month of embryogenesis an enamel organ moves away from a dental plate, uniting with it only by thin epithelial belt – neck of enamel organ. From circumferential the enamel organ of mesenchyma a dental sac appears as a result of its compression. An enamel organ, dental papilla and dental sac, is formed by dental rudiments. The rudiments of baby teeth are exposed to the further changes. Between the cells of central part of enamel organ a liquid begins to accumulate, as a result they are moved aside one from other, but the united cytoplasm bridges remain. Epithelial cells start to look like reticular cells. Pulp of enamel organ, which later will take part in cutification of the enamel is formed. At the same time the internal cells of enamel organ become high prismatic. Later they will form enamel, therefore they were named by enameloblasts (adamantoblasts). The cells of outward enamel epithelium, opposite, diminish in sizes.

The second stage of development is an embryonization of dental germs. An internal enamel epithelium unites with outer in the area of edge of enamel organ, cells which after forming of crown of the tooth will give beginning an epithelial root (Hertvig's) vagina which stipulates formation of root of tooth. The process of differentiation of dental papilla begins with its increase in sizes, excrescence in it of blood vessels. From the cells of mesenchyma on-the-surface dental papilla the prolate appear or pear-shaped cells with expressed basophilia of cytoplasm, located in a few rows. In future they will product a dentine; therefore they were named by dentinoblasts. From enameloblasts they are separated by a basal membrane.

The third stage of development (histogenesis of tissues of tooth) begins at the end of 4th month of embryonic development. A basale membrane under enameloblasts acts a part factor of embryonization. In the located under it the dentinoblasts organoids of synthesis (Golgy complex, granular cytoplasmic reticulum) takes place the considerable development. Cells begin to product the albumens of fibred structures. Formation of fibers is carried out outside dentinoblasts. Young precollagenous fibers are disposed radially; the radial fibers of Korf are so formed. Between them there are sprouts of dentinoblasts. Precollagenous fibers enter in the complement of basic substance of young uncalcified dentine - predentin. When the layer of predentin with the fibers of Korf reaches the certain thickness, driven back on periphery of the layer of predentin which appears again, but in it fibers go tangentially (parallel surfaces of dental papilla) are the tangential fibers of Ebner. Consequently, a cloak dentine (with the fibers of Korf), located under enameloblasts, appears above all things, and afterwards is a nearpulp dentine (with the fibers of Ebner). The sprouts of

dentinoblasts are formed at the same time, which get to the basic substance of predentin and wall up in it. Mineralization of dentine takes a place in the end of 5th month of embryonic development. The apical sprouts of dentinoblasts are not the subject of mineralization, as a result the system of radial dentin tubules appears in a dentine. Predentin and interglobular dentine also is not added mineralization. Also a dental papilla is given by beginning to the endodontium. The process of differentiation of pulp goes parallel to development of dentine. Fibroblasts form its basic substance, precollagenous and collagen fibers gradually. In peripheral part of pulp, in area of placing of dentinoblasts and predentine, enzymes (phosphohydrolase) due to which phosphatic ions are delivered in a dentine appear, and in future - in an enamel. Lying of the first layers of dentine induce the embryonization of internal cells of enamel organ - enameloblasts. The organoids of synthesis develop in their cytoplasm (Golgi complex, granular cytoplasmic reticulum, free ribosomes). With beginning of enamel formation in enameloblasts there is an inversion of nucleolus on the opposite pole of cage. Organoids are disposed above a nucleolus aside, turned to the dentine. A long sprout in which granules accumulate electronodense content appears on its pole of enameloblasts. They are selected in intercellular space and take part in formation of organic basis of enamel. The first rudiments of enamel appear as cuticle plates on that surface of enameloblasts, which is turned to the dentine in area of crown of the tooth. Their mineralization goes at once, due to the secretion by enameloblasts of the albumens of enamelogenines, cooperate rapid mineralization of enamel. The nutrition of enameloblasts after the change of poles of cage is carried out from the side of intermediate layer of enamel organ, but not from the side of dentine. Enamelblast diminish in sizes and are removed from a dentine. Outward enamel cells at an odontiasis meet with the epithelium of gums and collapse. Enamel appears to be covered a cuticle, forming from pulp of enamel organ. In the mesenchyma of dental sac two layers are differentiated: outer - dense and internal – loose. From the mesenchyma of internal layer in area of root cementoblasts, which synthesize collagen albumens are differentiated, that are selected in an intercellular substance. Cementoblasts transform in sprout cementocysts. Bodies and sprouts last located in the cavities of cement. From the mesenchyma of periblast of dental sac develops periodont tooth. Development of root, unlike development of crown, is carried out later and at times coincides from an eruption of tooth. The foundation of the second teeth begins at the end 4th, at the beginning of 5th month of intrauterine development. The rudiment of the second teeth appears from a dental plate, behind from the rudiment of baby tooth. So the enamel organs of permanent incisors, canines and small cheek-teeth appear. Small cheek-teeth replace molar of milk bite. Development of them takes place in the sequence, that milk teeth does. Rudiment of the first large cheek-tooth is founded in the middle of first-year of life of child, and rudiment of "wisdom tooth" - on 4-5th. The late foundation of large cheek-teeth is explained that at first the jaw has small sizes, therefore in a milk bite places are absent for their foundation. The foundation of large cheek-teeth takes place in postnatal life of child as far as the increase of jaws.

Terms of eruption and change of teeth. Eruption of **baby** teeth for children begins on 6-7 month of postnatal period. At this time a crown is formed only, and development of roots begins only. Tissues of gums atrophy in that area, where they are exposed to pressure from the side of apex of crown of the cutting through tooth. The apex of crown, which is in contact with the epithelium of gums, accretes with it. After it an epithelium breaks through, and a tooth appears in the cavity of mouth. The epithelium of gums in area of neck of tooth accretes with the cuticle of enamel, forming epithelial attachment. Eruption of baby and permanent teeth takes a place under constraint, which arises up in an endodontium as a result of formation of basic substance of connective tissue. Mineral substances (calcium, phosphorus, fluorine and other) and nutritives act in tissue of the ankylosed tooth only from blood, and after eruption the role of saliva increases in these processes. Eruption of the **second** teeth of a man begins in age 6-8 years, is closed to 20-25. Replacement of baby by permanent teeth takes a place thus: at first the rudiment of the second teeth lies in a general alveolus with milk. Later a bone partition appears between them. As far as development of the second teeth its pressure is increased on the root of baby tooth. With the help of osteoclasts resorption of partition and root of baby tooth takes place. Baby tooth are removed easily, and the permanent begin to develop quickly. Eruption is a physiological process which serves as the indirect index of correct or incorrect development of child. As a physiological act, eruption is not the sickly phenomenon, cannot cause some diseases therefore. It is placed in direct connection with the general state of health of child. Timely, in a certain sequence, a dentition testifies to normal development of organism. A delay of terms of eruption can be the investigation of rachitis, infectious disease, protracted parafunction intestine and changes in the exchange of substances. The early eruption can be the investigation of endocrine violations. The gap in mistiming of eruption of central incisors on 1-2 month from the set term can't be examined as pathology.

3.3. Literature recommended

Main Sources:

1. L.C. Junqueira, J. Carneiro - “Basic histology” – 11 edition - 2005.
2. A.S. Pacurar, J.W. Bigbee – “Digital histology” – Virginia - 2004.
3. Sadler T.V. – “Medical embryology” Montana – 1999.
4. Inderbir Singh Textbook of Human Histology.- Jaypee. India. - 1997.
5. Ten Cate A.R. Oral Histology.- St.Louis, Baltimore, Toronto.- 1995.

Additional ones:

1. Methodical Instructions.

3.4 How to work with the literature recommended:

Main tasks	Recommendations
To review the material	To use the material studied
To learn the material	To use the material on pages
To read and compose the plan	To learn the new material and be ready to write a summary
To answer the questions	To be ready to give an answer to the following:
To do the test on the material	
To be ready to answer the topic	

3.5. Self-control material:

A. *Questions to be answered:*

1. General characteristic of the tooth formation stages.
2. Derivation of dental germs. An epithelial tooth organ and germs of a mesenchymal parentage, their perspective value.
3. Differentiation of dental germs. Parts of the enamel organ and their perspective value to the tooth development.
4. Histogenesis of tissues of tooth.

B. *Test tasks to be done: Tests are applied*

4. Self-preparation in the classroom.

- 1) Listen to the information.
- 2) Work with the tables and a Light microscope.
- 3) Ask about the problems that haven't been found in the information given.
- 4) To sketch in the album the investigated preparations.

5. Self-preparation work at home.

- 1) Review the material learnt in the classroom.
- 2) Compose the plan of your answer.
- 3) Answer the questions to this topic.
- 4) Do the test given above.

<i>Subject</i>	<i>Histology, cytology and embryology</i>
<i>Modul №2</i>	<i>Histology, cytology and embryology</i>
<i>Submodul №4</i>	<i>Special histology</i>
<i>Topic 23</i>	ESOPHAGUS. STOMACH

Hours: 2

1. The topic basis: the topic “**ESOPHAGUS. STOMACH**” is very important for future doctors in their professional activity, positively influences the students in their attitude to the future profession, forms professional skills and experience as well as taking as a principle the knowledge of the subject learnt.

2. The aims of the training course:

- 1) To have general knowledge of the topic studied.
- 2) To understand, to remember and to use the knowledge received.
- 3) To learn the classification, structure and functions of the different histological methods.
- 4) To form the professional experience by reviewing, training and authorizing it.
- 5) To be able to carry out laboratory and experimental work.

3. Materials for the before – class work self – preparation work:

3.1 Basic knowledge, experience, skills necessary for studying the topic in connection with other subjects:

	To know	To be able to
Med. Biology	the structure of the cells and tissues	work with a light microscope
Med. Physics	the structure of the light and electron microscopes	work with a light microscope
Organic Chemistry	the chemical content of the cell	Speak of the topic

3.2 The contents of the topic:

GASTROINTESTINAL TRACT

General plan

1. Mucosa (innermost)

- *Epithelium, lamina propria* and smooth muscle *muscularis mucosae*.
- The epithelium in most places takes a *glandular* form, with simple tubular glands and a secreting surface epithelium.
- Some parts have discrete compound glands lying in the mucosa.
- Single lymphoid nodules can occur anywhere.

2. GI submucosa

- Of fairly dense CT, with blood and lymphatic vessels, and having a plexus of unmyelinated autonomic nerve fibres - *Meissner's submucosal plexus*.
- Glands are present in a few places.

3. GI muscularis externa

- Two or more helical layers of *smooth muscle*: the inner, tight 'circular'; the outer, loosely coiled 'longitudinal'.
- Served by a nerve fibre plexus - *Auerbach's myenteric plexus*, whose parasympathetic ganglion cells lie between the muscle layers.
- Circular coat is more developed at sphincters and valves.

4. GI serosa or adventitia/fibrosa (outermost)

- Of loose CT, with collagen and elastic fibres, nerves and vessels.

- The serosa has a smooth mesothelial covering, and that part of the tract is suspended on a mesothelium-covered tissue fold - omentum or mesentery.
- Mesothelial cells bear microvilli, are well attached, and secrete lubricants to allow viscera to move freely.

(If mesothelium is lost during inflammation or operations and replaced by the fibrous scar tissue of an *adhesion*, function is lost, e.g., uterine tubal adhesions can cause infertility.)

To avoid knots and obstruction, the plan for the GI tract is fasten, loosen, loosen and so forth, so that only the small intestine and transverse colon have long stretches of mobile tube: fastening requires an adventitia, mobility, a serosa.

Esophagus

1. *Mucosa* has stratified squamous epithelium ending sharply at the gastric junction, creating a white-pink distinction between proximal and distal sides of the Z-line in endoscopy. Here, abnormalities of the oesophageal epithelium and the position of the epithelial junction are quite common (Barrett's oesophagus).
2. *Muscularis mucosae* - longitudinal smooth muscle.
3. *Cardiac glands* - make neutral mucus and are branched tubular, in the mucosa near the gastric cardia and of the upper oesophagus; inconsistently present.
4. *Oesophageal glands* - acidic mucous, compound, tubulo-alveolar, and lying in the submucosa, less numerous in the middle segment of the oesophagus.
5. Circular and longitudinal *muscle coats* of skeletal muscle in the upper fifth or less give way progressively to only *smooth* muscle in the lower half.
6. Outermost coat is CT *adventitia*, except on a small piece below the diaphragm.
7. *Function* - rapid passage of food to (and from) the stomach.

Stomach

General structure

- *Anatomical regions* - cardia, fundus, corpus, pyloric antrum and pyloric canal: the regions are histologically distinct.
- Outer covering is a *serosa*, from which hang omenta.
- *Muscular coat* of three smooth muscle layers - outer, longitudinal; middle, circular; inner, oblique. The middle layer is more developed to form a sphincter at the pylorus. The muscle churns the contents (chyme), and passes them periodically in regulated amounts to the duodenum.
- *Submucosa* - no glands; CT carries vessels and the nerve plexus.
- *Muscularis mucosae* - two layers, with the inner circular one sending a few muscle fibres up towards the lumen.
- *Mucosa* is deep and glandular, with only a little lamina propria tissue; produces acid and enzymes for digestion, and undertakes some absorption, e.g., of water and alcohol.

Stomach mucosa

- Empty stomach's lining is folded in ridges - *rugae*.
- Surface is pitted by recesses - *gastric pits/foveolae gastricae*.
- Long tubular *glands* extend from the muscularis mucosae up to empty into the pits. A gland has a base, neck and isthmus.
- Surface of the stomach and the pits are lined by simple, columnar, special mucous epithelial cells.

- *Gastric glands* throughout the body and fundus of the stomach are simple, branched tubules with these cells:
 - *Chief/zymogenic/peptic* serous cells: in the majority; basophil with 'zymogen' granules and rich granular ER.
 - *Parietal/oxytic* cells: occur peripherally and singly; large and eosinophil; packed with mitochondria and smooth ER; have long secretory canaliculi, lined by microvilli, and opening to the gland's lumen.
 - *Mucous neck* cells: concentrated near the neck of the gland.
 - *Endocrine/enteroendocrine/argentaffin/enterochromaffin/* Kultschitsky cells: few in number, seen with EM, silver methods, or cytochemistry, but may be recognized from their empty look with H & E, and their rarity.
- In the narrow cardiac region lie cardiac glands - compound tubular, with mucous and parietal cells.
- In the *pylorus*, pits are deeper, and glandular tubules are wider and more branching. The main kind of cell present is pale and resembles fundic mucous neck cells.

Gastric secretions

- Surface mucous cells - *mucus*, believed to prevent auto-digestion of the mucosa, and *bicarbonate* ions.
- Chief/zymogenic cells - *enzymes*, e.g., pepsin, rennin, gastric lipase.
- Oxytic/parietal cells - $\text{Cl}^-/\text{HCO}_3^-$ is exchanged basolaterally to balance the apical Na^+/H^+ proton pump used to form the *hydrochloric acid* of the digestive juice.
(The stimulated active parietal cell has greatly extended canaliculi.)
- Mucous neck cells - *mucus* and *enzymes*, e.g., dipeptidases.
- Endocrine cells - *hormones* and amines; e.g., a hormone - *gastrin* - produced by the pyloric antral G cells controls the release and formation of acid from parietal cells, and of digestive enzymes from chief cells.
- Parietal cells - *intrinsic factor* - to assist in the absorption of vitamin B_{12} : this role is upset when the parietal cells' proton pump is an autoimmune target in pernicious anaemia, leading to the cells' destruction.

2. *Gastric protective mechanisms*

- *Digestive secretions* (survived by typhoid and other bacilli, and eggs of parasites).
- *Mucous* and *bicarbonate* outer coating of the epithelium.
- A film of surfactant-like *lipid* secreted by the epithelium.
- *Regenerative* power of the epithelium, by cell proliferation and migration (normally renewed every few days).
- *Lymphoid* nodules and lymphocytes, and other leucocytes, in the mucosa and submucosa.
- *Vomiting*.

3.3. Literature recommended

Main Sources:

8. L.C. Junqueira, J. Carneiro - "Basic histology" – 11 edition - 2005.
9. A.S. Pacurar, J.W. Bigbee – "Digital histology" – Virginia - 2004.
10. "Color Atlas of basic histology" – R.Berns – 2006.
11. Sadler T.V. – "Medical embryology" Montana – 1999.

Additional ones:

1. Methodical Instructions.

3.4 How to work with the literature recommended:

Main tasks	Recommendations
To review the material	To use the material studied
To learn the material	To use the material on pages
To read and compose the plan	To learn the new material and be ready to write a summary
To answer the questions	To be ready to give an answer to the following:
To do the test on the material	
To be ready to answer the topic	

3.5. Self-control material:

A. Questions to be answered:

1. Esophagus. Morphofunctional characteristic.
2. Features of the structural organization of esophagus departments.
3. Stomach. Morphofunctional characteristic.
4. Histophysiology of the stomach glands, their cellular content, functions.

4. Self-preparation in the classroom.

1) Listen to the information. 2) Work with the tables and a Light microscope. 3) Ask about the problems that haven't been found in the information given. 4) To sketch in the album the investigated preparations.

5. Self-preparation work at home.

1) Review the material learnt in the classroom. 2) Compose the plan of your answer. 3) Answer the questions to this topic. 4) Do the test given above.

6. The subject of the research work.

“Development of esophagus”

<i>Subject</i>	<i>Histology, cytology and embryology</i>
<i>Modul №2</i>	<i>Histology, cytology and embryology</i>
<i>Submodul №4</i>	<i>Special histology</i>
<i>Topic 24</i>	SMALL AND LARGE INTESTINE

Hours: 2

1. The topic basis: the topic “**SMALL AND LARGE INTESTINE**” is very important for future doctors in their professional activity, positively influences the students in their attitude to the future profession, forms professional skills and experience as well as taking as a principle the knowledge of the subject learnt.

2. The aims of the training course:

- 1) To have general knowledge of the topic studied.
- 2) To understand, to remember and to use the knowledge received.
- 3) To learn the classification, structure and functions of the different histological methods.
- 4) To form the professional experience by reviewing, training and authorizing it.
- 5) To be able to carry out laboratory and experimental work.

3. Materials for the before – class work self – preparation work:

3.1 Basic knowledge, experience, skills necessary for studying the topic in connection with other subjects:

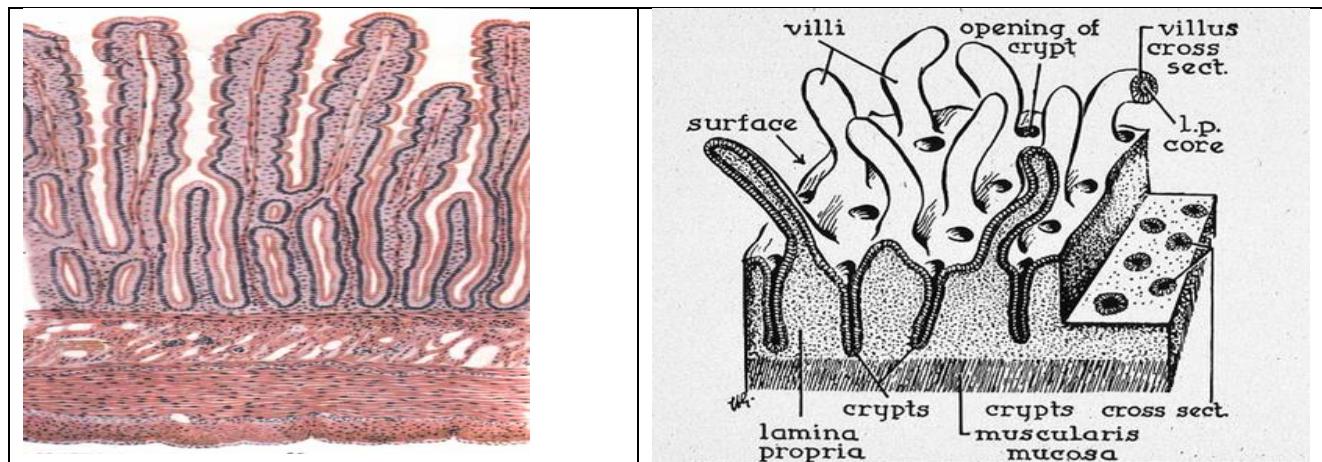
	To know	To be able to
Med. Biology	the structure of the cells and	work with a light

	tissues	microscope
Med. Physics	the structure of the light and electron microscopes	work with a light microscope
Organic Chemistry	the chemical content of the cell	Speak of the topic

3.2 The contents of the topic:

SMALL INTESTINE

- Three regions - *duodenum*, *jejunum* and *ileum*, anatomically and histologically distinguishable.
- *Serous coat* over all except part of the duodenum and the terminal ileum, which are fixed to the abdominal wall.
- Suspended on a *mesentery* carrying blood and lymphatic vessels, lymph nodes and nerves.
- *Muscularis externa* has two complete layers.
- *Submucosa* - occupied by *Brunner's mucous*, compound tubular glands in the duodenum; elsewhere is CT as for the rest of the tract.
- *Muscularis mucosae* - inner, circular, and outer, longitudinal smooth muscle.
- Mucosa has:

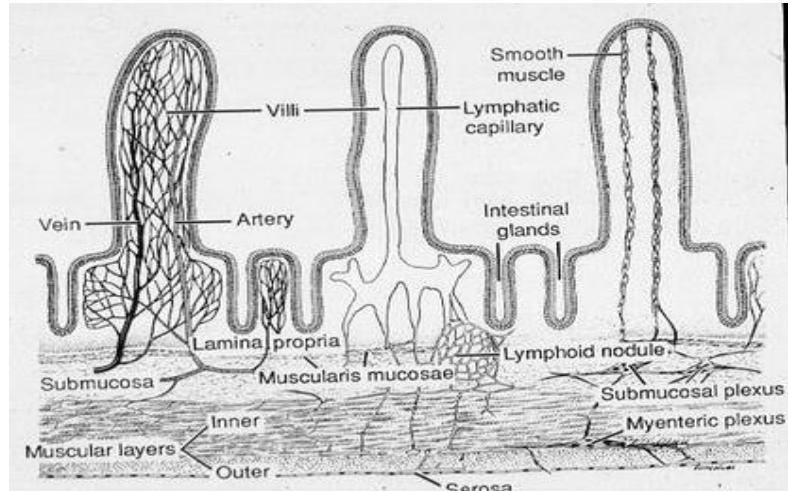


- Villi - finger- or leaf-like projections.
- Crypts of Lieberkühn - simple tubular glands.
- Lamina propria forming the core of each villus and lying between the gland tubules.
- Covering of simple columnar epithelium.

Cytology of small-intestinal mucosa

- *Enterocytes* are columnar absorptive epithelial cells on the villi; with a brush border (many microvilli); are held apically by junctional complexes; the many vesicles at the base of the microvilli communicate with agranular ER.
- *Goblet cells*, with the nucleus, GER and Golgi apparatus basally, stored mucigen droplets apically.
- *Paneth cells*, with eosinophil granules holding defensin and enzymes; remain at the base of the crypts.
- *Enteroendocrine cells* (other names 3.2.e.iv. above), with hormone- and serotonin-containing basal granules.
- *Undifferentiated columnar crypt stem cells*: few microvilli; able to divide, migrate, differentiate into the other kinds, function, and be extruded at the villus tip, over approximately four days.

- *Villus core* has the basal lamina for the epithelium, a central lymphatic capillary (lacteal), blood vessels, smooth muscle fibres. The loose stroma of reticular and elastic fibres is heavily infiltrated by WBCs, e.g., CD4+ helper-inducer lymphocytes and eosinophils, and plasma cells.
- Ileum has *Peyer's patches* of extensive lymphoid tissue, erasing villi, breaking into the epithelium, and interrupting the muscularis mucosae to invade the submucosa. Elsewhere, only solitary lymphoid nodules are to be seen. The epithelium domed over the Peyer's-patch follicles is specialized, with M cells, which transport antigen and otherwise assist immune functions.



Functions of small-intestinal mucosa

- *Secretory*
 - Goblet cells give *mucus*.
 - Columnar cells make their *glycocalyx*, and disaccharidase and other *digestive enzymes* for use by or in the microvilli.
 - Paneth cells form *defensins*, etc, for defence.
 - Endocrine cells produce *hormones* to coordinate the functions of the gut, liver and pancreas.
 - Simple tubular intestinal glands/glands of Lieberkühn also contribute to the enteric juice.

These secretions are additional to those already present from:

- Salivary and oesophageal glands.
- Stomach mucosa.
- Pancreas and liver, introduced into the duodenum.
- Brunner's duodenal glands (alkaline mucus led into the bottom of crypts).
- *Gut mucosal absorption of materials* degraded by the secretions.
- *Membrane transports*, active and passive, of many kinds, with appropriate pumps, channels, and transporters. The tricky part is to get lipid in across a barrier based on lipids - the cell membrane, and back out again.
- *Pathway*, through the absorptive cell, from the lumen to the lacteal capillary lumen for *lipid: hydrolysis*, by mostly pancreatic lipase, of the dietary triacylglycerols;
- interaction of the resulting free fatty acids and monoacylglycerol with bile, to form micelles for *solvabilization*;
- in this form, the lipids can be *transported* through the enterocyte's apical membrane;

- in the apical smooth ER, the lipids are *re-acylated*, and bound to a protein for intracellular transport.
- Meanwhile, the GER is producing proteins to which some lipid is added - apolipoproteins - which meet up with the apically reacylated lipid at the Golgi complex, where the apolipoprotein is used as a kind of cage, into the core/interior of which increasing amounts of lipid are introduced, as the lipid droplet - the *chylomicron* - is assembled,
- before its *basolateral secretion* by exocytosis from the Golgi complex into the basolateral intercellular space.
- The chylomicrons and similar smaller lipid bodies pass through the basal lamina to enter the *lacteal lymph capillary*, giving the gut and mesenteric lymphatic vessels their white colour, and constituting chyle.
- Devices for increasing the *effective gut surface area* for absorption:
- the long length of the gut;
- villi;
- microvilli on absorbing cells;
- plicae circulares/valves of Kerckring (high folds of mucosa and submucosa)
- contractions of villus muscle, muscularis mucosae, and two main muscle coats; (microvilli can slowly elongate, but not contract and relax.)

Changes within small intestine during descent:

- Goblet cells increase in number.
- Villi become more finger-like.
- Lymphoid tissue increases.
- Plicae circulares diminish.

Protective mechanisms of the gut:

- alkaline mucus of Brunner's glands;
- lubricating and protective goblet-cell mucus;
- immune responses by APCs, lymphocytes and plasma cells;
- rapid reactions of eosinophils, macrophages, and neutrophils
- lysozyme and other antimicrobial contributions of Paneth cells;
- barrier of tight junctions between the enterocytes;
- diarrhoea;
- rapid regeneration by the epithelium.

LARGE INTESTINE

General features

- Crypts, but no villi or plicae circulares.
- Columnar epithelial cells are: *undifferentiated*; *goblet* (numerous); *colonocytes*, absorbing, with microvilli, for water, and some products of bacterial metabolism of the faeces; (some excretion occurs). *Endocrine cells* are also present.
- Dehydrating faeces need lubrication, hence many goblet cells are present in the simple columnar epithelium.

Regional details of large intestine

- *Colon* and *caecum*: outer longitudinal muscle coat is gathered into three bands - *taeniae coli* - which pucker or sacculate the tube, forming haustrations.

- *Appendix*: continuous muscle coats; few crypts; the mucosa is mainly occupied by lymphoid tissue; the muscularis mucosae may be deficient and lymphoid tissue seen in the submucosa. The wall may be thick. With age the lumen may be blocked off/occluded by fibrosis.

- *Rectum*: outer longitudinal muscle is one continuous sheet.

- *Anal canal*

- Morgagni's anal columns are 6-10 vertical mucosal folds.

- *Dentate line* lies at the level of the bases of the columns, where there are tiny flaps and pockets - anal valves and sinuses.

- The histological epithelial *anal transitional zone* (ATZ) lies between unbroken simple columnar colo-rectal epithelium and lower stratified squamous epithelium.

- ATZ varies in extent and outline, in its epithelia, and the number of crypts.

- *Submucosal veins* display periodic dilations. Deterioration of their supporting connective tissue permits enlargement and prolapse - haemorrhoids.

- The complex *anal musculature* includes external skeletal-muscle and internal smooth-muscle sphincters. (The muscles and their innervation are particularly at risk of stretching and damage in women giving birth.)

3.3. Literature recommended

Main Sources:

10.L.C. Junqueira, J. Carneiro - "Basic histology" – 11 edition - 2005.

11.A.S. Pacurar, J.W. Bigbee – "Digital histology" – Virginia - 2004.

12."Color Atlas of basic histology" – R.Berns – 2006.

13.Sadler T.V. – "Medical embryology" Montana – 1999.

14.Ronald W., Dudek Ph.D. – "Embryology" 2 edition – 1998.

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17.William A., Beresford M.A. Cytology and Histology.- Anatomy department, West Virginia University, USA.- 1992.

18.K.E. Jonson - "Histology and cell biology" – 2 edition – Washington – 1991.

Additional ones:

1. Methodical Instructions.

3.4 How to work with the literature recommended:

Main tasks	Recommendations
To review the material	To use the material studied
To learn the material	To use the material on pages
To read and compose the plan	To learn the new material and be ready to write a summary
To answer the questions	To be ready to give an answer to the following:
To do the test on the material	
To be ready to answer the topic	

3.5. Self-control material:

A. Questions to be answered:

1. Small intestine. Morphofunctional characteristic.

2. Large intestine. Cellular structure and structure of the mucousa.

B. Test tasks to be done: Tests are applied

4. Self-preparation in the classroom.

- 1) Listen to the information.
- 2) Work with the tables and a Light microscope.
- 3) Ask about the problems that haven't been found in the information given.
- 4) To sketch in the album the investigated preparations.

5. Self-preparation work at home.

- 1) Review the material learnt in the classroom.
- 2) Compose the plan of your answer.
- 3) Answer the questions to this topic.
- 4) Do the test given above.

6. The subject of the research work.

<i>Subject</i>	<i>Histology, cytology and embryology</i>
<i>Modul №2</i>	<i>Histology, cytology and embryology</i>
<i>Submodul №4</i>	<i>Special histology</i>
<i>Topic 25</i>	SALIVARY GLANDS

Hours: 2

1. The topic basis: the topic “**SALIVARY GLANDS**” is very important for future doctors in their professional activity, positively influences the students in their attitude to the future profession, forms professional skills and experience as well as taking as a principle the knowledge of the subject learnt.

2. The aims of the training course:

- 1) To have general knowledge of the topic studied.
- 2) To understand, to remember and to use the knowledge received.
- 3) To learn the classification, structure and functions of the different histological methods.
- 4) To form the professional experience by reviewing, training and authorizing it.
- 5) To be able to carry out laboratory and experimental work.

3. Materials for the before – class work self – preparation work:

3.1 Basic knowledge, experience, skills necessary for studying the topic in connection with other subjects:

	To know	To be able to
Med. Biology	the structure of the cells and tissues	work with a light microscope
Med. Physics	the structure of the light and electron microscopes	work with a light microscope
Organic Chemistry	the chemical content of the cell	Speak of the topic

3.2 The contents of the topic:

In humans there are three pairs of major salivary glands: the parotid, the submandibular, and sublingual; they are located outside the oral cavity, are encapsulated, and have extended duct systems to discharge their secretions. There are also a multitude of smaller minor salivary glands, which are grouped for descriptive purposes, for example the labial, lingual, palatal, buccal, glossopalatine, and retromolar glands. These

are located just below and within the mucous membranes, are unencapsulated, and have short duct systems.

FUNCTIONS OF SALIVA

Mixed saliva has many functions, the most obvious being protection of the oral cavity.

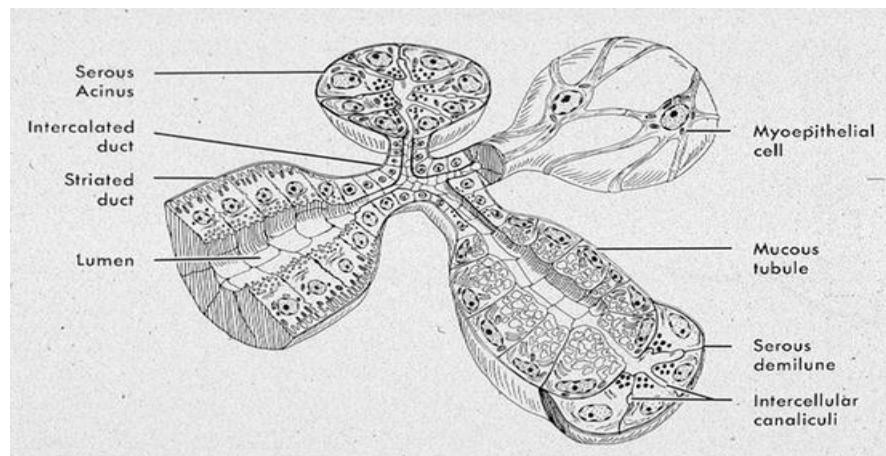
1. Protection
2. Buffering
3. Digestion
4. Taste
5. Antimicrobial
6. Maintenance of tooth integrity
7. Tissue repair

If the carious dissolution of enamel can be halted before cavitation of enamel occurs, remineralization of the lesion is possible. Remineralization is achieved largely through the ready availability of the phosphate and calcium ions in saliva. If the fluoride ion is also available as remineralization occurs, the repaired lesion is less susceptible to future decay.

STRUCTURE OF SALIVARY GLANDS

The parenchyma of the gland consists of a series of ducts ending in terminal secretory end-pieces much like a bunch of grapes, with the grapes representing the secretory end pieces and the stalks representing the duct system. Thus, following the pattern set by development, the main secretory duct of the salivary gland breaks up into a series of progressively smaller ducts, the striated ducts which in turn branch into smaller intercalated ducts that open into the blind terminal secretory end pieces. It is also easy to understand how every epithelial cell is always supported by some connective tissue, even though in some instances the connective tissue may be tenuous.

Terminal end pieces demonstrate great diversity in size, shape, and cell numbers when seen in section. The shape of end pieces varies from simple circular. They consist of a collection of cells, polygonal in section, supported by a basement membrane that encloses a central space, the lumen. The intercellular spaces between the cells open into the lumen, and technically these spaces constitute the start of the ductal system. In serous glands, such as the parotid, the cells in an end piece tend to be arranged in a roughly spherical form. In mucinous glands they tend to be arranged in a tubular configuration with a larger central lumen.



Three cell types may be found in a terminal secretory end piece: mucous cells; serous cells, and myoepithelial cells. The number and distribution of each type of cell vary from gland to gland and from secretory end piece to secretory end piece.

The basement membrane is continuous around the terminal end piece and the ducts. It forms complex tubular scaffolding within which the epithelial cells are arranged, and it probably influences the maintenance of normal glandular architecture.

The terminal secretory end piece is also known as an acinus, but the use of this term is confusing. Past practice has been to refer to the spherical serous end piece as an acinus and to the mucus-secreting component end piece as tubular secretory. However, when a tubular end piece is sectioned obliquely or transversely, the appearance of an acinus is created. If the term acinus is to be used to describe the morphology of the gland, it should be qualified as spherical acinus or tubular acinus.

The secretory cells in a salivary gland are described as either serous or mucous secreting, with both types exhibiting different and clear-cut histologic differences.

Serous cells

The so-called serous cell in human salivary glands also secretes demonstrable amounts of polysaccharide, and therefore these cells are more properly known as seromucous cells. With the light microscope the seromucous cell is readily identifiable as a pyramid shaped cell with its apex situated toward the central lumen. The nucleus is spherical and is situated in the basal third of the cell. The cytoplasm stains intensely with hematoxylin and eosin, giving the cell its characteristic dark color. In some hematoxylin-eosin stained sections, especially after good fixation, the apical cytoplasm of the seromucous cell can be seen to be filled with a number of eosinophilic secretory granules about 1 nm in diameter.

With the increased resolution of the electron microscope, the seromucous cell is found to have all the features of a cell specialized for the synthesis, storage, and secretion of protein. It has large amounts of rough endoplasmic reticulum arranged in parallel stacks packed basally and laterally to the nucleus. It also has a prominent Golgi complex situated either apically or laterally to the nucleus. The apical cytoplasm is filled with secretory granules, each surrounded by a unit membrane. All these cytoplasmic organelles are functionally related as the proteins, are synthesized at ribosomal sites on the rough endoplasmic reticulum, and pass into its cisternae. After complex interaction, either directly or indirectly with the Golgi complex (where carbohydrate moieties are added), the proteinaceous secretory material is concentrated in condensing vacuoles and then stored in secretory granules.

The secretory granules are discharged when required by a process known as exocytosis. This discharge occurs when granules move toward the apical portion of the cell, where the limiting membrane of the granule fuses with the plasma membrane of the seromucous cell lining the central cavity. As a result, the contents of the granule are released into the central lumen of the acinus. In common with most other cells, seromucous cells also contain other cytoplasmic organelles, such as mitochondria, found toward the lateral and basal portions of the cell, lysosomes, free ribosomes, a few microbodies or peroxisomes, microfilaments, and microtubules. It should be appreciated that this secretory process is continuous but cyclical, so that in any end piece seromucous cells at differing stages in the secretory cycle may be found. In a seromucous end piece the cells are supported by a basement membrane that separates the parenchyma from the connective tissue. The relationship between the basement membrane and the seromucous cell that it supports is complicated and shows

considerable variation. A straight relationship may exist with both the basement membrane and the basal plasma membrane running parallel and in close apposition. On the other hand, the space between the basement membrane and the basal plasma membrane may be increased extensively by complex foldings of the basal plasma membrane of the seromucous cell, especially when the cells are not fully distended with secretory material. In the submandibular gland the seromucous cells possess a more complicated basal specialization than in the parotid. The plasma membrane is thrown into a series of tall, narrow basal folds. The folds extend beyond the lateral border of the cell as foot processes that penetrate deeply into recesses of the folds of adjoining cells. The cell has been described as having the appearance of a multipointed star when viewed from above. This specialization increases the basal region of the cell by a factor of 60.

Laterally adjoining seromucous cells also have complex interrelationships. A well-defined intercellular space, or canaliculus, continues from the lumen of the end piece, between the seromucous cells. The canaliculus terminates in the form of a classical junctional complex consisting of, in order, a tight junction (zonula occludens), an intermediate junction (zonula adherens), and a desmosome (macula adherens). At various points in this canalicular complex apposing cells may contact and join in the form of desmosomal contacts and gap junctions. The surface of the seromucous cell, lining both the central lumen and the canaliculi possesses delicate microvilli, which extend into the luminal and canalicular space.

By virtue of the abundant amounts of rough endoplasmic reticulum, Golgi complexes, and secretory granules, proteins including salivary amylase are synthesized. The complex foldings of the cell surfaces are a reflection of the function of transporting fluid and electrolytes from the serum to saliva. Thus the seromucous cell is structurally adapted to fulfill its varied functions.

Mucous cell

Its secretory product differs from that of the seromucous cell in that it has a smaller enzymatic component and its proteins are linked to greater amounts of carbohydrate material-forming inucins. These differences are reflected in the structure of the cell. With the light microscope, the mucous cell appears as a pyramidal cell with a flattened nucleus situated toward its base. The apical portion of the cell does not stain strongly because of its higher carbohydrate content. On the other hand, if a mucous cell is stained specially for carbohydrates, the apical cytoplasm stains intensely.

Ultrastructurally, the mucous cell differs from the seromucous cell in that it contains more prominent Golgi complexes which reflect the cells in creased carbohydrate metabolism, and its secretory material is stored in droplets. In resting cells, the rough endoplasmic reticulum and other cytoplasmic organelles, such as mitochondria, are less conspicuous than in seromucous cells and are mainly confined to the base and lateral aspects of the cell. The number of interdigitations between adjacent mucous cells tends to be fewer than between seromucous cells. Intercellular canaliculi are found leading to demilunes and also occur between mucous cells. In the submandibular and sublingual glands, the mucous cells have a fairly complex system of basal folds, whereas in the labial glands the mucous cells exhibit complex lateral interdigitations.

The identification of a cell as seromucous or mucous by microscopy can be problematical because mucous cells at different stages of the functional cycle have different appearances. Thus the mucous cell at the beginning of its synthetic cycle may stain well with hematoxylin and closely resemble a seromucous cell. Recent studies taking this similarity into account have shown that the labial glands, previously regarded as mixed glands, are in fact mucous glands. It could be that some of the mixed secretory end pieces in the submandibular and sublingual glands also are entirely mucous cells, but this has not been established.

Myoepithelial cell

Myoepithelial cells are found in relation to the terminal secretory end piece and to the intercalated ducts occupying the space between the basement membrane and the basal plasma membrane of the secretory epithelial cells. There is usually one myoepithelial cell per secretory end piece, but two or three such cells per unit are not uncommon. They are not visible in ordinary hematoxylin and eosin stained light microscope sections.

The morphology of a myoepithelial cell depends on its location. Those associated with the secretory end pieces have been likened to an octopus sitting on a rock. Each cell consists of a central body where the nucleus is situated. From this central body radiate four to eight processes that follow the long axis of the secretory unit and from which other processes branch. The net effect is that the secretory end piece is encompassed by processes of the myoepithelial cell running between the basement membrane and plasma membrane of the secretory cells in depressions on the surface. Desmosomal attachments are present between the myoepithelial cells and the underlying secretory cells. Their processes contain many microfilaments (myofilaments) frequently aggregated to form dark bodies along the course of the process. The normal cytoplasmic organelles found in any cell are mainly located in the perinuclear region of the myoepithelial cell. The cytoplasm has been described as being sequestered into filamentous and nonfilamentous portions.

The myoepithelial cells related to the intercalated ducts are more spindle-shaped and have fewer processes. On occasion some myoepithelial cells are found with the cell body situated in the intercalated duct region and with processes extending backward onto parts of the secretory end piece.

The ultrastructural features of the myoepithelial cell are very similar to those of smooth muscle cell. The microfilaments, the desmosomal attachments, and the "dark bodies" are all found in myoepithelial cells, as well as in smooth muscle cells. Because of this similarity to smooth muscle, the myoepithelial cells are thought to have several possible functions, all related to ability to contract. One function may be to act as a support for the secretory cells, preventing an overdistention as secretory products accumulate within the cytoplasm. Another function may be to contract and widen the diameter of the intercalated ducts, thus lowering or raising their resistance to outflow. Finally, their contraction may aid in the rupture of the acinar cells packed with mucous secretion. The origin of the myoepithelial cell has not yet been determined. These cells are generally considered to be of epithelial origin, because they are always located between the parenchyma cell and its basement membrane.

Terminal end pieces produce acinar fluid, which is sometimes referred to as primary secretion. This fluid consists of water, ions, small molecules, and the secretory products of the secretory end piece cells. The fluid comes from interstitial fluid which in turn arises from blood in capillaries, in a manner similar to the formation of interstitial fluid elsewhere. This interstitial fluid must then pass through the basement membranes supporting the terminal secretory end piece and then through either the secretory cell or the intercellular spaces. The result is that the initial secretion is a protein-containing isotonic fluid characterized by a high sodium and low potassium electrolyte content. This fluid is then considerably modified by the ductal system as it passes toward the oral cavity.

DUCTAL SYSTEM

The ductal system of the salivary glands comprises a varied network of ducts characterized by progressively smaller membranes. This network contains three classes of ducts: intercalated ducts, striated ducts, and terminal ducts. The system is not a simple conduit, for it actively participates in the production and modulation of saliva.

Intercalated ducts

The secretion of the terminal end pieces passes first through the intercalated ducts. These ducts are of small diameter and are lined by short cuboid cells with a centrally placed nucleus and little cytoplasm containing some rough endoplasmic reticulum situated basally and some Golgi complexes situated apically. Secretory granules are occasionally found in these cells, especially in the cells closest to the secretory end piece.

These cuboid cells have a few microvilli projecting into the lumen of the duct, and their lateral borders interdigitate with each other and are connected by means of junctional complexes situated apically and by scattered desmosomal attachments below the junctional complexes. Myoepithelial cells, or their processes, are usually present between the basement membrane and the ductal cells. A high degree of structural pleomorphism has been described in the intercalated ducts of human labial and soft palatal glands with respect to arrangement, location, length, diameter, and epithelial thickness within individual lobules. The simplest form of duct is lined with simple cuboidal epithelium. In human soft palatal salivary glands, the intercalated ducts are more often relegated to the connective tissue septa, are long and highly convoluted, and consist of mucus-secreting cells, simple cuboidal epithelial cells, and myoepithelial cells. The functional activity of the intercalated duct cells is not properly understood. Intercalated ducts are especially prominent in salivary glands having a watery secretion and therefore occur frequently in the parotid gland. They may be difficult to distinguish if they are embedded in a mass of secretory units.

Striated ducts

The intercalated duct passes into the striated duct. The striated duct is lined by columnar cells, which have centrally placed nuclei and eosinophilic cytoplasm, characteristics that make the duct clearly recognizable in hematoxylin- and eosin-stained secretions. The most characteristic feature of such cells, however, is the prominent striations found at the basal ends of the cells, hence the name of the duct.

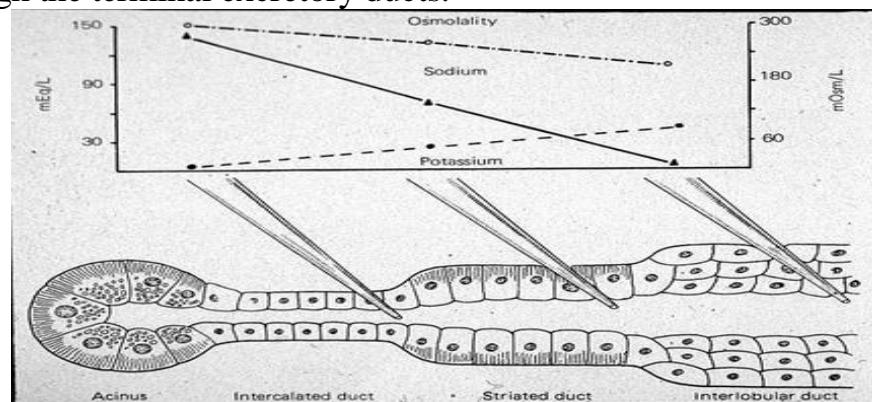
These striations are resolved by the electron microscope as particularly deep indentations of the basal plasma membrane into the cell. The basal folds also extend beyond the lateral boundaries of the cell as a series of foot processes, which in turn

possess complex secondary extensions. These lateral processes interlock in a highly complex fashion with adjacent cells, and at the same time they provide a very large increase in the surface area of the basal plasma membrane. Many large mitochondria, arranged along the long axis of the folds, occur in the cytoplasm between the folds. Around the nucleus a few profiles of rough endoplasmic reticulum are found, along with some Golgi complexes. The apical cytoplasm often contains a few scattered vesicles, smooth endoplasmic reticulum, free ribosomes, and lysosomes. The luminal surface of the striated cell is characterized by short stubby microvilli, and adjacent cells are again united by junctional complexes and desmosomal attachments. Occasional dark cells containing numerous mitochondria and scattered small basal cells are usually also present. Striated ducts are always surrounded by a number of longitudinally oriented small blood vessels.

The specialized structure of the striated ducts implies a particular function for them. Briefly stated, the cells are thought to modify the secretions passing through the striated duct. It will be recalled that this fluid is characterized by isotonic protein content, a high sodium content, and a low potassium content. As it passes along the striated duct, its composition changes into a hypotonic fluid with low sodium and chloride concentrations. The massive folding of the basal plasma membrane, associated with the elongated mitochondria, is thought to reflect the sodium-pumping capacity of the cell wall in this location. Thus sodium is depleted from the cell into the tissue fluid, establishing a concentration gradient between the cell and the luminal fluid. Sodium therefore diffuses into the cells from the luminal fluid; at the same time active transport of potassium occurs in the opposite direction. Bicarbonate ions are also actively secreted. Because the striated duct cells do not absorb water under normal conditions of flow, these ionic changes result in the formation of a hypotonic solution.

Terminal excretory ducts

After passing through the striated ducts, the salivary fluid is then secreted into the oral cavity through the terminal excretory ducts.



The histology of the terminal secretory ducts varies as they pass from the striated ducts to the oral cavity. Near the striated ducts it is lined by a pseudostratified epithelium consisting of tall, columnar cells much like the striated cells admixed with a number of small basal cells; goblet cells also occur.

As the duct approaches the oral cavity, the epithelium gradually changes to a true stratified epithelium that merges with the stratified epithelium of the oral cavity at the duct orifice. The main excretory ducts modify the final saliva by altering the electrolyte concentration and perhaps also by adding a mucoid component. Special eosinophilic

cells, loaded with mitochondria, tend to be found in the ducts, particularly in human mucosal glands. These cells are known as oncocytes, and they probably represent an age change.

CONNECTIVE TISSUE

The connective tissue component of the salivary gland is the same as connective tissue elsewhere and consists of such cells as fibroblasts, macrophages, mast cells, adipose cells, and plasma cells. These are embedded in an extracellular matrix of collagen fibres and a ground substance consisting of a mixture of glycoproteins and proteoglycans. Oxytalan fibres are found in the submandibular and minor salivary glands. They are located in the connective tissue supporting mucous end pieces and around the smaller intralobular ducts. They are thought to substitute for the elastic fibres found surrounding the larger extralobular ducts. The connective tissue stroma of the salivary gland serves to carry its nerve and blood supply which are both highly specialized.

MINOR SALIVARY GLANDS

The minor salivary lingual, buccal, and palatal glands are small mucosal glands with short ducts that produce a primarily mucoprotein-rich secretion. The exceptions are the serous glands of von Ebner. The mucins from these glands come into close contact with the tooth and mucosal surfaces, and as a result, they are important contributors to the protective mechanism of saliva. Since the minor salivary gland secretions are especially rich in mucosubstances, they are assumed to play an important role in the formation of acquired pellicle.

An interesting feature of the minor salivary glands is the occurrence of focal accumulations of lymphocytes around their duct walls, which are thought to have a role in the immune surveillance of the mouth.

SUMMARY OF MAJOR SALIVARY GLANDS

Parotid gland

In the parotid gland, the terminal secretory end pieces are seromucous. Pyramidal cells, which have a spherical, basally situated nucleus may be recognized surrounding a small central lumen. The basal cytoplasm stains blue (basophilic), and in well-fixed sections secretory granules can be seen. In older glands, fat cells can be readily seen.

Intercalated ducts in the parotid gland are numerous and elongated and in cross and oblique sections are found interposed between the seromucous acin. They have a narrow lumen surrounded by cuboidal cells with a round central nucleus and a sparse basophilic cytoplasm.

The striated ducts are easy to recognize and have been described as "pink necklaces" permeating the gland. The cells are columnar and stain intensely pink (acidophilic) with eosin. The nucleus is centrally located, and the striations can be recognized at higher magnifications adjacent to the basement membrane, not the lumen.

Submandibular gland

Approximately 80% of the secretory end pieces in the submandibular gland are seromucous and have the same features as those described in the parotid gland. The remaining secretory units are usually a mixture of mucous and seromucous cells. The mucous secretory cells can be identified by a larger lumen than that of the seromucous unit. It is surrounded by pyramidal cells whose nuclei are flattened and situated basally

and by cytoplasm that does not stain very strongly. The mixed units are easy to recognize because of the crescent-shaped caps, or demilunes, of seromucous cells at the terminal end of the mucus-secreting tubules. Intercalated ducts are shorter in the submandibular gland, and therefore fewer can be found in section. The striated ducts are well developed and are longer in the submandibular gland, have the characteristics already described, and are easy to recognize.

Sublingual gland

The most variable of the major salivary glands is the small, almond-shaped Sublingual gland. In hematoxylin and eosin-stained preparations the Sublingual glands appear to have a mixed complement of cells, with individual acini varying in the types of cells they contain. Some end pieces contain large mucous-filled cells, and other end pieces are composed of cells with few secretory granules. All gradations between these two types can be found. Seromucous end pieces are rarely found, but seromucous demilunes capping the mucous tubules exist. Morphologically, then, the Sublingual gland is described as a mixed gland. Intercalated ducts are either extremely short or absent and are difficult to find. Striated ducts also are short and difficult to find and may even be absent. In spite of these morphologic distinctions, histochemical studies indicate that the gland is purely a mucus-secreting gland.

3.3. Literature recommended

Main Sources:

1. L.C. Junqueira, J. Carneiro - "Basic histology" – 11 edition - 2005.
2. A.S. Pacurar, J.W. Bigbee – "Digital histology" – Virginia - 2004.
3. "Color Atlas of basic histology" – R.Berns – 2006.
4. Sadler T.V. – "Medical embryology" Montana – 1999.
5. Ten Cate A.R. Oral Histology.- St.Louis, Baltimore, Toronto.- 1995.

Additional ones:

1. Methodical Instructions.

3.4 How to work with the literature recommended:

Main tasks	Recommendations
To review the material	To use the material studied
To learn the material	To use the material on pages
To read and compose the plan	To learn the new material and be ready to write a summary
To answer the questions	To be ready to give an answer to the following:
To do the test on the material	
To be ready to answer the topic	

3.5. Self-control material:

A. Questions to be answered:

1. Major salivary glands. Features of the structure.
2. Micromorphology of secretory departments and duct's system of major salivary glands.
3. Minor salivary glands

B. Test tasks to be done: Tests are applied

4. Self-preparation in the classroom.

- 1) Listen to the information.
- 2) Work with the tables and a Light microscope.

- 3) Ask about the problems that haven't been found in the information given.
- 4) To sketch in the album the investigated preparations.

5. Self-preparation work at home.

- 1) Review the material learnt in the classroom.
- 2) Compose the plan of your answer.
- 3) Answer the questions to this topic.
- 4) Do the test given above.

6. The subject of the research work.

“Morphofunctional description of minor salivary glands”

<i>Subject</i>	<i>Histology, cytology and embryology</i>
<i>Modul №2</i>	<i>Histology, cytology and embryology</i>
<i>Submodul №4</i>	<i>Special histology</i>
<i>Topic 26</i>	LIVER

Hours: 2

1. The topic basis: the topic “LIVER” is very important for future doctors in their professional activity, positively influences the students in their attitude to the future profession, forms professional skills and experience as well as taking as a principle the knowledge of the subject learnt.

2. The aims of the training course:

- 1) To have general knowledge of the topic studied.
- 2) To understand, to remember and to use the knowledge received.
- 3) To learn the classification, structure and functions of the different histological methods.
- 4) To form the professional experience by reviewing, training and authorizing it.
- 5) To be able to carry out laboratory and experimental work.

3. Materials for the before – class work self – preparation work:

3.1 Basic knowledge, experience, skills necessary for studying the topic in connection with other subjects:

	To know	To be able to
Med. Biology	the structure of the cells and tissues	work with a light microscope
Med. Physics	the structure of the light and electron microscopes	work with a light microscope
Organic Chemistry	the chemical content of the cell	Speak of the topic

3.2 The contents of the topic:

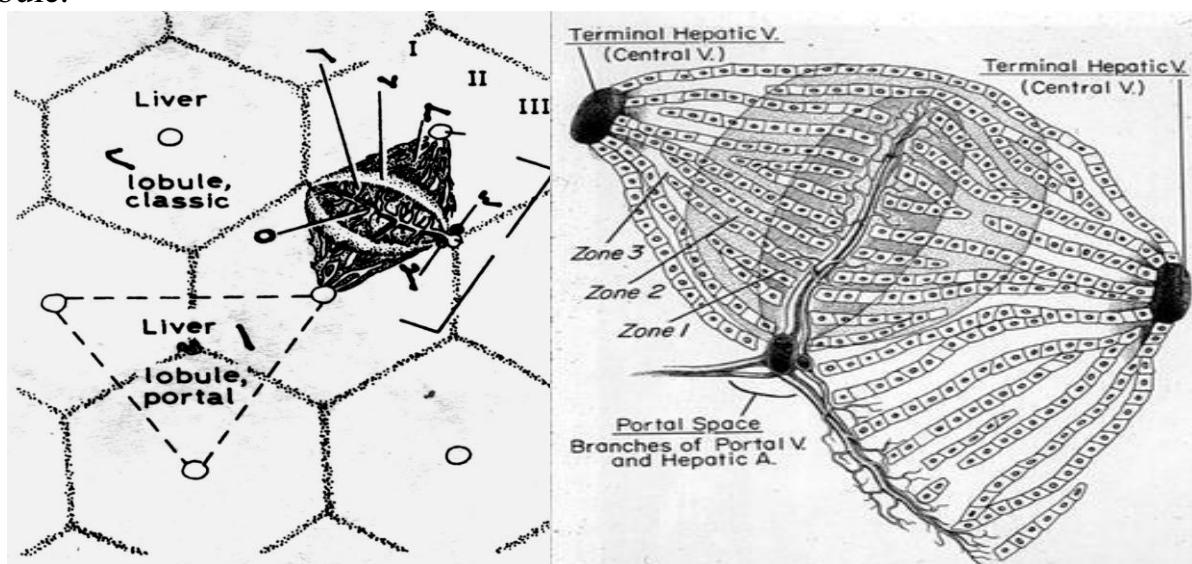
Liver's general features

1. Large, lobated exocrine and blood-processing gland, with vessels and ducts entering and leaving at the porta.
2. Enclosed by a thin CT capsule, mostly covered by mesentery.

3. CT of the branching vascular system provides gross support.
4. Parenchymal cells are supported by fine *reticular fibres*.
5. The internal structure is understandable in terms of the several vessels entering or leaving the organ;
 - o *Portal vein* bringing food-rich blood from the gut.
 - o *Hepatic artery* bringing arterial blood.
 - o *Hepatic veins* taking away processed blood into the vena cava.
 - o *Lymphatics* taking away some lymph.
 - o *Hepatic ducts* removing bile to the gallbladder and gut.

Liver lobule

1. First impression is of a uniform mass of large glandular cells throughout the liver substance.
2. Closer examination shows that the cells are arranged in perforated *plates*, one cell wide. Between the plates are *sinusoidal* blood channels 9-12 µm wide, lined by endothelial cells.
3. Scattered in the glandular mass are *blood vessels*, alone and accompanied by other vessels.
4. The distribution of these vessels defines or marks out the classic hepatic *lobules*.
5. *Varieties of liver vessel*
 - o *Central vein/terminal hepatic venule* - very thin wall; lies in the centre of a lobule, with sinusoids converging towards and opening into it.
 - o *Sublobular/intercalated vein* - thicker wall; lies alone at the periphery of the lobule.



- o *Branch of portal vein* - again at the periphery of the lobule, but accompanied by one or more small *hepatic arteries/arterioles*, one or more *bile ducts/ductules* lined by cuboidal epithelium, and lymphatics. Vein, artery, and bile duct constitute a *portal triad*; the area in which they lie is a *portal area/canal*. (The lymphatics are ignored for this naming).

6. In pig and camel, the lobules are separated from one another by CT and thus much more easily identified.
7. *Hepatic lobular blood flow* is:

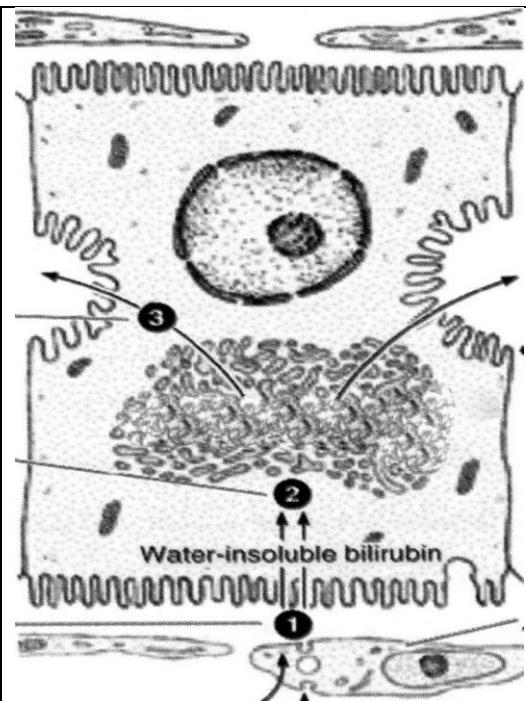
- from branches of the portal vein and hepatic artery; from the periphery towards the centre;
 - in the *sinusoids*, between the cell plates.
 - Blood collected in central veins goes to sublobular veins, thence to collecting veins, and then hepatic veins leaving the liver.
8. *Bile flow* is from the lobule's centre towards the peripheral bile ducts, and runs, within any one cell plate, between the liver cells in *bile canaliculi*.
9. Rappaport's *liver acinus* was a functional unit comprising parts of three or so lobules. It sought to account for differences in exposure to the blood supply among various parts of lobules. Such differences are reflected in varied functional activities and degrees of susceptibility to toxic agents - a *metabolic zonation*.

The territory of an acinus has, as its axis, one final branch of the portal vein, and is subdivided into: 1 periportal, 2 intermediate, and 3 perivenous (around the central vein) zones, with the initial periportal zone being roughly spheroid, and isolated from periportal zones of adjacent acini.

The concept is not easy for students to follow, nor, it seems, for hepatocytes, which, for many processes, heed different patterns. To best fit events to the architecture, hepatologists are now more likely to employ the simpler concept of separately continuous *periportal* and *perivenous/pericentral* zones, than that of discrete acini.

Sinusoids

1. Are lined by *fenestrated endothelial cells*, loosely attached, and hold phagocytic *Kupffer cells* (larger, stellate, with a pale oval nucleus), demonstrated by the vital intravascular injection of trypan blue or carbon particles, or latex particles for microscopy *in vivo*.
2. Fenestrated lining cells are not tightly attached and rest on microvilli of underlying hepatic cells, without a BL intervening.
3. Plasma can thus pass through the sieve plate, formed by the lining cells, out into the perisinusoidal *space of Disse* to interact with the hepatocytes. Some of this fluid may pass to the periphery of the lobule to be collected as lymph.
4. Disse's 'space' contains ECM materials, but not a visible basal lamina.
5. Scarce, fat-storing, *stellate cells* of Ito lie outside the endothelial cells. They store vitamin A. They respond to a variety of insults by making collagen and causing cirrhosis (fibrosis).
6. The sinusoidal wall provides for:
 - *blood cleansing*, e.g., of gut bacterial toxins;
 - *haemopoiesis* in the embryo;
 - bringing plasma into intimate contact with the hepatic cell for its many *metabolic functions* of storage, transformations, syntheses, regulation of plasma concentrations, detoxifications, the production of bile, and assisting *defence* by producing acute-phase proteins.



Hepatocyte/ hepatic cell

-large, spheroid *nucleus* (sometimes two), with membrane pores, and ribosomes on the outer membrane;

-extensive *granular ER* (protein synthesis for enzymes, plasma proteins, etc.);

-*smooth ER* (steroid hormone and cholesterol metabolism; lipids are taken in, processed, and secreted in a way very like the enterocyte's; SER carries enzymes for detoxifications);

-*mitochondria* (oxidative and other enzymes); actin and other *filaments*, near the bile canaliculi and elsewhere. cell membrane projecting *microvilli* into the space of Disse, and held firmly to adjacent cells, especially around the channel, the *bile canalculus*, formed by the separation of two or three cells' membranes and equipped with a few microvilli;

-*Golgi body* lying near the canalculus, as do the *lysosomes*; both appear to help form bile;

-*peroxisomes* with other enzymes, e.g., catalase;

-*glycogen granules* stored in association with smooth ER (an association seen elsewhere);

-*fat droplets* occurring briefly after meals;

-*lipofuscin* or aging pigment, as another normal inclusion; and sometimes brown haemosiderin, with its iron, may be seen.

Bile pathways

System of canaliculi (seen easily only with EM or special impregnation) between the hepatocytes leads to

1. *canals of Hering/cholangioles*, with both hepatocytes and pale duct cells in their walls. Next come, in the portal areas,
2. *bile ductules* with only small, pale cuboidal cells, firmly held by membrane interdigitations and junctional complexes, and having a few luminal microvilli.
3. *Bile ducts'* epithelium changes to columnar mucous cells and, extrahepatically, the ducts acquire smooth muscle as well as CT.
4. *Cystic duct* allows reflux into the *gallbladder*, when Boyden's sphincter choledochus at the duodenal outlet of the common bile duct is closed.

Gallbladder

1. Extensively folded *mucosa* of tall, simple, columnar epithelial cells with many microvilli, lying on a loose lamina propria.
2. Goblet cells are absent, but in the neck there may be small glands of uncertain function.
3. The middle layer has variously disposed (mainly circular) *smooth muscle* bundles.

- Outermost is a *serosa* of mesothelium-covered areolar CT with vessels and nerves, except where the gallbladder attaches to the liver.

Function - stores and concentrates the bile by actively absorbing sodium, coupled with water and anions. The hormone - cholecystokinin - released from gut endocrine cells in response to fat or amino acids causes contraction of the muscle to expel the bile.

3.3. Literature recommended

Main Sources:

- L.C. Junqueira, J. Carneiro - "Basic histology" – 11 edition - 2005.
- A.S. Pacurar, J.W. Bigbee – "Digital histology" – Verginia - 2004.
- "Color Atlas of basic histology" – R.Berns – 2006.
- Sadler T.V. – "Medical embryology" Montana – 1999.
- Ronald W., Dudek Ph.D. – "Embryology" 2 edition – 1998.
- Inderbir Singh Textbook of Human Histology.- Jaypee. India. - 1997.
- Ten Cate A.R. Oral Histology.- St.Louis, Baltimore, Toronto.- 1995.
- William A., Beresford M.A. Cytology and Histology.- Anatomy department, West Virginia University, USA.- 1992.
- K.E. Jonson - "Histology and cell biology" – 2 edition – Washington – 1991.

Additional ones:

- Methodical Instructions.

3.4 How to work with the literature recommended:

Main tasks	Recommendations
To review the material	To use the material studied
To learn the material	To use the material on pages
To read and compose the plan	To learn the new material and be ready to write a summary
To answer the questions	To be ready to give an answer to the following:
To do the test on the material	
To be ready to answer the topic	

3.5. Self-control material:

A. *Questions to be answered:*

- Morphofunctional characteristiof liver.
- Structure of hepatocytes.
- Structure of classic and portal lobes, acinuses.

B. *Test tasks to be done: Tests are applied*

4. Self-preparation in the classroom.

- Listen to the information.
- Work with the tables and a Light microscope.
- Ask about the problems that haven't been found in the information given.
- To sketch in the album the investigated preparations.

5. Self-preparation work at home.

- Review the material learnt in the classroom.
- Compose the plan of your answer.
- Answer the questions to this topic.
- Do the test given above.

6. The subject of the research work.

“Development of liver”

<i>Subject</i>	<i>Histology, cytology and embryology</i>
<i>Modul №2</i>	<i>Histology, cytology and embryology</i>
<i>Submodul №4</i>	<i>Special histology</i>
<i>Topic 27</i>	PANCREAS

Hours: 2

1. The topic basis: the topic “PANCREAS” is very important for future doctors in their professional activity, positively influences the students in their attitude to the future profession, forms professional skills and experience as well as taking as a principle the knowledge of the subject learnt.

2. The aims of the training course:

- 1) To have general knowledge of the topic studied.
- 2) To understand, to remember and to use the knowledge received.
- 3) To learn the classification, structure and functions of the different histological methods.
- 4) To form the professional experience by reviewing, training and authorizing it.
- 5) To be able to carry out laboratory and experimental work.

3. Materials for the before – class work self – preparation work:

3.1 Basic knowledge, experience, skills necessary for studying the topic in connection with other subjects:

	To know	To be able to
Med. Biology	the structure of the cells and tissues	work with a light microscope
Med. Physics	the structure of the light and electron microscopes	work with a light microscope
Organic Chemistry	the chemical content of the cell	Speak of the topic

3.2 The contents of the topic:

This gland combines *exocrine* and *endocrine* functions. The exocrine secretion passes via the duct of Wirsung (and any accessory duct) into the duodenum for digestive and neutralizing purposes.

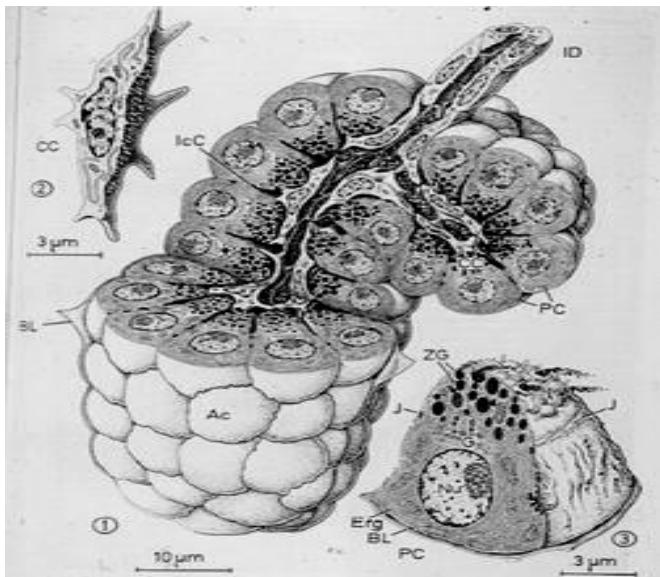
General structure

1. Elongated, lobulated, compound, acinar gland, with a very thin CT capsule and septa.
2. Long duct system and its CT provide support.

3. *Exocrine* part is major with very many serous acini and some ducts.
4. *Endocrine* part is minor: many small clusters of cells staining palely (with HE) - *islets of Langerhans*.

Exocrine pancreas

Acinar structure



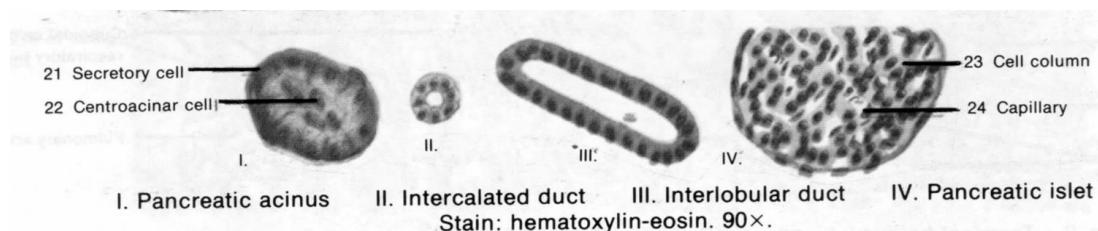
1. Pyramidal epithelial cells line the acini; are rich in *basal granular ER* (deeply basophil); have a prominent supranuclear *Golgi complex* and apical *zymogen granules* (precursors of several digestive enzymes).

2. Electron-radioautography with labelled leucine showed the secretory pathway through the cell and its time aspects.

3. A pale duct cell (or a pair) may be seen intruded into the centre of the acinus as a *centroacinar cell*.

Ducts

1. Commence as narrow *intercalated ducts* within the acini, although vagaries of section plane result in one finding centroacinar cells in only some acini.



2. Beyond the intercalated ducts, ducts have pale cuboidal cells, with few organelles and some microvilli, changing to columnar epithelial cells in the larger ducts.

3. Ducts are less often seen than in the serous parotid gland, and probably actively change the secretions only in the smaller, early ducts.

4. Ducts are accompanied by less connective tissue than in the salivary glands, which are exposed to masticatory forces.

Exocrine function

1. Formation of *alkaline secretions*, which counter the gastric fluid's acidity, thereby activating pancreatic *pro-enzymes* for digestion.

2. The release of alkaline and enzymatic secretions is under the hormonal control of secretin, and cholecystokinin/CCK, respectively.

Endocrine pancreas

Islet structure and functions

1. No ducts, but rich in capillaries with a fenestrated endothelium.
2. Pale cells contain granules differing in alcohol-solubility and staining characteristics (distinguishable also in EM and immunocytochemically) for the differentiation of:
 - o *Alpha cells*, 20 per cent, and large - produce the hormone, *glucagon*, which raises the blood's glucose level.
 - o *Beta cells*, 75 per cent, smaller - produce *insulin*, which promotes the intracellular movement of glucose and glycogen storage, thereby lowering the glucose level of the blood.
 - o *Delta cells*, 5 per cent, with large argyrophil granules; form *somatostatin*, which inhibits insulin and glucagon release.
 - o *F cells*, in islets and among exocrine cells, making *pancreatic polypeptide* (PP), acting centrally on the brainstem to influence the vagal control of GI functions, and on the liver.
3. Blood drained from the pancreas and bearing the polypeptide hormones passes, via the portal flow, to the liver.

3.3. Literature recommended

Main Sources:

1. L.C. Junqueira, J. Carneiro - "Basic histology" – 11 edition - 2005.
2. A.S. Pacurar, J.W. Bigbee – "Digital histology" – Virginia - 2004.
3. "Color Atlas of basic histology" – R.Berns – 2006.
4. Sadler T.V. – "Medical embryology" Montana – 1999.
5. Ronald W., Dudek Ph.D. – "Embryology" 2 edition – 1998.
6. Inderbir Singh Textbook of Human Histology.- Jaypee. India. - 1997.
7. Ten Cate A.R. Oral Histology.- St.Louis, Baltimore, Toronto.- 1995.
8. William A., Beresford M.A. Cytology and Histology.- Anatomy department, West Virginia University, USA.- 1992.
9. K.E. Jonson - "Histology and cell biology" – 2 edition – Washington – 1991.

Additional ones:

1. Methodical Instructions.

3.4 How to work with the literature recommended:

Main tasks	Recommendations
To review the material	To use the material studied
To learn the material	To use the material on pages
To read and compose the plan	To learn the new material and be ready to write a summary
To answer the questions	To be ready to give an answer to the following:
To do the test on the material	
To be ready to answer the topic	

3.5. Self-control material:

A. Questions to be answered:

1. Morphofunctional characteristic of pancreas.

2. Structure and functions of exocrine part.
3. Structure and functions of endocrine part. Cellular structure of the pancreatic island, functions of different types insulocytes.

B. Test tasks to be done: Tests are applied

4. Self-preparation in the classroom.

- 1) Listen to the information.
- 2) Work with the tables and a Light microscope.
- 3) Ask about the problems that haven't been found in the information given.
- 4) To sketch in the album the investigated preparations.

5. Self-preparation work at home.

- 1) Review the material learnt in the classroom.
- 2) Compose the plan of your answer.
- 3) Answer the questions to this topic.
- 4) Do the test given above.

6. The subject of the research work.

“Development of pancreas”

<i>Subject</i>	<i>Histology, cytology and embryology</i>
<i>Modul №2</i>	<i>Histology, cytology and embryology</i>
<i>Submodul №4</i>	<i>Special histology</i>
<i>Topic 28</i>	RESPIRATORY SYSTEM

Hours: 2

1. The topic basis: the topic “**RESPIRATORY SYSTEM**” is very important for future doctors in their professional activity, positively influences the students in their attitude to the future profession, forms professional skills and experience as well as taking as a principle the knowledge of the subject learnt.

2. The aims of the training course:

- 1) To have general knowledge of the topic studied.
- 2) To understand, to remember and to use the knowledge received.
- 3) To learn the classification, structure and functions of the different histological methods.
- 4) To form the professional experience by reviewing, training and authorizing it.
- 5) To be able to carry out laboratory and experimental work.

3. Materials for the before – class work self – preparation work:

3.1 Basic knowledge, experience, skills necessary for studying the topic in connection with other subjects:

	To know	To be able to
Med. Biology	the structure of the cells and tissues	work with a light microscope
Med. Physics	the structure of the light and electron microscopes	work with a light microscope
Organic Chemistry	the chemical content of the cell	Speak of the topic

3.2 The contents of the topic:

The tract rhythmically expels spent air and takes in fresh through conditioning passages, *conducting* it to the respiratory portion of the lungs, where the walls of the air-filled chambers are thin enough to permit an *exchange of gases* between blood and air. The respiratory movements involve chemoreceptors, brain centres, the thoracic cage, and various muscles: these structures belong, together with the respiratory tract, in the *respiratory system*. The lungs also have important *metabolic functions* not directly related to gas exchange, e.g., the activation of circulating angiotensin I, and the inactivation of some other vasoactive agents.

Development of the respiratory tract

1. From an *endodermal* bulge on the foregut, which gives the trachea, then two buds for the bronchi and lungs.
2. Continued *budding* and *branching*, and enclosure of the hollow buds by *mesenchyme*, produce a system of cuboidal epithelium-lined tubules with surrounding differentiating CT and vessels.
3. Early development thus is analogous to that of a compound exocrine gland, until the later phase, when the pulmonary alveoli form. Inadequately developed alveoli, with no surfactant, are a major hazard of premature birth.
4. Surfactant comprises lipids, and surfactant proteins SP-A, -B, -C, & -D, which variously cause the lamellar material to become a monolayer, enhance the lowering of surface tension, stabilise the lipids, and modify host defences.
5. For the development of glands and the lung, complex mesenchymal-epithelial inductive (instructional) interactions occur, and re-occur during repair and tumour development.

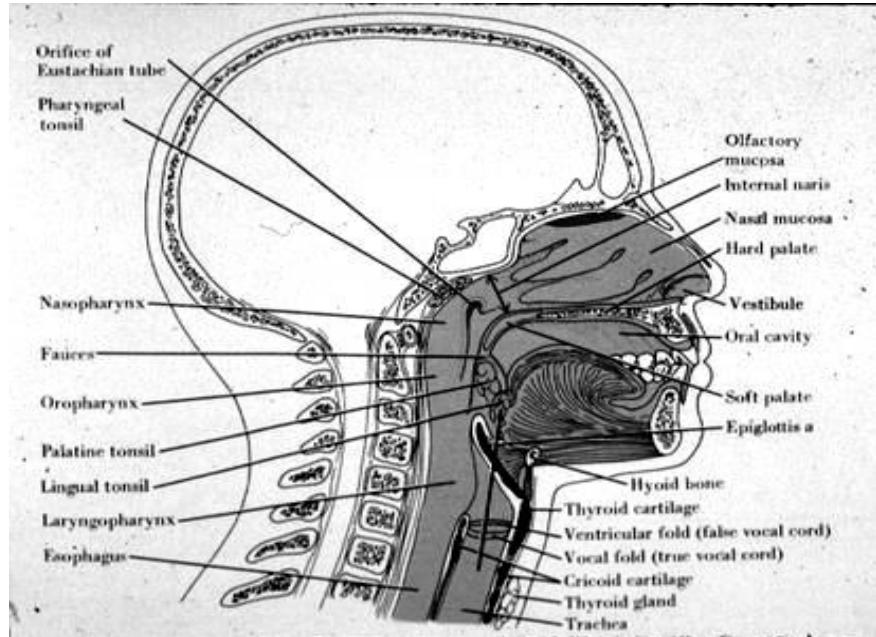
Respiratory protective mechanisms

1. Secretion of entrapping *mucus* by goblet cells and mixed glands, which is swept pharynx-wards by the *ciliary* beating action.
2. Solitary lymphoid nodules and tonsils, and their lymphocyte progeny, for *immune defence*.
3. *Phagocytic alveolar macrophages/dust cells*.

4. Reflex *coughing, sneezing*, and *constriction* of bronchioles.
5. Secretion of serous *bacteriolytic materials*, e.g., defensins and lysozyme.
6. Upper airway *recovers* water and heat, preventing too much loss in the expired air. Some protection is hazardous in that enzymes from WBCs can break down elastin; and activated lung macrophages stimulate fibroblasts to lay down movement-restricting collagen - an interstitial fibrosis. Various defects in the arms and microtubules of cilia (primary ciliary dyskinesia) can prevent proper clearance and cause recurrent lung infection. Affected men are often infertile from an accompanying paralysis of sperm.

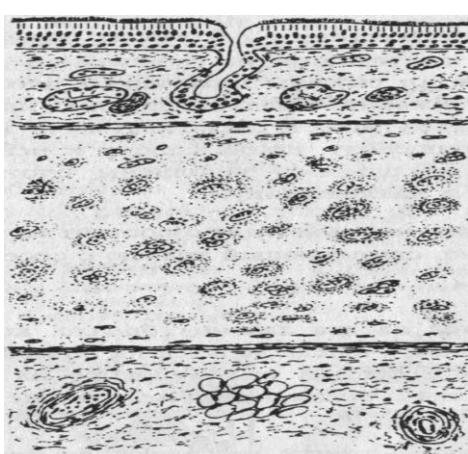
Nasal cavity

1. Divided by a hyaline-cartilage *nasal septum* in the midline.
2. Stratified squamous epithelium (hairy) of the *nares* changes to a lining *nasal mucosa* of:
 - pseudostratified, columnar, ciliated *epithelium* with mucus-secreting goblet cells,
 - a loose *lamina propria*, with many leucocytes, blood vessels, and mixed mucoseroous glands.
3. *Venous plexuses*, to warm the air, underlie the epithelium.
4. *Turbinate bones* in the conchae support the mucosa.
5. A small part of the mucosa is *olfactory*, with a neuroepithelium and Bowman's glands.
6. Paranasal *air sinuses* open off the main cavity.
7. The folded *pharyngeal tonsil*, covered by pseudostratified, columnar, ciliated epithelium, lies posteriorly in the pharynx.
8. *Nasal functions*:
 - air-filtering, material trapped in mucus is swept by the cilia towards the pharynx,
 - air-warming,
 - air-humidifying,
 - olfaction,
 - sensitivity for nasal reflexes such as sneezing,
 - resonating the voice.



Larynx

1. Hollow chamber, whose walls are supported by cartilages, connected by ligaments and membranes, and moved by skeletal muscles.
2. The *extrinsic* and *intrinsic muscles* move the larynx up and under the epiglottis in swallowing, and move the cartilages and tense the vocal cords during phonation and breathing.
3. The *cartilages* are *hyaline* tending to calcification, or *elastic* for the epiglottis, cuneiforms, corniculates, and the apices and vocal processes of the arytenoids.
4. *Mucosa* is mostly pseudostratified, columnar, ciliated epithelium with goblet cells, on a loose lamina propria rich in elastic fibres, mucous and mixed glands, leucocytes and sometimes lymphoid nodules.
5. Two constrictions occur: the *false vocal cords/ventricular folds*; and the lower, *true, cords*, with stratified squamous epithelium over elastic ligaments, and without glands in its lamina propria.
6. The *epiglottis*, too, has stratified squamous epithelium on its exposed tip and upper surface.



Trachea

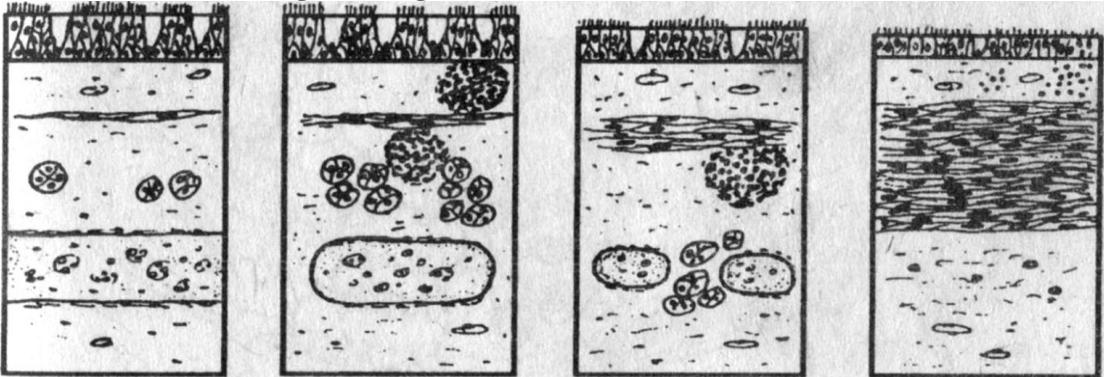
1. Flexible, extensible tube, with an always-patent lumen.
2. *Mucosa* as for the larynx, and the cilia sweep towards the pharynx, but the *elastic fibres* run longitudinally as a layer between mucosa and submucosa.
3. Supporting C-shaped pieces of *hyaline cartilage* are incomplete on their oesophageal side.
4. The gap in the C is crossed by trachealis *smooth muscle* and CT.
5. Outer *adventitia* is fibro-elastic CT.

Lungs

The structure of the lungs reflects the way in which the air is moved:

- the lungs are covered by a slippery *membrane* and are enclosed in *another membrane*, adherent to the inner chest wall, with a potential space between;
- the lungs are stretched out against their considerable *elasticity*, so that this space remains only a potential one;
- the larger conducting tubes of the lung need firm *cartilages* in their walls to prevent their collapsing during the inspiratory sucking in of air.

Bronchial tree serving the lungs



1. *Primary bronchi* branch to form the intrapulmonary *lobar bronchi*, branching to form *segmental bronchi*, then *lobular bronchioles*. After about 9-12 generations of branching, bronchioles replace bronchi.
2. *Terminal bronchioles* lead to *respiratory bronchioles*, off which open the respiratory exchange units, and not just at the end, but along the bronchiole.
3. *Bronchi* resemble the trachea in structure, except that the cartilage pieces in the wall have very irregular shapes, and the *smooth muscle* forms a nearly complete layer - muscularis mucosae - between the cartilages and the lumen.
4. *Bronchioles* are smaller than bronchi:
 - they have no cartilages;
 - their elastic fibres merge with those of the surrounding lung tissue;
 - the epithelium changes to simple, low ciliated columnar with a few goblet cells;
 - no mucous glands are present in the lamina propria, where the smooth muscle is relatively substantial.
5. Sharing the connective tissue of the branching bronchi are blood vessels, nerves and lymphatic vessels, entering or leaving at the hilum or lung root.
6. *Hilar structures* include arteries (bronchial and pulmonary), veins, lymphatics (from two systems), bronchi, lymph nodes, ganglia, nerves (to bronchial, bronchiolar, and vascular smooth muscles; and sensory), and adipose and other CT.

The carotid body-like glomus pulmonale in the pulmonary artery's adventitia is of uncertain function.

Mucosa of the lower airway

1. Cell types in the epithelium:
 - *ciliated* columnar cells, with lysosomes and some microvilli;
 - mucus-secreting *goblet* cells;
 - *basal* 'undifferentiated' cells to replace the specialized kinds;
 - *Clara's* non-ciliated bronchiolar secretory cells with granules and GER;
 - *neuroendocrine cells*;
 - *lymphocytes* migrated from the lamina propria.

2. A sheet of sticky mucus is moved by ciliary action over the mucosa to catch and remove particles - the *mucociliary escalator*.
3. The basal lamina typically is thick.
4. Muco-serous mixed glands, where present in the lamina propria, are small, compound tubular, and respond under nervous control to irritant stimuli, e.g., smoke.

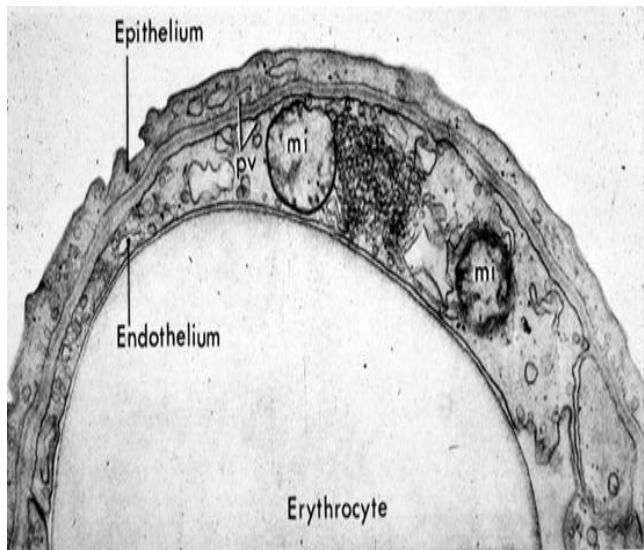
Respiratory chambers

1. *Respiratory bronchiole* has simple, low columnar or cuboidal bronchiolar and ciliated cells; elastic fibres and smooth muscle support the epithelium's BL.
2. Opening out along the respiratory bronchiole are *alveoli*, whose openings are ringed by smooth muscle.
3. At the end of the respiratory bronchiole are one or more long *alveolar ducts*.
4. Alveolar ducts can be viewed as being three to six *atria*, vestibules, leading to *alveolar sacs*, made up of varying numbers of *alveoli*.

Processing distortions in lung slides often make the atria and sacs hard to make out.

5. One alveolus or cubicle shares an *alveolar wall* with the ones adjacent and backing on to it. The wall is thus interalveolar and carries the many *capillaries*, whose blood is to receive oxygen and give up carbon dioxide.
6. *Angiotensin converting enzyme* in pulmonary capillaries cleaves angiotensin I to make it the potent angiotensin II.

Interalveolar wall



1. Air side - continuous *alveolar epithelium* with:
 - *type I pneumocytes*/squamous cells; and
 - *pneumocytes type II/septal* or great alveolar cells, with prominent lipid *cytosomes/multilamellar bodies* in their cytoplasm.
2. *Surfactant* is a stabilizing fluid film of lipids (90%) and proteins (10%), covering the epithelium and *lowering surface tension*. The principal surface-active agent is the lipid, dipalmitoyl phosphatidylcholine (DPPC). The type II cells synthesize this film, but also are the stem cell to replace themselves and Type I cells. Cytosomes are stored surfactant.
3. *Alveolar macrophages/dust cells* lie free in the alveoli.

4. Alveolar epithelium lies on a basal lamina sometimes merging with, and sometimes separated from, the *basal lamina* of a *blood capillary*, on which lies an *unfenestrated endothelium* on the blood side.
5. Where the two basal laminae are separated, the space - *zona diffusa* - is taken by elastic and reticular fibres, fibroblasts, macrophages and other CT cells.
6. Pulmonary *blood-air barrier* can therefore be as thin as 300 nm, and has a very extensive area.

7. Communication between adjacent alveolar sacs is through holes in the wall - *alveolar pores*.

8. Basal laminae, fibres, and surfactant maintain the shape and patency of alveoli during respiration.

Pleurae

are fibro-elastic vascular membranes with mesothelial coverings. From the visceral pleura, CT septa run in to subdivide the lung into lobules and carry lymphatic and venous vessels.

3.3. Literature recommended

Main Sources:

1. L.C. Junqueira, J. Carneiro - "Basic histology" – 11 edition - 2005.
2. A.S. Pacurar, J.W. Bigbee – "Digital histology" – Verginia - 2004.
3. "Color Atlas of basic histology" – R.Berns – 2006.
4. Sadler T.V. – "Medical embryology" Montana – 1999.
5. Inderbir Singh Textbook of Human Histology.- Jaypee. India. - 1997.
6. K.E. Jonson - "Histology and cell biology" – 2 edition – Washington – 1991.

Additional ones:

1. Methodical Instructions.

3.4 How to work with the literature recommended:

Main tasks	Recommendations
To review the material	To use the material studied
To learn the material	To use the material on pages
To read and compose the plan	To learn the new material and be ready to write a summary
To answer the questions	To be ready to give an answer to the following:
To do the test on the material	
To be ready to answer the topic	

3.5. Self-control material:

A. Questions to be answered:

1. Respiratory system. General plan of its structure.
2. Structure and functions of the trachea and bronchi of different calibre.
3. Lungs. Morphofunctional characteristic. Respiratory and non-respiratory departments.
4. Structure and functions of acini. Alveolocytes. Aero-haematic barrier.

B. Test tasks to be done: Tests are applied

4. Self-preparation in the classroom.

- 1) Listen to the information.
- 2) Work with the tables and a Light microscope.
- 3) Ask about the problems that haven't been found in the information given.
- 4) To sketch in the album the investigated preparations.

5. Self-preparation work at home.

- 1) Review the material learnt in the classroom.
- 2) Compose the plan of your answer.
- 3) Answer the questions to this topic.
- 4) Do the test given above.

6. The subject of the research work.

"Pulmonary surfactant"

<i>Subject</i>	<i>Histology, cytology and embryology</i>
<i>Modul №2</i>	<i>Histology, cytology and embryology</i>
<i>Submodul №4</i>	<i>Special histology</i>
<i>Topic 29</i>	URINARY SYSTEM. KIDNEYS. URINARY TRACT

Hours: 2

1. The topic basis: the topic “**URINARY SYSTEM. KIDNEYS. URINARY TRACT**” is very important for future doctors in their professional activity, positively influences the students in their attitude to the future profession, forms professional skills and experience as well as taking as a principle the knowledge of the subject learnt.

2. The aims of the training course:

- 1) To have general knowledge of the topic studied.
- 2) To understand, to remember and to use the knowledge received.
- 3) To learn the classification, structure and functions of the different histological methods.
- 4) To form the professional experience by reviewing, training and authorizing it.
- 5) To be able to carry out laboratory and experimental work.

3. Materials for the before – class work self – preparation work:

3.1 Basic knowledge, experience, skills necessary for studying the topic in connection with other subjects:

	To know	To be able to
Med. Biology	the structure of the cells and tissues	work with a light microscope
Med. Physics	the structure of the light and electron microscopes	work with a light microscope
Organic Chemistry	the chemical content of the cell	Speak of the topic

3.2 The contents of the topic:

Urinary system consists of the uro-generatind part and uro-conducting part. In the uro-conducting part there are intrakidney and extrakidney parts. The kidneys eliminate waste metabolic products using water, but conserve water, electrolytes and other materials to maintain the body *homeostatically* in fluid, pH and electrolyte balance. The urine produced is evacuated periodically via urinary passages.

Kidney

This separates from the blood large quantities of *ultra-filtered* fluid in more than a million small, tubular units, *nephrons*/uriniferous tubules. Most needed materials are then *recovered* to the bloodstream, and some *secretion* of other substances occurs, to give a solution of unwanted materials -the excretion - to be *collected* as urine from the tubules. The kidney is a compound, tubular, excretory gland, and an endocrine gland.

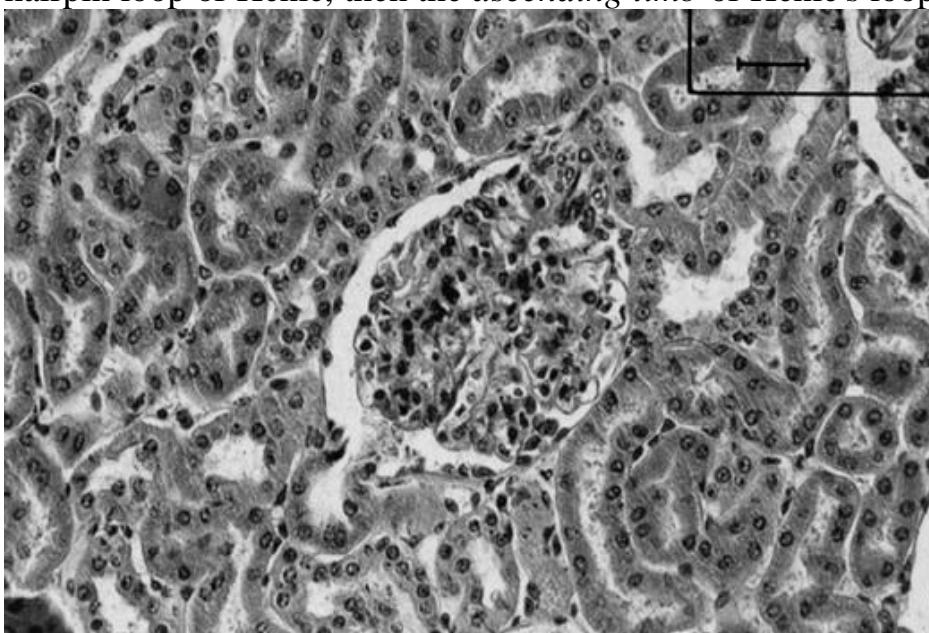
Kidney's general architecture

1. Outside are perirenal fat, and nearby suprarenal glands.
2. Thin, fibrous *capsule*.

3. Reniform (kidney-shaped!), around a *hilum* and *sinus* for the renal artery, renal vein, and ureter.
4. *Ureter* opens from a *renal pelvis*, for which major and minor *calyces** collect the urine from bluntly pointed apical *papillae* of *pyramids*.
5. Pyramid + overlying tissue constitute a *lobe*.
6. The human kidney is *multilobar*, with 8-18 lobes.
7. Pyramidal tissue has a pale striated appearance from many parallel tubules and blood vessels. It is the *medulla*.
8. The outer *cortex* of the kidney is darker, with many round structures - *renal corpuscles*/Malpighian corpuscles, and coiled tubules cut in cross and oblique section.
9. Cortical tissue - columns of Bertin - runs inward to partly separate the pyramids.
10. Medullary tissue extends *rays* up from the medulla into the cortex. A medullary ray defines the centre of a *lobule*, but the lateral limits of the lobule remain undefined in the cortical tissue.

Form of nephron and relations with cortex and medulla

Renal corpuscle (round, 150-240 μm diameter) - *glomerulus* of epithelium-invested capillaries, and enclosed in a *Bowman's capsule*, opening out at the urinary pole into the *proximal convoluted tubule*, which leads to the *Medulla descending limb* of the hairpin loop of Henle, then the *ascending limb* of Henle's loop.



Distal convoluted tubule follows, attached at one point to the renal corpuscle of origin; thence leading to an *arched collecting/junctional tubule* joining a *Medulla straight collecting tubule*, receiving many branches and running down from a medullary ray through the medulla to a *papillary duct of Bellini*, opening at the papilla of the pyramid. The papilla is cribriform from the many openings.

Alternative terms for these parts are:

- 2 may be termed the pars *convoluta* of the proximal tubule;
- 5 may be termed the pars *convoluta* of the distal tubule;
- the loop of Henle comprises the pars *recta* of the proximal tubule, the thin segment and the pars *recta* of the distal tubule.

Thin segments and loops vary in length dependent on the position in the cortex of their glomeruli of origin. The appearance of the kidneys is dominated by the nephrons, since the connective tissue element (reticular fibres) is slight, and the very many small blood vessels follow the pattern of the nephrons, because the two work together.

Functional unit of the kidney

Consists of nephron, blood vessels, interstitium, and collecting tubule.

The functions of the various parts of the unit are given briefly, so that all aspects of the finer structure can be presented together.

1. *Renal corpuscle*, with vascular glomerulus - ultrafiltration of arterial blood.
2. *Proximal convoluted tubule* - from the ultra-filtrate received from the corpuscle, the prompt massive recovery (reabsorption), by active transport, cotransport, facilitated and downhill diffusion, of sodium, chloride, glucose.
3. *Loop of Henle* - urine concentration by active and passive functions in a complicated counter-current osmotic multiplier interaction of loops of Henle, blood vessels, interstitium, and collecting tubules.
4. *Distal tubule* (partly in the loop) - continued active reabsorption of Na^+ under the control of aldosterone, and the secretion of potassium.
5. *Collecting tubule* - passive reabsorption of water to the blood, making the urine hypertonic, under the influence of pituitary antidiuretic hormone (ADH); and a variety of fine adjustments to electrolytes and acidity.
6. The nephron is controlled by hormones from other endocrine glands, but the kidney itself produces hormones that affect non-renal tissues.

Nephron cytology

1. Glomerulus

- Blood is fed, via an *afferent arteriole*, under pressure into groups of capillaries, tufting out as loops from the vascular pole, and ensheathed in *visceral squamous epithelium*.
- *Glomerular wall of*
 - *fenestrated endothelium*,
 - *thick basal lamina* (two laminae fused together),
 - *podocytes' pedicels* (visceral epithelial cells' feet), separated by filtration slits of controllable width, permit
- the *filtration* of water and solutes, with a molecular mass less than 70 kDa, into a *capsular space* between glomerular/visceral epithelium and the parietal squamous epithelium and BL of Bowman's capsule.
- The altered blood is collected from the capillary tufts, and passes out via the narrower *efferent arteriole*.
- Between the capillaries at their base lie *mesangial cells*, synthesizing and maintaining the glomerular basal lamina, and also probably phagocytic and contractile. Mesangial cells are significantly involved in renal disease, e.g., in diabetes and glomerular nephritis.

2. Proximal tubule (40-50 μm diameter)

- Most common of those tubules seen in the sectioned cortex, since it is longer than the distal tubule.
- Simple, acidophilic, cuboidal, epithelial lining cells with: large round nuclei;

- very many microvilli (brush border), and a surface glycoprotein coat containing peptidases to reduce polypeptides;
- vesicles and lysosomes just below the microvilli, and involved in endocytotic protein uptake and breakdown to amino acids;
- marked lateral membrane infoldings and interdigititation with adjacent cells, to which they attach with junctional complexes.
- The basal region has many membrane infoldings and long mitochondria (*basal striation*) for the provision of energy for active transport of Na^+ , and with it glucose and amino acids, through the basolateral membrane,
- basal lamina, and thence into adjacent capillaries, with their fenestrated endothelium.

3. *Thin segment* (15 μm diameter)

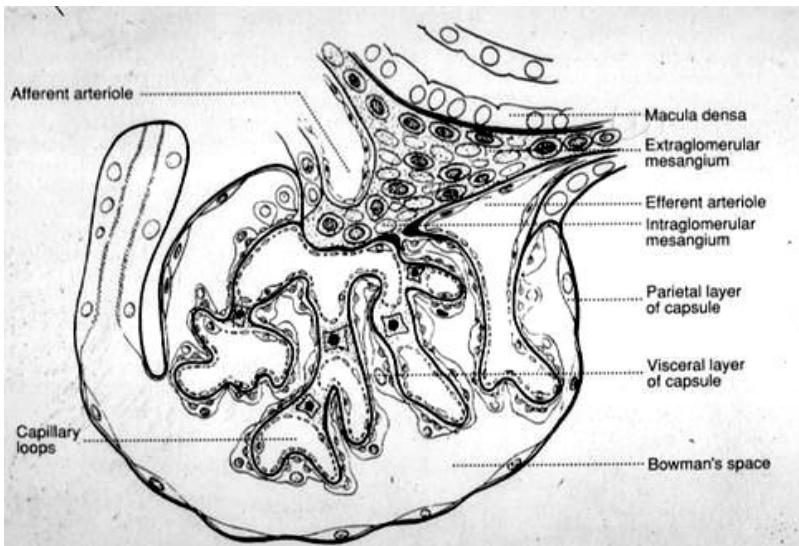
- Squamous epithelial lining on a BL.
- Cells are pale, tightly fastened, with small, short microvilli, and a few mitochondria scattered randomly.
- The lack of red blood corpuscles in the lumen, and plumper nuclei, distinguish thin segments from capillaries.

4. *Distal tubule* (20-50 μm diameter)

- Weakly acidophilic, cuboidal epithelial cells enclose large lumens.
- No brush border is seen because only a few short microvilli are present.
- Basal infoldings and interdigitations, with very many long mitochondria, give a basal striation.
- Cells lie on a BL, also supporting fenestrated endothelial cells of the surrounding capillaries.
- *Macula densa* is a specialized, more nucleated region of the epithelium, where it attaches to the arterioles of the glomerulus to form part of the juxtaglomerular apparatus. It senses the $[\text{Cl}^-]$ locally in the distal tubule and signals, via mesangial cells, for renin release, and arteriolar and mesangial contraction.

5. *Juxtaglomerular apparatus*

- Afferent arteriole, nearing the JGA, loses its elastica interna.
- Smooth muscle cells change to *epithelioid* with *secretory granules* and some GER.
- The juxtaglomerular secretory cells are in contact with the endothelium of the arteriole and, indirectly, with the macula densa of the distal tubule: for sensing renal tubular chemistry, and stretch, indicating blood pressure. The cells' sympathetic innervation is another element in the control matrix.
- Granules are the enzyme *renin* for release into the blood, where it cleaves a potentially hypertensive polypeptide (angiotensin I) from angiotensinogen.
- A juxtaglomerular interaction with the adrenal cortex and Na^+ excretion also occurs.
- Polkissen/Goormatigh/lacis cells lie in the angle between the afferent and efferent vessels and the attached distal tubule.



6. Collecting duct (40-200 µm diameter)

- Pale cuboidal cells, with the lateral cell membranes prominent because lateral interdigititation is lacking, are of three kinds: principal, and, set between them, alpha/A and beta/B intercalated cells, all differing in their ion-transport roles.
- *Principal cells* have few microvilli, and few mitochondria, but are tightly connected by occluding junctions. *Aquaporin 2* constructs the channels making the luminal cell membrane permeable to water in the presence of vasopressin/ADH, so that the cells reabsorb water. Basolaterally, a membrane Na,K-ATPase lets the cells secrete potassium, while absorbing sodium.
- *Intercalated cells* have darker cytoplasm, and more and darker mitochondria, than principal cells. The number of vesicles is highly variable, because they function to insert or remove ion pumps into the cell membrane, in a similar way to the gastric parietal cell.
- Type A intercalated cells bear a luminal-membrane H,K-ATPase to secrete hydrogen ions and reabsorb potassium; type B cells have a luminal Cl/HCO₃⁻ countertransporter to secrete bicarbonate and recover chloride.
- A simple columnar epithelium lines the final papillary ducts of Bellini, and covers the papillae.

Renal interstitium

1. lies between the kidney tubules and vessels.
2. It comprises: reticular fibres, a little ground substance, and interstitial fibroblasts, looking after the matrix and secreting erythropoietin.
3. The interstitial elements are more prominent in the medulla than the cortex.

Renal blood vessels

1. *Renal artery* branches to form *interlobar arteries* (interpyramidal), extending to the cortico-medullary junction, where they branch and turn as arching *arcuate arteries*, giving off outward branches called *interlobular arteries*; from which *intralobular arteries* provide *afferent arterioles* to *glomeruli*; from the capillaries of which the blood is taken via *efferent arterioles* to serve one or both of *two capillary beds* - around the convoluted tubules, and between the straight medullary tubules.
2. The blood collected in *stellate*, *deep cortical*, and *interlobular veins*, traces back the arterial path to the *renal vein*.

3. The sympathetic nervous supply to the kidney goes mainly to the renal vasculature, including the juxtaglomerular cells.

4. *Vasa recta* is a collective name for arteriolar, capillary, and venous *straight* blood vessels in the medulla. They participate in the counter-current exchange.

Urinary Passages

The kidney's calyces and pelvis, and the passages to the urethra are lined by transitional epithelium.

Transitional epithelium/urothelium

1. Multilayered, with large surface/*umbrella* cells, intermediate cells and basal cuboidal cells on a thin BL.

2. The surface cells have unique properties of:

- making a barrier impermeable to urine;
- changing their shape and extent during bladder distension.

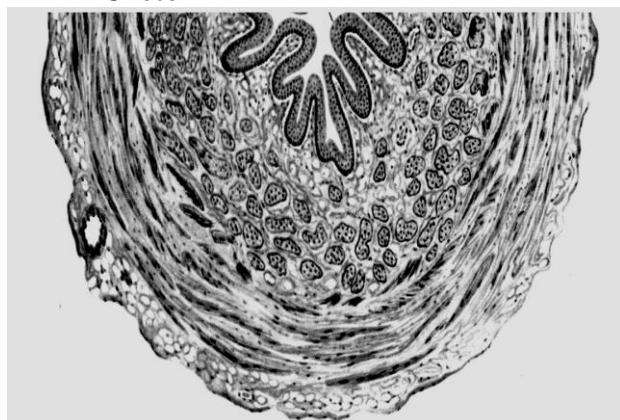
3. The luminal umbrella cell membrane is *asymmetrically thickened* (to 12 nm) and has unusual lipids and proteins, including uroplakins

4. The Golgi complex forms *fusiform vacuoles*, bounded by thick membranes. During bladder dilation, the vesicles attach to the thick luminal membrane and become part of it, thus increasing its extent and allowing the cell to flatten. No cell-over-cell sliding occurs, the cells being joined by tight and adherens junctions and desmosomes.

5. Large lysosomes destroy defective membrane.

6. The rate of cell turnover is very low for an epithelium.

Ureter



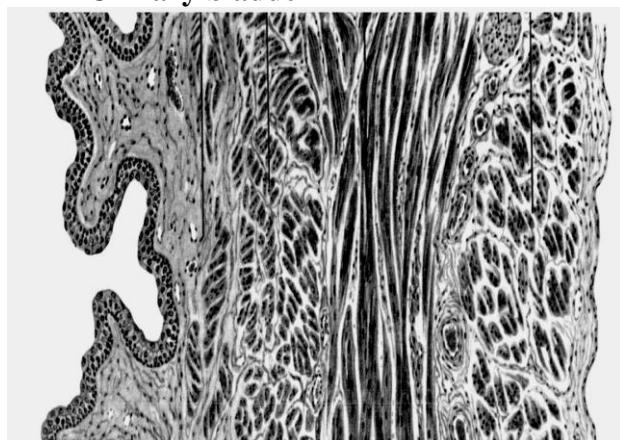
1. *Transitional epithelium* lies on a collagenous lamina propria.

2. Mucosa has several *longitudinal folds*, giving the lumen a stellate shape in the cross-section.

3. Two *smooth muscle coats*: outer, circular; inner, longitudinal;

4. CT *adventitia*, rich in vessels and nerves.

Urinary bladder



1. Transitional epithelium, on a wide collagenous lamina propria without glands, constitutes the *mucosa*.

2. Three smooth muscle tunics interweave in the *muscularis*.

3. A CT *adventitia* has blood and lymphatic vessels, nerve fibres and ganglion cells. The part of the bladder facing the pelvic cavity has a serosa.

4. The ureters enter obliquely, with mucosal flaps to prevent reflux; smooth muscle forms a sphincter at the urethral

outlet.

Urethra (male)

1. Epithelium lies on a very loose, elastic, vascular, distensible lamina propria. The lumen is stellate in cross-section.
2. *Epithelium* is transitional changing to pseudostratified columnar, stratified columnar, and finally stratified squamous, as it traverses the three sections: prostatic, membranous (short) and penile/cavernous (long).
3. Branching out in the penile mucosa are Littré's small tubular *mucous glands*.
4. There is a meagre smooth muscle *muscularis*, except at
5. the smooth and skeletal muscle *sphincters*
6. Female urethra is much shorter than the male; structurally it is similar, but, ending at the pelvic floor, has a skeletal muscle sphincter at its terminus.

3.3. Literature recommended

Main Sources:

1. L.C. Junqueira, J. Carneiro - "Basic histology" – 11 edition - 2005.
2. A.S. Pacurar, J.W. Bigbee – "Digital histology" – Virginia - 2004.
3. "Color Atlas of basic histology" – R.Berns – 2006.
4. Sadler T.V. – "Medical embryology" Montana – 1999.
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6. K.E. Jonson - "Histology and cell biology" – 2 edition – Washington – 1991.

Additional ones:

1. Methodical Instructions.

3.4 How to work with the literature recommended:

Main tasks	Recommendations
To review the material	To use the material studied
To learn the material	To use the material on pages
To read and compose the plan	To learn the new material and be ready to write a summary
To answer the questions	To be ready to give an answer to the following:
To do the test on the material	
To be ready to answer the topic	

3.5. Self-control material:

A. *Questions to be answered:*

1. Urinary system. General plan of organization.
2. Functions of urinary system.
3. Nephron: types and cytophysiology.
4. Urinary tract.

B. Test tasks to be done: Tests are applied

4. Self-preparation in the classroom.

- 1) Listen to the information.
- 2) Work with the tables and a Light microscope.
- 3) Ask about the problems that haven't been found in the information given.
- 4) To sketch in the album the investigated preparations.

5. Self-preparation work at home.

- 1) Review the material learnt in the classroom.
- 2) Compose the plan of your answer.
- 3) Answer the questions to this topic.
- 4) Do the test given above.

6. The subject of the research work.

“Sources of development and stages of embryogenesis of urinary system”

<i>Subject</i>	<i>Histology, cytology and embryology</i>
<i>Modul №2</i>	<i>Histology, cytology and embryology</i>
<i>Submodul №4</i>	<i>Special histology</i>
<i>Topic 30</i>	MALE REPRODUCTIVE SYSTEM. TESTIS

Hours: 2

1. The topic basis: the topic “**MALE REPRODUCTIVE SYSTEM. TESTIS**” is very important for future doctors in their professional activity, positively influences the students in their attitude to the future profession, forms professional skills and experience as well as taking as a principle the knowledge of the subject learnt.

2. The aims of the training course:

- 1) To have general knowledge of the topic studied.
- 2) To understand, to remember and to use the knowledge received.
- 3) To learn the classification, structure and functions of the different histological methods.
- 4) To form the professional experience by reviewing, training and authorizing it.
- 5) To be able to carry out laboratory and experimental work.

3. Materials for the before – class work self – preparation work:

3.1 Basic knowledge, experience, skills necessary for studying the topic in connection with other subjects:

	To know	To be able to
Med. Biology	the structure of the cells and tissues	work with a light microscope
Med. Physics	the structure of the light and electron microscopes	work with a light microscope
Organic Chemistry	the chemical content of the cell	Speak of the topic

3.2 The contents of the topic:

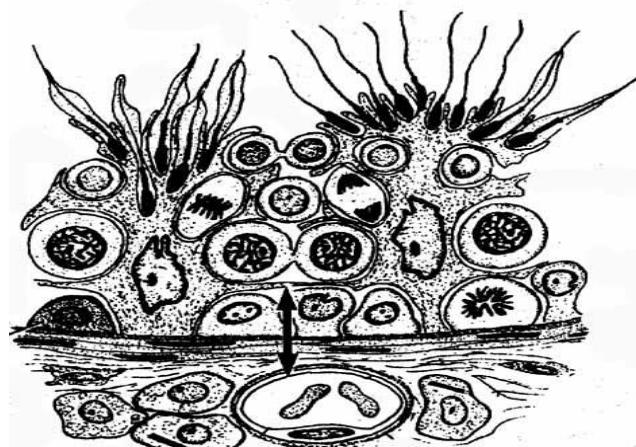
Male reproductive organs form spermatozoa, suspend them in secretions produced by accessory glands, and conduct them, via seminal pathways, to the female reproductive tract by mating behaviour. These activities are influenced by hormones, including ones formed by the testes. Male reproductive system consist of gametogenerative part, gametoconductive part and accessory glands. Seminiferous tubules forming gametogenerative part. Other tubular structures forming gametoconductive part.

Testis

1. Very dense CT capsule - *tunica albuginea*, with an outer mesothelium-covered visceral tunica vaginalis propria.
2. *Septa/septula* extend from the capsule to the CT *mediastinum*.
3. In the partitions thus formed (lobuli testis), lie looped, coiled *seminiferous tubules*, lined by germinal epithelium, and feeding via straight
4. *tubuli recti* into cuboidal epithelium-lined ducts of the
5. *rete testis*, which lead through the mediastinum to roughly 6-12
6. *ductuli efferentes*. These take the spermatozoa to a
7. single, coiled, tubular *epididymis* lying behind the testis.
8. Between, and outside, the coils of a seminiferous tubule lie blood and lymph capillaries, cells and fibres of CT, and hormone-secreting *Leydig interstitial cells*.
9. The testis is a mixed endocrine and compound, tubular, cytogenic exocrine gland.

Seminiferous tubule and spermatogenesis

1. The tubule has a substantial *support* of the basal lamina, plus two or more alternating layers of collagen fibres and muscle-like/myoid cells, with adherent external lamina.
2. The stratified *germinal epithelium* has cells of two kinds:
 - o *spermatogenic cells*, quiescent or in the various phases of development;
 - o *Sertoli supporting cells*; well attached, tall with an irregular columnar form, and a pale ovoid nucleus with a prominent *nucleolus*; taking up testosterone; and controlling spermatogenesis.



3. *Spermatogenesis* in the epithelium is initiated by the pituitary hormone FSH, and passes through these stages:
 - o *spermatogonium*, spheroid cell lying basally, divides mitotically for several generations, then become a
 - o *primary spermatocyte*, larger, divides by the first meiotic division (to halve the chromosome number to haploid 23 and introduce genetic variety), to produce

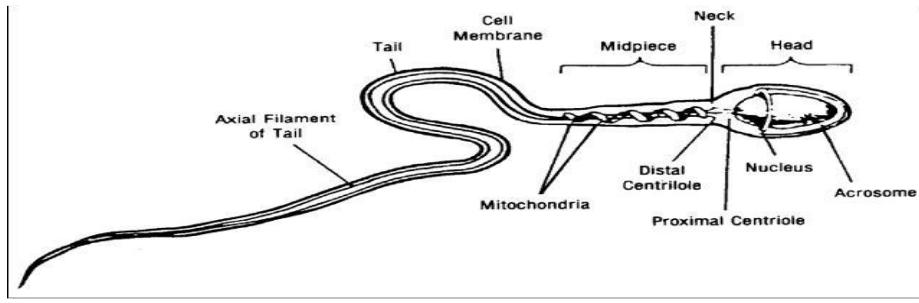
- *secondary spermatocytes*, small, soon undergoing the second meiotic division, maintaining the chromosome number at 23, to give
- *spermatids*, smaller and incompletely separated, which, without dividing, metamorphose by the process - *spermiogenesis* - into
- *spermatozoa*, released into the tubule's lumen.

The stages are not all seen at any one place in the germinal epithelium; various combinations exist and are distributed as a *mosaic* in the tubule's wall.

4. Spermatogenesis is *vulnerable* to heat, X-rays, dietary deficiencies, pesticides, and other poisons. Conventional microscopy reveals defects in sperm shape and motility, leading to infertility. FISH and other molecular techniques are needed to assess genetic damage, sometimes arising during.

Spermatogenesis is protected to a degree by the tight attachments between the capillary endothelial cells and, separately, between the Sertoli cells, creating a two-tiered *blood-testis barrier*, for example, against immune attack. The inner protected compartment of the seminiferous tubule is the 'adluminal' compartment.

5. The ***spermatozoon*** is a very elongated motile cell, with a cell membrane enclosing the:



- *acrosomal head cap*, with an enzyme - proacrosin - to aid binding to, and penetration of, the zona pellucida of the oocyte;
- *nucleus*, streamlined in shape, with dense chromatin;
- neck joining the *head* (nucleus and head cap) to the flagellar *tail*, which has the:
 - *middle piece*, with an axial *axonemal* core of microtubules in a cilium-like array, nine dense longitudinal fibres and, outermost, a sheath of mitochondria ending at the annulus;
 - *principal piece*, with both longitudinal and circumferential fibres around the axoneme;
 - *end piece*, with microtubules like a cilium, but no dense fibres.

6. *Spermiogenesis* - whereby the spermatid, a typical cell (except for its chromosomes) becomes a spermatozoon - involves:

- construction of the acrosome by the Golgi complex;
- the nucleus, thus polarized at one end, condenses and elongates;
- at the other end, one of the centrioles initiates formation of the flagellar tail;
- (d) mitochondria migrate to form a sheath in the tail;
- (e) excess cytoplasm is shed as a residual body;
- (f) the head of the spermatid throughout spermiogenesis stays held in a recess in a Sertoli cell.

7. *Sertoli cell functions*: to protect, nourish, and release the spermatids; to phagocytose residual bodies; and to make androgen-binding protein, fluid, and inhibin to influence pituitary FSH release.

Endocrine testis

1. *Leydig cells*, eosinophilic, with much smooth ER, lipid droplets, and crystals of Reinke, lie outside the tubules' BLs, constituting a diffuse, steroid-secreting endocrine gland.
2. Leydig interstitial cells are controlled by gonadotrophic interstitial cell-stimulating hormone (ICSH/LH) of the anterior pituitary, and produce the androgenic hormone - *testosterone*, responsible for: spermatogenesis; development and maintenance of reproductive ducts and accessory glands; secondary sexual characteristics; male mating behaviour; general anabolic effects on metabolism.

3.3. Literature recommended

Main Sources:

1. L.C. Junqueira, J. Carneiro - "Basic histology" – 11 edition - 2005.
2. A.S. Pacurar, J.W. Bigbee – "Digital histology" – Virginia - 2004.
3. "Color Atlas of basic histology" – R.Berns – 2006.
4. Sadler T.V. – "Medical embryology" Montana – 1999.
5. Inderbir Singh Textbook of Human Histology.- Jaypee. India. - 1997.
6. K.E. Jonson - "Histology and cell biology" – 2 edition – Washington – 1991.

Additional ones:

1. Methodical Instructions.

3.4 How to work with the literature recommended:

Main tasks	Recommendations
To review the material	To use the material studied
To learn the material	To use the material on pages
To read and compose the plan	To learn the new material and be ready to write a summary
To answer the questions	To be ready to give an answer to the following:
To do the test on the material	
To be ready to answer the topic	

3.5. Self-control material:

A. Questions to be answered:

1. Male reproductive system. General characteristic.
2. Development of male reproductive system.
3. Testis: structure, functions.

B. Test tasks to be done: Tests are applied

4. Self-preparation in the classroom.

- 1) Listen to the information.
- 2) Work with the tables and a Light microscope.
- 3) Ask about the problems that haven't been found in the information given.
- 4) To sketch in the album the investigated preparations.

5. Self-preparation work at home.

- 1) Review the material learnt in the classroom.
- 2) Compose the plan of your answer.
- 3) Answer the questions to this topic.
- 4) Do the test given above.

6. The subject of the research work.

"Endocrine functions of male reproductive systems"

<i>Subject</i>	<i>Histology, cytology and embryology</i>
<i>Modul №2</i>	<i>Histology, cytology and embryology</i>
<i>Submodul №4</i>	<i>Special histology</i>
<i>Topic 31</i>	MALE REPRODUCTIVE TRACT. ACCESSORIES

Hours: 2

1. The topic basis: the topic “**MALE REPRODUCTIVE TRACT. ACCESSORIES GLANDS**” is very important for future doctors in their professional activity, positively influences the students in their attitude to the future profession, forms professional skills and experience as well as taking as a principle the knowledge of the subject learnt.

2. The aims of the training course:

- 1) To have general knowledge of the topic studied.
- 2) To understand, to remember and to use the knowledge received.
- 3) To learn the classification, structure and functions of the different histological methods.
- 4) To form the professional experience by reviewing, training and authorizing it.
- 5) To be able to carry out laboratory and experimental work.

3. Materials for the before – class work self – preparation work:

3.1 Basic knowledge, experience, skills necessary for studying the topic in connection with other subjects:

	To know	To be able to
Med. Biology	the structure of the cells and tissues	work with a light microscope
Med. Physics	the structure of the light and electron microscopes	work with a light microscope
Organic Chemistry	the chemical content of the cell	Speak of the topic

3.2 The contents of the topic:

Efferent ducts/Ductuli efferentes

1. *Unevenly* lined by simple, columnar, epithelial cells, in groups of tall ciliated and short secretory; the wall has circular smooth muscle;
2. *Functions* - reabsorption of the fluid used to move sperm out of the testis; maturation of the sperm.

Epididymis/ductus epididymidis

1. *Regularly* lined by tall, absorptive, columnar cells with non-motile *stereocilia*, and smaller basal cells, together forming a *pseudostratified epithelium*. Outside the BL is a little smooth muscle and, between the coils, is a stroma of dense CT with capillaries. *Functions* - as for ductuli efferentes.

Ductus deferens/vas deferens

Lined by an *epithelium* similar to that of the epididymis, on a lamina propria; in the ampulla, this mucosa has many folds. Most of the very thick wall is *smooth muscle*: inner, longitudinal; middle, circular; outer, longitudinal. *Adventitia* of CT binds it to nerves, blood and lymphatic vessels, and the skeletal cremaster muscle, to comprise the *spermatic cord*. *Function* - rapid transport of sperm during ejaculation, under sympathetic control.

Ejaculatory ducts

Each occurs after a dilation of the ductus d. - the *ampulla*. Lined by pseudostratified or simple columnar epithelium on CT, without smooth muscle. Ducts open into the prostatic urethra through a hillock on the posterior urethral wall - *verumontanum/colliculus seminalis*, with its blind recess - *utriculus masculinus*.

Urethra - Three portions; prostatic, membranous, and cavernous.

Male Accessory Glands

Prostate gland

1. Lobulated by septa of CT, with much smooth muscle.
2. Divisible, with histology and rectal-probe ultrasound, into several *zones*:
 - *peripheral* (prone to cancer),
 - *transitional*,
 - *central*,
 - *peri-urethral* (subject to benign prostatic hypertrophy), and
 - an anterior non-glandular *fibromuscular zone*.
3. Large-lumened *secretory acini* are lined by pale columnar or cuboidal epithelial cells, on a BL. Epithelium is patchily *pseudostratified*, i.e., bearing some small basal cells.
4. Acini open into many ducts, entering the urethra *individually*, thus the prostate is a *collection* of compound tubuloacinar glands.
5. Laminated, rounded, *prostatic concretions* (originally glycoprotein, but later calcifying) - *corpora amyacea* - develop in some acini as age increases.
6. *Functions* - secretion of a watery fluid to dilute the semen; the protease - prostate-specific antigen (PSA) - liquifies the gel from the seminal vesicles to free the sperm; the roles of the citrate (the anionic counterpart to Na^+) and acid phosphatase are uncertain.
7. PSA serves as a *serum marker* of prostatic cancer, if excessive for the man's age.
8. The *stroma* has abundant smooth muscle to make the prostate a self-squeezing gland, without the need for myoepithelial cells. Stroma interacts with the epithelium in the control of growth and secretion, and is a major player in benign prostatic hypertrophy.

Seminal vesicles

1. Coiled, *convoluted, tubular structures*; with a very extensively *folded mucosa*, having a pseudostratified, columnar, secretory epithelium.
2. The wall has circular and longitudinal *smooth muscle*, and a thin, outer, fibro-elastic *adventitia*.
3. *Functions* - secretion of a viscid gel composed of *seminogelin*, with fructose to provide energy for the sperm, and prostaglandins that may alter contractions in the female tract.

Cowper's bulbo-urethral glands

1. Compound, tubulo-alveolar gland making special *mucus*, thought to lubricate and prepare the urethra for ejaculation.

Penis

1. The thin, elastic *skin* of the shaft is loosely attached.
2. Connective tissue capsules or *tunicae albugineae* enclose
3. Three roughly cylindrical *erectile bodies* - two corpora cavernosa penis, and one corpus spongiosum/cavernosum urethrae.
4. The two *corpora cavernosa* are incompletely separated by a sagittal pectiniform septum. Their endothelium-lined *venous sinuses*, between a meshwork of dense

trabeculae of muscular CT, can be engorged with blood from *helicine* (coiled) arteries causing erection.

5. *Corpus spongiosum*

- is erectile, but less turgid than the corpora cavernosa;
- has less smooth muscle in the CT trabeculae;
- originates proximally as the *bulbus urethrae* and
- extends distally to form the bulbous *glans*, occupied by many veins and nervous receptors, and covered by stratified squamous epithelium, variably keratinized;
- ensheaths the cavernous/penile *urethra*, lined by stratified columnar and finally stratified squamous epithelium.

6. *Erection* and *detumescence* are controlled by autonomic nerve fibres to the arteries and trabecular smooth muscle. Erection results from *parasympathetically* directed trabecular and arterial relaxation, and passive occlusion of the veins draining the corpora.

Sensory nerves serve the glans, skin and deep receptors.

7. *Functions* - urination/micturition; copulation.

Male & Female Reproductive Development

1. The primordial germ cells (prospective gametes) migrate to the gonadal ridges, then a system of dual paired tubules develops, to be either the male or female reproductive tract. Why dual sets of tubules?

2. The *para-mesonephric/Müllerian ducts* provide the *default* pathway to turn into female organs.

The *mesonephric/Wolffian ducts* furnish the *driven* pathway to a male tubular system.

3. How is the choice made? The male is male by virtue of the Y chromosome, bearing the SRY gene for the human testis-determining factor (SRY - Sex-determining Region on Y). The sequelae of the protein expression of *SRY* are:

- The indifferent gonad becomes a testis, with *Sertoli* and *Leydig cells*. Products of these cells act, gardening-style, as weed-killer and fertilizer.
- Sertoli cells make *Müllerian-inhibiting factor* (MIF), which causes the apoptosis and degeneration of almost all the Müllerian duct (MD).
- Leydig cells' *testosterone* boosts the growth and differentiation of the mesonephric/Wolffian duct (WD), to make the male tubules - efferent ducts to ejaculatory ducts, and the seminal vesicles.
- Testosterone, as 5alpha-dihydrotestosterone (DHT), also:
 - converts the urogenital sinus into the male urethra and prostate;
 - drives the external genitalia into male forms: larger phallus, urethra through the phallus, scrotal halves fused, etc. (The female-male homologues from embryology are needed to understand and correct inter-sex pathologies, seen in the newborn.)
- In the foetal girl, the Wolffian duct, left without testosterone, withers, while the Müllerian structures continue development.

4. *Outcomes of successful sexual development*

In lower case, are the epithelial-lined vestiges of the opposite sex's unneeded duct system. Note that the paradidymis is a remnant of male tubules in the male: surplus efferent ducts.

5. *Problems of sexual development* can arise at several points, thus:

- Absent or faulty SRY gene in the male;
- Failure of testis cells to respond to the gene's product;

- Absent or defective MIF gene; or problems in the MD's response;
- Leydig-cell failure to make and deploy the enzymes to produce testosterone;
- Defective or absent androgen receptor in the Wolffian-duct and external-genital targets for testosterone.

Meiosis provides an opportunity for such genetic defects to arise.

3.3. Literature recommended

Main Sources:

1. L.C. Junqueira, J. Carneiro - “Basic histology” – 11 edition - 2005.
2. “Color Atlas of basic histology” – R.Berns – 2006.
3. Sadler T.V. – “Medical embryology” Montana – 1999.
4. K.E. Jonson - “Histology and cell biology” – 2 edition – Washington – 1991.

Additional ones:

1. Methodical Instructions.

3.4 How to work with the literature recommended:

Main tasks	Recommendations
To review the material	To use the material studied
To learn the material	To use the material on pages
To read and compose the plan	To learn the new material and be ready to write a summary
To answer the questions	
To do the test on the material	To be ready to give an answer to the following:
To be ready to answer the topic	

3.5. Self-control material:

A. Questions to be answered:

1. General characteristic of the male reproductive tract.
2. Male Accessory Glands

B. Test tasks to be done: Tests are applied

4. Self-preparation in the classroom.

1) Listen to the information. 2) Work with the tables and a Light microscope. 3) Ask about the problems that haven't been found in the information given. 4) To sketch in the album the investigated preparations.

5. Self-preparation work at home.

1) Review the material learnt in the classroom. 2) Compose the plan of your answer. 3) Answer the questions to this topic. 4) Do the test given above.

6. The subject of the research work. “Development of male reproductive systems”

<i>Subject</i>	<i>Histology, cytology and embryology</i>
<i>Modul №2</i>	<i>Histology, cytology and embryology</i>
<i>Submodul №4</i>	<i>Special histology</i>
<i>Topic 32</i>	FEMALE REPRODUCTIVE SYSTEM. OVARIES

Hours: 2

1. The topic basis: the topic “**FEMALE REPRODUCTIVE SYSTEM. OVARIES**” is very important for future doctors in their professional activity, positively influences the students in their attitude to the future profession, forms professional skills and experience as well as taking as a principle the knowledge of the subject learnt.

2. The aims of the training course:

- 1) To have general knowledge of the topic studied.
- 2) To understand, to remember and to use the knowledge received.
- 3) To learn the classification, structure and functions of the different histological methods.
- 4) To form the professional experience by reviewing, training and authorizing it.
- 5) To be able to carry out laboratory and experimental work.

3. Materials for the before – class work self – preparation work:

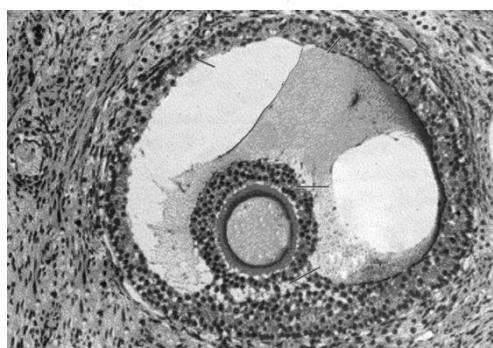
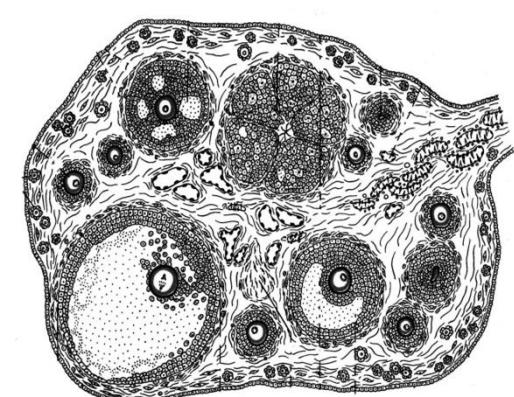
3.1 Basic knowledge, experience, skills necessary for studying the topic in connection with other subjects:

	To know	To be able to
Med. Biology	the structure of the cells and tissues	work with a light microscope
Med. Physics	the structure of the light and electron microscopes	work with a light microscope
Organic Chemistry	the chemical content of the cell	Speak of the topic

3.2 The contents of the topic:

Female reproductive system is a tubular system for the production of ova, and the reception of spermatozoa, their transport and union. It accommodates the fertilized oocyte and ensuing fetus, then expels the fetus at term. The ovary and placenta also have hormone-secreting functions, for instance, to prepare the uterine mucosa to receive, accept, and sustain the fertilized oocyte. Mammae are modifications of the skin for feeding the infant.

Ovary



1. Covered by mostly *simple epithelium* (variably columnar, cuboidal, or squamous), under which is a loose CT, a nominal capsule - *tunica albuginea*.
2. Has a *stroma* of atypical fibroblasts; collagen, as reticular fibres, is present, but not a dominant element; and stromal cells secrete hormones.
3. A fold of peritoneum, the *mesovarium*, connects the ovary at its hilum to the broad ligament, and sends many blood vessels to the fibrous, central, *medullary*, region of the ovary.
4. Peripheral, *cortical*, regions have many *primordial* and *primary follicles*, *maturing Graafian follicles*, which shed the ova (to be fertilized in the upper third of the Fallopian tube), and *glandular masses*.
5. Certain *vestigial structures* remain after development has ceased. These take the form of blind epithelium-lined tubules - *epoöphoron* and *paroöphoron* - lying in the broad ligament by the ovary.
6. Hilar stromal cells may include hormone-secreting *hilus cells*, resembling testicular Leydig

cells, which occasionally give rise to tumours causing a hyperandrogenic syndrome in the woman.

Maturation of the Ovum. Before an ovum can be fertilized it must undergo a process of **maturation** or **ripening**. This takes place previous to or immediately after its escape from the follicle, and consists essentially of an unequal subdivision of the ovum first into two and then into four cells.

Three of the four cells are small, incapable of further development, and are termed **polar bodies** or **polocytes**, while the fourth is large, and constitutes the **mature ovum**.

The process of maturation has not been observed in the human ovum, but has been carefully studied. The number of chromosomes found in the nucleus is constant for all the cells in an animal of any given species, and that in man the number is probably twenty-four.

This applies not only to the somatic cells but to the primitive ova and their descendants. For the purpose of illustrating the process of maturation a species may be taken in which the number of nuclear chromosomes is four. If an ovum from such be observed at the beginning of the maturation process it will be seen that the number of its chromosomes is apparently reduced to two. In reality, however, the number is doubled, since each chromosome consists of four granules grouped to form a **tetrad**.

During the metaphase each tetrad divides into two **dyads**, which are equally distributed between the nuclei of the two cells formed by the first division of the ovum. One of the cells is almost as large as the original ovum, and is named the **secondary oocyte**; the other is small, and is termed the **first polar body**. The secondary oocyte now undergoes subdivision, during which each dyad divides and contributes a single chromosome to the nucleus of each of the two resulting cells. This second division is also unequal, producing a large cell which constitutes the **mature ovum**, and a small cell, the **second polar body**.

3.3. Literature recommended

Main Sources:

1. L.C. Junqueira, J. Carneiro - "Basic histology" – 11 edition - 2005.
2. A.S. Pacurar, J.W. Bigbee – "Digital histology" – Verginia - 2004.
3. "Color Atlas of basic histology" – R.Berns – 2006.
4. Sadler T.V. – "Medical embryology" Montana – 1999.
5. Inderbir Singh Textbook of Human Histology.- Jaypee. India. - 1997.

Additional ones:

1. Methodical Instructions.

3.4 How to work with the literature recommended:

Main tasks	Recommendations
To review the material	To use the material studied
To learn the material	To use the material on pages
To read and compose the plan	To learn the new material and be ready to write a summary
To answer the questions	To be ready to give an answer to the following:
To do the test on the material	
To be ready to answer the topic	

3.5. Self-control material:

A. Questions to be answered:

1. Female reproductive system. Development. Morphofunctional characteristic.
2. Structure of the ovaries. Exocrine and endocrine functions.

B. Test tasks to be done: Tests are applied**4. Self-preparation in the classroom.**

1) Listen to the information. 2) Work with the tables and a Light microscope. 3) Ask about the problems that haven't been found in the information given. 4) To sketch in the album the investigated preparations.

5. Self-preparation work at home.

1) Review the material learnt in the classroom. 2) Compose the plan of your answer. 3) Answer the questions to this topic. 4) Do the test given above.

6. The subject of the research work. "Endocrine functions of female reproductive systems"

<i>Subject</i>	<i>Histology, cytology and embryology</i>
<i>Modul №2</i>	<i>Histology, cytology and embryology</i>
<i>Submodul №4</i>	<i>Special histology</i>
<i>Topic 33</i>	FEMALE REPRODUCTIVE SYSTEM. UTERUS. MAMMARY GLAND

Hours: 2

1. The topic basis: the topic "**FEMALE REPRODUCTIVE SYSTEM. UTERUS. MAMMARY GLAND**" is very important for future doctors in their professional activity, positively influences the students in their attitude to the future profession, forms professional skills and experience as well as taking as a principle the knowledge of the subject learnt.

2. The aims of the training course:

- 1) To have general knowledge of the topic studied.
- 2) To understand, to remember and to use the knowledge received.
- 3) To learn the classification, structure and functions of the different histological methods.
- 4) To form the professional experience by reviewing, training and authorizing it.
- 5) To be able to carry out laboratory and experimental work.

3. Materials for the before – class work self – preparation work:**3.1 Basic knowledge, experience, skills necessary for studying the topic in connection with other subjects:**

	To know	To be able to
Med. Biology	the structure of the cells and tissues	work with a light microscope
Med. Physics	the structure of the light and electron microscopes	work with a light microscope
Organic Chemistry	the chemical content of the cell	Speak of the topic

3.2 The contents of the topic:

UTERUS
Fallopian/Uterine Tube (oviduct)

1. Four parts: *infundibulum* with the *fimbria* - a fringe of processes, engorgeable with blood and moved by smooth muscle to catch the oocyte, wide *ampulla*, with a cell-

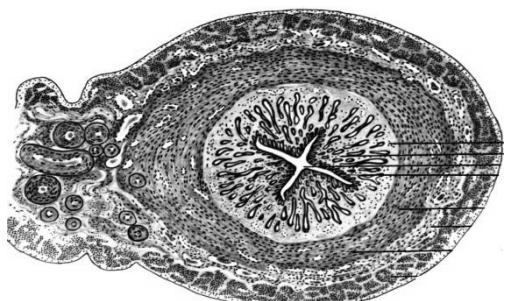
ensnaring labyrinth of protruding mucosal processes, narrow *isthmus* down to the uterus, and an *intramural/ interstitial* section through the uterine wall.

2. Lined by a *highly folded mucosa*, comprising a cellular lamina propria covered by a simple columnar epithelium of columnar *ciliated cells*, and *secretory* cells, varying in height and secretory activity during the menstrual cycle. Secretion is more in the late oestrogen phase around ovulation than in the post-ovulatory progesterone phase. Cilia beat toward the uterus.

3. *Muscularis* of inner, circular, smooth muscle, and a few outer, longitudinal bundles.

4. Covered outside by a *serosa*, with nerves and blood vessels.

5. *Functions* - meeting place for sperm and oocyte; helps 'capacitation' of sperm to their most energetic and zona pellucida-penetrating state; nourishes and transports the zygote.



Corpus uterine

1. Outer serous coat (*perimetrium*), with vessels, nerves, and ganglia.

2. **Myometrium** of interwoven smooth muscle, capable of a great hypertrophy during pregnancy, with many blood vessels in the middle stratum vasculare.

3. **Mucosa/endometrium** with:

1. Simple, columnar, epithelial lining (some cells ciliated);

2. Simple, tubular mucous glands;

3. Loose vascular *stroma* of special fibroblasts, reticular fibres and much ground substance; some stromal cells can become *decidual* around the implantation site;

4. Helicine/coiled *spiral arteries*, a capillary bed, and veins.

4. **Mucosa** of the sexually mature woman experiences cyclic menstrual changes, involving all elements and considerable changes in mucosal thickness, and driven hormonally by the ovary:

1. *Oestrogens*, e.g., oestradiol, from the growing follicle cause cell *proliferation*, and an increase in endometrial height.

2. *Progesterone*, formed by the corpus luteum, then increases cell *secretion* and glycogen accumulation, and the stroma dilates with fluid. The *glands* coil and sacculate. Spiral arteries continue to grow up towards the surface.

3. *Hericine arteries* rhythmically constrict, then dilate, inducing menstruation or breakdown of the endometrium, altered in the last few days of the secretory phase by a reduction in progesterone level, and cytokine signals for cellular apoptosis. This sloughing of the *functional layer* of the endometrium is unaccompanied by blood clotting.

4. *Regeneration* (physiological) takes place from the *basal layer* of the endometrium, where the epithelium survives at the bottom of the glands.

5. The mucosa may experience these cyclic changes minimally, even though no oocyte was shed from the Graafian follicle - an *anovulatory cycle*.

5. **Uterine cervix** differs from the corpus thus:

1. It has more collagen and elastic in the wall than muscle.

2. Mucosa is furrowed by complex clefts - *plicae palmatae*; and does not participate in menstruation.

3. Lining columnar epithelial cells produce a mucus, richly hydrated and penetrable at mid-cycle.

4. Epithelium changes to *stratified squamous* on the portio vaginalis. The boundary between simple columnar and stratified squamous epithelia is unstable, and shifts position by a process of columnar-to-squamous conversion. This *transformation zone* is prone to dysplasia, then malignant change, which can be detected early by examining 'Pap' smears.

Vagina

1. *Adventitia* of CT, with abundant nerves and blood vessels, merges with some longitudinal and a few circular *smooth muscle* bundles, around a wide collagenous lamina propria. All these layers loosen in gestation.

2. *Epithelium* is stratified squamous, rich in glycogen (to promote the growth of benign lactobacilli in the lumen), and influenced by gonadal hormones, but not to the degree seen in rodents.

3. Mucosa has transverse folds or *rugae*, and may have lymphoid nodules, but is without glands.

External Genitalia/Vulva

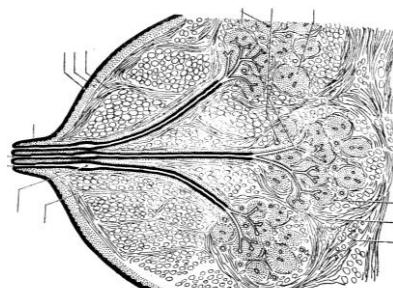
1. *Labia majora* and *minora*, *vestibule* and *hymen* - skin, or stratified squamous epithelium on a loose, fatty or vascular lamina propria.

2. *Clitoris* and *vestibular bulbs* - erectile tissue.

3. *Sensory receptors* are distributed widely in the clitoris, vestibule and labia.

4. *Bartholin's glands* - mucus-secreting, compound, tubulo-alveolar - are homologues of the male Cowper's glands. Other, minor, vestibular, mucous glands lie near the urethra and clitoris. **Mammary Gland/Breast/Mamma**

Structure



1. A collection of compound, tubular (tubulo-alveolar, when active) glands grouped around the *nipple*, where the *lactiferous duct* of each gland opens.
2. Glands are in lobes, separated by dense interlobar CT.
3. In each lobe are:

- a *stroma* of CT - loose collagenous and adipose tissue, with many lymph and blood vessels;

parenchymal tissue of alveoli and ducts, lined with secretory, cuboidal and columnar epithelia.

- Alveoli and ducts also have *myoepithelial cells* between epithelium and basal lamina.

4. *Lactiferous ducts* are lined successively by cuboidal, columnar, stratified columnar, and stratified squamous epithelia. Each duct widens below the nipple into a *sinus*.

Nipple

1. Cornified stratified squamous epithelium covers a stroma of *elastic fibres*, *smooth muscle*, and collagen, through which pass the lactiferous ducts.

2. Epithelium is continuous with the somewhat pigmented, glabrous (hairless) epidermis of the surrounded *areola*, with its sebaceous glands and high dermal papillae.

3. The many *autonomic nerve fibres* to the nipple's *smooth muscle* control its rigidity for suckling, and the relaxation of the milk sinuses.
4. Numerous *sensory receptors* and nerve fibres are present.

3.3. Literature recommended

Main Sources:

1. L.C. Junqueira, J. Carneiro - "Basic histology" – 11 edition - 2005.
2. A.S. Pacurar, J.W. Bigbee – "Digital histology" – Virginia - 2004.
3. "Color Atlas of basic histology" – R.Berns – 2006.

Additional ones:

1. Methodical Instructions.

3.4 How to work with the literature recommended:

Main tasks	Recommendations
To review the material	To use the material studied
To learn the material	To use the material on pages
To read and compose the plan	To learn the new material and be ready to write a summary
To answer the questions	To be ready to give an answer to the following:
To do the test on the material	
To be ready to answer the topic	

3.5. Self-control material:

A. Questions to be answered:

1. Uterus. Morphofunctional characteristic.
2. Mammary glands. Features of its structure during lactation. Hormonal regulation.

B. Test tasks to be done: Tests are applied

4. Self-preparation in the classroom.

- 1) Listen to the information.
- 2) Work with the tables and a Light microscope.
- 3) Ask about the problems that haven't been found in the information given.
- 4) To sketch in the album the investigated preparations.

5. Self-preparation work at home.

- 1) Review the material learnt in the classroom.
- 2) Compose the plan of your answer.
- 3) Answer the questions to this topic.
- 4) Do the test given above.

6. The subject of the research work.

"Endocrine and Female reproductive systems"

<i>Subject</i>	<i>Histology, cytology and embryology</i>
<i>Modul №2</i>	<i>Histology, cytology and embryology</i>
<i>Submodul №4</i>	<i>Special histology</i>
<i>Topic 34</i>	MENSTRUAL CYCLE

Hours: 2

1. The topic basis: the topic “**MENSTRUAL CYCLE**” is very important for future doctors in their professional activity, positively influences the students in their attitude to the future profession, forms professional skills and experience as well as taking as a principle the knowledge of the subject learnt.

2. The aims of the training course:

- 1) To have general knowledge of the topic studied.
- 2) To understand, to remember and to use the knowledge received.
- 3) To learn the classification, structure and functions of the different histological methods.
- 4) To form the professional experience by reviewing, training and authorizing it.
- 5) To be able to carry out laboratory and experimental work.

3. Materials for the before – class work self – preparation work:

3.1 Basic knowledge, experience, skills necessary for studying the topic in connection with other subjects:

	To know	To be able to
Med. Biology	the structure of the cells and tissues	work with a light microscope
Med. Physics	the structure of the light and electron microscopes	work with a light microscope
Organic Chemistry	the chemical content of the cell	Speak of the topic

3.2 The contents of the topic:

Hormonal background

1. Dealing with changing structures, either developing or degenerating; with marked changes in events and appearances at the *menarche*, when ovarian cycles begin, and the *menopause*, when they end. Period between these events called reproductive period.
2. The constant physiological change makes difficult recognizing pathological changes, e.g., uterine bleeding. Female reproduction is a considerable burden in its energy demands, e.g., for fat storage and lactation, which can only be met on an intermittent, i.e., cyclic, basis.
3. FSH and LH/ICSH are pituitary *gonadotrophins* - hormones with the gonads as their target organ.
4. Corpus luteum is also influenced by hormones produced by the *placenta*, if fertilization has occurred - chorionic gonadotrophins.
5. Distinguish between hormones acting on the gonads, and those produced by the gonads and acting on other organs, e.g., uterus.

3. Ovarian/menstrual cycle

1. Maturation of oocyte

- o Oocyte increases in size.
- o Golgi complex and other organelles become more dispersed in the cytoplasm, and lipid droplets appear.

- *Zona pellucida* of glycoprotein forms between the oocyte and surrounding follicular cells; both extend processes into it. The zona pellucida may protect the ovulated and fertilized oocyte from phagocytosis and immune rejection.

2. Development of follicular/granulosa cells and follicle

- Follicular cells are present as a single squamous layer, encircling the dormant oocyte (stage of *primordial follicle*).
- The primary follicle arises by enlargement of the follicular cells - they become cuboidal - and of the oocyte.
- Follicular cells proliferate to a multilayered state (*secondary/preantral follicle*).
- Primary oocyte moves to an eccentric position. Fluid forms, separating follicular cells and collecting in *antra* (spaces). Further cell multiplication, and fluid coalescence, lead to a large follicle, with *liquor folliculi* filling a single antrum (*antral/vesicular/tertiary/Graafian follicle*).
- In the follicular lining of *granulosa cells*, a hillock - *cumulus oophorus* - encloses the oocyte.
- The granulosa cells synthesize materials for the oocyte, and also oestrogens, and inhibin to reduce FSH release from the pituitary.

3. Changes in stroma around maturing follicle

- Stromal fibroblast cells build a capsular *theca*, which differentiates into:
 - an inner *theca interna*: ovoid secretory cells, with lipid droplets; vascular;
 - an outer *theca externa*: fusiform fibroblastic cells packed densely.
- The growing theca interna secretes androgenic precursors of *oestradiol-17beta* for aromatase-mediated conversion by the granulosa cells.
- A glassy *basal lamina* develops between the theca cells and the membrana granulosa lining the follicle.

4. Ovulation

- A sudden surge in LH, coupled with an increase in FSH and a peaking oestrogen level, triggers ovulation, after the completion of meiosis I by the oocyte.
- *Graafian/antral follicle*, grown huge (15 mm diameter), extends to and protrudes from the ovarian surface.
- Protruding apical tissue weakens at the *stigma*, by apoptosis, and enzymatic action on its matrix, and ruptures, helped by thecal cellular contractions; the fluid flows out.
- The fluid takes with it the already floating *secondary oocyte* (a first maturation division having recently occurred), and some attached granulosa cells as a *corona radiata*.

5. Corpus luteum: formation, function and fate

- Burst follicle's walls collapse, becoming folded/plicated.
- Lining granulosa cells become secretory *granulosa lutein cells* - the main component of the *corpus luteum of menstruation* (CLM), or of *pregnancy* (CLP); theca interna cells become secretory *theca lutein cells* (found as small nests of darker cells at the periphery of the main mass of granulosa lutein cells, and accompanying vascular septa into the CLM).
- Lutein cells become enlarged, with many lipid droplets (vacuoles, in H&E preparation) and much smooth ER, and secrete the steroid hormone - *progesterone*, which is collected in capillaries that grow in from the theca interna.

- Progesterone makes the uterine mucosa secretory; and inhibits menstruation and uterine muscle contraction, if implantation occurs.
- The centre of the collapsed follicle fills with clotted blood, which is reorganized by ingrowing fibroblasts and capillaries to form a pale, *central core* of CT.
- Late in pregnancy, or late in the menstrual cycle (if the shed oocyte is not fertilized), the glandular lutein cells degenerate; the corpus luteum shrinks, and is replaced by a small pale mass of hyalinized CT - *corpus albicans* (white to the naked eye in the fresh, unstained ovary).

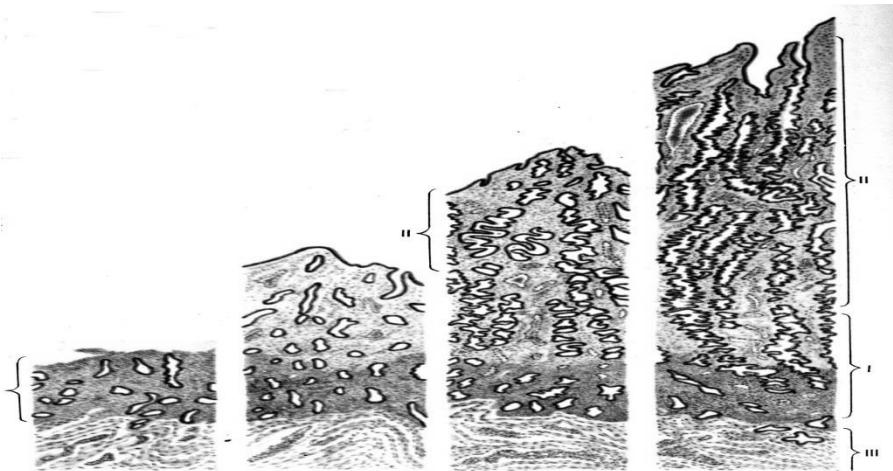
6. Signs of follicular atresia (aborted development)

- Granulosa lining breaks up and sheds apoptotic cells into the antrum.
- Follicle's wall collapses; vessels and CT cells invade.
- Basal lamina thickens to become a 'glassy membrane'.
- Oocyte's nucleus shrinks and becomes pyknotic.
- Zona pellucida folds in, as the oocyte degenerates.
- Theca interna cells enlarge, becoming more glandular to form a temporary interstitial gland.

The Endometrium

The endometrium undergoes marked cyclical changes that constitute the menstrual cycle. The most prominent feature of this cycle is the monthly flow of blood from the uterus. This is called menstruation. The menstrual cycle is divided (for descriptive convenience) into the following phases: postmenstrual, proliferative, secretory and menstrual. The cyclical changes in the endometrium take place under the influence of hormones (oestrogen, progesterone) produced by the ovary.

1. In the postmenstrual phase the endometrium is thin. It progressively increases in thickness being thickest at the end of the secretory phase. At the time of the next menstruation the greater part of its thickness (called the pars functionalis) is shed off and flows out along with the menstrual blood. The part that remains is called the pars basalis.



2. The uterine glands are straight in the postmenstrual phase. As the endometrium increases in thickness the glands elongate, increase in diameter, and become twisted on themselves. Because of this they acquire a saw-toothed appearance in sections. At the time of menstruation the greater parts of the uterine glands are lost (along with the entire lining epithelium) leaving behind only their most basal parts. The lining epithelium is reformed (just after the cessation of menstruation) by proliferation of

epithelial cells in the basal parts of the glands.

The stroma and blood vessels of the endometrium also undergo cyclical changes.

Histophysiology

1. Prepubertal period

- Nipple remains small and weakly pigmented.
- Glands stay rudimentary as multiple, branched, tubular units in a CT stroma.

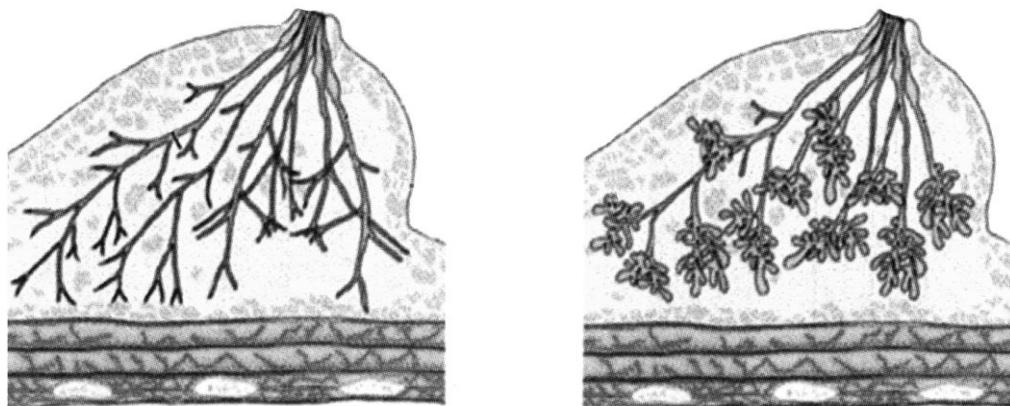
2. Puberty

- *Oestrogen* promotes ductal growth, and the formation of stromal adipose tissue.
- Increasing levels of *progesterone* cause some alveoli to bud out from the duct ends.

3. Early pregnancy: Progesterone and oestrogen cause a marked epithelial proliferation, with increased branching of ducts, which bud out and form many alveoli; these form at the expense of stromal tissue.

4. Late pregnancy and post-parturition

- *Prolactin/mammotrophic hormone* of the anterior pituitary and placenta promotes an 'apocrine' secretory activity in alveolar cells; first of protein-rich colostrum, then milk.
- Milk comprises: proteins, e.g., casein (seen as granules in EM); lactose; minerals; fat (seen as osmophilic droplets in EM) extruded apically as large, membrane-bound bodies; water.
- Secretion needs adequate nutrition, and proper levels of thyroid, adrenal, and other hormones.



5. Lactation

- Numerous white blood cells infiltrate the stroma; some of which on gaining access to alveolar lumens, phagocytose the secretion and become *colostrum bodies*, seen in the first few days after parturition.

- The actual release of milk depends on the stimulus of suckling, acting on receptors in the nipple, which inform the brain to liberate *pitocin* (let-down hormone) from the pituitary's posterior lobe. This hormone makes the *myoepithelial cells* of ducts and alveoli contract.

6. Post-lactational regression and post-menopausal involution

- If the milk is not suckled, it accumulates and secretion slows down.
- Alveolar cells die by apoptosis. The secretions and degenerating alveolar cells are resorbed, leaving the gland with ducts, but fewer alveoli.
- After the menopause or surgical oophorectomy, the alveoli and ducts regress further, cysts may form, and the CT tends to become pale, acellular and hyalinized.

3.3. Literature recommended

Main Sources:

1. L.C. Junqueira, J. Carneiro - "Basic histology" – 11 edition - 2005.
2. A.S. Pacurar, J.W. Bigbee – "Digital histology" – Verginia - 2004.
3. "Color Atlas of basic histology" – R.Berns – 2006.
4. Sadler T.V. – "Medical embryology" Montana – 1999.
5. Inderbir Singh Textbook of Human Histology.- Jaypee. India. - 1997.
6. K.E. Jonson - "Histology and cell biology" – 2 edition – Washington – 1991.

Additional ones:

1. Methodical Instructions.

3.4 How to work with the literature recommended:

Main tasks	Recommendations
To review the material	To use the material studied
To learn the material	To use the material on pages
To read and compose the plan	To learn the new material and be ready to write a summary
To answer the questions	To be ready to give an answer to the following:
To do the test on the material	
To be ready to answer the topic	

3.5. Self-control material:

A. Questions to be answered:

1. Phases of the menstrual cycle.

B. Test tasks to be done: Tests are applied

4. Self-preparation in the classroom.

- 1) Listen to the information.
- 2) Work with the tables and a Light microscope.
- 3) Ask about the problems that haven't been found in the information given.
- 4) To sketch in the album the investigated preparations.

5. Self-preparation work at home.

- 1) Review the material learnt in the classroom.
- 2) Compose the plan of your answer.
- 3) Answer the questions to this topic.
- 4) Do the test given above.

6. The subject of the research work.

<i>Subject</i>	<i>Histology, cytology and embryology</i>
<i>Modul №2</i>	<i>Histology, cytology and embryology</i>
<i>Submodul №4</i>	<i>Special histology</i>
<i>Topic 35</i>	CONTROL TESTS 4

Hours: 2

1. The topic basis: the topic “**CONTROL TESTS 4**” is very important for future doctors in their professional activity, positively influences the students in their attitude to the future profession, forms professional skills and experience as well as taking as a principle the knowledge of the subject learnt.

2. The aims of the training course:

- 1) To have general knowledge of the topic studied.
- 2) To understand, to remember and to use the knowledge received.
- 3) To learn the classification, structure and functions of the different histological methods.
- 4) To form the professional experience by reviewing, training and authorizing it.
- 5) To be able to carry out laboratory and experimental work.

3. Materials for the before – class work self – preparation work:

3.1 Basic knowledge, experience, skills necessary for studying the topic in connection with other subjects:

	To know	To be able to
Med. Biology	the structure of the cells and tissues	work with a light microscope
Med. Physics	the structure of the light and electron microscopes	work with a light microscope
Organic Chemistry	the chemical content of the cell	Speak of the topic

3.2 The contents of the topic:

3.3. Literature recommended

Main Sources:

- 10.L.C. Junqueira, J. Carneiro - “Basic histology” – 11 edition - 2005.
- 11.A.S. Pacurar, J.W. Bigbee – “Digital histology” – Verginia - 2004.
- 12.“Color Atlas of basic histology” – R.Berns – 2006.
- 13.Sadler T.V. – “Medical embryology” Montana – 1999.
- 14.Ronald W., Dudek Ph.D. –“Embryology” 2 edition – 1998.
- 15.Inderbir Singh Textbook of Human Histology.- Jaypee. India. - 1997.
- 16.Ten Cate A.R. Oral Histology.- St.Louis, Baltimore, Toronto.- 1995.
- 17.William A., Beresford M.A. Cytology and Histology.- Anatomy department, West Virginia University, USA.- 1992.
- 18.K.E. Jonson - “Histology and cell biology” – 2 edition – Washington – 1991.

Additional ones:

1. Methodical Instructions.

3.4 How to work with the literature recommended:

Main tasks	Recommendations
To review the material	To use the material studied
To learn the material	To use the material on pages
To read and compose the plan	To learn the new material and be ready to write a summary
To answer the questions	To be ready to give an answer to the following:
To do the test on the material	
To be ready to answer the topic	

3.5. Self-control material:

A. Questions to be answered:

<i>Subject</i>	<i>Histology, cytology and embryology</i>
<i>Modul №2</i>	<i>Histology, cytology and embryology</i>
<i>Submodul №4</i>	<i>Special histology</i>
<i>Topic 36</i>	MODULE 2

Hours: 2

LIST OF THEORETICAL QUESTIONS TO FINAL CONTROL OF THE MODULE 2. SPECIAL HISTOLOGY AND EMBRYOLOGY.

1. The development of the nervous system.
2. Regeneration of nerves.
3. Brainstem.
4. Age-related changes in the nervous system.
5. The development of the eye.
6. Auxiliary apparatus of the eye.
7. Development of the ear.
8. The development of the organ of smell.
9. Age-related changes of the senses.
10. Derivatives skin.
11. Age-related changes in the skin.
12. The development of the cardiovascular system.
13. Embryonic hematopoiesis.
14. Characteristic of immunoglobulins.
15. Mechanisms of integration of elements of the immune system.
16. Morphofunctional characteristics of the lymphatic system.
17. Organ structural features of the blood vessels.
18. Haemolymphatic nodes.
19. Dissociated endocrine system.
20. Morphofunctional characteristics of gastrointestinal endocrinocytes.
21. Development of oral cavity and digestive system.
22. Lymphoid ring Valdeyera-Pirogov.
23. Morphofunctional characteristics of the salivary glands.
24. Age-related changes in the tissues of the tooth.
25. Histophysiology processes of digestion and absorption in the small intestine.
26. Morphofunctional characteristics of the appendix.
27. Blood supply of the nephron.
28. Endocrine system kidneys.
29. Features of male and female reproductive systems.
30. Endocrine function of female and male reproductive systems.

