MINISTRY OF HEALTH PROTECTION OF UKRAINE
ODESSA NATIONAL MEDICAL UNIVERSITY

Faculty of **medicine**

Department **of general and clinical pathophysiology**

I APPROVE

Vice-rector for scientific and pedagogical work

Ass. Prof. _____ Eduard BURYACHKIVSKYJ

September 1, 2023

METHODOLOGICAL DEVELOPMENT
TO PRACTICAL LESSONS
FROM EDUCATIONAL DISCIPLINE

Faculty of Medicine, course 3

Educational discipline - " **pathophysiology"**

Approved:
At the meeting of the Department of *General and Clinical Pathological Physiology named after V.V. Podvysotsky* Odesa National Medical University

Protocol No. 1 of August 31, 2023

Head of the Department _____ Professor Ruslan VASTYANOV

Developers:

_____ prof. R.S. Vastyanov
_____ prof. S.G. Kotyuzhynska
_____ ace I.O. Ostapenko
_____ Assoc. V.P. Babyi
_____ Assoc. D.E. Lapshyn
_____ Assoc. O.M. Pospelov
_____ Art. off L.V. Goncharova
_____ as. V.V. Kirchev
_____ as. V.M. Sarahan

PRACTICAL TRAINING

Content module 1. General nosology. Pathophysiology of the cell.

Practical lesson No. 1

Topic: Subject, methods and tasks of pathophysiology. The history of its development. General etiology and pathogenesis.

Practical lesson No. 2

Typical reactions of cells to damage: types, mechanisms of development. Apoptosis and necrosis.

Practical lesson No. 3

Topic: Typical disorders of peripheral blood circulation and microcirculation: classification, etiology and pathogenesis.

Practical lesson No. 4

Topic: Inflammation: etiology, pathogenesis . Mediators. Local signs. Exudation and proliferation.

Practical lesson No. 5

Topic: Exudation and proliferation. General disorders of microcirculation in the focus of inflammation.

Practical lesson No. 6

Topic: Disorders of thermoregulation: hypo and hyperthermia. Fever: etiology, pathogenesis.

Purpose: Acquisition by the student of higher education of knowledge and formation of elements of professional competences in the field of medicine from the sub-division of pathophysiology:

Topic 1. About health, disease, general concepts of etiology and pathogenesis.
Topic 2. About cell damage. Apoptosis . Necrobiosis. Necrosis.
Topic 3. Typical disorders of peripheral blood circulation and microcirculation: classification, etiology and pathogenesis.
Topic 4 . Inflammation: etiology, pathogenesis. Mediators.
Topic 5 . Exudation and proliferation. General disorders of microcirculation in the focus of inflammation.
Topic 6 . Violations of thermoregulation: hypo and hyperthermia. Fever: etiology, pathogenesis.

Improvement of skills and competences acquired during the study of previous disciplines.

Basic concepts:

Topic 1. About health, disease, general concepts of etiology and pathogenesis.
Topic 2. About cell damage. Apoptosis . Necrobiosis. Necrosis.
Topic 3 . Typical disorders of peripheral blood circulation and microcirculation: classification, etiology and pathogenesis.
Topic 4 . Inflammation: etiology, pathogenesis. Mediators.
Topic 5 . Exudation and proliferation. General disorders of microcirculation in the focus of inflammation.
Topic 6 . Violations of thermoregulation: hypo and hyperthermia. Fever: etiology, pathogenesis.

Equipment: Multimedia presentations, tables.

Plan:

1. **Organizational activities (greetings, verification of those present, announcement of the topic, purpose of the lesson, motivation of higher education seekers to study the topic).**
2. **Control of the reference level of knowledge:**

Topic 1. Subject, methods and tasks of pathophysiology. The history of its development. General etiology and pathogenesis.

"Pathophysiology" is the science of the vital activity of a sick organism ("pathology" from the Greek . Pathos - disease, suffering + 1oroc - teaching, science; "physiology" (from the Greek . Phusis - nature + 1oroc).

Pathological physiology studies the main regularities of the occurrence, development and outcome of the disease. The ultimate goal of pathophysiology is to reveal the laws by which the disease develops.

The pathophysiology course consists of 2 sections: general pathophysiology and private pathophysiology.

The first section - general pathophysiology consists of general nosology and the doctrine of typical pathological processes. General nosology considers the essence of diseases , causes (etiology) and mechanisms of development (pathogenesis), as well as mechanisms of recovery (sanogenesis).

Nosology forms the basic concepts and categories of pathology, creates classifications and nomenclature of diseases , studies the social aspects of the disease.

Basic concepts of general nosology:

Health is a state of complete physical, mental and social well-being, and not just the absence of disease or physical defects (WHO definition, 1946). This is, first of all, the state of the organism, in which the correspondence of structure and function, as well as the ability of regulatory systems to maintain the constancy of the internal environment (homeostasis), is noted.

The norm is a state of optimal life activity and development of the organism.

A disease is a violation of the normal vital activity of an organism when it is affected by harmful agents, as a result of which its adaptive capabilities are reduced

(MM Zaiko).

Classification of diseases is a certain system of distribution of diseases and pathological conditions into classes, groups and other headings according to established criteria.

1. Etiological principle - hereditary and acquired, infectious and non-infectious , etc.

2. Anatomical and topographic principle - cardiovascular diseases, respiratory diseases, kidney diseases , etc.

3. By age and gender - children's diseases, women's diseases, diseases of old age.

4. Pathogenetic principle - allergic diseases, inflammatory diseases, metabolic diseases , etc.

5. Depending on the state of structural and functional disorders - organic and functional diseases.

6. According to the clinical course - acute and chronic, subacute .

7. Depending on the methods that are mainly used to treat the disease - therapeutic and surgical.

A pathological reaction is an inadequate and biologically inappropriate response of the body to the action of ordinary or excessive stimuli. Examples: various types of pathological reflexes, allergies, a short-term increase in blood pressure after nervous tension or a decrease in blood sugar due to the introduction of large doses of insulin , etc.

A pathological process is a sequence of reactions that naturally occur in the body to the harmful effect of a pathogenetic factor . Examples of pathological processes are inflammation of lung tissue in pneumonia, hypoxia in obliterating endarteritis , inflammation of the heart muscle during myocardial infarction, fever during typhoid fever , etc.

A pathological condition is a set of pathological changes in the body that arise as a result of the development of a pathological process. In the narrow sense of the word, it is a persistent deviation from the norm that has a negative biological meaning. Examples of pathological conditions are a stump after amputation of a limb, cicatricial tissue changes after a thermal burn, atrophy of the alveolar processes of the jaw in connection with the removal or loss of teeth, an acquired defect of the valve apparatus hearts

Typical pathological processes are such processes that have the same laws of development regardless of the cause, localization, species of animals and individual characteristics of the organism. Examples: inflammation, tumor growth, local circulatory disorders, hypoxia, starvation, fever.

In the development of the disease, 4 periods (stages) are distinguished:

- latent (regarding infectious diseases - incubation) lasts from the moment of exposure to the cause until the appearance of the first clinical manifestations of the disease;
- prodromal is the period of time from the first non-specific signs of the disease to the full manifestation of its symptoms;
- the period of exacerbation of the disease is characterized by the full development of

the clinical picture: convulsions in parathyroid insufficiency , leukopenia in radiation sickness, hyperglycemia and glucosuria in diabetes;

- the period of the end of the disease: complete and incomplete recovery, relapse, transition to a chronic form, remission, complications, death.

Complete recovery is a state in which all manifestations of the disease disappear and the body fully restores its functions.

In case of incomplete recovery, the consequences of the disease are pronounced. They remain for a long time or forever.

Remission is a temporary improvement of the patient's condition, which manifests itself in slowing down or stopping the disease process, partially reversing the development or disappearance of clinical manifestations or the pathological process.

Exacerbation is a stage of the course of a chronic disease characterized by an increase in existing symptoms or the appearance of new ones.

A complication is a pathological process secondary to the existing diseases , which arises in connection with the peculiarity of the pathogenesis of the primary (main) disease or as an unforeseen consequence of medical measures.

Relapse - restoration or strengthening of the manifestations of the disease after their temporary disappearance, weakening or termination of the pathological process.

Death is the most unfavorable outcome of the disease. It can be natural (physiological from aging) and premature, which can be violent (murder) and from disease. In addition, there is brain death (sudden death of the brain against the background of all healthy organs supported by artificial ventilation) and somatic death, which occurs as a result of irreversible, incompatible with life damage to any organ, organs or systems. It occurs more often in chronic diseases, when the cerebral cortex and internal organs die simultaneously, but slowly.

The terminal state is a reversible fading of the body's functions , which precedes biological death, when the complex of protective and compensatory mechanisms is insufficient to eliminate the effects of the pathogenic factor on the body. The cessation of vital functions occurs gradually, and the dynamics of this process allows us to distinguish several phases that are observed during the death of an organism: preagony , agony, clinical and biological death.

Clinical death is a terminal state that occurs after cessation of cardiac activity and breathing and continues until the onset of irreversible changes in the higher departments of the central nervous system. During clinical death, external signs of life (consciousness, reflexes, breathing, heart rate) are absent, but the body as a whole has not yet died, energy substrates are stored in its tissues and metabolic processes continue, therefore, with timely resuscitation measures, it is possible to restore all body functions.

Biological death is an irreversible state, when reviving the organism as a whole is no longer possible, and the restoration of its individual functions (for example, cardiovascular activity) with the help of resuscitation measures loses its meaning.

General etiology (Greek . Aitia - cause, logos - science, teaching) - teaching

about the causes and conditions of disease occurrence and the principles of etiotropic prevention and therapy.

The cause of the disease should be considered the pathogenic factor without which it cannot occur under any conditions. Conditions for the occurrence of the disease are factors that reliably increase the probability of the occurrence of the disease. Example: the cause of ARVI is a virus, the conditions are hypothermia, fatigue, reduced immunity.

A risk factor is a general name for factors that are not the direct cause of a certain disease, but increase the likelihood of its occurrence.

Classification of etiological factors.

- physical - mechanical action, ionizing radiation, high and low temperature, electric current, etc.;
- chemical - inorganic and organic compounds of natural and artificial origin;

rickettsia , bacteria, protozoa, etc.

- psychogenic - negative emotions, etc.

General pathogenesis (pathos - disease, suffering; genesis - origin , birth) - the doctrine of the general mechanisms of development, course and consequences of the disease and the principles of pathogenetic prevention and therapy.

The relationship between the cause of the disease and its pathogenesis.

1. The etiological factor plays the role of a trigger and includes the process of disease development. For the further course of pathogenesis, the continued existence of the cause is not mandatory (for example, radiation sickness, mechanical trauma, thermal injuries).

2. Parallel existence of the cause and pathogenesis. The mechanism of disease development functions as long as the causative factor operates. Most infectious diseases can serve as an example of this type of interaction between the cause and the mechanism of the disease.

3. Persistence of the etiological factor . Disease-causing agents stay in the body longer than the pathogenesis itself. At the same time, the properties of the etiological factor may change under the influence of the organism. An example is bacteremia after infectious diseases.

Adaptation - this is the adaptation of the organism and its structures to the changing conditions of the external environment. Adaptation ensures preservation of homeostasis and prevents damage under the influence of normal environmental factors.

Compensation is a condition that develops as a result of the implementation of compensatory reactions and processes aimed at restoring disturbed homeostasis due to the influence of pathogenic factors.

The second section of general pathological physiology is the study of typical pathological processes. The section contains data on the processes underlying many diseases, namely: inflammation, tumor growth, fever, hypoxia, typical metabolic disorders, starvation.

The second section of pathological physiology - private pathophysiology - examines disorders in individual organs or systems: blood circulation, breathing, endocrine, nervous systems , etc.

Research methods, significance of the experiment in pathophysiology

Pathophysiology is an experimental science. Therefore, its main method is an experiment on living objects. A pathophysiological experiment differs from a physiological one by modeling a human disease on laboratory animals. Currently, it is possible to reproduce such pathological processes on animals as traumatic shock, diabetes, atherosclerosis, myocardial infarction, kidney inflammation, arterial hypertension , etc. Meanwhile, we must not forget that the human body is much more complex than even the most highly organized animals and is under the constant influence of social factors, which is why it is almost impossible to get the full extent of human diseases on animals. It is possible to reproduce only some pathogenetically important links, symptoms and syndromes of a human disease. Physiological, electrophysiological, biophysical, biochemical, hematological, morphological, immunological, mathematical research methods are used in the experiment. Pathophysiological experiment, in contrast to clinical observation, has a number of beneficial advantages. These benefits include the ability to:

1. Clarification of the causal factors of the disease;
2. Observations from the pre-disease period and the earliest stage of the disease to the result;
3. Research of incurable forms of the disease;
4. Conducting experimental therapy.

All these possibilities are sharply limited in clinical conditions. All experiments can be acute and chronic. An acute experiment is needed to study the effects of blood loss. Tumor development is studied in a chronic experiment. Conducting the experiment involves humane treatment of animals (using anesthesia). It is unacceptable to conduct an experiment that will cause suffering to the animal.

Topic #2 Typical reactions cells for damage : types , mechanisms development _ Apoptosis and necrosis.

Cell damage, as a typical pathological process , is its basis

Pathogenetic mechanisms of cell damage - violent; cytopathic .

Lipid mechanisms 1) peroxide oxidation of lipids (POL), 2) activation of membrane phospholipases, and 3) detergent effect of an excess of free fatty acids. Activation of membrane phospholipases . Determination of cell damage, its specification.

Prove that cell damage is a typical pathological process. Describe the causes of cell damage . Role peroxide lipid oxidation (POL) in cell membrane damage. Molecular mechanisms of damage development.

Pathogenesis of cell damage - mechanisms

1) lipid,
2) calcium,
3) electrolyte -osmotic,
4) acidotic ,
5) protein and
6) nucleic.

Cell damage is a typical pathological process , the basis of which is a violation of intracellular homeostasis, which leads to a violation of the structural integrity of the cell and its functional capabilities .

Cell damage classify:

1) Depending on the speed of damage development, the following are distinguished: a) acute - develops quickly, as a rule, as a result of a one-time, but intensive impact of a damaging agent , b) chronic - runs slowly and is the result of long-term, but less intense pathogenic influence.

2) Depending on the degree of violations of intracellular homeostasis, they are distinguished: a) reverse - disappear after the cessation of the harmful effect factor , b) irreversible - lead to cell death.

3) Depending on the period of the cell life cycle: a) mitotic and b) interphase .

4) Depending on the etiological factor : a) direct (primary) damage and b) indirect damage.

Direct (primary) damage occurs as a result of the direct effect on the cell of the pathogenic agent :

- physical (mechanical impact, high and low temperature, ultraviolet and ionizing radiation, etc.) ;
- chemical (inorganic and organic substances artificial and natural origin);
- biological (bacteria, viruses, fungi, protozoa).

Indirect damage occurs as a result of primary disturbances in the stability of the internal environment of the body and is caused by hypoxia, hypo - and hyperthermia, acidosis, alkalosis, hyper- and hyposmia , hyper- and hypoglycemia, hypo- and avitaminosis , an increase in the content of the final toxic products of metabolism (ammonia , bilirubin, indole, skatole, etc.) in the body .

5) Depending on the pathogenetic mechanisms, cell damage is divided into: a) violent and b) cytopathic .

Violent - occurs in in case of action on a healthy cell by physical, chemical and biological factors, the intensity of which exceeds the threshold stimuli to which the cell has adapted

Cytopathic - occurs as a result of a primary violation of the protective and adaptive mechanisms of the cell and then natural for irritations of this cell become harmful .

The following signs indicate cell damage:

1) Structural - detected using histological and electron microscopic methods.

2) Functional - accompanied by: a) violation of electrophysiological processes, b) violation of contractility, c) violation of exo - and endocytosis ; violation of cell division , etc.

3) Physico-chemical - accompanied by: a) disruption of cellular colloids, b) changes in water-electrolyte exchange , etc.

4) Biochemical - accompanied by a violation of internal and extracellular concentration of various substances.

5) Thermodynamic - accompanied by conformational changes of macromolecules that occur in the direction of the most favorable thermodynamic state (denaturation).

• Pathogenesis of cell damage.

There are 6 groups of molecular mechanisms that are important in the pathogenesis of cell damage: 1) lipid, 2) calcium, 3) electrolyte -osmotic, 4) acidotic , 5) protein and 6) nucleic.

I. Lipid mechanisms

include:

1) lipid peroxidation (POL),
2) activation of membrane phospholipases
3) detergent effect of an excess of free fatty acids.

Peroxide oxidation of lipids is the free radical oxidation of unsaturated fatty acids that are part of the phospholipids of cell membranes.

The initiators of POL are free radicals - these are molecules or atoms with an odd number of electrons, which gives them high reactivity and the ability to interact with different substances.

Among them, the most important are:

a) $^{\bullet}O_2$) $HO_2^{\bullet}$) - superoxide radical;
b) $OH^{\bullet}$ - hydroxyl radical;
c) $H^{\bullet}$ - hydrogen radical;
d) $^{\bullet}O_2$ - singlet (excited) oxygen.

One of these primary free radicals (A*) interacts with a molecule of an unsaturated fatty acid (FA), resulting in the formation of a free radical of this acid (X*) and a molecular reaction product (CA):

A* + ZK = Z* + KA.

The free radical of the fatty acid (F*) further interacts with molecular oxygen (O_2), which is always present in the cell, as a result of which the peroxide radical of this acid is formed:

F* + O_2 = VHOO*

Peroxide radical (ZHOO*), v own in turn, interacts with the adjacent molecule of unsaturated fatty acid (FA), resulting in the formation of hydroperoxide (FAO) and a new free radical (F*):

Vocational school* + ZhK = Vocational school + Zh* .

It should be noted 2 important features of POL:

□ First: LPO reactions have a chain character. This means that free radicals are not destroyed in the course of LPO reactions and more and more molecules of unsaturated fatty acids are involved in the process.

□ Secondly: LPO reactions have a branched nature. In other words, free radicals appear in increasing quantities in LPO reactions, the source of which are the LPO intermediates themselves. An example can be the formation of free radicals from lipid hydroperoxides during their interaction with metals of variable valency present in the cell:

$$XOOH + Fe^{2+} \rightarrow XO^{\bullet} + OH + Fe^{3+}.$$

□ In the course of many normal biochemical reactions in the body, a small amount is formed the number of free radicals. But there is always a danger of LPO activation in the cell. However, this does not happen under natural conditions, since the cell

has antioxidant protection mechanisms at its disposal, thanks to which the inactivation of free radicals, limitation and inhibition of LPO is achieved.

The cell has the following antioxidant systems:

I) Enzymatic antioxidant systems:

A) Superoxide dismutase , which includes superoxide dismutase (SOD) and catalase (K). Inactivates superoxide radicals ($HO_2^{\bullet}$):

B) Glutathione , which includes: glutathione (G), glutathione peroxidase (GP), glutathione reductase (GR), NADP•H_2 . Inactivates and destroys lipid hydroperoxides .

2) Non-enzymatic antioxidants:

A) "Real" antioxidants include: tocopherols, ubiquinones , naphthoquinones , flavonoids , steroid hormones, biogenic amines. Inactivate free radicals of fatty acids.

B) Auxiliary antioxidants include: ascorbic acid and sulfur-containing compounds (glutathione , cystine , cysteine). Restore (regenerate) "real" antioxidants.

LPO activation occurs in 2 cases:

□ The first is associated with the excessive formation of primary free radicals, due to which the antioxidant systems present in the cell are unable to overcome reactions of lipid peroxidation.

According to this mechanism, LPO is activated in the event of a damaging effect on cells: a) ultraviolet and ionizing radiation (the burning process should be regulated), b) under the influence of some poisons (carbon tetrachloride), c) under conditions of stress, since free radicals are formed from catecholamines , d) with hypervitaminosis D, since free radicals are formed during autooxidation ergocalciferol .

□ The second is related to the malfunctioning of antioxidant systems of cells. In this case, the initiator of POL is primary free radicals, which are formed under conditions of naturally occurring metabolism. The lack of antioxidants can be caused by:

a) hereditary and acquired disorders of their synthesis,

b) deficiency of metals (iron, copper, selenium) necessary for the functioning of these enzymes,

c) hypo- and vitamin deficiency IS and C (that's why you need to eat walnuts - a lot of vitamin E, sauerkraut - a lot of vitamin C),

d) violations of the pentose cycle and cycle Krebs, which leads to a decrease in the formation of NADPH•N and NAD•N, which under normal conditions ensure the restoration of true and auxiliary antioxidants.

Activation of membrane phospholipases . Excessive activation of phospholipase A_2 - an enzyme that cleaves phospholipids of cell membrane structures into a) unsaturated fatty acids and b) lysophospholipids is important in the pathogenesis of cell damage .

Unsaturated fatty acids, in particular arachidonic, under the influence of certain enzymes, they are transformed into biologically active substances - e and cosanoids, which include: a) prostaglandins , b) prostacyclin , c) thromboxane , and d) leukotrienes .

Lysophospholipids have the ability to form micelles and are very strong detergents. WITH the detergent effect of lysophospholipids and the related damage to membranes in conditions of excessive activation of phospholipase A_2 , and the main factor causing such activation is a high concentration of Ca ions in the cytoplasm.

Detergent action of an excess of free fatty acids . Free fatty acids in high concentrations, as well as lysophospholipids, show a detergent effect. and cause damage to the lipid bilayer of cell membranes.

4 main mechanisms can be distinguished increasing the content of free fatty acids in the cell:

1) Increased influx of free fatty acids into the cell with hyperlipacytemia (increased concentration of free fatty acids in the blood), which is observed when lipolysis processes are activated in adipose tissue (stress, diabetes).

2) Enhanced formation of free fatty acids from the triglyceride part of lipoproteins in lysosomes (with atherosclerosis).

3) Increased release of free fatty acids from phospholipids of cell membranes under the influence of phospholipases.

4) Violated use of free fatty acids by the cell as a source of energy (reduction of beta-oxidation enzymes and the Krebs cycle at hypoxia).

The lipid mechanisms of cell damage described above lead to a violation of the main functions of the lipid biolayer of cell membranes: a) barrier and b) matrix.

IN there are two main mechanisms underlying the disruption of the barrier function: a) ionophore and b) an electrical breakdown mechanism.

The first is due to the appearance in the cell of substances that have the properties of ionophores , i.e. compounds capable of facilitating the diffusion of ions through the membrane by forming complexes ion and ionophore . In the professional cycle , the activation of POL especially appears ionophores relative to Ca and H ions , which facilitates their easier passage through cell membranes.

The second mechanism is implemented through existing on many membranes the difference in biopotentials . The above-mentioned shifts in lipid metabolism disrupt the electrical insulating properties of cell membranes, reduce their electrical stability, which leads to an electrical breakdown of the membrane, that is, to its electromechanical rupture with the formation of new transmembrane channels of ion conduction.

certain enzymes and some specialized proteins embedded in the lipid biolayer . There is no doubt that changes in the lipid components of membranes largely determine the properties of protein molecules and enzymes.

IN the basis of violations of the barrier functions of cell membranes during LPO activation are the following mechanisms:

1) The ionophore mechanism is due to the appearance in the cell of substances that have the properties of ionophores , i.e. , compounds capable of facilitating the

diffusion of ions through the membrane due to the formation of ion and ionophore complexes . In the process of LPO activation, ionophores appear , which the permeability of cell membranes for calcium and hydrogen ions increases.
2) The mechanism of electrical breakdown is associated with the existence of a potential difference on many membranes. As a result of the appearance of hydrophilic lipid products, the electroinsulating properties of the hydrophobic layer of cell membranes are disturbed, which leads to an electrical breakdown of the membrane, that is, to an electromechanical rupture of it with the formation of new transmembrane channels of ion conduction.
3) Violation of the matrix function of the lipid biolayer of membranes, which under normal conditions is determined by the enzymes embedded in it and some specialized proteins that change their activity in the LPO process, as their lipid microenvironment changes.

II. Calcium mechanisms

Damage to cellular structures can be caused by a persistent increase in the concentration of Ca^{2+} ions in the cell cytoplasm. Such a situation arises: 1) as a result of an excessive influx of ions Ca^{2+} into the cytoplasm (hypercalcemia , increased permeability of the plasma membrane), or as a result of disruption of the mechanisms that ensure removal of Ca^{2+} ions from the cytoplasm (disruption of Ca pumps, Na - Ca exchange mechanism, Ca-accumulating function of mitochondria).

An increase in the concentration of Ca^{2+} ions in the cytoplasm causes:
a) contracture of the fibrillar structures of the cell (myofibrils , elements of the cytoskeleton); b) activation of phospholipase A_2 ; c) violation of the connection between oxidation and phosphorylation processes .

III. Electrolyte -osmotic mechanism

Cell damage is caused by changes in the content of basic cellular cations Na^+ and K^+. Equalization of ion concentrations Na^+ and K^+ on both sides of the plasma membrane (an increase in the content Na^+ and decrease in content K^+ in the cytoplasm) can basically have two mechanisms: 1) increased diffusion of ions through the plasma membrane along the existing concentration and electrical gradient and 2) disruption of active transport mechanisms Na^+ and K^+ (Na -K-pump).

The first mechanism is implemented in conditions of general disturbances of water-electrolyte exchange (hypernatremia , hypokalemia) and violation of the barrier function of the plasma membrane (increased ion permeability).

Function disorders Na -K-pumps can be due to a deficiency of ATP in the cell, an increase in the cholesterol content in the lipid bilayer of the membrane (for example, in atherosclerosis), the action of a number of specific inhibitors Na -K-ATP-ases (for example, strophanthin).

Changes in the content of ions Na^+ and K^+ cause: a) loss of the cell's electric membrane potential (resting potential); b) cell swelling; c) osmotic stretching of cell membranes, which is accompanied by an increase in their permeability.

I. Reactions aimed at restoring disturbed intracellular homeostasis: a) activation of the mechanisms of active transport of substances (Na -K-, Ca - pumps; Na-Ca -, Na -H exchange mechanisms, microvesicular transport); b) increased regeneration of antioxidants; c) binding of free fatty acids (synthesis of triglycerides); d) activation of the synthesis of proteins, nucleic acids, phospholipids, etc.

An indispensable condition for the implementation of these mechanisms is sufficient energy supply of the cell. This is achieved by increasing the intensity of energy exchange (activation of glycolysis, cellular respiration, pentose cycle) and redistribution of energy resources available in the cell.

II. Reactions aimed at creating a functional rest of the damaged cell.

Their goal is to eliminate possible additional shifts in intracellular homeostasis under the influence of physiological pathogenic factors (damage stabilization) and to minimize energy costs for the performance of specific cell functions.

Such reactions include: a) production of prostaglandins by the cell and blockade by them β- adrenoceptors ; b) inhibition of adenylate cyclase and increase in the activity of phosphodiesterase , which destroys cAMP ; c) the formation of adenosine - a natural blocker of Ca channels, etc.

Topic 3. Typical disorders of peripheral blood circulation and microcirculation: classification, etiology and pathogenesis.

Definition of the concept of local blood circulation disorders. General characteristics of forms of local circulatory disorders. Arterial hyperemia: definition, classification, general signs. Causes and mechanisms of development of physiological arterial hyperemia. Pathological arterial hyperemia: causes, mechanism of development, experimental models, consequences.

Venous hyperemia: definition, causes, mechanism of development, general signs, consequences. Ischemia: definition, mechanism of development, general signs. Characteristic etiological compression ischemia factors, obturational and angiospastic types Mechanism of ischemic damage to cells. Factors determining high tissue sensitivity to ischemia. Possible consequences of ischemia.

Thrombosis: definition, causes, mechanism of development, consequences. Stasis: definition, classification, characteristic features, etiology, pathogenesis. Embolism: definition, principles of classification, etiology and pathogenesis of certain types of embolism.

Arterial hyperemia - an increase in blood filling of an organ or a tissue area due to an increase in arterial blood flow.

Reasons:

- physical (temperature, UV radiation);
- chemical (turpentine , mustard powder);
- biological (toxins);
- psychogenic (emotions).

Species:

- ***physiological*** (develops in connection with the increased need of tissue for oxygen and nutrients): *working* (functional) - caused by the metabolic needs of an organ or tissue in connection with an increase in their functioning. For example, hyperemia in the muscle during physical work, hyperemia of the pancreas and intestinal wall at the time of digestion, hyperemia of the endocrine gland during secretion, hyperemia of the salivary glands. An increase in the contractile activity of the myocardium leads to an increase in coronary blood flow, activation of the brain is accompanied by an increase in its blood supply. *Reactive* (postischemic) arterial hyperemia is observed after a temporary cessation of blood flow (temporary ischemia) and has a protective and adaptive nature (removal of the tourniquet).

- ***pathological*** - develops during pathological processes, such as allergy, fever, inflammation.

The leading link of pathogenesis: dilation of arterioles and increase in arterial blood flow.

Mechanism of arterial expansion:

- **neurogenic:** decrease in the tone of vasoconstrictors (neuroparalytic), increase in the tone of vasodilators due to acetylcholine (neurotonic);

- **humoral** (myoparalytic) - expansion of blood vessels with the help of BAV: histamine , bradykinin , lactic acid, excess carbon dioxide, nitric oxide, adenosine, hypoxia, some prostaglandins , etc.

Manifestations arterial hyperemia:

- reddening of a tissue area due to an increase in the number of functioning capillaries and arterialization of venous blood;

- local increase in temperature (increased arterial blood flow and increased redox processes in the tissue;

- increase in tissue turgor (dilation of blood vessels, increase in blood supply);

- dilation of arterioles, increase in blood flow rate, increase in intracapillary pressure, increase in the number of functioning capillaries.

Consequences: - *positive* : improvement of delivery of oxygen and nutrients to the body , strengthening of metabolic processes and function of the body ; - *negative* : rupture of a vessel with hemorrhage in the presence of pathology, generalization of infection, progression of tumor growth and metastasis.

Venous hyperemia - increased blood supply to an organ or tissue area due to obstruction of venous blood outflow.

Reasons:

- vein thrombosis;

- compression of veins from the outside by a tumor, enlarged uterus during pregnancy, scar, exudate, tourniquet;

- violation of general hemodynamics in right ventricular heart failure;

- constitutional insufficiency of the valve apparatus of veins.

The leading link of pathogenesis: obstruction of the outflow of venous blood.

Mechanism of development: circulatory hypoxia → cell damage → cell death → sclerosis; local intoxication due to the accumulation of lactic acid, carbon dioxide → metabolic acidosis

Manifestations venous hyperemia:

- cyanosis of a tissue area due to increase in the blood of reconstituted hemoglobin ;
- local decrease in temperature (reduction of regenerative processes in the tissue, increase in heat transfer);
- increase in organ volume (increased blood supply, edema);
- expansion of veins and capillaries, slowing of blood flow;
- increase in fluid filtration, decrease in its reabsorption, difficulty in lymphatic outflow .

Consequences: - *positive* : slowing down the development of the local infectious process, facilitating the migration of leukocytes to the focus of inflammation; *negative* - atrophy of parenchymal elements, growth of connective tissue and development of sclerosis.

Ischemia - decrease in blood supply to an organ or tissue area due to a decrease in arterial blood flow.

Reasons:

- compression of arteries from the outside,
- arterial thrombosis and embolism,
- angiospasm of arteries,
- atherosclerotic damage to the inner lining of arteries.

The leading link of pathogenesis: decrease in arterial blood flow.

Mechanism of development: Violation of energy metabolism: $\downarrow O_2 \rightarrow$ violation of oxidative phosphorylation in mitochondria $\rightarrow \downarrow$ ATP $\rightarrow$ violation of contractile and secretory functions of cells, violation of active transport of substances $\rightarrow$ necrosis, increased biosynthesis of connective tissue components $\rightarrow$ sclerosis.

Manifestations of ischemia:

- paleness of the tissue area at the expense of decrease in blood supply and the number of functioning capillaries;
- local decrease in temperature (decrease in flow of warm arterial blood, decrease in redox processes in the tissue);
- pain or paresthesias (irritation of nerve endings by products of metabolism (H^+, K^+);
- organ size reduction (reduction in blood supply);
- reduction of intravascular pressure, slowing of blood flow, reduction of the number of functioning capillaries, reduction of fluid filtration, reduction of lymph outflow .

Consequences of ischemia: restoration of blood circulation in collateral vessels, impaired nutrition and tissue death (necrosis).

Stasis - stoppage of blood flow in the vessels of the microcirculatory channel.

Species:

- ischemic due to cessation of arterial blood flow;
- venous in connection with termination outflow of venous blood;
- capillary (true) - intracapillary aggregation of erythrocytes.

Pathogenesis of erythrocyte aggregation in capillary stasis: etiological factors → damage to capillary walls → increase in their permeability → filtration of fluid and albumins into the surrounding tissues → increase in the level of high molecular weight proteins (globulins and fibrinogen) in the blood → adsorption of proteins on erythrocyte membranes → changes in the surface potential of erythrocyte membranes → aggregation of erythrocytes. Etiological factors → damage to erythrocyte membranes → changes in physicochemical properties of membranes (decreased ability to deform) → changes in surface potential of erythrocyte membranes → aggregation.

Consequences stasis: restoration of blood circulation (reversible stasis), necrosis (irreversible stasis).

Thrombosis - intravital deposition of a clot of stabilized fibrin and formed blood elements on the inner surface of blood vessels with partial or complete obturation of their lumen.

Mechanisms formation and structure blood clots depend on the characteristics of the blood flow in the vessel. Basically *arterial thrombosis* - thrombus formation in the arterial system with a high blood flow rate, - the activation of vascular and platelet (primary) hemostasis lies in the basis *venous thrombosis* - formation of blood clots in the venous system, which is characterized by a low blood flow rate, - activation of coagulation (plasma) hemostasis.

Virchow's triad :

1. Damage to the endothelium: death of endotheliocytes ; violation of their function - endothelial dysfunction; death of endotheliocytes → exposure of the basement membrane → unmasking of collagen → ↑ adhesion of platelets; endotheliocytes release Willebrand factor , which forms "bridges" between collagen and platelets.

2. Violation current of blood - when changing current of blood from laminar to turbulent formative elements of the blood acquire opportunities contact with the endothelium.

3. Increase viscosity of blood

Embolism - movement by blood flow (lymph) and clogging of blood vessels by foreign bodies (embolomas).

Embolism of endogenous origin:

and) thromboembolism ;

b) tissue - pieces of tissue in case of injuries or tumors when they disintegrate;

c) fat - droplets of fat in case of fractures of tubular bones or damage adipose tissue during liposuction ;

d) amniotic fluid embolism - getting into the amniotic fluid water during childbirth into the damaged vessels of the uterus.

Embolism of exogenous origin:

a) air - air bubbles entering from the environment environment in large veins (superior cava, jugular, subclavian), in which blood pressure may be lower than atmospheric;

b) gas - gas bubbles that form in the blood during a rapid decrease in barometric pressure, for example, during the rapid ascent of divers from the area of

high pressure to normal; when depressurizing the aircraft cabin at high altitudes (transition from normal to low atmospheric pressure);

c) foreign bodies - in case of gunshot wounds.

Topic 4 . Inflammation: etiology, pathogenesis . Mediators. Local signs.

Changes in metabolic processes in inflamed tissue.

Reasons for changes in osmotic and oncotic pressure in the focus of inflammation . Reasons for the development of acidosis in inflamed tissue. The essence of Schade's physicochemical theory of inflammation and Menkin's theory of inflammation . Mechanisms of the development of cardinal signs of inflammation (swelling, heat, redness, pain, impaired function).Morphological and biochemical composition of exudate.Mechanisms of proliferationThe influence of the nervous system on the development of inflammation. The role of the endocrine system in the pathogenesis of inflammation. The importance of inflammation for the body.

Inflammation is a typical pathological process that occurs under the action of phlogogenic factors, characterized by alteration phenomena, microcirculation disorders (with exudation and emigration) and proliferation aimed at localization, destruction and removal of the damaging agent , as well as for the restoration (or replacement) of tissues damaged by it.

The causes of inflammation are phlogogens . Classification of phlogogenic factors:

Exogenous:

- Physical (mechanical injury, exposure to high and low temperatures, ionizing radiation);
- Chemical (acids, alkalis, salts of heavy metals);
- Biological (bacteria, viruses, fungi).

Endogenous:

- Products of tissue decay during tumor growth;
- Toxic metabolites formed in the event of impaired kidney and liver function;
- Products of tissue decay during heart attack, burns ;
- Immune complexes.

Components of inflammation:

1. Alteration
2. Exudation and emigration of leukocytes
3. Proliferation

Alteration - violation of the structure and function of cells, intercellular substance, nerve endings, blood vessels. Alteration can be primary or secondary. ***The primary alteration*** develops immediately after exposure to a harmful factor and is formed at the level of the functional element of the organ. ***Secondary alteration*** is a consequence of the primary alteration and is associated with changes in metabolism, physical and chemical changes, and the action of inflammatory mediators.

Mediators of inflammation are biologically active substances, the

appearance of which in the focus of inflammation determines its further course.

Name	Characteristic
Cellular mediators Histamine	Expands arterioles, increases the permeability of the vascular wall, irritates nerve endings, causes spasm of the smooth muscles of the bronchi, uterus, intestines
Serotonin	Increases the permeability of the vascular wall, expands an intact vessel, narrows a damaged one
Lysosomal enzymes	They cause secondary tissue alteration, chemotaxis, increase the permeability of the vessel wall, activate the systems of complement, blood coagulation and fibrinolysis, facilitate the migration of leukocytes
Cationic non-enzymatic proteins	Increase the permeability of the vessel wall, stimulate the emigration of leukocytes, cause a bactericidal effect on microbes
Leukotrienes	They stimulate chemotaxis of neutrophils , narrowing of arterioles, increased permeability of the vascular wall, bronchospasm
Prostaglandins	They cause dilation of arterioles, increased permeability of blood vessels, chemotaxis of leukocytes, decreased sensitivity of nerve endings to stimuli
Thromboxanes	Activate adhesion and aggregation of platelets, vasoconstriction , increase blood coagulation
Prostacyclins	Cause disaggregation of platelets, dilation of blood vessels
Cytokines: - Interleukins - Interferons - Colony-stimulating factors - Chemokines - Apoptosis factors	Stimulate increased adhesion and emigration of leukocytes, increased vascular permeability, stimulation of neutrophils and monocytes. Stimulate phagocytosis, antibody formation , cell proliferation and differentiation
Active metabolites of O_2: O_2-, HO-, H_2O_2 Nitric oxide (NO)	They increase the permeability of blood vessels, the bactericidal effect of phagocytosis, the expansion of blood vessels, the bactericidal effect
Humoral mediators Proteins of the complement system C3a, C5a, C3c, complex C5c-C9	They cause chemotaxis, increased postcapillary permeability venules , release of cellular mediators, cytolysis
Kinins (bradiki - nin , kalidin)	Expand arterioles, increase permeability of venules , stimulate T-lymphocytes, proliferation of fibroblasts, release of cellular mediators, pain, itching

Factors of coagulation and fibrinolysis systems	Regulate blood coagulation, chemotaxis

Topic 5 . Exudation and proliferation. General disorders of microcirculation in the focus of inflammation.

Vascular reactions during inflammation:

1) short-term vasospasm (reflex spasm, action of endothelin , catecholamines , thromboxane A_2);

2) arterial hyperemia (paralysis of vasoconstrictors, the influence of mediators with vasodilating activity - histamine , bradykinin , nitric oxide);

3) venous hyperemia (*intravascular factors* : blood thickening; formation of microthrombi ; leukocyte margination ; swelling of formed elements

blood and vessel walls in an acidic environment; *extravascular factors:* compression of the walls of venous and lymphatic vessels by exudate and cellular infiltrate; destruction of connective tissue fibers surrounding the walls of capillaries and venules).

4) stasis.

Exudation is the exit of the liquid part of the blood, which contains proteins, and formed elements into the center of inflammation.

Pathogenesis of exudation:

1. Increased vascular permeability: reduction of endothelial cells under the influence of histamine , bradykinin , leukotrienes ; direct damage to arterioles, capillaries, venules ;

2. Increase in hydrostatic pressure in capillaries and venules ;

3. Increase in osmotic and oncotic pressure in the center of inflammation - due to electrolytes and protein in tissues.

Types of exudates:

- ***serous*** - contains 2-3% protein (albumin), transparent, observed in viral, allergic inflammation, burns ;

- ***hemorrhagic*** - contains a significant number of erythrocytes, is formed in case of severe damage to blood vessels with destruction of the basement membrane, develops in case of influenza pneumonia, anthrax;

- ***purulent*** - yellow-green in color, contains destroyed cells, leukocytes, bacteria, caused by bacterial microflora;

- ***putrid*** - gray in color with an unpleasant smell, develops when an anaerobic infection occurs;

- ***catarrhal*** – transparent, contains mucus, lysozyme, immunoglobulin A, develops during viral infections;

- ***fibrinous*** - **in** the case of significant damage to the endothelium, it contains fibrinogen, which turns into fibrin when in contact with tissues (in diphtheria, dysentery).

Value of exudation:

- *positive:* dilution of the concentration of bacterial and other toxins and their

destruction by proteolytic enzymes that come from the blood plasma; arrival of serum antibodies in the center of inflammation; emigration of blood leukocytes, which promotes phagocytosis; localization of the pathological process;

- *negative:* microcirculation disorders and ischemic tissue damage; excessive growth of connective tissue; organ dysfunction.

Emigration of leukocytes is the release of leukocytes into the focus of inflammation.

Stages of emigration:

1. Marginal standing of leukocytes near the inner wall of blood vessels and rolling :

- slowing of blood flow;
- activation and expression of E and P - selectins on the surface of the endothelium;
- receptor interaction of L- selectins of leukocytes with E- and P -selectins of the endothelium → rolling → reversible adhesion;
- expression of integrins on the surface of leukocytes and their interaction with adhesive molecules on the endothelium (ICAM, VCAM) → irreversible adhesion to the endothelium.

2. Egress of leukocytes through the vessel wall:

- formation of pseudopodia and passage between endothelial cells
- lysis of the basal membrane by proteases;
- thixotropy effect.

3. Movement of leukocytes to the center of inflammation:

- chemotaxis - chemoattractants → interaction with receptors on the surface of leukocytes → increase of Ca^{2+} in the cytoplasm → activation of the microtubular system of the leukocyte, formation of pseudopodia, activation of intracellular enzymes → active movement of the leukocyte (energy due to anaerobic glycolysis).

Proliferation - reproduction of cellular elements of connective tissue. Stimulators of proliferation: epidermal and endothelial growth factor, platelet growth factor, cytokines (IL-1). Proliferation inhibitors: keylons , tumor necrosis factors.

Local signs of inflammation (pentad Celsus Galena):

- redness (development of arterial hyperemia);
- local fever (inflow of warm arterial blood and increased metabolic rate);
- swelling (exudation and inflammatory infiltrate);
- pain (irritation of nerve endings of BAR, K^+, H^+; mechanical compression by exudate);
- dysfunction .

General signs of inflammation:

- fever - due to IL-1;
- synthesis of acute phase proteins in the liver: C-reactive protein, fibrinogen, ceruloplasmin, haptoglobin ;
- neutrophilic leukocytosis with a shift to the left - leukopoietins stimulate leukopoiesis ;
- accelerated ESR due to an increase in the amount of globulins and

fibrinogen.

Topic 6 . Violations of thermoregulation: hypo and hyperthermia. Fever: etiology, pathogenesis.

Definition of fevers .

Etiology of fever: exogenous and endogenous pyrogens.

Pathogenesis of fever, stages.

Types of temperature curves.

The difference between fever and hyperthermia.

The importance of fever for the body.

Fever is a typical pathological process, which is characterized by a change in thermoregulation under the influence of pyrogenic stimuli, which is expressed by the rearrangement of the thermoregulatory homeostasis of the body.

Stages of fever:

1) Stadium incrementi - the stage of rising body temperature,

2) Stadium fastigii - the stage of standing temperature at a high level,

3) Stadium decrementi - the stage of lowering the temperature and returning it to normal.

Clinical characteristics of the stages:

The 1st stage - an increase in temperature - is characterized by chills accompanied by a feeling of cold. ***Pathogenesis of chills*** - there is a spasm of skin vessels and a decrease in skin temperature. This causes irritation of cold receptors (sensation of cold) and the corresponding reaction to cold - muscle tremors. Subjectively, all this is perceived as a chill. Heat production prevails over heat output.

In the second stage , it is characterized by the appearance of a feeling of heat, which is caused by the expansion of skin vessels at a high body temperature. Heat transfer is equal to heat production. According to the features of the temperature curve (height of rise), depending on the nature of its fluctuations during the day, the following types of fever are distinguished :

1) subfebrile - up to 38 ^{0} ,

2) moderate - 38-39 ^{0} ,

3) high - 39-40 ^{0} and

4) excessive - hyperpyretic (41 ^{0} and above). When this limit is exceeded, deep disorders of the CNS function occur and the patient's life may be threatened.

Types of (temperature) curves:

1) constant temperature curve (**febris continua**) - temperature fluctuations in the range of no more than 1 ^{0} (observed in typhoid and typhoid fever, croup pneumonia);

2) relaxing (**febris remittens)** - temperature fluctuations in the range of 1.5 - 2 ^{0}) (with viral infections);

3) intermittent or intermittent - **febris intermittents** - this is the correct alternation of normal temperature with periods of rise (with malaria);

4) rotary - **febris recurrens** - the intervals between the febrile period and normal periods are usually not the same (5-7 days of fever and 3-4 days of normal)

- relapsing typhus;

5) exhausting or hectic - **febris hectica** - temperature fluctuations during the day reach 3-5 ^{0} (normal in the morning, 40 $^{0 \text{ in the evening}}$) - with sepsis. At the same time, fever can be atypical, when the temperature is higher in the morning than in the evening.

Pathogenesis of the 3rd stage (decrease in temperature) is manifested clinically by sweating. Sweating is the main form of heat transfer during the period of lowering the temperature and returning it to normal. Body temperature can decrease quickly (critically) and slowly (lytically). Lytic hypothermia can be dangerous, especially in the elderly who have had a myocardial infarction or have cardiosclerosis. A crisis can lead to collapse from acute heart failure.

Heat production returns to normal due to the decrease in the effect of pyrogens on the set point, the heat output is increased.

Etiological factors of fever are pyrogens. They are divided into *infectious* and *non-infectious:* these are lipopolysaccharides of bacteria, their exo- and endotoxins, viruses, rickettsiae, cells of a foreign transplant, products of decay of own tissues, lymphokines , chemotaxins , allergen-antibody complex, allergens.

By origin, pyrogens are divided into:

1. Exopyrogens (from endotoxins of microbes - bacterial), according to their chemical structure, are high-molecular lipopolysaccharides .

2. Endopyrogenes (cellular).

It is established that:

1) **exopyrogens** cause fever indirectly through the formation of endopyrogens , so the temperature rises after 45-60 minutes and its maximum after 3-4 hours,

2) non-toxic,

3) heat-resistant (for destruction, it is necessary to autoclave for 1-2 hours at a temperature of 200 ^{0}),

4) non-allergenic,

5) are not antigenic, but carry antigenic chemical specificity - that is, they are haptens . To acquire antigenic properties, they must combine with the proteins of cells and tissues,

7) with daily administration 5-6 times to exopyrogens, tolerance occurs and fever does not develop,

8) exopyrogens cause a number of protective effects.

Endogenous pyrogens: their source is neutrophils , macrophages and blood lymphocytes - these are leukocyte pyrogens.

Properties of leukopyrogens :

1) are produced only by living leukocytes, the structure is an albumin-type protein,

2) unstable to heating - they are destroyed at a temperature that causes protein coagulation (60-70 ^{0}),

3) the temperature reaction to endopyrogen develops after 10-15 minutes. The maximum rise in temperature after the introduction of endopyrogen after 1-2 hours (exopyrogen 3-4).

Characteristics of interleukin-1:

1) it is produced in micro- and macrophages, does not cause tolerance, is non-toxic, acts on all the main regulatory systems of the body and, above all, those that determine reactivity and resistance - nervous and endocrine,

2) acts on the cells of the hypothalamus and enhances the production of CRF, which trigger a stress reaction, mobilize energy resources, develop hyperglycemia, lipemia .

Endopyrogens have the same biological effect as exopyrogens , increasing the body's protective properties:

1) enhance phagocytosis,

2) enhance the production of glucocorticoids ,

3) enhance tissue regeneration,

4) strengthen the detoxification function of the liver,

5) improve microcirculation processes - this is why pyrogens are used in the sluggish course of diseases, in chronic stomach ulcers to accelerate the healing and scarring of ulcers, in renal hypertension to improve microcirculation processes in the kidneys (in the nephron, glomeruli) and reduce renin production.

Pathogenesis of fever . A rise in temperature in the initial stage is associated with a decrease in heat transfer - this is *the main link of pathogenesis* . Increasing heat production helps to raise the temperature faster.

Chains of pathogenesis of fever:

1) entry of exogenous pyrogens into the body,

2) interaction of exopyrogens with the body's phagocytes,

3) activation of phagocytes,

4) secretion of endopyrogens by activated phagocytes - **IL-1** , IL-6, IL-8, TNF (factor tumor necrosis),

5) transfer of IL-1 by blood flow to the center of thermoregulation in the hypothalamus,

6) interaction of IL-1 with receptors located on endothelial cells of hypothalamic capillaries,

7) the release of arachidonic acid from membrane phospholipids under the action of Ca^{2+} ions and the formation under the action of COX of $PGE_{1,2}$ (prostaglandins) and their effect on set point neurons,

8) distortion of information from peripheral thermoreceptors (normal temperature is perceived as low),

9) limitation of heat transfer (due to spasm of surface vessels) and increase in heat production,

10) shift of the set point of temperature homeostasis to a higher level.

The biological significance of fever is mainly the creation of a higher temperature background for metabolic processes, which leads to an increase in the level of protective reactions:

1) activation of enzymes,

2) increased phagocytosis,

3) activation of antibody formation ,

4) synthesis of interferon,

5) violation of the reproduction of microbes and viruses,

6) increased sensitivity of microbes to antibiotics.

The difference between fever and hyperthermia:

1) various etiological factors: in case of fever – pyrogenic factors, in case of hyperthermia – environmental factors,

2) various manifestations of the stage of temperature rise - with fever - chills and moderate stimulation of functions (with an increase in temperature by 1^0 - an increase in the pulse by 8-10 beats per minute and by 2-3 respiratory movements), and with hyperthermia, sharp sweating, a feeling of heat , a sharp increase in pulse and breathing - by 10-15 respiratory movements when the body temperature rises by 1^0),

3) when cooling the body in case of fever, the temperature does not change, in case of hyperthermia - it decreases,

4) antipyretic drugs reduce the temperature in case of fever and do not affect in case of hyperthermia.

During fever, oxidative phosphorylation processes are activated, ATP synthesis increases, and protective reactions are accelerated. With hyperthermia, there is a blockade of ATP synthesis and their breakdown, a lot of heat is generated.

3. Formation of professional skills, skills related to topics that are part of the content module (mastery of communication skills, clinical examination, determination of treatment scheme, conducting laboratory research, etc.) mastery of skills:

Topic 1

1. Acquaintance and teaching with the definition , essence and history of the subject.

Topic 2

1. Cells are damaged in the body of an animal that has undergone radioactive irradiation. Give examples of mechanisms in the pathogenesis of damage that occur under these conditions.

2. Present in the form of a scheme the mechanism of detergent action of lysophospholipids and free fatty acids.

3. Present in the form of a scheme the causes and consequences of increasing the concentration of calcium ions in the cell.

4. Compile a comparative table of the two main mechanisms of cell death: necrosis and apoptosis .

Topic 3

Task 1. To study blood circulation disorders with arterial hyperemia

the spinal cord with the help of a probe . Fix the frog on the rubber stand with the back up so that the mouth opening is near the lower edge of the triangular opening of the stand. Carefully pull out the tongue with tweezers (in a frog, the root of the tongue is located in front , and the tongue is thrown back) and fix it around the hole of the stand. Place the rubber stand on the microscope stage. Under a small

magnification of the microscope, study blood circulation in the vessels of the tongue. Apply turpentine on the surface of the tongue , note changes in blood circulation in the vessels of the tongue: dilation of arterioles, capillaries, acceleration of blood flow, presence of central and parietal blood flow. Wash off the turpentine .

Task 2. To study the peculiarities of blood circulation in venous hyperemia.

Use tweezers to open the frog's mouth. Consider the location of blood vessels in the area of the root of the tongue. On both sides of the tongue, the vein is located laterally (outside), and a thinner artery passes around it, medially . Pass a ligature under one of the marginal veins, using a surgical needle with a thread for this. Bandage the vein. Under a small magnification of the microscope, observe the expansion of venous vessels, the slowing down of blood flow in them, the absence of distribution into central and parietal blood flow.

Task 3. To study blood circulation during ischemia.

Conduct the experiment on the same frog. Tie the artery in the area of the root of the tongue on the side opposite to the one where the vein was tied. Observe the pallor of the ischemic part of the tongue, as well as under the microscope the decrease in the lumen of arterial vessels and the speed of blood movement, the disappearance of previously visible capillaries, the cessation of blood circulation.

Topic 4

Task 1. Determine amylolytic activity of purulent exudate.

Method: Take 8 tubes. Pour 1 ml of the working solution of purulent exudate diluted 1:10 into the first two test tubes. Then add 1 ml of physiological solution to all test tubes, starting with the second one. After mixing, transfer 1 ml of the mixture from the 2nd test tube to the 3rd, from the 3rd to the 4th , etc. Pour 1 ml of the mixture from the 7th test tube. Thus, the 8th test tube will be a control containing only saline. From the 1st to the 7th test tube there are manure dilutions (1:10; 1:20; 1:40, etc.) . Add 2 ml of 0.1% starch solution (substrate for amylase action of manure) to all test tubes (1-8) and mix well. Put the test tubes in a thermostat for 30 minutes. at 37 ° C. After incubation, add 2 drops of Lugol's solution to each test tube .

Amylolytic activity of purulent exudate determine by diluting the manure in the last test tube, where starch has been split into achrodextrins (yellow color of the mixture).

Topic 5

Task 2. To determine the proteolytic activity of purulent exudate.

Method: As in the previous experiment, take 8 test tubes and dilute the working manure solution (1:10). Then add 1 ml of 10% casein solution (substrate for proteases) to all test tubes and place in a thermostat for 30 minutes. at 37 ° C. After that, add 2 drops of acetic alcohol to each test tube. The solution is clear in the test tubes where the protein was completely split, and the solution is cloudy in those where the protein was not split.

The proteolytic activity of pus is determined by diluting the pus in the last test tube, where complete protein cleavage is detected.

Topic 6

Task 1. Reproduce fever in an experimental animal (rat) and study the dependence of body temperature on the level of heat production.

Methodology: Measure the rat's rectal temperature with a thermometer, count the breathing rate in 1 minute. Measure the volume of oxygen absorbed by a rat in 10 minutes using Kalabukhov's apparatus .

Intraperitoneally inject the rat with pyrogenal solution (1 mg per 1 kg of body weight). Observe the animal's behavior. After 1-1.5 hours, measure temperature, respiratory rate, oxygen absorption for 10 minutes a second time. Compare the results obtained at the beginning and at the end of the experiment, draw conclusions.

Initial indicators (control)			Indicators after the introduction of pyrogenal		
t,°C	Oxygen absorption , ml/min	Breathing rate, in 1 min	*t, °C*	Oxygen absorption , ml/min	Breathing rate, in 1 min

4. Summary : testing

PRACTICAL TRAINING

Content module 2. Typical pathological processes.

Practical lesson No. 7

Topic. Pathophysiology of the immune system. Immunodeficiency and immunodepressive conditions.

Practical lesson No. 8

Topic. Allergy: classification, etiology, pathogenesis.

Practical lesson No. 9

Topic. Allergy: Allergic reactions of types I - IV. Pseudoallergic reactions. Autoimmune reactions.

Practical lesson No. 10

Topic. Pathophysiology of tissue growth. Tumors: etiology, pathogenesis.

Practical lesson No. 11

Topic. General nosology. Typical pathological processes.

Current control of knowledge

Purpose: Acquisition by the student of higher education of knowledge and formation of elements of professional competences in the field of medicine from the pathophysiology division:

Topic 7. Pathophysiology of the immune system. Immunodeficiency and immunodepressive states.

Topic 8 Allergy: classification, etiology, pathogenesis.

Topic 9. Allergic reactions of types I - IV. Pseudoallergic reactions.

Autoimmune reactions.

Topic 10. Pathophysiology of tissue growth. Tumors: etiology, pathogenesis.

Topic 11. Verification of assimilation of acquired knowledge and skills by applicants.

Improvement of skills and competences acquired during the study of previous disciplines.

Basic concepts:

Topic 7. Pathophysiology of the immune system. Immunodeficiency and immunodepressive states.

Topic 8. Allergy: classification, etiology, pathogenesis.

Topic 9. Allergic reactions of types I - IV. Pseudoallergic reactions. Autoimmune reactions.

Topic 10. Pathophysiology of tissue growth. Tumors: etiology, pathogenesis

Topic 11. Verification of assimilation of acquired knowledge and skills by applicants.

Equipment: Multimedia presentations, tables.

Plan:

3. **Organizational activities (greetings, verification of those present, announcement of the topic, purpose of the lesson, motivation of higher education seekers to study the topic).**

4. **Control of the reference level of knowledge:**

Topic 7. Pathophysiology of the immune system. Immunodeficiency and immunodepressive conditions.

1. What is immunological reactivity and how it is formed

2. What is immunological tolerance and means and achievements

3. T- and B-lymphocytes and their functions. Mechanism of humoral and cellular immune response.

4. Causes and mechanism of primary (hereditary) immune deficiency, classification, characteristics of species.

5. Etiology and pathogenesis of secondary (acquired) immune deficiency. Examples

6. AIDS - etiology, pathogenesis.

Primary immunological deficiency

The failure of specific immune mechanisms can refer separately to the T-system of immunity, the B-system of immunity or be combined.

The insufficiency of the T-system is caused by a genetic blockade of the multi-

stage process of formation and maturation of T-lymphocytes. Since this blockade can occur at different levels, its clinical manifestations will not be the same. Some diseases associated with insufficient formation or functional failure of T-lymphocytes are briefly described below.

Hypoplasia of the retrosternal gland (Di Giorgi syndrome) is a consequence of the disruption of the lining and the development of the 3-4 pharyngeal pockets up to the 8th week of pregnancy. Children (more often - girls) are born without a mammary gland, with defects in the development of the thyroid and parathyroid glands, the face and large vessels. The depth of suppression of cellular immunity is different - from the complete absence of T-lymphocytes to barely noticeable inhibition of their functions. If the child survives, the T-lymphocytic insufficiency disappears completely by the age of 5 years. The disease is not transmitted by heredity.

Lymphocytic dysgenesis (Nezelof's syndrome) occurs due to early atrophy of the retrosternal gland and lymph nodes. Lymphopenia and a decrease in the functional activity of T-lymphocytes are characteristic . Immediately after birth, such children develop purulent inflammatory processes on the skin and internal organs, which are complicated by sepsis and, as a rule, end in death in the first months of life.

Insufficiency of purine nucleotide phosphorylase leads to the accumulation of toxic products of purine metabolism, which suppress the function of T-lymphocytes.

The insufficiency of the B-lymphocyte system is manifested by a violation of the synthesis of antibodies. Depending on the level at which their differentiation is blocked, this violation can be general or selective.

Primary agammaglobulinemia Bruton's disease is characterized by inhibition of immunoglobulin synthesis Ig M, Ig A and Ig G. Such children (boys) have a sharply reduced resistance to staphylococci, pneumococci, meningococci and other microorganisms. At the age of 8 months to 3 years, they begin to suffer from severe recurrent infections - bronchitis, pneumonia, sinusitis, purulent arthritis, meningitis, sepsis. Their lymph nodes and spleen are completely devoid of plasma cells , there are no B-lymphocytes in the blood. The retrosternal gland is normal, T-cell immunity is not impaired. The inheritance of the disease is linked to the X-chromosome.

Selective deficiency of Ig A is associated with the blockade of the final stage of differentiation of plasma cells , which synthesize this particular immunoglobulin. The synthesis of other immunoglobulins is not disturbed. In some patients, deletion of chromosome 18 and antibodies to Ig A are found.

Combined immunodeficiencies are accompanied by simultaneous suppression of cellular and humoral immunity. Such patients have neither T nor B lymphocytes, they are not viable. The following forms of combined immunodeficiencies are best studied .

"Swiss" type - characterized by lymphopenia and hypogammaglobulinemia . The retrosternal gland is underdeveloped, there are few lymphocytes and plasma cells in the lymph nodes and spleen. Recurrent infectious diseases with hemorrhages and diarrhea lead to the child's death in the first months of life.

Immunodeficiency with ataxia and telangiectasia (Louis-Bar syndrome) begins in early childhood with progressive cerebellar ataxia (impaired coordination of movements). It is accompanied by the expansion of peripheral blood vessels - telangiectasia . Older children are prone to recurrent infectious diseases and malignant tumors. Their retrosternal gland is very small, with a small number of lymphocytes. 70% of patients have absent or sharply reduced Ig A in their blood.

Wiskott-Aldrich syndrome manifested by thrombocytopenia , eczema and various infectious diseases that begin at the end of the first year of life. Children are prone to malignant tumors, leukemia, hemorrhages and rarely reach adulthood. The retrosternal gland and lymph nodes are not changed in them, but they contain a smaller number of lymphocytes. The number of lymphocytes in the blood may also be reduced. The content of Ig M often decreases.

Secondary immunological deficiency

Immunodepressive states of secondary origin are a much more common phenomenon than primary immunodeficiencies . Their reasons are various. General suppression of all links of the immune system is observed in case of massive damage to the bone marrow, for example, when it is replaced by tumor metastases or connective tissue (myelofibrosis). Acute and chronic infectious diseases (influenza, measles, tuberculosis) also cause a general depression of immunity. Ionizing rays are powerful immunosuppressants . Predominant suppression of the T-system occurs after surgical removal of the retrosternal gland due to its malignant transformation. Gross violations of the B-system are accompanied by tumors from immunocompetent cells - plasmacytoma , lymphoma, chronic lymphocytic leukemia . Antibody synthesis suffers in exhausted patients who have lost a lot of protein (starvation, burns, chronic renal failure). Immunodepression can be caused by medical effects - administration of cytostatics and glucocorticoids , irradiation of patients with tumors and leukemias. The intensity of immune reactions decreases with age.

Acquired immunodeficiency syndrome (AIDS)

This recently discovered disease is caused by the human immunodeficiency virus (HIV). It is manifested by signs of depression of the T-system of immunity and

a sharp decrease in the body's resistance to bacteria, viruses, fungi and pathogenic protozoa. It has been found that HIV damages some immunocompetent cells, primarily T- helpers and macrophages. The reason is that their membranes have receptors on which the virus is absorbed . Having penetrated into the cell, it can remain inactive for a long time (up to 10 years). Under the influence of provoking factors, for example, during the layering of another viral disease, it begins to multiply and spread throughout the body, destroying more and more T- helpers . Under these conditions, their stimulating effect on the immune system is removed. On the contrary, the inhibitory effect of T- suppressors begins to prevail . The immunological capacity of the organism weakens sharply, and it becomes defenseless not only against pathogenic microorganisms, but also against saprophytic flora. Antitumor immunity, which is normally carried out by the same T-lymphocytes, is also suppressed.

It has been proven that, in addition to T- helpers and macrophages, HIV multiplies in glial cells of the brain and β-cells of the pancreas. Damage to brain cells causes mental disorders and multiple sclerosis.

Immunological basis of transplantation

Transplantation refers to the transplantation of tissues and organs within the same organism or from one to another. The following types of transplantation are distinguished:

a) autotransplantation - transplantation of one's own tissue, for example, skin, bone, cartilage;

b) isotransplantation - transplantation of tissue or organ to a person with an identical genotype (identical twin);

c) allotransplantation (homotransplantation) - transplantation within the limits of one biological species (from person to person);

d) xenotransplantation (heterotransplantation) - transplantation of a tissue or organ from a representative of one biological species to a representative of another species, for example, from a pig to a human.

The organism to which the transplant was carried out is called the recipient, and the one from which the tissue was taken for transplantation is called the donor.

Despite the achievements of transplantology , the ancient dream of mankind to replace lost or damaged organs with healthy ones has not been finally realized. Transplantation immunity, which is based on the antigenic incompatibility of donor and recipient tissues, became the main obstacle. Transplantation immunity reactions are directed against foreign antigens that are located on the surface of transplanted cells and are called transplantation or histocompatibility antigens . They are present in all cells that contain a nucleus. Most of them are in organs rich in lymphoid tissue - lymph nodes and spleen. There are much fewer of them in the liver, lungs, kidneys, heart and stomach, and none at all - in fat cells and erythrocytes.

Thanks to the mechanisms of transplantation immunity, genetically foreign

cells are recognized and removed from the body, and its antigenic homeostasis is preserved. The very process of elimination of foreign material is called graft rejection. This reaction is absent only under the condition of antigenic identity of the donor and recipient (auto- and isotransplantation). Allo- and xenografts are always rejected as a result of an immune conflict.

The reaction of rejection consists of two phases - afferent and efferent. During the first phase, the recipient's lymphocytes penetrate the transplant through the vessels that have sprouted from the surrounding tissues. Penetrated lymphocytes recognize foreign antigens and specifically are sensitized to them. It has been proven that this sensitization can occur not only inside the transplant, but also outside it in the lymphoid organs. After a few hours, the sensitized lymphocytes attach to the cells of the transplant.

In the second stage, sensitized lymphocytes (T- killers) deal a devastating blow to the transplant cells. They destroy these target cells using two main mechanisms - by releasing soluble cytostatics and by activating membrane enzymes that cause the destruction of foreign cell membranes.

The need for organ transplantation raised the problem of preventing the rejection reaction. For this, in addition to careful selection of the donor, agents are used that suppress the intensity of the immune response, that is, cause artificial immunodepression. These include ionizing rays, glucocorticoids , antilymphocyte serum, chemical immunosuppressants (azathioprine , cyclosporine A).

Another method of preventing the rejection reaction is at the stage of experimental research - the induction of immunological tolerance to foreign antigens. It is known that humans and animals with a highly developed immune system do not have cellular or humoral immunological reactions to their own antigens. The immune system is tolerant to them, and this tolerance developed during embryonic development. Immunocytes and antigens of the embryo came into contact with each other and formed a mechanism of peaceful coexistence in the form of natural tolerance.

Proteins and synthetic polypeptides belong to thymus-dependent antigens, that is, those that require the presence of the retrosternal gland and T-lymphocytes to trigger an immune response. Thymus-dependent antigens in very low doses are unable to activate T- helpers and cause an immune response, but their amount may be sufficient to stimulate T- suppressors . Then T-helpers become the target cells for their inhibitory effect , and the response to the antigen becomes impossible. This state of immunological reactivity is called low-dose tolerance.

Some antigens (bacterial lipopolysaccharides , polyvinylpyrrolidone) cause the formation of antibodies without the participation of T-lymphocytes, that is, by direct activation of B-cells. Such antigens were called thymus-independent . With their help, you can also induce a state of tolerance, but for this you have to administer

very large doses, much higher than what is necessary for an optimal immune response. This type of induced tolerance is called high-dose tolerance .

Immunological tolerance is characterized by specificity . It is caused by an antigen and deprives the body of an immune response only against this antigen . This is fundamentally different from immunodepression, which is caused by non-specific influences and in which the formation of antibodies against many antigens is blocked.

Clinical organ transplantation has now become widespread. The best results are given by autotransplantation, for example replantation of traumatically amputated organs - fingers, limbs. Allotransplantation of the cornea and cartilage is possible without suppression of the immune system. These tissues do not have a vascular system, and therefore they lack immunoreactivity .

Hundreds of thousands of kidney transplants have been performed. Reliable results have been achieved in cases of identical twins. Engraftment of the transplanted kidney is facilitated by the fact that the recipient has been suffering from chronic renal failure for a long time before the operation and is in a state of immunodepression under the influence of uremic toxins.

A human heart transplant was first performed by K. Bernard in 1978. Now there are several thousand such operations. 80% of heart transplant patients live longer than 1 year.

Bone marrow transplantation is performed in patients with immunological deficiency, aplastic anemia, those who were exposed to radiation as a result of an accident or radiotherapy of malignant tumors and leukemias.

Topic 8. Allergy: classification, etiology, pathogenesis.

Allergy is an immune reaction (a qualitatively altered immune response) accompanied by damage to the body's own tissues.

The causes of allergies are **allergens.**

Classification of allergens : exoallergens and endoallergens .

Exoallergens :

1) infectious: a) bacterial, b) viruses, c) fungi,

2) pollen of flowering plants, fluff of poplar, dandelion, ambrosia, cotton,

3) household - detergents, household and library dust, as a product of the vital activity of a house mite, specific for a particular apartment,

4) food products - especially for children - cow's milk, chicken eggs, chocolate, citrus fruits, strawberries, fish, crabs, lobsters, cereals,

5) medicines - especially therapeutic serums, antibiotics, vitamins,

6) products of chemical synthesis.

Endoallergens :

a) natural (primary): lens and retina of the eye, tissues of the nervous system, thyroid gland, male gonads,

b) acquired (secondary), induced from own tissues under the influence of external influences: infectious, non-infectious (cold, burns, radiation).

1. Allergy, definitions, concepts, types
2. Prove that allergy is a typical pathological process 3. Give the classification of

allergens and find out the nature of endogenous allergens (natural and acquired)
4. Find out what active and passive sensitization are
5. Prove how an allergic reaction of the immediate type differs from an allergic reaction of a delayed or cellular type. Give examples and find out the features of the immenological stage.
6. Find out why large doses of antireticulated cytotoxic serum of Bogomolets (ACS) cause an allergic reaction
7. Give the characteristics of delayed-type hypersensitivity (GST) and give examples.
8. What diseases are associated with the stimulating (type 5 according to Coombs and Gell) nature of the allergic reaction.
9. How are biologically active substances (BAR) formed and what role do they play in the functional and structural breakdowns of the body10. Find out the pathogenesis of auto allergic diseases.

Classification of allergic reactions:

1. According to the reaction time after repeated exposure to the allergen (according to Cook):

- Allergic reactions of the immediate type (hypersensitivity of the immediate type) - I, II, III - develop 15-20 minutes after repeated exposure to the allergen.
- Allergic reactions of the delayed type (hypersensitivity of the delayed type) - IV - develop 24-48 hours after repeated exposure to the allergen.

2. According to pathogenesis (according to Coombs and Jell):

- I. Anaphylactic;
- II. Cytotoxic;
- III. Immunocomplex ;
- IV Hypersensitivity of delayed type.

General pathogenesis of allergic reactions:

I. Immunological stage

1. Formation of antibodies or sensitized T-lymphocytes upon initial contact with an allergen (sensitization);
2. Formation of complexes allergen + antibody (type I, II, III) or allergen + sensitized T-lymphocyte (type IV) upon repeated contact with the allergen.

II. Pathochemical stage. It is characterized by the release, activation, synthesis of biologically active substances - allergy mediators.

III. Pathophysiological stage (stage of clinical manifestations). It is characterized by structural and functional changes in organs and tissues:

- vasomotor reactions (local and systemic), leading to changes in blood pressure, peripheral blood circulation and microcirculation;
- increased permeability of vessel walls, which leads to the development of edema;
- spastic contractions of the smooth muscles of the bronchioles and intestines, which may manifest as asphyxiation, dyspeptic disorders;
- an imbalance between the factors of coagulation, anticoagulation and fibrinolytic systems of blood, which can lead to both hemorrhagic syndrome and thrombosis;

- irritation of nerve receptors, which leads to the development of a feeling of pain, itching , burning;
- inflammatory reactions accompanied by significant cell infiltration of tissues.

Sensitization - formation of increased sensitivity of the body to this allergen. It is characterized by the formation of specific antibodies or sensitized T-lymphocytes to a specific allergen. Clinically, sensitization is not manifested. The state of sensitization can be detected with allergy tests.

Distinguish ***active*** (develops 10-14 days after the introduction of the allergen into the body; the immune system of the body is actively involved in the process of formation of specific antibodies or sensitized T-lymphocytes) and ***passive*** sensitization (develops after the introduction of serum containing ready-made antibodies or a cell suspension with sensitized T-lymphocytes; at the same time, the body's own immune system does not participate in the formation of antibodies and sensitized T-lymphocytes).

Topic 9. Allergy: Allergic reactions of types I - IV. Pseudoallergic reactions. Autoimmune reactions.

ALLERGIC REACTION TYPE I (anaphylactic)

Immunological stage: allergen → recognition of allergens by dendritic cell (DC) → reading of information, its processing, isolation of AG determinants and its incorporation into the membrane of DC → activation of T- helpers (Th_0) → formation of Th_2 → B-lymphocytes → transformation of B-lymphocytes into plasma cells → synthesis of antibodies - immunoglobulins Ig E, G4 → fixation of antibodies on the surface of mast cells (antibodies with their end Fc (constant fragment) are fixed on the corresponding receptors of mast cells and basophils; nerve receptors of blood vessels, smooth muscles of intestinal bronchi and blood cells → repeated contact with the allergen → formation of allergen-antibody complexes on the surface of mast cells (Fab (antigen-binging fragment) antibody fragment binds to AG, and 1 molecule of IgE can bind 2 molecules of AG).

There is activation of the cell and transition of the process to **the pathochemical stage** , which includes degranulation mast cells (Fig. 1) and the release of granules from them: histamine , heparin, chemotaxis factors of eosinophils and neutrophils ; formation of leukotrienes and prostaglandins from phospholipids of membranes ; migration of eosinophils, neutrophils to the zone of allergic reaction and their release of secondary mediators: histamines , arylsulfatases , proteases, phospholipases

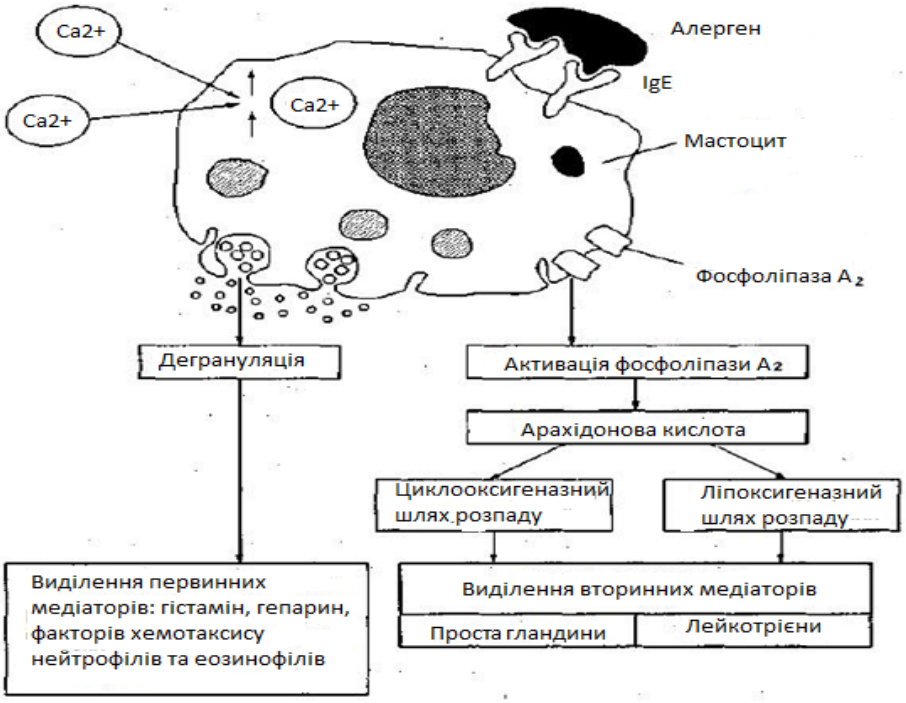


Fig. 1. Isolation of primary and secondary mediators from mast cells .

Pathophysiological stage: spasm of bronchial smooth muscles → bronchospasm ; dilation of blood vessels → arterial hyperemia; increased permeability of the vascular wall → edema; hypersecretion of mucus, irritation of nerve endings → itching, pain. *Clinical forms:* urticaria, pollinosis , Quincke's edema , bronchial asthma, anaphylactic shock.

ANAPHYLACTIC SHOCK

Bronchospasm

Mucus hypersecretion Increase vascular permeability

Violation of pulmonary ventilation

Expansion of arterioles

Lower blood pressure

Violation of microcirculation

Hypoxia

Dysfunction of the respiratory and cardiovascular centers

↓

Death

TYPE II ALLERGIC REACTION (cytotoxic)

Immunological stage: allergen (changed components of cellular and basal membranes (autoallergens) → recognition of allergens by dendritic cells (DC) → reading of information, its processing, isolation of AG determinants and its incorporation into the DC membrane → activation of T- helpers (Th_0) → formation of Th_2 → B-lymphocytes → transformation of B-lymphocytes into plasma cells → synthesis of Ig $G_{1,2,3;}$ IgM → fixation of antibodies on the surface of target cells → upon repeated contact with an allergen, the formation of an allergen + antibody complex on their surface.

Pathochemical stage: activation of complement components; release of lysosomal enzymes and superoxide radicals (O, OH, H_2O_2) during phagocytosis; granzyme , perforin from NK cells.

Pathophysiological stage. Lysis of target cells, destruction of basement membranes:

1. Complement-dependent cytolysis (activation of individual fragments of complement components): C3a, C5a - chemotaxis of neutrophils and phagocytosis; C5b-C9 - formation of channels in the cell membrane and osmotic cell lysis.

2. Complement-independent cytolysis (the role of opsonins is performed by antibodies (IgG).

3. Antibody-dependent cellular cytotoxicity (NK cells are activated, which have receptors for the Fc fragment of antibodies on their surface).

Clinical forms: hemotransfusion shock, hemolytic disease of newborns, autoimmune thrombocytopenic purpura, autoimmune agranulocytosis, Dressler's syndrome (postinfarction myocarditis), acute rheumatic fever, hyperthyroidism, drug allergy.

ALLERGIC REACTION TYPE III (immune complex)

Immunological stage: allergen (soluble proteins, drugs, therapeutic serums) → recognition of allergens by dendritic cells (DC) → information reading, its processing, isolation of AG determinants and its incorporation into the DC membrane → activation of T- helpers (Th_0) → formation of Th_2 → B-lymphocytes → transformation of B-lymphocytes into plasma cells → synthesis of precipitating antibodies - Ig G; Ig M → upon repeated contact with the allergen, the formation of soluble complexes → fixation of allergen + antibody complexes on the walls of microvessels .

Pathochemical stage: activation of complement components; chemotaxis of granulocytes and macrophages (C3a, C5a); activation of phagocytosis (C3b) and release of lysosomal enzymes and superoxide radicals by phagocytes; activation of mast cells (C3a, C5a), their degranulation and release of histamine , heparin, chemotactic factors; factor selection Hageman in case of damage to the endothelium of vessels by immune complexes; and activation with its help of the kallikrein-kinin system, coagulation, anticoagulation and fibrinolysis systems .

Pathophysiological stage. Circulating immune complexes are deposited in the vessels of kidney glomeruli and cause various types of glomerulonephritis , alveolitis in the lungs , and dermatitis in the skin. In severe cases, inflammation can take on an alterative character with tissue necrosis, partial or complete thrombosis, and hemorrhage . Initially, the focus is dominated by neutrophils , which actively phagocytose immune complexes, releasing lysosomal enzymes and factors that increase permeability and chemotaxis for macrophages. Macrophages accumulate in the focus of inflammation and phagocytose destroyed cells, cleaning the affected area. Inflammation ends with the proliferation of cellular elements.

Clinical forms: serum sickness, nodular periarteritis , Artus phenomenon , poststreptococcal glomerulonephritis , vasculitis , systemic lupus erythematosus, rheumatoid arthritis , etc.

TYPE IV ALLERGIC REACTION (delayed type hypersensitivity)

Immunological stage: allergen → recognition of allergens by dendritic cell (DC) → reading of information, its processing, isolation of AG determinant and its incorporation into the membrane of DC → activation of T- helpers (Th_0) → accumulation of Th_1 clones (sensitized T-lymphocytes), in the cell membrane of which are embedded structures that perform the role of AT, able to connect with the relevant allergen → upon repeated application of the allergen, T-lymphocytes diffuse from the bloodstream to the site of application and connect with the allergen, which is located on the target cells.

Pathochemical stage: lymphocytes are thrown out lymphokines , NK cells secrete granzyme and perforin .

Pathophysiological stage: the development of foci of allergic exudative inflammation of a dense consistency.

Clinical forms: contact dermatitis, infectious and allergic diseases (tuberculosis, brucellosis, syphilis, fungal diseases); tuberculin reaction; graft rejection reaction.

Hyposensitization - a decrease in the body's sensitivity to an allergen. There is a distinction between specific and non-specific hyposensitization.

Specific hyposensitization is achieved by the introduction of the allergen that caused the allergy (introduction of serum according to the method of A.M. Bezredka). Specific hyposensitization is effective for type I allergic reactions.

Nonspecific hyposensitization is achieved by changes in the body's reactivity (normalization of the function of the neuroendocrine system: working conditions, rest, nutrition, reflexology , physiotherapy ; administration of drugs (antihistamines , GCS, leukotriene receptor blockers).

Pseudoallergic reactions are a group of reactions that are similar in appearance to allergies, but differ in the absence of an immunological stage. They develop under the action of factors that cause degranulation mast cells and the release of biologically active substances.

Mechanisms of development:

- Histamine : degranulation mast cells , violation of histamine inactivation , increased intake of histamine with food, dysbacteriosis .

- Violation of activation of the complement system : excessive activation of the complement system , deficiency of complement inhibitors .
- Disruption of the metabolism of the arachidonic system: imbalance between prostaglandins and leukotrienes (aspirin use).

Topic 10. Pathophysiology of tissue growth. Tumors: etiology, pathogenesis

1. Determination of the tumor process. Features of tumors.
2. Characteristics of carcinogenic factors: a) chemical. Including endogenous (hormones, tryptophan derivatives, etc.), b) physical, c) biological.
4. Molecular mechanisms of carcinogenesis due to:
A) non-inverse molecular mechanisms of activation of cell reproduction (growth factors, growth factor receptors of molecules - mediators of cell division excitation)
B) loss of brakes (repressors) of cell division
5. Concepts of tumor progression and its mechanisms
6. Organism-tumor relationship: a) effect of tumor on the organism; b) the effect of the body on the tumor; c) immunological mechanisms of impact on the tumor (changes in the antigenic composition of the tumor, mechanisms of tumor escape from – under immune surveillance)

Tumors are a typical pathological process, the main feature of which is the endless and uncontrolled reproduction of cells with a violation of their ability to differentiate and form organized structures.

Comparative characteristics of benign and malignant tumors

	Benign tumors	**Malignant tumors**
Tempo	Slow growth	Rapid growth
The nature of growth in relation to adjacent tissues	Expansive growth	Infiltrating (invasive) growth
A type of atypism	Fabric atypism	Cellular and tissue atypism
The degree of maturity (differentiation) of cells	Mature, well-differentiated cells	Immature cells that have varying degrees of anaplasia (insufficient cellular differentiation)
Necrosis of tumor tissue	Rarely occur (in large and long-lived tumors)	Characteristic feature, more pronounced in advanced stages
Metastases	As a rule, they do not metastasize	Lymphogenic , hematogenous, perineural , implantation metastases
Recurrences after removal	After complete surgical removal, as a rule, they do not recur	After complete surgical removal, they often relapse

Forecast	The prognosis is usually favorable	The prognosis is often (often) unfavorable

Features of tumor growth:

1. Atypia of reproduction : unregulated, unlimited growth, loss of the "limit" of the number of cell divisions (Hayflick's limit). *Pathogenesis:*

- Activation of oncogenes of tumor cells, as a result of which cells switch to autocrine regulation - synthesize proliferation stimulators themselves.

- Changes in the structure and function of tumor cell membranes:

- decrease in the number of receptors that provide control from the nervous and endocrine systems;
- appearance of "defective" receptors;
- decrease in the number of adhesive molecules that provide intercellular contacts and contact inhibition of division. The loss of the upper "limit" of the number of cell divisions is associated with a change in the function of genes that regulate apoptosis .

1. Morphological atypia (cellular and tissue).

Tissue atypia	Cellular atypia
Violation of the normal ratio of tissue structures. In each tumor, it is possible to distinguish parenchyma, which consists of specific elements of this tumor, and stroma, which contains vessels, nerves, collagen, argyrophilic fibers and amorphous substance. Large vessels in tumors are deformed. In some malignant tumors, vascular sinusoids are partially lined not by endothelium, but by the tumor cells themselves. The tumor is most abundantly supplied by capillaries, but they are unevenly distributed, and prevail in the peripheral regions. Nerves in the area of tumor growth most often undergo degeneration and die.	Tumor cells have different shapes and sizes, cell nuclei are enlarged, contain a large amount of chromatin, are hyperchromic , the number of nucleoli is increased, the number, shape and size of chromosomes have changed. Mitochondria become atypical, they increase or decrease in size, the number of cristae often decreases. The endoplasmic reticulum expands unevenly, the number of ribosomes, lysosomes , and various inclusions increases in the cytoplasm. is the interconnection of cell membranes of various organelles, which is found in embryonic cells. The structure of the outer membrane changes - many microvilli and outgrowths appear on it.

Atypia of differentiation - partial or complete cessation of differentiation of cells - *anaplasia* .

3. Biochemical atypia (peculiarities of metabolism in tumor tissue).

1) Features of carbohydrate metabolism:

a) a tumor is a "trap" of blood glucose;

b) Pasteur's negative effect - glycolysis in tumor cells can continue even in the presence of oxygen;

c) activation of the pentose phosphate pathway of glucose oxidation.

2) Features of protein metabolism:

a) tumor cells - blood nitrogen "trap" - tumor cells intensively capture nitrogen-containing substances from the blood (amino acids, nitrogenous bases) and use them for the synthesis of their own proteins;

b) protein synthesis prevails over decay - sharply increased synthesis of DNA, RNA. The activity of nucleic acid synthesis enzymes is increased, while the activity of enzymes that break them down is decreased;

c) synthesis of oncoproteins ;

d) synthesis of embryonic proteins (alpha- fetoprotein);

e) decrease in the synthesis and content of histones - proteins - suppressors of DNA synthesis;

f) the content of c-AMP decreases, which, as a rule, has an inhibitory effect on cell division; the content of c-GMP increases, which stimulates cell proliferation.

3) Features of fat metabolism:

a) tumor cells capture LDL (low-density lipoproteins) and antioxidants (alpha-tocopherol) from the blood;

b) weakened synthesis of fatty acids, enhanced synthesis of altered membrane phospholipids.

4. Antigenic atypia:

a) antigenic simplification - a decrease in the number of organ-specific antigen proteins (antigens of the main complex disappear on the surface of many cells histocompatibility);

b) antigenic complication:

- antigenic divergence - synthesis of antigens peculiar to other tissues;
- antigenic reversion - synthesis of embryonic antigens.

5. Functional atypia:

a) a decrease in tissue function (with gastric cancer , the secretion of gastric juice decreases; with leukemia, immature leukocytes are unable to participate in phagocytosis);

b) increase in tissue function (endocrine gland adenomas enhance hormone synthesis);

c) performance of a function that is not characteristic of the tissue from which the tumor grows (lung and bronchial tumor cells can synthesize pituitary hormones).

6. Monoclonality - tumor growth from 1 transformed cell.

7. Autonomy of growth - tumor growth does not depend on the regulatory influences of the body.

8. Neovascularization - the formation of new blood vessels.

Biological features that are characteristic of malignant tumors:

1. Infiltrative (invasive) growth - the main sign of malignant tumors - the penetration of tumor cells into the surrounding tissues. *Pathogenesis:*

a) reduction of adhesion forces between tumor cells:

- decrease in the number of adhesive molecules - cadherins (E- cadherin), integrins on the surface of tumor cells, which ensure adhesion of cells to each other;
- change in the location of receptors for connective tissue proteins.

b) increased mobility of tumor cells:

- cell movement is stimulated by growth factors, products of destruction of connective tissue;

- tumor cells synthesize cytokines (chemokines) and oncoproteins that have the properties of chemoattractants .

c) secretion of hydrolytic enzymes by tumor cells:

- tumor cells themselves secrete hydrolytic enzymes - matrix enzymes metalloproteinases (proteases, collagenases , glycosidases);

- cytokines of tumor cells stimulate the release of enzymes and cells of the host's body (fibroblasts);

- decrease in the activity of tissue inhibitors of hydrolases .

d) violation of neuroendocrine regulation of tumor cells.

Benign tumors are characterized by expansive growth , limited inside the capsule and without penetration into the surrounding tissues

2. Metastasis is the process of transfer of individual tumor cells to other organs and the development of secondary tumor nodes of the same histological structure in them.

Ways of metastasis of tumor cells:

- lymphogenic (transfer of cells by lymph through lymphatic vessels) - characteristic of carcinomas,
- hematogenous (through blood vessels) - characteristic of sarcoma ,
- hematolymphogenic ,
- "cavity" (transfer of tumor cells by fluids in body cavities, for example, cerebrospinal fluid),
- implantation - direct transfer of tumor cells from the surface of the tumor to the surface of the organ or tissue with which it is in contact.

Stages of lymphogenic and hematogenous ways of metastasis:

1. *Intravasation stage* - penetration of tumor cells through the wall of a blood or lymphatic vessel into its lumen. *Pathogenesis:*

a) disruption of intercellular connections and active cell motility.

b) increased proteolytic activity of cells.

c) the presence of receptors for type IV collagen, laminin , fibronectin

d) inferiority of tumor vessels, which are arranged according to the type of capillaries.

e) angiogenesis - vascular neoplasms.

f) immunodepression.

2. *Dissemination stage* - transportation of tumor cells through blood vessels and formation of cell emboli .

3. *The stage of extravasation* - the exit of tumor cells from blood vessels and their penetration into normal tissue, reproduction and formation of new tumor nodes.

3. Recurrence – repeated development of a tumor at the site of its removal.

Reasons for relapses:

a) incomplete removal of tumor cells.

b) implantation of tumor cells in normal tissue during gross, massive surgical

interventions .

c) immunodepression.

d) the action of carcinogens, which is still ongoing or the preservation of the causal factors of tumor growth.

4. Cachexia - a syndrome of exhaustion and general weakness of the body. *Pathogenesis:*

a) the phenomenon of " substrate traps";

b) synthesis of toxohormone by tumor cells , which reduces catalase activity, iron content in the blood, causes the breakdown of skeletal muscle protein, inhibits erythropoiesis ;

c) formation of interleukin-1 and tumor necrosis factor by tumor cells and macrophages , which have a systemic effect on the body (decrease in appetite, breakdown of muscle proteins, fever);

d) anorexia and impaired intake of food into the body. Anorexia - lack of appetite - a symptom that often occurs in tumors. In the pathogenesis of anorexia lies a violation of the central mechanisms of appetite regulation;

e) violation of the neuro -endocrine regulation of the metabolism of the tumor-carrying organism;

e) intoxication by tumor decay products.

The causes of tumors are carcinogens.

Classification of carcinogenic factors:

- physical;
- chemical;
- biological.

Physical carcinogens:

1. *Ionizing radiation* : X-rays, γ-radiation. Ionizing radiation has a mutagenic effect: it causes breaks in DNA strands, translocations , point mutations.

2. *Ultraviolet rays* damage DNA, causing the formation of pyrimidines dimers _ These damages are repaired by DNA repair enzymes. With a hereditary defect of DNA repair enzymes, the frequency of skin cancer increases. People with fair skin are most sensitive to the effects of ultraviolet rays.

kangri " cancer in people who use for heating clay pots filled with hot coals, which are fixed on the skin of the abdomen; cancer of the esophagus when eating excessively hot food).

4. Repeated mechanical impact (improperly selected prostheses).

Chemical carcinogens:

- By origin:
  - exogenous;
  - endogenous;
- According to the mechanism of action:
  - direct (alkylating compounds capable of attaching alkyls to DNA);
  - indirect - procarcinogens - induce tumors after metabolic transformations in the body.

Classification of exogenous chemical carcinogens:

Polycyclic aromatic hydrocarbons (surfactants): 3,4-benzpyrene dimethylbenzanthracene	They have a local effect: when injected under the skin, they cause sarcoma, when applied to the skin - cancer. When introduced into the body, they cause tumors in those organs where they accumulate. They are widespread in nature (soil , volcanic emissions), are products of incomplete combustion, are found in exhaust gases, bitumen, asphalt, tobacco smoke and resin, over-fried oil, and smoked products.
Amino compounds: b - naphthalamine	They have organotropy : they cause bladder and liver cancer. They are part of aniline and some food dyes.
Nitrosocompounds : nitrosoamines , nitrosoamides	They have organotropy . They can be synthesized in the stomach from non-carcinogenic precursors (nitrates and amines) in the presence of hydrochloric acid.
Aflatoxins	Formed by Aspergillus mold flavum , which affects foodstuffs (especially peanuts). Joint action with hepatitis B virus - causes liver cancer.
Simple chemical compounds Cr , As , Co , Ni , Be , Pb , Cd	They belong to industrial carcinogens, cause skin, lung, and prostate cancer

Endogenous chemical carcinogens:

- tyrosine and tryptophan derivatives,
- cholesterol and its metabolites,
- free radicals and lipid peroxides,
- some hormones in large doses (estrogens).

Endogenous carcinogens are characterized by: formation in the body, weak carcinogenic effect, long latent period.

Biological carcinogens - oncoviruses :

- RNA- containing viruses (it is necessary to synthesize DNA- provirus) - human T- lymphotropic virus HTLV-1 (causes T-cell leukemia in humans). Similar action with HIV.

- DNA- containing viruses:

- papova viruses: human papilloma virus,
- adenoviruses: not oncogenic for humans,
- herpesviruses : Epstein-Barr virus (causes Burkitt's lymphoma , nasopharyngeal cancer),
- hepadnoviruses : hepatitis B virus (causes liver cancer, especially when combined with aflatoxin).

Carcinogenesis is a long process of accumulation of genetic damage.

Stages of carcinogenesis:

1. *Initiation*

2. Promotion

3. Progression

Initiation - irreversible violations of the genotype of a normal cell and its transition into a state prone to transformation (latent cell). Initiation consists in the occurrence of mutations of one of the genes that regulate cell reproduction under the influence of various carcinogens:

- Activation of oncogenes (transformation of proto-oncogenes into oncogenes),
- Inactivation of suppressor genes (anti-oncogenes),
- Damage to genes that regulate apoptosis ,
- Damage to DNA repair genes.

Mechanisms of transformation:

1. *Transformation of proto-oncogenes into oncogenes - activation of oncogenes* .

Proto-oncogenes are normal genes that stimulate cell division. They encode the synthesis of growth factors, receptors for growth factors, secondary mediators of the transmission of the mitogenic signal to the nucleus, and transcription factors.

The mechanism of transformation of proto-oncogenes into oncogenes :

1) Point mutation of the proto-oncogene ,

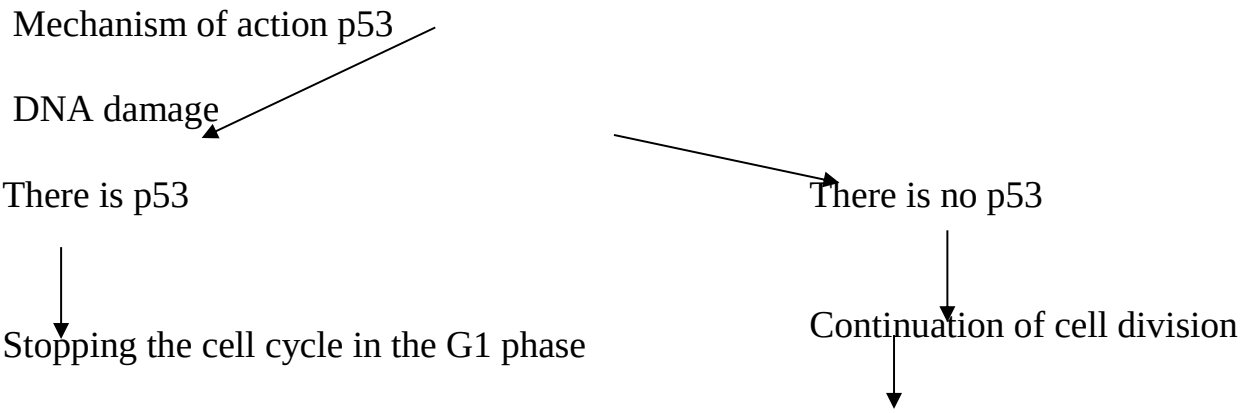
2) Translocation proto-oncogenes ,

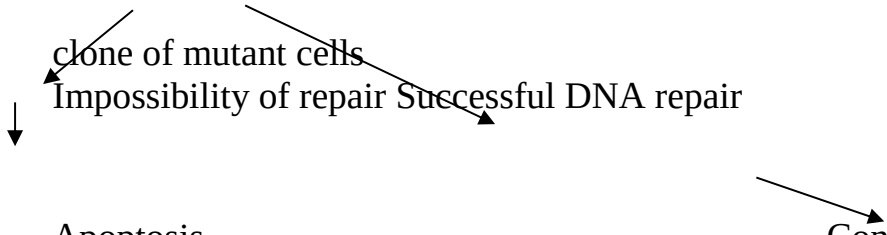
3) Amplification of a proto-oncogene - an increase in the number of proto-oncogenes that normally have a low activity,

4) Inclusion (insertion) of a promoter - a section of DNA that activates nearby genes.

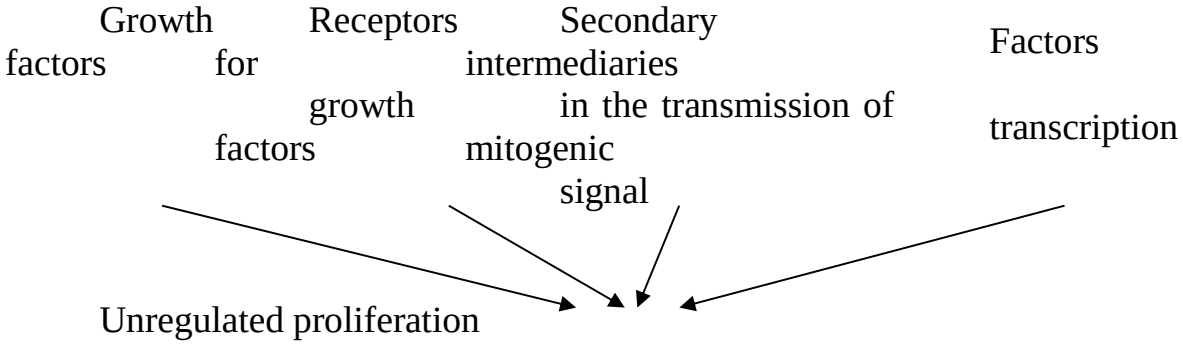
2. *Inactivation of cell division suppressor genes.*

To transform a normal cell into a tumor in In vivo , in addition to oncogene activation, inactivation of proliferation suppressor genes , including the p53 system, is necessary.





As a result of oncogene activation and inactivation of cell proliferation suppressor genes, oncoproteins are synthesized that perform the following functions:



3. *Suppression of the activity of genes that regulate apoptosis* .

Apoptosis is programmed cell death, which is triggered by various stimuli external to the cell and intracellular "conflicts" that cannot be resolved (impossibility of DNA repair, increase of intracellular calcium). External stimuli include tumor necrosis factor (TNF), the action of ionizing radiation, and free radicals.

4. *Damage to DNA repair genes.*

Damage to the repair genes weakens the cell's ability to correct errors that occur when the DNA structure is broken.

The II phase of carcinogenesis - **promotion** , unlike the initiation stage, is reversible at an early stage of the process. During promotion, the cell initiated as a result of gene changes acquires the phenotypic properties of a transformed cell. However, a long and continuous effect of promoters is necessary for the emergence of a tumor: they affect cellular differentiation and block intercellular connections, contribute to the formation of free radicals, induce the exchange of sister chromatids , stimulate the expression (power of expression) of DNA - proviruses and some retroviruses that have a revertase (reverse transcriptase , which synthesizes DNA on the RNA matrix, that is, there is a reverse flow of information from RNA to DNA). During the promotion stage, cell division is stimulated, which leads to the formation of a tumor node.

Progression is the stage of carcinogenesis, when more malignant clones of tumor cells appear - the most resistant to the body's defense forces and the effects of drugs.

Mechanisms of antiblastoma resistance:

1. Anticarcinogenic - act against carcinogens:

- reactions of inactivation of carcinogens (oxidation, reduction, methylation , acetylation , conjugation with glucuronic acid);
- elimination of carcinogens in the composition of bile, urine, feces;

- formation of antibodies against carcinogens;

- activation of the antioxidant system and inhibition of the formation of free radicals;

- destruction of oncogenic viruses.

2. Anti-transformational - prevent the transformation of a normal cell into a tumor (function of DNA repair enzymes, suppressor genes, apoptosis genes).

3. Anticellular - aimed at destroying or suppressing the growth of tumor cells (natural killers (NK-cells), sensitized T-lymphocytes (T- killers), macrophages and interferons released by them, tumor necrosis factor, immunoglobulins , keylons , heparin.

Classical methods of experimental oncology:

1. Tumor transplantation is the transplantation of a tumor from one animal to another. The following conditions are important for successful tumor transplantation: a) transplantation must be carried out within the same animal species; b) live viable tumor cells should be transplanted; c) transplantation must be done under sterile conditions to avoid the inflammatory process in the tissue.

2. Tumor induction. It involves the reproduction of malignant tumors by introducing carcinogenic factors into the body. Chemical carcinogenic compounds and cell-free filtrates of tumor tissue containing oncogenic viruses are most often used for this purpose. In addition, for the purpose of tumor induction, physical effects (X-ray radiation, ultraviolet radiation) are sometimes used.

3. Tumor explantation - tumor cultivation outside the body. This method makes it possible to study the influence of various factors on tumor growth, to search for means of therapy for malignant tumors.

Topic 11. General nosology. Typical pathological processes.
Current control of knowledge

3. Formation of professional skills, skills related to topics that are part of the content module (mastery of communication skills, clinical examination, determination of treatment scheme, conducting laboratory research, etc.) mastery of skills:

Topic 7.

1. A patient with an infectious disease has reduced phagocytosis. What are the reasons that led to a decrease in phagocytosis and how can this be related to the development of infection? What is primary?
2. Hypoplasia of the retrosternal gland was detected in the newborn . What consequences will this lead to and what is their pathogenesis?
3. In the first patient, the immunodeficient state is accompanied by mycosis and a viral disease, in the second - by purulent coccal infection. Which systems are deficient in each patient? What are the commonalities and differences in the manifestations of immunodeficiency of these systems?

Answer standard:

1. Insufficient number and quality of phagocytes, which leads to the development of infection.
2. To the insufficiency of T-Lymphocytes and related mechanisms of immunological cellular insufficiency3. The first patient has a deficiency of T-lymphocytes and cellular immune reactions. In the second patient, the lack of immunoglobulins is related to B-lymphocytes.

Topic 8.

1. In connection with an open leg injury, the victim was once again given anti-tetanus serum under the protection of antihistamine drugs. On the 9th day after the last serum injection, his body temperature rose to 38C, severe weakness, soreness and swelling of the shoulder and knee joints appeared, a generalized itchy rash on the skin, and enlarged popliteal and inguinal lymph nodes.

1) What form of pathology can be established in the patient? *Reaction of slow hypersensitivity*
2) What additional data are needed to conclude this pathology? Detection *of a precipitant in the blood IgG, IgM , level of mediators, allergen, complement system*

3) What is the possible cause and mechanism of development of this pathology?
Violation of microcirculation. With serum sickness, the impression of the wall of microvessels occurs intra- and extravascularly .

Topic 9.

1. On the 6th week of the patient's stay in the clinic due to a myocardial infarction, against the background of good treatment, dull pains and pericardial friction noise appeared in the area of the heart, the temperature rose to 39C. A blood test revealed eosinophilic leukocytosis, an increased titer of anticardiac blood pressure. The doctor diagnosed post-infarction syndrome.

1. It is known that Dressler's syndrome has an immunogenic nature, where does the AH causing it come from?
Ag is a destructively altered protein of the myocardium. Development on the background of myocardial infarction, with fever necrotized and affected myocardial cells become foreign and turn into an antigen.
2) To what type of reaction can the syndrome be classified? *Type 2 Allergic myocarditis*

3) What type of Ig do anticardial antihypertensive drugs belong to? *To IgG , IgM*

Topic 10.

1. A 50-year-old patient who, 1.5 years before consulting a doctor, took part in the liquidation of an accident at a nuclear reactor, complained of high fatigue,

weakness, dizziness, insomnia, constant cough with minimal sputum secretion. He has been a heavy smoker for 20 years, but has stopped smoking in the last 2 years, however, in the last 6 months. He suffered from bronchitis, catarrh of the upper respiratory tract, and pneumonia more than once. Bronchoscopic and histological examination determined the presence of a tumor in the right bronchus, in which there are malignant cells. 1. Specify the cause and conditions that contribute to the development of cancer. 2. What is the mechanism of carcinogenesis: initiation, promotion, progression? 3. What antiblastoma mechanism needed to be activated in this patient.

Answer standard:

1. Smoking
2. Promotion, initiation
3. Anticellular mechanism

2. hypoacid gastritis for 15 years , complained of increased weakness, a sharp decrease in appetite, nausea, vomiting, severe pain in the epigastric region, a sharp decrease in body weight over the past 3 months, and constant fever. The examination showed the presence of anemia, leukocyte count, hypochlorhydria , decreased activity of gastric juice enzymes. Gastroscopy revealed a diffuse tumor in the pyloric part of the stomach with an ulcerated center. 1. Could hypoacid gastritis be a precancerous process that stimulates tumor development? 2. What is the mechanism of fever and anemia in this patient?

Answer standard:

1. Maybe
2. A large number of pyrogenic factors.

4. Summary: testing

Topic 11.

General nosology. Typical pathological processes. Current

knowledge control

PRACTICAL TRAINING

Content module 3. Typical metabolic disorders.

Practical lesson No. 12

Topic. Violation of water-salt metabolism: etiology, pathogenesis. Dyshydria , edema.

Practical lesson No. 13

Topic. Pathophysiology of acid-base metabolism: acidosis, alkalosis

Practical lesson No. 14

Topic. Pathophysiology of energy and protein metabolism. Etiology and pathogenesis. Starvation.

Practical lesson No. 15

Topic. Pathophysiology of carbohydrate metabolism: etiology and pathogenesis.

Practical lesson No. 16

Pathophysiology of fat metabolism: etiology and pathogenesis. Atherosclerosis.

Practical lesson No. 17

Topic. Pathophysiology of extreme conditions. Etiology and pathogenesis of shock and colaptoid states.

Practical lesson No. 18

General metabolic disorders. Current control of knowledge

Purpose: Acquisition by the student of higher education of knowledge and formation of elements of professional competences in the field of medicine from the pathophysiology division:

Topic 12. Violation of water-salt exchange: etiology, pathogenesis . Dyshydria , edema.

Topic 13. Pathophysiology of acid-base metabolism: acidosis, alkalosis

Topic 14. Pathophysiology of energy and protein metabolism. Etiology and pathogenesis. Starvation.

Topic 15. Pathophysiology of carbohydrate metabolism: etiology and pathogenesis.

Topic 16. Pathophysiology of fat metabolism: etiology and pathogenesis. Atherosclerosis.

Topic 17. Pathophysiology of extreme conditions. Etiology and pathogenesis of shock and colaptoid states.

Topic 18. Verification of assimilation of acquired knowledge and skills by applicants.

Improvement of skills and competences acquired during the study of previous disciplines.

Basic concepts:

Topic 12. Violation of water-salt exchange: etiology, pathogenesis . Dyshydria , edema.

Topic 13. Pathophysiology of acid-base metabolism: acidosis, alkalosis

Topic 14. Pathophysiology of energy and protein metabolism. Etiology and

pathogenesis. Starvation.

Topic 15. Pathophysiology of carbohydrate metabolism: etiology and pathogenesis.

Topic 16. Pathophysiology of fat metabolism: etiology and pathogenesis. Atherosclerosis.

Topic 17. Pathophysiology of extreme conditions. Etiology and pathogenesis of shock and colaptoid states.

Topic 18. Verification of assimilation of acquired knowledge and skills by applicants.

Equipment: Multimedia presentations, tables.

Plan:

5. **Organizational activities (greetings, verification of those present, announcement of the topic, purpose of the lesson, motivation of higher education seekers to study the topic).**
6. **Control of the reference level of knowledge:**

Topic 12. Violation of water-salt exchange: etiology, pathogenesis. Dyshydria , edema.

The role of water and electrolytes in the body.

Concept of osmolarity , its correction.

Clinical signs of dehydration and hyperhydration .

Hypertonic dehydration. Causes, clinical signs, methods of correction.

Isotonic dehydration. Causes, clinical signs, methods of correction.

Hypotonic dehydration. Causes, clinical signs, methods of correction.

Hypertensive hyperhydration . Causes, clinical signs, methods of correction.

Isotonic hyperhydration . Causes, clinical signs, methods of correction.

Hypotonic hyperhydration . Causes, clinical signs, methods of correction.

Causes and signs of hypo- and hypernatremia , methods of treatment.

Pathophysiological disorders in hypo- and hyperkalemia , clinic, diagnosis, correction.

Violation of chlorine metabolism.

Characteristics of solutions for infusion therapy.

Water is the main component that ensures the stability of the body's internal environment. In an adult, about 2/3 of water is in the intracellular sector and 1/3 - in the extracellular sector.

The exchange of water and salts between the plasma and the extracellular environment takes place in the capillaries. Osmotic pressure in conditions of normal water-salt exchange has no significant value. Filtration is carried out due to the difference in hydrostatic (32-35 mm Hg) and oncotic (22-25 mm Hg) pressure at the arterial end of the capillary. At the venous end of the capillary, the hydrostatic pressure is 13-15 mm Hg . Art., so the liquid moves to the venous part. Most of the filtered fluid leaves the interstitial space through the lymphatic vessels.

Violation of water and electrolyte balance (dyshydria). Dyshydria is

divided into 2 groups: **dehydration** (dehydration) and **hyperhydration** (water retention). Depending on the predominance of disorders in the cellular or extracellular space, **intracellular** and **extracellular are distinguished** dyshydria . According to the concentration of electrolytes in the blood plasma, dyshydria is distinguished **hyperosmolar** , **isoosmolar** and **hypoosmolar** .

Hyperosmolar dehydration is characterized by the predominance of water loss over electrolytes during hypersalivation , overheating, hyperventilation, and diabetes insipidus. Dehydration of cells develops, catabolic processes and cellular exicosis increase . Neurological disorders appear, body temperature rises.

Isoosmolar dehydration occurs with simultaneous loss of water and electrolytes during acute blood loss. Circulatory disorders develop with a decrease in blood pressure up to hypovolemic shock, neurological disorders, dryness of the skin and mucous membranes, soft eyeballs appear.

Hypoosmolar dehydration develops due to a deficiency of electrolytes in the plasma - losses during diarrhea and vomiting. High osmotic pressure inside the cell promotes the movement of water into the cell, causing its hyperhydration . This redistribution of water leads to circulatory disorders - tachycardia, hypotension , dryness of mucous membranes, decrease in tissue turgor.

Hyperosmolar hyperhydration occurs with increased reabsorption of sodium (forced consumption of sea water, use of hypertonic solutions, hyperaldosteronism) with subsequent retention of water in tissues. An excess of sodium in the extracellular space is accompanied by the development of edema and the appearance of fluid in the cavities.

Isoosmolar hyperhydration occurs when the plasma and extracellular space are filled with isotonic fluid (transfusion of a large amount of isotonic solutions (0.9% NaCl , 5% glucose); heart failure; oligo- and anuria in renal failure), while the intracellular sector remains normal. Edema at isosmolar hyperhydration appears when the concentration of protein in the blood plasma begins to decrease. Diluted plasma due to low oncotic pressure is not retained in the vascular bed and passes into the interstitial space.

Hypoosmolar hyperhydration occurs during the overflow of the extracellular space with a liquid with low osmotic pressure (hyponatremia) - with a long-term diet without salt, hyperproduction of antidiuretic hormone. As a result of the decrease in plasma osmolality , water enters the cells and cellular hyperhydration develops - "water poisoning" of the body with pronounced neurological disorders, vomiting, convulsions, loss of consciousness up to coma.

Edema - retention of water in the body mainly in the intercellular space with an excess of water and sodium retention. In the pathogenesis of edema, an increase in the hydrostatic pressure in the vessels, a decrease in the oncotic pressure of the blood plasma, an increase in the permeability of the vascular wall, and a violation of lymph flow are important .

The main pathogenetic factors of edema development:

1. *Hydrodynamic.* An increase in filtration pressure due to: a) an increase in venous pressure (general venous congestion associated with heart failure, impaired patency of veins, insufficiency of venous valves, etc.); b) narrowing of venules .

2. *Osmotic.* A decrease in the osmotic pressure gradient between the blood and the interstitial medium due to the accumulation of osmotically active substances (electrolytes, metabolic products) in the intercellular space.

3. *Oncotic* . A decrease in oncotic blood pressure, or an increase in it in tissues, intercellular fluid. Hypoonxia of the blood is most often due to a decrease in the level of protein and, mainly, albumins due to: a) insufficient intake of protein in the body; b) violation of albumin synthesis; c) excessive loss of blood plasma proteins with urine in some kidney diseases.

4. *Membranogenic* . Increased permeability of capillary vessels due to: a) the effects of humoral factors (histamine , serotonin, kinins , prostaglandins , etc.); b) violation of the trophic state of the wall of capillary vessels (violation of the neurotrophic supply, starvation, hypoxia, etc.).

5. *Lymphatic.* Violation of outflow, stagnation of lymph in the organ (damage or obturation of lymphatic vessels, elephantiasis, etc.).

6. *Violation of nervous and humoral regulation* of water-electrolyte exchange (violation of the sensitivity of volume and osmoreceptors, secondary aldosteronism , hypothyroidism, etc.).

Depending on the causes and mechanisms of development, the following are distinguished:

Cardiac or congestive edema is associated with difficulty in blood flow. As a result of an increase in venous pressure (hydrostatic factor), liquid from vessels more actively moves into the interstitial space, which is facilitated by increased permeability in connection with the development of hypoxia. The same mechanism is associated with increased permeability of kidney glomerular tubules and limited reabsorption of protein in them, increased production of renin, angiotensin I and II, stimulated production of aldosterone, increased sodium reabsorption, increased secretion of ADH, increased reabsorption of water in the distal parts of the renal tubules. The consequence of these processes is an increase in the mass of circulating blood, the filtration pressure in the vessels becomes higher - and water again moves into the interstitial sector.

Renal edema is often associated with a decrease in glomerular filtration (acute glomerulonephritis), the osmotic pressure of plasma increases. With nephrotic syndrome, the permeability of the glomeruli to protein increases, the oncotic pressure of the plasma decreases and the fluid moves into the interstitial space.

Starvation (cachectic) edema develops with protein deficiency, especially with chronic diseases of the stomach and intestines. Hypovolemia develops and, as a compensatory reaction, the reabsorption of sodium and water increases, which worsens edema.

Inflammatory edema is associated with increased vascular permeability, high osmotic and oncotic pressure in tissues.

Violation of electrolyte exchange:

I. ***Na*** $^{+}$ *(extracellular electrolyte, 130-145 mmol/l).*

1. Primary hypernatremia (an absolute increase in sodium ions in the body) can occur either as a result of an increase in the intake of sodium into the body (intake of a large amount of sodium chloride, introduction of its hypertonic solution), or as

a result of a decrease in the removal of sodium from the body (primary and secondary hyperaldosteronism , renal failure).

Secondary (relative) hypernatremia is an increase in the content of sodium ions in the blood and intercellular fluid as a result of water loss by the body. At the same time, the total sodium content in the body may not change, and sometimes it decreases. This condition occurs with hyperventilation, diarrhea, increased sweating, and diabetes insipidus.

Protective and compensatory reactions : as a result of hypernatremia , the osmotic pressure of the extracellular fluid increases, central and peripheral osmoreceptors are disturbed, and the amount of antidiuretic hormone in the blood increases. The latter enhances the reabsorption of water in the kidneys, as a result of which the volume of extracellular fluid increases and its osmotic pressure decreases.

Consequences: the development of intracellular dehydration.

2. Primary (absolute) hyponatremia develops as a result of a decrease in the intake of sodium in the body (salt-free diet, anorexia) or as a result of an increase in the excretion of sodium from the body by the kidneys (hypofunction of the adrenal cortex, renal failure).

Secondary (relative) hyponatremia is excessive intake of water in the body or its retention - hyponatremia due to dilution.

Protective and compensatory reactions : a decrease in the concentration of sodium ions in the extracellular fluid causes, on the one hand, an increase in the secretion of aldosterone through the renin-angiotensin mechanism, on the other hand, a decrease in the flow of antidiuretic hormone into the blood, since the impulse from osmoreceptors decreases. Strengthening the reabsorption of sodium ions and inhibiting the reabsorption of water in the kidneys - the osmotic pressure of the extracellular fluid is restored.

Consequences: generalized cell swelling.

II. K^+ *(intracellular electrolyte, 3.5-5.5 mmol/l).*

1. Hyperkalemia . Reasons: 1) excess intake of potassium in the body; 2) the transition of potassium ions from the intracellular to the extracellular space with massive damage to cells, with an increase in the intensity of catabolic processes and acidosis; 3) impaired excretion of potassium from the body (oligo- and anuria, insufficiency of the function of the adrenal cortex).

Protective and compensatory reactions: an increase in the concentration of potassium ions in the blood directly activates the cells of the glomerular zone of the adrenal cortex and causes an increase in the secretion of aldosterone. The latter increases the secretion of potassium ions in the renal nephrons and thus restores their concentration in the blood.

Consequences: 1) violation of the activity of excitable tissues (nervous and muscular), as a result of which disorders of the central nervous system, cardiovascular system, skeletal muscles, and smooth muscles of the alimentary canal develop; 2) development of non-gaseous acidosis.

2. Hypokalemia . Reasons: 1) insufficient intake of potassium in the body with food (long-term use of a diet that does not contain products of plant origin); 2) increased transition of potassium ions from the extracellular space into the cells,

which occurs with increased anabolic processes and alkalosis; 3) loss of potassium in the body (polyuria, hyperaldosteronism , long-term use of diuretics).

Protective and compensatory reactions : the development of hyperpolarization of the membranes of secretory cells and in this connection the secretion of aldosterone by the adrenal cortex decreases. This causes a decrease in the secretion of potassium ions by cells of the renal epithelium.

Consequences: a) the threshold of cell excitability increases and, as a result, general weakness, flatulence, hypotonia of skeletal muscles appear, skin sensitivity decreases; 2) hypokalemic alkalosis develops.

III. Ca^{2+} *(2.25-2.75 mmol/l).*

1. Hypocalcemia . Reasons: - decrease in the flow of calcium from the small intestine into the blood: a) decrease in calcium content in food products; b) violation of the ratio of calcium / phosphorus in food products; c) formation of insoluble calcium compounds in the intestines ; d) violation of absorption of calcium in lesions of the small intestine (enteritis); e) hypovitaminosis D; - loss of ionized calcium by the body: a) with urine in case of reabsorption disorders; b) during pregnancy - losses associated with the formation of the fetal skeleton; - violation of mobilization of calcium from bone tissue: a) hypoparathyroidism ; b) tumors of C-cells of the thyroid gland, which produce calcitonin ; - mineralization of soft tissues: a) hyperphosphatemia ; b) alkalosis; - transition of blood plasma calcium from an ionized form to a non-ionized one - into complexes with proteins and organic acids: a) oxalic acid poisoning, transfusion of citrated blood; b) increasing the concentration of serum proteins; c) alkalosis.

Protective and compensatory reactions : 1) increased parathyroid hormone secretion ; 2) increased formation of 1,25 $(OH)_2$ -vitamin D in the kidneys; 3) reduction of calcitonin secretion . Thanks to these reactions, the absorption of calcium and phosphorus in the intestines increases, and their transfer from the bones to the blood increases.

Consequences: 1) disturbance of skeletal bones - development of rickets in children and osteomalacia in adults; 2) syndrome of increased neuromuscular excitability - tetany.

2. Hypercalcemia . Reasons: - increased influx of calcium from the small intestine into the blood: a) excessive calcium content in food products; b) enhanced

absorption of calcium in the intestines, which happens most often with hypervitaminosis D; - reduction of calcium removal from the body: a) acquired disorders - chronic renal failure; b) hereditary disorders - familial hypocalciuria hypercalcemia ; - increased influx of calcium into the blood from bone tissue: a) hyperparathyroidism ; b) malignant tumors with bone metastases; c) multiple bone fractures; - violation of calcium deposition in bone tissue, which is observed in hypophosphatemia .

Protective and compensatory reactions: 1) decrease in parathyroid hormone secretion ; 2) a decrease in the formation of 1.25 $(OH)_2$ -vitamin D in the kidneys and an increase in the formation of 24.25 * $(OH)_2$ -vitamin D; 3) increased secretion of calcitonin .

Consequences: 1) damage to cells by calcium ions; 2) calcification of soft

tissues - calcification ; 3) decrease in excitability of excitable tissues; 4) formation of calcium stones in the kidneys; 5) increased gastric secretion with the formation of peptic ulcers in the stomach; 6) development of arterial hypertension.

IV. P (0.87-1.45 mmol/l).

1. Hypophosphatemia . Reasons: a) decrease in the intake of inorganic phosphorus in the body (starvation, malabsorption syndrome , hypovitaminosis D); b) increased excretion of phosphates by the kidneys (hyperparathyroidism , phosphate diabetes, Fanconi syndrome).

Consequences: disorders of oxidative phosphorylation in cells, a decrease in the formation of 2,3-diphosphoglycerate in erythrocytes, as a result of which the oxyhemoglobin dissociation curve shifts to the left and hypoxia develops. At the same time, there are disturbances in the digestive system (dyspeptic phenomena, anorexia), blood system (hemolytic anemia, leuko- and thrombocytopenia), nervous system (paresthesia, ataxia, confusion of consciousness, in severe cases - coma), musculoskeletal system (osteomalacia, myopathy, phosphopenic rickets in children).

2. Hyperphosphatemia . Reasons: a) increased influx of phosphates from the cells and tissues of the body into the blood (heavy physical exertion, hemolysis of erythrocytes, leukemia, metastases and primary malignant bone tumors); b) impaired removal of phosphates by the kidneys (hypoparathyroidism , kidney failure).

Consequences: calcification of soft tissues.

Topic 13. Pathophysiology of acid-base metabolism: acidosis, alkalosis

What is the acid-base state (KOS) and pH ?

Why should the body maintain pH stability ?

Physico-chemical and physiological mechanisms of maintaining the constancy of COS.

Buffer systems, their meaning and functioning mechanisms.

The value of bicarbonate buffer for maintaining normal extracellular fluid pH .

Relationship between disorders of electrolyte metabolism and KOS.

The role of the lungs in controlling blood pCO2.

Renal mechanisms of compensation in cases of COS disorders.

Mechanisms and purpose of renal ammonogenesis .

Classification of KOS violations by pathogenesis and degree of compensation.

Etiology and pathogenesis of various forms of COS disorders.

Mechanisms of development of metabolic acidosis in the course of diabetes, starvation and hypoxia.

Types and mechanisms of development of renal tubular acidosis.

Acidosis is *a disorder of the digestive system in which the blood increases the level of acids decreases level bicarbonate* . **Alkalosis** *is a violation of the KOS, in which the blood is increasing level bicarbonates and decreases acid level* . In dependence from the degree of compensation (pH shift beyond normal values - 7.4 ± 0.05) *of acidosis and alkalosis* are divided into:

- *compensated* (pH capillary blood does not exceed 7.4±0.05);

- *decompensated* (pH capillary blood exceeds the limits of 7.4±0.05).

With *compensated acidosis and alkalosis* the absolute amount changes [HCO_3] and PCO_2, but the ratio [HCO_3-]/(0.03*PCO_2) remains within the normal range (20:1). While maintaining this ratio pH blood does not change significantly , that is, it remains within 7.35-7.45. Accordingly decompensated are such violations of KOS, when not only the absolute quantity changes components bicarbonate buffer and others ratio , as a result of which there is a shift in pH beyond normal parameters .

According to *the mechanism intelligence* all violations of the Code of Civil Procedure are divided into *respiratory* and non - *respiratory* . The first arise as a result excretion of CO_2 by the lungs.

The key mechanism for the development of this disorder is an increase or decrease in PCO_2 and therefore carbonic acid.

Non-respiratory disorders are called COS disorders caused by primary growth in the blood the concentration of non-volatile acids and bases, as a result of which there is a shift in the buffer bases - BE and the concentration bicarbonate . This may be due to:

- increasing the introduction of non-volatile acids and bases from the outside ;
- metabolic disorder accompanied by accumulation organic acids;
- disorders of the kidneys and gastrointestinal tract as a result of the delay or excess excretion of acids and bases.

In this connection , non-respiratory acidosis are divided into *metabolic and excretory and exogenous* , and alkalosis on *excretory and exogenous* .

Classification of violations of the Code of Criminal Procedure

1. Acidosis :

1) respiratory (respiratory, gas);

2) non-respiratory (non-gaseous);

a) metabolic ,

b) isolated

c) exogenous

3) *combined (respiratory + non-respiratory*)

2. Alkalosis :

1) respiratory (respiratory. gas)

2) non-respiratory (non-gaseous)

a) secretory (excretory);

b) exogenous;

3) combined (respiratory + non-respiratory)

3. Mixed forms of violations of the Code of Civil Procedure:

1) primary respiratory acidosis and secondary non-respiratory acidosis alkalosis ;

2) primary non-respiratory acidosis and secondary respiratory acidosis alkalosis ;

3) primary respiratory alkalosis and secondary non-respiratory acidosis;

4 *) primary non-respiratory alkalosis and secondary respiratory acidosis*

Evaluation of KOS. Laboratory indicators of blood used in the clinic to characterize KOS

No	KOS indicators	Marking	Normal value
1	Indicator [H^+]	pH	7.4±0.05
2	Voltage CO_2	RSO_2	40±5 mm Hg .
3	Shift of buffer bases	VE	± 2.5 mmol/l
4	Buffer bases	VV	48±2.5 mmol/l
5	Standard bicarbonate	SB	24±3 mmol/l

Respiratory (respiratory, gas) acidosis is a frequent form of COS disorders caused by an increase in the blood of PSO_2 more than 45 mm. RT _ Art.

Causes of respiratory acidosis:

- all types of deficiency external breathing, when gas exchange is disturbed between external air and alveoli (bronchial attack asthma , aspiration foreigners body , hemo-, pneumothorax, suppression of the respiratory center) aba between alveoli and blood (pulmonary edema , thromboembolism pulmonary arteries and others);
- breathing air or mixtures with a large content carbon dioxide.

KOS indicators in respiratory diseases acidosis

Gas acidosis	**pH**	**pCO_2**	**SB**
Compensated	=	↑↑	↑↑
Partially compensated	↓	↑↑	↑
Decompensated	↓↓	↑↑	=

Non-respiratory acidosis - develops with a decrease in VE blood below -2.5 mmol/l, is the most frequent and severe form of COS impairment.

KOS indicators in non-respiratory conditions acidosis

Gaseous acidosis	pH	pCO_2	SB
Compensated	=	↓↓	↓↓
Partially compensated	↓	↓	↓↓
Decompensated	↓↓	=	↓↓

Metabolic non-respiratory acidosis develops as a result of increased formation of organic acids in the body's cells in the process of metabolism.

There are two main types of *non-respiratory metabolic acidosis* :

– **lactic acidosis –** lactic acid is formed in excess in muscle and other cells as a result of activation of glycolysis during heavy physical exertion or generalized hypoxia of any kind;

– **keto-acidosis –** ketone bodies in excess are formed in liver cells as a result of activation of ketogenesis from free fatty acids with a deficiency of insulin in the body and an excess of counterinsular hormones.

Isolated non-respiratory acidosis develops in various kidney diseases, which are accompanied by disturbances in the mechanisms of secretion in the tubules of hydrogen ions and reabsorption of sodium and bicarbonate. It is also possible to lose bicarbonate with secretions of the pancreas and intestinal glands (diarrhea, fistulas of the intestine and pancreatic ducts)

Exogenous non-respiratory acidosis caused by an excess of acids entering the body from the outside, mainly from the gastrointestinal tract (acid poisoning, overdose with acidic drugs), or by intravenous administration of acidic solutions .

KOS indicators in non-respiratory acidosis: pH = 7.35; PCO_2 =36 mm Hg ; BE= -4 mmol/l (compensated); pH = 7.15; PCO_2 =38 mm Hg ; BE=-16 mmol/l (decompensated).

Respiratory alkalosis is formed when the blood $PCO_{2\ decreases}$ to less than 35 mm Hg , which is observed in severe conditions accompanied by a significant increase in lung ventilation at a normal level of metabolism.

Causes of respiratory alkalosis:

1) high-altitude respiratory hypoxia;
2) hyperventilation lungs of central genesis (tumors, injuries, encephalitis, stroke);
3) long-term enhanced artificial ventilation of the lungs .

KOS indicators in respiratory alkalosis : pH = 7.45; PCO_2 =30 mm Hg ; BE= -2 mmol/l (compensated); pH = 7.52; PCO_2 =26 mm Hg ; BE= -0.5 mmol/l (decompensated).

Non-respiratory alkalosis occurs when the VE of the blood increases above +2.5 mmol/l

Isolated non-respiratory alkalosis can be formed with significant losses of anions of strong acids - most often chloride ion Cl^-, and along with them, H^+ ions . This loss can occur:

1) through the mucous membrane of the stomach;
2) through the kidneys:

a) with an overdose of loop diuretics

b) with excessive secretion of corticosteroid hormones or with long-term treatment with these hormones;

c) with hypofunction of the parathyroid glands and lack of parathyroid hormone .

Exogenous non-respiratory alkalosis is formed with excessive use of bases.

KOS indicators in non-respiratory alkalosis : pH = 7.45; PCO_2 =41 mm Hg ; BE= +3.5 mmol/l (compensated); pH = 7.5; PCO_2 =45 mm Hg ; BE= +10 mmol/l (decompensated).

Term	Definition
pH	Negative decimal logarithm concentration H^+, which in extracellular liquid in norms is equal to 7.4 ± 0.05, in cytoplasm cells – 7.0 - 7.2, and in activated lysosomes - 5.0 - 5.5
pCO_2 of blood	Partial pressure CO_2 plasma, which in arterial of blood in norms is equal to 40 ±4 mm RT _ Art.
Buffer system	Mixture weak acid and her salt, atwhen added to which strong acid most of the hydrogen ions bind to the conjugate base to formweak acid and neutral salt, which reduces number free H^+ and those by myself prevents landslide pH
Acidosis	State, what characterized by decrease pH or tends to lower pH because of reduction correlation between metabolic and respiratory components bicarbonate buffer($NaHCO_3/PCO_2$)
Alkalosis	A condition characterized by an increase pH or tends to increase pH because of magnification correlationbetween metabolic and respiratorycomponents bicarbonate buffer ($NaHCO_3/PCO_2$)
Gaseous acidosis	acidosis, what is caused primaryby increasing PSO_2 of blood due to hypoventilation lungs
Gaseous alkalosis	alkalosis, what is caused primaryadecreasin blood PSO_2 due to hyperventilation lungs

Non-gasacidosis	acidosis, which occurs because of decrease in bicarbonate, whichis caused by a decrease correlation between fixed cations and anions
Non-gas alkalosis	alkalosis, which occurs because of an increase in bicarbonate thatcaused by an increase correlation between fixedcations and anions
fixed	Such contents whose in body changes
cations and anions	only at their introductions or output (Na^+, K^+, Cl^- and others)
Semi-fixed cations and anions	Those that are formed and are metabolized in process exchange with small speed (NH_4^+, lactate, pyruvate, ketones bodies, proteins)
Unfixed cations and anions	Such which are formed and disappear in exchangeprocess almost instantly (bicarbonate and ion hydrogen)
Metabolic acidosis	occurs at excessive formation in body anions lactate at hypoxia and diabetes or ketone anions bodies during starvation and diabetes
Exogenous acidosis	occurs under time introduction in organism acids or of salt strong acids from cations, what are metabolized (example, NH_4Cl)
Excretory acidosis	occurs because of losses fixedcations with diarrhea or dysfunction renal tubules
Exogenous alkalosis	occurs at introductions in organism meadowsor of salt with organic anions, that are metabolized
Excretory alkalosis	occurs or at increase in kidneys Na^+ reabsorption , or at loss of Cl^- because of vomiting or reduction his renal reabsorption
Renal ammonogenesis	The process of formation of glutamine in nephrocytes NH^+, which is secreted into the urine in exchange for Na^+, which is reabsorbed

Topic 14. Pathophysiology of energy and protein metabolism. Etiology and pathogenesis. Starvation.

Define the concept of basic exchange
The level of basic metabolism of an adult depends on age.
Methods of determining the main exchange

In the case of which pathological changes there is an increase and decrease in the basic metabolism.

Starvation. Characteristic. Kinds Stages.

Manifestations and clinical symptoms.

Complication.

Fats are contained in all human tissues, and are the main and mandatory components of human food. The need for fats depends on age, lifestyle, climate and other factors (on average, you need to consume 80-100 g of fats per day).

Lipids include triglycerides , glycerophosphates , cholesterol and its esters, bile acids, fatty acids (unsaturated and saturated) and other compounds. Lipids are part of cell membranes, are the main sources of energy, solvents of vitamins A, D, E, F, participate in the synthesis of steroid hormones, in the creation of protective heat-insulating and water-repellent coatings, play a mechanical role (fixation of the kidneys). Lipids (prostaglandins) are regulators of the functions of various organs in normal and pathological conditions, participate in the transmission of nerve impulses, in the creation of intercellular contacts. Enzyme complexes that are part of lipids play an important role in blood clotting, digestion, and immunological processes. The lack of lipids in the body leads to a violation of these functions. Some lipids enter the body with food, other lipids are synthesized in the body. Some polyunsaturated acids (linoleic , linolenic, etc.) are introduced into the body with vegetable fats, which belong to essential fatty acids, because they are not synthesized in the human body, their function is extremely important. Therefore, the European Association of Experts for the Elimination of Fat Metabolism Disorders recommends limiting only the total consumption of fats, especially of animal origin, and not completely eliminating the consumption of fatty acids and dietary cholesterol. It is also recommended to increase the consumption of products enriched with polyunsaturated fatty acids (liquid vegetable oils, fish, poultry, seafood). If there is insufficient intake of fats in the body, the probability of oncological diseases increases sharply.

Pathological changes in fat metabolism can occur at various stages in the event of a violation:

processes of digestion and absorption of fats;

transport of fat and its transition into tissues;

oxidation of fats in tissues;

intermediate fat metabolism;

fat exchange in adipose tissue (excess or insufficient formation and deposition).

The pathology of fat metabolism is manifested by various types of hyper-lipoproteidemia and alipoproteidemia .

Hyperlipoproteinemia . There are 5 types of hyperlipoproteinemia :

Type I – fat-induced lipemia ;

II type – hyper -α- lipoproteidemia (multiple nodular xanthoma). Characteristic early manifestations of atherosclerotic changes in vessels, especially coronary, xanthomatous changes in the endocardium and heart valves, tendon xanthomas (hard deposits of fat), peri-orbital xanthelasma , rheumatoid joint pain.

There are known cases of death from myocardial infarction in childhood. In these patients, a defect of LDL receptors on skin fibroblasts was detected, which leads to a decrease in the breakdown of LDL and an increase in cholesterol synthesis.

type – dys -β- lipoproteidemia (“ floating ” hyperlipemia). Patients are characterized by hypertrophy of lipocytes , atherosclerosis of coronary arteries, angina pectoris, myocardial infarction, obturation diseases of peripheral arteries, yellowish-brown deposits of lipids in the skin of the lines of the palms in places where wedding rings are stamped, and xanthomas . These manifestations are observed already in early childhood. Obesity, diabetes, and fatty liver disease develop.

type – hyperpre -γ- lipoproteidemia (familial essential hyperlipemia), in which the presence of a genetic defect is assumed. Fatty liver, diabetes mellitus, coronary sclerosis and organ angiopathy , general obesity, intermittent lameness develop. Clinical manifestations of atherosclerosis are observed more often in adults and the elderly.

Type V – hyperchylomicronemia (combined lipemia caused by disturbances in the metabolism of both fats and carbohydrates). Patients have symptoms similar to type IV. In addition, pancreatitis, neuropathy with painful paresthesias of hands and feet, and vascular complications are possible. The presumed cause is secondary inhibition of chylomicron cleavage .

Treatment of familial hyperlipoproteinemias includes limiting the intake of neutral fats and carbohydrates while introducing short-chain fatty acids into the diet.

α- lipoproteidemia . α- lipoproteidemia – Tenzhi disease . The type of inheritance is autosomal recessive. The basis of the defect is a violation of the synthesis of the protein component. The following signs are observed in homozygous representatives: there is no normal α- lipoprotein , only the altered α-lipoprotein "Tenti - LP" is present. The pathogenetic mechanism is based on insufficient evacuation of cholesterol esters.

Symptoms: enlarged tonsils, hepatosplenomegaly , enlarged lymph nodes (accumulation of cholesterol esters), diarrhea, retinitis, clouding of the cornea.

Patients feel relatively well because α- lipoprotein has a short half-life.

α-β- lipoproteidemia – Bassen-Kornzweig disease . The type of inheritance is autosomal recessive.

Etiology: inability of the liver to synthesize active aprotein or the possibility of synthesis of only inactive aprotein B.

Bassen-Kornzweig disease can also develop as part of autoimmune processes in diseases of the liver and gastrointestinal tract (the formation of LP is disturbed), in diseases of the thyroid gland (the splitting of LP increases).

Symptoms: steatorrhea , progressive dystrophy. In the walls of the intestines fat stagnation is detected. In many body systems, the structure of cell membranes is disturbed. On the surface of erythrocytes, thyroid bulges (acanthocytes) are observed, anemia develops with reticulocytosis and bone marrow hyperplasia. Damage to the myelin sheaths leads to disorders of the peripheral nerves and the central nervous system (pyramidal tract and cerebellum). The first symptom in the second year of life is the fading of tendon reflexes. Ataxic gait , characteristic

nystagmus, violation of vibration sensation. Patients have mental retardation, myopathy. Pigmentary retinopathy develops, which causes scotoma and blindness.

The role of lipid metabolism disorders in the pathogenesis of atherosclerosis. Atherosclerotic changes in blood vessels are characteristic of almost all people over 40 years old, the difference is only in the degree of changes. The development of atherosclerosis is closely related to the processes of cholesterol transport into the arterial wall, removal of cholesterol from the arterial wall. Violation of this process occurs in the absence of specific receptors on the surface of cells, increased affinity of lipoproteins with the membrane, direct damaging effect of excess cholesterol on the endothelium and vascular smooth muscle cells. An excess of lipoproteins accelerates the development of atherosclerosis.

Hereditary forms of accelerated atherosclerosis are caused by a defect in lipoprotein genes and their receptors, enzymes of lipoprotein and cholesterol metabolism, the rate of production and catabolism of lipoproteins circulating in the blood changes in the liver. Various molecular defects have been noted in different families, which lead to an imbalance of cholesterol either in the cells or in circulating blood lipids.

Cholesterol, triglycerides , and saturated fatty acids have atherogenic properties. An increase in the concentration of atherogenic lipoproteins in the blood can be caused by a decrease in the rate of their removal from the blood to the liver; increasing the speed of their synthesis; violation of metabolism in plasma, taking into account the formation of abnormal modified lipoproteins . Phospholipids and polyunsaturated fatty acids have antiatherogenic properties . They limit the absorption of dietary cholesterol in the small intestine, stimulate the synthesis of bile acids in the liver, inhibit the synthesis and secretion of various lipoproteins.

Fat infiltration and fatty dystrophy

If the fat entering the cells is not split, oxidized , or removed from it, this indicates fatty infiltration. If it is not combined with a violation of the plasma structure and its protein component, then it is called fatty dystrophy. The general cause of fatty infiltration and fatty dystrophy is considered to be suppression of the activity of oxidizing and hydrolytic enzymes of fat metabolism (in case of arsenic, chloroform poisoning, vitamin deficiency , etc.).

Fatty infiltration develops with alimentary and transport hyperlipemia and with a violation of the formation of phospholipids, which is a consequence of insufficient intake of choline, methionine and other lipotropic factors with food, insufficient secretion of lipocaine by the pancreas , which activates the formation of phospholipids in the liver and oxidation of fatty acids in it.

Disruption of fat metabolism in adipose tissue is manifested by obesity.

Obesity *is the tendency of the body to excessively increase body weight under the influence of certain conditions.*

At the same time, the body weight increases (Fig. XIV) due to the abnormal accumulation of fat in the depot.

By etiology, obesity is divided into three types: alimentary, hormonal (Fig. XV), cerebral. The essential role of heredity in the pathogenesis of obesity. Obesity develops as a result of three main pathogenic factors:

increased intake of carbohydrates and fats in food with inappropriate use of fat for energy;

insufficient use (mobilization) of fat from the depot as a source of energy;

excessive formation of fat from carbohydrates.

Consequences of obesity: impaired glucose tolerance, hyperglycemia, hyperinsulinemia ; increased excretion of glucocorticoids with urine (in contrast to patients with Ishchenko- Cushing syndrome , the ratio of excretion of glucocorticoids and creatinine remains normal in obese patients) after exercise, during sleep; after the introduction of arginine, smaller fluctuations in the concentration of somatotropic hormone in the plasma are observed; decrease in insulin sensitivity of enlarged alipocytes and muscles; increase in the content of unsaturated fatty acids in the blood - increased consumption of them by the muscles; hypertrophied lipocytes are more responsive to norepinephrine and other lipotic substances.

Starvation is a typical pathological process that develops as a result of a complete lack of food or insufficient intake of nutrients in the body, as well as in conditions of a sharp violation of the composition of food and its assimilation.

Classification of starvation:

Physiological, pathological and therapeutic fasting are distinguished by origin. Physiological starvation is characteristic of some animal species during hibernation.

The pathological type of starvation is divided into:

1. Complete fasting: a) with drinking water; b) without drinking water (absolute).

2. Incomplete starvation (malnutrition).

3. Partial starvation (quality).

Complete fasting with water. *Pathogenesis:*

I. The period of uneconomic energy consumption . Lasts 2-4 days. A strong feeling of hunger is characteristic, due to the excitation of the food center. With complete starvation, it lasts up to 5 days, and then disappears. Rapid weight loss occurs. The main source of energy during this period is *carbohydrates* , as evidenced by the value of the respiratory coefficient, equal to 1.0. Hypoglycemia occurs, which increases the secretion of glucocorticoids by the adrenal cortex. This results in increased catabolism of proteins in peripheral tissues, in particular muscle, and activation of gluconeogenesis in the liver. The main exchange first increases slightly, and then gradually decreases and becomes 10-20% less than the original. A negative nitrogen balance develops .

II. The period of maximum adaptation . Its average duration is 40-50 days. The pace of body weight loss slows down to 0.5-1% per day. The feeling of hunger disappears. The main source of energy is *fats*, which is evidenced by the value of the respiratory coefficient, equal to 0.7. Hypoglycemia increases the flow of lipolytic hormones (adrenaline, glucocorticoids , glucagon) into the blood. As a result, fat is mobilized from the depot and hyperlipacidemia develops . It, in turn, is the cause of increased formation of ketone bodies in the liver. The resulting ketonemia can lead to metabolic acidosis. The main exchange during this period is 10-20% below the

initial level. The nitrogen balance is negative.

III. Terminal period. Duration - 2-3 days. Intensive decay of tissues occurs, intoxication develops. The main source of energy is *proteins* , as evidenced by the value of the respiratory coefficient, equal to 0.8. Urinary excretion of nitrogen, potassium, and phosphates increases (signs of destruction of cells and tissue proteins). Death occurs when the body weight decreases to 50% of the original.

Absolute fasting is complete fasting without drinking water. Its duration is 2-3 times less than the duration of complete fasting with water, due to the fact that there is an increased splitting of fats to form endogenous, as a result of which ketonemia and non-gaseous acidosis develop rapidly. The severity of the course of absolute starvation is also due to the accumulation of a large number of end products of metabolism and other toxic products, which require water to be removed from the body.

Incomplete starvation (energy deficiency) develops when the energy value of food does not satisfy the body's energy needs.

Protein-energy deficiency is a condition that occurs as a result of a combination of incomplete and high-quality protein starvation. *Species:*

a) alimentary dystrophy - in its pathogenesis, in addition to protein and energy deficiency, additional factors are also important: cold, physical fatigue, neuropsychological tension;

b) alimentary fever . It develops in children up to one year of age. Energy deficiency comes first;

c) kwashiorkor . It develops in children aged 3-6 years. the main factor in pathogenesis is protein deficiency, the energy deficit is compensated by excessive consumption of carbohydrates.

Clinical manifestations of protein-energy deficiency:

1. Insufficient intake of proteins in the body leads to a violation of the liver's biloxinthetic function. This is the cause of hypoproteinemia , which, in turn, causes the development of oncotic edema.

2. Energy deficiency is the cause of a decrease in basic metabolism. This is manifested by a decrease in body temperature (hypothermia).

3. Atrophic syndromes. Their development is associated with violations of the plastic and energy supply of cells. A manifestation of atrophic changes in the central nervous system is the slowing of mental development, in the digestive system - malabsorption and diarrhea, in the cardiovascular system - hypotension , in the immune system - a decrease in the synthesis of antibodies and increased sensitivity to infections, in the red bone marrow - the development of anemia, in the skeletal in muscles - hypodynamia and muscle weakness, in bones - retardation of skeletal growth.

Partial (qualitative) starvation is the insufficient intake of one or more nutrients with the normal energy value of food. Types: protein, fat, carbohydrate, vitamin, mineral, water fasting.

Topic 15. Pathophysiology of carbohydrate metabolism: etiology and pathogenesis.

The importance of fats for the body, their metabolism in the body.

Lipids and lipoproteins of blood plasma, lipid transport.

Sources of blood plasma cholesterol and its metabolism

Anatomical and physiological features of blood vessels. Prerequisites for the formation of an atherosclerotic lesion.

Atherosclerosis. Pathogenetic mechanisms of development. Stages. Signs. Complication.

Normally, the fasting blood plasma glucose level ranges from *3.3 to 5.5 mmol/l.*

Hypoglycemia is a condition characterized by a decrease in blood plasma glucose below 3.3 mmol/l.

Etiology:

• Carbohydrate starvation is observed as a result of prolonged general starvation. Deficiency in food of only carbohydrates does not lead to hypoglycemia due to the activation of gluconeogenesis .

• Liver pathology. In most hereditary and acquired diseases of the liver, the deposition of glucose in it in the form of glycogen is disturbed and the intensity of gluconeogenesis decreases . As a result, the body is not able to maintain the level of glucose within normal limits for a long time without receiving glucose from the outside.

• Indigestion. Violation of cavity and parietal cleavage and absorption of carbohydrates lead to the development of hypoglycemia.

• Kidney pathology. Hypoglycemia develops when glucose reabsorption is impaired in the proximal tubules of the nephron of the kidneys, which leads to the development of a syndrome characterized by hypoglycemia and glucosuria (renal glucosuria).

• Endocrinopathies. The main causes of the development of hypoglycemia in endocrinopathies: insufficiency of endocrine hormones (adrenal glands, hypothyroidism, pituitary insufficiency) or excess insulin (insulinoma). Glucocorticoids , thyroid hormones, THG, catecholamines , and glucagon are included *in the contінsular hormones* . An excess of insulin activates the utilization of glucose by cells, inhibits gluconeogenesis , and inhibits glycogenolysis . These effects are observed with insulinomas or insulin overdose.

• Long-term intensive physical work leads to depletion of glycogen reserves deposited in the liver and skeletal muscles (marathon running).

• Uptake of glucose by tumor cells.

Clinical manifestations of hypoglycemia:

Hypoglycemic syndrome - a steady decrease in blood glucose below the norm, which is combined with a violation of vital activity. Manifestations of hypoglycemic syndrome can be adrenergic (due to excessive secretion of catecholamines) and neurogenic (due to disorders of the central nervous system).

• Adrenergic manifestations: hunger, anxiety, fear of death, muscle tremors, tachycardia, sweating.

• Neurogenic manifestations: headache, confusion, dizziness, visual disturbances.

Hypoglycemic coma is a condition characterized by a decrease in the level of blood glucose below normal (as a rule, less than 2.0-1.5 mmol / l), loss of consciousness, lack of reaction to external and internal stimuli, impaired cardiovascular activity and breathing.

Pathogenesis of hypoglycemic coma:

• The energy supply of cells, especially neurons, is disrupted due to a lack of glucose; deficiency of metabolites of free fatty acids - acetoacetic and β-hydroxybutyric acid , which can provide neurons with energy even in conditions of hypoglycemia. Ketonemia develops only after a few hours and in case of acute hypoglycemia cannot eliminate energy deficiency in neurons.

• Imbalance of ions and water in cells due to malfunction of energy-dependent ion carriers: loss of K^+, accumulation of H^+, Na^+, Ca^{2+}, water.

↓ influx of glucose into neurons → substrate hypoxia → violation of ATP formation → damage to neurons → coma

Principles of hypoglycemia therapy:

Etiotropic treatment is aimed at filling the deficit of glucose and eliminating the cause of its occurrence.

• Eliminating hypoglycemia is achieved by introducing glucose into the body.

• Therapy of the main disease that caused hypoglycemia (diseases of the liver, kidneys, gastrointestinal tract, glands of internal secretion).

Pathogenetic treatment is aimed at blocking the main pathogenetic links (energy supply disorders, damage to membranes and enzymes, water-electrolyte imbalance).

Symptomatic treatment is aimed at eliminating symptoms that worsen the patient's condition (severe headache, feeling of fear of death, sharp blood pressure fluctuations, tachycardia).

Hyperglycemia is a condition characterized by an increase in blood plasma glucose level above 5.5 mmol/l.

Etiology:

• Alimentary overeating. When consuming easily digestible carbohydrates in large quantities, the glucose level rises quickly and exceeds the ability of hepatocytes to form glycogen.

• Endocrinopathies are the most common cause of hyperglycemia. In this case, they are caused by an excess of constitutive hormones or a deficiency of insulin effects. 1. *Insulin deficiency:*

a) violation of glucose utilization by cells,

b) activation of glycogen synthetase → glycogenesis ,

c) inhibition of the transition of glucose into fats,

d) activation of gluconeogenesis .

2. *Hyperproduction contrainsular hormones* (adrenaline - pheochromocytoma , glucagon , GCS - Itsenko-Cushing's disease and syndrome , thyroid hormones - thyrotoxicosis, STH - gigantism and acromegaly against the background of pituitary adenoma): activation of glycogenolysis and / or gluconeogenesis (formation of glucose from proteins and fats)

• Neurological and psychogenic disorders. States of mental excitement and

stress are characterized by activation of the sympathoadrenal , hypothalamic - pituitary -adrenal and thyroid systems. Hormones of these systems (catecholamines , glucocorticoids , T4 and T3) activate glycogenolysis and gluconeogenesis , suppress glycogenesis .

• Liver pathology. With liver failure (hepatitis, cirrhosis), hyperglycemia may develop after eating due to the inability of hepatocytes to transform glucose into glycogen.

Clinical manifestations of hyperglycemia:

Hyperglycemic syndrome is a condition characterized by a long-term increase in the level of blood glucose above the norm, which is combined with a disturbance of vital activity. Hyperglycemic syndrome includes a number of interconnected symptoms.

• Glucosuria - the result of exceeding the possibility of tubular reabsorption of glucose from primary urine at a blood glucose level of more than 10 mmol / l (physiological renal threshold for glucose).

• Polyuria - the formation and excretion of urine in an amount exceeding the norm (more than 1800-2000 ml / day), which is associated with an increase in the osmolality of urine due to the presence of glucose in it (glucose increases the osmotic pressure of primary urine, which prevents water reabsorption) .

• Hypohydration (dehydration) - a decrease in fluid content in the body due to polyuria.

• Polydipsia (thirst) - increased fluid intake due to thirst caused by hypohydration and increased blood plasma osmolality (hyperosmolar hypohydration).

• Arterial hypotension is caused by hypovolemia due to hypohydration of the body.

Diabetes mellitus (DM) Type 1 is a disease based on an absolute lack of insulin in the body, which occurs as a result of the death of b-cells of the pancreatic islets, which causes metabolic disorders .

Etiology of type 1 diabetes:

Insulin deficiency can occur under the influence of factors of a biological, chemical, physical nature, as well as inflammation of the pancreas.

• Biological factors

♦ Genetic defects of β-cells of the islets of Langerhans . Genetic defects of the MHC system cause the inclusion of immune autoaggressive damage to the pancreas or the repression of genes encoding insulin synthesis.

♦ Immune factors. Autoaggressive immunoglobulins and cytotoxic T-lymphocytes are able to damage β-cells.

♦ Viruses that are tropic to β-cells: Coxsackie , hepatitis, measles, chicken pox, epidemic parotitis, rubella. Viruses have a direct cytolytic effect and initiate autoimmune processes.

♦ Endogenous toxic substances. As a result of disruption of pyrimidine metabolism , alloxan is formed , which blocks the synthesis of insulin.

• Chemical factors: high doses of ethanol, some anticancer drugs (cytostatics).

• Physical factors: ionizing radiation, mechanical trauma, compression by a

tumor.

• Inflammatory processes in the pancreas caused by factors of a chemical, physical or biological nature. Chronic pancreatitis is the cause of insulin deficiency in about 30% of cases.

Pathogenesis:

The basis of insulin deficiency is the development of an immunoaggressive process, which is accompanied by the gradual destruction of β-cells. There are two options for development:

1. A) Entry into the body of persons genetically predisposed to diabetes by carriers of foreign AGs, usually viruses. B) Formation of an immune response with the formation of AT and cytotoxic lymphocytes to foreign AGs. C) Specific AT and lymphocytes act on the antigenic structures of the β-cell, which have a similar structure to foreign AG. This phenomenon is referred to as "cross-immunoaggressive reaction". In the course of this reaction, β-cells are destroyed, and individual proteins of the plasma membrane are also denatured and become autoantigenic .

2. A) The pancreas is primarily damaged under the influence of factors of a chemical, physical or infectious nature. B) Release of "foreign" proteins for the immune system (normally they are found only intracellularly and do not enter the blood): cytoplasmic proteins of heat shock, proinsulin . Some proteins are denatured and become autoantigenic . C) Formation of an immune response with the formation of AT and cytotoxic lymphocytes to denatured and intracellular proteins that have entered the blood. D) Autoaggressive AT and lymphocytes act on the antigenic structures of their own β-cells, which is accompanied by their destruction.

Hereditary predisposition (connection with the HLA gene system) in 80% of cases of ICD develops in persons with HLA-DR-3, HLA-DR-4

↓

Immune damage normal and/or damaged beta cells ← pathogenic factors:
viruses (mumps, measles, rubella, coxsackie B)
chemical factors (alloxan , salts heavy metals, etc.)
physical factors (mechanical trauma, ionizing radiation)

↓

destruction of beta cells

↓

violation of the synthesis and secretion of insulin - lina (absolute insulin resistance adequacy)

↓

Type 1 diabetes

Type 1 diabetes manifests itself at a young age, the blood insulin level is low. Polyuria, polydipsia , polyphagia, weight loss develop rapidly , and ketoacidosis develops . Legitimate complications. Insulin treatment is necessary.

Diabetes mellitus (DM) Type 2 is a disease based on relative insulin deficiency or insulin resistance , which causes metabolic disorders.

Type 2 diabetes manifests itself in most cases after the age of 40, develops slowly, often in people who are obese. Polyuria, polydipsia , weakness develops. The insulin level is high or normal. Complications and ketoacidosis occur less often. Insulin is not used in its treatment.

Hereditary predisposition to type 2 diabetes, unlike type 1 diabetes, is not associated with HLA genes.

Risk factors:

• Excess body weight, which is combined with an increase in insulin resistance of target tissues and stimulation of the production of counterinsular hormones. This excessively activates the synthesis of insulin by β-cells of the pancreas, leading to their "exhaustion" and damage.

• Arterial hypertension, which leads to a violation of microcirculation in the pancreas.

• Chronic stress, which is accompanied by a steady increase in the level of counterinsular hormones in the blood.

Conditionally, two stages of pathogenesis are distinguished:

1. Hyperinsulinemic stage. Consuming a large amount of food by obese individuals causes an increase in insulin secretion (hyperinsulinemia). This reaction is aimed at activating the processes of depositing nutrients in adipose tissue in the muscles, there is no need for the action of insulin. Therefore, they protect themselves from an excess of this hormone by reducing the number of receptors on the surface of muscle cells. The phenomenon of insulin resistance of muscle tissue develops - its sensitivity to the action of insulin decreases.

2. Hypoinsulinemic stage. Increased load on the insular apparatus can lead to functional exhaustion of cells. This is facilitated by their genetically determined defects and an excess of counterinsular hormones in the body. As a result, the amount of secreted insulin decreases and its relative insufficiency develops. At the same time, the effect of insulin on adipose tissue is preserved (there are many insulin receptors on fat cells), and on muscle tissue it decreases due to the development of insulin resistance .

Metabolic disorders in diabetes.

- *Violation of fat metabolism:*

1. Hyperlipacidemia (activation of lipolysis). Increase in blood LDL and VLDL.

2. Ketonemia , ketonuria = ketoacidosis :

a) Excessive production of ketone bodies: activation of lipolysis □□ UHD in the blood □ entering the liver □ activation of beta-oxidation □□□ Acetyl CoA □ increased synthesis of ketone bodies (acetoacetic acid, beta- oxybutyric acid,

acetone),

b) Violation of utilization of ketone bodies as a source of energy in the Krebs cycle.

3. Fat infiltration liver (increased intake of UHD in the liver, reduced synthesis of lipoproteins and their secretion into the blood).

- *Disorders of protein metabolism:*

1. Decreased protein synthesis (transmembrane transport of amino acids due to insulin deficiency, degradation of polysomes, disruption of translation processes) hyperaminoacidemia , aminoaciduria .

2. Activation of protein catabolism negative nitrogen balance, hyperazotemia .

3. Decrease in the synthesis of antibodies and the body's resistance to infection.

- *Violation of carbohydrate metabolism:*

1. Hyperglycemia occurs as a result of insufficient insulin effects and impaired utilization of glucose by cells.

2. Glycosuria is mainly a consequence of hyperglycemia.

3. Hyperlactatacidemia - develops due to inhibition of lactate catabolism in the Krebs cycle, violation of glycogen resynthesis from lactate.

Acute complications of diabetes - coma. Species:

Ketoacidotic	**Hyperosmolar**	**Lactatacidemic**
High content of ketone bodies, significant hyperglycemia	A very high level of glucose in the blood, a significant increase in the osmotic pressure in the blood, an insignificant level of ketone bodies (since the level of insulin is sufficient for the oxidation of fats)	An increased level of lactic acid with an insignificant level of glucose and ketone bodies in the blood

Chronic complications of diabetes:

Microangiopathies are pathological changes in the vessels of the microcirculatory channel.

Pathogenesis:

- Glycosylation of capillary basement membrane proteins in conditions of hyperglycemia.
- Thickening and compaction of the vascular wall under the influence of excess sorbitol . Normally, no more than 1-2% of intracellular glucose is transformed into sorbitol , and with diabetic hyperglycemia, the level of conversion increases 8-10 times due to the activation of aldose reductase .
- Swelling, thickening and dystrophy of the endothelium of vessels.

- A change in the structure of the proteins of the basal membrane of vessels and their acquisition of antigenic properties, which leads to immune-mediated damage to the walls of microvessels .
- Tissue ischemia caused by a decrease in the lumen of vessels due to a decrease in the formation of NO and thickening of the vascular wall. The specified changes lead to a violation of transcapillary exchange and the formation of microthrombi .

Macroangiopathy - the development of sclerotic changes in the walls of medium- and large-caliber arteries. Atherosclerosis of blood vessels appears early and progresses rapidly in diabetes mellitus.

Pathogenesis:

- Glycosylation of basement membrane proteins and the interstitium of vessel walls. Modification of protein molecules stimulates atherogenesis .
- Accumulation of sorbitol in the wall of arterial vessels.
- An increase in the level of atherogenic LDL and a decrease in the level of anti-atherogenic HDL.
- Activation of the synthesis of thromboxane A_2 by platelets, which potentiates vasoconstriction and platelet adhesion on vessel walls.
- Stimulation of proliferation of smooth myocytes of arterial vessels.
- These changes lead to the formation and calcification of atherosclerotic plaques, thrombus formation and occlusion of arteries, impaired blood supply to tissues with the development of heart attacks and gangrene.

Neuropathies

- Glycosylation of proteins of peripheral nerves.
- The formation of AT to modified proteins with the development of reactions of immune autoaggression .
- sorbitol in neurons and Schwann cells .
- Decreased intraneural blood supply with the development of chronic ischemia and hypoxia of nervous structures. The main factor in ischemic nerve tissue is considered to be a deficiency of the vasodilator NO.
- Violation of myelin synthesis and demyelination of nerve fibers; slowing down the speed of conduction of nerve impulses.
- These changes lead to *peripheral polyneuropathy* , which is characterized by damage to several nerve trunks and is manifested by paresthesia of the feet, less often - hands; loss of pain and vibration sensitivity, more often in the distal parts of the lower extremities; decreased expression of reflexes, necrosis of foot tissues (diabetic foot syndrome). *Vegetative neuropathy* is manifested by disorders of the gastrointestinal tract (swallowing difficulties, constipation or diarrhea), dystrophy of the urinary bladder (urinary retention), impaired vascular tone (hypotension or fainting), cardiac disorders, sexual dysfunction (erectile dysfunction, decreased libido and other disorders). *Radiculopathy* due to changes in the roots of the spinal cord. They are characterized by pain and increased sensitivity along the course of one or more spinal nerves (usually in the chest and abdomen).

Retinopathy. Causes: microangiopathies in eye tissues and hypoxia of eye tissues, especially the retina. Types and manifestations:

- Nonproliferative retinopathy is manifested by the formation of microaneurysms of arterioles and venules , microhemorrhages in the retina and vitreous body (which can cause blindness), the development of microthrombi with occlusion of vessels and the formation of edema.
- Proliferative retinopathy is characterized by new formation of blood vessels of the microcirculatory bed (stimulated by hypoxia), which sprout into the vitreous body; formation of scars and detachment of the retina in the regions of large hemorrhages.

Nephropathy. Diabetic nephropathy is characterized by:

- thickening and compaction of the walls of glomerular arterioles;
- thickening of the basal membranes of the glomeruli and tubules with disturbances in the processes of filtration, reabsorption, and secretion;

an increase in blood pressure as a result of activation of the SAS and RAAS.

Topic 16. Pathophysiology of fat metabolism: etiology and pathogenesis. Atherosclerosis.

VASCULAR FAILURE. ATHEROSCLEROSIS.

Vascular insufficiency is a pathological condition characterized by disorders of general or local blood circulation, the basis of which is the insufficiency of the hemodynamic function of blood vessels due to violations of their tone, patency, and a decrease in the volume of blood circulating in them.

Depending on the prevalence of manifestations, vascular insufficiency is divided into systemic, the main pathogenetic link of which is a pathological decrease in systemic blood pressure, and regional, which is manifested by local disorders of blood supply to organs and tissues.

According to the rates of development and course, vascular insufficiency is divided into acute and chronic.

An obligatory manifestation of systemic acute and chronic vascular insufficiency is arterial hypotension . At the same time, acute vascular insufficiency is characterized by a rapid and pronounced drop in blood pressure - collapse, which can be progressive in nature, be a component of severe generalized hemodynamic disorders in shock, or be expressed by a short-term, but deep violation of the blood supply to organs and tissues, in which, first of all, the function of the most sensitive to ischemia of the cerebral cortex, manifested by a temporary loss of consciousness - fainting.

ETIOLOGY AND pathogenesis

Acute vascular insufficiency is one of the most common forms of the so-called urgent pathology. It occurs when:

> Severe general and craniocerebral injuries,

> Blood loss,

> Various heart diseases,

> Large burns ,

> Acute poisonings,

> Severe infectious diseases,
> Organic lesions and functional disorders of the central nervous system.,
> Hypersensitivity of carotid sinus baroreceptors,
> Adrenal insufficiency, etc.

Both acute and chronic systemic vascular insufficiency are characterized by a decrease in the volumetric rate of blood flow and the intensity of metabolism through the membranes of capillaries in all organs and tissues of the body due to a decrease in blood pressure in the arterial system and capillaries. The consequence of this is hypoxia, a lack of energy supply and disruption of metabolism in the cells of various organs, leading to a partial or complete loss of their functions. The hemodynamic basis of hypotension may be a decrease in cardiac output (CO), including due to a decrease in venous return; reduction of peripheral blood flow resistance (mainly at the precapillary level), reduction of BCC or a combination of these factors.

In case of acute vascular insufficiency, three types of collapse can be distinguished - cardiogenic , angiogenic , and hypovolemic . The latter develops as a result of an absolute decrease in BCC with blood loss (a component of the manifestation of hemorrhagic shock), plasma loss (with large burns), dehydration of the body.

Hypovolemic collapse is accompanied by compensatory reactions of the central blood circulation (reduction of brain tone and sharp hypertension of peripheral arteries), increased tone of systemic veins. However, this does not prevent a critical decrease in venous return when the body is upright, as a result of which orthostatic fainting easily occurs. Due to a significant increase in peripheral resistance to blood flow, diastolic blood pressure decreases more slowly than systolic blood pressure, so a drop in pulse blood pressure is noted first.

At the heart of cardiogenic collapse is a sharp decrease in the pumping function of the heart with a drop in IOC. The latter is observed with sudden significant bradycardia, for example with complete transverse heart block, with paroxysmal tachycardia and paroxysmal fluttering or flickering of the atria (see. Fibrillation arrhythmia) with a very high frequency of contractions of the ventricles of the heart or with their fibrillation (so-called arrhythmogenic collapse); with a significant decrease in the contractile function of the heart in patients with acute myocardial infarction, myocarditis, as well as with cardiac tamponade.

Angiogenic collapse is most often caused by a pathological increase in the capacity of the venous bed with partial sequestration of blood in it and a decrease in its venous return to the heart (at the same time, the volume of blood in the arterial bed decreases and reactions of centralization of blood circulation develop, as in hypovolemic collapse), and in some cases (for example, with infectious -toxic collapse) its development is facilitated by acute systemic arterial hypotension, which leads to a pathological decrease in peripheral resistance to current.

The reason for the increase in the capacity of the venous bed can be both organic damage to the walls and functional hypotonia of the veins as a result of disturbances in the regulation of vascular tone: weakening of adrenergic, in particular sympathotonic , effects, predominance of vagotonia , imbalance of effects on the tone of humoral

vasoactive factors (for example, with hypocapnic fainting). Violations of nervous regulation leading to vascular insufficiency can be psychogenic (so-called simple fainting), reflex (most characteristic of hypersensitivity syndrome cardiogenic sinus); caused by intoxication of the central nervous system (in case of poisoning, infections), drug blockade of adrenergic states (in case of overdose of hypotensive agents) or related to organic damage of the sympathetic division of the central nervous system (Shy-Dreiger syndrome). Without a violation of the regulation of vascular tone, short-term functional vascular insufficiency is possible in cases where the rate of redistribution of a large mass of blood in the venous channel exceeds the rate of development of the adaptive tonic reaction of the veins (the so-called redistributive syncope). This is observed, for example, in the case of sudden expansion of the veins of the abdominal cavity due to a sharp decrease in intra-abdominal pressure during rapid puncture evacuation of fluid in ascites, standing up after a long period of squatting , when the gravitational redistribution of blood is accelerated by the mechanism of reactive hyperemia. Angiogenic collapse underlies most acute orthostatic circulatory disorders and is often accompanied by orthostatic syncope. Hypocapnia-induced narrowing of cerebral arteries (instead of their compensatory expansion when blood pressure drops) is of significant importance in the pathogenesis of fainting that develops during hyperventilation.

The above hemodynamic factors of the pathogenesis of acute vascular insufficiency, even in the case of its manifestations in the form of short-term fainting, are usually combined. So, in the development of vasovagal fainting in hypersensitivity syndrome of the carotid sinus, both vasodepressor (due to reflex asympaticotonia) and cardiodepressor (due to reflex excitation of the vagus) mechanisms of blood pressure drop are involved . However, the total BCC in short-term acute vascular insufficiency, which is manifested only by fainting, does not decrease (it is only redistributed from the arterial to the venous). Longer and more pronounced vascular insufficiency, that is, collapse as an independent form of its clinical manifestations, regardless of its primary hemodynamic nature (hemorrhagic, cardiogenic , angiogenic) and whether the collapse is accompanied by fainting or not, is characterized by the indispensable participation in its pathogenesis of hypovolemia , the origin of which is vascular insufficiency of various etiology. Thus, in the case of infectious -toxic collapse, which develops as a result of acute hypotonia of blood vessels, usually against the background of a critical decrease in body temperature (see Fever), hypovolemia is important in the mechanism of its development from the very beginning , due to the loss of fluid and salts due to profuse sweating and excessive filtration of liquid from the blood into the tissues due to the increased permeability of the capillary walls. The latter mechanism is always involved in the pathogenesis of hypovolemia in shock of any etiology, which is characterized by impaired cell membrane function, including in capillaries. At the same time, the collapse is only part of the manifestations of shock, characterized by a total disorganization of the regulation of vegetative functions at all levels. A distinctive feature of shock is deep disorders of microcirculation in all organs and tissues with a blockade of cellular respiration and a sharp disruption of cellular

metabolism, for the elimination of which the restoration of blood pressure to normal values in itself is usually insufficient.

hemodynamic disturbances as in acute conditions are involved , but they are formed on the basis of a constantly active cause - a chronic disease of the heart, blood vessels or their regulation apparatus (see Arterial Hypotension). The simultaneous involvement of hypovolemia , cardio- and angiogenic factors in the pathogenesis of chronic systemic vascular insufficiency is characteristic of its development in Addison's disease .

Clinical picture and diagnosis

An objective and sufficient sign to substantiate the diagnosis of systemic vascular insufficiency is a pathological decrease in blood pressure. However, the absolute value of blood pressure due to pronounced fluctuations in the individual norm cannot be assessed as pathological without taking into account other manifestations of vascular insufficiency, especially acute, because the latter can develop at a value of blood pressure that is determined within the formal norm (for example, in people with initial arterial hypertension) and be absent at blood pressure values below 100/60 mm Hg . (In persons with so-called physiological arterial hypotension). Therefore, the diagnosis of acute vascular insufficiency is established on the basis of a set of symptoms of systemic hemodynamic insufficiency, which can form a clinical picture of fainting, collapse or shock .

Chronic systemic vascular insufficiency has its own characteristics, which depend on its etiology and pathogenesis, but a set of symptoms common to most of its etiological forms is also distinguished. These include:

> low blood pressure,

> General3 weakness and rapid fatigue during exercise, often frostbite,

> Tendency to hypothermia (if there is no current chronic infectious intoxication),

> Orthostatic fainting,

> Tachycardia (with the exception of vascular insufficiency in Addison's disease , Shay-Dreiger syndrome and other diseases accompanied by bradycardia).

> A small pulse on the radial arteries, especially when the body is in a vertical position. The pathogenetic diagnosis is specified by means of the study of the value of the cardiac output (in the conditions of the polyclinic, it can be determined by the rheocardiography method) and the average arterial pressure (by the mechanocardiography method) to calculate the total peripheral blood flow resistance, conducting orthostatic tests.

Usually, chronic vascular insufficiency is established with an already known underlying disease, but in some cases, vascular insufficiency is detected at the patient's first visit to the doctor, and its etiological diagnosis requires a targeted examination of the patient.

ATHEROSCLEROSIS

One of the most common diseases that plays the most important role in the development of other pathological processes affecting the cardiovascular system is atherosclerosis (from the Greek Athere - porridge, sclerosis - compaction).

Atherosclerosis is a disease that occurs as a result of primary alteration of the endothelium of vessels, affecting mainly arteries of the muscular and muscular-elastic type, which is based on the inflammatory process and a violation of the transport function of lipoproteins , which is manifested by imbibition of the vascular wall with lipids with further development around of these deposits of reactive changes.

Topic 17 . Pathophysiology of extreme conditions. Etiology and pathogenesis of shock and colaptoid states.

Definition of terms: extreme conditions, shock, collapse, coma

Etiology of shock

Types of shocks

General elements of the pathogenesis of shock states

Disruption of the neuroendocrine system during shock

Hemodynamic disorders in shocks - systemic hemodynamic disorders, microcirculation disorders

Cellular disturbances in shocks. Multiple organ failure.

Pathogenesis of acute respiratory distress syndrome in adults.

Features of the development of various types of shock: hypovolemic , cardiogenic , traumatic, Crash syndrome , burn shock, anaphylactic, septic.

Types of collapse - by etiology, by pathogenesis.

Pathogenesis of collapse.

Etiology of comatose states

Pathogenesis of certain types of coma: in case of mechanical damage to the brain, metabolic coma - diabetic, hepatic, uremic.

Shock is a generalized form of acute circulatory failure that is life-threatening and associated with insufficient oxygen consumption by cells. It is a condition in which the cardiovascular system does not supply the tissues with oxygen in an amount adequate to their needs (but the sole or dominant cause of reduced oxygen transport is not respiratory failure or anemia). As a result, dysoxia occurs at the cellular level (the independence between the utilization of oxygen and its supply is lost), which leads to an increase in anaerobic metabolism and an increase in lactate production. It is most often accompanied by a decrease in blood pressure (hypotension), which, however, can be within the normal range (and even elevated) in the initial phase of shock (which is called compensated shock).

Causes and mechanisms of development

Shock develops as a result of one of the mechanisms listed below or (more often) as a result of their coexistence.

1. ***Hypovolemic shock*** — a decrease in the total volume of blood (absolute hypovolemia):

1) blood loss (bleeding, or massive external or internal bleeding) — hemorrhagic shock;

2) decrease in plasma volume due to:

a) transition of plasma to crushed tissues (injury) or its loss from the surface of the skin (burns, Lyell's syndrome, Stevens -Johnson syndrome , exfoliative dermatitis);

b) a decrease in the volume of extracellular fluid (states of dehydration) - insufficient water intake (most often in the elderly [due to thirst disorders] and people who have lost the ability to self-care) or excessive loss of water and electrolytes through the gastrointestinal tract (diarrhea and vomiting), kidneys (osmotic diuresis in diabetic ketoacidosis and hyperosmolar non-ketoacidemic hyperglycemia), polyuria and excessive sodium removal with gluco- and mineralocorticoid deficiency , rarely hypothalamic or renal diabetes insipidus) , skin (fever, hyperthermia);

c) loss of fluid to the so-called the third space — intestinal lumen (paralytic or mechanical obstruction), less often — serous cavities (peritoneal — ascites);

d) increased permeability of vessel walls in anaphylactic and septic shocks.

2. ***Redistributive (vasogenic) shock*** — expansion of blood vessels, which is accompanied by an increase in the volume of the vascular bed, a decrease in vascular resistance and a violation of blood flow distribution, which lead to relative hypovolemia (a decrease in effective volemia , i.e., blood filling of the areas of the blood circulation that are monitored baro -, volumo -, and chemoreceptors [practically this applies to the arterial system], with a simultaneous increase in blood volume in venous and capillary vessels; then, as a rule, there is a hyperkinetic type of circulation (increased cardiac output), while peripheral (tissue) blood flow is reduced:

1) *septic shock* — sepsis (sometimes toxic shock — caused by staphylococcal or streptococcal toxins);

2) *anaphylactic shock* — anaphylaxis;

3) *neurogenic shock* — damage to the spinal cord (spinal shock); injuries, strokes and cerebral edema; orthostatic hypotension (long-term); expansion of blood vessels in response to pain ("pain shock");

4) *shock caused by hormonal disorders* (in addition to vasodilation, heart failure and other mechanisms are possible) — acute adrenal insufficiency, thyrotoxic crisis, hypothyroid coma.

3. ***Cardiogenic shock*** is a violation of cardiac activity (as a rule, as a result of an acute myocardial infarction, heart rhythm disorders, or valve dysfunction), which causes a decrease in cardiac output (as a result of a violation of myocardial contractility or serious heart rhythm disorders.

4. ***Obstructive shock*** — causes of a mechanical nature (obstruction in blood circulation as a result of vessel obstruction or compression of the heart and vessels from the outside):

1) left ventricular filling disorder due to heart tamponade;

2) a significant decrease in venous return as a result of compression of the venous system (tension pneumothorax, abdominal compression syndrome);

3) difficulty in filling the ventricles caused by intracardiac causes (heart tumors and blood clots in the chambers of the heart);

4) sudden increase in resistance in the circulatory system (thromboembolism of the pulmonary artery, acute pulmonary hypertension with acute respiratory failure)

Consequences

1. ***Compensatory reactions*** (as a rule, they are exhausted over time) — the most important are:

1) excitation of the sympathetic nervous system and increased secretion of adrenaline by the medulla of the adrenal glands → tachycardia and centralization of blood circulation (narrowing of precapillary and venous vessels of the skin, and then muscles, visceral and renal blood circulation → decrease in blood flow and filling of venous vessels in these areas → preservation of blood flow in vital organs [heart and brain]); in case of hypovolemia , restoration of plasma volume by percolation of intercellular fluid to capillaries (due to spasm of precapillary vessels and decrease of intracapillary hydrostatic pressure with unchanged oncotic pressure); in some cases of non-cardiogenic shock, an increase in myocardial contractility (and even an increase in ejection volume); hyperventilation; hyperglycemia;

2) stimulation of the renin-angiotensin- aldosterone system and the secretion of vasopressin (ADH) and GC → leads to the centralization of blood circulation and promotes the retention of sodium and water in the body;

3) increased extraction of oxygen in response to a decrease in its supply → greater deoxygenation of hemoglobin → decrease in hemoglobin oxygen saturation of venous blood (SvO2).

2. ***Metabolic and electrolyte disturbances due to hypoxia*** :

1) increased anaerobic metabolism and increased production of lactate → metabolic lactic acidosis;

2) the transfer of potassium, phosphates and some enzymes (LDH, KFC, AST, ALT) from cells to the extracellular space, increased sodium flow to cells (due to impaired ATP synthesis) → possible hyponatremia , hyperkalemia , and hyperphosphatemia .

3. Consequences of organ ischemia: multiple organ failure (acute prerenal kidney damage, impaired consciousness [including coma] and other neurological deficits, acute respiratory failure, acute liver failure, CVD syndrome), bleeding from the gastrointestinal tract (as a result of acute hemorrhagic [erosive] gastropathy , stress ulcers of the stomach and duodenum or ischemic colitis), paralytic intestinal

obstruction and penetration of microorganisms from the lumen of the gastrointestinal tract into the blood (can cause sepsis).

Symptoms of organ hypoperfusion :

1) skin — paleness, cooling, and sweating (but in septic shock, the skin is usually dry and warm at the beginning, and in states of dehydration — dry and inelastic), slowing of capillary refill (after stopping pressure on the nail, the pallor disappears after >2 s) , cyanosis, marbled skin;

2) Central nervous system — feeling of fear, restlessness, confusion, psychomotor excitement, drowsiness, stupor, coma, focal neurological deficit;

3) kidney — oliguria or anuria and other symptoms of acute failure;

4) muscles — weakness;

5) gastrointestinal tract — nausea, vomiting, flatulence, weakening or absence of peristalsis, bleeding;

6) liver — jaundice is a symptom that appears rarely and late, or already after recovery from shock;

7) respiratory system — various disturbances of the breathing rhythm are possible, at the beginning breathing may be shallow and accelerated, then slowed down, residual or apnea (with metabolic acidosis, it is slow and deep, it can also be accelerated and deep — Kussmaul breathing); acute respiratory failure with hypoxemia (type I) and/or hypercapnia (type II) may occur .

Symptoms related to the cause of shock : symptoms of dehydration, bleeding, anaphylaxis, infection (sepsis), heart or large vessel disease, pulmonary embolism , tension pneumothorax, intestinal obstruction, etc.

All components of the classic triad (hypotension , tachycardia, oliguria) are not always present.

Traumatic shock (TS) is characterized by acute-phase interrelated disorders of important body functions, which lead to critical disorders of perfusion, hypoxia, and disorders of the functions of vital organs.

Among victims who are in a serious condition, clinical signs of TS are observed in two-thirds of patients with a mortality rate of up to 40% of cases.

Researches of recent years show that the disturbances of vital functions caused by mechanical trauma have a prolonged phase character, have a specific pathogenesis, defined clinical forms and are no longer included in the framework of

the doctrine of TS.

The following periods are distinguished in the clinical course of a traumatic disease:

- shock period - acute reaction to injury (duration up to 1-2 days)
- the period of early manifestations - the danger of early complications (duration up to 14 days);
- the period of late manifestations - the danger of late complications (duration of several weeks);
- the period of final recovery and rehabilitation (duration from several weeks to many months and even years).

Thus, a traumatic disease is the life of an organism from the moment of injury to recovery or death. It is characterized by the presence of local and general pathological processes caused by trauma, within which traumatic shock is considered as the first period of a traumatic disease.

Coma is a state characterized by unconsciousness, impaired reflex activity of functions of vital organs and systems.

Comatose states are classified by the causes of occurrence:

- Coma in diseases of internal organs: hepatic, uremic, eclamptic, hypoxemic , anemic, hungry (alimentary- dystrophic).
- Neurological (cerebral) comas: traumatic, epileptic, apoplectic.
- Coma in diseases of the endocrine glands: diabetic, hypoglycemic , adrenal (hypocorticoid), thyrotoxic , hypothyroid .
- Coma of infectious origin: malarial, pneumatic, septic, with acute neuroinfections .
- Coma of non-infectious origin: alcoholic, narcotic.
- Coma due to the influence of physical factors: cold, thermal, electrical.

Since the brain is the highest center of regulation of the functions of vital organs, its damage leads to a pronounced violation of their functions: deterioration of breathing, blood circulation, disorder of metabolic processes.

Violations of the functions of other organs that occur under the influence of extreme factors (liver, kidneys, pancreas) can also be the reason for the development

of coma.

Despite the large number of reasons that lead to the development of comatose states, there are signs that are similar in all types of coma: fainting, changes in reflexes, convulsions, breathing disorders, a decrease in blood pressure with a pulse disorder, a decrease or absence (anuria) of urine output, disorders swallowing, water-electrolyte exchange, acid-base status, thermoregulation, joining infections with the development of sepsis.

According to the depth or degree of severity, comatose states are divided as follows:

1. Light coma - lack of consciousness (unconsciousness); the victim does not answer questions; protective reactions (corneal, pupillary to light, tendon reflexes) are preserved, but may be weakened; vital functions (breathing, blood circulation) are not disturbed, but may be weakened.

2. Significant coma - lack of consciousness (unconsciousness); protective reactions are weakened, reflexes are almost not triggered; disturbed functions of breathing, blood circulation, pelvic organs, swallowing disorders.

3. Deep coma - consciousness and protective reactions, reflexes are absent, muscle atony, a decrease in body temperature (hypothermia), dilated pupils, significant disturbances of breathing, blood circulation, and functions of internal organs.

4. Terminal coma is a critical disorder of vital functions that requires special measures (resuscitation) to maintain the vital activity of the body.

Collapse — threatening for life a person state, what characterized by fall bloody pressure and deterioration blood supply vitally important bodies Appears sharp weakness sharpened features face, pallor, chillslimbs occurs at infectious diseases, poisonings, big blood loss, overdose and others

Pathogenesis of collapse

sharp vascular insufficiency (GSO) is developing in cases occurrence pronounced inconsistencies between capacity vascular channels and volume of circulating blood. One of the leading factors that determine GOS, there is a decrease in BCC (anhydremia with dehydration of the most diverse origin).

With hypovolemia the blood filling of the heart cavities decreases sharply and aorta, the systolic volume of the heart falls, and on this basis the protective one is activatedneuro-reflex mechanism in the form of spasm of arterioles and relaxation capillary circulation (primarily in muscles, skin, internal organs). It the first phase of shock. In the future, in the absence of the effect of such protective reactions, happens reflexive expansion arteriole and peripheral resistibility current of blood is decreasing

Significantly filling by blood peripheral vessels may strengthen paresis of peripheral arterioles due to damage to the vasomotor center toxins bacterial and another origin, toxic damage vascular membranes and increase their permeability IN as a result violation peripheral hemodynamics suffers function internal bodies CNS activity, are getting worse redox processes and exchange substances, arise hypoxemia and hypoxia , azotemia and acidosis _ IN such conditions depressed function adrenal glands, on this soil is falling tone

sympathetic nervous system, peripheral hemodynamics deteriorates due to additional vasodilators neurogenic influences

A mild form of GOS can develop as a consequence of an acute reflexparesis vascular tone with temporary anemia brain and short-termloss consciousness

STR is a polyetiopathogenetic , dynamic phase process, which is based on neurohumoral and immunological changes against the background of toxemia, plasma-blood loss, violation of vital body functions, primarily hemodynamics and kidney function.

The pathogenesis of STR consists of the following main factors:

1) neuro -humoral
2) toxemic
3) plasma and blood loss
4) immunological

According to the clinical manifestations of SDR, three periods are distinguished:

1. Early period (period of traumatic shock) - observed during the first day.
2. Intermediate (ANN period) - observed up to 8-12 days.
3. Late (period of late complications or recovery) - lasts more than a month.

3. Formation of professional skills, skills related to topics that are part of the content module (mastery of communication skills, clinical examination, determination of treatment scheme, conducting laboratory research, etc.) mastery of skills:

Topic 12. Violation of water-salt exchange: etiology, pathogenesis. Dyshydria , edema.

1. In a patient injured during a car accident, there is a decrease in the amount of water in the extracellular space. Blood plasma osmolarity remains within normal limits. To draw a conclusion about the type of violation of water-electrolyte exchange in a melon patient and its specific cause.

the end of a shift , a worker in a hot shop has an unbearable feeling of thirst, an increase in body temperature, and a short-term loss of consciousness. The consequences of which violations of water-electrolyte exchange are the observed

symptoms? The etiology and pathogenesis of disorders will be explained . What preventive measures should be taken to prevent these violations? If the matter will be alleviated by drinking water without salt, to which, in turn, violation of the water-electrolyte exchange can this lead to?

3. In a patient with enteritis accompanied by significant diarrhea, there is a decrease in the amount of water in the extracellular space, an increase in it in the middle of the cell, and a decrease in blood osmolarity . What is this violation of water - electrolyte exchange called? What is its pathogenesis? Would it be correct to prescribe this patient an infusion of 5% glucose solution?

4. A patient with kidney pathology has significant proteinuria and accumulation of water mainly in the intercellular space. What is the name of such a violation of water-electrolyte exchange and what is its pathogenesis in this patient?

5. The child developed dehydration as a result of diarrhea. A system with isotonic sodium solution will be prescribed. Chloride and deoxycorticosterone . After some time, the child developed weakness. At the same time, sodium in the plasma was 180 mmol/l, potassium – 3.4 mmol/l. What is the mechanism of the complication that has arisen ? Was the treatment strategy correctly developed?

Answers:

1. Blood loss that provoked simple hypovolemia .
2. In connection with increased sweating, there were disturbances of water-electrolyte exchange in the form of hypoosmolar hypohydration
3. Dehydration. Exykosis .
4. Extracellular hyperhydration . Hypoproteinemia .

Topic 13. Pathophysiology of acid-base metabolism: acidosis, alkalosis

- What form of acid-base disturbance is characteristic of metabolic acidosis that occurred in a patient in a hypoxic state?

A. Accumulation of organic acids in the body
B. Accumulation of alkalis in the body
C. Violation of $CO_{2\ release}$
D. Reduction of carbonic acid content
E. Loss of acidic compounds

- Which metabolite plays a leading role in the development of acidosis in hypoxic conditions

states?

A. Lactic acid
B. Fatty acids
S. Succinic acid
D. Ketone bodies
E. Glutamic acid

- The patient's condition deteriorated sharply due to a viral infection, which was complicated by liver failure. What metabolite, included in gluconeogenesis , causes metabolic acidosis?

A. Lactic acid

B. Glutamic acid

S. Fatty acids

D. Ketone bodies

E. Carbon dioxide

- Which of the listed buffer systems is an open system that most informatively characterizes the state of acid-base balance?

A. Bicarbonate

B. Hemoglobin

S. Phosphatna

D. Bilkova

E. Ammonia

- What type of acid-base disorder is characterized by the following indicators: blood pH – 7.2, pCO_2 – 55 mm Hg . st., AB – 15 mmol/l, VE (excess acids) –„– ”3.7?

Decompensated respiratory acidosis

B. Metabolic acidosis is compensated

S. Metabolic decompensated alkalosis

D. Compensated respiratory alkalosis

decompensated acidosis

-. What type of disorder did the patient have if the pH of the blood is 7.4, pCO_2 is 49 mm Hg . st., AB (current bicarbonates) – 18 mmol/l?

A. Compensated respiratory acidosis

B. Metabolic acidosis is compensated

Decompensated metabolic acidosis

Decompensated respiratory acidosis

E. Metabolic alkalosis is compensated

-What type of acid-base disorder is characterized by the following indicators: pH – 7.24, pCO_2 – 50 mm Hg . st., VE (excess acids) – “–”3.5?

Decompensated respiratory acidosis

Decompensated metabolic acidosis

C. Compensated metabolic acidosis

Decompensated respiratory alkalosis

E. Metabolic alkalosis is compensated

Topic 14. Pathophysiology of energy and protein metabolism. Etiology and pathogenesis. Starvation.

1. In the patient, an increase (by 30%) of the basic metabolism and absorption of radioactive iodine, as well as an increase in the thyroid gland, was established. Body temperature is 37C, heart rate is 120 per minute. The number of breaths is 28 per minute. What is the cause and pathogenesis of the increase in basic metabolism?
2. In an animal that was starving, there is general excitement, an increase in basic

metabolism by 25%, a respiratory rate of 1, a heart rate of 78 in 1 minute. Determine the period of complete starvation and explain the mechanism of increasing the basic metabolism. 3. In an animal that was starving, there is general depression, a decrease in basic metabolism by 18%, body weight by 20%, and hyperglycemia. Body temperature is 36.2C, heart rate is 68 per 1 minute, respiratory rate is 0.7. Determine the period of complete starvation and the mechanism of its main manifestations. **Reference answers:**
1. Hyperfunction of the thyroid gland2. The first period of complete starvation3. The second period of complete starvation.

Topic 15. Pathophysiology of carbohydrate metabolism: etiology and pathogenesis.

Task 1. The obtained laboratory analyzes showed: total lipids – 12 g/l, free fatty acids – 1.01 mmol/l, ketone bodies – 0.98 mmol/l, glucose – 3.5 mmol/l, total protein 65 g/l , albumins – 32 g/l, creatinine – 0.07 mmol/l, urea – 4 mmol/l, triglycerides – 65%, cholesterol – 10%, phospholipids – 15%, protein – 10%.

Describe the state of lipid metabolism, establish the state of other types of metabolism, name the probable mechanism of the pathology, show the ways of occurrence of these disorders on the diagram.

Topic 16. Pathophysiology of fat metabolism: etiology and pathogenesis. Atherosclerosis.

Task 2. The obtained laboratory analyzes showed: total protein – 60g/l, albumins – 28g/l, globulins – 32g/l, α-I-globulins – 5%, α-II-globulins – 10%, β-globulins – 13 %, γ-globulins – 29%, ALT activity – 40 units, residual blood nitrogen – 57 mmol/l, urea nitrogen – 44.3 mmol/l, blood urea – 20.8 mmol/l, ketone bodies – 2.5 mmol/l, total bilirubin – 17.0 mmol/l, direct bilirubin – 2 mmol/l.

Evaluate protein metabolism indicators, give a conclusion about the nature of protein metabolism disorders in your patient.

Topic 17. Pathophysiology of extreme conditions. Etiology and pathogenesis of shock and colaptoid states.

The driver , who got into a road accident, was injured and is in a state of shock, has a decrease in the daily amount of urine to 300 ml. What is the main pathogenetic factor of this change in diuresis?

(Drop in **blood** pressure)

Topic 18. General metabolic disorders. Current control of knowledge

4. Summary: testing

PRACTICAL TRAINING

Content module 4. Pathophysiology of the blood system.

Practical lesson No. 19

Topic. Pathophysiology of the blood system. Changes in total volume.

Practical lesson No. 20

Topic. Pathophysiology of the blood system. Blood loss. Erythrocytosis

Practical lesson No. 21

Topic. Anemia : Etiology and pathogenesis. Classification of anemias. Posthemorrhagic anemia, etiology, pathogenesis .

Practical lesson No. 22

Topic. Hemolytic anemias, etiology, pathogenesis

Practical lesson No. 23

Topic. B12 - folic acid deficiency , iron deficiency anemia, etiology, pathogenesis.

Practical lesson No. 24

Topic. Leukocytosis and leukopenia: etiology, pathogenesis. A picture of blood. Leukemoid reactions.

Practical lesson No. 25

Topic. Leukemias: etiology, classification, pathogenesis. A picture of blood.

Practical lesson No. 26

Topic. Pathophysiology of the hemostasis system: hemorrhagic syndrome, thrombosis and DVZ-syndrome.

Practical lesson No. 27

Topic. Pathophysiology of the blood system. Current control of knowledge

Purpose: Acquisition by the student of higher education of knowledge and formation of elements of professional competences in the field of medicine from the pathophysiology division:

Topic 19. Pathophysiology of the blood system. Changes in the total volume .

Topic 20. Blood loss. Erythrocytosis .

Topic 21. Classification of anemias, posthemorrhagic anemias, etiology, pathogenesis.

Topic 22. Hemolytic anemias

Topic 23. B12 - folate-deficient and iron-deficient anemias, etiology, pathogenesis

Topic 24. Leukocytosis and leukopenia: etiology, pathogenesis. A picture of blood. Leukemoid reactions.

Topic 25. Leukosis: etiology, classification, pathogenesis. A picture of blood.

Topic 26. Pathophysiology of the hemostasis system: hemorrhagic syndrome, thrombosis and DVZ-syndrome.

Topic 27. Verification of assimilation of acquired knowledge and skills by

applicants.

Improvement of skills and competences acquired during the study of previous disciplines.

Basic concepts:

Topic 19. Pathophysiology of the blood system. Changes in the total volume .

Topic 20. Blood loss. Erythrocytosis .

Topic 21. Classification of anemias, posthemorrhagic anemias, etiology, pathogenesis.

Topic 22. Hemolytic anemias

Topic 23. B12 - folate-deficient and iron-deficient anemias, etiology, pathogenesis

Topic 24. Leukocytosis and leukopenia: etiology, pathogenesis. A picture of blood. Leukemoid reactions.

Topic 25. Leukosis: etiology, classification, pathogenesis. A picture of blood.

Topic 26. Pathophysiology of the hemostasis system: hemorrhagic syndrome, thrombosis and DVZ-syndrome.

Topic 27. Verification of assimilation of acquired knowledge and skills by applicants.

Equipment: Multimedia presentations, tables.

Plan:

7. **Organizational activities (greetings, verification of those present, announcement of the topic, purpose of the lesson, motivation of higher education seekers to study the topic).**
8. **Control of the reference level of knowledge:**

Topic 19. Pathophysiology of the blood system. Changes in total volume.

General characteristics of pathological processes in the blood system Changes in the total volume of blood, types of changes, characteristics. Signs. Blood loss: etiology, pathogenesis. Compensation mechanisms.

Erythrocytosis : definition, etiology and pathogenesis. Characteristics of individual species. Physiological and pathological forms of erythrocytes.

Etiology and pathogenesis of posthemorrhagic anemia, types. Posthemorrhagic anemia characteristics, blood picture. Clinical signs, mechanisms of compensation.

Violation of circulating blood volume (CCB). Violations of blood volume are manifested in the form of *hypovolemia* or *hypervolemia* - a decrease or increase in blood volume compared to the norm (*normovolemia*). Hypo- and hypervolemia are divided into *simple* (the normal ratio of plasma and blood cells is preserved), *polycythemic* (blood cells predominate) and *oligocythemic* (plasma predominates).

Blood volume disorders also include changes in the volume ratio between cellular elements and plasma with a normal total blood volume - oligo - and polycythemic normovolemia (hemodilution and hemoconcentration). An indicator

of the volume ratio is **the hematocrit** , which determines the content of cellular elements (mainly erythrocytes) in the total volume of blood (normally 0.36-0.48, or 36-48%).

Hypovolemia is simple - a decrease in BCC without a change in hematocrit. It occurs immediately after acute blood loss and persists until the fluid passes from the tissue into the blood.

Hypovolemia oligocythemic - a decrease in BCC with a predominant decrease in cells - erythrocytes. It is observed with acute blood loss in those cases when the influx of blood and tissue fluid into the bloodstream does not compensate for the volume and especially the composition of the blood.

Hypovolemia polycythemic - a decrease in BCC due to a decrease in the volume of plasma with a relative increase in the content of erythrocytes. It develops when the body is dehydrated (diarrhea, vomiting, increased sweating, hyperventilation), shock (leaking of fluid into tissues as a result of increased permeability of the vessel wall).

Hypervolemia is simple - an increase in BCC while maintaining a normal ratio between erythrocytes and plasma. Occurs immediately after transfusion of a large amount of blood. However, the fluid soon leaves the bloodstream, and the red blood cells remain, which leads to blood clotting. Simple hypervolemia with increased physical work is due to the entry of blood from the depot into the general bloodstream.

Hypervolemia oligocythemic - increase in BCC due to plasma. It develops when water is retained in the body due to kidney disease, when blood substitutes are administered. It can be modeled in an experiment by intravenously injecting animals with an isotonic sodium chloride solution.

Hypervolemia polycythemic - an increase in BCC due to an increase in the number of erythrocytes. It is observed with a decrease in atmospheric pressure, as well as with various diseases associated with hypoxia (heart disease, emphysema), and is considered a compensatory phenomenon. However, in the case of Waquez's disease, it is the result of tumor growth of cells of the erythrocyte row of the bone marrow.

Oligocythemic normovolemia occurs with anemia as a result of blood loss (blood volume has normalized due to tissue fluid, and the number of erythrocytes has not yet recovered), hemolysis of erythrocytes, hematopoiesis disorders .

Polycythemic normovolemia is observed when transfusing small amounts of erythrocyte mass.

Topic 20. Pathophysiology of the blood system. Blood loss. Erythrocytosis

Blood loss is a pathological process that occurs as a result of bleeding and is characterized by a complex complex of pathological disorders and compensatory reactions aimed at reducing BCC and hypoxia caused by a decrease in the respiratory function of the blood.

Etiological factors that cause bleeding include:

1) violation of the integrity of blood vessels in case of injury or damage by a pathological process (atherosclerosis, tumor, tuberculosis); 2) increased

permeability of the vascular wall (acute radiation sickness);

3) reduction of blood coagulation (hemorrhagic diathesis).

Stages of the pathogenesis of acute blood loss:

I. Initial stage. It is characterized by a decrease in BCC - simple hypovolemia , a decrease in blood pressure, hypoxia mainly of the circulatory type.

P. Compensatory stage. It is due to the inclusion of a complex of protective and compensatory reactions aimed at eliminating the consequences of blood loss.

Sh. Terminal stage. It is characterized by an increase in pathological changes in the body up to the point of death. It develops when compensatory reactions are insufficient.

Protective and compensatory reactions during blood loss:

I. Reduction of the volume of the vascular bed :

1) spasm of arterioles of the skin, muscles, organs of the digestive system;

2) opening of arteriovenous anastomoses of the specified organs and tissues as a result of spasm of precapillary sphincters;

3) venoconstriction (contraction of the smooth muscles of the veins), which increases the flow of blood to the heart and reduces the capacity of the venous section of blood circulation.

The pathogenesis of the corresponding changes:

a) decrease in blood pressure → disturbance of baroreceptors → activation of sympathoadrenal system → action of catechamines on α- adrenoceptors of smooth muscles of arteries, arterioles, precapillary sphincters and veins;

b) a decrease in the volume of circulating blood and arterial blood pressure: excitation of volume and baroreceptors → activation of neurosecretory cells of the hypothalamus, which produce vasopressin → action of this hormone on Vj - receptors of vascular smooth muscles with subsequent vasoconstriction ;

c) decrease in the volume of circulating blood and activation of the sympathoadrenal system: release by cells of the juxtaglomerular renal renin apparatus → activation of the renin- angiotensin system with the formation of angiotensin II → spasm of smooth muscles of blood vessels.

II. Increase in BCC:

1) transition of tissue fluid and blood vessels. As a result of the decrease in BCC, the hydrostatic pressure in the capillaries decreases, which leads to a decrease in the filtration of water in the arterial part of the capillaries and an increase in the reabsorption of liquid in the venous part;

2) increased reabsorption of water and sodium ions in the kidneys:

a) the action of vasopressin on the receptors of the epithelium of the distal convoluted tubules and collecting tubules of the kidneys, as a result of which the facultative reabsorption of water increases;

b) activation of the renin- angiotensin system with subsequent release of aldosterone, which increases sodium reabsorption in the distal convoluted tubules;

c) activation of the sympathoadrenal system, which leads to a redistribution of blood flow between the vessels of cortical and juxtamedullary nephrons, as a result of which the area and intensity of tubular reabsorption of water and sodium increases.

3) the release of blood from the depot into the bloodstream - activation of the sympathoadrenal system and the action of catecholamines on the vessels of the liver, spleen, and subcutaneous fat.

III. Restoration of the composition of peripheral blood during blood loss: develops as a result of hypoxia of the kidneys, the result of which is the formation and entry into the blood of a large amount of renal erythropoietins , which, stimulating erythropoiesis , increase the entry of young regenerative forms of erythrocytes into the peripheral blood.

Pathological changes in blood loss:

1. Violation of systemic hemodynamics (decrease in BCC, decrease in blood pressure) and local blood circulation (microcirculation) up to the development of shock.

2. Development of acute posthemorrhagic anemia.

3. Development of hypoxia, first circulatory , and then hemic type.

4. The development of metabolic acidosis due to the entry of lactic acid into the blood in connection with the occurrence of hypoxia.

5. Violations of the excretory function of the kidneys: a decrease in the intensity of filtration and the development of the phenomena of acute renal failure: oligo - and anuria, intoxication (azotemia).

Hemorrhagic shock is a shock that occurs as a result of abundant acute blood loss. The leading mechanism of its development is the reduction of BCC, which causes a decrease in blood pressure, microcirculation disorders, disorders of blood supply to vital organs (brain, heart, kidneys). This results in the development of hypoxia, acidosis, and intoxication, which complicates the course of shock, creates "vicious circles" in its pathogenesis, and ultimately leads to death.

Disorders of the erythrocyte system. Normally, the number of erythrocytes in men is $4*10^{12}$ -$5*10^{12}$ /l, in women - $3.5*10^{12}$ -$4.5*10^{12}$ /l. The concentration of hemoglobin (Hb) in men is 130-160 g/l, in women - 120-140 g/l.

Under conditions of pathology, two types of changes in the number of erythrocytes and Hb in peripheral blood are possible:

1) erythrocytosis - an increase in the content of erythrocytes and hemoglobin;

2) anemia - a decrease in their number.

Quantitative changes in erythrocytes can be due to:

a) violation of the relationship between their formation and destruction;

b) loss of erythrocytes in case of violation of vascular integrity (blood loss);

c) redistribution of erythrocytes.

Qualitative changes of erythrocytes :

1) the appearance of their regenerative forms (violation of the maturation of erythrocytes in the red bone marrow or an increase in the permeability of the bone barrier, as a result of which the influx of immature cells with a low hemoglobin content into the blood increases):

a) *reticulocytes* (Rt) - normally their content in the blood is 0.2-2%. With increased regeneration of red blood cells, their number can increase to 50%;

b) *polychromatophiles* are anucleate cells, the cytoplasm of which shows the ability to perceive both acidic and basic dyes, they differ from mature erythrocytes

by their bluish shade of color, together with reticulocytes are the immediate precursors of erythrocytes;

c) *normoblasts* - nuclear precursors of erythrocytes, normally absent in peripheral blood, found only in red bone marrow. With increased regeneration of cells of the erythroid row, acidophilic and polychromatophilic , less often basophilic , may appear in the blood normoblasts . Sometimes, with hyperregenerative anemias, erythroblasts (precursors of normoblasts) can be detected in the blood.

2) degenerative changes of erythrocytes (acquired and hereditary disorders of metabolism, composition and structure of erythrocytes, including hemoglobin synthesis). Such changes are characterized by the following phenomena:

a) *anisocytosis* - a change in the size of erythrocytes. The appearance of macrocytes - erythrocytes with a diameter of more than 8 μm and microcytes - cells whose diameter is less than 6.5 μm (the average diameter of a normal erythrocyte is about 7.2 μm) is possible;

b) *poikilocytosis* - a change in the shape of erythrocytes. Normally, erythrocytes have the shape of biconcave discs. In pathological conditions, pear-shaped, elongated, sickle-shaped, oval erythrocytes, as well as spherical erythrocytes may appear;

c) *a change in the color of erythrocytes* , which depends on the content of Hb in them . Intensely colored erythrocytes are called hyperchromic , with pale color - hypochromic . Erythrocytes, in which only the peripheral part, where hemoglobin is located, is colored in the form of a ring, and there is an uncolored light in the center, are called annulocytes . In the case of pronounced differences in the color of erythrocytes, they speak of anisochromia ;

d) *the presence of pathological inclusions:* Jolly bodies - 1-2 μm size formations , which are remnants of a nuclear substance; Cabot rings - remnants of the nuclear envelope, having the shape of a ring or a figure of eight; basophilic granularity - remnants of the basophilic substance of the cytoplasm, which indicate a toxic lesion of the red bone marrow.

3) the appearance of cells of pathological regeneration (a change in the type of hematopoiesis from erythroblastic to megaloblastic , when megaloblasts and megalocytes appear in the bone marrow and blood . The appearance of these cells in the red bone marrow and blood is characteristic of B_{12} foliodeficiency anemia.

Erythrocytosis is an increase in the number of erythrocytes in the blood over $6*10^{12}$ /l and hemoglobin concentration over 170 g/l.

Absolute erythrocytosis - is an increase in the content of erythrocytes and hemoglobin in a unit of blood volume due to increased erythropoiesis .

1. *Acquired absolute erythrocytosis* occurs as a result of increased production of erythropoietin mainly in the kidneys due to hypoxia and ischemia, production of erythropoietin by some tumors (hypernephroma , liver cancer, etc.).

In addition, absolute erythrocytosis develops in true polycythemia (Vakeza's disease), which is a type of chronic leukemia.

2. *Hereditary absolute erythrocytosis* - a genetically determined globin defect in the hemoglobin molecule or a deficiency in erythrocytes of 2,3-diphosphoglycerate, which is a regulator of oxygenation and deoxygenation of

hemoglobin. At the same time, the affinity of hemoglobin for oxygen increases and its return to tissues decreases. Hypoxia develops, the production of erythropoietins is stimulated, under the influence of which erythropoiesis increases .

Relative erythrocytosis - this is an increase in the content of erythrocytes and hemoglobin in a unit of blood volume due to a decrease in plasma volume. Its development is associated with the action of factors that cause dehydration of the body or redistribution of blood, which causes polycythemia hypovolemia (eg, shock, burns).

Topic 21. Anemias: Etiology and pathogenesis. Classification of anemias. Posthemorrhagic anemia, etiology, pathogenesis.

General characteristics of pathological processes in the blood system

Etiology and pathogenesis of the above-mentioned anemias, types. Characteristics of the above-mentioned anemias, blood picture. Clinical signs, compensation mechanisms for the above-mentioned anemias. Modern understanding of the etiology and pathogenesis of the above-mentioned anemias. **Anemia** is a hematological syndrome or an independent disease characterized by a decrease in the number of erythrocytes and (or) the hemoglobin content per unit volume of blood, as well as qualitative changes in erythrocytes.

Classification of anemias:

I. *By etiology:*

1) hereditary (for example, thalassemia);

2) acquired (for example, chronic posthemorrhagic anemia).

II. *By pathogenesis:*

1) post-hemorrhagic anemia (for example, anemia after acute blood loss);

2) hemolytic anemias (for example, sickle cell anemia);

3) anemia caused by disorders of erythropoiesis (for example, iron deficiency).

III. *According to the regenerative ability of red bone marrow:*

1) regenerative (Rt up to 3%, for example, acute posthemorrhagic anemia);

2) hyperregenerative (Rt > 3%, for example, acquired hemolytic anemia);

3) hyporegenerative (Rt < 0.2%, for example, iron deficiency anemia);

4) aregenerative (Rt 0%, for example, aplastic anemia).

IV. *According to the color index (CP):*

1) normochromic (this variant of anemia indicates a proportional, uniform decrease in Hb and erythrocytes per unit volume of blood, CP = 0.85-1.05; for example, acute posthemorrhagic anemia in the first few days after blood loss);

2) hypochromic (this type of anemia indicates that the number of Hb is reduced more than the number of erythrocytes, CP <0.85; for example, iron deficiency anemia);

3) hyperchromic (this type of anemia is found in those cases when the total number of erythrocytes is reduced to a greater extent than the total number of Hb , KP> 1.05; for example, B_{12} foliodeficiency anemia).

V. *By type of hematopoiesis:*

1) anemia with erythroblastic type of hematopoiesis (for example, iron

deficiency anemia);

2) anemias with a megaloblastic type of hematopoiesis (for example, B_{12} foliodeficiency anemia).

VI. *According to the size of erythrocytes:*

1) normocytic (≈ 7.1 – 7.9 μm);

2) macrocytic (>7.9 μm);

3) microcytic (< 7.1 μm);

4) megalocytic (> 12 μm).

VII. *According to the clinical course:*

1) acute (for example, anemia after hemotransfusion shock);

2) chronic (for example, hypoplastic anemia).

VIII. *By degree of severity:*

1) mild degree (Hb 120-90 g/l, er. – not lower than $3.0*10^{12}$ /l);
2) of medium degree (Hb 90-70 g/l, er. – not lower than $2.5*10^{12}$ /l);
3) of severe degree (Hb < 70 g/l, er. – below $2.5*10^{12}$ /l).

Posthemorrhagic anemia can be acute or chronic.

Acute posthemorrhagic anemia occurs after a sudden , rapid, massive blood loss. This situation occurs when large blood vessels are injured, bleeding from internal organs.

Stages of acute posthemorrhagic anemia:

1) In the first time after acute blood loss, there is an approximately equal decrease in the number of erythrocytes and hemoglobin in the blood, the color index (CP) is within the normal range (normochromic anemia).

2) 2-3 days after blood loss, the number of erythrocytes decreases slightly due to the influx of tissue fluid into the vessels (relative erythropenia) and the destruction of erythrocytes in the cells of the mononuclear phagocyte system (absolute erythropenia).

3) On the 4th-5th day, erythropoiesis increases due to an increase in the production of erythropoietin during hypoxia . The number of polychromatophilic erythrocytes and reticulocytes increases in the blood , normoblasts appear (regenerative anemia), the central nervous system decreases (hypochromic anemia), because accelerated regeneration precedes the maturation of cells that do not have time to lose signs of their immaturity (nucleus, granules) and become saturated with Hb . In addition, acute blood loss will lead to iron deficiency and reduced heme synthesis.

Chronic posthemorrhagic anemias occur with small in volume, but frequent and prolonged bleeding (with gastric ulcer disease , hemorrhoids, hyperpolymenorrhea , etc.), with a violation of hemostasis (hemorrhagic diathesis). *Blood picture:* strong hypochromia of erythrocytes, which indicates a sharp decrease in Hb synthesis due to iron deficiency, microcytosis, hyporegenerative .

Topic 22 . Hemolytic anemias, etiology, pathogenesis

Hemolytic anemias are characterized by the predominance of the processes of destruction of erythrocytes over the process of their formation. Increased breakdown of erythrocytes can be due to acquired or hereditary changes in the

metabolism and structure of the membrane, stroma of erythrocytes or Hb molecules ; the harmful effect of physical, chemical, biological hemolytic factors on the membrane of erythrocytes; slowing down the movement of erythrocytes in the intersinus spaces of the spleen, which contributes to their destruction by macrophages ; by increasing the activity of macrophages .

Types of hemolysis:

- ***intravascular hemolysis*** occurs in blood vessels under the influence of factors that damage erythrocytes: a) physical factors (mechanical trauma, ionizing radiation, ultrasound, temperature); b) chemical agents (hemolytic poisons); c) biological factors (causing agents of infectious diseases, toxins, enzymes); d) immune factors (antibodies).

Mechanisms of intravascular hemolysis.

I. Mechanical hemolysis. It occurs as a result of mechanical destruction of erythrocyte membranes, for example, when erythrocytes are crushed in the vessels of the foot (marching hemolysis).

II. Osmotic hemolysis. It occurs when the osmotic pressure inside the erythrocyte is greater than the osmotic pressure of the blood plasma. In this case, according to the laws of osmosis, water enters the erythrocyte, its volume increases, and eventually the membrane ruptures.

III. Oxidative hemolysis. It develops as a result of free radical oxidation of lipids and proteins of the plasma membrane of erythrocytes. The result of this is an increase in the permeability of the erythrocyte membrane, which further leads to the implementation of the osmotic mechanism of hemolysis.

IV. Detergent hemolysis. Associated with the dissolution of lipid components of the erythrocyte membrane by detergent substances. This type of hemolysis is caused by bile acids (cholemic syndrome), fat-soluble chemical agents, and some bacterial toxins.

V. Complement-dependent hemolysis caused by destruction of the erythrocyte membrane by active complement. This mechanism is the basis of immune hemolysis.

- ***intracellular hemolysis*** develops as a result of absorption and digestion of erythrocytes by macrophages. Reasons:

a) appearance of defective erythrocytes. Reduction of plasticity of erythrocytes, their ability to deform;

b) the appearance on the surface of erythrocytes of chemical groups capable of specifically interacting with macrophage receptors. Such groups are detected during the aging of erythrocytes, as well as when antibodies are fixed on their surface;

c) hypersplenism - increased phagocytic activity of spleen macrophages.

Hemolytic anemias:

● *Hereditary:*

1. **Membranopathies :** violation of the membrane structure with a change in shape (hereditary microspherocytosis or Minkovsky-Shoffar anemia , hereditary ovalocytosis). The type of inheritance is autosomal dominant. Hereditary defect of membrane proteins of erythrocytes - spectrin and ankerin . As a result, the

permeability of the erythrocyte membrane for sodium ions increases significantly , as a result of which erythrocytes acquire a spherical shape. Spherocytes . lose their ability to deform and therefore cannot pass through the narrow interendothelial slits of the venous sinuses of the spleen and remain in it for a long time. Macrophages of the spleen fragment part of the membrane of erythrocytes and turn them into microspherocytes . During subsequent passages of microspherocytes through the spleen, macrophages completely phagocytize the changed erythrocytes - intracellular hemolysis occurs.

2. **Fermentopathies :** deficiency of enzymes of the pentose-phosphate cycle, glycolysis, ATP utilization and enzymes of the glutathione cycle (glucose-6-phosphate-dehydrogenase deficiency anemia).

3. **Hemoglobinopathy :**

a) hereditary defect in the synthesis of chains of globin molecules (α- and β-thalassemia). Thalassemias are hereditary hemolytic anemias with intracellular hemolysis. If the synthesis of α-chains is disturbed, then α- thalassemia develops . At the same time, HbA1, HbA2 and HbF are not formed , but pathological forms of hemoglobin appear: in adults - HbH , and in newborns - HbBart , which are unstable and therefore easily precipitate, as a result of which erythrocytes take the form of targets. Changed erythrocytes are phagocytosed by macrophages - intracellular hemolysis develops.

In β- thalassemia (Culi's disease), the synthesis of β-chains of hemoglobin molecules is disturbed. Therefore, HbA1 is absent, compensatory formation of HbA2 increases. HbF synthesis is not impaired in newborns .

b) hereditary defect of the primary structure of globin (sickle cell anemia). The essence of the defect is that glutamic acid is replaced by valine in the β-chain of the hemoglobin molecule in the 6th position from the N-end. This leads to the appearance of a pathological form of hemoglobin - HbS . Unlike the usual forms of hemoglobin, HbS in the reduced state reduces its solubility, which leads to its precipitation with the formation of crystals that deform erythrocytes. As a result, erythrocytes do not pass through the narrow capillaries and interendothelial space of the venous sinuses of the spleen and intensively phagocytosed by macrophages (intracellular hemolysis).

Blood picture in hereditary hemolytic anemias: enhanced regeneration of the erythrocyte sprout is noted, but erythropoiesis can often be ineffective (when the nuclear forms of erythrocytes are destroyed in the bone marrow). In a blood smear, along with regenerative forms (high reticulocytosis , polychromatophilia , single nuclear forms of erythrocytes), there are degeneratively changed cells (for example, microspherocytes in Minkovsky-Shoffar disease).

● Purchased:

a) **toxic** (hemolytic poisons: compounds of arsenic, lead; toxins of infectious agents: hemolytic streptococcus, anaerobic malarial plasmodium, snake, bee venom);

b) **immune** (transfusion of incompatible blood, Rh incompatibility of mother and fetus; formation of autoantibodies against own erythrocytes when their antigenic properties change under the influence of drugs, viruses).

Hemolytic disease of newborns is a disease that occurs as a result of hemolysis of erythrocytes of the fetus and newborn, caused by antibodies of the mother. Two variants of hemolytic disease of newborns are most common: Rhesus-conflict and ABO-conflict.

Rhesus conflict. It develops in the case of an Rh^- mother's pregnancy with an Rh^+ fetus (most often during a second pregnancy). First, there is immunization of the mother with Rh^+ erythrocytes of the fetus, which can enter the mother's body during childbirth or with placental defects. Antibodies against the D-antigen are synthesized in response to the arrival of Rh^+ erythrocytes in the mother's body. These antibodies (IgG) are able to penetrate through the placenta into the body of the fetus and cause hemolysis of its erythrocytes.

ABO-conflict. It most often occurs in situations where the mother has blood group 0 (I), and the fetus - A (II) or B (III). Normal isoagglutinins in the ABO system belong to the IgM class . These antibodies do not penetrate the placenta and therefore cannot be the cause of ABO-conflict. However, 10% of healthy people who have blood group 0 (I) have antibodies against agglutinogens A and B, represented by IgG . The presence of these antibodies does not depend on previous immunization. IgG agglutinins penetrate the placenta and can cause hemolysis of fetal erythrocytes with blood groups A (II), B (III). Among first-born children, hemolytic anemia as a result of ABO-conflict occurs with the same frequency as in children born after the second, third and subsequent deliveries, in contrast to Rhesus-conflict, where the frequency of hemolytic anemia increases with an increase in the number of deliveries.

c) **mechanical** (mechanical damage to erythrocytes during prosthetics of vessels and valves);

d) **acquired membranopathies** are hemolytic anemias that arise as a result of defects in erythrocyte membranes acquired in the course of individual development, for example, paroxysmal nocturnal hemoglobinuria . This disease occurs as a result of a somatic mutation of hematopoietic cells, as a result of which abnormal populations of erythrocytes, leukocytes, platelets with membrane defects appear, which are associated with a change in the ratio of fatty acids included in the composition of their phospholipids (the content of unsaturated decreases and the content of saturated fatty acids). Erythrocytes of an abnormal population acquire the ability to fix complement, which is a prerequisite for complement-dependent hemolysis. A decrease in the pH of the environment is a factor that provokes intravascular hemolysis. This explains the fact that the destruction of erythrocytes develops most often at night (at night the pH of the blood decreases somewhat).

The blood picture in acquired hemolytic anemias: according to the type of hematopoiesis - normoblastic , according to the regenerative capacity of the bone marrow - hyperregenerative , according to KP - normochromic . The degree of reduction in the number of erythrocytes and hemoglobin depends on the intensity of hemolysis. Cells of physiological regeneration and degeneratively changed erythrocytes (poikilocytosis, anisocytosis) are detected in the blood smear. The appearance of a large number of erythroblasts and normoblasts is characteristic of hemolytic disease of newborns.

Clinical signs and syndromes in hemolytic anemias:

1. Hypoxia. It is caused by anemia and is manifested by sharp weakness, unpleasant sensations in the area of the heart, palpitations, shortness of breath.

2. Hemolytic jaundice.

3. Increased formation of gallstones , especially bilirubin stones . It is explained by a significant increase in the content of bilirubin in bile and an increase in its viscosity.

4. Hemoglobinuria . If it is not possible to bind all the hemoglobin that is released from the destroyed erythrocytes with the blood plasma protein haptoglobin , then the unconjugated hemoglobin passes through the kidney filter and appears in the urine.

5. Splenomegaly - enlargement of the spleen. It is characteristic of the intracellular mechanism of erythrocyte hemolysis. The basis of this phenomenon is an increase in the functional activity of macrophages, which causes their intensive proliferation. Splenomegaly is often accompanied by liver enlargement (proliferation of liver macrophages).

6. Hemosiderosis - deposition of hemosiderin in macrophages.

7. Violation of microcirculation. They often occur with intense hemolysis and are caused by the development of DIC syndrome.

8. Fever. It develops as a result of sharp activation of the phagocytic function of macrophages, as a result of which they secrete interleukin-1.

Topic 23. B12 - folate-deficient and iron-deficient anemias, etiology, pathogenesis

B $_{12}$ -deficient and folate-deficient anemia are anemias associated with a violation of the synthesis of nucleic acids and the replacement of the normoblastic type of hematopoiesis by a megaloblastic one due to a lack of vitamin B $_{12}$ and folic acid in the body.

Etiology:

1. Lack of vitamin in food.

2. Non-absorption of vitamin B $_{12}$ in the stomach, which may be associated with a violation of the function of the fundal part of the stomach , which produces gastromucoprotein (vitamin B $_{12}$ is absorbed in a complex with gastromucoprotein). Violation of the function of lining cells is caused by the influence of autoantibodies on them (pernicious anemia or Addison-Birmer). In addition, a similar condition can occur after resection of the stomach .

3. Non-absorption of vitamin B $_{12}$ in the intestines (with resection of the small intestine, tumors, diphyllobotryosis , alcoholism).

4. Increased consumption of vitamins during pregnancy.

5. Violation of deposition of vitamins in the liver with its diffuse damage.

Pathogenesis. Deficiency of vitamin B $_{12}$ and folic acid, which participate in the formation of thymine, which is part of DNA, reduces the rate of its formation. Slowing down of DNA replication is first of all noticeable in tissues where normally cell division occurs most often - in blood cells and the epithelium of the gastrointestinal tract. Violation of cell division leads to the formation of large blood

cells: megalocytes , megaloblasts , giant megakaryocytes. The maturation of megaloblasts to megalocytes is accompanied by a violation of enucleation (this is evidenced by the appearance of Jolly bodies (remains of the nucleus) and rings in megalocytes Cabot (remains of the nuclear envelope)). The presence of a large number of megaloblasts and megalocytes , saturated with hemoglobin, causes hyperchromia (KP> 1.05).

Normal physiological exfoliation of the epithelium of the gastrointestinal tract due to disruption of cell division is not restored. Therefore, atrophic -inflammatory processes develop in the epithelium of the entire gastrointestinal tract. At the same time, the absorption of vitamins is even more impaired.

As a result of a lack of vitamin $B_{12,}$ methylmalonic acid accumulates in the body , which is toxic to nerve cells. In addition, with vitamin $B_{12\ deficiency}$, fatty acids with a changed structure are synthesized in nerve fibers, which affects the synthesis of myelin and leads to axon damage. Degeneration of the posterior and lateral columns of the spinal cord develops (funicular myelosis), cranial and peripheral nerves are affected.

Blood picture: megaloblastic , hyperchromic , macrocytic anemias . Megalocytes and megaloblasts appear in the blood smear , poikilocytosis, anisocytosis is revealed, the number of reticulocytes decreases , thrombocytopenia and leukocytopenia are observed .

Iron-deficiency anemia is an anemia caused by a lack of iron in the body as a result of an imbalance between its intake, consumption and loss.

Etiology:

1. Chronic blood loss, leading to the loss of iron along with erythrocytes.
2. Increased need for iron (during growth, maturation, pregnancy, lactation).
3. Dietary iron deficiency.
4. Failure to absorb iron:

a) with achlorhydria (hydrochloric acid ionizes iron, which is necessary for its assimilation);

b) with vitamin C deficiency (vitamin C stabilizes iron in its divalent form, because trivalent iron is not absorbed by the body);

c) with enteritis and resection of the small intestine.

5. Violation of iron transport (deficiency of transferrin in liver lesions).
6. Insufficient utilization of iron from its reserve (in case of infection, intoxication).
7. Violation of iron deposition (ferritin deficiency in hepatitis, cirrhosis).

Pathogenesis : with iron deficiency in the body, its inclusion in erythrocytes is disturbed, while the synthesis of heme and globin decreases , the activity of some enzymes in erythrocytes decreases, which causes an increase in their sensitivity to oxidants . The lifespan of erythrocytes decreases.

Along with pathological changes in erythropoiesis , iron deficiency in the body leads to a decrease in myoglobin and the activity of iron-containing factors of tissue respiration. Hemic anemic hypoxia develops , and this leads to atrophic and dystrophic processes in tissues and organs (especially in the gastrointestinal tract and myocardium).

Blood picture: anemia is normoblastic , hypochromic , anisocytosis (microcytosis) is observed, anemia can be regenerative at first, and then hyporegenerative .

Hypoplastic (aplastic) anemia is a disease of the blood system, which is characterized by suppression of the hematopoietic function of the red bone marrow and is manifested by insufficient formation of erythrocytes, granulocytes and platelets (pancytopenia) or only erythrocytes (partial hypoplastic anemia).

Etiology:

1) physical factors (ionizing radiation);

2) chemical agents (benzene, lead, mercury vapor, drugs: cytostatic agents, chloramphenicol, sulfonamides);

3) biological factors (hepatitis virus).

Pathogenesis:

1. Damage to stem cells with the development of pancytopenia .
2. Damage to the cells of the microenvironment is a violation of stromal cells that have a significant impact on the processes of reproduction and maturation of blood cells.

Blood picture: normochromic anemia, aregenerative anemia , agranulocytosis, thrombocytopenia , the number of lymphocytes may remain unchanged. In the red bone marrow, the number of hematopoietic cells decreases with an increase in the content of adipose tissue.

Topic 24. Leukocytosis and leukopenia: etiology, pathogenesis. A picture of blood. Leukemoid reactions.

Leukocytosis . Leukopenia. Nuclear shifts left and right. Characteristic. The value for the diagnosis of bacterial and viral diseases

Definition and classification of leukemia with an indication of the principles underlying it.

Etiology of leukemia. The role of oncogenic viruses, ionizing radiation, chemical carcinogens, genetic abnormalities hematopoiesis in the development of leukemia.

Pathogenesis of leukemia. Mono - and polyclonal stage of development of leukemia. Tumor progression in leukemia.

Blood picture in acute and chronic leukemia (myelo- and lymphatic leukemia).

The difference between leukemias and leukemic reactions.

The content of leukocytes per unit volume of blood is normally $4.0*10^{9}$/l-$9.0*10^{9}$/l.

The leukocyte formula is the percentage ratio of various forms of leukocytes in the peripheral blood.

Leukocytosis is an increase in the number of leukocytes in a unit of blood volume by more than $10*10^{9}$/l.

Classification of leukocytosis :

I. Depending on the causes of development, *physiological* and *pathological*

leukocytosis are distinguished. Physiological leukocytosis is a physiological reaction of the body to strong emotions (emociogenic), during intense physical work (myogenic), after eating (alimentary), when a person moves from a horizontal to a vertical position, in pregnant women and newborns.

Pathological leukocytosis is associated with the course of a pathological process in the body during infectious diseases, inflammatory and allergic processes, intoxication of exo - and endogenous origin.

II. Leukocytosis can be *absolute* and *relative.* Absolute leukocytosis is characterized by an increase in the absolute number of leukocytes per unit volume of blood. We are talking about relative leukocytosis in the case when the relative content of individual forms of leukocytes in the peripheral blood increases.

III. By pathogenesis:

a) *reactive* , which occurs as a reaction of the red bone marrow to a pathogenic influence in infectious diseases, inflammation, the action of low doses of toxic substances. *Pathogenesis:* increased proliferation and maturation of leukocytes in the red bone marrow under the action of leukopoietins ; increasing the transfer of reserve leukocytes from the red bone marrow with the help of interleukin-1 and bacterial endotoxins, which increase the permeability of the wall of blood vessels of the red bone marrow.

b) *redistribution* , which occurs as a result of the transition of leukocytes from the parietal pool to the circulating one. Most forms of physiological leukocytosis are redistributive in their mechanism of development. Its features are: a) short-term nature with a rapid return of the number of leukocytes to normal after the end of the cause; b) preservation of the normal quantitative ratio of different types of leukocytes (the leukocyte formula does not change); c) absence of degenerative changes in leukocytes.

c) *tumor origin* .

IV. Depending on the types of leukocytes, the content of which is increased in the blood, the following are distinguished:

a) *neutrophilic leukocytosis* - observed in: a) purulent-inflammatory processes caused by purulent bacteria (abscesses, phlegmons, sepsis); b) severe hypoxia (acute blood loss, acute hemolysis); c) endogenous intoxication (uremia);

b) *eosinophilic leukocytosis* - occurs in: a) allergic reactions of type I according to the classification of Coombs and Jell ; b) helminthiasis; c) chronic myelogenous leukemia;

c) *basophilic leukocytosis* - occurs in: a) chronic myelogenous leukemia; b) hemophilia; c) Waquez's disease (polycythemia);

d) *lymphocytic leukocytosis* - observed in: a) acute infectious diseases (whooping cough, viral hepatitis); b) some chronic infectious diseases (tuberculosis, syphilis, brucellosis); c) chronic lymphocytic leukemia ;

e) *monocytic leukocytosis* – characteristic of: a) chronic infections (tuberculosis, brucellosis); b) infectious mononucleosis; c) infections caused by rickettsia and protozoa (typhus, malaria).

Leukopenia is a decrease in the number of leukocytes in peripheral blood below $4*10^{9}$/l.

Classification of leukopenia :

I. By origin, leukopenias are *acquired* and *hereditary.* Acquired leukopenia can be caused by physical (ionizing radiation), chemical (benzene, cytostatics, drugs), biological (hepatitis viruses, infectious mononucleosis) and immune factors.

Examples of hereditary leukopenias are neutropenia Kostman , hereditary neutropenia of the autosomal dominant type, "lazy leukocyte" syndrome.

II. According to the type of leukocytes, the number of which is reduced, the following are distinguished:

a) neutropenia ;

b) lymphopenia ;

c) eosinopenia .

III. According to pathogenesis, the following are distinguished:

a) leukopenia caused by a violation of the flow of leukocytes from the red bone marrow into the blood. *Pathogenesis:* damage to hematopoietic cells of a cytolytic and antimetabolic nature; violation of mitosis (inefficient leukopoiesis) due to deficiency of vitamin B_{12} , folic acid and leukopoietins ; violation of maturation of leukocytes; violation of the release of leukocytes from the red bone marrow into the blood; reduction of the bridgehead of leukopoiesis .

b) leukopenia associated with a reduction in the residence time of leukocytes in the peripheral blood. *Pathogenesis:* destruction of leukocytes, which is due to autoimmune mechanisms and hypersplenism (increased phagocytic activity of spleen macrophages); increased use of leukocytes; increased removal of leukocytes from the body.

c) redistributive leukopenia.

Agranulocytosis is a clinical and hematological syndrome, which is characterized by a sharp decrease in the content of neutrophils below $0.75*10^{9}$ /l with a decrease in the total number of leukocytes below $1-10^{9}$ /l.

Pathogenesis:

a) Myelotoxic lesion of red bone marrow;

b) Immune destruction of granulocytic cells by anti-leukocyte antibodies.

Agranulocytosis is accompanied by a weakening of the body's reactivity due to the exclusion of the protective function of leukocytes.

A shift in the leukocyte formula (nuclear shift) is a violation of the ratio between immature and mature forms of neutrophils . An increase in the content of young forms of neutrophils in the blood indicates *a nuclear shift to the left* , a predominance of mature neutrophils with a large number of segments against the background of the disappearance of younger cells - a *nuclear shift to the right* .

Types of nuclear shift to the left:

1. Regenerative shift is an indicator of reactive activation of granulocytopoiesis .

2. Hyperregenerative shift reflects excessive hyperplasia of leukopoietic tissue with impaired cell maturation and marked rejuvenation of the blood composition.

3. Degenerative shift indicates suppression and deep disorders of leukopoiesis .

4. Regenerative -degenerative shift is observed with hyperproduction of pathologically changed leukocytes in the bone marrow and violation of their maturation.

Hemoblastosis is a collective name for neoplastic diseases of the blood system, which are malignant neoplasms from the cells of hematopoietic and lymphatic tissues involving a number of organs and body systems. Typical forms of hemoblastosis are neoplasias arising in the bone marrow (leukemia) and outside the bone marrow (lymphomas).

Leukemia is a systemic neoplastic disease in which a mutant tumor clone originates from progenitor (stem) cells and progenitor cells of hematopoietic cells. It occurs primarily in the bone marrow; it is manifested by uncontrollable proliferation and rejuvenation of hematopoietic elements with a delay in their maturation and metaplasia of hematopoietic tissue.

Classification of leukemias:

- According to the degree of differentiation (maturity) of leukemic cells, *acute* and *chronic leukemias are distinguished* .

Acute leukemias are a heterogeneous group of tumor diseases of the blood system, the substrate of which are young immature hematopoietic cells that displace normal elements. All acute leukemias arise from one mutated hematopoietic cell.

Currently, clinical practice is often guided by the classification of acute leukemias developed in 1976 - FAB (FAB) and subsequently modified. It is based on the cytological characteristics of the dominant population of blasts , taking into account cytochemical reactions and the ultrastructure of leukemic cells.

In acute leukemias, the substrate of the tumor is blast cells.

In acute leukemias, more than 30% of leukemic blasts are detected in the bone marrow , they are more numerous in peripheral blood, complete delay in maturation is characteristic, there are no or significantly reduced maturing and differentiated forms of leukocytes (leukemic failure - hiatus leucemicus , especially expressed in acute myeloid leukemia). *Leukemic failure* is an unfavorable prognostic sign ("white gate to the black kingdom of death"). The content of Hb drops sharply , irreversible anemia and hemorrhagic diathesis develop (hematopoiesis disorders already at the beginning of the disease).

In chronic leukemias, the maturation of cells is partially delayed, the substrate of the tumor is maturing and mature cells, which are mainly found in the peripheral blood.

Over time, acute leukemia does not turn into chronic, because the neoplasm does not regain the previously lost ability to differentiate. However, chronic leukemia can transform into an acute one.

- According to the number of leukocytes in the peripheral blood . Leukemias at one or another stage of their course are classified as:

- leukemic (a sharp increase in the number of leukocytes - from 50.0-100.0*10^9/l);

- subleukemic (increase in the number of leukocytes from 20.0-50.0*10^9/ l);

- leukemic (the number of leukocytes has not changed);

- leukopenic (the number of leukocytes is reduced - <4*10^9/l).

Topic 25. Leukemias: etiology, classification, pathogenesis. A picture of blood.

The etiology of leukemia is similar to that of most malignant neoplasms. Their development is caused by the action of chemical, physical, and biological carcinogens. Among them, ionizing radiation, other types of exposure, chemicals (benzene and its derivatives), cytostatics, RNA and DNA- oncoviruses are of particular importance . Moreover, the carcinogenic effect is realized in conditions of impaired resistance and reactivity of the body, especially with hereditary and acquired defects of the immune system.

The pathogenesis of leukemias is characterized by staged molecular genetic disorders that underlie carcinogenesis. Leukemias, like other malignant tumor diseases, are monopathogenetic . The stages of the pathogenesis of leukemias reflect the typical phasic development of malignant neoplasms.

I stage - initiation (tumor transformation). Under the influence of carcinogens, point mutations (deletions) of suppressor genes (anti-oncogenes) and oncogenes occur in the stem hematopoietic cell of the bone marrow, with the shutdown of the antiblastoma program, including apoptosis . These key gene disruptions give the mutated stem cell the ability to divide indefinitely, a fundamental property of tumor growth. A hematopoietic stem cell becomes a leukemic (cancer) stem cell.

II stage - promotion . In the presence of promotor factors in the body that enhance cell proliferation, the leukemic stem cell divides indefinitely, which leads to the formation of an immortal monoclone with further increase in its number. Thus, the formation of a tumor population in the bone marrow is based on the initial appearance of one malignant stem cell, and then - a clone of leukemic cells.

III stage - progression . During this stage, the following multiple mutations contribute to the increasing destabilization of the genome of the transformed cells of the monoclonal with hyperexpression of new oncogenes and suppression anti-oncogenes . This leads to the emergence of more aggressive subclones , the cells of which acquire the properties of malignancy with replacement (metaplasia) of normal hematopoiesis , spread (dissemination) by hematogenous route into the tissues of the body of the carrier and the formation of proliferating infiltrates in them blasts , foci of perverted (aberrant) hematopoiesis .

The main feature of the pathogenesis of acute leukemias is that leukemic cells, having acquired the ability for unlimited uncontrolled growth, have completely lost the ability to mature, that is, to differentiate into the following forms.

At the same time, in chronic leukemias, leukemic cells, along with the ability to grow indefinitely, retain the ability to mature and give the following forms.

Thus, in acute leukemia, tumor cells only divide and do not mature, in chronic - they divide and mature. Taking into account this circumstance, acute leukemia should be considered a more malignant type of disease.

The source of acute leukemias can be hematopoietic cells of the first four classes. If leukemia develops from cells of classes I-III, which do not have specific morphological and cytochemical features, then such leukemia is called

undifferentiated. If leukemia develops from cells of class IV, then with the help of morphological and cytochemical methods, it is possible to establish the cell from which the tumor arises.

If the source of leukemic cells is lymphoblasts , then such leukemia is called *acute lymphoblastic* , if myeloblasts are *acute myeloblastic* , etc.

Acute myeloblastic leukemia develops mainly in young and middle-aged people. Characteristic features:

- tumor cells - myeloblasts , which are the source of the tumor, will be detected in the blood;

- since the cells of normal hematopoiesis are preserved in the red bone marrow, they will be the source of the influx of normal leukocytes into the blood, that is, those that should be in the blood normally - metamyelocytes , rod-nuclear and segment-nuclear neutrophils ;

- in the blood, there are no transitional forms of leukocytes from myeloblasts to those cells that are found in the blood normally, that is, there are no promyelocytes and myelocytes. A similar phenomenon was called *leukemic failure* .

- the total number of leukocytes is reduced or corresponds to the norm.

Acute lymphoblastic leukemia. It is a typical childhood leukemia. Characteristic features:

- tumor cells - lymphoblasts , which are the source of the tumor, will be detected in the blood;

- along with lymphoblasts , all those cells that should be normal (due to foci of normal hematopoiesis) are also found;

- there are no transitional forms of leukocytes from lymphoblasts to those cells that are normally found in the blood, that is, there are no prolymphocytes (leukemic failure);

- the total number of leukocytes is reduced or corresponds to the norm.

Chronic leukemias develop from hematopoietic cells of class IV.

Chronic myelocytic leukemia. Myeloblasts are the most likely source of the development of this leukemia . Since leukemia is chronic, it means that leukemic myeloblasts retain the ability to differentiate into the following forms. Therefore, all cells originating from myeloblasts , namely promyelocytes , myelocytes, metamyelocytes , rod-nuclear and segmentonuclear granulocytes, enter the blood in large quantities from the leukemic tissue of the red bone marrow (there is no leukemic failure). Cellular elements of the myeloid series predominate in the red bone marrow.

Chronic lymphocytic leukemia. The source of its development is lymphoblasts , which have retained the ability to differentiate into the following forms - prolymphocytes and lymphocytes. Therefore, the main mass of leukemic blood cells is represented by lymphocytes. Their number in the leukocyte formula is 80-90%. In addition to leukemic lymphocytes, prolymphocytes and single lymphoblasts can be detected in the blood . Characteristic is the appearance of the so-called shadows of Botkin- Gumprecht - half-destroyed nuclei of lymphocytes, which arise as an artifact during the preparation of blood smears.

Chronic leukemias are most often characterized by leukemic and subleukemic

variants of the course.

Clinical syndromes in the development of leukemia:

I. Hematological syndromes:

1. Pancytopenia - decrease in the content of all formed blood elements.

2. Anemia . The basis of its pathogenesis is a violation of erythropoiesis .

3. Hemorrhagic syndrome . It is caused mainly by thrombocytopenia and leukemic infiltrates in the walls of blood vessels.

4. Violation of non-specific antimicrobial protection , due to which the body's resistance to infections decreases.

5. Immunological deficiency. It develops as a result of lymphopenia or deficiency of leukemic lymphocytes.

II. Syndromes associated with the peculiarities of the functioning of leukemic cells:

1. Fever. For the most part, fever has a non-infectious origin.

2. Intoxication . Many components of dead leukemic cells have a toxic effect on the central nervous system. Hence fatigue, general weakness, nausea, etc.

3. Autoimmune processes.

III. Syndromes associated with the metastasis of leukemic cells and the development of leukemic proliferates in various organs and tissues:

1. Enlargement of lymph nodes, liver and spleen.

2. Skin syndrome. Caused by the appearance of proliferated leukemic cells - leukemias in the skin .

3. Ulcerative and necrotic lesions of mucous membranes (stomatitis, sore throat, enteropathy).

4. Bone-joint syndrome , manifested by pain in the bones and joints.

5. Neuroleukosis syndrome . It can be manifested by the syndrome of increased intracranial pressure, various neurological disorders: paresis, paralysis, paresthesias.

6. Leukemic pneumonitis . Leukemic proliferates disrupt the respiratory function of the lungs - insufficiency of external breathing develops.

7. Heart failure. It may be a consequence of the proliferation of leukemic cells in the heart muscle.

Leukemoid reactions are reactive, to a certain extent, functional states of the hematopoietic apparatus, lymphatic and immune systems of the body, arising against the background of various diseases. Leukemoid reactions are not independent diseases, but changes in peripheral blood (leukocytosis and a change in the leukocyte formula) and hematopoietic organs that resemble leukemia and other tumors, but do not transform into them.

Differences between leukemias and leukemic reactions.

Sign	Leukosis	Leukemoid reaction
Causative factor	Unknown	Often known (sepsis, dysentery, scarlet fever, diphtheria, purulent infection, croup pneumonia, some

		stages of radiation sickness, etc.)
Antibacterial therapy	Does not give an effect	Gives an effect
The nature of changes	Irreversible	Temporary, reversible
Transformation into a tumor	Transforms	Does not transform
Changes in the bone marrow	Blastna metaplasia of the corresponding sprout	Reactive hyperplasia of leukopoietic tissue
Change of red and platelet germ	IS	There is none
Cell metastasis	Yes (leukemic infiltrates)	There is none

Topic 26. Pathophysiology of the hemostasis system: hemorrhagic syndrome, thrombosis and DVZ-syndrome.

Definition of the term "hemorrhagic shock".

Risk factors for the development of hemorrhagic shock.

Pathogenesis of hemorrhagic shock.

Classification of hemorrhagic shock.

Diagnosis of hemorrhagic shock of various degrees.

Basic principles of treatment of hemorrhagic shock.

Definition of the concept of "DVZ-syndrome".

Causes and risk factors for the development of DVZ-syndrome.

Pathogenesis of DVZ-syndrome.

Classification of DVZ-syndrome by clinical course and stages.

Clinical manifestations of DVZ-syndrome.

Measures of prevention and treatment of DVZ-syndrome.

Hemostasis is a complex system of homeostasis, which on the one hand maintains blood in a liquid state, ensures normal blood supply to organs and tissues, and on the other hand - stops bleeding and prevents blood loss from the body by maintaining the structural integrity of the walls of blood vessels and rapid thrombus formation during their damage

Hemostasis is realized by three interacting structural components:

1. walls of blood vessels,

2. blood cells,

3-plasma enzyme systems (coagulation, fibrinolytic (plasmin), kallikreinkinin , etc.).

Vascular -platelet hemostasis. The main role in the implementation of primary hemostasis belongs to platelets. As a result of damage to blood vessels, platelets come into contact with the subendothelium - mainly with the main stimulator of adhesion - collagen - they swell, form processes and stick together. The duration of this phase is 1-3 seconds. This requires Ca ions and a protein synthesized in the endothelium - Willebrand factor (VIII, PV), and in platelets - a membrane

glycoprotein that interacts with this factor Ib (HP- Ib), which in its absence leads to Bernard-Soulier disease .

Adhesion is followed by rapid aggregation of platelets on the damaged area - II phase (tens of seconds), which leads to rapid growth of the thrombus. The primary stimulus for aggregation is provided by collagen and, to an even greater extent, by ADP, catecholamines , and serotonin released from the vascular wall, from platelets hemolyzed in the area of damage and already adhered platelets.

Platelets that have undergone adhesion and aggregation actively secrete granules with substances that enhance the aggregation process and form its second wave: adrenaline, norepinephrine , serotonin, antiheparin factor. Later, granules containing lysose are secreted omal enzymes .

As a result of the interaction of platelet and plasma factors in the zone of hemostasis, thrombin is formed, small doses of which sharply increase and complete the aggregation process and at the same time start blood coagulation, as a result of which the platelet clot acquires great density and undergoes retraction - III phase - viscous metamorphosis.

After the aggregation of platelets and the formation of fibrin, under the influence of retractozyme , the special contractile protein of platelets - thrombostenin is reduced , which leads to the convergence of platelets and fibrin threads. Retraction requires thrombin, which promotes viscous metamorphosis.

Arachidonic acid derivatives released from the membrane phospholipids of platelets and the vascular wall due to the activation of phospholipases play an important role in the regulation of platelet hemostasis. Under the influence of cyclooxygenase, prostaglandins are formed , from them an extremely powerful agent - thromboxane A_{2} - is formed in platelets under the influence of thromboxane synthetase . The lifetime of thromboxane , prostacyclin and other prostaglandins is a few minutes, but their importance in the regulation and pathology of hemostasis is very great. At the same time, paraproteins , cryoglobulins and fibrinolysis products inhibit platelet aggregation.

Coagulation hemostasis. Blood coagulation is a complex multistage process involving a number of protease proteins, non-enzymatic accelerator proteins that ensure the interaction of coagulation factors on phospholipid matrices (platelet factor 3, micromembranes of other cells), and calcium ions.

It is conventionally divided into 3 phases:

1 - formation of thromboplastin ,

2 - formation of thrombin

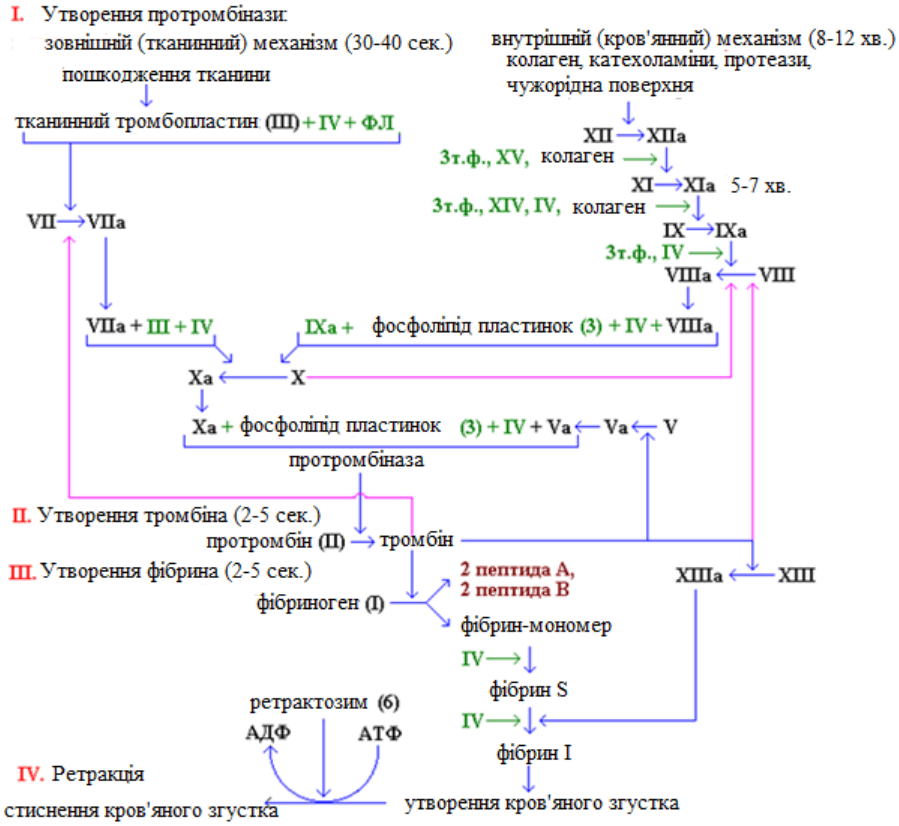
3 - the final stage, where, under the influence of thrombin, fibrinogen is first transformed into fibrin monomers, and then into its polymer, which is stabilized by activated factor XIII.

According to the modern cascade -complex theory of blood coagulation, activation of prothrombin is the result of a multistage enzymatic process in which various coagulation factors are sequentially activated and interact with each other. Among them, factors III, VII, IX, X, XI and XII, as well as prekallikrein are protease enzymes, and factors VIII and V are non-enzymatic accelerators of the process, which accelerate the interaction and activation of enzyme factors many thousands of

times.

There are two main mechanisms for starting the folding process - external and internal. With the external mechanism, blood coagulation is stimulated by the entry of tissue thromboplastin into the plasma . With the internal mechanism of blood coagulation occurs without the participation of tissue thromboplastin . The starting factor here is factor XII (Hagemann), the activation of which occurs either as a result of contact with a foreign surface (glass, metal) or due to its enzymatic cleavage by kallikrein , plasmin or in contact with subendothelium (collagen) and other components of connective tissue in case of injuries, vasculitis , atherosclerosis.

Scheme of the cascade -complex mechanism of blood coagulation:



Mechanism of transformation of fibrinogen into fibrin. The essence of this stage is that the proteolytic enzyme thrombin (formed from prothrombin) cleaves two peptides A and two peptides B from the fibrinogen molecule. As a result, fibrin monomers are formed, each of which has 4 free bonds. These connections are connected to each other first in pairs (dimers), and then into a polymer (connecting end-to-end and side-to-side) and fibrin fibers are formed. This fibrin is soluble and is designated as fibrin S (soluble). Under the influence of factor XIIIA (which is also activated by thrombin in the presence of Ca^{2+} ions), additional disulfide bonds are formed in fibrin . Insoluble fibrin I (insoluble) is formed.

Physiological anticoagulants are necessary to maintain the blood in a liquid state and to limit the process of thrombus formation. They are divided into two main groups:

1. primary, or independently synthesized and constantly contained in the blood,

2. secondary, formed in the process of proteolysis during blood coagulation and fibrinolysis.

Among the primary, the following inhibitory proteins are most important:

Heparin is a natural anticoagulant (together with fibrinolysin, it is part of the physiological blood clotting system). It is produced in basophils and labrocytes . Heparin directly affects blood clotting factors, blocking or reducing their activity. With intravenous administration, the effect occurs almost instantly and lasts 4-6 hours. Heparin is destroyed in the tissues with the participation of heparinase (uroheparin is formed , which is excreted through the kidneys). Heparin has antithromboplastin , antiprothrombin and antithrombin effects, delays the transition of fibrinogen to fibrin, increases fibrinolysis, in large doses inhibits aggregation and adhesion of platelets, increases vascular permeability.

Antithrombin III is a universal inhibitor of almost all enzyme coagulation factors, primarily thrombin - IIa and Xa . It accounts for more than 75% of the total anticoagulant activity of plasma. It is the main plasma cofactor of heparin, and if there is not enough antithrombin III in the blood, it makes no sense to administer heparin to the patient for the treatment of thrombosis. With a hereditary or acquired decrease in antithrombin III, a severe thrombophilic condition occurs with recurrent thrombosis of the trunk veins of the limbs and internal organs, thromboembolism of the pulmonary artery, and organ infarctions.

Secondary physiological anticoagulants are formed in the process of blood coagulation and fibrinolysis as a result of further enzymatic degradation of a number of coagulation factors. After initial activation, they lose their ability to participate in hemostasis and often acquire the properties of anticoagulants. Thus, fibrin adsorbs and inactivates a large amount of thrombin (and is designated as antithrombin I). The products of enzymatic cleavage of fibrinogen / fibrin by plasmin (fibrinolysin) inhibit both platelet aggregation and self-formation of fibrin monomers - that is, the formation of fibrin. Adrenaline in a complex with fibrinogen and heparin turns from a stimulator of platelet aggregation and blood coagulation into a factor that prevents hemocoagulation and into an activator of non-enzymatic fibrinolysis.

Fibrinolysis - an enzyme system (which causes asymmetric splitting of fibrin / fibrinogen into smaller fragments) is called fibrinolytic or plasmin . The main component of this system is the enzyme plasmin (fibrinolysin), which is contained in plasma in the form of a proenzyme - plasminogen . Active plasmin is quickly blocked by antiplasminogens and removed from the bloodstream. When streptokinase or urokinase is administered, the level of plasminogen in the blood decreases very quickly and deeply due to the transition to active plasmin, and then recovers within 18-28 hours. In the body, the activation of fibrinolysis (as well as the activation of coagulation) can be by both external and internal pathways.

Mechanisms and factors of maintaining blood in a liquid state. Blood is kept in a liquid state thanks to the presence of anticoagulants, the activity of which should be higher than that of coagulants. Taking into account the multitude of coagulation factors, there is a powerful system of anticoagulants. It contains antithromboplastins , antithrombin , enzymes that prevent the transition of fibrinogen into fibrin. When thrombin enters the blood, it irritates the chemoreceptors of the vascular wall. From

here, the irritation is reflexively transmitted to the medulla oblongata, and as a result, heparin and heparin-like anticoagulants are released from the vascular wall , which delay the formation of fibrin and its transformation into fibrinogen (spherical).

Thrombosis occurs more often when the biological reliability of the hemostasis system is violated when its regulatory mechanisms are damaged, which leads to thrombophilia . Thrombophilia occurs as a result of a change in one or more components of the hemostasis system, that is, activation of the external and internal systems.

Causes of intravascular thrombosis:

1. Pathology of the vascular wall (intima and media):

a) atherosclerosis (vessel damage with increased platelet aggregation) and hypertension (vessel spasm) (in 80% of diseases - thrombosis),

b) inflammatory vascular lesions, rheumatism (50% is accompanied by thrombosis),

c) postoperative thrombosis (in case of severe operations under general anesthesia - violation of the regulation of the hemostasis system),

d) myocardial infarction - both spasm and thrombosis,

e) with the disintegration of malignant tumors (increased tissue thromboplastin),

f) diabetes (vessel damage and physical and chemical blood changes).

In addition, there are conditions that contribute to thrombosis - emotional stress, endocrine diseases, obesity, general anesthesia, hypodynamia (because movement activates fibrinolysis), and with age, fibrinolysis fluctuations become monotonous and do not provide the required level.

Differences between intravascular thrombosis and protective hemostasis:

Signs	**Thrombosis**	**Protective hemostasis**
Vascular rupture and bleeding	missing	is
Duration of coagulation	long time (hours , days, up to a week)	quickly (seconds, maximum - minutes)
The length of the vessel area	extensive, sometimes the entire venous system	limited by the area of rupture of the vessel
Reversibility of the blood coagulation process	often irreversible and sprouts connective tissue	reversible, the fibrin plug dissolves - sewage
Harmony	disharmoniously with the addition of new areas of thrombosis	harmonic - stages: vessel injury → coagulation → fibrinolysis

Hemorrhagic diatheses (HD) are a group of hereditary or acquired diseases , the main feature of which is bleeding. The mechanism of the development of HD

is diverse and is associated with the pathology of various components of the coagulation system (plasma and platelet), increased fibrinolysis, the presence of DIC, the circulation of anticoagulants in the blood, increased vascular permeability or vascular wall abnormalities. Each of these mechanisms can be primary or accompany other diseases. *Primary HD* belongs to family-hereditary diseases, the characteristic feature of which is the deficiency of any one blood coagulation factor (for example, VIII). *Secondary* , symptomatic HD is characterized by the insufficiency of several blood coagulation factors.

Classification according to the mechanism of occurrence:

I. Violation of vascular and platelet hemostasis: a) vasopathy ; b) thrombocytopenia ; c) thrombocytopenia .

II. Violation of coagulation hemostasis - coagulopathy .

Violation of vascular and platelet hemostasis

Thrombocytopenia is a decrease in the content of platelets in a unit volume of peripheral blood below $150*10^{9}$ / l.

Etiology:

1. violation of the production of platelets in the bone marrow (Werlhoff's disease) or essential thrombocytopenia ;

2. death of platelets in the bloodstream due to the influence of autoantibodies , infections, intoxications, increased spleen function (hypersplenism);

3. increased consumption of platelets in DIC - thrombocytopenia of consumption.

Pathogenesis:

1) violation of the angiotrophic function of platelets, as a result of which dystrophic changes occur in the endothelium and the fragility of microvessels increases ;

2) violation of platelet adhesion and aggregation. This causes a violation of the formation of a platelet thrombus and leads to an increase in bleeding time (Duke's test);

3) violation of secondary spasm of damaged arterioles. With thrombocytopenia , little biogenic amines (catecholamines , serotonin) are released, which cause contraction of vascular smooth muscles;

4) blood coagulation disorders. Caused by insufficient release of platelet factor 3 and thrombostenin . As a result, the first phase of blood coagulation and clot retraction is disrupted .

Pathogenetic therapy - replacement - introduction of fresh blood or platelet mass.

Thrombocytopathy is a violation of the functional properties of platelets, their qualitative inferiority. At the same time, the number of platelets may remain normal.

Etiology:

1. violation of the ability of platelets to adhesion, aggregation and release of blood coagulation factors;

2) lack of factor 3 - thromboplastic factor - thrombocytodystrophy ;

3) lack of factor 6 - retractozyme - thrombocytoasthenia .

Vasopathies are hereditary or acquired hemorrhagic diatheses that occur as a result of primary vascular wall disorders. Species:

1) inflammatory vasopathies - vasculitis :

- infectious vasculitis (for viral hemorrhagic fevers, typhus, sepsis);
- immune vasculitis (as a result of immune complex diseases (type III allergic reactions according to the classification of Coombs and Jelly), for example, with systemic lupus erythematosus);

3) infectious -immune vasculitis .

2) dysplastic Vasopathies are damage to blood vessels associated with a violation of their connective tissue (inferiority of the vascular wall). Causes: hypovitaminosis C, telangiectasias (hereditarily determined local defects of the connective tissue of vessels, which cause thinning of their walls and expansion of their lumen), hemangiomas, genetically determined collagen defects.

Violation of coagulation hemostasis.

The working classification can be based on the scheme of normal blood coagulation. Then the diseases can be grouped according to the phases of blood coagulation:

● HD (coagulopathy) caused by violation of the I phase of coagulation (deficiency of factors VIII, IX, XI and XII), the presence of inhibitors to factors VIII (hemophilia A) and IX (hemophilia B), deficiency of the platelet component of thromboplastin formation , angiohemophilia .

Hemophilia is characterized by bleeding from large vessels - bruising (90% in children). Hemophilia is transmitted by women, and manifests itself in men. In children, hemophilia is manifested to a greater extent by damage to blood vessels, since they have traumatized surfaces, the joints swell - ankylosis, severe pain, restriction of movement → disability. Pathogenesis - blood coagulation factors are poorly activated, or their immune damage develops.

Laboratory diagnosis - clinical - bruises, slowing of blood coagulation, decrease in thromboplastic activity of blood.

Treatment - replacement of the missing factor (fresh plasma or cryoprecipitate or specific factors - VIII, IX).

● HD caused by violation of the II phase of blood coagulation: deficiency of plasma components of thrombin formation - factors II, V, VII and X in liver pathology, presence of antagonists of thrombin formation (antithrombin I - fibrin, antithrombin II - heparin, antithrombin III, IV, V, VI) , the presence of antagonists to factors of the prothrombin complex (II, V, VII, X).

Coagulopathy with damage to the prothrombin complex resembles hemophilia - large bruises (with vitamin K deficiency, cirrhosis , jaundice), heparin overdose.

Laboratory diagnostics - a decrease in the prothrombin index.

Therapy - replacement of the missing factor or blockade of heparin with protamine sulfate.

● GD with violation of phase III. Reasons:

a) violation of fibrinogen formation in liver pathology,

b) increased consumption of fibrin in thrombosis, CVD syndrome,

c) pathological increase in fibrinolysis. There may be a congenital insufficiency of factor XIII . The run is difficult.

Laboratory diagnostics - determination of fibrinogen and its fractions, level of fibrinolysis.

Therapy - administration of fibrinogen and, if necessary, blockade of fibrinolysis.

Disseminated intravascular coagulation (IVC) is one of the severe and dangerous disorders of the hemostasis system. It is a nonspecific reaction characterized by the widespread formation of microclots and aggregates of cells in the vascular bed, which cause a violation of peripheral blood circulation with the development of generalized hemorrhages and severe multiple organ failure.

Etiology:

• all types of shock (anaphylactic, traumatic, burn, cardiogenic),
• acute blood loss,
• infection,
• acute intravascular hemolysis,
• immune conflict,
• massive hemotransfusion ,
• tumors,
• obstetric pathology (premature detachment of the placenta, intrauterine death of the fetus, cystic implantation, eclampsia),
• severe poisoning with hemolytic poisons,
• acute and chronic leukemias

The pathogenesis of DVZ-syndrome consists in activation of blood coagulation, formation of thrombin, widespread deposition of fibrin and systemic thrombus formation in the microcirculatory channel. Widespread intravascular coagulation leads to intensive consumption of coagulation factors and platelets (coagulopathy and consumption thrombocytopenia) with the development of a hemorrhagic syndrome, which is also facilitated by the activation of the fibrinolysis and proteolysis system in general. An obligatory component of DVZ is a hemorrhagic diathesis in the form of petechial hemorrhages in the skin, mucous membranes, under the endocardium, pericardium, in the pleura, peritoneum, meninges, internal organs, possible large hemorrhages in the pleural and abdominal cavities, gastrointestinal tract. The severity of DIC syndrome is determined by the severity of consumption coagulopathy and thrombocytopenia .

Stages of DVZ-syndrome:

Stage 1 - <u>hypercoagulation and aggregation of platelets.</u> It is characterized by the activation of platelet and coagulation hemostasis and the beginning of microthrombus formation .

2nd stage - <u>increasing hypocoagulation .</u> This phase develops as a result of exhaustion of the mechanisms of vascular- platelet and coagulation hemostasis as a result of a decrease in the activity of the coagulation system (consumption of factors I, V, VIII); activation of the fibrinolytic system (a large number of fibrinolysis activators enter the blood); increase in anticoagulant activity of blood due to the formation of fibrinolysis products; the development of consumption

thrombocytopenia ; increasing the permeability of the vessel wall (the formation of large amounts of kinins is important).

3rd stage - restorative. Occurs after elimination of acute disorders of hemostasis and multiple organ failure. It is characterized by the gradual normalization of indicators of all hemostasis links, improvement of the function of affected organs, stabilization of the general condition of patients.

3. Formation of professional skills, skills related to topics that are part of the content module (mastery of communication skills, clinical examination, determination of treatment scheme, conducting laboratory research, etc.) mastery of skills:

Topic 19

1. Patient S., 35 years old, was brought to the surgical clinic due to a bullet wound to the chest.
Objective clinical data: pale skin, blood pressure 9.3/5.3 kPa (70/40 mm Hg), frequent weak pulse, rapid shallow breathing, massive internal bleeding due to damage to one of the branches of the pulmonary artery.
the results of blood analysis 4 days after the operation, which stopped the bleeding: Hb - 4.1 mmol/l, erythrocytes 3*1012 in 1 л, color index - x, reticulocytes -15%, leukocytes 10.2*10-12 in 1l, ESR - 10 mm/ hours Blood smear: many polychromatophilic erythrocytes, 5 adidophilic normoblasts .

-What method of blood smear staining reveals reticulocytes , polychromatophilic normoblasts ?

- What does the picture of the blood smear indicate?

- Name the pathology of blood (erythrocytes) in the patient. To characterize it according to five classifications with the definition of indicators, laying them in their basis. -=What is the color indicator for this bleeding?

Answer standard : Reticulocytes - young erythrocytes are detected by supravital staining of a blood smear, polychromatophilic normoblasts - when stained according to Romanovsky. The blood picture indicates reticulocytosis and good bone marrow regeneration, as there are many polychromatophilic erythrocytes and acidophilic normoblasts . The color index is normal (0.85 – 1). This is polychromic anemia, posthemorrhagic . The bone marrow's ability to regenerate is good, that is, hyperregenerative anemia .

Topic 20

1. Patient D., 42 years old, was hospitalized in a gynecological clinic with complaints of prolonged (2 to 3 weeks in total) and heavy uterine bleeding during the last year. Objective clinical data: pale skin, accelerated pulse, myoma of the uterine body (benign tumor).

Blood analysis results: Hb - 3.6 mmol/l, erythrocytes 1.8*1012 in 1 л, color index - x, reticulocytes - 0.05%, leukocytes 4*109 in 1 л, ESR - 15 mm/h.
Blood smear: hypochromia of erythrocytes, anisocytosis (microcytosis), poikilocytosis, atypical polychromatophiles . The iron content in blood serum is 6 μmol /l (normally 12.3–30.4 μmol /l).
-What is the color index?

-Name the patient's blood (erythrocyte) pathology. To characterize it according to five classifications with the definition of indicators, laying their foundation.

- What regenerative forms and degenerative changes of erythrocytes are detected in a blood smear?

- Why does the patient's blood iron concentration decrease?

Answer standard: Chronic posthemorrhagic anemia, hypsochromic - color index less than 1, due to a decrease in iron in the blood, as the whites continued to bleed. Hypogenerative - reticulocytes of only 0.05% with a norm of 0.5 - 2%. Degenerative changes in erythrocytes are observed - azisocytosis , poikilocytosis. There are also few regenerative forms (polychmatophiles).

Topic 21

- A three-year-old girl (Moroccan by nationality) was hospitalized in a children's hospital in serious condition due to pneumonia and hematuria. (Objective clinical data: yellow skin and sclera, body temperature 39C, frequent shallow breathing, adynamia, right-sided croup pneumonia, enlarged spleen and liver, black urine, contains hemoglobin and hemosiderin .
Results of blood analysis: Hb – 4.2 mmol / d, erythrocytes 2.3.*1012 in 1 л, color index - X, leukocytes 15* 10^{9} in 1 л, neutrophilic leukocytosis with nuclear shift to the left, ESR - 25 mm/h.
Blood smear: poikilocytosis, anisocytosis , erythrocytes with basophilic granularity, single sickle-shaped erythrocytes (drepanocytes), many polychromatophiles . During electrophoresis of hemoglobin, HA, HBs were found .

A sample with sodium meta bisulfate (reducing agent) reveals the phenomenon of ser similarity of erythrocytes.
Name the pathology of erythrocytes that the child suffers from.

Is this disease hereditary or acquired?

If it is hereditary, the type of inheritance should be indicated and the conclusion justified. Calculate the color index.

Explain the mechanism of hemoglobinuria in the patient.
Answer standard: sickle cell anemia. The disease is hereditary. Type of inheritance - incomplete dominance (erythrocytes contain both normal adult hemoglobin and fetal hemoglobin)
Color indicator is less than or equal to 1. As a result of hemolysis of erythrocytes, there is a lot of free hemoglobin in the blood, which is filtered in the kidneys and enters the urine - hemoglobinuria .

Topic 22.

- In a 55-year-old patient who suffered from chronic myeloid leukemia for two years and received cytostatic drugs, the number of blast cells in the blood increased sharply (up to 80%). Anti-leukemia therapy (chemical, hormonal, radiation) becomes ineffective.

Name and explain the pathogenesis of hematological changes in the patient and the lack of effect from cytostatic treatment.

Answer standard: " Blastny crisis". Caused by tumor progression - the transition of the monoclonal stage of chronic myelogenous leukemia to the more "malignant" polyclonal one . Due to the instability of the genetic apparatus, its increased mutability , new clones of tumor cells arise. The selection leads to the death of cells SENSITIVE to cytostatic therapy and the maintenance of leukemic cells' resistance to them.

-Indicate the similarities and differences between leukocyte changes in sepsis, the course of which is characterized by a hyperregenerative nuclear shift of neutrophil granulocytes to the left, and chronic myelogenous leukemia.

Answer standard: In sepsis, a leukemic reaction similar to leukemia develops, but there is a significant difference between them, which is that:

a) causes of leukemic reactions are factors of infectious (viruses, bacteria, parasites, etc.), allergic, tumor processes; leukemias are caused by carcinogenic agents;

b) in leukemoid reactions, the proliferation of normal healthy cells of leukopoietic tissue is activated, in chronic leukemia, the transformation of normal leukopoietic cells into a tumor occurs. In the peripheral blood in sepsis there are leukocytes with toxogenic granularity and

signs of degeneration, they are absent in chronic myeloid leukemia.

In addition, chronic myelogenous leukemia is characterized by " eosinophilic-basophilic association", which is usually absent in sepsis.

Topic 25

- The action of ionizing radiation on the body can lead to the development of both acute radiation sickness and leukemia. In both cases, pathological changes in the blood and a sharp decrease in immunological reactivity are observed.

Specify the characteristic changes in the blood in these diseases and explain their occurrence, the pathogenesis of impaired immunological reactivity. Name the clinical consequences that lead to a decrease in reactivity.

Answer standard:

Agranulocyte leukopenia, acute lymphopenia , thrombocytopenia are characteristic of acute radiation sickness.

High leukocytosis up to 80-90%, single prolymphocytes , lymphoblasts , anemia, thrombocytopenia , relative neutropenia - for leukemia.

In addition, in acute radiation sickness there is suppression of hematopoiesis as a result of decreased cell division under the influence of radiolysis products, decreased phagocytic activity of granulocytes and synthesis of antibodies as a result of impaired T- and B-lymphocytes. Everything leads to the occurrence of secondary and autoinfections . In leukemia, replacement of normal hematopoiesis by tumor

growth of cells of the lymphocytic series is observed. Tumor lymphocytes do not produce antibodies, which also leads to auto- and secondary infections.

- The patient is 45 years old, hospitalized in a therapeutic clinic for exudative pleurisy. In the anamnesis - recurrent angina, bronchopneumonia, furunculosis. Objective clinical data: pale skin, lymph nodes (cervical, submandibular, axillary) enlarged in size, but painless and not fused together ; spleen and liver enlarged; right-sided exudative pleurisy.

Blood analysis results: Hb - 5.6 mmol/l, erythrocytes - 2.8*10 " in 1 л, color index - 1, leukocytes - 100*10 ^{9} in 1 л, platelets 160*10 ^{9} in 1 л, ESR - 30 mm/h; leukogram : basophilic granulocytes - 0%, eosinophilic granulocytes - 1, segmentonuclear neutrophil granulocytes -9, lymphoblasts -1, prolymphocytes - 5, lymphocytes - 80, monocytes - 4%. The smear is dominated by micro- and mesogenerations of lymphocytes, many Gumprecht shadows (lymphocytes in a state of lysis).

What pathology was detected in the patient?

Justify the conclusion.

In this case, is exudative pleurisy a primary or secondary disease?

What is associated with the frequency of angina and bronchopneumonia in the patient?

Explain the mechanism of change in the number of erythrocytes.

Answer standard:

Chronic lymphocytic leukemia .

Secondary disease.

Decrease in immunological reactivity.

Metaplastic anemia / displacement of the erythrocyte sprout of the bone marrow by a leukemic infiltrate.

Topic 23.

-A patient with hemorrhagic shock of the 4th degree was transfused with 200 ml of single-group and single-rhesus erythrocyte mass. The patient's condition did not change during the transfusion. What research and laboratory methods of examination should be performed by the doctor who transfused the erythrocyte mass within a day after the transfusion?

After hemotransfusion, the doctor observes the patient:

1) bed rest and fasting for 2 hours after hemotransfusion ;

2) measurement of body temperature and blood pressure every hour for 2 hours after hemotransfusion ;

3) medical control of the general condition of the patient, the amount and nature of urine in the first 6 hours after hemotransfusion ;

4) laboratory control of urine, blood and, if necessary, other indicators the next day.

- O., a 16-year-old woman in labor, started hypotonic bleeding in the early postpartum period. The volume of blood loss is 1.6% of body weight, pulse is 115 bpm , blood pressure - 80/40 mm Hg , CVT - 35 mm of water. Art.

What is the diagnosis?

A. Hypotonic bleeding in the early postpartum period. Hemorrhagic shock of the 1st degree.

B. Hypotonic bleeding in the early postpartum period. Hemorrhagic shock of the II degree

C. Hypotonic bleeding in the early postpartum period. III degree hemorrhagic shock.

D. Hypotonic bleeding in the early postpartum period. IV degree hemorrhagic shock.

- After bleeding during childbirth, the woman in labor complains of weakness, dizziness, darkening of the eyes, nausea. Objectively: BP – 80/60 mm Hg . Art., pulse – 110/min., hemoglobin – 74 g/l. The bleeding stopped. The diagnosis was established - hemorrhagic shock, post-hemorrhagic anemia.

What are the driving tactics?

A. Introduction of fresh frozen plasma and erythrocyte mass, crystalloids and colloids

B. Direct blood transfusion, infusion reopolyglukin , dry plasma.

C. Antianemic therapy using iron preparations, cyanocobalamin , dizinon .

D. Infusion therapy with solutions of crystalloids and colloids. Pathological obstetrics

4. Summary of results : testing, differential assessment.

PRACTICAL TRAINING

Content module 5. Pathophysiology of the cardiovascular and respiratory systems.

Practical lesson No. 28

Topic. Pathophysiology of systemic circulation. Heart failure: classification, overload mechanisms

Practical lesson No. 29

Topic. Coronary heart disease. Coronary insufficiency. Myocardial necrosis .

Practical lesson No. 30

Topic. Violation of blood circulation is caused by a violation of the functions of blood vessels. General characteristics of the occurrence of hypertension. Atherosclerosis: etiology, pathogenesis.

Practical lesson No. 31

Topic. General characteristics of arrhythmias: etiology, classification, pathogenesis.

Practical lesson No. 32

Topic. Pathophysiology of external respiration. Respiratory failure.

Practical lesson No. 33

Topic. Hypoxia : classification, etiology, pathogenesis.

Practical lesson No. 34

Topic. Pathophysiology of the heart. Current control of knowledge.

Purpose: Acquisition by the student of higher education of knowledge and formation of elements of professional competences in the field of medicine from the pathophysiology division:

Topic 28. Pathophysiology of systemic circulation. Heart failure: classification, overload mechanisms.

Topic 29. Coronary heart disease. Coronary insufficiency. Myocardial necrosis .

Topic 30. Violation of blood circulation is caused by a violation of the functions of blood vessels. General characteristics of the occurrence of hypertension. Pathogenesis of atherosclerosis.

Topic 31. General characteristics of arrhythmias: etiology,
classification, pathogenesis.

Topic 32. Pathophysiology of external breathing. Respiratory failure.

Topic 33. Hypoxia: classification, etiology, pathogenesis.

Topic 34. Verification of assimilation of acquired knowledge and skills by applicants.

Improvement of skills and competences acquired during the study of previous

disciplines.

Basic concepts:

Topic 28. Pathophysiology of systemic circulation. Heart failure: classification, overload mechanisms.

Topic 29. Coronary heart disease. Coronary insufficiency. Myocardial necrosis .

Topic 30. Violation of blood circulation is caused by a violation of the functions of blood vessels. General characteristics of the occurrence of hypertension. Pathogenesis of atherosclerosis.

Topic 31. General characteristics of arrhythmias: etiology,
classification, pathogenesis.

Topic 32. Pathophysiology of external breathing. Respiratory failure.

Topic 33. Hypoxia: classification, etiology, pathogenesis.

Topic 34. Verification of assimilation of acquired knowledge and skills by applicants.

Equipment: Multimedia presentations, tables.

Plan:

9. **Organizational activities (greetings, verification of those present, announcement of the topic, purpose of the lesson, motivation of higher education seekers to study the topic).**
10. **Control of the reference level of knowledge:**

Topic 28. Pathophysiology of systemic circulation. Heart failure: classification, overload mechanisms.

- Definition of the concept of blood circulation insufficiency, principles of its classification, characteristics of cardio and hemodynamic disorders.

The concept of acute and chronic ("congestive") circulatory failure.

Etiology, pathogenesis, stages of chronic circulatory failure.

Development mechanisms of the main clinical manifestations of chronic circulatory failure (dyspnea, cyanosis, edema).

Definition of the concept of heart failure, principles of classification.

Heart failure due to overload.

Causes of cardiac volume and resistance overload.

Mechanisms of immediate and long-term adaptation of the heart to excessive load: tachycardia, hyperfunction (hetero-, homeometric), myocardial hypertrophy.

Coronary insufficiency (relative and absolute; acute and chronic), mechanisms of development.

-Classification of heart rhythm disorders.

Violation of automatism. Causes and mechanisms of occurrence.

Arrhythmias associated with conduction disturbances.

Arrhythmias in connection with a simultaneous violation of automatism and

conduction.

Mechanisms of atrial fibrillation.

TYPICAL FORMS OF CIRCULATORY SYSTEM PATHOLOGY

Normally, in a healthy person, the circulatory system optimally meets the blood supply needs of organs and tissues.

The optimal level of systemic blood circulation is determined by its three components: 1) heart activity; 2) vascular tone; 3) the condition of the blood (the amount of its total and circulating mass, as well as its rheological properties). a disturbance in any link of the circulatory system can lead to insufficient blood circulation.

INSUFFICIENCY OF BLOOD CIRCULATION

Circulatory insufficiency (CI): a condition in which the circulatory system does not meet the needs of tissues and organs for optimal blood supply.

TYPES: INSUFFICIENCY OF BLOOD CIRCULATION:

PC is divided according to several criteria: - compensated (or uncompensated) disorders associated with it, - acuteness of its development and course, - expressiveness of its signs; - Predominant damage to the structures of the circulatory system.

According to compensation of disorders in PC, it is differentiated into: - Compensated PC (Signs of blood circulation disorders are revealed during exercise); - uncompensated PC (signs of impaired blood circulation are at rest).

According to the speed of development and course of PC, it is divided into: - acute (occurs within hours and days); - chronic PC (develops over several months or years).

According to the severity of symptoms, PC is divided into three stages: - stage I (initial or PC of the first degree; this stage is characterized by a decrease in the speed of myocardial contraction, ejection fraction, shortness of breath, palpitations, fatigue. It is important that all the indicated signs are manifested during physical exertion and are absent at rest); - stage II (NC of the second degree; NK is expressed moderately or significantly. The signs of NK indicated for the initial stage are manifested not only during physical exertion, but also at rest); - stage III (final, PC of the third degree. It is characterized by significant disturbances of cardiac activity and hemodynamics at rest, as well as the development of significant dystrophic and structural changes in organs and tissues).

According to the predominant damage to the structures of the circulatory system, NK is differentiated into two groups: - violation of the central circulation, i.e. blood flow in the cavities of the heart and large vessels leaving it and entering it;

- disorders of peripheral blood circulation: blood flow in vessels of medium diameter (arteries and veins), as well as in the microcirculatory channel.

RISK FACTORS OF INSUFFICIENCY OF BLOOD CIRCULATION

The main risk factors for the development of PC in a modern person include:

- repeated and prolonged episodes of stress; - chronic hypodynamia; - alcohol intoxication; - smoking; - excessive consumption of tea, coffee and other "household doping"; - low-quality, unbalanced nutrition and overeating; - Obesity. in total, at least 50 risk factors are known that contribute to the occurrence of NK .

THE INITIAL CAUSES OF CIRCULATORY SYSTEM INSUFFICIENCY ARE VIOLATIONS:

- Cardiac activity,
- tone and structure of blood vessel walls,
- BCC and/or rheological properties of blood.

INSUFFICIENCY OF BLOOD CIRCULATION AS A CONSEQUENCE OF HEART DISORDERS

Most cardiac disorders are classified into three groups of typical forms of pathology:

- coronary insufficiency,
- arrhythmias,
- Heart failure.

Topic 28. Coronary heart disease. Coronary insufficiency. Myocardial necrosis .

CORONARY INSUFFICIENCY

Coronary insufficiency: a typical form of heart pathology.

KN is characterized by an excess of the myocardium's need for oxygen and metabolic substrates over their real inflow through the coronary arteries, as well as a violation of the outflow of metabolites, BAV, ions and other substances from the myocardium.

The main pathogenetic factor of coronary insufficiency: myocardial ischemia.

Clinically, coronary insufficiency is manifested as coronary heart disease (CHD, syn.: coronary heart disease - CHD). When the coronary arteries are damaged, various forms of angina pectoris, myocardial infarction, arrhythmias, heart failure, and cardiac death can develop.

TYPES OF CORONARY INSUFFICIENCY

All varieties of CN, depending on the degree and reversibility of myocardial damage, are divided into reversible and irreversible

REVERSIBLE DISORDERS OF CORONARY BLOOD FLOW

Reversible (transient) disorders of coronary blood flow are manifested by two categories of disorders:

- various forms of angina pectoris and
- states after the start of reperfusion (revascularization) of the previously ischemic area of the myocardium

ANGINA

Angina: a typical form of coronary insufficiency.

Angina is characterized by a reversible local mismatch of the myocardium's need for oxygen and metabolic substrates in comparison with their inflow through the coronary arteries, as well as a violation of the outflow of metabolites, BAV, ions and other substances from the myocardium.

With angina pectoris, the need for blood supply is always higher than its actual level.

THERE ARE SEVERAL TYPES OF ANGINA:

- angina pectoris of a stable (typical) course. This is the most common type of angina pectoris. It is usually the result of a decrease in coronary blood flow to a critical level or a significant increase in the work of the heart, or a combination of both;

- angina pectoris of an unstable course (syn.: increasing, unstable, threatening the development of myocardial infarction). It is characterized by episodes of angina pectoris that increase in frequency, duration, and severity, often even at rest. These episodes are usually the result of the destruction of the atherosclerotic plaque and the development of a thrombus at the site of the defect, or an embolism of the coronary artery, or a long-term spasm of its branch. Often, episodes of angina are prolonged and end with a myocardial infarction. In this regard, such episodes are designated as a pre-infarction state;

- Variant angina (Prinzmetal's angina). It is the result of long-term spasm of the walls of the branches of the coronary arteries. Repeated, even short-term (up to 3-8 min) episodes of angina pectoris can lead to the formation of small areas of myocardial necrosis with subsequent development of small focal cardiosclerosis.

STATE AFTER REPERFUSION (REVASCULARIZATION) OF MYOCARDIA.

Such conditions develop in patients with coronary artery disease after:

- surgical restoration or significant increase in blood flow in the coronary artery (for example, after coronary artery bypass grafting, coronary artery stenting or percutaneous intravascular angioplasty);

- medicinal restoration of blood flow in coronary arteries (for example, as a result of thrombolysis , disaggregation of formed blood elements with the help of clots and fibrinolytics or disaggregants).

IRREVERSIBLE DISORDERS OF CORONARY BLOOD FLOW

Irreversible cessation or long-term significant reduction (compared to the required!) blood flow through the coronary arteries in some region of the heart usually results in a myocardial infarction.

Myocardial infarction: a typical form of coronary insufficiency, characterized

by focal necrosis of the heart.

A heart attack develops as a result of a significant and long-term mismatch between the myocardium's need for oxygen and metabolic substrates and their delivery through the coronary arteries, as well as a violation of the outflow of metabolites, BAV, ions and other substances from the myocardium.

Myocardial infarction threatens the patient with life-threatening complications:

- acute heart failure,
- cardiogenic shock,
- Lung edema;
- rupture of the walls of the ventricle, interventricular septum or aneurysm;
- Insufficiency of heart valves;
- Violations of heart rhythm;
- Thromboembolism .

If a myocardial infarction does not lead to the death of the patient, then the dead part of the heart is replaced by connective tissue - cardiosclerosis develops.

CAUSES OF CORONARY FAILURE

The numerous conditions and factors capable of causing coronary insufficiency fall into three main interrelated and interdependent groups

- reduce blood flow to the myocardium through coronary arteries;
- They increase the consumption of oxygen and metabolic substrates by the myocardium;
- which reduce the content of oxygen and/or metabolic substrates in blood and myocardial cells.

Decreased blood flow to the myocardium as a cause of heart failure

Factors leading to an absolute decrease in blood flow to the myocardium through the coronary arteries occur most often. The most significant among them include:

- atherosclerotic lesion of coronary arteries. In more than 90% of patients with angina, significant local narrowing of the lumen of at least one of the coronary arteries of the heart is detected on coronary angiograms ;
- aggregation of formed blood elements (mainly erythrocytes, platelets) with the formation of blood clots in the coronary arteries of the heart. Atherosclerotic changes in vessel walls, turbulent nature of blood flow in coronary vessels, increased content and/or activity of blood coagulation factors released from damaged blood cells and vessel wall contribute to these processes to a large extent;
- Spasm of coronary arteries. Catecholamines are of decisive importance in the development of coronary spasm . In real life, coronary insufficiency is the result of a complex of interrelated factors: - contraction of smooth muscle cells of coronary arteries and reduction of their lumen under the influence of catecholamines , thromboxane A2, PgF2α and other vasoconstrictors; -Reduction of the internal

diameter of the lumen of the coronary arteries as a result of thickening of its wall (due to atherosclerotic changes, hypertrophy of the muscular membrane, fibrous changes, edema, etc.) ; - narrowing and closing of the vessel lumen by aggregates of formed blood elements. These ideas are summarized in the concept of dynamic stenosis of coronary arteries.

Increased consumption of oxygen and metabolic substrates by the myocardium as a cause of heart failure

The factors that most often and significantly increase the consumption of oxygen by the myocardium, as well as the substrates of metabolism and lead to coronary insufficiency include: - an excess of catecholamines in the heart and - the increased work of the heart.

of catecholamines in the heart has a pronounced cardiotoxic effect. It is implemented with the participation of several mechanisms.

Coronary insufficiency with excessive activation of the sympathoadrenal system is characterized both by an increase in the consumption of O2 and metabolites by the hyperfunctioning myocardium, and by a limitation of their inflow to the myocardium by the coronary arteries.

Increased work of the heart, as well as the reasons that caused it, always lead to the activation of the sympathoadrenal system. The latter is accompanied by the release of an excess of catecholamines and the realization of their cardiotoxic effect.

A decrease in the content of oxygen and/or metabolic substrates in the blood and cells of the myocardium as a cause of heart failure

Systemic deficiency of O2 (general hypoxia) and metabolic substrates is often observed in patients with various forms of pathology. Yes, it naturally manifests itself in respiratory insufficiency, in all forms of anemia, insufficiency of blood circulation, endo - and exogenous intoxications, long-term and significant physical exertion, in diabetes mellitus (glucose deficiency in cells), in hypo- and dyslipidemias (insufficiency in VLDL cells). etc. _ _ conditions It is known that under aerobic conditions the main substrates for ATP synthesis in cells are fatty acids (65–70%), glucose (15–20%) and lactic acid (10–15%).

MECHANISMS OF HEART DAMAGE IN CORONARY FAILURE

A lack of oxygen and/or metabolic substrates in the myocardium, as well as a violation of the outflow of products of disturbed metabolism, ions, BAV in conditions of coronary insufficiency lead to the inclusion of a number of typical mechanisms of myocardial damage.

The specified mechanisms are implemented both in the ischemia zone and its borders, although in the latter - to a much lesser extent.

DISORDER OF ENERGY SUPPLY OF CARDIOMYOCITES IN

CORONARY INSUFFICIENCY.

In the conditions of increasing ischemia in the myocardium, the oxygen associated with myoglobin is depleted and the intensity of oxidative phosphorylation decreases. As a result of these changes , the content of ATP and then creatine phosphate in cardiomyocytes decreases .

Disruption of the energy supply processes of cardiomyocytes leads to a decrease in the contractile function of the myocardium, impaired blood circulation in organs and tissues, and the development of cardiac arrhythmias. Heart rhythm disorders, in turn, are often the cause of sudden death in patients with coronary insufficiency.

cardiomyocyte membranes and enzymes in coronary insufficiency.

The main properties of the myocardium (automatism, excitability, conduction, contractility), as well as their regulation, largely depend on the condition of the membranes and enzymes of cardiomyocytes . In the case of ischemia, their damage is the result of a number of common factors. The main mechanisms of damage to cell membranes and enzymes are shown on.

IONS AND FLUID IMBALANCE IN CORONARY INSUFFICIENCY.

Ionic imbalance develops as a result of disturbances in the energy supply of cardiomyocytes , as well as damage to their membranes and enzymes.

The total content of ions in the cells of the ischemic myocardium increases significantly. Intra- and extracellular ratio and distribution of individual ions, as well as fluid in cardiomyocytes varies in different ways.

The following – typical for myocardial ischemia – changes in ion content are especially important:

- an increase in [K+] outside cardiomyocytes as a result of a decrease in the activity of Na +, K+ATPase , a deficiency of ATP and an increase in the permeability of the plasma membrane; the loss of K+ by cardiomyocytes is accompanied by an increase in its content in the interstitial fluid and blood.

Hyperkalemia is one of the characteristic signs of coronary insufficiency, especially in myocardial infarction.

- increasing the content of Na + ions in cardiomyocytes ;
- an increase in [Ca2+] in myocardial cells . The above-mentioned changes lead to the accumulation of excess fluid in myocardial cells;
- Dysregulation of the volume of myocardial cells.

The imbalance of ions and fluid causes a violation of fundamental processes in the myocardium, primarily its contractile function and electrogenesis .

in connection with a significant disorder of transmembrane electrogenesis .

Disorders of mechanisms of regulation of cardiac activity in coronary insufficiency.

The change in the function of the heart as a whole, as well as the nature and degree of damage to its cells in coronary insufficiency is the result not only of their

direct alteration by pathogenic factors of ischemia. To a large extent, these changes are caused by disorders of the mechanisms of cardiac activity regulation. They develop at one (less often) or several (more often) levels: - interaction of BAS (hormones, neurotransmitters) with receptors; - formation of cellular (second) mediators of regulatory influences; - metabolic cellular.

Coronary insufficiency is characterized by stage changes in the activity of sympathetic and parasympathetic regulation mechanisms:

- at the initial stage of myocardial ischemia, as a rule, significant activation of the sympathoadrenal system is observed. This is accompanied by an increase in the content of noradrenaline and especially adrenaline in the myocardium. As a result, tachycardia develops, cardiac output increases, which usually decreases immediately after the onset of an episode of coronary insufficiency. In parallel with this, parasympathetic effects may increase (as evidenced by an increase in the content of acetylcholine in the myocardium), but the degree of their increase is less than sympathetic;

- in the later stages of coronary insufficiency (after several tens of minutes, sometimes hours), a decrease in the content of norepinephrine in the myocardium and the preservation of an elevated level of acetylcholine are usually recorded. At the same time, there are signs of the dominance of parasympathetic regulatory influences: bradycardia, a decrease in cardiac output, the rate of contraction and relaxation of the myocardium;

- in conditions of coronary insufficiency (especially with prolonged ischemia and at the initial stage of myocardial reperfusion), an important pathogenetic phenomenon naturally develops: hormone-neuromediated dissociation of catecholamines (the ratio of the neurotransmitter norepinephrine and the hormone adrenaline).

PHENOMENON: HORMONE-NEUROMEDIATOR DISSOCIATION catecholamines is characterized by:

- a significant increase in the concentration of adrenaline in the ischemic myocardium and the realization of its cardiotoxic effects.

- A simultaneous decrease in the content of noradrenaline in the ischemic myocardium .

The phenomenon of hormone-neurotransmitter dissociation of catecholamines causes the potentiation of ischemic and reperfusion damage to the myocardium.

Coronary insufficiency is accompanied by other changes in neurohumoral regulation of heart function. As a rule, they are individualized (depending on the duration of the episode of coronary insufficiency, the number of them in the anamnesis, the age of the patient, the severity of heart failure, etc.) and are specifically considered in clinical manuals.

The most common forms of coronary insufficiency — angina pectoris of various currents — are characterized by a spontaneous or drug-induced change in a more or less prolonged period of myocardial ischemia by a period of restoration of coronary blood flow — reperfusion .

The frequency of conditions caused by postocclusion (poststenotic) reperfusion of the myocardium has significantly increased in recent decades due to the introduction into clinical practice of various surgical (aorto-coronary bypass, stenting of coronary arteries) and/or medicinal (fibrinodiaz) and fibrinolysis . methods of eliminating stenosis or occlusion of main branches of coronary arteries

Restoration of blood flow (reperfusion) is the most effective way to stop the action of pathogenic factors of myocardial ischemia and eliminate the consequences of their impact on the heart.

Adaptive effects of reperfusion :

- prevention of myocardial infarction;
- prevention of aneurysm formation in the previously ischemic area of the heart;
- Stimulation of the formation of connective tissue in the wall of the aneurysm, if it has already developed;
- Potentiation of the process of restoring the contractile function of the heart.

At the same time, the initial stage of postocclusion reperfusion of coronary vessels and myocardium is often accompanied by significant heart function disorders:

- the development of arrhythmias, including ventricular fibrillation, which threatens the death of the patient;
- destabilization of indicators of central and organ tissue blood circulation; - imbalance of biochemical and electrophysiological parameters of the heart.

In this regard, at the early stage of reperfusion , prolongation and even potentiation of damage to the reperfused heart area is possible .

Coronary insufficiency is a combination of two syndromes: ischemic and reperfusion , and not just one – ischemic (as previously believed).

DAMAGE TO MYOCARDIA DURING ITS REPERFUSION

Postocclusion reperfusion of coronary arteries has, along with the main: reparative, restorative effect, as well as a pathogenic effect on the myocardium. The latter is a cumulative consequence of the prolongation of its ischemic damage, and even additional alteration of the myocardium by the factors of reperfusion and reoxygenation .

The main mechanisms of additional - reperfusion - damage to myocardial cells are:

- Worsening of the violation of the energy supply of the cells of the myocardium, which is reperfused at the stages of resynthesis , transport, utilization of ATP energy. This is characterized by: - A decrease in the efficiency of ATP resynthesis . The causes of additional - reperfusion - inhibition of ADP rephosphorylation are: hyperhydration , swelling and destruction of mitochondria in the reperfused myocardium (the result of osmotic swelling of organelles, overstretching and rupture of their membranes in connection with excessive accumulation of Ca2; Ca2; release of ADP, AMP and other purine of compounds

from the mitochondria of cardiomyocytes into the intercellular fluid; - Violation of the ATP energy transport mechanism in myocardial cells; - Reduction of the efficiency of ATP energy utilization mechanisms;

- increasing degree of damage to membranes and enzymes of cells and myocardium. The reasons for this are: reperfusion (oxygen-dependent) intensification of the lipoperoxide process, calcium activation of proteases, lipases , phospholipases and other hydrolases , as well as osmotic swelling and rupture of the membranes of myocardial cells and their organelles;

- Potentiation of ion and fluid imbalance in cardiomyocytes . The reasons for this are considered to be reperfusion disorders of energy supply processes and damage to membranes and enzymes. As a result, an excess of Na + and Ca2+ accumulates in the cells of the myocardium, as a result - liquid;

- a decrease in the effectiveness of regulatory (nervous, humoral) effects on myocardial cells (normally, contributing to the integration and normalization of intracellular processes);

- increasing severity of hormone-neuromediated dissociation of catecholamines .

Effective prevention and therapy of postischemic reperfusion conditions allows:

- prevent the development of a myocardial infarction or significantly reduce the volume of the affected area of the myocardium;
- to stimulate repair processes in the heart muscle;
- Normalize the contractile function of the heart;
- Restore optimal parameters of blood circulation in the body.

CHANGE OF HEART FUNCTION IN CORONARY INSUFFICIENCY

Coronary insufficiency is accompanied by characteristic changes on the ECG and indicators of the contractile function of the heart.

Changes on the ECG during an acute episode of coronary insufficiency: at the time of a pain attack, as a rule, the following are recorded: - at the initial stage of the episode: a temporary elevation of the ST segment (as a rule, with variant angina); - later there is a decrease (depression) of the ST segment and inversion of the T wave.

CHARACTERISTIC CHANGES IN THE REDUCTION FUNCTION OF THE HEART DURING AN ACUTE EPISODE OF CORONARY INSUFFICIENCY:

- shock and cardiac output, as a rule, decrease. The reason for this: "turning off" the ischemic region of the myocardium from the contractile process. Tachycardia is one of the mechanisms for compensating for a decrease in cardiac output. It is mainly caused by the activation of the sympathoadrenal system (in response to a drop in cardiac output), as well as an increase in blood pressure in the vena cava and atria;

- The end-diastolic pressure in the heart cavities usually increases. The main reasons for this are: - a decrease in the contractile function of the damaged myocardium and - a decrease in the degree of diastolic relaxation of the myocardium.

This is caused by its subcontracted state in connection with an excess of Ca2+ in the cytosol and myofibrils cardiomyocytes ;

- the rate of systolic contraction and diastolic relaxation of the myocardium significantly decreases. The main reasons for these changes: - ATP energy deficiency; - damage to myofibril membranes , sarcoplasmic network and sarcoplasm; - Decrease in the activity of Ca2+-dependent ATPases .

HEART FAILURE

Heart failure (HF) is one of the most common causes of disability, disability and death in patients suffering from diseases of the circulatory system.

Heart failure is not a nosological form. This is a syndrome that develops in many diseases, including those affecting organs and tissues that do not belong to the cardiovascular system.

Heart failure: a typical form of heart pathology, in which it does not meet the needs of organs and tissues in adequate (their functions and the level of plastic processes in them) blood supply.

Heart failure is revealed by a smaller (compared to the required) amount of cardiac output, as well as primary circulatory hypoxia.

The essence of HF lies in the fact that the heart (with OPSS and BCC) cannot move all the blood flowing to it through the veins into the arterial channel.

CAUSES OF HEART FAILURE

The action of two groups of factors leads to the development of HF:

- have a direct harmful effect on the heart;
- which determine the functional load of the heart.

DAMAGE TO THE HEART AS A CAUSE OF SLEEP

Factors directly damaging the heart can be physical, chemical, and biological in nature.

Physical factors. Most often it is: - compression of the heart (exudate, blood, emphysematous lungs, tumor); - Exposure to electric current (in case of electrocution, heart defibrillation procedure); - mechanical injury (in the case of clogged chest areas, penetrating wounds, surgical manipulations).

Chemical factors. These include: - non-medicinal chemical compounds (for example, oxidative phosphorylation uncouplers, calcium and heavy metal salts, inhibitors of enzymes, lipid hydroperoxide); - medicines in inadequate dosage (for example, calcium antagonists, cardiac glycosides, adrenoblockers); - lack of oxygen or substances necessary for metabolism (for example, ions).

Biological factors Most often these are: - high levels of BAS (for example, catecholamines or thyroid hormones); - deficiency or absence of BAS necessary for myocardial metabolism (for example, enzymes, vitamins, etc.); - cardiomyopathy (heart damage, mainly non-inflammatory in nature, characterized by changes in electrophysiological and other biological properties of the heart).

OVERLOAD OF THE HEART AS A CAUSE OF SLEEP

The causes of heart overload are divided into two subgroups, which cause: - increased preload and/or - increased afterload on it.

Types of heart failure

Differentiation of types of SN is based on several main criteria: - its origin; - speed of its development; - predominant damage to the heart; - predominant insufficiency of the cardiac cycle phase; - primary myocardial damage.

TYPES OF SN BY ORIGIN:

Myocardial form: develops mainly as a result of direct damage to the myocardium.

Congestive form: occurs mainly as a result of cardiac overload (increased pre- or afterload).

Mixed form: the result of a combination of direct damage to the myocardium and its load.

TYPES OF SN BY SPEED OF DEVELOPMENT:

Acute HF (Develops within minutes and hours). It is the result of a myocardial infarction, acute insufficiency of the mitral and aortic valves, rupture of the walls of the left ventricle.

Chronic heart failure (formed gradually, over weeks, months, years). It is a consequence of arterial hypertension, chronic respiratory failure, long-term anemia, heart defects.

TYPES OF SN REGARDING THE INITIAL DEVELOPMENT MECHANISM

Primary or cardiogenic. It develops as a result of a predominant decrease in the contractile function of the heart with a venous blood flow to it that is close to normal. It is most often observed in coronary artery disease, myocarditis , cardiomyopathies.

Secondary or non-cardiogenic . It arises as a result of primary preferential reduction of venous inflow to the heart with close to the normal value of the contractile function of the myocardium. It is most often found with acute massive blood loss, violation of diastolic relaxation of the heart and filling of its chambers with blood (for example, when the heart is squeezed by fluid in the pericardial cavity - blood, exudate), episodes of paroxysmal tachycardia, collapse.

TYPES OF SLEEP BY THE PART OF THE HEART MAINLY AFFECTED

Left ventricular heart failure. It can be caused by an overload of the left ventricle (for example, in the case of stenosis of the mouth of the aorta) or a decrease in its contractile function (for example, in the case of a myocardial infarction).

Right ventricular heart failure. Occurs with mechanical overload of the right ventricle (for example, with narrowing of the opening of the pulmonary artery valve)

or high pressure of the pulmonary artery (with pulmonary hypertension).

Total heart failure. With this form of HF, there are signs of both left ventricular and right ventricular heart failure.

TYPES OF MI REGARDING THE PREDOMINANT FAILURE OF THE PHASE OF THE CARDIAC CYCLE

Predominantly diastolic heart failure. With it, the relaxation and filling of the ventricles of the heart is disturbed. This leads to an increase in end-diastolic pressure. This is due to hypertrophy or fibrosis of the myocardium.

Predominantly systolic heart failure. As a rule, it has a chronic course. With it, the pumping function of the heart is disturbed , which is manifested by a decrease in cardiac output.

GENERAL MECHANISMS OF THE DEVELOPMENT OF HEART FAILURE

The myocardial form of HF is characterized by a decrease in the tension developed by the heart, and is manifested by a decrease in the strength and speed of its contraction and relaxation.

The overload form of HF is formed against the background of a more or less prolonged period of its hyperfunction and also leads to a decrease in the force and speed of contraction and relaxation of the heart.

In both cases (both with overload and with damage to the heart), a decrease in its contractile function is accompanied by the inclusion of extra- and intracardial mechanisms to compensate for this shift. All these mechanisms, despite the known originality, are interconnected under the conditions of a whole organism.

COMPENSATORY HEART HYPERFUNCTION

The functioning of the Frank Starling mechanism and the homeometric mechanism provides emergency compensation of the contractile function of an overloaded or damaged myocardium. This is accompanied by a significant and more or less long-lasting increase in the intensity of the heart's functioning: its compensatory hyperfunction.

COMPENSATORY HEART HYPERTROPHY

Hyperfunction of the myocardium determines the expression of certain genes of cardiomyocytes . This is manifested by an increase in the intensity of the synthesis of nucleic acids and proteins. Acceleration of the synthesis of nucleic acids and proteins of the myocardium leads to an increase in its mass - compensatory hypertrophy of the heart (CHT).

The value of compensatory hypertrophy of the heart is that the increased function of the myocardium is performed by the increased mass.

MECHANISMS OF DECOMPENSATION OF THE HYPERTROPHATED HEART

The potential for a hypertrophied myocardium to increase force and speed of

contraction is not limitless.

If the increased load continues to act on the heart or it is additionally damaged, the strength and speed of its contractions decrease, and their energy "cost" increases: decompensation of the hypertrophied heart develops.

The basis of decompensation of a long-term hypertrophied myocardium is a violation of the balanced growth of its various structures. These shifts, along with others, cause a decrease in the force of heart contractions and the speed of the contractile process, i.e. - Development of heart failure.

CELLULAR AND MOLECULAR MECHANISMS OF SN

A decrease in the contractile function of the heart is the result of the development of HF of various etiologies.

Despite the difference in the causes and the known originality of the initial stages of the pathogenesis of HF, its mechanisms at the cellular and molecular levels are the same.

DISORDERS OF THE NEUROHUMORAL REGULATION OF THE HEART IN SLEEP

A general description of disturbances in the regulation of cellular functions is given in chapter 5 "Damage, adaptation and pathology of cells". Only important for the development of HF, changes in sympathetic and parasympathetic regulation of the heart are discussed below.

Changes in sympathetic regulation mechanisms include:

- Decrease in the content of the neurotransmitter of the sympathetic nervous system: norepinephrine in the heart tissue. The reasons for this are: - reduction of norepinephrine synthesis in neurons of the sympathetic nervous system due to suppression of the activity of the tyrosine hydroxylase enzyme and -inhibition of norepinephrine uptake by nerve endings;

- Reduction of adrenoreactive properties of the heart, i.e. severity of ino -, chrono -, dromo - and bathmotropic effects of norepinephrine and adrenaline.

The change in the mechanisms of parasympathetic regulation consists in increasing the effects of acetylcholine on Mcholine receptors . This causes a decrease in the heart rate, inhibiting the formation of TsAMP and stimulating the formation of CGMP. The latter activates cGMP -dependent kinase , which suppresses the activity of potential-dependent Ca2+ channels.

The change in the mechanisms of parasympathetic regulation in HF is much less pronounced than that of sympathetic regulation. This is the result of higher resistance of parasympathetic mechanisms to damaging factors.

The main pathogenic consequence of disruption of sympathetic and parasympathetic effects on the myocardium in heart failure is a decrease in the degree of controllability and reliability of heart regulation. This leads to a decrease in the rate and magnitude of mobilization of the contractile function of the heart, especially in emergency conditions.

MANIFESTATIONS OF HEART FAILURE
CLINICAL OPTIONS OF HEART FAILURE

ACUTE HEART FAILURE

Acute heart failure: a sudden disruption of the pumping function of the heart, leading to the inability to maintain adequate blood circulation.

Etiology of acute HF

Acute HF develops in conditions that lead to a rapid and significant decrease in cardiac output. This is most often observed in myocardial infarction. However, acute HF is also possible with high cardiac output.

Acute HF has three main clinical variants:

- cardiac asthma,
- acute cardiogenic pulmonary edema,
- Cardiogenic shock.

Cardiac asthma

Cardiac asthma (asphyxia, paroxysmal nocturnal dyspnea) occurs as a result of blood stagnation in the small blood circulation as a manifestation of interstitial pulmonary edema and a rapid increase in blood pressure in the blood vessels of the small blood circulation.

Cardiogenic flow of the lungs

Pulmonary edema is divided into interstitial (observed in cardiac asthma) and alveolar, which are considered as two stages of the same process.

Interstitial pulmonary edema: swelling of the lung parenchyma without the release of transudate into the lumen of the alveoli. It is clinically manifested by shortness of breath and cough without sputum. As the process progresses, alveolar edema occurs.

Alveolar edema of the lungs is characterized by transudation of plasma into the lumen of the alveoli. Patients develop a cough with frothy sputum, wheezing, and wheezing sounds are heard in the lungs. Pulmonary edema develops with an increase in the pressure of jamming of the pulmonary capillaries. 25 mm Hg .

CARDIOGENIC SHOCK

Cardiogenic shock develops as a result of a sharp decrease in cardiac output. As a rule, it occurs with extensive myocardial infarction against the background of multiple lesions of the coronary arteries.

CHRONIC HEART FAILURE

Chronic heart failure: a clinical syndrome that complicates the course of a number of diseases. It is characterized by the development of shortness of breath (first during physical exertion, and then at rest), peripheral edema and signs of cardiac dysfunction at rest.

ETIOLOGY AND PATHOGENESIS OF CHRONIC SYSTOLIC

HEART FAILURE

Under the influence of these reasons, the pumping function of the heart is disturbed . This leads to a decrease in cardiac output. As a result, hypoperfusion of organs and tissues develops . The greatest importance is the decrease in perfusion of the heart, kidneys, and peripheral muscles.

A decrease in blood supply to the heart and the development of its insufficiency leads to the activation of the sympathoadrenal system and increased heart rate. A decrease in kidney perfusion causes stimulation of the renin-angiotensin system. Angiotensin II causes vasoconstriction , fluid retention (edema, increase in BCC) and further increase in preload on the heart. Decreased perfusion of peripheral muscles (and, as a result, the development of hypoxia) leads to the accumulation of underoxidized metabolic products in them and, as a result, pronounced fatigue.

CHRONIC DIASTOLIC SN

Chronic diastolic heart failure is characterized by impaired relaxation and filling of the left ventricle . It is caused by myocardial hypertrophy, fibrosis, or cellular (leukocyte) infiltration. This leads to an increase in end-diastolic pressure in the left ventricle and the development of heart failure.

Etiology and pathogenesis of chronic diastolic heart failure

The occurrence of diastolic heart failure is most often caused by: - ischemic heart disease (with or without myocardial infarction), - hypertrophic cardiomyopathy, - cardiac amyloidosis, - arterial hypertension, - valvular heart defects, - diabetes mellitus, - constrictive pericarditis .

As a result of reduced compliance and impaired filling of the left ventricle, end-diastolic pressure increases in it, which causes a decrease in cardiac output. The pressure in the left atrium, the small circle of blood circulation, increases. In the future , right ventricular heart failure may occur .

PRINCIPLES OF NORMALIZATION OF HEART FUNCTION DUE TO ITS FAILURE

Treatment measures for HF are carried out comprehensively. They are aimed at stopping (reducing the degree of) the pathogenic effect of the causative factor (etiotropic therapy), breaking the links of its development (pathogenetic therapy), potentiating adaptive processes (sanogenetic therapy).

With timely initiation of therapy and its rational implementation, long-term normalization of cardiac activity and systemic hemodynamics is possible.

Topic 30. Violation of blood circulation is caused by a violation of the functions of blood vessels. General characteristics of the occurrence of hypertension. Atherosclerosis: etiology, pathogenesis.

VASCULAR FAILURE. ATHEROSCLEROSIS.

Vascular insufficiency is a pathological condition characterized by disorders of general or local blood circulation, the basis of which is the insufficiency of the

hemodynamic function of blood vessels due to violations of their tone, patency, and a decrease in the volume of blood circulating in them.

Depending on the prevalence of manifestations, vascular insufficiency is divided into systemic, the main pathogenetic link of which is a pathological decrease in systemic blood pressure, and regional, which is manifested by local disorders of blood supply to organs and tissues.

According to the rates of development and course, vascular insufficiency is divided into acute and chronic.

An obligatory manifestation of systemic acute and chronic vascular insufficiency is arterial hypotension . At the same time, acute vascular insufficiency is characterized by a rapid and pronounced drop in blood pressure - collapse, which can be progressive in nature, be a component of severe generalized hemodynamic disorders in shock, or be expressed by a short-term, but deep violation of the blood supply to organs and tissues, in which, first of all, the function of the most sensitive to ischemia of the cerebral cortex, manifested by a temporary loss of consciousness - fainting.

ETIOLOGY AND pathogenesis

Acute vascular insufficiency is one of the most common forms of the so-called urgent pathology. It occurs when:

> Severe general and craniocerebral injuries,
> Blood loss,
> Various heart diseases,
> Large burns ,
> Acute poisonings,
> Severe infectious diseases,
> Organic lesions and functional disorders of the central nervous system.,
> Hypersensitivity of carotid sinus baroreceptors,
> Adrenal insufficiency, etc.

Both acute and chronic systemic vascular insufficiency are characterized by a decrease in the volumetric rate of blood flow and the intensity of metabolism through the membranes of capillaries in all organs and tissues of the body due to a decrease in blood pressure in the arterial system and capillaries. The consequence of this is hypoxia, a lack of energy supply and disruption of metabolism in the cells of various organs, leading to a partial or complete loss of their functions. The hemodynamic basis of hypotension may be a decrease in cardiac output (CO), including due to a decrease in venous return; reduction of peripheral blood flow resistance (mainly at the precapillary level), reduction of BCC or a combination of these factors.

In case of acute vascular insufficiency, three types of collapse can be distinguished - cardiogenic , angiogenic , and hypovolemic . The latter develops as a result of an absolute decrease in BCC with blood loss (a component of the manifestation of hemorrhagic shock), plasma loss (with large burns), dehydration of the body.

Hypovolemic collapse is accompanied by compensatory reactions of the central blood circulation (reduction of brain tone and sharp hypertension of peripheral arteries), increased tone of systemic veins. However, this does not prevent

a critical decrease in venous return when the body is upright, as a result of which orthostatic fainting easily occurs. Due to a significant increase in peripheral resistance to blood flow, diastolic blood pressure decreases more slowly than systolic blood pressure, so a drop in pulse blood pressure is noted first.

At the heart of cardiogenic collapse is a sharp decrease in the pumping function of the heart with a drop in IOC. The latter is observed with sudden significant bradycardia, for example with complete transverse heart block, with paroxysmal tachycardia and paroxysmal fluttering or flickering of the atria (see. Fibrillation arrhythmia) with a very high frequency of contractions of the ventricles of the heart or with their fibrillation (so-called arrhythmogenic collapse); with a significant decrease in the contractile function of the heart in patients with acute myocardial infarction, myocarditis, as well as with cardiac tamponade.

Angiogenic collapse is most often caused by a pathological increase in the capacity of the venous bed with partial sequestration of blood in it and a decrease in its venous return to the heart (at the same time, the volume of blood in the arterial bed decreases and reactions of centralization of blood circulation develop, as in hypovolemic collapse), and in some cases (for example, with infectious -toxic collapse) its development is facilitated by acute systemic arterial hypotension, which leads to a pathological decrease in peripheral resistance to current.

The reason for the increase in the capacity of the venous bed can be both organic damage to the walls and functional hypotonia of the veins as a result of disturbances in the regulation of vascular tone: weakening of adrenergic, in particular sympathotonic , effects, predominance of vagotonia , imbalance of effects on the tone of humoral

vasoactive factors (for example, with hypocapnic fainting). Violations of nervous regulation leading to vascular insufficiency can be psychogenic (so-called simple fainting), reflex (most characteristic of hypersensitivity syndrome cardiogenic sinus); caused by intoxication of the central nervous system (in case of poisoning, infections), drug blockade of adrenergic states (in case of overdose of hypotensive agents) or related to organic damage of the sympathetic division of the central nervous system (Shy-Dreiger syndrome). Without a violation of the regulation of vascular tone, short-term functional vascular insufficiency is possible in cases where the rate of redistribution of a large mass of blood in the venous channel exceeds the rate of development of the adaptive tonic reaction of the veins (the so-called redistributive syncope). This is observed, for example, in the case of sudden expansion of the veins of the abdominal cavity due to a sharp decrease in intra-abdominal pressure during rapid puncture evacuation of fluid in ascites, standing up after a long period of squatting , when the gravitational redistribution of blood is accelerated by the mechanism of reactive hyperemia. Angiogenic collapse underlies most acute orthostatic circulatory disorders and is often accompanied by orthostatic syncope. Hypocapnia-induced narrowing of cerebral arteries (instead of their compensatory expansion when blood pressure drops) is of significant importance in the pathogenesis of fainting that develops during hyperventilation.

The above hemodynamic factors of the pathogenesis of acute vascular insufficiency, even in the case of its manifestations in the form of short-term fainting, are usually combined. So, in the development of vasovagal fainting in hypersensitivity syndrome of the carotid sinus, both vasodepressor (due to reflex asympaticotonia) and cardiodepressor (due to reflex excitation of the vagus) mechanisms of blood pressure drop are involved . However, the total BCC in short-term acute vascular insufficiency, which is manifested only by fainting, does not decrease (it is only redistributed from the arterial to the venous). Longer and more pronounced vascular insufficiency, that is, collapse as an independent form of its clinical manifestations, regardless of its primary hemodynamic nature (hemorrhagic, cardiogenic , angiogenic) and whether the collapse is accompanied by fainting or not, is characterized by the indispensable participation in its pathogenesis of hypovolemia , the origin of which is vascular insufficiency of various etiology. Thus, in the case of infectious -toxic collapse, which develops as a result of acute hypotonia of blood vessels, usually against the background of a critical decrease in body temperature (see Fever), hypovolemia is important in the mechanism of its development from the very beginning , due to the loss of fluid and salts due to profuse sweating and excessive filtration of liquid from the blood into the tissues due to the increased permeability of the capillary walls. The latter mechanism is always involved in the pathogenesis of hypovolemia in shock of any etiology, which is characterized by impaired cell membrane function, including in capillaries. At the same time, the collapse is only part of the manifestations of shock, characterized by a total disorganization of the regulation of vegetative functions at all levels. A distinctive feature of shock is deep disorders of microcirculation in all organs and tissues with a blockade of cellular respiration and a sharp disruption of cellular metabolism, for the elimination of which the restoration of blood pressure to normal values in itself is usually insufficient.

hemodynamic disturbances as in acute conditions are involved , but they are formed on the basis of a constantly active cause - a chronic disease of the heart, blood vessels or their regulation apparatus (see Arterial Hypotension). The simultaneous involvement of hypovolemia , cardio- and angiogenic factors in the pathogenesis of chronic systemic vascular insufficiency is characteristic of its development in Addison's disease .

Clinical picture and diagnosis

An objective and sufficient sign to substantiate the diagnosis of systemic vascular insufficiency is a pathological decrease in blood pressure. However, the absolute value of blood pressure due to pronounced fluctuations in the individual norm cannot be assessed as pathological without taking into account other manifestations of vascular insufficiency, especially acute, because the latter can develop at a value of blood pressure that is determined within the formal norm (for example, in people with initial arterial hypertension) and be absent at blood pressure values below 100/60 mm Hg . (In persons with so-called physiological arterial hypotension). Therefore, the diagnosis of acute vascular insufficiency is established on the basis of a set of symptoms of systemic hemodynamic insufficiency, which can form a clinical picture of fainting, collapse or shock .

Chronic systemic vascular insufficiency has its own characteristics, which depend on its etiology and pathogenesis, but a set of symptoms common to most of its etiological forms is also distinguished. These include:

> low blood pressure,

> General3 weakness and rapid fatigue during exercise, often frostbite,

> Tendency to hypothermia (if there is no current chronic infectious intoxication),

> Orthostatic fainting,

> Tachycardia (with the exception of vascular insufficiency in Addison's disease , Shay-Dreiger syndrome and other diseases accompanied by bradycardia).

> A small pulse on the radial arteries, especially when the body is in a vertical position. The pathogenetic diagnosis is specified by means of the study of the value of the cardiac output (in the conditions of the polyclinic, it can be determined by the rheocardiography method) and the average arterial pressure (by the mechanocardiography method) to calculate the total peripheral blood flow resistance, conducting orthostatic tests.

Usually, chronic vascular insufficiency is established with an already known underlying disease, but in some cases, vascular insufficiency is detected at the patient's first visit to the doctor, and its etiological diagnosis requires a targeted examination of the patient.

ATHEROSCLEROSIS

One of the most common diseases that plays the most important role in the development of other pathological processes affecting the cardiovascular system is atherosclerosis (from the Greek Athere - porridge, sclerosis - compaction).

Atherosclerosis is a disease that occurs as a result of primary alteration of the endothelium of vessels, affecting mainly arteries of the muscular and muscular-elastic type, which is based on the inflammatory process and a violation of the transport function of lipoproteins , which is manifested by imbibition of the vascular wall with lipids with further development around of these deposits of reactive changes.

Topic 31 . General characteristics of arrhythmias: etiology, classification, pathogenesis.

ARRHYTHMIAS OF THE HEART

Arrhythmia: a typical form of heart pathology, characterized by a violation of the frequency and periodicity of the generation of excitation pulses and/or the sequence of excitation of the atria and ventricles of the heart.

ETIOLOGY AND PATHOGENESIS OF ARRHYTHMIAS.

Arrhythmias are the result of a violation of the following basic properties of the heart:

- automatism,
- conductivity,

- excitability and
- their combined disorders.

IMPORTANT : contractility disorders are not (!) the cause of heart rhythm disorders. Violation of contractility is the cause of heart (myocardial) failure.

ARRHYTHMIAS DEVELOPING AS A RESULT OF AUTOMATIC DISRUPTION

The change in normal automatism is due to a violation of the functions of the sinus-atrial node, pacemakers of the second and third orders.

The emergence of pathological automatism (ectopic activity) can be observed in the atria, ventricles, bundle of His , Purkinje fibers with partial depolarization of cardiomyocytes and cells of the conducting system.

Trigger activity (early and late afterdepolarization) determines the occurrence of ectopic impulses: early afterdepolarization develops during the third phase of PD (repolarization), late after its end.

With early postdepolarization, ectopic impulses are formed in the phase of early repolarization with a slow rhythm due to an increase in the duration of PD (with a prolongation of the QT interval or a low intracellular content of potassium ions). An example can be ventricular tachycardia of the "pirouette" type (torsade de pointes) under conditions of dominance of parasympathetic influences on the heart (for example, with neuroses or hypothyroidism).

With late postdepolarization, ectopic impulses occur instead of an accelerated rhythm. Their main cause is considered to be overloading of cardiomyocytes with calcium ions as a result of excessive adrenergic effects on the heart during myocardial hypertrophy and heart failure, intoxication with cardiac glycosides, myocardial reperfusion (restoration of impaired blood flow in the heart vessels with the help of thrombolytics).

TYPES OF ARRHYTHMIAS AS A CONSEQUENCE OF DISORDER OF AUTOMATICITY OF THE HEART.

Depending on the place (topography) of the generation of the abnormal excitation pulse, nomotopic and heterotopic arrhythmias are distinguished.

NOMOTOPIC ARRHYTHMIAS.

They arise in the sinus-atrial nodes _

To nomotopy Arrhythmia includes: - sinus tachycardia, - sinus bradycardia, - sinus arrhythmia.

HETEROTOPE ARRHYTHMIAS . These are ectopic rhythms. They are formed outside the sinus-atrial node and are caused by a decrease in the automatism of the higher centers of rhythmogenesis .

Heterotopic arrhythmias include : - migration of the supraventricular pacemaker; - Atrial slow rhythm; - atrioventricular (AV, node) rhythm; - idioventricular (ventricular) rare rhythm (heterotopic heart rhythm, in which the

pacemaker is located in the myocardium of the ventricles); - idioventricular accelerated heart rhythm with a heart rate of 60-120 per 1 minute (occurs with pathological circulation of excitation through the myocardium of the ventricles); - atrioventricular dissociation: cessation of excitation from the atria to the ventricles. At the same time, the atria and ventricles contract independently of each other (complete transverse block).

PATHOGENESIS AND MANIFESTATIONS OF NOMOTOPIC ARRHYTHMIAS

SINUS TACHYCARDIA

Sinus tachycardia is characterized by an increase in the resting frequency of excitation impulses in the sinus-atrial knots (usually more than 100 per minute) with equal intervals between them.

The electrophysiological mechanism of sinus tachycardia is the acceleration of spontaneous diastolic depolarization of the plasmolemma of cells of the sinus-atrial node.

Causes of sinus tachycardia:

- Activation of the effect on the heart of the sympathoadrenal system. This situation is most often observed with: - emotional stress, - physical exertion, - neuroses, -

acute arterial hypotension (which is accompanied by activation of afferent impulse from baroreceptors); - heart failure (due to increased blood flow to the right atrium and activation of the Bainbridge reflex);

- reduction of the influence of the parasympathetic nervous system on the heart. This may be the result of damage to: - central nerve formations (subcortical nuclei , reticular formation, nuclei of the medulla oblongata), - conducting pathways, - parasympathetic ganglia and nerve trunks, - cholinergic receptors of the myocardium, which leads to a decrease in the cholinergic properties of the heart;

- direct effect on the cells of the sinus-atrial node of damaging factors of various nature (Physical, chemical, biological). The latter is often observed in myocarditis , myocardial infarction, pericarditis , mechanical trauma, cardiosclerosis.

SINUS BRADYCARDIA

Sinus bradycardia is characterized by a decrease in the resting frequency of excitation impulses by the sinus-atrial node below the norm (as a rule, up to 40-60 per minute) with the same intervals between them.

The electrophysiological mechanism of sinus bradycardia is the slowing down of the process of spontaneous diastolic depolarization of cell membranes of the sinus-atrial node

Causes of sinus bradycardia:

- Predominance of the effects of the parasympathetic nervous system on the heart. Observed in case of: - Irritation of the nuclei of the vagus nerve (in particular, as a result of increased intracranial pressure in meningitis , encephalitis, etc.) or its endings; - Increased intraventricular pressure and myocardial tone; - pressing on the eyeballs (Ashner's reflex Danyini), as well as in the area of the projection of the bifurcation of the carotid artery (Hering's reflex) and in the area of the solar plexus;

- Reduction of sympathoadrenal effects on the heart. Sinus bradycardia can develop with: - neurosis; - damage to brain structures (for example, the hypothalamus), conduction pathways, intracardiac ganglia and endings of sympathetic nerve fibers in the myocardium; - reduction of adrenoreactive properties of the heart;

- Direct damage to the cells of the sinus-atrial node. Such damaging factors can be: - mechanical trauma, - hemorrhage or heart attack in the area of the sinus-atrial node, - toxins and drugs (quinine, digitalis drugs, opiates , cholinomimetics), - individual metabolites (indirect bilirubin), bile acids.

The above-mentioned factors can cause not only the development of sinus bradycardia, but also a significant decrease in the frequency of pulse generation (less than 50 per minute) or the cessation of pulse generation by the sinus-atrial node. Such conditions are called " sinus-atrial node weakness syndrome " and " sinus-atrial node arrest" (stage III sinoatrial block), respectively.

SINUS ARRHYTHMIA

Sinus arrhythmia is a heart rhythm disorder characterized by irregular intervals between separate impulses of excitation emanating from the sinus-atrial node.

Sinus arrhythmia is manifested by a change in periods of normal rhythm with periods of tachy and bradycardia or slow recovery of sinus rhythm after an episode of tachycardia (the latter is a manifestation of the syndrome of weakness of the sinus-atrial node). Sinus arrhythmia is observed in various forms of neurosis, encephalitis, angina pectoris, poisoning, etc.

The electrophysiological mechanism of sinus arrhythmia consists in the fluctuation of the speed (increase, decrease) of the process of slow spontaneous diastolic depolarization of pacemaker cells.

THE MOST COMMON CAUSES OF SINUS ARRHYTHMIA:

- fluctuation (strengthening/weakening) of parasympathetic effects on the heart;

- Violation of the ratio of sympathoadrenal and parasympathetic effects on the myocardium;

- fluctuations in the blood content of gases (O2 and CO2), metabolites (lactate, pyruvate, bile acids), drugs (digitalis, opiates , cholinos and sympatholytics , cholinos and sympathomimetics);

- change in cholino and adrenoreactive properties of the heart;

- the action of physical factors directly on the cells of the sinus-atrial node (Trauma, hemorrhage, neoplasm, etc.).

SYNDROME OF WEAKNESS OF SINOATRIAL NODE

Syndrome of weakness of the sinus-atrial node (bradycardia-tachycardia syndrome) - the inability of the sinus-atrial node to provide a heart rhythm adequate to the level of vital activity of the body.

The electrophysiological mechanism of the development of the syndrome of weakness of the sinus-atrial node is a violation (often temporary cessation) of the process of automatic generation of excitation impulses by this node. To the greatest extent, this is associated with disorders of the phases of repolarization and spontaneous diastolic depolarization of the action potential. Under these conditions, heterotopic (ectopic) centers of rhythmic activity are formed.

The main causes of the syndrome of weakness of the sinus-atrial node:

- a disorder in the balance of sympathoadrenal and parasympathetic effects on the heart, with a predominance of the latter. This is found in patients with neurotic conditions (psychasthenia, hysteria, neurosis of obsessive states), incorrect dosage of drugs (for example, ßadrenoblockers , calcium antagonists, some antiarrhythmic drugs);
- violation of adreno and cholinergic properties of cells of the sinus atrial node. More often there is a decrease in their adreno and/or an increase in cholinoreactivity ;
- Direct damage to the heart in the area of the sinus-atrial node (Ischemia, hemorrhages, tumors, injuries, inflammatory processes).

The main ECG-manifested syndrome of weakness of the sinus-atrial node include:

- Intermittent or constant sinus bradycardia, alternating with sinus tachycardia;
- transient atrial flutter or flickering;
- Slow restoration of sinus rhythm after termination of sinus tachycardia;
- episodes of sinus-atrial node arrest.

sinus atrial node weakness syndrome :

- an increase in cardiac output during sinus tachycardia and during a similar period of sinus arrhythmia (due to an increase in heart rate) and a slight increase in systolic blood pressure;
- reduction of cardiac output in case of sinus bradycardia and in the similar period of sinus arrhythmia. At the same time, the shock output increases slightly due to the lengthening of diastole and the increase in blood filling of the heart chambers;
- decrease in blood pressure (and loss of consciousness in connection with brain ischemia at a heart rate of 35 and below).

sinus-atrial node impulses (sinus-atrial node arrest syndrome) for more than 10-20 seconds causes loss of consciousness and the development of seizures. This condition is known as Morgana Adams Stokes syndrome. The pathogenetic basis of the syndrome is brain ischemia.

The consequences of the syndrome of weakness of the sinus-atrial node are:

- A significant decrease in cardiac output;

- a drop in perfusion pressure in the coronary arteries of the heart and the development of coronary insufficiency (both with pronounced bradycardia and with prolonged significant tachycardia).

PATHOGENESIS AND MANIFESTATIONS OF HETEROTOPIC (ECTOPIC) HEART ARRHYTHMIAS

Decreased activity or cessation of activity of the sinus-atrial node of the heart as a result of its functional or organic damage creates conditions for the activation of automatic centers of the second and third orders. At the same time, the ectopic (relative to the sinus-atrial node) focus with its rarer rhythm assumes the function of a pacemaker . Such rhythm disturbances of this type are called heterotopic , passive or substitute (sinus rhythm) arrhythmias. The following are the most common

Atrial slow rhythm. An ectopic pacemaker is usually located in the left atrium. Rare (less than 70-80 min) impulses of excitement are detected on the ECG. Atrial slow rhythm will be observed in neuroses, acquired (rheumatic) or congenital heart defects and cardiomyopathies.

Atrioventricular rhythm (nodal rhythm) is observed in those cases when impulses in the sinus-atrial nodes do not arise at all or are generated with a lower frequency than in the cells of the atrioventricular (AV) node. The source of excitation pulses can be the upper, middle or lower part of the AV node. The higher the localization of the pacemaker , the more pronounced its influence and the higher the frequency of the pulses generated by it.

Variable ("floating") heart rhythm (syn.: " supraventricular pacemaker migration"). It is the result of the movement of the pacemaker from the sinus-atrial node to the lower departments (mainly to the AV node) and back. This, as a rule, occurs when the automatism of the sinus-atrial node is suppressed as a result of a transient increase in the effects of the vagus nerve . The rhythm of the heart depends on the new source of impulses and therefore becomes irregular.

Idioventricular ventricular rhythm. It develops as a substitute when suppressing the activity of first- and second-order pacemakers. Impulses are generated, as a rule, in the bundle of His of the upper part of the interventricular septum, in one of its legs or in their branches (the rhythm of the legs of the bundle of His), and less often — in the fibers of the Purkinje network . Most often liquid ventricular heterotopic rhythm is observed when the pacemaker is located in the myocardium of the ventricles.

Idioventricular accelerated (heart rate 60-120 per 1 min) heart rhythm occurs with pathological circulation of excitation through the myocardium of the ventricles. The presence of three or more ventricular complexes with a frequency of 50–100 per minute is considered an accelerated idioventricular rhythm. It usually occurs during a myocardial infarction, is asymptomatic and requires intervention.

Atrioventricular dissociation is a complete cessation of conduction of excitation from the atria to the ventricles. At the same time, the atria and ventricles contract independently of each other (complete transverse block).

Dissociation with interference. This phenomenon is included in the

simultaneous, but uncoordinated operation of two heart rhythm generators: as a rule, nomotopic - sinus and heterotopic - more often atrioventricular , less often ventricular .

" Pop-up " contractions are the appearance of separate (substitute) contractions of the heart under the influence of impulses generated by centers of second- or third-order automatism and instead a temporary decrease in the automatic function of the sinus-atrial node. A typical example of this: supraventricular extrasystoles.

ARRHYTHMIAS OF THE HEART AS A CONSEQUENCE OF VIOLATIONS IN THE CONDUCTION OF THE EXCITATION IMPULSE

Conduction is the property of the conducting pathways of the heart and cardiomyocytes to conduct an excitation impulse.

Types of disturbances in conduction of the excitation impulse

They consist in slowing down (up to blockade) or speeding up the conduction of the excitation impulse through the heart.

Slowing down and/or blocking the conduction of the excitation impulse is a consequence of functional or organic changes in the conduction system of the heart.

The reasons for slowing down and blocking the propagation of the excitation pulse with the development of arrhythmias can be:

- increasing the effects of the vagus nerve on the heart and/or its cholinergic properties. This leads to a significant slowing down of the speed of propagation of the excitation pulse along the conduction system, especially at the level of the AV node (negative dromotropic effect of acetylcholine);
- direct damage to the cells of the conducting system of the heart and cardiomyocytes by various factors of physical, chemical and biological origin. It is most often observed in myocardial infarction, myocarditis , hemorrhages in the tissue of the myocardium, in its operative (cardiosurgical) injuries, its tumors, scars in it, in intoxication with alcohol, nicotine, medications (for example, digitalis drugs, quinidine) , the effects of bacterial poisons (with diphtheria, scarlet fever, typhoid, and other infections), with a violation of the transmembrane distribution of ions (most often in conditions of hyperkalemia).

DISORDERS OF SYSTEMIC HEMODYNAMICS WHEN SLOWING AND BLOCKING THE SPREAD OF THE EXCITATION PULSE THROUGHOUT THE HEART.

Disorders of hemodynamics in the body depend on the duration of the episode of impaired conduction, the nature of the underlying disease and the level of damage to the conduction system of the heart:

- slowing or short-term blockade of the sinus atrial is accompanied by a decrease in cardiac output, blood pressure with the development of ischemia of organs and tissues. If the blockade lasts several minutes and is not accompanied by

the development of a substitute heterotopic (nodal or ventricular rhythm), this can end in cardiac asystole and death of the patient;

- slowing down of the intraatrial and intraventricular conduction of the excitation impulse by itself does not significantly change the frequency and rhythm of heart contractions, and even - systemic hemodynamics ;

- Complete AV blockade leads to pronounced bradycardia, reduced cardiac output and venous blood stagnation;

- blockade of conduction of the excitation impulse at any level of the conduction system of the heart (more often with complete AV blockade) can be complicated by the development of Morgana Adams-Stokes syndrome . Pathogenetic basis of the syndrome: a significant decrease up to the cessation of the effective work of the heart. Clinically, the syndrome is manifested by sudden loss of consciousness, absence of pulse and heart sounds. Epileptiform seizures are possible . The attack usually lasts 5-20 seconds, rarely 1-2 minutes.

DISORDER OF CORONARY BLOOD FLOW WHEN SLOWING AND BLOCKING THE CONDUCT OF THE EXCITATION IMPULSE THROUGH THE HEART.

Coronary blood flow under conditions of inhibition of the speed of propagation of excitation through the heart decreases with a significant drop in systemic blood pressure. This leads to a decrease in perfusion pressure in the coronary arteries of the heart and can lead to coronary insufficiency due to a decrease in the delivery of oxygen and metabolic substrates to the myocardium.

ACCELERATION OF CONDUCT OF EXCITATION BETWEEN ATRIA AND VENTRICLES OR SEPARATE AREAS OF THE HEART.

The reasons for the acceleration of the conduction of the excitation impulse are: - the presence of additional impulse conduction paths and/or - increased excitability of heterotopic centers of rhythmic activity.

Additional (bypassing the AV node) ways of conducting excitation.

In this case, impulses from the sinoatrial node enter the ventricles both by the main atrioventricular pathway and by additional bundles of conducting tissue. Behind them, the excitation spreads faster and reaches the ventricles earlier than the same impulse passing through the AV node.

Increased excitability of heterotopic cells.

Certain regions of the heart can become foci of heterotopic rhythmic activity under the influence of a number of factors: the impulse of excitement, which spreads through the heart system; electrical or mechanical (for example, when the myocardium is stretched by excess blood) irritation; activation of sympathoadrenal effects on the heart

Disorders of systemic hemodynamics with accelerated conduction of excitation between the atria and ventricles:

- reduction of shock and cardiac output (due to reduced filling of heart

chambers with blood in conditions of tachycardia, atrial fibrillation, atrial flutter);

- a drop in systolic and, often, diastolic blood pressure (caused by a decrease in cardiac output and total peripheral vascular resistance).

Coronary blood flow, as a rule, is reduced to a greater or lesser extent, which threatens the development of coronary insufficiency (angina, myocardial infarction).

COMBINED HEART RHYTHM DISORDERS

Combined heart rhythm disorders are caused by a combination of changes in its properties of excitability, conduction, and automaticity.

The reasons for the violation of the properties of excitability, conduction and automaticity of the heart are:

- functional disorders of the nervous system (neurosis, stress, vagotonia);

– organic lesions of the nervous system (brain tumors, skull injuries, impaired cerebral circulation);

- Damage to the myocardium (myocardial dystrophy, myocarditis , cardiosclerosis, cardiomyopathy, myocardial infarction);

- Violation of the electrolyte balance (Changes in the content of potassium, calcium, magnesium ions in the myocardium);

- Exposure to toxic substances (carbon monoxide, bacterial toxins, nicotine, alcohol, industrial toxins).

- drug intoxication (antiarrhythmic drugs, adrenomimetics , cardiac glycosides).

- Hypoxemia (with heart failure, "pulmonary heart").

Excitability: the ability of cells to receive an electrical impulse and respond to it with an excitation reaction.

The excitability of the heart muscle is manifested in the ability to generate PD. The property of heart excitability should be distinguished from automatism, which consists in the spontaneous generation of impulses.

MECHANISMS OF COMBINED ARRHYTHMIAS

Abnormal automatism This mechanism of arrhythmias is characterized by the presence of an ectopic center that generates its own rhythm, protected by the so-called input blockade: a zone of impaired conduction that prevents suppression of the ectopic focus by sinus impulses. Thus, conditions are created for the simultaneous coexistence of two sources of heart activation: - normal (sinus) and - alternative (parasystolic), which works in an autonomous mode.

Cardiocyte post-depolarization and trigger activity (generation of an excitation pulse shortly after depolarization).

Reentry and movement of the excitation pulse in the heart along a closed loop .

Violation of conduction of the excitation impulse.

Most often, several mechanisms of arrhythmogenesis are triggered at once .

TYPES OF COMBINED ARRHYTHMIAS

Rhythm disorders caused by combined changes in the properties of excitability, conduction, and automaticity include:

- Extrasystole: (sinus, atrial , atrioventricular , ventricular);
- paroxysmal tachycardia (atrial , atrioventricular , ventricular);
- fluttering and flickering of the ventricles.

EXTRASYSTOLY

Extrasystole: the most common typical form of cardiac arrhythmias. It occurs as a result of the generation of an extraordinary impulse of excitation (premature depolarization) and is manifested, as a rule, by an extraordinary contraction of the whole heart or its individual parts (atria or ventricles).

Extrasystoles are often recorded repeatedly. If three or more extrasystoles follow each other, it is called extrasystole.

The most frequent types of extrasystole:

- alorhythmia : a combination of a certain sequence of normal (timely) pulses with extraordinary ones. The most frequent forms: bigeminy - extrasystole after each (one) next pulse, trigeminy - extrasystole after two next pulses, quadrigeminy - extrasystole after three next pulses;
- Parasystole : there is a coexistence of two or more independent, simultaneously functioning foci of impulse generation that cause contraction of the whole heart or its individual parts. One of the cells determines the main rhythm of the heart. As a rule, it is the sinus-atrial node. Another focus is ectopic (parasystolic). It is usually located in the ventricles.

PAROXISMAL TACHYCARDIA

Paroxysmal tachycardia: a typical form of cardiac arrhythmias. It is characterized by an attack-like increase in the frequency of impulses of excitation above the norm of the correct rhythm, which is generated by an ectopic focus in the heart.

Paroxysm of tachycardia is said when the number of ectopic pulses exceeds 3-5, and the frequency is usually from 160 to 220 per minute (when the heterotopic focus is located in the atrium) or from 140 to 200 (when the focus is located in the ventricles).

ATRIAL AND VENTRICULAR FLUBRING

Atrial and ventricular flutter is manifested by a high frequency of excitation pulses and, as a rule, contractions of the heart, the correct rhythm (atria usually 220-350 per minute; ventricles - 150-300 per minute).

Tremor is characterized by the absence of a diastolic pause and superficial,

hemodynamically ineffective myocardial contractions

With atrial flutter, as a rule, AV block develops. In this regard, only every second to fourth atrial impulse is conducted in the ventricle, since the functional features of the AV node are such that it is usually capable of conducting no more than 200-250 impulses per minute.

ATRIUM AND VENTRICULAR FIBRILLATION

Atrial and ventricular fibrillation (fibrillation) is the irregular, erratic electrical activity of the atria and ventricles.

Fibrillation is accompanied by the cessation of the effective pumping function of the heart.

Atrial fibrillation develops at a frequency of ectopic impulses over 400-500 per minute, ventricular - over 300-500.

At such a frequency of generation of excitation pulses, myocardial cells cannot respond with a synchronous, coordinated contraction covering the entire myocardium. Individual fibers or microregions of the heart contract irregularly as they exit the refractory period.

CHANGES IN THE MYOCARDIA PRECEDING ARRHYTHMIAS

The development of paroxysmal tachycardia, flutter and fibrillation is preceded by typical metabolic disorders in the myocardium.

The most important metabolic changes in the myocardium during arrhythmias are considered to be:

- Increase in the extracellular content of potassium ions.

- decrease in pH (acidosis) in myocardial cells. The arrhythmogenic effect of an excess of H+ ions in the myocardium is very similar to that of an increase in the concentration of K+ ions in the interstitium (see above). However, the severity of these effects is less;

- Accumulation of excess cAMP in cardiomyocytes . The reasons for this are: - activation of adenylate cyclase (as a result of the influence of many factors, but mainly - catecholamines) and - suppression of the activity of phosphodiesterases that destroy cAMP . This is naturally observed in myocardial ischemia, myocarditis , cardiomyopathies. The arrhythmogenic effects of an excess of cAMP are realized due to stimulation under the influence of cAMP of a slow incoming calcium current;

- Increase in the content of UHD in the cells of the myocardium. The main reasons for the increase in the level of VHD are considered to be: - An increase in the content of catecholamines in the myocardium (they have pronounced lipolytic activity); -myocardial ischemia (it is characterized by an increase in the content of catecholamines in the myocardium and activation of lipolysis); -Increased capture of VHD by damaged cardiomyocytes (caused by alteration of cardiomyocyte membranes and increase in their permeability, including for VHD); - activation of hydrolysis of membrane phospholipids (under the influence of catecholamines ,

Ca2+ and other factors)

The arrhythmogenic effect of an excess of VHD is associated with: - disconnection of the processes of oxidation and phosphorylation in mitochondria, which leads to the potentiation of ATP deficiency and the release of K + ions into the intercellular fluid (the mechanisms of the development of arrhythmias under the influence of hyperkalemia are discussed above) and - inhibition of resynthesis . that ATP of glycolytic origin is used by cationic pumps in the formation of MP, as well as in the development of PD).

ELECTROPHYSIOLOGICAL MECHANISMS OF EXTRASYSTOLE, PAROXISMAL TACHYCARDIA, FLUTTERING, ATRIAL AND VENTRICULAR FIBRILLATION

As the leading electrophysiological mechanisms of the development of extrasystole, paroxysmal tachycardia, flutter and fibrillation of the atria and ventricles of the heart, two are distinguished:

- circulation of the excitation pulse along a closed loop (Syn.: Reversal excitation, excitation circulation, reentry);
- abnormal automatism.

Repeated circulation of the excitation impulse in the heart along a closed circuit as a mechanism of the development of its arrhythmias.

The development of reentry is possible on the basis of three electrophysiological phenomena: - its retrograde propagation, - longitudinal dissociation of the conduction and - reflection of the excitation pulse.

Retrograde conduction of the impulse. Slowing down or blocking the conduction of the excitation impulse in one direction (anterograde) is combined with the possibility of its conduction in another (retrograde). This situation usually occurs in a microarea on the periphery of the conduction system, as well as in the contact zones of Purkinje fibers with cardiomyocytes .

Longitudinal dissociation of impulse conduction . This phenomenon develops in areas with parallel course of the fibers of the conducting system and the presence of anastomoses between them . The conditions for its occurrence are the blockade of conduction of the excitation impulse in one fiber and its delayed conduction in another.

Display of the excitation pulse. It is observed in the area of cicatricial changes or significant changes in the concentration of cations in the myocardium, where the impulse changes the direction of propagation (ie. "reflected").

ABNORMAL HETEROTOPIC AUTOMATISM AS A MECHANISM OF THE DEVELOPMENT OF HEART ARRHYTHMIAS.

The development of arrhythmias is possible on the basis of the phenomenon of abnormal heterotopic automatism, in which a pacemaker with a higher frequency of generation of excitation pulses than other pacemakers is formed and works . That is why the abnormal rhythm "subordinates" to itself the rhythm of the normal pacemaker of the heart. This is observed, for example, in the conditions of short-term slowing of the normal rhythm of the pacemaker . This phenomenon is also

referred to as "replacement of activity" of the abnormal pacemaker. The formation of abnormal heterotopic automatism is also possible in "worker" cardiomyocytes , especially with their partial depolarization.

Topic 32. Pathophysiology of external breathing. Respiratory failure.

What is external respiratory failure ?

What are the main indicators of the effectiveness of external breathing ?

What are the main causes of the development of insufficiency of external breathing ?

What are the main signs of insufficiency of external breathing ?

What are the main consequences of insufficient external breathing ?

What is tachypnea ?

What is bradypnea ?

What is dyspnea ?

What are the main types of shortness of breath ?

TYPICAL FORMS OF DISORDERS EXTERNAL BREATHING SYSTEMS

Breathing is the process of gas exchange of oxygen, carbon dioxide and other gaseous substances by diffusion along their concentration gradient. The determining factor of gas exchange is the partial pressure of gases, for example, pO2 and pCO2. External and tissue ("internal") respiration are conventionally distinguished.

External breathing: two-way diffusion of gases between the air of the alveoli of the lungs and the blood of the blood capillaries of the interalveolar septa (aerogematic barrier).

Tissue respiration: two-way diffusion of gases between the blood of the capillaries and the internal environment of the cells of organs and tissues (the term "tissue respiration" has another meaning: a broader meaning is the process of using O2 in cell metabolism.

Evaluation of the body's external breathing function

To characterize the function of external breathing, indicators are used that allow us to adequately evaluate the functions of the airways (in particular, in obstructive diseases, i.e. related to restriction: a decrease in the respiratory surface).

When examining lung function, three groups of indicators are evaluated:

- lung volumes,
- volumetric exhalation rate,
- diffusion capacity of the lungs.

Lung volumes:

- static indicators of lung volumes reflect the elastic properties of the lungs and chest.

- dynamic indicators of lung volumes characterize the patency of the respiratory tract.

Volumetric rate of exhalation

The speed of the air flow depends on the indicators of the lung volumes and the force of exhalation. The air flow increases with an increase in the force of exhalation, especially at the beginning of forced exhalation (over 75% of the vital capacity of the lungs, counting from the beginning of exhalation).

The volumetric velocity is also affected by the elastic thrust of the lungs, the resistance of the small airways, and the cross-sectional area of the larger airways.

Diffusion capacity (capacity) of the lungs

Diffusion capacity, or diffusion capacity (Ds) of the lungs (more precisely, of the aerogematic membrane!) is an indicator of the efficiency of gas transfer from the air of the alveoli to the blood of the pulmonary capillary.

Spirometry and its indicators

Spirometry (spirography): measurement of the vital capacity of the lungs (LVC) and other lung volumes.

The analysis of pyrometry data allows to differentiate obstructive lung diseases from restrictive ones , to assess the severity of respiratory failure and its dynamics during treatment.

Many parameters of the spirogram are expressed in relative values (%) from the average values of physiological values (gender, age, height are taken into account). The normal range is considered to be 80-120%.

Tidal volume (DI): the volume of air entering the lungs during inhalation during calm breathing (normal 500-800 ml). The part of DO that is in gas exchange is called alveolar volume (AT); the rest - about 30% of TO - harmful volume, or anatomically dead space.

LVEF: the maximum volume of air expelled from the lungs after a maximum inhalation. Since VLDL progressively decreases in restrictive lung diseases, this indicator, in combination with diffusion capacity, helps to evaluate the dynamics of the disease and the effectiveness of treatment in patients with restrictive lung pathology.

Forced vital capacity (FVC) is similar to FVC, except that breathing is carried out with the maximum possible force and speed. Forced exhalation causes narrowing of the respiratory tract, slowing down its speed.

Forced expiratory volume in 1 s (FEV1): the volume of air expelled with maximum effort from the lungs during the first second of exhalation after a deep breath; i.e. the part of the LVEF that is exhaled in the first second. FEV1 reflects the condition of the large airways and is most often found as a percentage of LVEF (normal value of FEV1 = 75% of LVEF).

FEV1/FVOL: the ratio of FEV1 to FVOL (Tiffno index), expressed as a percentage (normally greater than or equal to 70%). The value of FEV1/FVOL, which is directly proportional to the force of exhalation, is an important detection of obstructive disorders. It also helps in the diagnosis of restrictive disorders. A decrease in only FEV1 (FEV1/FJOL <70%) indicates obstruction; a decrease in both indicators (FEV1/FVL = 70%) indicates a restrictive pathology.

Obtaining other information indicators requires the use of both spirometry and a helium dilution test (determines the volume of gas in the lungs). Such indicators include:

Total lung capacity (TLC): the volume of air contained in the lungs at the height of maximum inspiration.

Functional residual capacity (FRE): the volume of air remaining in the lungs at the end of a normal exhalation. FOE is represented by two components:

- exhalation reserve volume (ROvid): part of the FOE, which can be expelled from the lungs with maximally intensified exhalation;

- residual lung volume (RLV): the volume of air remaining in the lungs after maximum exhalation (normally 25–30% of FOE).

Relationships of lung volumes.

ОЕЛ = ХОВ + ООЛ

ООЛ = FOE - ROvid

Other indicators of lung function

Diffusion capacity (diffusion capacity, Ds) of the lungs for carbon monoxide (DsCO) reflects the state of the alveolar-capillary membrane: the aerogematic barrier. DSCO is determined by measuring the amount of carbon monoxide (CO) that has entered from the alveolar air into the blood of the pulmonary capillaries after the patient has inhaled a known amount of CO (0.1%); expressed in ml/min/mm of mercury column.

Respiratory tract (SDP): reflects the condition of the large airways, since 80-90% of the resistance to air flow occurs in them. SDP is usually determined by dynamic lung volumes and expiratory volume velocities. SDP values are increased in mild obstructive diseases and decreased in restrictive lung diseases.

Ventilation-perfusion ratio (V/Q). In general, the V/Q ratio in the lungs is 0.8 (normally, a physiological V/Q imbalance equivalent to 2% shunting of pulmonary arterial blood directly into the pulmonary venous circulation without gas exchange is allowed). Low V/Q values indicate inadequate ventilation of areas of the lung that are normally supplied with blood. As a result, there is a decrease in pO2 (hypoxemia). If there is no alveolar ventilation in the area of the lung, then V/Q = 0, i.e. there is no gas exchange. Because of the war, there is a shunting of blood from right to left, i.e. venous blood is combined with arterial blood. High values of V/Q indicate adequate ventilation of areas of the lungs that are poorly supplied with blood. The level of oxygen exchange is low , because available Hb is able to bind a limited amount of oxygen.

TYPICAL FORMS OF EXTERNAL RESPIRATORY DISORDERS

Typical forms of external breathing disorders include:

- ventilation of lung alveoli;

- perfusion of the lungs with blood;

- adequacy of ventilation and perfusion of the lungs (violation of ventilation and perfusion compliance);

- diffusion of O2 and CO2 through the alveolar-capillary (aerohematic) membrane.

VIOLATION OF VENTILATION ALVEOLI LUNGS

They cause two groups of lung ventilation disorders:

- alveolar hypoventilation ,

- Alveolar hyperventilation.

ALVEOLAR HYPOVENTILATION

Hypoventilation of alveoli with air (alveolar hypoventilation): a typical form of pathology of external breathing. With alveolar hypoventilation, the real volume of ventilation of the alveoli per unit of time is lower than that required by the organism under these conditions.

Causes of alveolar hypoventilation

There are two groups of factors that decrease the ventilation of the lung alveoli:

- Disorders of the biomechanics of external breathing;
- Violation of regulation of external breathing

Disorders of the biomechanics of external breathing. as a cause of alveolar hypoventilation .

By origin, two types of breathing biomechanics disorders are distinguished:

- mostly obstructive and
- Mostly restrictive .

Obstructive type of alveolar hypoventilation .

Obstruction of respiratory tracts and reduction of their patency is characterized by:

- by increasing the resistance of the air flow,
- a decrease in the volume of ventilation of the corresponding areas of the lungs,
- increased work of respiratory muscles,
- By increasing the energy expenditure of the external breathing apparatus.

The most common causes of alveolar hypoventilation are:

- obstruction of the lumen of the upper and/or lower respiratory tract by food and other foreign bodies (for example, when vomiting or inhaling polluted air), the tongue falling down (for example, in a coma, during sleep, anesthesia), sputum, mucus, exudate, blood (for example, with tracheitis, bronchitis, cystic fibrosis , bronchiolitis , tumor growth), neoplasms of the airways;
- muscle spasm of the bronchi and/or bronchioles (for example, during an attack of bronchial asthma). Bronchospasm , as a rule, is combined with swelling of the mucous membrane and the formation of viscous sputum;
- spasm of the muscles of the larynx (for example, when inhaling irritating substances or in neurotic states);
- compression (compression) of the respiratory tract from the outside (for example, by a tumor, enlarged lymph nodes, thyroid gland);
- dynamic compression of medium- and small- diameter bronchi during increased intrapulmonary pressure during exhalation (especially forced exhalation). This phenomenon is known as "expiratory compression of the bronchi" (syn. phenomenon of "expiratory compression", " hyperventilation of the lung", "expiratory collapse of the bronchi"). This phenomenon is observed with a strong cough, in patients with emphysema of the lungs, with forced breathing during physical exertion.

Manifestations of obstructive lung hypoventilation .

Restrictive type of alveolar hypoventilation .

Restrictive disorders of alveolar ventilation consist in reducing (restricting) the degree of lung expansion. In this connection, ventilation of the lungs decreases, the load on the respiratory muscles increases, and the energy cost of breathing increases.

Causes of restrictive disorders of alveoli of lung ventilation.

According to their origin, they are divided into two groups: - Intrapulmonary and - extrapulmonary .

The essence of the intrapulmonary (or parenchymal) causes of restriction is a decrease in the extensibility of lung tissue, as a result, for example, of their sclero- and fibrosis in pneumoconiosis , infiltrative growth of lung sarcoma or atelectasis in pneumo- or hematorax . .

Extrapulmonary causes of the restrictive type of hypoventilation of the lungs determine the limitation of the size of the respiratory excursions of the lung (for example, with exudative pleurisy , pronounced ossification of costal cartilages and/or reduced mobility of the joints of the chest in osteochondrosis, compression of the chest in the case of blockages or car accidents).

Manifestations of restrictive type of lung hypoventilation .

In restrictive disorders, ventilation naturally decreases:

- Indicators of total lung capacity,
- residual lung volume,
- XOB (This indicator directly reflects the degree of lung restriction).

Violation of external breathing regulation mechanisms as a cause of alveolar hypoventilation .

Breathing disorders often arise as a result of disturbances: - activity of the respiratory center, - its afferent and - efferent connections .

Disorders of the central regulation of external breathing.

The most common causes of centrogenic respiratory disorders are:

- injuries and neoplasms in the medulla oblongata;
- Compression of the brain (with its swelling or inflammation, hemorrhages in the substance of the brain or its ventricles);
- acute pronounced hypoxia of various genesis;
- intoxication (for example, with ethanol, narcotic drugs, endotoxins formed in uremia or liver failure);
- destructive changes in brain tissue (for example, with encephalitis, multiple sclerosis, syringomyelia , syphilis).

Manifestations of centrogenic respiratory disorders.

Clinically significant forms of centrogenic breathing regulation disorders include: - apneic breathing, - labored breathing and - periodic forms of breathing.

Apneic breathing: this is breathing with temporary stops. It is characterized by a prolonged inhalation due to convulsive contraction of the respiratory muscles and a relatively short exhalation. Apneic breathing is observed in brain bridge infarction, acute pronounced hypoxia, barbiturate poisoning.

Gasping - type breathing _ _ _ Observed in an agonal state. It is characterized

by deep convulsive short breaths, large intervals between them, lack of reactions to afferent influences (for example, painful or increased carbon dioxide content in the blood).

Periodic forms of breathing are characterized by periods of increased respiratory movements followed by their weakening and periods of apnea. They include the breath of Biot, Cheyne-Stokes , Kussmaul .

The basis of the mechanism of the development of periodic breathing is: - periodically increasing insufficiency (up to critical) of the energy supply of the neurons of the respiratory center; - due to this, as well as damage to membranes, disorder of transmembrane distribution of ions, formation of MP and PD; - The excitability of the neurons of the respiratory center, which changes periodically, and as a result, the frequency and depth of breaths .

Violation of afferent regulation of neurons of the respiratory center.

They consist in the development of states of: - either insufficient or - excessive afferent impulse to the neurons of the respiratory center.

Reasons for insufficient excitatory afferentation:

- poisoning with narcotic drugs or ethanol. Lead to the restriction of the conduction of the respiratory center of excitatory stimuli;

- low excitability of chemoreceptors, which perceive the content of oxygen and/or carbon dioxide in the blood (Observed, for example, in premature babies or with abnormalities of brain development);

- reduction of non-specific tonic activity of neurons of the reticular formation of the brain stem (inherited or acquired, for example, with an overdose of narcotic analgesics, barbiturates, tranquilizers and other neuro- and psychoactive substances).

Causes of excessive excitatory afferentation:

- Stress reactions (accompanied by the activation of stimulating impulses to the respiratory center from the receptors of vessels and bronchi);

- encephalitis;

- hemorrhage or ischemia in the medulla oblongata;

- neurotic conditions (for example, hysteria or phobias);

- excessive irritation of the night -, chemo and mechanoreceptors in case of trauma to the respiratory organs, abdominal cavity or burns of the skin and mucous membranes.

Manifestations of conditions with excessive excitatory afferentation to neurons of the respiratory center.

These conditions are characterized by: - frequent shallow breathing (tachypnea), - respiratory hypoxia, - hypercapnia , - acidosis.

Excess inhibitory afferentation.

The most frequent causes: - severe pain in the area of the chest and/or respiratory tract (for example, in case of injury, burns , pleurisy); air in acute bronchitis and/or tracheitis).

Damage to the efferent pathways of the nervous regulation of breathing.

They are the result of alteration of the effector conducting pathways to the

respiratory muscles at different levels:

- from the respiratory center to the diaphragm (for example, in case of ischemia or injury of the spinal cord, multiple sclerosis or poliomyelitis) are manifested by the loss of respiratory automatism and the transition to voluntary breathing. It becomes uneven and stops when falling asleep (" Undine's curse " syndrome);

- through the corticospinal pathways to the respiratory muscles (for example, in the case of tumors, injury or ischemia of the spinal cord, syringomyelia) leads to the loss of voluntary (conscious) breathing control and the transition to "automated" (" machine-like ", "stabilized") breathing;

- descending spinal tracts, motoneurons of the spinal cord, nerve trunks to the respiratory muscles (for example, in case of injury or ischemia of the spinal cord, poliomyelitis, botulism, neuritis; blockade of neuromuscular conduction in myasthenia or the use of curare drugs). Manifestations: decrease in the amplitude of respiratory movements and periodic apnea.

ALVEOLAR HYPERVENTILATION

Hyperventilation of the lungs (alveolar hyperventilation) is a typical form of impaired external breathing, characterized by an excess of the actual ventilation of the lungs per unit of time compared to that required by the body under these conditions.

Causes of alveolar hyperventilation

Most often, hyperventilation is caused by:

- inadequate mode of mechanical ventilation (for example, during anesthesia, transfer of the patient to artificial respiration in case of brain injury or coma; the hyperventilation that develops is called passive);

- stress reactions , neurotic states (for example, hysteria or phobias);

- organic brain damage (for example, as a result of hemorrhage, ischemia, intracranial tumors, stroke and concussion);

- hyperthermic conditions (fever, heat stroke, etc.).

- Exogenous hypoxia.

DISORDERS OF LUNG BLOOD PERFUSION

Significant violations of lung perfusion in most forms of pathology are observed with hypo and hypertension in the vessels of the small blood circulation. These states denote, respectively, as:

- pulmonary hypertension and

- Pulmonary hypotension .

Pulmonary hypertension

Pulmonary hypertension is characterized by a persistent increase in blood pressure in the small vessels.

There are three forms of pulmonary hypertension:

- precapillary ,

- postcapillary ,

- Mixed

Precapillary form of pulmonary hypertension.

It is characterized by an increase in blood pressure in the precapillaries and capillaries above the norm (more than 30 mmHg systolic and 12 mmHg diastolic).

The most common causes of precapillary pulmonary hypertension are:

- spasm of smooth muscle cells of the walls of arterioles (for example, during stress, pulmonary embolism, release of catecholamines from pheochromocytoma , during acidosis, a sharp decrease in the partial pressure of oxygen in inhaled air). Hypoxia is the strongest factor of vasoconstriction , causing the formation of mediators of vasoconstriction : catecholamines , endothelin , thromboxane A2 and others.

- obturation of lung microvessels (for example, microthrombi , emboli , hyperplastic endothelium);

- Compression of lung arterioles (for example, by a tumor, enlarged lymph nodes, increased air pressure in the alveoli and bronchi during an acute attack of coughing).

Postcapillary form of pulmonary hypertension.

This form of pulmonary hypertension is characterized by impaired outflow of blood from vessels to the left atrium and accumulation of its excess in the lungs.

The most common causes of postcapillary form of pulmonary hypertension:

- stenosis of the mitral valve opening (for example, as a result of endocarditis),

- Compression of the pulmonary veins (for example, by enlarged lymph nodes or a tumor),

- left ventricular heart failure (for example, with myocardial infarction, hypertension, myocardial dystrophy).

Mixed form of pulmonary hypertension.

It is often the result of progression and complications of pre- or post-capillary pulmonary hypertension. For example, the obstruction of blood flow from the pulmonary veins to the left atrium (characteristic of postcapillary hypertension) leads to a reflex decrease in the lumen of the pulmonary arterioles (characteristic of precapillary hypertension).

Manifestations of a mixed form of pulmonary hypertension:

- signs of left ventricular and/or right ventricular heart failure (blood stasis in venous vessels, edema, ascites, etc.);

- reduction of XOB;

- hypoxemia and hypercapnia ;

- acidosis (Respiratory, with a chronic course - mixed).

Pulmonary hypotension

Pulmonary hypotension is characterized by a steady decrease in blood pressure in the small vessels.

The most frequent causes of pulmonary hypotension :

- heart defects with shunting of blood " from left to right ". In this case, there is a "dumping" of venous blood into the arterial system (for example, with Fallot's syndrome , insufficiency of pulmonary artery valves);

- hypovolemia of various genesis (for example, with prolonged diarrhea, shock states, due to chronic blood loss);

- systemic arterial hypotension (For example, with collapse or coma).

VIOLATION OF VENTILATION AND PERFUSION COMPLIANCE

Normally, the ratio between the volume of ventilation of the lungs and the amount of their perfusion with blood is optimally related both in individual areas and in the lungs in general: blood flow is realized in those areas of the lung in which ventilation is carried out and vice versa.

This provides such a ratio of CO2 excretion by the lungs to O2 consumption that is adequate for the respiratory rate, which reflects the intensity of metabolism. These coefficients: ventilation-perfusion and respiratory are normally equal to approximately 0.8).

Violation of the combination of ventilation and perfusion of the lungs leads to the development of respiratory failure.

The quantitative relationship between ventilation (v) and perfusion (q) of the lungs is expressed by the indicator of ventilation-perfusion correspondence: v/q, which normally ranges from 0.8 to 1.0.

Causes of ventilation and perfusion imbalance

The main causes of violation of the ratio of ventilation and perfusion of the lungs, leading to either their local hypoperfusion or local hypoventilation .

Factors leading to local hypoventilation of the lungs.

These factors are described in the Alveolar hypoventilation section . They cause a regional decrease in air flow to the alveoli. At the same time, the volume of alveolar ventilation and the volume of blood circulation in some region of the lung becomes smaller than in the lungs as a whole.

Consequences of local hypoventilation of the lungs:

- Increase in functional dead space;
- decrease in oxygenation blood flowing from the hypoventilated area of the lung.

Factors leading to local hypoperfusion of the lungs.

These include influences that cause:

- obturation of the branches of the pulmonary artery (for example, by a thrombus or embolus in the case of disseminated blood clotting, fat embolism, aggregates of formed blood elements in sepsis or shock);
- Compression of the vessels of the pulmonary artery (for example, by a neoplasm, foreign body, scar tissue);
- spasm of smooth muscle cells of the wall of any branch of the pulmonary artery;
- shunting blood into the lungs - bypassing the alveoli. This happens, for example, in the presence of messages between the branches of the pulmonary artery and vein.

The mentioned changes cause:

- decrease in perfusion of one of the areas of the lung (as a result, an alveolar dead space is formed - ventilated, but not supplied with blood);
- undemanding alveolar ventilation (Normal or even increased) level of lung perfusion;

- hypoxemia in the outflow of blood from the lungs; at the same time, the tension of CO2 in the blood, as a rule, remains normal (normocapnia), since the diffusion of this gas is not reduced.

DIFFUSION OF OXYGEN AND CARBON DIOXIDE GAS THROUGH THE ALVEOLO-CAPILLARY MEMBRANE

The area of the diffusion membrane (aerogematic barrier) reaches 180-200 m2, and the thickness is 0.2-2 μm .

The transfer of oxygen and carbon dioxide is optimal with a sufficient concentration gradient of O2 and CO2 in the alveolar air and blood, adequate blood flow in the lungs, while preserving the size of the membrane area, the normal structure and physicochemical state of the aerogematic barrier.

The diffusion capacity of the lungs (DL) for oxygen and carbon dioxide is calculated as the ratio of the volume of the gas diffusion flow (V ml/min) and the difference in the partial gas pressures (P in mm Hg) on different sides of the membrane:

This value reflects the volume of gas in ml that diffuses through the alveolocapillary membrane at a pressure gradient of 1 mmHg . in 1 min. Normally, the DL for oxygen is about 15, and for CO2 about 300 (the latter indicates that the possibility of disordered diffusion of oxygen is very high, and that of carbon dioxide is low).

Reasons for the decrease in diffusivity

They are caused by an increase in:

- Alveolar-capillary membrane thicknesses and/or
- Its density.

An increase in the thickness of the aerogematic membrane is the result of:

- an increase in the amount of liquid on the surface of the alveolar epithelium (for example, due to mucus or exudate in allergic alveolitis or pneumonia);
- edema of the interstitium (accumulation of fluid between the basal membranes of the endothelium and epithelium);
- an increase in the thickness of the cells of the endothelium of the capillaries and the epithelium of the alveoli (For example, as a result of their hypertrophy or hyperplasia, the development of sarcoidosis).

An increase in membrane density develops as a result of:

- Its calcifications (for example, interstitial structures);
- increase in the viscosity of the gel of the interstitial space
- increase in the number of collagen, reticulin and elastic fibers in the interalveolar walls.

Examples of pathological conditions characterized by a decrease in the diffusion capacity of the aerogenous membrane:

- pneumonia (especially with chronic current diffuse interstitial pneumonia);
- Pneumoconiosis . They develop when inhaling dust containing silica (silicosis), asbestos (asbestosis), beryllium (beryliosis);
- fibrosing alveolitis (diffuse or focal);

- Allergic alveolitis (for example, with hay fever);
- heart failure.

Topic 33. Hypoxia: classification, etiology, pathogenesis.

HYPOXIA. RESPIRATORY FAILURE.

Respiratory insufficiency: a typical form of pathology of the external respiratory system, in which this system does not provide the level of gas exchange necessary for optimal implementation of body functions and plastic processes in it.

Respiratory (pulmonary) failure is revealed by the development of hypoxemia and, as a rule, hypercapnia (but not always).

Causes of respiratory failure.

They are divided into two groups:

- Caused by lung pathology;
- caused by extrapulmonary forms of pathology (Fig. 24-8).

Pulmonary (intrapulmonary) causes of respiratory failure.

These include all variants of disorders (partial and mixed) of the gas exchange function of the lungs:

- their air ventilation,
- perfusion with their blood,
- ventilation-perfusion ratios,
- diffusion of gases through the alveolar-capillary membrane.

EXTRA-PULMONARY CAUSES OF RESPIRATORY FAILURE.

Most often, this is a violation:

- mechanisms of neurogenic regulation of external breathing (for example, in case of injuries, strokes, brain tumors);
- implementation of efferent regulatory influences in neuromuscular synapses of intercostal muscles and diaphragm (for example, in poliomyelitis, myasthenia gravis , polyneuritis);
- functions of the respiratory muscles (for example, with myalgias and myodystrophies of the intercostal muscles);
- respiratory excursions of the chest (for example, with injuries to the ribs or spine, ankylosis of the rib joints);
- blood circulation in the lungs (for example, with heart failure or anemia).

Forms of respiratory failure.

There are three main forms of respiratory failure:

- hypoxemic (parenchymal, type I);
- hypercapnic (hypoventilation , type II);
- Mixed.

Hypoxemic (parenchymal, type I) form of respiratory failure.

It is characterized by a decrease in the partial tension of oxygen in the arterial blood (hypoxemia).

The main causes of the parenchymal form of respiratory failure: - Violation of gas diffusion through the alveolocapillary membrane (the most frequent factor);

- Pulmonary perfusion disorders;
- Violation of ventilation-perfusion ratios;
- Exogenous hypoxia (hypo and normobaric).

The hypoxemic form of respiratory failure is found in severe lesions of the lung parenchyma: this is what determines its name (for example, in cases of generalized infection, fluid aspiration, bronchitis and bronchiolitis , inhalation of toxic gases, pulmonary edema, shock).

Hypercapnic (hypoventilation type II) form of respiratory failure.

It is characterized by hypoxemia and hypercapnia .

The main causes of the hypoventilation form of respiratory failure:

- alveolar hypoventilation ;
- Violation of entilation-erfusion ratios (due to insufficient ventilation of the alveoli).

The hypercapnic form of pulmonary insufficiency is observed in bronchitis, bronchopneumonia, bronchial asthma, and bronchial tumors.

Mixed form of respiratory failure.

hypercapnia and hypoxemia naturally develop .

The main causes of mixed respiratory failure are acute and chronic lung diseases leading to obstructive hypoventilation (for example, bronchitis, bronchial asthma, obstructive emphysema, bronchiectasis , pneumonia, and lung abscesses).

RESPIRATORY DISTRESS SYNDROME.

Respiratory distress syndrome of adults ("wet lung"): a typical form of pathology of the external respiratory system, characterized by acute respiratory failure, mainly hypoxemic type.

The name of the syndrome reflects a certain similarity of clinical, morphological and functional changes with respiratory distress syndrome of newborns. However, the main causes of the latter (in contrast to the distress syndrome of adults) are a violation of the synthesis of surfactant and its release on the surface of alveolocytes , as well as excessive compliance of the chest.

Pathogenesis of respiratory distress syndrome

The end result of any variant of the development of the distress syndrome is hypoxemia .

Manifestations of respiratory distress syndrome

Distress syndrome develops, as a rule, after 20-40 hours. after the action of the causative factor and is characterized by a progressive course.

The following manifestations are most characteristic:

- tachypnea (shortness of breath);
- Increase of MOD;
- reduction of lung volumes (total lung capacity, residual lung volume, LVEF, functional residual lung capacity);
- hypoxemia , acute respiratory alkalosis;
- increase in cardiac output (in the terminal stage of the syndrome - decrease).

3. Formation of professional skills, skills related to topics that are part of the content module (mastery of communication skills, clinical examination, determination of treatment scheme, conducting laboratory research, etc.) mastery of skills:

Topic 29.

1. The patient, 65 years old, complains of general weakness, palpitations and shortness of breath during moderate physical exertion, occasionally dizziness. In the evening, he notes swelling of the lower extremities. Heart rate - 80 per minute, AT - 140/70 mm Hg . Heart tones are muffled. On the ECG, there are signs of myocardial ischemia and dystrophy. A decrease in stroke volume was detected during the ultrasound examination . It was concluded that the woman had heart failure.

1. Give the definition of "heart failure".
2. Give the classification of heart failure by pathogenesis.
3. Name the main pathogenetic principles of heart failure treatment.

2. A 28-year-old man complains of shortness of breath, rapid fatigue while walking. Considers himself sick from birth, when congenital insufficiency of aortic valves was established. Physically developed satisfactorily, the skin is pale, weak cyanosis of the lips. The left border of the heart is enlarged. Heart rate - 78 bpm , blood pressure - 110/80 mm Hg .

1. What type of heart failure is the patient's pathogenesis ?
2. What mechanism of intracardiac adaptation is activated in this type of heart failure?
3. Reveal the mechanisms of intracardial adaptation.

Topic 30.

1. A 27-year-old man complains of shortness of breath, rapid fatigue while walking. He considers himself sick after suffering from rheumatism, when insufficiency of the mitral valves was established.

1. What is the type of heart failure according to the pathogenesis of the patient?
2. What mechanism of intracardiac adaptation is activated in this type of heart failure?
3. Name the indicators of hemodynamics in heart failure.

2. A girl, 18 years old, complains of shortness of breath, rapid fatigue during physical exertion. She considers herself sick since birth, when congenital stenosis of the aortic orifice was established.

1. What is the type of heart failure according to the pathogenesis of the patient?

2. Reveal the mechanism of intracardiac adaptation that works in this type of heart failure?

3. A 35-year-old woman complains of shortness of breath, rapid fatigue while walking. An ultrasound of the heart revealed stenosis of the mitral orifice. Physically developed satisfactorily, the skin is pale, weak cyanosis of the lips. The left border of the heart is enlarged. Heart rate - 78 bpm , blood pressure - 110/80 mm Hg . Art.

1. What is the type of heart failure according to the pathogenesis of the patient?

2. What mechanism of intracardiac adaptation is activated in this type of heart failure?

Topic 31.

A 17-year-old girl periodically has palpitations that last several minutes. At the same time, the pulse rate reaches 200 in 1 minute. The pulse is rhythmic. What heart rhythm disorder occurred ? What is its mechanism?

Answer standard: The girl developed paroxysmal tachycardia - a group of extrasystoles that repeat many times and completely suppress the normal physiological rhythm. This type of arrhythmia belongs to disorders of automatism, and is associated with the occurrence of out-of-order excitement and premature contractions of the heart.

Topic 32.

1. A patient, 62 years old, in serious condition, was admitted to the neurology department due to cerebral hemorrhage. An increase in the depth and frequency of breathing is observed, and then it decreases to apnea, after which the cycle of respiratory movements resumes.

What type of breathing did the patient have?

Answer standard: In the patient, *Cheyne -Stokes breathing , because it is characterized by an increase in the amplitude of breathing to pronounced hyperpnea , and then a decrease in apnea, after which a cycle of respiratory movements begins again, which also ends in apnea.*

2. A patient with diphtheria develops swelling of the larynx. What type of respiratory failure can occur and why? What type of breathing is observed in the patient? Explain the mechanism of development of dyspnoea in this condition?

3. The child was diagnosed with bilateral pneumonia. Specify the possible mechanisms that can lead to insufficient external respiration.

Topic 33.

1. The patient had an attack of bronchial asthma. What type of breathing is observed in this case and why? What are the mechanisms underlying the patient's respiratory failure? What is the likely pathogenesis of shortness of breath?

2. Emphysema of the lungs was detected in a cement factory worker. What is the mechanism of disease development in this case? What changes in lung volumes

and capacities are characteristic of this disease.

Topic 34.

4. Summary : testing

PRACTICAL TRAINING

Content module 6.

Pathophysiology of digestion, liver, kidneys.

Practical lesson No. 35
Topic. Digestive disorders in the gastrointestinal tract.
Ulcer disease.
Practical lesson No. 36
Topic. Pathophysiology of the intestine. Pancreatitis.
Practical lesson No. 37
Topic. Pathophysiology of the liver. Liver failure.
Practical lesson No. 38
Topic. Pathophysiology of the liver. Komi, Zhovtyanitsy.
Practical lesson No. 39
Topic. Pathophysiology of kidneys. Violations of the main functions of the kidneys.
Practical lesson No. 40
Topic. Kidney failure. Nephrotic syndrome.
Practical lesson No. 41
Topic. Pathophysiology of digestion. Current control of knowledge.

Purpose: Acquisition by the student of higher education of knowledge and formation of elements of professional competences in the field of medicine from the pathophysiology division:

Topic 35. Indigestion in the gastrointestinal tract. Ulcer disease.
Topic 36. Pathophysiology of the intestine. Pancreatitis.
Topic 37. Pathophysiology of the liver. Liver failure.
Topic 38. Pathophysiology of the liver. Comas . Jaundice
Topic 39. Pathophysiology of kidneys. Violations of the main functions of the kidneys.
Topic 40. Kidney failure. Nephrotic syndrome.
Topic 41. Verification of assimilation of acquired knowledge and skills by applicants.

Improvement of skills and competences acquired during the study of previous disciplines.

Basic concepts:

Topic 35. Indigestion in the gastrointestinal tract. Ulcer disease.

Topic 36. Pathophysiology of the intestine. Pancreatitis.

Topic 37. Pathophysiology of the liver. Liver failure.

Topic 38. Pathophysiology of the liver. Comas . Jaundice

Topic 39. Pathophysiology of kidneys. Violations of the main functions of the kidneys.

Topic 40. Kidney failure. Nephrotic syndrome.

Topic 41. Verification of assimilation of acquired knowledge and skills by applicants.

Equipment: Multimedia presentations, tables.

Plan:

11. **Organizational activities (greetings, verification of those present, announcement of the topic, purpose of the lesson, motivation of higher education seekers to study the topic).**

12. **Control of the reference level of knowledge:**

Topic 35. Indigestion in the gastrointestinal tract. Ulcer disease.

Enzymes that break down proteins, fats and carbohydrates. The role of bile and pancreatic juice in digestion.

Causes and consequences of body- and hypersecretion of saliva.

Periodontitis, caries. Basic theories of etiology and pathogenesis.

Consequences of removal of different parts of the stomach (experiments by U.S. London.)

Disorders of the secretory and motor function of the stomach .

Ulcer disease and pancreatitis

The average human body consists of water - 60-65%, proteins - 15-20%, fats - 19%, salts - 5.8%, carbohydrates - 0.6%. All these substances must be constantly replenished. Unlike plants, animals (including humans) do not create nutrients themselves, but obtain them from the environment. To do this, they consume food, process it and extract nutrients necessary for their vital activity, which enter the blood and are absorbed from it by cells.

Digestive insufficiency is a discrepancy between the ability of the digestive system to digest and absorb nutrients with the volume and/or composition of the incoming food. Digestive insufficiency accompanies a wide range of diseases of the gastrointestinal tract, and can also occur in a healthy person as a result of an unbalanced diet or too much food eaten, and therefore it is very common in the daily practice of a gastroenterologist. The consequence of indigestion is insufficiency of digestion. Currently, the main pathophysiological mechanisms of indigestion can be classified as follows: cavity digestion disorders, parietal digestion disorders, mixed form of indigestion syndrome.

Causes of insufficiency of cavitary digestion

• Diseases of the pancreas, both hereditary and acquired (chronic pancreatitis, condition after pancreatectomy , pancreatic cancer, cystic fibrosis).

• Secretory insufficiency of the stomach (atrophic gastritis, post-gastrectomy syndrome).

• Deficiency of bile acids or asynchrony of the flow of bile into the small intestine in case of biliary obstruction, hepatitis, cirrhosis , CKD, after cholecystectomy .

• Inactivation of digestive enzymes in gastroduodenitis , peptic ulcer disease, dysbacteriosis of the small intestine.

• Violation of transit of intestinal contents and mixing of enzymes with chyme in duodenal and gastrostasis , irritable bowel syndrome. Causes of parietal digestive disorders

Disturbances of parietal digestion are associated with impaired function of parietal digestive enzymes (for example, lactase deficiency). Disturbances of parietal digestion develop as a result of disaccharidase deficiency (congenital and acquired lactase deficiency); dystrophic changes or death of enterocytes (gluten enteropathy , sarcoidosis , Crohn's disease, excessive bacterial growth). With insufficiency of digestion, a large amount of undigested remains in the intestinal cavity nutrients , which leads to a violation of the composition of the internal environment of the intestines, including changes - 5 pH , osmotic pressure, chemical composition. These changes lead, on the one hand, to secondary damage to the intestinal mucosa and even greater disruption of digestive processes, and on the other hand, to a change in the composition of the intestinal microflora, which exacerbates existing disorders. In the clinic, digestive insufficiency, manifested by a number of rather characteristic syndromes and laboratory changes, is designated as "dyspepsia" or " **dyspeptic syndrome".**

The manifestations of dyspeptic syndrome traditionally include: heartburn, nausea and vomiting, belching, unpleasant sensations (discomfort or pain) in the epigastric region, flatulence, and bowel disorders. Symptoms of dyspepsia can be observed both together and separately and accompany almost any disease of the gastrointestinal tract. At the same time, each of them has a different origin and different mechanisms of occurrence, and also requires completely different approaches to treatment, which makes it impractical to combine all symptoms so widely with a single term. Clinical manifestations of indigestion are found in 25–41% of the population. Insufficiency of digestion can occur even without obvious clinical manifestations and consist in the weakening of the participation of any organ of the digestive system in the digestion process, which is compensated by the activity of other organs of the digestive system. This is due to the fact that its various departments are functionally a single system. This unity is due to the commonality of neuro-humoral regulation. E. S. London showed that a dog's life is possible even after the (staged) removal of its stomach , the entire ileum and most of the small intestine, as well as almost the entire colon. In addition, this unity is especially manifested in pathological conditions, when a violation of the functions of some

links of the system entails a violation of the functions of others: superior - inferior and vice versa. Insufficiency of digestion can be a consequence of the influence of external alimentary factors (quantitatively or qualitatively unbalanced nutrition), violations of the mechanisms of regulation of water and food intake (disorders of the feeling of hunger and thirst), violations of the central nervous, endocrine, local neurohumoral -hormonal mechanisms that control the functions of the digestive organs system, various combinations of these factors. Most often, insufficiency of digestion occurs with diseases of the organs of the digestive system.

Indigestion in the stomach

At the heart of digestive disorders in the stomach are partial, and more often combined disorders of the secretory, motor, absorptive, barrier and protective functions of the stomach . In general, secretion disorders cause a discrepancy between the dynamics and/or level of secretion of various components of gastric juice with the current real needs for them. 6 Types of gastric secretion disorders Normally, the amount of gastric juice is 2–2.5 liters per day. Disorders of gastric secretion include hypersecretion, hyposecretion and achillea. Hypersecretion - an increase in the amount of gastric juice, an increase in its acidity (hyperchlorhydria) and digestive abilities.

The main causes of hypersecretion

• Increase in the mass of secretory cells of the stomach (genetically determined).

• Activation of the effects of the vagus nerve (BN) (for example, in neurotic conditions or constitutional vagotonia): acetylcholine stimulates all types of secretion in the stomach, duodenum, pancreas, as well as gastric motility and intestinal peristalsis.

• Increasing the synthesis and/or effects of gastrin (stimulates the secretion of mucus, bicarbonate, enzymes, hydrochloric acid in the stomach, inhibits evacuation from the stomach , stimulates intestinal peristalsis and insulin secretion, stimulates the proliferation of cells in the mucous membrane).

• Hypertrophy and/or hyperplasia of enterochromaffin (enteroendocrine) cells (for example, with hypertrophic gastritis).

• Overstretching antral part of the stomach (pylorostenosis , pylorospasm).

• Action of some drugs (for example, acetylsalicylic acid or corticosteroids, insulin).

• Smoking, drinking alcohol.

• Rough, spicy, hot (irritating) food. Possible consequences of hypersecretion: slowing down of the evacuation of food mass from the stomach , erosion and ulceration of the mucous membrane of the stomach , indigestion in the intestines. Hyposecretion is a decrease in the volume of gastric juice, a decrease in its acidity and splitting efficiency. The main causes of hyposecretion

• Decrease in the mass of secretory cells (for example, with hypo- and atrophic forms of chronic gastritis or disintegration of a stomach tumor).

• Reduction of the effects of BN (for example, with neuroses or constitutional

sympathicotonia).

• Reduction of gastrin formation .

• Deficiency of proteins and vitamins in the body.

• Dehydration.

• Action of drugs that reduce or eliminate the effects of BN (for example, cholinergic blockers or cholinesterase activators).

It is also possible to develop an anacid state, or achlorhydria , when there is no free hydrochloric acid in the gastric juice. In the case when not only free hydrochloric acid, but also enzymes are not found in the gastric juice, we speak of achilia (absence of gastric secretion). 7 Achillia can be functional (caused by inhibition of secretion) and organic (associated with atrophy or replacement of the mucous membrane - anadenia). They are distinguished using a histamine test. This is important, because it depends on the tactics of treatment (stimulation of secretion or replacement of gastric juice components). Achillia is characteristic for late stages of chronic hypoacidic (atrophic) gastritis, stomach cancer , pernicious anemia. Possible consequences of hyposecretion: digestive disorders in the stomach and intestines, appearance of motor disorders (nausea, vomiting), violation of the antiseptic properties of gastric juice, development of fermentation and putrefaction processes, violation of the optimal amount of mucus in the stomach, alkalosis. Types of impaired motor function Violation of the tone of the muscular membrane of the stomach : excessive increase (hypertonus), excessive decrease (hypotonus) and atony - lack of muscle tone. Changes in muscle tone lead to disturbances of the peristalsis - covering food masses with the stomach wall and forming a portion of food for intragastric digestion, as well as its evacuation into the duodenum (DPK). Disorders of the activity of the muscular sphincters of the stomach in the form of a decrease (up to their atony; causes long-term opening - "gaping" of the cardiac and/or pyloric sphincters) and increased tone and spasm of the sphincter muscles (leading to cardiospasm and/or pyloric spasm). Violation of gastric peristalsis in the form of its acceleration (hyperkinesis) and slowing (hypokinesis). Evacuation disorders. Combined and/or separate disorders of tone and peristalsis of the stomach wall lead to either acceleration or slowing down of the evacuation of food from the stomach .

Causes of impaired motor function

Violation of the nervous regulation of the motor function of the stomach : increasing the influence of the BN stimulates its motor function, and activation of the effects of the sympathetic nervous system suppresses it. Disorders of humoral regulation of the stomach . For example, a high concentration of hydrochloric acid in the stomach cavity , as well as secretin, cholecystokinin inhibits the motility of the stomach . On the contrary, gastrin , motilin , reduced content of hydrochloric acid in the stomach stimulate motility. Pathological processes in the stomach (erosions, ulcers, scars, tumors can weaken or strengthen its motility depending on their localization or severity of the process). Consequences of impaired motor function As a result of impaired motility of the stomach , the development of early satiety syndrome, heartburn, nausea, vomiting and dumping syndrome is possible. 8

Absorption disorders in the stomach Normally, water, alcohol, and electrolytes are absorbed in the stomach. In case of accidental or deliberate intake, toxic agents can be absorbed. In the case of destructive changes in the stomach wall (including when the barrier function is impaired), it is possible for protein to enter the internal environment of the body, which threatens the development of immunopathological processes: allergic reactions and states of immune autoaggression .

Violation of the barrier and protective function of the stomach

The mucous-bicarbonate barrier protects the mucous membrane from acid, pepsin and other potential damaging agents. Components of the stomach barrier (mucus is constantly secreted on the surface of the epithelium). • Bicarbonate (HCO_3^- ions). It is secreted by superficial mucous cells, providing a neutralizing effect. • pH . The mucus layer has a pH gradient . On the surface of the mucus layer, the pH is 2.0, and in the pre-membrane part it is more than 7.0. • H^+ . . The permeability of the plasmolemma of mucous cells of the stomach for H^+ is different. It is insignificant in the membrane facing the lumen of the organ (apical), and quite high in the basal part. In case of mechanical damage to the mucous membrane, when it is exposed to oxidation products, alcohol, weak acids or bile, the concentration of H^+ in the cells increases, which leads to their death and destruction of the barrier. • Dense contacts. Formed between the surface cells of the epithelium. When their integrity is violated, the barrier function is violated.

Regulation of the stomach barrier .

The secretion of bicarbonate and mucus is enhanced by glucagon , prostaglandin E, gastrin , and epidermal growth factor (EGF). Antisecretory agents (for example, histamine receptor blockers), Pg , gastrin , sugar analogs (for example, sucralfate) are used to prevent damage and restore the barrier . Under adverse conditions, the barrier breaks down within a few minutes, epithelial cells die, swelling and hemorrhages occur in the own layer of the mucous membrane. Factors adverse to maintaining the barrier. NSAIDs (aspirin, indomethacin), ethanol, salts of bile acids. • Helicobacter pylori is a gram-negative bacterium that survives in the acidic environment of the stomach . N. pylori infects the surface epithelium of the stomach and destroys the barrier, contributing to the development of gastritis and ulcerative defects of the stomach wall . This microorganism is isolated in 70% of patients with gastric ulcer and 90% of patients with gastric ulcer or antral gastritis. A decrease in acidity in the stomach creates favorable conditions for the life and reproduction of many microbes, such as cholera vibrio, Shigella , and amoeba. Thus, patients with gastric achilles are more likely to suffer from infectious diseases (transmitted through the oral -fecal route), are exposed to intoxication, and have a higher risk of developing stomach neoplasms .

Topic 36. Pathophysiology of the intestine. Pancreatitis.

Indigestion in the intestines

Digestive disorders in the intestine are caused by a violation of its main

functions: digestive , absorptive, motor and barrier protective . 1. Disorders of the digestive function of the intestines The main causes of disorders of the digestive function of the intestines: • disorders of the exocrine function of the pancreas (P); • violation of bile secretion in the small intestine; • violation of the secretion of mucus and bicarbonate into the lumen of the small intestine by the own (Brunner's) glands of the wall of the small intestine and mucus by numerous goblet cells of the villi and crypts of the intestine. 2. Disorders of intestinal absorptive function The main causes of intestinal absorptive function disorders: • insufficient cavity and membrane digestion; • acceleration of the evacuation of intestinal contents (for example, with diarrhea); • atrophy of the villi of the intestinal mucosa; • excess content of exudate on the surface of the mucous membrane (for example, with acute intestinal infections, chronic enteritis); • resection of a large fragment of the small intestine (for example, with tumor damage and/or necrosis); • disorders of blood and lymph circulation in the intestinal wall; • disorders of intestinal absorption are a significant component of the pathogenesis of malabsorption syndrome .

Violation of the motor function of the intestines.

There are various forms of intestinal motility disorders. Extreme variants of violations are diarrhea and constipation.

Ulcer disease

The terms "ulcer", "ulcer disease", "peptic ulcer disease" are used in relation to a group of diseases of the gastrointestinal tract characterized by the formation of areas of destruction of the mucous membrane of the organs of the gastrointestinal tract. Ulcers are more often found in the stomach and the proximal part of the gastrointestinal tract, sometimes in the distal part of the esophagus and rarely in the small intestine (usually combined with Meckel's diverticulum containing fragments of the mucous membrane of the gastric type). Zollinger - Ellison syndrome can also be considered as a type of HV. Damage to the protective barrier of the mucous membrane of the stomach , as well as dysregulation of the acid-forming , acid-neutralizing , evacuation functions of the stomach and gastrointestinal tract, genetic, bacterial and other factors are of primary importance in the ulcer process. Etiology of ulcer disease

The main role in the development of HC is played by Helicobacter pylori . Among other causes of the disease, there are nutritional errors (violation of the regime and 10 nature of nutrition: long-term use of rough food, dry food, long breaks between meals, etc.), neuropsychological (stress) factor, increased secretion of gastric juice and decreased activity protective factors (mucoproteins , bicarbonates), the presence of harmful habits (smoking, alcohol abuse), hereditary factors, etc. HC is the result of the action of many mutually potentiating etiological factors. Pathogenesis of HC The pathogenesis of HC is based on a violation of the dynamic balance between the factors of aggression and protection of the gastric mucosa : the predominant role is played by a decrease in the effectiveness of protective factors, and in the development of peptic ulcers, the activation of aggression factors. As a result, proteolytic tissue destruction by gastric juice and the formation of an ulcer

defect are observed. There are three phases of ulcer formation: neurovascular dystrophy; necrobiosis in the submucosal basis and ulcerative destruction of the mucous membrane as a result of proteolysis. General manifestations of ulcer disease. Pain syndrome.

Dyspeptic syndrome. Asthenovegetative syndrome.

Seasonality of the disease (spring and autumn), period of remission and exacerbation. Complications of peptic ulcer disease Penetration – penetration of the ulcer into nearby neighboring organs. If the ulcer, which has eaten away the walls, does not meet an organ on its way and opens directly into the abdominal cavity, then such a condition will not be called penetration , but perforation. Perforation of an ulcer is a breakthrough of the wall of the organ in which the ulcer is located. Gatekeeper's stenosis. *Malabsorption syndrome*

Malabsorption syndrome (" malabsorption " literally means "bad absorption)" is a complex of disorders that develop as a result of disturbances in the processes of food digestion and absorption of its components. The syndrome of impaired intestinal absorption is nonspecific; it develops with many hereditary and acquired diseases, not only of the intestines, but also of other organs and systems of the body. Currently, the term " malabsorption syndrome " unites more than 70 diseases and syndromes.

Topic 37.

Pathophysiology of the liver. Liver failure.

Violation of the bile-forming and bile-secreting function of the liver.

Etiology and pathogenesis of jaundice - mechanical, hemolytic, parenchymal. Cholemic and aholic syndromes.

Dyscholia .

Violation of carbohydrate metabolism in case of liver pathology. Hereditary glycogenoses .

Violation of fat metabolism in liver diseases. Pathogenesis of fatty infiltration of the liver.

Violation of protein metabolism in case of liver pathology.

Violation of the metabolism of vitamins, hormones and biologically active substances and in case of liver failure.

Violation of the protective function of the liver. Etiology and pathogenesis of hepatic coma.

Glycogenoses .

Liver failure

Liver pathology can be manifested both in the form of independent diseases and liver syndromes (jaundice, cholestasis , cholemia , portal hypertension, etc.), highlighting the clinic of concomitant diseases of other organs and systems, in connection with which primary and secondary liver lesions are distinguished.

Etiology

All liver lesions are divided into hereditary and acquired. Damage to the liver can be caused by: physical factors - ionizing radiation, mechanical trauma; chemical agents that have a toxic (hepatotropic) effect. They can be of exogenous origin (alcohol, industrial poisons - carbon tetrachloride , organophosphorus compounds, chloroform, arsenic; drugs - PASK-sodium, sulfonamides, cytostatics, some antibiotics; plant poisons - aflatoxin , muscarine, heliotrope alkaloids), so and endogenous (tissue decay products during burns , necrosis ; toxicosis of pregnant women); infectious agents - viruses (viral hepatitis, infectious mononucleosis), causative agents of tuberculosis, syphilis, protozoa (giardia, amoeba), fungi (actinomycetes), helminths (echinococcus, roundworms); nutritional factors – protein, vitamin starvation, very fatty food; allergic reactions to the introduction of vaccines, serums, food products and medicines; violation of blood circulation in the liver of a local (ischemia, venous hyperemia, thrombosis, embolism) and general (insufficiency of blood circulation) nature; endocrine and metabolic disorders in the body (diabetes, hyperthyroidism, obesity); tumors (hepatocellular cancer) and their metastases in the liver (cancer of the stomach , lungs, mammary gland, leukemic proliferations); genetic defects of metabolism (hereditary enzyme diseases), congenital malformations of the liver.

Pathogenesis

Two types of pathological reactions are defined:

1. Direct damage to the liver by an etiological factor.

2. Autoimmune damage due to the appearance of autoantigens (pathologically altered components of hepatocytes) and the development of humoral and cellular autoallergic reactions, which deepen liver damage as a result of microcirculatory disturbances (action of biologically active substances) and immune cytolysis with the participation of T- killers .

Damage to the liver is often combined with a violation of the organs of the digestive system, spleen, kidneys, which is caused by their anatomical and functional connections and is manifested by the development of a number of **syndromes (hepatolienal , hepatorenal)** .

Pathological processes such as inflammation, disorders of peripheral blood circulation, metabolism, tumors are most often the basis of various liver diseases. Inflammatory lesions are called **hepatitis** , the primary change in the metabolism of hepatocytes with the development of dystrophy is hepatosis and metabolic diseases of the liver (fatty hepatosis or fatty liver dystrophy; glycogenosis), and diffuse growth of connective tissue against the background of dystrophy, necrosis of the parenchyma and restructuring of the liver structure is cirrhosis. It should be noted a certain interrelationship of pathological processes in the liver: hepatitis and hepatosis usually end with the development of cirrhosis.

Cirrhosis of the liver is a chronic, progressive disease characterized by 12 growth of connective tissue, pathological regeneration of liver tissue and restructuring of the organ structure , which is manifested by signs of liver failure. Cirrhosis is the result of irreversible damage to a large number of liver cells.

Depending on the reasons that caused such damage, three pathogenetic variants of liver cirrhosis are distinguished:

- post-necrotic : manifested by signs of hepatocellular liver failure;
- biliary : accompanied by cholestatic liver failure;
- portal: is the structural basis of hepatovascular insufficiency of the liver.

Topic 38.
Pathophysiology of the liver. Komi, Zhovtyanitsy.
Jaundice

Jaundice (lat. Icterus - yellow) is a syndrome caused by an increase in the level of bilirubin in the blood, manifested by a yellow color of the skin and mucous membranes.

There are three types of jaundice:

1. Hemolytic (suprahepatic). It occurs as a result of hemolysis of erythrocytes and increased formation of bilirubin in the cells of the mononuclear phagocyte system.

2. Parenchymatous (hepatic). Its development is associated with liver damage.

3. Mechanical (obturation or subhepatic).

It occurs as a result of a violation of the outflow of bile through the biliary tract. Jaundice appears with bilirubinemia over 35 μmol /l. The skin is most strongly colored (pigments are deposited in the Malpighian layer), mucous membranes, the inner wall of blood vessels (bilirubinophilic tissues), parenchymal organs are less, and the cornea, cartilage, muscles, and peritoneum are less. Brain tissue and cerebrospinal fluid are almost not stained, as the blood-brain barrier is impassable for bile pigments.

Jaundice can be accompanied by the accumulation of bile acids in the blood along with other components of bile (cholemia).

Cholemic syndrome (cholestasis syndrome) is caused by the entry of bile components (bile acids, direct bilirubin, cholesterol) into the blood due to impaired bile formation and outflow.

Aholic is a syndrome caused by the absence of bile in the intestines due to violations of its formation and outflow. Violations of the hemodynamic functions of the liver are manifested by the development of portal hypertension syndrome. Portal hypertension syndrome Hemodynamics in the liver depends, first of all, on the pressure gradient in the arterial, portal and hepatic vena cava systems. Normally, the pressure in the own hepatic artery is about 120 mm Hg . art., 13 in the portal vein - 5–10 mm Hg . century, in the hepatic veins and inferior vena cava - 2–5 mm Hg . Art. The difference in blood pressure is so pronounced that it ensures liver perfusion. The average linear velocity of blood flow in the portal vein is about 15 cm/s. In some types of portal hypertension syndrome, it is significantly reduced. With a significant increase in pressure in the portal vein and its tributaries, expansion of the portocaval occurs anastomoses , which to some extent determines the clinical picture of the disease.

Portal hypertension is a syndrome characterized by a number of specific manifestations and occurs in some congenital and acquired diseases of internal organs that lead to impaired blood flow from the portal vein and its branches. Changes affecting both the physical and chemical properties and the cellular composition of blood often develop with liver damage. As a result of violations of the protein-synthesizing function of the liver, hypoproteinemia develops , blood oncotic pressure decreases (hypoonkia), the ratio of albumins and globulins (albumin- globulin ratio) decreases, which is manifested by an increase in ESR. Changes in the cellular composition of blood include anemia, leukopenia, and thrombocytopenia . The development of anemia can be associated with various pathogenetic mechanisms: a violation of erythropoiesis (decreased deposition of cyanocobalamin, folic acid, iron in the liver), hemolysis of erythrocytes (hypersplenism , detergent effects of bile acids in cholemic syndrome), blood loss (hemorrhagic syndrome). Leukopenia and thrombocytopenia , as well as anemia, can be due to the deficiency of some substances necessary for hematopoiesis (cyanocobalamin, folic acid) and the destruction of formed blood elements by macrophages during hypersplenism . Liver damage is often accompanied by hemorrhagic diathesis - *coagulopathy* . At the basis of their development are violations of synthesis in the liver of prothrombin, factors V, VII, IX, X, fibrinogen; Violation of absorption of vitamin K in hypo - and acholia. Disorders of vascular and platelet hemostasis are added to thrombocytopenia .

Gallstone disease

It is characterized by the formation of stones in the gallbladder and bile ducts. They can be of infectious -inflammatory (cholesterol-pigment -salt) and non-inflammatory origin (disorders of metabolism - cholesterol and pigment, biliary stasis - bilirubin -calcium). Consequences: pain attacks with irradiation in the right shoulder and shoulder blade; development of mechanical jaundice; traumatization leads to the spread of infection through the bile ducts, its transfer to the liver, damage to hepatocytes and hepatic jaundice.

Topic 39. Pathophysiology of kidneys. Violations of the main functions of the kidneys.

Define acute renal failure

Name the classification of acute renal failure

Tell the main links of the pathogenesis of ARF

Define chronic renal failure

What stages of chronic kidney failure do you know?

Renal syndromes. Etiology and pathogenesis. Signs. Characteristic

Kidneys are the main organ for excretion of metabolic products, regulation of osmotic pressure, acid-base balance and water-electrolyte balance. The main function of the kidneys is excretory.

Kidneys play an important role in all metabolic processes and maintenance of energy balance. In the kidneys, the processes of gluconeogenesis and glucogenesis

take place intensively . During fasting, half of all blood glucose is provided by renal gluconeogenesis .

The kidneys take part in the regulation of lipid metabolism, with chronic renal failure, hyperlipoproteinuria develops . Biomembrane components of a lipid nature (phospholipids) are synthesized in the kidneys , TAG is formed, and the active form of vitamin D is formed.

Important metabolic processes of amino acid conversion, the initial stage of creatine biosynthesis from argin and glycine are carried out in the kidneys.

In the kidneys, the processes of utilization of intermediate acidic metabolites (oxy- and ketoacids) into glucose take place, the vasoactive hormone renin is synthesized, insulin, THG, glucagon , prolactin are destroyed , 45% of exogenous insulin is destroyed in the kidneys.

Kidneys play an important role in maintaining the homeostasis of the human body, they are characterized by a high intensity of metabolism, the water content in the kidneys is about 83%.

An important feature of metabolic processes in the kidneys is the high activity of oxidative processes and related phosphorylation . Kidneys make up 0.5% of the body weight, and absorb 10% of the oxygen used by the body. The intensity of exchange is due to increased blood circulation.

Filtration-reabsorption processes take place in the kidneys , as the necessary energy material (carbohydrates, lipids and oxygen) is delivered by blood, which ensures the possibility of effective functioning of the kidneys. Oxygen consumption and the intensity of tissue respiration are maximum in the cortical layer.

Energy for the work of the kidneys is mainly provided by the oxidation of carbohydrates and lipids. Oxidation processes of acetoacetic acid - an important intermediate product of lipid metabolism - are actively taking place in the kidneys.

Acute renal failure (**ANN** , *Insuficiencia renalis acuta)* is an acute, usually reversible impairment of kidney function, primarily oligo- , anuria that develops over several days, rarely weeks, and causes azotemia.

Classification of acute renal failure

Prerenal ARF - occurs as a result of impaired general blood circulation: in heart failure (blood circulation and glomerular filtration rate in the kidneys are sharply reduced), vascular diseases that provide renal blood circulation, in bleeding due to a decrease in BCC and/or a drop in vascular tone.

Renal ARF - develops as a result of primary damage to the renal parenchyma: rapidly progressing forms of glomerulonephritis , damage to tubular cells (acute tubular necrosis) by toxins or ischemia, blockage of the lumen of the nephron by a precipitate of crystals or protein, acute interstitial nephritis caused by infection or a reaction to drugs, diseases of the renal arterioles.

Postrenal ARF is caused by obstruction of the urinary tract anywhere along its length (stone, tumor, blood clots, etc.). Pathogenesis consists in deep disorders of the body's homeostasis. Metabolic products accumulate: urea, uric acid, creatinine,

indican, phenol, various compounds of sulfur, phosphorus, and magnesium. Acidosis develops. The function of the cardiovascular, nervous, and digestive systems is disturbed.

Clinic

ARF increases rapidly and is manifested by a severe general condition, vomiting, clouded consciousness, impaired breathing and heart activity. Oliguria occurs , in severe cases - anuria.

There are four stages of ANN.

- 1 *The initial* stage, lasting 6-7 days, is characterized by symptoms of the underlying disease.
- 2 *The oligoanuric* stage (up to full anuria) is manifested by uremic intoxication, water-electrolyte disturbances, urinary syndrome (proteinuria, cylinduria, erythrocyturia). The stage ends with the recovery or death of the patient. its duration is from 7-11 days to 4 weeks or more. Patients are inhibited, sleepy, they may develop coma, sometimes psychosis, dry or purulent pericarditis, hydrothorax , ascites, the liver is often enlarged. The content of creatinine, urea, uric acid and other nitrogen compounds increases rapidly , hyperkalemia , hypocalcemia , and hypermagnesemia increase . metabolic acidosis, increased ESR, proteinuria (up to 3.5 g/l and more), erythrocyturia , leukocyturia . Bacteriuria is often detected .
- 3 *Stage of polyuria* (beginning of recovery) - sudden or gradual increase in diuresis (3-5 liters of urine is released per day, sometimes more, with a low relative density). Proteinuria and cylindruria decrease, leukocyturia and bacteriuria may last longer.
- 4 *Stage of recovery.* It begins from the moment of normalization of diuresis and lasts from 3 to 12 months until the normalization of tubular reabsorption and concentration function of the kidneys.

Chronic kidney failure

Topic 40 .

Kidney failure. Nephrotic syndrome.

Chronic kidney failure (**CKD** , *Insuficienia renalis chronica)* is a syndrome that develops as a result of any chronic pathology of the kidneys, characterized by a decrease in the number of nephrons, a violation of the excretory and secretory functions of the kidneys, which lose the ability to maintain the normal composition of the body's internal environment.

The combination of all clinical and laboratory signs that develop in CKD characterizes uremia. CKD is the final phase of progressive kidney damage in a wide variety of pathological conditions.

Etiology

The most frequently recognized causes of chronic renal failure are: 1) diseases with damage to the glomeruli - glomerulonephritis ; 2) damage to renal vessels: renal artery stenosis, arterial hypertension (hypertensive disease, malignant hypertension); 3) diseases with primary tubule damage and kidney interstitium - chronic pyelonephritis, interstitial nephritis; 4) diseases of the urinary system: urolithiasis, hydronephrosis, tumors of the renal system; 5) systemic diseases of

connective tissue; b) metabolic diseases: diabetes, amyloidosis, gout, calcium metabolism disorders; 7) congenital diseases of the kidneys: polycystosis , hypoplasia of the kidneys.

Pathogenesis

Despite various causative factors, morphological changes in the kidneys are of the same type, characterized by the development of sclerotic processes, desolation of the affected glomeruli with the loss of morphological features of the primary pathological process and hypertrophy of functioning nephrons. Such nephrons are structurally and functionally defective, the degree of enhancement of their functions is insufficient. The significance of the decrease in the mass of functioning nephrons in CKD is manifested by the inability of the kidneys to maintain normal homeostasis.

With CKD, products of protein metabolism - nitrogenous wastes (creatinine, urea, uric acid, etc.) are retained in the body. The water-electrolyte balance is disturbed. In the early stages of CKD, the concentration function of the kidneys changes. Nephrons that remained functioning under conditions of increased osmotic load must excrete much more soluble substances per minute than under normal conditions. To do this, they need to increase the volume of excreted urine - polyuria develops (more than 2.5 liters of urine per day), the daily rhythm of urine excretion changes (nocturia), iso- and/or hyposthenuria occurs (relative density of urine 1010-1012). At the terminal stage of chronic renal failure, the volume of urine decreases sharply, oliguria and anuria develop. With increasing CKD, the kidneys lose their ability to store sodium - mineral depletion occurs. However, some patients have a tendency to delay it. Hypokalemia is characteristic of the early polyuric stage of CKD .

The acid-alkaline balance is disturbed, acidosis develops, which is facilitated by the marked loss of bicarbonates in the urine (as a result of impaired reabsorption in conditions of decreased activity of the carbonic anhydrase enzyme), as well as a decrease in the secretion of hydrogen ions and organic acids by tubules.

Phosphorus -calcium exchange changes – hypocalcemia develops due to decreased absorption of calcium in the intestines, as well as hyperphosphatemia .

of erythropoietin by the kidneys is disturbed , which leads to the development of anemia.

Renin production persists, which leads to the development of hypertension. In some patients, sodium and fluid retention are also links to the pathogenesis of a high level of AT.

3. Formation of professional skills, skills related to topics that are part of the content module (mastery of communication skills, clinical examination, determination of treatment scheme, conducting laboratory research, etc.) mastery of skills:

Topic 35.

The patient complains of flatulence, weight loss. During a microscopic

examination of feces, many drops of neutral fat and muscle fibers and a radical decrease in the number of enzymes in the duodenal contents were found ; increased amount of diastase in urine.

1. What form of violation is present in this case?

Answer standard: Chronic pancreatitis, this is evidenced by an increase in amylase in the urine and the presence of neutral fat in the feces - steatorrhea , which indicates a lack of pancreatic lipase. Presence of muscle fibers (absence of digestive proteases)

2. What is the mechanism of these violations?

Answer standard: The mechanism of these disorders is due to a decrease in the synthesis of pancreatic enzymes or difficulties outflow of pancreatic secretion. A lack of proteases leads to a violation of protein digestion, and a lack of lipase and phospholipids - fat digestion. This leads to disturbances in the processes of digestion in the intestine, a decrease in peristalsis and an increase in the processes of putrefaction and fermentation, flatulence, which leads to weight loss and weight loss.

Topic 36.

1. What factors play a leading role in the pathogenesis of ascites in portal hypertension?

1)
2)
3)
4)

2. What can explain the development of gynecomastia , testicular atrophy, and decreased sexual function in men with liver cirrhosis?

Q. Hepatic coma is characterized by an increase in aldosterone in the blood due to a violation of its metabolism in the liver, which is accompanied by by increasing excretion from the body……., with increased transition to cells of hydrogen and sodium ions, the development of intracellular……and extracellular……

Topic 37.

1. A farmer, 24 years old, suffered from angina. After 2 weeks in the morning, he noticed swelling under the eyes, t 37.7C, weakness, aching pains in the lower back. General analysis of urine: specific gravity - 1026, protein - 1.66 g/l, erythrocytes - 25-30 in p/z, cylinders: granular - 2-3 in p/z, hyaline 4-5 in p/z, daily diuresis - 0.5 l. Previous diagnosis?

A. Acute glomerulonephritis with isolated urinary syndrome;

B. Acute glomerulonephritis , nephrotic syndrome;
B. Chronic glomerulonephritis , period of exacerbation;
D. Acute pyelonephritis;
D. Chronic pyelonephritis, period of exacerbation.

Topic 38 .

1. A 60-year-old patient complains of headache, dry mouth, and thirst. Objectively: pulse 86 bpm, blood pressure 140/80 mm Hg . Art. S- m weakly positive case. Blood creatinine - 468 mmol/l. An . urine: specific gravity 1008, protein - 0.198 g/l, leukocytes - 30 in p/z, leached erythrocytes - 6-8 in p/z. The most likely preliminary diagnosis?

A. Chronic pyelonephritis, CKD III stage ;
B. Chronic pyelonephritis, CKD II stage ;
B. Chronic glomerulonephritis , CKD II stage ;
G. Chronic glomerulonephritis , CKD I stage ;
D. Renal amyloidosis, CKD III stage.

Topic 39.

from insulin-dependent diabetes mellitus for 20 years . Receives 80 units of insulin. Increasing proteinuria has been noted for the last 2 years. The patient is exhausted. The skin is dry with a coating of urea. Blood creatinine 1200 μmol /l.

A. Acute renal failure;
B. Chronic kidney failure due to diabetic nephropathy;
B. Chronic pyelonephritis;
G. Chronic glomerulonephritis ;
D. Hypoglycemic coma.

Topic 40.

1. A 61-year-old patient has severe leg swelling, ascites, and shortness of breath. He has been suffering from chronic glomerulonephritis for about 10 years. Objectively: there are wet rales in the lungs, the abdomen is enlarged due to free fluid in the abdominal cavity. Pronounced edema, when pressed, they are dense. Diuresis 1.5 l. What syndrome does this patient have?

A. Nephrotic ;
B. Tubulopathy ;
V. Ostronephriticheskiy ;
H. Sechovyi;
D. Chronic kidney failure.

2. Patient M., 37 years old, complains of a dull pain in the lower back on the left, which periodically worsens, an increase in body temperature to 38.7 0C,

frequent urination. He has been sick for about 4 years, the disease occurred after hypothermia. Objectively: pulse 80 per minute, rhythmic, blood pressure 160/100 mm Hg . Art. Pain is noted during palpation of both kidneys, more on the left, there is also a positive symptom of tingling . There are no swellings. In urine: specific gravity 1012, protein 0.99 g/l, 12-14 leukocytes in the field of vision, 2-3 erythrocytes in the field of vision. ESR 22 mm/h. Your diagnosis?

A. Chronic pyelonephritis;
B. Chronic glomerulonephritis ;
B. Acute pyelonephritis;
G. Renal colic;
D. Chronic cystitis.

ANSWERS
A, B, B, A, A

4. Summary : testing

PRACTICAL TRAINING

Content module 7.

Pathophysiology of regulatory systems (endocrine, nervous).

Practical lesson No. 42

Topic: General etiology and pathogenesis of endocrine disorders. Pathophysiology of the pituitary gland and adrenal glands. Pathophysiology of the thyroid and parathyroid glands.

Practical lesson No. 43

Topic. Disruption of the endocrine function of the pancreas. Diabetes mellitus: etiology, pathogenesis, types.

Practical lesson No. 44

Topic. Pathophysiology of the nervous system. General signs and pathogenesis of disorders. Pathophysiology of higher nervous activity . Current control of knowledge.

Practical lesson No. 45

Topic. Pathophysiology of motor disorders. Etiology, pathogenesis. Pathophysiology of sensitivity.

Practical lesson No. 46

Topic. Pain. Etiology and pathogenesis.

Practical lesson No. 47

Topic. Pathophysiology of the endocrine and nervous systems. Current control of knowledge.

Practical lesson No. 48

Topic. Final test control

Purpose: Acquisition by the student of higher education of knowledge and

formation of elements of professional competences in the field of medicine from the pathophysiology division:

Topic 42. General etiology and pathogenesis of endocrine disorders. Pathophysiology of the pituitary gland and adrenal glands. Pathophysiology of the thyroid and parathyroid glands.
Topic 43. Disorders of the endocrine function of the pancreas.
Topic 44. Pathophysiology of the nervous system.
Topic 45. General signs and pathogenesis of disorders of the nervous system.
Topic 46. Pathophysiology of higher nervous activity.
Topic 47. Pathophysiology of pain.
Topic 48. Final test control

Improvement of skills and competences acquired during the study of previous disciplines.

Basic concepts:

Topic 42. General etiology and pathogenesis of endocrine disorders. Pathophysiology of the pituitary gland and adrenal glands. Pathophysiology of the thyroid and parathyroid glands.
Topic 43. Disorders of the endocrine function of the pancreas. Diabetes mellitus: etiology, pathogenesis, types.
Topic 44. Pathophysiology of the nervous system.
Topic 45. General signs and pathogenesis of disorders of the nervous system.
Topic 46. Pathophysiology of higher nervous activity.
Topic 47. Pathophysiology of pain.
Topic 48. Final test control

Equipment: Multimedia presentations, tables.

Plan:

13. **Organizational activities (greetings, verification of those present, announcement of the topic, purpose of the lesson, motivation of higher education seekers to study the topic).**
14. **Control of the reference level of knowledge:**

Topic 42.

General etiology and pathogenesis of endocrine disorders. Pathophysiology of the pituitary gland and adrenal glands. Pathophysiology of the thyroid and parathyroid glands.

1. Pathophysiology of the endocrine system (hypothalamus, pituitary gland, adrenal glands). Pathology of the hypothalamic-pituitary system. The causes and mechanisms of the development of syndromes of excess and lack of pituitary hormones. General characteristics of hypothalamic-pituitary-thyroid , hypothalamic-pituitary-adrenal , hypothalamic-pituitary-gonadal system disorders. Etiology, pathogenesis, clinical manifestations of panhypopituitarism . Causes, mechanisms, clinical manifestations of partial insufficiency of adenohypophysis hormones (STH, TSH, ACTH, gonadotropins). Etiology, pathogenesis, clinical manifestations of partial hyperfunction of the adenohypophysis . Pathophysiology of the neurohypophysis . Diabetes insipidus: causes and mechanisms of development, clinical manifestations.

2. Pathology of the adrenal glands. Insufficiency of the adrenal cortex: types, etiology, pathogenesis, clinical manifestations. Hyperfunction of the adrenal cortex: types, etiology, pathogenesis, clinical manifestations. Itsenko-Cushing syndromes , Conn . Types, causes, mechanisms of development, clinical manifestations of disorders of the medulla of the adrenal glands.

3. Pathophysiology of the endocrine system (thyroid, parathyroid glands). Pathology of the thyroid gland. Hypothyroidism: causes and mechanisms of development, pathogenesis of the main disorders in the body. Hyperthyroidism: causes and mechanisms of development, pathogenesis of the main disorders in the body.

4. Dysfunction of the parathyroid glands: types, causes, mechanisms of development, manifestations.

5. Definition of diabetes; epidemiology of diabetes in Ukraine and in the world, prevalence in different age groups; - risk factors for the development of diabetes; mechanism of violation of carbohydrate, protein and lipid metabolism in diabetes; etiology and pathogenesis of diabetes mellitus types 1 and 2; clinical picture of diabetes, diabetes symptoms of different types of diabetes; features of damage in diabetes of the cardiovascular, hepatobiliary systems, urinary excretion and the development of osteoarthropathies ; diagnostic value of determination of glycosylated hemoglobin, fructosamines , C-peptide, glucosuria, ketonuria .

In recent years, the frequency and prevalence of diseases of the endocrine system (including the thyroid and parathyroid glands) has increased significantly. This is connected, on the one hand, with the sharp deterioration of the ecological situation in Ukraine, and on the other hand, with the consequences of the accident at the Chernobyl gas station. We are talking about a possible mutation spillover into the gene pool of the entire population of Ukraine, and not just the 30-kilometer zone around Chernobyl, as a number of domestic and foreign scientists claimed a few years ago. Of all the factors that affect the thyroid gland, radioactive iodine-131 is in the first place. It can accumulate in it and cause its disruption.

Hypofunction of the thyroid gland . Hyperthyroidism is reproduced in animals by complete or partial removal of the gland, its destruction with the help of radioactive iodine, which selectively accumulates in the parenchyma of the gland, as well as by the introduction of thermostatic drugs that prevent the synthesis and

release of thyroid hormones (metnlthiouracil , mercazolil , betazin , potassium perchlorate). The condition that occurs after thyroidectomy is called thyroid-induced cachexia. The consequences of thyroidectomy are more severe the earlier the operation is performed. In young dogs, rats, rabbits and other animals, sharp growth retardation , sexual underdevelopment, disorder of all types of metabolism, and trophic disorders are observed. As a result of the decrease in the level of oxidative processes, the basic metabolism decreases by 25-40%, the body temperature decreases, there is a tendency to hyperglycemia and an increase in glucose tolerance. Due to a decrease in the breakdown of cholesterol and its utilization in tissues, the concentration of cholesterol in the blood increases by 2-3 times. Against this background, the effect of atherogenic factors increases. The results of radiological studies indicate inhibition of the incorporation of labeled amino acids into proteins. Retention of water in tissues is observed.

Thyroidectomized animals are sedentary. Disorders of the functions of the higher departments of the central nervous system are manifested *in* the absence of the formation of conditioned reflexes, the predominance of inhibition processes, and differentiation disorders. Etiological factors in the development of hyperthyroidism in humans are congenital defects in the biosynthesis of thyroid hormones; congenital hypoplasia or aplasia of the thyroid gland; autoimmune and infectious inflammatory processes in the gland; removal of a large amount of glandular epithelium during surgical intervention; damage to the gland by thermostatic drugs, radioactive iodine as a result of exceeding permissible therapeutic doses, as well as under the influence of ionizing radiation, etc. Most often, the cause of hyperthyroidism is insufficient intake of iodine and, possibly, cobalt. In the case of severe thyroid insufficiency (if the disease occurred in early childhood or is congenital), cretinism develops, in adults - myxedema (hyperthyroidism, which is accompanied by mucous swelling of the skin).

Disorders of mental activity, trophic, water-mineral, protein and lipid metabolism, growth and sexual development, thermoregulation and other body functions characteristic of hyperthyroidism reach an extreme degree in cretinism. A decrease in metabolism, obesity, inactivity , and a decrease in body temperature are typical for myxedema. As a result of increased hydration of the skin and subcutaneous tissue and excessive accumulation of hydrophilic mucous substances in them, the patient's face becomes puffy, with poor facial expressions, thickened nose and lips. Brittle nails, hair loss and other trophic disorders are observed. Sexual function gradually fades, intelligence decreases, memory deteriorates, apathy, drowsiness appear, and in the late period of the disease - dementia.

Enlargement of the thyroid gland with iodine deficiency is known as endemic goiter. This disease is common in the Alps, Carpathians, Himalayas, Andes and other mountainous regions of the globe, where the soil and water contain little iodine. Iodine deficiency causes a decrease in the synthesis of thyroxine and triiodothyronine , as a result of which the production of thyrotropin slows down in the pituitary gland . This, in turn, causes hyperplasia of the thyroid gland, the mass of which sometimes reaches several kilograms.

The etiological role of iodine deficiency in the development of endemic goiter is confirmed by such an experiment. If a dog is fed with water that does not contain iodine during the first year and a half of its life, the mass of the thyroid gland reaches 100 g with a norm of 1 g. The most convincing evidence is the successful prevention of endemic goiter with iodine in the foci of its spread. As the experience of many endocrinologists shows, adding sodium or potassium iodide to drinking water or table salt prevents the development of diseases.

Thyroid hyperfunction glands

An increase in the production of thyroid hormones (hyperthyroidism), a weakening of the strength of the connection between thyroxine and thyroxine-binding globulin, a violation of the metabolism of thyroid hormones, or an increase in the sensitivity of target tissues to their action lead to the development of thyrotoxicosis. Its most common manifestation is diffuse toxic goiter (Based's disease, Graves' disease).

Diffuse toxic goiter is characterized by a typical symptom complex: enlargement of the thyroid gland, exophthalmos, increased basal metabolism, increased heat production, tachycardia, tremors, increased mental excitability. No and many other pathological phenomena are caused by the toxic effect of thyroxine and triiodothyronine , which are produced in excess.

The most important etiological factor of thyrotoxicosis in humans is mental trauma. Developmental diseases are promoted by infection, hypothermia, as well as physiological fluctuations in the functional activity of the gland associated with the menstrual cycle. The notion of hyperproduction of thyrotropin as the leading pathogenetic link of diffuse toxic goiter are currently under review. The main importance is given to the violation of immune processes and the increase in sensitivity of adrenoceptorin lol catecholamines . In the blood of patients there is a long - acting stimulator of the thyroid gland (English Long acting thyroid stimulator - LATS) — an immunoglobulin of the IgO type (see the "Allergy" section). The pathogenic role of prostaglandins of the thyroid gland in disorders of its function has been proven. In the pathogenesis of thyrotoxicosis and its complications, antibodies circulating in the blood against brain tissue proteins, thyroglobulin , thyrotropin receptors , microsomal and other antigens are also important. Exophthalmos is caused by an exophthalmic factor, which has a pituitary origin and is similar in a number of features to thyrotropin . These factors act even after surgical treatment of patients and can cause hypogyrsotoxicity eiscephaloophthalmopathy or hypertension. The main manifestations of thyrotoxicosis were studied in animals that were administered thyroid hormone preparations or added dried thyroid gland to food. At the same time, n dogs observed loss of body weight, increased activity of the heart and lungs, increased basic metabolism, body temperature, trophic disorders, diarrhea, vomiting. The sensitivity to hypoxia increased, the excitability of all links of the reflex bladder increased, motor activity increased. The leading mechanism of the toxic effect of an excess of thyroxine and hrnhyudthyronine is an increase in the permeability of the mitochondrial membrane. Violation of the functional integration of mitochondria leads to the disconnection of oxidative

phosphorylation , as a result of which energy accumulation in macroergic phosphate bonds of adenosine triphosphoric acid and other compounds decreases . The free energy of oxidation is released in the form of heat. A negative nitrogen balance in thyrotoxicosis indicates the predominance of protein catabolism. As a result of increased breakdown of glycogen in the liver and muscle tissue, hyperglycemia is observed. The utilization of glucose by tissues is accelerated, the activity of hexokinase is increased.

An excess of thyroid hormones inhibits the transition of carbohydrates into fats, accelerates the breakdown of cholesterol and its utilization in tissues, intensifies the oxidation of fats in the liver, and also increases the sensitivity of adipose tissue to the lipolytic effect of adrenaline. As a result of the listed changes, the mobilization of fat from the depot increased, which explains the weight loss of patients with thyrotoxicosis, hypocholesterolemia , and hypoxarctonemia .

Thyroid hormones disrupt the metabolism of the heart muscle. Dystrophic changes in the myocardium, violations of cardiac - ventricular conduction, overload of the left ventricle are revealed. The peroxidation of lipids in the membranes of cardiomyocytes , energy and plastic support of cardiac activity is disturbed . A " thyrotoxic " heart responds inadequately to cholinergic and adrenergic influences.

Violation of calcitonin secretion . Some consequences of thyroidectomy are obviously caused by the loss of secretion of the protein hormone of the thyroid gland - calcitonin . The formation of calcitonin is also disturbed in hypofunction of the thyroid gland caused by gnreostatic substances and hyperthyroidism of endogenous and exogenous origin, sometimes excessive secretion of calcitonin is associated with tumors, then they originate from interfollicular C-cells of the thyroid gland, in which this hormone is synthesized.

Very little is known about the violation of calcitonin secretion in humans. Perhaps the origin of false hypoparathyroidism is associated with its increase — a disease in which, despite the normal functioning of the prostate glands, hypocalcism and other disorders of phosphorus -calcium metabolism are observed.

DISORDERS OF THE FUNCTIONS OF THE THYROID GLANDS

Hypofunction of parathyroid glands. Loss of function of the parathyroid glands leads to the development of parathyroiditis Tegania . In the experiment, it is reproduced by removing glands from dogs and cats. One or two days after the operation, the guards become lethargic, refuse to eat, have thirst, a decrease in body temperature, and shortness of breath. As a result of a decrease in the concentration of calcium in the blood (from 2.25-2.99 to 1-1.25 mmol/l), the ratio of monovalent (La $^{+}$, K) and divalent (Ca $^{?}$+, M£ ^{2}') ions changes . The consequence of this is a sharp increase in neuromuscular excitability. Muscle stiffness appears, gait is disturbed. At the same time, multiple fibrillar contractions of the muscles of the whole body are observed, which are then joined by clonic attacks convulsions _ Clonic convulsions turn into tonic convulsions, opisthotonus develops (a sharp

bending of the body with the head thrown back). Convulsive contractions can also spread to internal organs (pilorospasm , laryngospasm). During one of these attacks, the animal dies. Against the background of hyiocalcism, the content of inorganic phosphorus in the blood increases. Violations of mineral metabolism are due to inhibition of bone tissue resorption, absorption of calcium in the intestines, and increased phosphate reabsorption in nephron tubules. In the pathogenesis of paratnreopryvnoy tetany, certain importance is attached to the violation of the detoxification function of the liver. Feeding meat from dogs with parathyroid glands removed increases tetany due to insufficient elimination of products of nitrogenous metabolism, in particular, weakening of the ability of the liver to convert ammonia into urea. In the case of additional parathyroid glands (in rabbits , rats) or preservation of a piece of the parathyroid gland during surgery, the animals develop chronic hypoparathyroidism , the clinical picture of which is known as parathreonopreptive cachexia. It is characterized by weight loss, anorexia, increased neuromuscular excitability, dyspepsia and various trophic disorders.

Hypoparathyroidism in humans develops most often as a result of accidental damage or removal of the parathyroid glands during surgery on the thyroid gland. Relative hypofunction of the glands is observed during intensive growth, pregnancy, lactation and other conditions characterized by an increased need for calcium salts in the body.

Pathogenesis and clinical picture of hypoparathyroidism : in humans, they are close to those observed in the experiment. An increase in neuromuscular excitability is determined by the appearance of muscle contractions during stimulation of the motor nerves with a galvanic current of a certain strength, when the hand is pressed above the elbow or lightly tapped on the skin at the exit of the facial nerve in front of the external auditory canal. Children in the first or second year of life, usually in combination with rickets, often experience spasmophilia — periodic muscle spasms that occur when the ambient temperature rises and other adverse effects occur. Especially dangerous is laryngospasm , which can cause asphyxiation and death.

Hyperfunction of parathyroid glands. As a result of the increased secretion of paragnrin, the formation and activity of osteoclasts , which carry out bone resorption, increases, and their differentiation into osteoblasts, which take part in new formation of bone tissue, is inhibited. At the same time, the absorption of calcium in the intestines increases, the reabsorption of phosphates in the tubules of the nephrons decreases , the formation of soluble calcium salts in bone tissue and insoluble calcium phosphate in various organs, including the kidneys, increases. Hyperparathyroidism in experimental animals is reproduced by the introduction of an extract of the parathyroid glands of animals or purified parathyroid under the influence of large doses of the hormone, the level of calcium in the blood reaches 4.99 mmol/l, the concentration of peorianic phosphorus decreases, and the excretion of phosphorus in the urine increases. Although parathyrin somewhat enhances tubular reabsorption of calcium ions, excretion; their excretion in urine increases due

to significant hypercalcism . Dehydration of the body, vomiting, fever, acute kidney failure occur, as a result of which the animal dies. Experimental chronic hyperparathyroidism differs from acute parathyroid intoxication . At the same time, there is progressive thinning of bone tissue (osteoporosis), deposition of calcium salts in the kidneys, lungs, heart, and other internal organs up to their complete calcification. The walls of blood vessels become hard and brittle, blood pressure rises. Animals die, as a rule, from uremia.

The origin of hyperparathyroidism in humans is associated with adenoma or hyperplasia of the parathyroid glands. Generalized fibrous osteodystrophy, which develops at the same time, is characterized by pain in muscles, bones and joints, softening of bones, and sharp deformation of the skeleton. Mineral components are washed out of the bone tissue and deposited in the muscles and internal organs (this phenomenon is figuratively called the movement of the skeleton into soft tissues). Nephrocalcinosis develops , the narrowing of the lumen of nephron tubules and their blockage with stones (nephrolithiasis) and, as a result, severe kidney failure. As a result of deposits of calcium salts in the walls of main vessels, hemodynamics and blood supply to tissues are disturbed.

Topic 43. Disorders of the endocrine function of the pancreas. Diabetes mellitus: etiology, pathogenesis, types.

Diabetes mellitus (DM) Type 1 is a disease based on an absolute lack of insulin in the body, which occurs as a result of the death of b-cells of the pancreatic islets, which causes metabolic disorders.

Etiology of type 1 diabetes:

Insulin deficiency can occur under the influence of factors of a biological, chemical, physical nature, as well as inflammation of the pancreas.

• Biological factors

♦ Genetic defects of β-cells of the islets of Langerhans . Genetic defects of the MHC system cause the inclusion of immune autoaggressive damage to the pancreas or the repression of genes encoding insulin synthesis.

♦ Immune factors. Autoaggressive immunoglobulins and cytotoxic T-lymphocytes are able to damage β-cells.

♦ Viruses that are tropic to β-cells: Coxsackie , hepatitis, measles, chicken pox, epidemic parotitis, rubella. Viruses have a direct cytolytic effect and initiate autoimmune processes.

♦ Endogenous toxic substances. As a result of disruption of pyrimidine metabolism , alloxan is formed , which blocks the synthesis of insulin.

• Chemical factors: high doses of ethanol, some anticancer drugs (cytostatics).

• Physical factors: ionizing radiation, mechanical trauma, compression by a tumor.

• Inflammatory processes in the pancreas caused by factors of a chemical, physical or biological nature. Chronic pancreatitis is the cause of insulin deficiency in about 30% of cases.

Pathogenesis:

The basis of insulin deficiency is the development of an immunoaggressive process, which is accompanied by the gradual destruction of β-cells. There are two options for development:

1. A) Entry into the body of persons genetically predisposed to diabetes by carriers of foreign AGs, usually viruses. B) Formation of an immune response with the formation of AT and cytotoxic lymphocytes to foreign AGs. C) Specific AT and lymphocytes act on the antigenic structures of the β-cell, which have a similar structure to foreign AG. This phenomenon is referred to as "cross-immunoaggressive reaction". In the course of this reaction, β-cells are destroyed, and individual proteins of the plasma membrane are also denatured and become autoantigenic .

2. A) The pancreas is primarily damaged under the influence of factors of a chemical, physical or infectious nature. B) Release of "foreign" proteins for the immune system (normally they are found only intracellularly and do not enter the blood): cytoplasmic proteins of heat shock, proinsulin . Some proteins are denatured and become autoantigenic . C) Formation of an immune response with the formation of AT and cytotoxic lymphocytes to denatured and intracellular proteins that have entered the blood. D) Autoaggressive AT and lymphocytes act on the antigenic structures of their own β-cells, which is accompanied by their destruction.

Hereditary predisposition (connection with the HLA gene system) in 80% of cases of ICD develops in persons with HLA-DR-3, HLA-DR-4

↓

Immune damage normal and/or damaged beta cells ← pathogenic factors: viruses (mumps, measles, rubella, coxsackie B) chemical factors (alloxan , salts heavy metals, etc.) physical factors (mechanical trauma, ionizing radiation)

↓

destruction of beta cells

↓

violation of the synthesis and secretion of insulin - lina (absolute insulin resistance adequacy)

↓

Type 1 diabetes

Type 1 diabetes manifests itself at a young age, the blood insulin level is low. Polyuria, polydipsia , polyphagia, weight loss develop rapidly , and ketoacidosis

develops . Legitimate complications. Insulin treatment is necessary.

Diabetes mellitus (DM) Type 2 is a disease based on relative insulin deficiency or insulin resistance , which causes metabolic disorders.

Type 2 diabetes manifests itself in most cases after the age of 40, develops slowly, often in people who are obese. Polyuria, polydipsia , weakness develops. The insulin level is high or normal. Complications and ketoacidosis occur less often. Insulin is not used in its treatment.

Hereditary predisposition to type 2 diabetes, unlike type 1 diabetes, is not associated with HLA genes.

Risk factors:

• Excess body weight, which is combined with an increase in insulin resistance of target tissues and stimulation of the production of counterinsular hormones. This excessively activates the synthesis of insulin by β-cells of the pancreas, leading to their "exhaustion" and damage.

• Arterial hypertension, which leads to a violation of microcirculation in the pancreas.

• Chronic stress, which is accompanied by a steady increase in the level of counterinsular hormones in the blood.

Conditionally, two stages of pathogenesis are distinguished:

1. Hyperinsulinemic stage. Consuming a large amount of food by obese individuals causes an increase in insulin secretion (hyperinsulinemia). This reaction is aimed at activating the processes of depositing nutrients in adipose tissue in the muscles, there is no need for the action of insulin. Therefore, they protect themselves from an excess of this hormone by reducing the number of receptors on the surface of muscle cells. The phenomenon of insulin resistance of muscle tissue develops - its sensitivity to the action of insulin decreases.

2. Hypoinsulinemic stage. Increased load on the insular apparatus can lead to functional exhaustion of cells. This is facilitated by their genetically determined defects and an excess of counterinsular hormones in the body. As a result, the amount of secreted insulin decreases and its relative insufficiency develops. At the same time, the effect of insulin on adipose tissue is preserved (there are many insulin receptors on fat cells), and on muscle tissue it decreases due to the development of insulin resistance .

Metabolic disorders in diabetes.

- *Violation of fat metabolism:*

1. Hyperlipacidemia (activation of lipolysis). Increase in blood LDL and VLDL.

2. Ketonemia , ketonuria = ketoacidosis :

a) Excessive production of ketone bodies: activation of lipolysis □□ UHD in the blood □ entering the liver □ activation of beta-oxidation □□□ Acetyl CoA □ increased synthesis of ketone bodies (acetoacetic acid, beta- oxybutyric acid, acetone),

b) Violation of utilization of ketone bodies as a source of energy in the Krebs cycle.

3. Fat infiltration liver (increased intake of UHD in the liver, reduced synthesis of lipoproteins and their secretion into the blood).

- *Disorders of protein metabolism:*

1. Decreased protein synthesis (transmembrane transport of amino acids due to insulin deficiency, degradation of polysomes, disruption of translation processes) hyperaminoacidemia , aminoaciduria .

2. Activation of protein catabolism negative nitrogen balance, hyperazotemia .

3. Decrease in the synthesis of antibodies and the body's resistance to infection.

- *Violation of carbohydrate metabolism:*

1. Hyperglycemia occurs as a result of insufficient insulin effects and impaired utilization of glucose by cells.

2. Glycosuria is mainly a consequence of hyperglycemia.

3. Hyperlactatacidemia - develops due to inhibition of lactate catabolism in the Krebs cycle, violation of glycogen resynthesis from lactate.

Acute complications of diabetes - coma. Species:

Ketoacidotic	**Hyperosmolar**	**Lactatacidemic**
High content of ketone bodies, significant hyperglycemia	A very high level of glucose in the blood, a significant increase in the osmotic pressure in the blood, an insignificant level of ketone bodies (since the level of insulin is sufficient for the oxidation of fats)	An increased level of lactic acid with an insignificant level of glucose and ketone bodies in the blood

Chronic complications of diabetes:

Microangiopathies are pathological changes in the vessels of the microcirculatory channel.

Pathogenesis:

- Glycosylation of capillary basement membrane proteins in conditions of hyperglycemia.
- Thickening and compaction of the vascular wall under the influence of excess sorbitol . Normally, no more than 1-2% of intracellular glucose is transformed into sorbitol , and with diabetic hyperglycemia, the level of conversion increases 8-10 times due to the activation of aldose reductase .
- Swelling, thickening and dystrophy of the endothelium of vessels.
- A change in the structure of the proteins of the basal membrane of vessels and their acquisition of antigenic properties, which leads to immune-mediated damage to the walls of microvessels .

- Tissue ischemia caused by a decrease in the lumen of vessels due to a decrease in the formation of NO and thickening of the vascular wall. The specified changes lead to a violation of transcapillary exchange and the formation of microthrombi .

Macroangiopathy - the development of sclerotic changes in the walls of medium- and large-caliber arteries. Atherosclerosis of blood vessels appears early and progresses rapidly in diabetes mellitus.

Pathogenesis:

- Glycosylation of basement membrane proteins and the interstitium of vessel walls. Modification of protein molecules stimulates atherogenesis .
- Accumulation of sorbitol in the wall of arterial vessels.
- An increase in the level of atherogenic LDL and a decrease in the level of anti-atherogenic HDL.
- Activation of the synthesis of thromboxane A_2 by platelets, which potentiates vasoconstriction and platelet adhesion on vessel walls.
- Stimulation of proliferation of smooth myocytes of arterial vessels.
- These changes lead to the formation and calcification of atherosclerotic plaques, thrombus formation and occlusion of arteries, impaired blood supply to tissues with the development of heart attacks and gangrene.

Neuropathies

- Glycosylation of proteins of peripheral nerves.
- The formation of AT to modified proteins with the development of reactions of immune autoaggression .
- sorbitol in neurons and Schwann cells .
- Decreased intraneural blood supply with the development of chronic ischemia and hypoxia of nervous structures. The main factor in ischemic nerve tissue is considered to be a deficiency of the vasodilator NO.
- Violation of myelin synthesis and demyelination of nerve fibers; slowing down the speed of conduction of nerve impulses.
- These changes lead to *peripheral polyneuropathy* , which is characterized by damage to several nerve trunks and is manifested by paresthesia of the feet, less often - hands; loss of pain and vibration sensitivity, more often in the distal parts of the lower extremities; decreased expression of reflexes, necrosis of foot tissues (diabetic foot syndrome). *Vegetative neuropathy* is manifested by disorders of the gastrointestinal tract (swallowing difficulties, constipation or diarrhea), dystrophy of the urinary bladder (urinary retention), impaired vascular tone (hypotension or fainting), cardiac disorders, sexual dysfunction (erectile dysfunction, decreased libido and other disorders). *Radiculopathy* due to changes in the roots of the spinal cord. They are characterized by pain and increased sensitivity along the course of one or more spinal nerves (usually in the chest and abdomen).

Retinopathy. Causes: microangiopathies in eye tissues and hypoxia of eye tissues, especially the retina. Types and manifestations:

- Nonproliferative retinopathy is manifested by the formation of microaneurysms of arterioles and venules , microhemorrhages in the retina and vitreous body (which can cause blindness), the development of microthrombi with occlusion of vessels and the formation of edema.
- Proliferative retinopathy is characterized by new formation of blood vessels of the microcirculatory bed (stimulated by hypoxia), which sprout into the vitreous body; formation of scars and detachment of the retina in the regions of large hemorrhages.

Nephropathy. Diabetic nephropathy is characterized by:

- thickening and compaction of the walls of glomerular arterioles;
- thickening of the basal membranes of the glomeruli and tubules with disturbances in the processes of filtration, reabsorption, and secretion;

an increase in blood pressure as a result of activation of the SAS and RAAS.

Topic 44. Pathophysiology of the nervous system. General signs and pathogenesis of disorders. Pathophysiology of higher nervous activity . Current control of knowledge.

-General characteristics of the pathology of the nervous system, principles of classification of disorders of its activity. Features of the development of typical pathological processes in the nervous system. The role of changes in the blood-brain barrier in the pathogenesis of disorders of the central nervous system.

- Violation of the sensory function of the nervous system. Disorders of mechano- , thermo- , proprio- and nociception . Violation of the conduction of sensory information. Manifestations of damage to thalamic centers and sensory structures of the cerebral cortex.

-Pain. Principles of classification. Somatic pain. Modern ideas about the causes and mechanisms of pain development: the theory of impulse distribution, the theory of specificity. Pathological pain. Body reactions to pain. Natural antinociceptive mechanisms.

- Violation of the motor function of the nervous system. Experimental modeling of movement disorders. Peripheral and central paralysis and paresis: causes, mechanisms, manifestations. Spinal shock. Movement disorders of subcortical origin. Disorders associated with damage to the cerebellum. Convulsions Myasthenia.

-Disruption of vegetative functions of the nervous system, methods of experimental modeling. Syndrome of vegetative-vascular dystonia.

- Violation of the trophic function of the nervous system. Neurogenic dystrophies. Structural, functional and biochemical changes in denervated organs and tissues.

- Causes and mechanisms of disturbances of electrophysiological processes in

neurons. Violation of the function of ion channels, violation of neurochemical processes. Mechanisms of pathological excitation and pathological inhibition of nerve centers.

-Damage of neurons as a cause of disorders of the integrative functions of the nervous system.

-Properties of nerve centers; principles of coordination of nervous activity; the structure of the human nervous system; the importance of NS in human life; vpatterns of reflex activity of the central nervous system, excitation and inhibition; functions of CNS departments: spinal, and brain departments; the importance of the higher departments of the central nervous system.

-The role of the cortex of the large hemispheres in the integration of the body's behavior; patterns of conditionally reflex activity of the cortex; anatomical and physiological mechanisms of GNI in humans; typology of higher nervous activity;

- Signs of pathological changes in the higher nervous activity of a person. types and physiological mechanisms of memory. physiological mechanisms of sleep.

The nervous system is very sensitive to damaging influences. Disorders of its activity can be caused by physical factors /mechanical trauma, electric current, heat and cold, noise and vibration, low atmospheric pressure/, poisons /narcotics, nicotine, carbon monoxide/, pathogens of infectious diseases - encephalitis, poliomyelitis, rabies, bacterial toxins / botulinum , tetanus, diphtheria/, parasites - echinococcus, cysticercosis, toxoplasma. Functional and organic disorders of cerebral circulation are frequent causes of nervous system damage: arteriosclerosis, thrombosis, embolism, arterial hyperemia and ischemia, hemorrhages, as well as tumors and inflammatory processes. Violation of motor function. Movements are divided into voluntary and involuntary. Voluntary movements are controlled by the pyramidal system, which consists of two neurons: central and peripheral. Processes of peripheral neurons innervate muscles . Involuntary movements are regulated by the extrapyramidal system. It includes the caudate nucleus, shell, globus pallidus, substantia nigra, red nucleus, subthalamic nuclei. Body balance, coordination of movements and muscle tone are provided by the cerebellum. Central and peripheral paralysis. Complete loss of a central or peripheral neuron leads to the appearance of central or peripheral paralysis. Partial damage to these neurons gives the corresponding paresis. In many ways, central paralysis differs from peripheral paralysis. Central paralysis (spastic) is characterized by increased muscle tone, increased tendon reflexes, and the appearance of pathological reflexes. Peripheral /flabby/ paralysis is characterized by a complete loss of movements - both voluntary and reflex. There is no muscle tone, tendon reflexes disappear, denervated muscles undergo atrophy.

Topic 45. Pathophysiology of motor disorders. Etiology, pathogenesis. Pathophysiology of sensitivity.

The following types of paralysis are distinguished: monoplegia - one nail is affected ; hemiplegia - affected muscles of half of the body; paraplegia - affected upper or lower limbs; tetraplegia - all limbs are affected. Myasthenia. Symptoms of

this disease are associated with rapid fatigue and muscle weakness. The most frequent pathological weakness covers all muscles / generalized form/, less often - individual muscle groups. In myasthenia, the transmission of nerve impulses in neuromuscular synapses, where acetylcholine serves as a mediator, is disturbed. The synthesis of the mediator decreases, while the activity of cholinesterase , which destroys it, increases. Hyperkinesias are involuntary violent pyramidal or extrapyramidal movements origin _ Pyramidal hyperkinesis manifests itself in the form of a convulsive state. Prolonged involuntary muscle contractions are called tonic convulsions. If muscle contractions alternate with relaxation, such convulsions are called clonic . To hyperkinesis extrapyramidal origin includes tremor, myoclonus , chorea, athetosis. Tremor is characteristic of parkinsonism. It appears mainly in a state of rest and is combined with rigidity muscles , stiffness of movements and poor facial expressions. . ; Myoclonia is a fast and short muscle twitch that occurs isolated or in bursts and is not accompanied by a motor act. They are observed in encephalitis, atherosclerosis, hypertension. Chorea - non-rhythmic, fast, sweeping movements of the limbs and trunk with elements of unnaturalness, picturesqueness. The reason is rheumatism, atherosclerosis. Athetosis - slow worm-like movements in the distal parts of the arms and legs, occasionally - on the face and neck. The generalized form of athetosis is called torsion dystonia. When the cerebellum is damaged, the following movement disorders develop: atony - a decrease in muscle tone; astasia - inability to hold a pose; ataxia - impaired coordination of movements; dysmetria - unevenness of movements by force; asthenia - quick fatigue. Sensitivity disorders. The sensitive function of the nervous system consists in conducting four types of sensitivity from the periphery to the brain: pain, temperature, proprioceptive and tactile. Violations of sensitivity are possible when any part of the sensory pathway is affected. Damage to a peripheral nerve /traumatic cutting, inflammation/ leads to the loss of all types of sensitivity in the zone of its innervation. A complete loss is called anesthesia, a decrease in sensitivity is called hypoesthesia .. A complete interruption of the spinal cord is also accompanied by the disappearance of all types of sensitivity below the interruption. A local lesion of the spinal cord or brain /tumor, traumatic compression, hemorrhage/ causes a selective loss of sensitivity depending on which ascending pathways are damaged. Loss of tactile sensitivity is called tactile anesthesia, loss of pain sensitivity - analgesia, loss of thermal sensitivity - thermoanesthesia . Increased sensitivity is called hyperesthesia , and the appearance of unusual sensations / tingling, crawling flies / - paresthesia. Pain. Belongs to the most striking manifestations of the sensitive function of the nervous system. Pain is aimed at protecting the body from damage, signals the appearance of a pathological process: inflammation, tumor, ischemia, hemorrhage, nerve irritation with a scar. Factors that cause pain are called algogenic , or nociceptive . They are divided into external and internal. External nociceptive factors include mechanical (impact, rupture, compression, excessive contraction or stretching of a muscle, intestine, pleura), physical (heat over 40 C, cold below 10 C, low and high barometric pressure, light, sound), chemical /alkalis, acids, salts/. The group of internal nociceptive factors consists of biologically active substances: bradykinin , substance P, histamine ,

serotonin, prostaglandins , acetylcholine, potassium and hydrogen ions.

Topic 46. Pain. Etiology and pathogenesis.

Physiological and pathological pain are distinguished. Physiological pain is an adequate reaction of the nervous system to a potentially dangerous situation for the body. This is a factor of warning and prevention. Pathological pain is manifested due to the presence of the receptor apparatus, conductors and central brain structures. Acute and chronic pain are also distinguished. Acute pain is short-lived. At first, age is localized, and later, as biologically active substances accumulate, it becomes spilled and burning. Chronic pain lasts for a long time - hours, days, weeks... Pain is a reflex process. It is formed due to the presence of the receptor apparatus, conductors and central brain structures. Chronic pain occurs with long-term tissue damage /fracture, inflammation, tumor/. Viv is formed in the same way as acute pain, but constant pain impulses cause much greater activation of the hypothalamus, pituitary gland, and sympatho-adrenal system. Chronic pain is manifested by several pain syndromes: a/ Phantom pain in amputated limbs. Most patients note that they feel a phantom limb almost immediately after amputation. It can last for years and decades b/ Causalgia - severe burning pain associated with nerve deformation when wounded by high-speed projectiles /bullet, shrapnel/. It is characterized by unrelenting intense pain, which intensifies under the action of stimuli that normally do not cause pain / touch, unexpected noise, flash of light / c/ Neuralgia - characterized by severe pain, also associated with peripheral nerve damage . Its manifestations are similar to phantom pain and causalgia, but it has a different origin. Its cause is a viral infection, nerve degeneration in diabetes, insufficient blood supply to the extremities, vitamin deficiency, arsenic or lead poisoning. Trigeminal neuralgia is particularly severe . It is characterized by paroxysms of pain that occur when talking, eating, or generally spontaneously. d/ Radiating pain is pain in certain areas of the skin when internal organs are affected. d/ Projection pain - occurs when the nerve is compressed and damaged or posterior spinal roots. Territorially, it is limited to the area of innervation of a sensitive nerve and is connected with the fact that excitation from the place of nerve damage spreads both to the central nervous system and to the periphery, in the zone of innervation. The biological meaning of pain is ambiguous. Acute pain serves as a signal about the threat of damage or its presence, it mobilizes protective processes in the body. Chronic pain is characterized by disorganization of regulatory mechanisms, it becomes unnecessary and dangerous. Shifts in chronic pain lose their adaptive meaning and acquire the importance of independent pathogenetic links in the development of the pathological process. Violation of the functions of the autonomic nervous system. The autonomic nervous system consists of two divisions: sympathetic and parasympathetic. Their functional tension is not the same in all people: in some, sympathetic tone prevails, in others - parasympathetic. This is where the doctrine of sympathetic and vagotonia arose . Sympatheticotonia is characterized by the following signs: pale dry skin, shiny eyes with wide pupils, mild exophthalmos, tendency to tachycardia, arterial hypertension, tachypnea , constipation, hyperthermia, hyperglycemia. With vagotonia , the skin is cold, moist, cyanotic, the pupils are narrowed . Bradycardia,

arterial hypotension , respiratory arrhythmia, diarrhea, hypersalivation , tendency to hypothermia, drowsiness are characteristic. Clinically expressed violations of vegetative regulation are manifested by a number of syndromes, the most important of which is the syndrome of vegetative dystonia. Three separate syndromes are distinguished in the clinical picture of vegetative dystonia. The first of them, psychovegetative , is associated with damage to the limbic system. At the same time, vegetative symptoms are combined with mental disorders of an anxious, depressive, asthenic, hysterical nature. The second syndrome of progressive autonomic failure is polyneuria - damage to the peripheral autonomic system that innervates internal organs. The syndrome is manifested by orthostatic hypotension , loss of consciousness , impotence, general weakness, weight loss, urinary incontinence, constipation, angina pectoris. The third syndrome is vegetative-vascular-trophic. It occurs on the hands and feet when the corresponding mixed nerves /neuropathy/, plexuses / plexopathy / anterior roots / radiculopathy / or neurons of the lateral horns are affected. There are many causes of vegetative dystonia : hereditary nerve damage, puberty and menopause, numerous somatic diseases - arterial hypertension, bronchial asthma, peptic ulcer disease, diabetes, as well as occupational poisoning. Vegetative dystonia syndrome is characteristic of most mental illnesses, especially depression dominates their clinical picture. Disorders of nervous trophism. Nervous trophism is the regulation of metabolic processes in tissues through nervous influences. The nervous system exerts trophic effects through intracellular regulatory mechanisms in close connection with the endocrine apparatus. The process that develops after denervation is called neurogenic dystrophy. Proteins with autoantigenic properties are formed in the neurodystrophic focus . Trophic ulcers are characterized by an indolent course and do not have a tendency to heal. Destructive processes in them always prevail over regenerative ones. Violations of higher nervous activity. Such processes as speech, memory, emotions, thinking, skills are called higher nervous activity. They are carried out by the cortex of the large hemispheres and the nearest subcortical centers.

Speech disorders are called aphasias . Sensory aphasia is a violation of the understanding of spoken language, motor aphasia is a violation of the pronunciation of words, amnestic inability to name well-known objects. Aphasia can be combined with disorders of reading /alexia/ and writing /agraphia/. Disorders of short-term memory consist in the fact that it is difficult for the patient to remember ordinary words, events, numbers, and names. With disorders of long-term memory, knowledge acquired during life is lost, for example, historical facts, dates, names of literary characters. Closely related to memory is the ability to recognize objects and phenomena of the surrounding world and interpret them. Violation of these processes was called agnosia. There are several types of agnosia : visual, auditory, agnosia of smells, taste, and one's own body. The impossibility of performing movements acquired in everyday life and in the process of work is called apraxia. Neuroses The cause of neuroses is mental trauma. Mental injuries are chronic, if they are repeated many times, or acute, when too strong a stimulus acts once. Especially strong traumatic vpllv make unexpected messages that a person did not expect. The mechanism of this influence is explained on the basis of the concept of

forecasting. It has been proven that the psychotraumatic value of an unpleasant event is greater, the greater the discrepancy between the expected and real situations. In the pathogenesis of neuroses, the main role is played by disturbances in the activity of those higher parts of the brain that adapt the body to psychotraumatic situations. Under conditions of emotional stress, there is a strong nervous tension with vegetative and endocrine changes, which eventually manifests itself in inappropriate behavior. I.P. Pavlov saw the nature of neuroses in the overstrain of the processes of excitation and inhibition or in their collision. The basis of these ideas was the doctrine of the types of higher nervous activity. However, experimental models, according to modern views, have very little in common with neuroses in humans. Meningitis - inflammation of the membranes of the brain and spinal cord. Inflammation of the soft membrane is called leptomeningitis , of the arachnoid membrane, and of the hard membrane - pachymeningitis . The disease is caused by various pathogenic bacteria, viruses, fungi, protozoa. The entrance gate is the mucous membrane of the nasopharynx, bronchi, and gastrointestinal tract. From the primary focus, the infection spreads lymphogenously or hematogenously to the meninges. Often, inflammation of the meninges is the result of contact transfer of infection in otitis, mastoiditis , epitympanitis . Forms of inflammation, as a rule, are determined by the properties of the causative agent. Serous meningitis is more often observed with a viral infection, purulent - with a bacterial one, and chronic productive meningitis is caused by pathogenic fungi and protozoa . Hemorrhagic meningitis is distinguished as a separate form. Due to the hyperproduction of cerebrospinal fluid, patients with meningitis may experience acute hydrocephalus and swelling of the brain with its wedging in the large occipital foramen. Microscopically, the vessels of the soft meninges are sharply filled with blood, the subarachnoid space is expanded, impregnated, depending on the form of inflammation, with serous, purulent, fibro -purulent or hemorrhagic exudate. The process from the choroid can move to the brain tissue with the development of meningoencephalitis . Timely treatment gives favorable results. Sometimes the process turns into a chronic form with progressive hydrocephalus and atrophy of the brain substance. Encephalitis. Encephalitis - inflammation of the brain of an infectious or infectious -allergic nature. Lesions of white matter are called leukoencephalitis , gray matter - polioencephalitis, together - panencephalitis , inflammation of the brain and its membranes - meningoencephalitis , brain and spinal cord - encephalomyelitis . Primary encephalitis is caused by neurotropic viruses - tick-borne, mosquito-borne. Secondary encephalitis occurs as a complication of a number of diseases: measles, rubella, epidemic parotitis, influenza, chicken pox, vaccination (serum encephalitis), and also as a side effect of drugs. The development of encephalitis is often a leading link in the pathogenesis of neuroinfections : botulism, rabies, poliomyelitis, tetanus, typhus. In the pathogenesis of primary encephalitis, the main role is played by the neurotropism of infectious agents that penetrate the brain by hematogenous and cerebrospinal fluid. Secondary encephalitis is characterized by other ways of damage to brain tissue: contact - otogenic , rhinogenic , orbitogenic , as well as metastatic - through blood and lymphatic vessels. Macroscopically , with encephalitis, hyperemia of cerebral

vessels, edema and swelling of the brain substance, and point hemorrhages are found. Microscopic changes depend on the course of the disease. When acute Circulatory disturbances, exudative phenomena, inflammatory mononuclear infiltration, and neurophagy prevail in the firm . The protracted form is characterized by the proliferation of glia and destruction of the nervous system, the chronic form by fibrillary gliosis , demyelination , brain atrophy. The use of modern treatment methods allows to stabilize the process. But with a prolonged and chronic course, residual phenomena such as paresis, paralysis, hydrocephalus remain . Damage to vital centers can lead to death.

Topic 47. Pathophysiology of the endocrine and nervous systems. Current control of knowledge.

Topic 48. Final test control

<u>3. Formation of professional skills, skills related to topics that are part of the content module (mastery of communication skills, clinical examination, determination of treatment scheme, conducting laboratory research, etc.) mastery of skills:</u>

Topic 42.

Task No. 1.

Patient Sh., 47 years old, complains of insomnia, irritability, feeling hot, sweating, and increased fatigue. In the evening, the body temperature rises to 37.3 C. The patient is very mobile, talks a lot and quickly. The eye slits are wide open. Sharply pronounced bulging of the eyes. Blinking is rare. The look is scared. The skin is moist, thin. The face is pink . The thyroid gland is diffusely enlarged on the neck . A tremor of the fingers is noted. Tendon reflexes are enhanced. Blood pressure 130/50 mm Hg . Art. Pulse 98 beats per minute. The blood shows leukopenia (leukocytes - 3.8 g/l) with relative lymphocytosis (lymphocytes - 46%). Chair frequent, rare Total exchange increased by 40%

Question:

1. What are the mechanisms of goiter, bulging eyes and tachycardia in the patient?
2. How do thyroid hormones affect protein, fat-lipid and carbohydrate metabolism?
3. How do thyroid hormones affect energy metabolism?

Topic 4 3 .

Task No. 1 .

Patient K., 25 years old, complains of periodic attacks of spasms in the muscles of the face and limbs, increased irritability, numbness of the fingers and toes, pain behind the sternum and in the substernal area, difficulty breathing, constipation. The disease has begun ; but after surgically removing part of the thyroid gland from the drive) [1] thyrotoxicosis)'. The patient is pale. The skin is cold to the touch, moist. Hair is thin, cropped. Claws are brittle and fragile. There are

many carious teeth in the oral cavity . No deviations from the norm were found on the part of the internal organs. The neurological examination revealed a sharp increase in the excitability of the nervous and muscular system. Significantly increased electrical excitability of motor nerves. The content of calcium in the blood is reduced to 7 mg%, the content of phosphorus and potassium is increased. The alkaline blood reserve is increased.

Question:

1. The function of which endocrine glands is impaired in the patient and why?
2. What is the mechanism of seizures?
3. How does parathyroid hormone affect calcium and phosphorus metabolism ?

Task No. 2 .

Patient V. is 49 years old, complains of muscle weakness, bone pain, poor appetite, weight loss , strong thirst, constipation. There are periodic attacks of hepatic colic . Over the past year, the patient, Hiel, suffered two minor injuries and fractured the bones of the shins.

When outside examination revealed pronounced kyphosis of the spine. The gait was unsteady. Bones are excessively mobile. During palpation on the neck *in* the area of the right lobe of the thyroid gland, there are dense formations the size of a pea. On the part of the internal organs, during the physical examination, no abnormalities were found. Neurological; the study revealed a decrease in the excitability of nerves and muscles. Radiography of the bones revealed diffuse osteoporosis (thinning of the bone substance). The pigtails of the skull have been eaten by moths . There is a cystic cavity in the left thigh . On X-ray images of the limbs, you can see the peripheral vessels. During the examination of the kidneys, a stone was found in the right ureter. In the blood, the level of calcium is increased (up to 15 mg %) and the phosphorus content is reduced (where it is 2.5 mg %). Daily diuresis 4 л. A lot of phosphates were found in the urine.

Question:

1. How can the patient's complaints and bone fractures be explained?
2. What explains the changes in blood and urine?
3. What is the common etiology of parathyroid diseases ?

Topic 4 4 .

Task No. 1

Patient R., suffering from diabetes, was delivered by "ambulance" in an unconscious state. Objectively : the skin is dry, the eyeballs are soft, there are no reflexes, the breathing is noisy, deep, there is a sharp smell of acetone from the mouth. Blood pressure - 95/65 mm Hg . Art. Pulse - 110 bpm , rhythmic.

1. Assess the patient's condition.
2. Identify the patient's actual and potential problems.
3. Form the goal of nursing care.
4. Specify the emergency measures.

Answer standard

HYPERGLYCEMICAL COMA.

Actual problems: lack of consciousness, dry skin, breathing disorders (Kussmaul's breathing), the smell of acetone from the mouth, a decrease in blood pressure, an acceleration of the pulse. Potential problems: death due to ketoacidosis . The goal of care: to normalize the level of glucose in the blood.

Emergency measures:

- urgent hospitalization;
- express examination of blood and urine for sugar level;
- administration of insulin under blood sugar control;
- to reduce acidosis, inject 200 ml of 5% sodium bicarbonate intravenously ;
- to combat cardiovascular insufficiency, 0.5-1.0 ml of 0.05% strophantin or 1 ml of 0.06% corglycon are administered intravenously .

Task #2

According to the prescription sheet, 24 units of insulin were administered subcutaneously to patient K., who is suffering from diabetes. In 20 minutes. after the injection, he complained of dizziness, trembling hands, sweating, and a sharp feeling of hunger.

1. Assess the patient's condition.

2. Identify the patient's actual and potential problems.

3. Form the goal of nursing care.

4. Specify the emergency measures

Answer standard

HYPOGLYCEMICAL STATE.

Actual problems: dizziness, sweating, hunger.

Potential problems: hypoglycemic coma.

Emergency measures:

- seat the patient;
- let him drink sweet tea, eat a piece of bread;
- if the condition has not improved, repeat the use of sweets;
- explain the cause of such a condition and the need to eat after an insulin injection.

Topic 45.

1. A 27-year-old woman's vision in her left eye deteriorated dramatically after a psychotic trauma . The ophthalmologist diagnosed retrobulbar neuritis of the left optic nerve . Objectively: sharply reduced visual acuity in the left eye, absent abdominal reflexes, increased deep reflexes from the limbs, positive Babinski cm bilaterally , slight muscle weakness in the right leg, decreased vibration sensitivity in the legs up to 5 seconds , in the hands up to 7 seconds .

What disease does the patient have ?

Topic 46.

1. A 35-year-old woman developed diplopia and decreased vision against a background of normal temperature. After 3 months, the condition worsened - there was weakness in the limbs, increased urination, unsteadiness when walking. In the neurological statue : horizontal nystagmus, diplopia when looking to the sides, spastic tetraparesis , absence of abdominal reflexes, decreased vibration sensitivity on the legs. Subatrophy of optic nerve discs on the fundus .

What disease are we talking about?

2. The patient complains of discomfort in the left hand, numbness of the right foot, which occurred acutely, at the same time, for the first time in his life. On MRI, there are 4 foci of size 3-4 mm in the parietal lobes (one paraventricularly) and in the brain stem.

What disease are we talking about? What are these lesions?

4. Summary : testing, differential assessment.

List of recommended literature (main, additional, electronic information resources):

Recommended Books

Main:

1. 1. Ataman O.V. Pathophysiology: General pathology. – Vinnytsia: New book, 2018. – Volume 1. - 584 p.
2. 2. Ataman O.V. Pathophysiology: Pathophysiology of organs and systems. – Vinnytsia: Nova kniga, 2019. – Vol. 2. – 448 p.
3. 3. Yu.V. Byts, G.M. Butenko, A.I. Gozhenko . Pathophysiology: a textbook / edited by M.N. Zaika , Yu.V. Bytsia, M.V. Crystal . - Kyiv: VSV "Medicine", 2015. - 752 p.
4. 4. Zaiko M.N., Byts Y.V., Kryshtal M.V. etc. Pathophysiology: a textbook / edited by M.N. Zaika , Yu.V. Bytsia, M.V. Crystal . – Kyiv: Medicine, 2017. - 736 c.

Additional:

1. 1. Ataman O.V. Pathological physiology in questions and answers. – Vinnytsia: New book - 2007. – 512 p.
2. 2. Zaiko M.N., Byts Yu.V., Butenko H.M. and others. Pathophysiology: a textbook / edited by M.N. Zaika , Yu.V. Bytsa . - K.: Medicine, 2008. - 704 p.
3. 3. Krishtal NV, Mikhnev VA, Zayko NN et al . Pathophysiology : Textbook / Ed . by NV Krishtal , VA Mikhnev : Textbook , the 3rd Edition . — Kyiv : AUS Medicine Publishing , 2019. - 656 p.
4. 4. Robbins and Cotran pathological basis of disease / Ed. by Vinay Kumar, Abul K. Abbas, Jon C. Aster : Textbook, the 9 th Edition. - Philadelphia: Elsevier Saunders, 2015. - 1392 p. 952

13. Electronic information resources

1. https://info.odmu.edu.ua/chair/pat_physiology/ - information resource of the department of general and clinical pathological physiology
2. http://moz.gov.ua – Ministry of Health of Ukraine
3. www.who.int - World Health Organization
4. www.dec.gov.ua/mtd/home/ - State Expert Center of the Ministry of Health of Ukraine
5. http://bma.org.uk - British Medical Association