MINISTRY OF HEALTH OF UKRAINE
ODESA NATIONAL MEDICAL UNIVERSITY

Faculty **Medicine**

Department **General and Clinical Pathophysiology**

CERTIFY

Vice-rector for scientific and pedagogical work
Profesor _____ Svitlana KOTYUZHYNSKA

01 September 2022

MANUAL
FOR SEMINAR CLASSES
FROM EDUCATIONAL DISCIPLINE

Faculty **Medicine**, course 3, 5

Educational selective discipline - **"Clinical Pathophysiology"**

Certify:
At the meeting of V.V. Pidvysotsky General and Clinical Pathological Physiology Department of Odesa National Medical University

Protocol N 1 dated 31 August 2022

Head of Department _____ profesor Rooslan VASTYANOV

Developers:

_____ prof. R.S. Vastyanov
_____ prof. S.G. Kotyuzhynska
_____ Asst. Prof. I.O. Ostapenko
_____ Ass. Prof. I.A. Kuzmenko
_____ Ass. Prof. V.P. Babiy
_____ Ass. Prof. D.Ye. Lapshin
_____ Ass. Prof. O.M. Pospelov
_____ Ass. Prof. L.V. Goncharova
_____ Asst. Prof. V.V. Kirchev
_____ Asst. Prof. V.M. Sarakhan

PRACTICAL TRAINING

Seminar lesson N 1

Topic: Inflammation. The main components of the inflammatory process. Features of vascular reaction, exudation and emigration of leukocytes. Pathological principles of anti-inflammatory therapy.

Seminar session N 2

Topic: Allergy. General characteristics of allergic reactions. The nature of allergens. Principles of allergy detection. The role of allergies in transplantology. Types and mechanisms of desensitization. Principles and treatment of allergic reactions.

Seminar session N 3

Topic: Typical metabolic disorders: mechanisms of hyper- and dehydration. Principles of edema therapy. Characteristics of acidosis and alkalosis, main laboratory criteria and mechanisms of detected disorders in the patient's body.

Seminar session N 4

Topic: Clinical pathophysiology of extreme conditions: shock, collapse, coma. Pathophysiological basis of shock prevention and therapy. The role of homeostasis disorders in the pathogenesis of coma. Principles of coma therapy.

Seminar session N 5

Topic: Clinical pathophysiology of red blood: changes in total volume, anemia and erythrocytosis. Pathogenetic characteristics of anemia classifications for the analysis of their manifestations. Principles of prevention and treatment.

Seminar lesson N 6

Topic: Identify typical disorders in the white blood system: leukocytosis, leukopenia, hemoblastosis, leukemia. Analysis of the mechanism of development and causes of changes in the cellular composition of "white blood" and their clinical consequences; pathogenetic principles of leukemia diagnosis, features of the results of therapy and bone marrow transplantation.

Seminar lesson N 7

Topic: Modern ideas about the mechanisms of damage to the gastrointestinal tract. Principles of prevention and treatment of peptic ulcer disease. Pathogenetic mechanisms of development of acute pancreatitis. Local and systemic changes in the pathogenesis of pancreatic shock and their rationale.

Seminar session N 8

Topic: Modern concepts of pathogenetic mechanisms of disorders of the nervous system. Motor and sensory disorders, their etiological-pathogenetic features, basic principles of pathogenetically determined pharmacological correction. The concept of the determinant of the pathological process in the nervous system, the generator of pathologically enhanced excitation and the systemic and anti-systemic mechanisms of regulation in the formation of the pathology of the nervous system.

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

Topic 1. Inflammation. The main components of the inflammatory process. Features of vascular reaction, exudation and emigration of leukocytes. Pathological principles of anti-inflammatory therapy.
Topic 2. Allergy. General characteristics of allergic reactions. The nature of allergens. Principles of allergy detection. The role of allergies in transplantology. Types and mechanisms of desensitization. Principles and treatment of allergic reactions.
Topic 3. Typical metabolic disorders: mechanisms of hyper- and dehydration. Principles of edema therapy. Characteristics of acidosis and alkalosis, main laboratory criteria and mechanisms of detected disorders in the patient's body.
Topic 4. Clinical pathophysiology of extreme conditions: shock, collapse, coma. Pathophysiological basis of shock prevention and therapy. The role of homeostasis disorders in the pathogenesis of coma. Principles of coma therapy.
Topic 5. Clinical pathophysiology of red blood: changes in total volume, anemia and erythrocytosis. Pathogenetic characteristics of anemia classifications for the analysis of their manifestations. Principles of prevention and treatment of anemia.
Topic 6. Identify typical disorders in the white blood system: leukocytosis, leukopenia, hemoblastosis, leukemia. Analysis of the mechanism of development and causes of changes in the cellular composition of "white blood" and their clinical consequences; pathogenetic principles of leukemia diagnosis, features of the results of therapy and bone marrow transplantation.
Topic 7. Modern ideas about the mechanisms of damage to the gastrointestinal tract. Principles of prevention and treatment of peptic ulcer disease. Pathogenetic mechanisms of development of acute pancreatitis. Local and systemic changes in the pathogenesis of pancreatic shock and their rationale.
Topic 8. Modern concepts of pathogenetic mechanisms of nervous system disorders. Motor and sensory disorders, their etiological-pathogenetic features, basic principles of pathogenetically determined pharmacological correction. The concept of the determinant of the pathological process in the nervous system, the generator of pathologically enhanced excitation and the systemic and anti-systemic mechanisms of regulation in the formation of the pathology of the nervous system.

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

Basic concepts:
Topic 1. Inflammation: etiology, pathogenesis. Mediators. Local signs. Exudation and proliferation.
Topic 2. Allergy: Allergic reactions of types I - IV. Pseudoallergic reactions.
Autoimmune reactions.
Topic 3. Violation of water-salt exchange: etiology, pathogenesis. Dyshydria, edema. Pathophysiology of acid-base metabolism: acidosis, Alkalosis.
Topic 4. Pathophysiology of extreme conditions. Etiology and pathogenesis shock and colaptoid states.
Topic 5. Pathophysiology of the blood system. Changes in the total volume. Blood oss.

Erythrocytosis, posthemorrhagic anemia, etiology, pathogenesis. Hemolytic, B12-folate-deficient, iron-deficient anemias, etiology, pathogenesis.
Topic 6. Leukocytosis and leukopenia: etiology, pathogenesis. A picture of blood. Leukemoid reactions. Leukemias: etiology, classification, pathogenesis. A picture of blood.
Topic 7. Indigestion in the gastrointestinal tract. Ulcer disease. Pathophysiology of the intestine. Pancreatitis.
Topic 8. Pathophysiology of the nervous system. General signs and pathogenesis violations Pathophysiology of higher nervous activity.

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. Inflammation. The main components of the inflammatory process. Features of vascular reaction, exudation and emigration of leukocytes. Pathological principles of anti-inflammatory therapy.

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 physico-chemical 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 proliferation. The 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 at 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 in case of 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	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. They 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 permeability of postcapillary venules, release of cellular mediators, cytolysis
Kinins (bradykinin, kalidin)	Dilate 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

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 clotting; 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 of Celsus-Galen):

- 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 2. Allergy. General characteristics of allergic reactions. The nature of allergens. Principles of allergy detection. The role of allergies in transplantology. Types and mechanisms of desensitization. Principles and treatment of allergic reactions.

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

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 (HST) 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 body
10. 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).

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 Fc end (constant fragment) are fixed on the corresponding receptors of mast cells and basophils; nerve receptors of blood vessels ,

smooth muscles of the 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 AG).

There is cell activation and transition of the process to **the pathochemical stage**, which includes degranulation of mast cells 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 and neutrophils into the allergic reaction zone and their release of secondary mediators: histamines, arylsulfatases, proteases, phospholipases

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.

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 (Th0) → 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 sera) →

recognition of allergens by dendritic cells (DC) → reading information, processing it, isolating AG determinants and embedding it in the DC membrane → activation of T-helpers (Th0) → 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, 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; release of Hageman factor in 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 the 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 (Th0) → 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 introducing 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, corticosteroids, 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 influence of factors that cause degranulation of mast cells and the release of biologically active substances.

Mechanisms of development:

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

- **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 humanity 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. Infiltrated lymphocytes recognize foreign antigens and are specifically 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, cyclosporin 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 mandatory 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 are devoid of 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 3 . Typical metabolic disorders: mechanisms of hyper- and dehydration. Principles of edema therapy. Characteristics of acidosis and alkalosis, main laboratory criteria and mechanisms of detected disorders in the patient's body.

1. The role of water and electrolytes in the body.
2. Concept of osmolarity, its correction.
3. Clinical signs of dehydration and hyperhydration.
4. Hypertonic dehydration. Causes, clinical signs, methods of correction.
5. Isotonic dehydration. Causes, clinical signs, methods of correction.
6. Hypotonic dehydration. Causes, clinical signs, methods of correction.
7. Hypertonic hyperhydration. Causes, clinical signs, methods of correction.
8. Isotonic hyperhydration. Causes, clinical signs, methods of correction.
9. Hypotonic hyperhydration. Causes, clinical signs, methods of correction.
10. Causes and signs of hypo- and hypernatremia, methods of treatment.
11. Pathophysiological disorders in hypo- and hyperkalemia, clinic, diagnosis, correction.
12. Violation of chlorine metabolism.
13. 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.

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

Why should the body maintain a constant pH?

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.

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

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. The 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 the 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 overflowed 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 in isoosmolar 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 lymphatic drainage 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) 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 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 the outflow of blood. 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), and plasma osmotic pressure 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, administration 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) calcium malabsorption in the case of 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 hypocalciuric 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 excretion of phosphates by the kidneys (hypoparathyroidism, kidney failure).

Acidosis is *a disturbance of the KOS in which the level of acids in the blood increases and the level of bicarbonate decreases* . **Alkalosis** *is a BOS disorder in which the level of bicarbonates in the blood increases and the level of acids decreases* . Depending on the degree of compensation (pH shift beyond normal values - 7.4 ± 0.05), *acidosis and alkalosis* are divided into:

- *compensated* (pH of capillary blood does not exceed 7.4±0.05);
- *decompensated* (pH of capillary blood exceeds 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). When maintaining this ratio, the pH of the blood does not change significantly, that is, it remains within the range of 7.35-7.45. Correspondingly, such

violations of KOS are called decompensated, when not only the absolute number of components of the bicarbonate buffer and their ratio change, as a result of which there is a shift in pH beyond normal parameters.

According to *the mechanism of detection*, all violations of COS are divided into *respiratory* and *non-respiratory* . The first arise as a result of the release 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 due to the primary increase in the concentration of non-volatile acids and bases in the blood, as a result of which there is a shift in the buffer bases - BE and the concentration of 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 regard, non-respiratory acidosis is divided into *metabolic, excretory and exogenous* , and alkalosis on *secretory 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) separated
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 alkalosis acidosis;
4 *) primary non-respiratory alkalosis and secondary respiratory alkalosis acidosis*

Evaluation of KOS. Laboratory indicators of blood are 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 blood PSO_2 of more than 45 mm. mercury Art.

Causes of respiratory acidosis:

- all types of insufficiency of external breathing, when the gas exchange between the external air and alveoli is disturbed (bronchial asthma attack, aspiration of foreign bodies, hemo-, pneumothorax, suppression of the respiratory center) and between alveoli and blood (pulmonary edema, thromboembolism of the pulmonary artery, etc.) ;

- breathing air or mixtures with a high content of carbon dioxide.

KOS indicators in respiratory 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 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 nonrespiratory acidosis is 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 PCO_2 in the blood decreases to less than 35 mm Hg, which is observed in severe conditions that are 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 of the lungs of central genesis (tumors, injuries, encephalitis, stroke);
3) prolonged 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 strong acid anions - most often the 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 parathyroid hormone deficiency.

Exogenous non-respiratory alkalosis is caused by 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 mercury 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 myselfprevents 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 primarydecrease blood PSO_2 due to hyperventilation lungs
Non-gasacidosis	acidosis, which occurs because of decrease in bicarbonate, which is caused by a decrease correlation between fixed cations and anions
Non-gasalkalosis	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 andare 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 exchange process almost instantly (bicarbonate and ion hydrogen)
Metabolicacidosis	occurs at excessive formation inbody anions lactate at hypoxia and diabetes or ketone anions bodies during starvation and diabetes
Exogenousacidosis	occurs under time introduction in organism acids or of salt strong acids from cations, what are metabolized (example, NH_4Cl)
Excretoryacidosis	occurs because of losses fixedcations with diarrhea or dysfunction renal tubules
Exogenousalkalosis	occurs at introductions in organism meadows or of salt with organic anions, that are metabolized
Excretoryalkalosis	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 4. Clinical pathophysiology of extreme conditions: shock, collapse, coma. Pathophysiological basis of shock prevention and therapy. The role of homeostasis disorders in the pathogenesis of coma. Principles of coma therapy .

1. Definition of terms: extreme conditions, shock, collapse, coma
2. Etiology of shock
3. Types of shocks
4. General elements of the pathogenesis of shock states
5. Disruption of the neuroendocrine system during shock
6. Hemodynamic disorders in shocks - systemic hemodynamic disorders, microcirculation disorders
7. Cellular disturbances in shocks. Multiple organ failure.
8. Pathogenesis of acute respiratory distress syndrome in adults.
9. Features of the development of various types of shock: hypovolemic, cardiogenic, traumatic, Crash syndrome, burn shock, anaphylactic, septic.
10. Types of collapse - by etiology, by pathogenesis.
11. Pathogenesis of collapse.
12. 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. Most often, it is accompanied by a decrease in blood pressure (hypotension), which, however, can be within the normal range (and even increased) in the initial phase of shock (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*** — decrease in total blood volume (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 nonketoacidemic hyperglycemia), polyuria and excessive sodium removal in glucocorticoid 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*** — the 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 by baro-, volume-, 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, a hyperkinetic type of blood circulation (increased cardiac output) occurs, 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.

Violation of the functions of other organs, which occurs 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 blood 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 is sharply reduced 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 is 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.

Topic 5. Clinical pathophysiology of red blood: changes in total volume, anemia and erythrocytosis. Pathogenetic characteristics of anemia classifications for the analysis of their manifestations. Principles of prevention and treatment of anemia.

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, compensation mechanisms.

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* (a normal ratio of plasma and blood cells is preserved), *polycythemic* (predominance of blood cells) and *oligocythemia* (predominance of plasma).

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.

Oligocythemic hypovolemia - 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.

Polycythemic hypovolemia - 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.

Oligocythemic hypervolemia - an 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.

Polycythemic hypervolemia - 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 Waquez's disease, it is the result of tumor growth of cells of the erythrocyte row of the bone marrow.

Oligocytemic normovolemia occurs with anemia due to 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.

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 → the effect 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 the 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 exhibits the ability to perceive both acid 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

erythroid cells, acidophilic and polychromatophilic, less often basophilic normoblasts may appear in the blood. 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);

b) *poikilocytosis* - a change in the shape of erythrocytes. Normally, erythrocytes have the shape of biconcave disks. 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's bodies - formations 1-2 μm in size, 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 as a result of hypoxia and ischemia, production of erythropoietin by some tumors (hypernephroma, liver cancer, etc.).

In addition, absolute erythrocytosis develops in true polycythemia (Vakez'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 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 polycythemic hypovolemia (for example, shock, burns).

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 occurs in cases where 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) 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. In the blood, the number of polychromatophilic erythrocytes and reticulocytes increases, 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 post-hemorrhagic anemia occurs 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.

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 caused by 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; increasing the activity of macrophages.

Types of hemolysis:

- ***intravascular hemolysis*** occurs in blood vessels under the influence of factors that damage erythrocytes: a) factors of a physical nature (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:** violations of the structure of the shell with a change in shape (hereditary microspherocytosis or Minkovsky-Shoffar anemia, hereditary ovalocytosis). The type of inheritance is autosomal dominant. Hereditary defect of erythrocyte membrane proteins - 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 erythrocyte membrane 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) a hereditary defect in the synthesis of globin molecule chains (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 are 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 isogglutinins 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, which is released from the destroyed erythrocytes, to 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 hepatic 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.

Anemia due to impaired erythropoiesis.

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 impaired 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 gastric resection.

3. Non-absorption of vitamin B_{12} in the intestine (in case of resection of the small intestine, tumor, 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 into megaloblasts is accompanied by a violation of enucleation (this is evidenced by the appearance of Jolly bodies (remains of the nucleus) and Cabot rings (remains of the nuclear envelope) in megaloblasts). 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 $B_{12\ \text{deficiency}}$, 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 detected, 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 6. Identify typical disorders in the white blood system: leukocytosis,

leukopenia, hemoblastosis, leukemia. Analysis of the mechanism of development and causes of changes in the cellular composition of "white blood" and their clinical consequences; pathogenetic principles of leukemia diagnosis, features of the results of therapy and bone marrow transplantation.

1. Leukocytosis. Leukopenia. Nuclear shifts left and right. Characteristic. The value for the diagnosis of bacterial and viral diseases
2. Definition and classification of leukemia with an indication of the principles underlying it.
3. Etiology of leukemia. The role of oncogenic viruses, ionizing radiation, chemical carcinogens, genetic abnormalities hematopoiesis in the development of leukemia.
4. Pathogenesis of leukemia. Mono- and polyclonal stage of development of leukemia. Tumor progression in leukemia.
5. Blood picture in acute and chronic leukemia (myelo- and lymphatic leukemia).
6. 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 Kostman's neutropenia, autosomal dominant hereditary neutropenia, "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 (ineffective 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 damage 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 inhibition and deep disorders of leukopoiesis.

4. Regenerative-degenerative shift is observed with hyperproduction in bone marrow of pathologically changed leukocytes 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, maturing and differentiated forms of leukocytes are absent or

significantly reduced (leukemic failure - hiatus leucemicus, especially pronounced 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).

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.

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 greater destabilization of the genome of the transformed cells of the monoclone with hyperexpression of new oncogenes and suppression of anti-oncogenes. This leads to the emergence of more aggressive subclones, the cells of which acquire malignant properties with replacement (metaplasia) of normal

hematopoiesis, spread (dissemination) by hematogenous route into the tissues of the body of the carrier and the formation of infiltrates of proliferating blasts, foci of perverted (aberrant) hematopoiesis in them.

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 cells of normal hematopoiesis are preserved in the red bone marrow, they will be the source of entry into the blood of normal leukocytes, that is, those that should be in the blood normally - metamyelocytes, rod-shaped and segmented 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 - a 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 in the skin of proliferated leukemic cells - leukemic cells.

3. Ulcerative-necrotic lesions of mucous membranes (stomatitis, sore throat, enteropathies).

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 respiration 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	Blast 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 7. Modern ideas about the mechanisms of damage to the gastrointestinal tract. Principles of prevention and treatment of peptic ulcer disease. Pathogenetic mechanisms of development of acute pancreatitis. Local and systemic changes in the pathogenesis of pancreatic shock and their rationale.

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 nutrients remains in the intestinal cavity, which leads to a violation of the composition of the internal environment of the intestine, including changes in pH, osmotic pressure, and 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 diet), 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 of the 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 the evacuation of food mass from the stomach, erosion and ulceration of the gastric mucosa, 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, in 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 (due to 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 of 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 deceleration (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 analogues (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 subject to intoxication, and have a higher risk of developing stomach neoplasms.

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; • excessive content of exudate on the surface of the mucous membrane (for example, in 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 duodenum, sometimes in the distal part of the esophagus and rarely in the small intestine (usually combined with Meckel's diverticulum, which contains fragments of the mucous membrane of the gastric type). Zollinger-Ellison syndrome can also be considered as a type of VT. 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 of the gastric mucosa, the activation of aggression factors plays a predominant role. 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 8. Modern concepts of pathogenetic mechanisms of nervous system disorders. Motor and sensory disorders, their etiological-pathogenetic features, basic principles of pathogenetically determined pharmacological correction. The concept of the determinant of the pathological process in the nervous system, the generator of pathologically enhanced excitation and the systemic and anti-systemic mechanisms of regulation in the formation of the pathology of the nervous system.

-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; anatomic 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. The following types of paralysis are distinguished: monoplegia - one knuckle 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 - separate 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 movements of pyramidal or extrapyramidal 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. Hyperkinesias of extrapyramidal origin include tremor, myoclonus, chorea, and athetosis. Tremor is characteristic of parkinsonism. It appears mainly in a state of rest and is combined with muscle stiffness, 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. Complete loss is called anesthesia, reduced sensitivity - hypoesthesia. 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.

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 prevention 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/. Chronic pain 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 is aggravated by stimuli that normally do not cause pain / touch, sudden 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 a nerve or posterior spinal roots are compressed and damaged. 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 with damage to the corresponding mixed nerves /neuropathy/, plexuses /plexopathy/ anterior roots /radiculopathy/ or neurons of the lateral horns.

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 understanding spoken language, motor aphasia is a violation of word pronunciation, 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. Unexpected messages that a person did not expect have a particularly strong traumatic effect. 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 full of blood, the subarachnoid space is expanded, impregnated, depending on the form of inflammation, with serous, purulent, fibrous-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. White matter lesions 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 brain tissue damage: 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. Circulatory disorders, exudative phenomena, inflammatory mononuclear infiltration, and neurophagy predominate in the acute form. 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, and hydrocephalus persist. Damage to vital centers can lead to death.

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

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 saline 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 2.

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*

precipitating IgG, IgM, level of mediators, allergen, complement system in the blood

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.

2. 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 heart area, 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 against the background of a myocardial infarction, when necrotized and affected cells of the myocardium 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*

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Topic 3.

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.

2. At 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

occurred? Was the treatment strategy correctly developed?

Answers:

1. Blood loss that provoked simple hypovolemia. 2. In connection with increased sweating, water-electrolyte metabolism disorders in the form of hypoosmolar hypohydration occurred3. Dehydration. Exykosis.4. Extracellular hyperhydration. Hypoproteinemia.

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} secretion

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, which is 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?

A. Decompensated respiratory acidosis

B. Metabolic acidosis is compensated

S. Metabolic decompensated alkalosis

D. Compensated respiratory alkalosis

E. Mixed 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

C. Decompensated metabolic acidosis

D 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?

A. Decompensated respiratory acidosis

B. Decompensated metabolic acidosis

C. Compensated metabolic acidosis

D. Decompensated respiratory alkalosis

E. Metabolic alkalosis is compensated

Topic 4.

The driver who was involved in the accident was injured and is in a stable condition

shock, a decrease in the daily amount of urine to 300 ml is observed.

What is the main pathogenetic factor of this change in diuresis?

(Drop in **blood** pressure)

Topic 5.

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, accelerated shallow breathing, massive internal bleeding due to damage to one of the branches of the pulmonary artery. blood analysis results after 4 days after the operation that 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/h. Blood smear: many polychromatophilic erythrocytes, 5 adiophilic normoblasts.

-What method of staining a blood smear 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 blood smear staining, polychromatophilic normoblasts - by Romanovsky staining. 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, post-hemorrhagic. The bone marrow's ability to regenerate is good, that is, hyperregenerative anemia.

2. 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).

- 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 mmaol/ 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. The type of inheritance is 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 6.

- 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. As a result of 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, in chronic myeloid leukemia they are absent.

In addition, chronic myelogenous leukemia is characterized by "eosinophilic-basophilic association", which is usually absent in sepsis.

- 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 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, segmented neutrophilic 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 7.

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 in the 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 8.

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, abdominal reflexes are absent, deep reflexes from the limbs are increased, positive Babinski cm bilaterally, slight muscle weakness in the right leg, reduced vibration sensitivity in the legs up to 5 seconds, in the hands up to 7 seconds.

What disease does the patient have?

2. 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 in the legs. Subatrophy of optic nerve discs on the fundus.

What disease are we talking about?

3. 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 3-4 mm in size in the parietal lobes (one paraventricularly) and in the brain stem.

What disease are we talking about? What are these lesions?

Summary : testing, differential assessment.

List of recommended literature (main, additional, electronic information resources):

Recommended Books

Main:

1. Ataman O.V. Pathophysiology: General pathology. – Vinnytsia: New book, 2018. – Volume 1. - 584 p.
2. Ataman O.V. Pathophysiology: Pathophysiology of organs and systems. – Vinnytsia: Nova kniga, 2019. – Vol. 2. – 448 p.
3. Yu.V. Byts, G.M. Butenko, A.I. Gozhenko. Pathophysiology: a textbook / edited by M.N. Zayka, Yu.V. Bytsia, M.V. crystal – Kyiv: VSV "Medicine", 2015. – 752 p.
4. Zaiko M.N., Byts Y.V., Kryshtal M.V. etc. Pathophysiology: a textbook / edited by M.N. Zayka, Yu.V. Bytsia, M.V. crystal – Kyiv: Medicine, 2017. - 736 p.

Additional:

1. Ataman O.V. Pathological physiology in questions and answers. – Vinnytsia: New book - 2007. – 512 p.
2. Zaiko M.N., Byts Yu.V., Butenko G.M. and others. Pathophysiology: a textbook / edited by M.N. Zaika, Yu.V. Bytsia. - K.: Medicine, 2008. - 704 p.
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. 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.

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