PATHOPHYSIOLOGY OF ORGANS AND SYSTEMS

Methodical instructions for the practical class for foreign students (majoring in «Medicine» and «Dentistry»)

МІНІСТЕРСТВО ОХОРОНИ ЗДОРОВ'Я УКРАЇНИ
Харківський національний медичний університет

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ПАТОФІЗІОЛОГІЯ ОРГАНІВ ТА СИСТЕМ

Методичні вказівки для практичних занять з підготовки іноземних студентів (спеціальність «Медицина» та «Стоматологія»)

Затверджено
Вченою радою ХНМУ.
Протокол № 10 від 26.10.2023.

Харків
ХНМУ
2023

Pathophysiology of organs and systems : methodical instructions for the practical class for foreign students (majoring in «Medicine» and «Dentistry») / comp. M. S. Myroshnychenko, V. O. Bibichenko M. O. Kucheriavchenko et al. Kharkiv : KhNMU, 2023. 240 p.

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Патофізіологія органів та систем : метод. вказ. для практ. занять з підготовки іноземних студентів (спеціальність «Медицина» та «Стоматологія») / упоряд. М. С. Мирошниченко, В. О. Бібіченко М. О. Кучерявченко та ін. Харків : ХНМУ, 2023. 240 с.

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Topic 1. Changes in the total volume of the blood. Qualitative changes of erythrocytes and leukocytes. Erythrocytosis

Justification of the topic: The internal environment of the body, which unites all organs and systems at the humoral level, is represented by three components - blood, lymph and interstitial fluid, the composition and properties of which are closely related to each other, and consistency in work ensures the maintenance of the stability of the internal environment of the body – homeostasis. The blood system, as well as other systems of the human body, can change under the influence of environmental factors, or as a result of a violation of the activity of certain organs and systems that maintain the stability of morphological, protein, ion, electrolyte, gas and other blood components. As a result, the inherent functions of the blood are disturbed. The ability to interpret changes in the total volume (mass) of blood and its constituent elements (erythrocytes and leukocytes) is important for a doctor of any specialty.

Purpose of the lesson:

General – to be able to determine changes in the total volume of blood, as well as qualitative changes of erythrocytes and leukocytes.

Specifically:

Know:

1. Know the normal parameters of hematocrit in an adult.
2. Describe the main stages of erythrocyte formation.
3. Know the normal parameters of the number of reticulocytes in an adult.
4. Determine the number of reticulocytes in the blood.
5. Prepare and stain a blood smear according to Romanovsky-Giemsa and recognize the cellular elements of the erythrocyte series under its microscopy.

Be able to:

1. On the basis of hematocrit data, identify changes in the total volume of blood and give their characteristics.
2. To characterize the possible qualitative changes of erythrocytes occurring in anemia, to detect their presence during microscopy of a blood smear of an animal with experimental anemia.
3. Describe possible qualitative changes in leukocytes.

Practical experience:

1. Identify regenerative forms of erythrocytes in peripheral blood smears (stained according to Romanovsky or Pappenheim), interpret their presence or absence.
2. Identify the regenerative forms of erythrocytes in stained blood smears it is vital to evaluate the value of their presence or absence in the blood.
3. Describe the degenerative forms of erythrocytes in blood smears stained by Romanovsky or Pappenheim, to interpret their presence in the blood.

4. Determine the pathological forms of erythrocytes in a smear of peripheral blood, interpret their presence in the blood.

5. Calculate the content of erythrocytes in a unit of blood volume, draw a conclusion about violation of the quantitative composition of "red" blood (anemia, erythrocytosis).

The graphological structure of the topic "Changes in the total volume of the blood. Qualitative changes of erythrocytes and leukocytes. Erythrocytosis." is attached.

Material and methodological support of the topic "Changes in the total volume of the blood. Qualitative changes of erythrocytes and leukocytes. Erythrocytosis":

1. Lectures;
2. Methodical instructions for teachers;
3. Methodical instructions for students;
4. Set of test tasks to determine the basic level of knowledge;
5. Set of situational tasks to determine the final level of knowledge;
6. Set of KROK-1 tasks;
7. Set of schemes and tables (presentation);
8. Set of forms with a clinical blood test;
9. Video films;
10. For the experiment (experimental animals – rabbit, microscopes, immersion oil, subject slides, polish slides, hydrochloric acid solution, distillates for painting of smears, fixation, Romanovsky staining, injector, pins, Petri-dish, solution of brilliant cresyl blue).

Oriented map of students' work on the topic "Changes in the total volume of the blood. Qualitative changes of erythrocytes and leukocytes. Erythrocytosis"

No	Stage of lesson	Academic time, min	Educational guide		Place holding a class
			Educational tools	Equipment	
1	Determination of the basic level of knowledge	10	Written answer to test tasks	Test tasks	Study room
2	Analysis of theoretical material	35	Analysis of theoretical material based on control questions of the topic, situational tasks, tasks of KROK-1	Topic control questions, KROK-1 tasks, situational tasks	
3	Practical part (conduct experiment)	30	Introduction and preparation for setting up the experiment. Setting up the experiment. Discussion of the results of the experiment and formulation the conclusions	Rabbit, microscopes, immersion oil, subject slides, polish slides, hydrochloric acid solution, distillates for painting of smears, fixation, Romanovsky staining, injector, pins, Petri-dish, solution of brilliant cresyl blue	

No	Stage of lesson	Academic time, min	Educational guide		Place holding a class
			Educational tools	Equipment	
4	Determination of the final level of knowledge and skills. Summarizing the results	15	Determination of the final level of knowledge and skills. Summarizing the results	KROK-1 tasks, situational tasks	

CHANGES IN THE TOTAL VOLUME OF BLOOD

In norm the volume of the blood is 1/13 of the body weight, i.e. 7 %.

The normal volume of the blood is called normovolemia (from the Latin word volumen – volume). In pathology there are not only the changes in the volume of the blood, but also in hematocrit without changes in the volume of the blood. Therefore normovolemia may be:

1) simple, i.e. without changes in hematocrit, when the volume of the formed elements is 43–45 %, and the volume of the plasma is 55–57 %;

2) polycythemic, i.e. with an increased number of erythrocytes, when the volume of the formed elements is 58 % and more. It is observed in transfusion of a small amount of erythrocytes, in the secondary erythrocytosis (polycythemia), when the total volume of the blood is not increased yet;

3) oligocythemic, i.e. with a decreased number of erythrocytes, when the volume of the formed elements is 35% and less – in anemias, which are not accompanied by changes in the volume of the blood, as well as in cachexia, avitaminoses.

Besides normovolemia, which is characterised by changes in hematocrit, there are the changes in the total volume of the blood: hypervolemia (plethora), an increase in the total volume of the blood, and hypovolemia (oligemia), a decrease in the total volume of the blood.

Hypervolemia and hypovolemia may be: 1) simple, i.e. with a normal plasma-erythrocyte ratio, i.e. without changes in hematocrit; 2) polycythemic – with an excess of the formed elements; 3) oligocythemic – with an excess of plasma.

Hypervolemia

1) Simple one. It may arise for a short time following transfusion of a large amount of blood, ejection of the blood from the blood depots (in the beginning of strenuous work, or under high external temperature). Plethora with a 150 % or higher increase in the mass of blood imperils the life because of disturbed circulation.

2) Polycythemic one, or true plethora (true polyemia; plethora vera). It is characterised by increased number of erythrocytes as a result of increased hematopoiesis and is observed in Vaquez's disease and in the secondary erythrocytoses (polycythemias).

3) Oligocythemic one, or hydremic plethora. It arises in retention of water as a result kidney diseases, disturbed circulation and water metabolism.

Hypovolemia

1) Simple one. It is observed in the beginning of acute hemorrhage.

2) Polycythemic, or anhydremic, one. It is observed in anhydremias and is characterised by hemoconcentration and increased viscosity of the blood.

3) Oligocythemic one. It is observed after hemorrhages in cases of increased passage of fluid from tissues into the vascular system and in certain forms of anemia, for example, pernicious anemia.

HEMORRHAGE

It is the pathologic process which is characterised by the set of pathologic and compensatory reactions to reduction in the volume of the blood and connected with it disturbance of circulation, respiration (hypoxia) and metabolism.

The cause of hemorrhage is injury of large vessel (trauma, atherosclerosis, tumor, tuberculosis, ulcer, etc.). As a condition a decrease in blood clotting is important.

Hemorrhage may be acute and chronic, external and internal. The decisive significance in the course and outcome of hemorrhage has the rate of the blood flow, the mass of blood lost and the general condition of the organism. For a healthy organism a single loss of 50–60 % of the total amount of blood is fatal.

Hemodynamic disturbances in hemorrhage

1. Reduction in the volume of the circulating blood [i.e. reduction in the mass of the blood (simple and then oligocythemic hypovolemia) plus the deposition of blood].
2. Decrease of the blood pressure.
3. Reduction in the volume of coronary blood flow.
4. Decrease of venous inflow to heart.
5. Reduction of the heart volume.
6. Tachycardia.
7. Disturbance of microcirculation.

As a result hypoxia, acidosis, shock and asphyxia are developed.

Compensatory reactions in haemorrhage

The urgent (emergency) and nonurgent reactions are distinguished.

The urgent reactions include:

1. Reflex spasm of peripheral vessels owing to irritation of pressoreceptors and activation of the vasomotor centre. It results in inflow of blood from depots, increased blood pressure and volume of the circulating blood.
2. Redistribution of blood (the vessels of heart, brain, adrenals do not constrict).
3. Restoration of the volume of the circulating blood, mainly by inflow the tissue fluid.
4. Reflex tachycardia and intensification of heart activity.
5. Reflex intensification of respiration.
6. Increased utilisation of oxygen by tissues (the shift of the curve of oxyhemoglobin dissociation left to right).
7. Increased blood clotting.

Nonurgent reactions:

1. Restoration of the protein composition of blood by mobilization of tissue resources (first 2–3 days), increased synthesis of proteins in the liver (results in normalization of protein content in the blood through 8–9 days).

2. Increased hematopoiesis. The starting factor is hypoxia which stimulates the production of erythropoietin in kidneys. It influences the generic apparatus of erythropoietin-sensitive cell and its differentiation into erythroblast and further up to mature erythrocytes. As a parameter of increased hematopoiesis is increased number of reticulocytes in the blood (on the 5-th day).

The most effective measure in hemorrhage is the transfusion of blood or blood substitutes.

CHANGES IN ERYTHROCYTES

The qualitative changes of erythrocytes

1. Degenerative forms involve the changes of colouring (content of gemoglobin), sizes and structure – hypochromic, hyperchromic and anisochromic erythrocytes, anisocytes, poikilocytes, availability inclusions, for example, Jolly bodies and Cabot's ring bodies.

2. Regenerative forms: reticulocytes, polychromatophils, normocytes.

3. Pathologic forms: megalocytes and megaloblasts. These cells are found in the blood in pernicious anemia, severe sepsis and tuberculosis.

After the ability to regeneration of blood there are regenerative, hyporegenerative and aregenerative anemias. Most anemias are regenerative. Hypo- and aregenerative forms develop in avitaminoses, intoxications, infections, chronic hemorrhages, radiation sickness.

The qualitative changes in leukocytes

Qualitative changes in leukocytes are mostly degenerative. They manifest themselves through nucleus and cytoplasm disorders.

They are:

- anisocytosis (change in the size of leukocytes);
- poikilocytosis (change in the form of leukocytes);
- absence of normal granulation;
- pathological inclusions in the cytoplasm (toxic granulosity, large azurophilic granules, basophilic bundles of cytoplasm);
- vacuolization of the nucleus and cytoplasm;
- swelling of the nucleus;
- karyorrhexis;
- hypo- and hypersegmentation of the nucleus;
- cytolysis.

Degenerative changes are caused by the influence of different pathologic factors (chemical toxins, bacteria, viruses and antibodies) that damage leukocytes in the hemopoietic organs and blood. Leukocyte metabolism disorders lead to structural anomalies.

Production of pathologic leukocytes may arise as a result of neoplastic transformation of the leukopoietic tissue in leukemia.

Structural disturbances may be genetically conditioned (e.g. hereditary PelgerHuet anomaly of granulocytes, when neutrophils have round rod-shaped or twosegment nuclei after maturation).

Erythrocytosis (polycythemia)

It is an increased number of erythrocytes in the blood. It may be relative or absolute.

Relative one is observed as a result of loss of water (hemoconcentration), rapid mobilisation of depot blood and redistribution of blood. The number of erythrocytes arises per unit of blood only.

Absolute polycythemia is characterised by an increase in the total number of erythrocytes, i.e. in hemopoiesis. It may be primary and secondary one.

The primary absolute polycythemia is so-called true polycythemia or erythremia, or Vaquez's disease. It is characterised by an increased volume of blood (true plethora). The disease is stipulated by hyperplasia of bone marrow.

The secondary absolute polycythemia is observed more often, arises as a symptom, as a rule is not accompanied by increase of volume of blood. It is developed as the compensatory reaction to hypoxia.

Setting up the experiment. Discussion the results and formulation the conclusions

- **Studying the qualitative changes of erythrocytes in experimental hemolytic anemia.**

The conduction of the experiment: take the blood from the marginal vein of the ear of the anemic and control rabbits. Prepare smears. Put the blood on the fatless subject slide. The polished slide place slopingly to the subject slide (angle of slopy is 45 degree) till the contact with the drop. When the drop of blood spills on the rim of polished slide, move it along the subject slide. The smear must be rather thin and pro-portional. Dry the smear, and then fix it in the mixture of spirit with the ether for 5 min., after that stain according to Romanovsky during 15 min. After that wash the smear by thin stream of the water and dry it. Microscope the smear. Put the drop of immersion oil on the smear and look at it under the microscope with immersion objective. Pay attention to hypochromic erythrocytes, anisocytosis, poikilocytosis, polychromatophils (erythrocytes stained by acid and basic stains, which have violet or violet-blue colour in destinction from mature erythrocytes stained in pink colour) and normoblasts erythrocytes with nuclears. Compare the content of qualitative changed erythrocytes in the blood of experimental and control rabbits.

Describe and draw the slides in details.

- **Studing the reticylocytes in experimental hemolytic anemia**

The conduction of the experiment: take the thin part of brilliant cresyl blue subject slide and mark this site by colour pencil. Make the smear of the blood and without drying quickly place it into a humid chamber (Petri-dish with humid filter paper). In 15 min. take the smear off, dry it in the air and microscope it. Erythrocytes are stained into green colour. In some of them there is

a thin dark blue net which is placed either in all cells or in its center, where the denser ball is formed. This net is called substantia reticulogranulofilamentosa. Erythrocytes with such granules are called reticulocytes. Compare the amount of reticulocytes in the blood of experimental and control rabbits.

Describe and draw the slides in details.

Discussion of the results of the experiment

Changes on the part of red blood cells are expressed primarily in changes in form, that is, a change in the quality of erythrocytes - quantity, anisocytosis, a change in color – hypochromic, hyperchromic erythrocytes; possible pathological inclusions in erythrocytes - Cabot rings, Zolla bodies.

Changes in the structure of leukocytes are also possible. List again the degenerative forms of leukocytes.

With hemolytic anemia, the release of reticulocytes from the bone marrow into the peripheral blood stream increases.

Formulation the conclusions based on the experiment

A change in the shape of blood cells – erythrocytes and leukocytes, ultimately leads to a violation of their physiological functions. A change in structure entails a change in function, which, in turn, leads to the development of pathological conditions associated with a disturbance in the blood cells themselves.

An increase in the number of reticulocytes in the peripheral blood indicates hemlytic or posthemorrhagic anemia and is a compensatory reaction of the body aimed at normalizing the number of erythrocytes.

Tasks for independent work on the topic "Changes in the total volume of the blood. Qualitative changes of erythrocytes and leukocytes. Erythrocytosis"

The student is offered to investigate the results of a clinical blood analysis of a patient with a disorder in the blood system. It is necessary to determine the signs and type of violation. Be able to explain the mechanism of occurrence. Analysis the errors with an explanation of the correct answers.

List of questions and works to be studied:

1. Violations of total amount of blood. Normovolemia. Types of a normovolemia, causes of their development.
2. Hypervolemia. Types of a hypervolemia, causes and mechanisms of development. Pathogenetic value of a hypervolemia.
3. Hypovolemia. Types of a hypovolemia, causes and mechanisms of development. Pathogenetic value of a hypovolemia.
4. Definition of the terms "blood loss", "bleeding", "hemorrhage", "hematoma". Etiology and classification of blood loss.
5. Acute blood loss. Pathogenesis. The pathological changes happening at blood loss. Protective and compensatory reactions at blood loss.
6. Qualitative changes of erythrocytes, their causes.
7. Qualitative changes of leukocytes, their causes.

List of practical skills that must be mastered:

1. Identify the regenerative forms of erythrocytes in peripheral blood smears (stained according to Romanovsky or Pappenheim), interpret their presence or absence.
2. Identify the regenerative forms of erythrocytes in stained blood smears it is vital to evaluate the value of their presence or absence in the blood.
3. Describe the degenerative forms of erythrocytes in blood smears stained by Romanovsky or Pappenheim, to interpret their presence in the blood.
4. Determine the pathological forms of erythrocytes in a smear of peripheral blood, interpret their presence in the blood.
5. Calculate the content of erythrocytes in a unit of blood volume, draw a conclusion about violation of the quantitative composition of "red" blood (anemia, erythrocytosis).

Situational tasks KROK-1 to determine the final level of knowledge

1. A 32-year-old patient was admitted to the hospital with gross blood loss due to auto accident trauma. Ps – 110 Bpm, RR – 22 pm, BP – 100/60 mm Hg. What changes in the blood will occur in an hour after the blood loss?

A. Hypovolemia. *C. Hypochromia of erythrocytes.* *E. Hypoproteinemia.*
B. Erythropenia. *D. Leukopenia.*

2. A 26-year-old pregnant woman is under treatment in hospital. After a continuous attack of vomiting she was found to have reduced volume of circulating blood. What kind of change in general blood volume is the case?

A. Polycythemic hypovolemia. *D. Simple hypovolemia.*
B. Oligocythemic hypervolemia. *E. Oligocythemic hypovolemia.*
C. Polycythemic hypervolemia.

3. In a car accident a man got injured and lost a lot of blood. What changes in peripheral blood are most likely to occur on the 2nd day after the injury?

A. Erythropenia. *C. Anisocytosis.* *E. Significant reticulocytosis.*
B. Microplania. *D. Hypochromia.*

4. On the fifth day after the acute blood loss a patient has been diagnosed with hypochromic anemia. What is the main mechanism of hypochromia development?

A. Release of immature red blood cells from the bone marrow.
B. Increased destruction of red blood cells in the spleen.
C. Increased excretion of body iron.
D. Impaired iron absorption in the intestines.
E. Impaired globin synthesis.

5. A 42 year old patient complains of pain in the epigastral area, vomiting; vomit masses have the colour of “coffee-grounds”, the patient has also melena. Anamnesis records gastric ulcer. Blood formula: erythrocytes – 2.8×10^{12}/l, leukocytes – 8×10^{9}/l, Hb – 90 g/l. What complication is it?

A. Haemorrhage. *C. Perforation.* *E. Pyloric stenosis.*
B. Penetration. *D. Canceration.*

6. A 30-year-old patient's blood test revealed the following: erythrocyte count is 6×10^{12}/l, hemoglobin is 10.55 mmol/l. Vaquez disease was diagnosed. Name the leading part of pathogenesis:

A. B12-deficiency. *C. Neoplastic erythroid hyperplasia.* *E. Acidosis.*
B. Iron-deficiency. *D. Hypoxia.*

7. As a result of increased permeability of the erythrocyte membrane in a patient with microspherocytic anaemia (Minkowsky-Shauffard disease) cells receive sodium ions and water. Erythrocytes take form of spherocytes and can be easily broken down. What is the leading mechanism of erythrocyte damage in this case?

A. Electrolytic osmotic. *C. Acidotic.* *E. Nucleic.*
B. Calcium. *D. Protein.*

8. A 32-year-old patient was delivered to the clinic with massive blood loss as a result of an accident. Ps – 110 beats/min., RR – 22 per minute, blood pressure – 100/60 mm Hg. Art. Which of the following blood changes will be the most characteristic 1 hour after blood loss?

A. Erythropenia. *C. Leucopenia.* *E. Hypovolemia.*
B. Hypochromia of erythrocytes. *D. Hypoproteinemia.*

9. In a person weighing 80 kg, after prolonged physical activity, the volume of circulating blood decreased, hematocrit – 50 %, total blood protein – 80 g/l. Such blood counts are the result, first of all:

A. Increased diuresis.
B. Increased plasma oncotic pressure.
C. Increase in the number of red blood cells.
D. Water loss through sweat.
E. Increase in blood proteins.

10. A week after massive blood loss, a patient has a large number (5 %) of regenerative forms of erythrocytes in the blood. Which ones?

A. Reticulocytes. *C. Megalocytes.* *E. Spherocyto.*
B. Megaloblasts. *D. Microcytes.*

Standards of correct answers to the task KROK-1

1	2	3	4	5	6	7	8	9	10
A	*A*	*A*	*A*	*A*	*C*	*A*	*E*	*D*	*A*

Recommendations for registration of work results

1. Written answer to test tasks (initial level of knowledge).
2. The results of the experiment are drawn up in the form of an experiment protocol with the determination of relevant conclusions.
3. Protocol for the study of the results of the patient's clinical blood analysis.
4. Protocol for solving situational tasks with an explanation of the correct answers.

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Topic 2. Anemia: definition, clinical and hematologic signs. Posthemorragic anemia

Justification of the topic: Anemia are very frequent hematologic symptoms at the diverse diseases (diseases of a digestive tract, kidneys, collagenases, infectious and parasitic diseases, malignant new growths, obstetric and gynecologic pathology, a number of endocrine diseases, a number of congenital and acquired diseases of children of early age, various intoxications, etc.). Besides, erythrocytosis and anemia can have primary character, act as an independent hematologic disease. Thus, pathophysiological mechanisms of development of erythrocytosis and the anemic states are very difficult and various. The knowledge of the main hematologic manifestations of an erythrocytosis and anemia, the reasons and mechanisms of development in each case gives the chance to the doctor to make the diagnosis, but also to plan actions for prevention and rational pathogenetic therapy of this type of pathology.

Purpose of the lesson:

General – to be able to define, using data of quantitative and qualitative changes of erythrocytes, existence of an erythrocytosis or anemic state and their character according to the available classifications.

Specifically:

Know:

1. According to number of erythrocytes to resolve an issue of existence of an erythrocytosis or anemia.
2. According to concentration of hemoglobin and a color indicator to resolve an issue of existence of anemia.
3. To classify anemias by their etiology, pathogenesis, quantitative and qualitative changes of erythrocytes and an erythropoesis, dynamics of a curse.
4. To generalize the obtained data on quantitative and qualitative changes of erythrocytes at an animal and on the basis of it to give a conclusion concerning character of anemia.

Be able to:

1. To give the characteristic of the main stages of formation of erythrocytes.
2. To know normal parameters of number of erythrocytes, concentration of hemoglobin, a color indicator and quantity of reticulocyte at the adult.
3. To define number of erythrocytes, concentration of hemoglobin, a color indicator and quantity of reticulocyte in blood.

Practical experience:

Determination of anemia in a patient based on symptoms and data hemogram, description of peripheral blood smear.

The graphological structure of the topic "Anemia: definition, clinical and hematologic signs. Posthemorragic anemia." is attached.

Material and methodological support of the topic "Anemia: definition, clinical and hematologic signs. Posthemorragic anemia.":

1. Lectures;
2. Methodical instructions for teachers;

3. Methodical instructions for students;
4. Set of test tasks to determine the basic level of knowledge;
5. Set of situational tasks to determine the final level of knowledge;
6. Set of KROK-1 tasks;
7. Set of schemes and tables (presentation);
8. Set of forms with a clinical blood test
9. Video films.

Oriented map of students' work on the topic " Anemia: definition, clinical and hematologic signs. Posthemorragic anemia"

No	Stage of lesson	Academic time, min	Educational guide		Place holding a class
			Educational tools	Equipment	
1	Determination of the initial level of knowledge	15	Written answer to test tasks	Test tasks	Study room
2	Analysis of theoretical material	50	Analysis of theoretical material based on control questions of the topic, situational tasks, tasks of KROK-1	Topic control questions, KROK-1 tasks, situational tasks	
3	Determination of the final level of knowledge and skills. Summarizing the results	25	Determination of the final level of knowledge and skills. Summarizing the results	KROK-1 tasks, situational tasks	

ANEMIA

The function of red cells is the transport of oxygen into tissues. In physiologic terms, therefore, anemia may be defined as a reduction in the oxygen transport capacity of the blood. Since in most instances the reduced oxygen-carrying capacity of blood results from a deficiency of red cells, *anemia may be defined as a reduction below normal limits of the total circulating red cell mass.* This value is not easily measured, however, and therefore anemia has been defined as a reduction below normal in the volume of packed red cells, as measured by the hematocrit, or a reduction in the hemoglobin concentration of the blood. It hardly needs pointing out that fluid retention may expand plasma volume and fluid loss may contract plasma volume, creating spurious abnormalities in clinically measured values.

As the main phenomenon in anemia serves hypoxemia and anemic hypoxia. There are paleness, dizziness, fatigue, easy tiring dyspnea, tachycardia.

The ratio between erythrocytes and hemoglobin is frequently disturbed. There are following anemias after the colour index:

1. Normochromic one – colour index is about 1. It is observed in the beginning after hemorrhage, in hemolytic anemias.

2. Hypochromic one – when the synthesis of hemoglobin is insufficient. The colour index is less than 1. It is observed in iron-deficiency anemias.

3. Hyperchromic one – colour index is more than 1 (up to 1,8). It is observed in an increased volume of erythrocytes (macrocytes, megalocytes, megaloblasts), mainly in pernicious (Addison's, Biermer's) anemia connected with a deficiency of vitamin B_{12}.

CLASSIFICATION OF ANEMIA ACCORDING TO UNDERLYING MECHANISM

Blood Loss

• Acute: trauma

• Chronic: lesions of gastrointestinal tract, gynecologic disturbances

Increased Rate of Destruction (Hemolytic Anemias)

• Intrinsic (intracorpuscular) abnormalities of red cells

Hereditary

Red cell membrane disorders

Disorders of membrane cytoskeleton: spherocytosis, elliptocytosis

Disorders of lipid synthesis: selective increase in membrane lecithin

Red cell enzyme deficiencies

Glycolytic enzymes: pyruvate kinase deficiency, hexokinase deficiency

Enzymes of hexose monophosphate shunt: G6PD, glutathione synthetase

Disorders of hemoglobin synthesis

Deficient globin synthesis: thalassemia syndromes

Structurally abnormal globin synthesis (hemoglobinopathies): sickle cell anemia, unstable hemoglobins

Acquired

Membrane defect: paroxysmal nocturnal hemoglobinuria

• Extrinsic (extracorpuscular) abnormalities

Antibody mediated

Isohemagglutinins: transfusion reactions, erythroblastosis fetalis

Autoantibodies: idiopathic (primary), drug-associated, systemic lupus erythematosus, malignant neoplasms, mycoplasmal infection

– Mechanical trauma to red cells

Microangiopathic hemolytic anemias: thrombotic thrombocytopenic purpura, disseminated intravascular coagulation

Cardiac traumatic hemolytic anemia

– Infections: malaria

– Chemical injury: lead poisoning

Sequestration in mononuclear phagocyte system: hypersplenism

Impaired Red Cell Production

• Disturbance of proliferation and differentiation of stem cells: aplastic anemia, pure red cell aplasia, anemia of renal failure, anemia of endocrine disorders

• Disturbance of proliferation and maturation of erythroblasts

• Defective DNA synthesis: deficiency or impaired use of vitamin B_{12} and folic acid (megaloblastic anemias)

• Defective hemoglobin synthesis

Deficient heme synthesis: iron deficiency

Deficient globin synthesis: thalassemias

General clinical manifestations of anemia

Anemic syndrome (pallor of the skin and visible mucous membranes and symptom, caused by hypoxia – rapid fatigue, weakness, dizziness). Syndromes due to the peculiarity of the pathogenesis of each individual type of anemia (for example, with iron-deficiency anemia, sideropenic syndrome, with B_{12}-foliodeficiency anemia – neurological disorders and damage to the gastrointestinal tract, with haemolytic anemia – jaundice).

Clinical symptoms caused by compensatory reactions aimed at hypoxia compensation (hyperventilation, tachycardia, etc.)

Hematological signs of anemia

Hematological signs of anemia are divided into quantitative and qualitative.

Quantitative hematological signs of anemia

A decrease in the number of erythrocytes in a unit of blood volume (in men, less than 4×10^{12}/l, in women and children less than 3.5×10^{12}/l).

Decreased hemoglobin concentration (in men less than 130 g/l, in women less than 120 g/l, in children under 6 years less than 110 g/l, in children older than 6 years less than 120 g/l).

Decrease in hematocrit (in men less than 43 %, in women less than 40 %).

Changes in color index (norm 0.85–1).

Qualitative hematological signs of anemia

The presence of regenerative forms of erythrocytes. Presence of degenerative changes in cells erythrocyte series. The presence of cells of pathological regeneration.

POSTHEMORRHAGIC ANEMIA

Posthemorrhagic anemia refers to a reduced number of red blood cells in the body due to bleeding.

There are two types of anemias of this group according to the character of hemorrhage:

1) acute posthemorrhagic

2) chronic posthemorrhagic anemia.

Symptoms of Posthemorrhagic anemia:

- Reduced red blood cell count, asymptomatic in mild cases, loss of appetite, pale lips, pale eyelids, weakness, fatigue, lightheadedness, tiredness, headache, early symptoms are mild, shortness of breath on exertion, pallor, concentration problems, rapid heartbeat, irregular heartbeat, chest pain, dizziness, impaired cognitive ability, cold skin, shock – severe acute cases, lactic acidosis – severe acute cases.

ACUTE BLOOD LOSS

The clinical and morphologic reactions to blood loss depend on the rate of hemorrhage and whether the blood is lost externally or internally. With acute blood loss, the alterations reflect principally the loss of blood volume

rather than the loss of hemoglobin. Shock and death may follow. If the patient survives, the blood volume is rapidly restored by shift of water from the interstitial fluid compartment. The resulting hemodilution lowers the hematocrit. Reduction in the oxygenation of tissues triggers the production of erythropoietin, and the marrow responds by increasing erythropoiesis. When the blood is lost internally, as into the peritoneal cavity, the iron can be recaptured; but if the blood is lost externally, the adequacy of the red cell recovery may be hampered by iron deficiency when insufficient reserves are present.

Soon after the acute blood loss, the red blood cells appear normal in size and color (normocytic, normochromic). However, as the marrow begins to regenerate, changes occur in the peripheral blood. *Most striking is an increase in the reticulocyte count, reaching 10 % to 15 % after 7 days.* The reticulocytes are seen as polychromatophilic macrocytes in the usual blood smear. These changes of red cell regeneration can sometimes be mistaken for an underlying hemolytic process. Mobilization of platelets and granulocytes from the marginal pools leads to thrombocytosis and leukocytosis in the period immediately after acute blood loss.

CHRONIC BLOOD LOSS

Chronic blood loss induces anemia only when the rate of loss exceeds the regenerative capacity of the erythroid precursors or when iron reserves are depleted. In addition to chronic blood loss, any cause of iron deficiency such as malnutrition, malabsorption states, or an increased demand above the daily intake as occurs in pregnancy will lead to an identical anemia, discussed later.

Tasks for independent work on the topic "Anemia: definition, clinical and hematologic signs. Posthemorragic anemia."

The student is offered to investigate the results of a clinical blood analysis of a patient with a disorder in the blood system. It is necessary to determine the signs and type of violation. Be able to explain the mechanism of occurrence. Analysis of errors with an explanation of the correct answers

List of questions and works to be studied:

1. Erythrocytosis. Definition of term, types, etiology, pathogenesis.
2. Clinical manifestations, changes in peripheral blood and marrow at an erythrocytosis.
3. Anemia. Definition of term. Classification of anemias.
4. General clinical and hematologic symptoms of anemias.
5. Posthemorrhagic anemia.

List of practical skills that must be mastered:

Determination of anemia in a patient based on symptoms and data hemogram, description of peripheral blood smear.

Situational tasks KROK-1 to determine the final level of knowledge

1. A 46-year-old female patient complaining of having alveolar haemorrhage for 6 hours after a tooth extraction, general weakness and dizziness was delivered to a hospital. The patient has a history of essential hypertension. Objectively: pale skin and mucous membranes. In blood: Hb – 80 g/l, Ht – 30 %, bleeding and coagulation time is normal. What complication had been provoked by the haemorrhage?

A. Acute posthaemorrhagic anaemia. *D. Haemolytic anaemia.*
B. Chronic posthaemorrhagic anaemia. *E. Iron deficiency anaemia.*
C. Folic acid deficiency anaemia.

2. A 42 year old patient complains of pain in the epigastral area, vomiting; vomit masses have the colour of "coffee-grounds", the patient has also melena. Anamnesis records gastric ulcer. Blood formula: erythrocytes - $2,8 \times 10^{12}$/l, leukocytes – 8×10^{9}/l, Hb – 90 g/l. What complication is it?

A. Haemorrhage. *C. Perforation.* *E. Pyloric stenosis.*
B. Penetration. *D. Canceration.*

3. A 55 y.o. woman consulted a doctor about having continuous cyclic uterine hemorrhages for a year, weakness, dizziness. Examination revealed skin pallor. Hemogram: Hb – 70 g/l, erythrocytes – $3,2 \times 10^{12}$/l, color index – 0,6, leukocytes – $6,0 \times 10^{9}$/l, reticulocytes – 1 %; erythrocyte hypochromia. What anemia is it?

A. Chronic posthemorrhagic anemia. *D. B_{12}-folate-deficiency anemia.*
B. Hemolytic anemia. *E. Iron-deficiency anemia.*
C. Aplastic anemia.

4. A 30-year-old patient's blood test revealed the following: erythrocyte count is $6 \times 10_{12}$/l, hemoglobin is 10,55 mmol/l. Vaquez's disease was diagnosed. Name the leading part of pathogenesis:

A. B_{12}-deficiency. *D. Hypoxia.*
B. Iron-deficiency. *E. Acidosis.*
C. Neoplastic erythroid hyperplasia.

5. A 38-year-old woman with gastric bleeding was brought to the admission and diagnostic department. What changes are most likely in the blood in a day?

A. Increased hematocrit. *C. Leukopenia.* *E. Leukocytosis.*
B. Decreased hematocrit. *D. Erythrocytosis.*

6. A 32-year-old patient was delivered to the clinic with massive blood loss as a result of an accident. Ps – 110 beats/min., RR – 22 per minute, blood pressure – 100/60 mm Hg. Art. Which of the following blood changes will be the most characteristic 1 hour after blood loss?

A. Erythropeniaю *C. Leucopenia.* *E. Hypovolemia.*
B. Hypochromia of erythrocytes. *D. Hypoproteinemia.*

7. Due to injury, the patient lost 25 % of the volume of circulating blood. Name the urgent mechanism for compensating for blood loss.

A. Entry of interstitial fluid into the vessels
B. Restoration of the protein composition of the blood
C. Increase in the number of reticulocytes
D. Recovery of red blood cells
E. Erythropoiesis activation

8. A general examination of the patient revealed hyperemia of all skin with a cyanotic tint. Attention is drawn to the patient's lethargy and slowing down movements. Blood analysis showed: erythrocytes 9×10^{12}/l, hematocrit 60 %. At what pathological condition is absolute erythrocytosis:

A. Megaloblastic anemia. *C. Hemodilution.* *E. Vaquez's disease.*
B. Hemoconcentration. *D. Lymphoma.*

9. On the fifth day after acute blood loss, the patient was diagnosed with hypochromic anemia. What is the main mechanism in the development of hypochromia?

A. Bone marrow supply of immature erythrocytes.
B. Intestinal iron malabsorption.
C. Increased destruction of red blood cells in the spleen.
D. Impaired synthesis of globin.
E. Increased excretion of iron from the body.

10. An ambulance delivered a 46-year-old patient to the clinic with complaints of alveolar bleeding within 6 hours after tooth extraction, general weakness, dizziness. She has a history of hypertension. Objectively: pale skin and visible mucous membranes. In the blood: Hb – 80 g/l, Ht – 30 %, indicators of bleeding time and blood clotting are within normal limits. What complication developed in the patient due to bleeding?

A. Hemolytic anemia. *D. Acute posthemorrhagic anemia.*
B. Iron deficiency anemia. *E. Chronic posthemorrhagic anemia.*
C. Folate deficiency anemia.

Standards of correct answers to the task KROK-1

1	2	3	4	5	6	7	8	9	10
A	*A*	*A*	*C*	*B*	*E*	*A*	*E*	*A*	*D*

Recommendations for registration of work results

1. Written answer to test tasks (initial level of knowledge).
2. Protocol for the study of the results of the patient's clinical blood analysis.
3. Protocol for solving situational tasks with an explanation of the correct answers.

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Topic 3. Anemia, witch duo to disturbances of erythropoiesis. Hemolytic anemia

Justification of the topic: Anemia is a very frequent hematologic symptom at the diverse diseases (diseases of a digestive tract, kidneys, collagenoses, infectious and parasitic diseases, malignant tumors, obstetric and gynecologic pathology, a number of endocrine diseases, a number of congenital and acquired diseases of children of early age, various intoxications, etc.). Besides, anemia can have primary character, act as an independent hematologic disease. Thus, pathophysiological mechanisms of development the anemic states are very difficult and various. The knowledge of the main hematologic manifestations of anemia, the causes and mechanisms of development in each case gives the chance to the doctor not only to make the diagnosis, but also to plan actions for prevention and rational pathogenetic therapy of this type of pathology.

Purpose of the lesson:

General – to be able to define, using data of quantitative and qualitative changes of erythrocytes, existence of an anemic state and character of anemias according to the available classifications.

Specifically:

Know:

1. According to number of erythrocytes, concentration of hemoglobin and a color indicator to resolve an issue of existence of anemia.
2. Characterize the possible qualitative changes of erythrocytes which are found at anemias to find their existence at blood dab microscopy of an animal with experimental anemia.
3. Classify anemias by their etiology, pathogenesis, quantitative and qualitative changes of erythrocytes and an erythropoesis, dynamics of a current.
4. Generalize the obtained data on quantitative and qualitative changes of erythrocytes at an animal and on the basis of it to give a conclusion concerning character of anemia.

Be able to:

1. To give the characteristic of the main stages of formation of erythrocytes.
2. To know normal parameters of number of erythrocytes, concentration of hemoglobin, a color indicator and quantity of retikulocyte at the adult.
3. To define number of erythrocytes, concentration of hemoglobin, a color indicator and quantity of retikulocyte in blood.
4. To prepare and paint dab of blood according to Romanovsky-Geimsa and to distinguish at its microscopy cellular elements of an erythrocyte row.

Practical experience:

1. Definition of hemoglobin amount in experimental hemolytic anemia.
2. Calculation of the number of erythrocytes in experimental hemolytic anemia.
3. Determination of anemia in a patient based on symptoms and data hemogram, description of peripheral blood smear.

The graphological structure of the topic "Anemia, witch duo to disturbances of erythropoiesis. Hemolytic anemia" is attached.

Material and methodological support of the topic "Anemia, witch duo to disturbances of erythropoiesis. Hemolytic anemia":

1. Lectures;
2. Methodical instructions for teachers;
3. Methodical instructions for students;
4. Set of test tasks to determine the basic level of knowledge;
5. Set of situational tasks to determine the final level of knowledge;
6. Set of KROK-1 tasks;
7. Set of schemes and tables (presentation);
8. Set of forms with a clinical blood test
9. Video films;
10. For the experiment (experimental animals – rabbit, microscopes, immersion oil, Vidal's tubes, injectors, micropipets, 5,0 ml pipets, 10 % sol. Natrium chloridum, calculating chamber, hemometers, injectors, 0,1 % hydrochloric acid solution, distill water.).

Oriented map of students' work on the topic "Anemia, witch duo to disturbances of erythropoiesis. Hemolytic anemia"

No	Stage of lesson	Academic time, min	Educational guide		Place holding a class
			Educational tools	Equipment	
1	Determination of the initial level of knowledge	10	Written answer to test tasks	Test tasks	Study room
2	Analysis of theoret-ical material	35	Analysis of theoretical material based on control questions of the topic, situational tasks, tasks of KROK-1	Topic control questions, KROK-1 tasks, situational tasks	
3	Practical part (conduct experiment)	30	Introduction and preparation for setting up the experiment. Setting up the experiment. Discussion of the results of the experiment and formulation of conclusions	Microscopes, Vidal's tubes, injectors, micropipets, 5,0 ml pipets, 10 % sol. Natrium chloridum, calculating chamber, hemometers, injectors, 0,1 % hydrochloric acid solution, distill water	
4	Determination of the final level of knowledge and skills. Summarizing the results	15	Determination of the final level of knowledge and skills. Summarizing the results	KROK-1 tasks, situational tasks	

CLASSIFICATION OF ANEMIA ACCORDING TO UNDERLYING MECHANISM

Blood Loss

- Acute: trauma
- Chronic: lesions of gastrointestinal tract, gynecologic disturbances

Increased Rate of Destruction (Hemolytic Anemias)

• Intrinsic (intracorpuscular) abnormalities of red cells

Hereditary

Red cell membrane disorders

Disorders of membrane cytoskeleton: spherocytosis, elliptocytosis

Disorders of lipid synthesis: selective increase in membrane lecithin

Red cell enzyme deficiencies

Glycolytic enzymes: pyruvate kinase deficiency, hexokinase deficiency

Enzymes of hexose monophosphate shunt: G6PD, glutathione synthetase

Disorders of hemoglobin synthesis

Deficient globin synthesis: thalassemia syndromes

Structurally abnormal globin synthesis (hemoglobinopathies): sickle cell anemia, unstable hemoglobins

Acquired

Membrane defect: paroxysmal nocturnal hemoglobinuria

• Extrinsic (extracorpuscular) abnormalities

Antibody mediated

Isohemagglutinins: transfusion reactions, erythroblastosis fetalis

Autoantibodies: idiopathic (primary), drug-associated, systemic lupus erythematosus, malignant neoplasms, mycoplasmal infection

✓ Mechanical trauma to red cells

Microangiopathic hemolytic anemias: thrombotic thrombocytopenic purpura, disseminated intravascular coagulation

Cardiac traumatic hemolytic anemia

✓ Infections: malaria

✓ Chemical injury: lead poisoning

Sequestration in mononuclear phagocyte system: hypersplenism

Impaired Red Cell Production

• Disturbance of proliferation and differentiation of stem cells: aplastic anemia, pure red cell aplasia, anemia of renal failure, anemia of endocrine disorders

• Disturbance of proliferation and maturation of erythroblasts

• Defective DNA synthesis: deficiency or impaired use of vitamin B_{12} and folic acid (megaloblastic anemias)

• Defective hemoglobin synthesis

Deficient heme synthesis: iron deficiency

Deficient globin synthesis: thalassemias

Anemias of Diminished Erythropoiesis

Diminished erythropoiesis may result from a deficiency of some vital substrate necessary for red cell formation. Included in this group are anemia of vitamin B_{12} and folate deficiency, characterized by defective DNA synthesis (megaloblastic anemias), and iron deficiency anemias, in which heme synthesis is impaired. Other causes of decreased erythropoiesis include anemia of

chronic disease and "marrow stem cell failure," which embraces such conditions as aplastic anemia, pure red cell aplasia, and anemia of renal failure.

MEGALOBLASTIC ANEMIAS

The following discussion attempts first to characterize the major features of these anemias and then to discuss the two principal types of megaloblastic anemia: (1) pernicious anemia, the major form of vitamin B12 deficiency anemia,

(2) folate deficiency anemia.

The megaloblastic anemias constitute a diverse group of entities, having in common impaired DNA synthesis and distinctive morphologic changes in the blood and bone marrow. As the name implies, the erythroid precursors and erythrocytes are abnormally large, thought to be related to defective cell maturation and division. The precise basis of these changes is not fully understood.

Because of these maturational derangements, there is an accumulation of megaloblasts in the bone marrow, yielding too few erythrocytes; hence, the anemia. Two concomitant processes further aggravate the anemia:

(1) ineffective erythropoiesis

(2) increased hemolytic destruction of red cells. Ineffective erythropoiesis results from intramedullary destruction of megaloblasts, which undergo autohemolysis more readily than do normoblasts and are more vulnerable to phagocytosis by mononuclear phagocytic cells in the morrow than are normal erythroid precursors. Premature destruction of granulocytic and platelet precursors also occurs, resulting in leukopenia and thrombocytopenia. The basis of the increased hemolysis of the mature erythrocytes is not entirely clear. Both an intracorpuscular defect, related perhaps to the defective red cells, and a poorly characterized plasma factor are believed to contribute. As in other hemolytic states, accelerated destruction of the red cells may lead to anatomic signs of mild to moderate iron overload after several years.

Anemias of Vitamin B12 Deficiency: Pernicious Anemia

As mentioned at the outset, pernicious anemia is an important cause of vitamin B12 deficiency. The feature that sets pernicious anemia apart from the other vitamin B12 deficiency megaloblastic anemias is the cause of the vitamin B12 malabsorption: atrophic gastritis with failure of production of intrinsic factor.

It is well to discuss first the economy of vitamin B12 in the body to place pernicious anemia in perspective relative to the other forms of vitamin B12 deficiency anemia.

Etiology of Vitamin B12 Deficiency.

Vitamin B12 is a complex organometallic compound known as cobalamin. Under normal circumstances, humans are totally dependent on dietary animal products for their vitamin B12 requirement. Microorganisms are the ultimate origin of cobalamin in the food chain. Plants and vegeta-bles contain little cobalamin save that contributed by microbial contamination;

strictly vegetarian or macrobiotic diets, then, do not provide adequate amounts of this essential nutrient. The daily requirement is of the order of 2 to 3 mg, and the normal balanced diet contains significantly larger amounts. The reserves in the body, when fully maintained, are sufficient for years.

CAUSES OF MEGALOBLASTIC ANEMIA

• Vitamin B12 Deficiency

– Decreased intake

Inadequate diet, vegetarianism

– Impaired absorption

Intrinsic factor deficiency

Pernicious anemia

Gastrectomy

Malabsorption states

Diffuse intestinal disease, e.g., lymphoma, systemic sclerosis

Ileal resection, ileitis

Competitive parasitic uptake

Fish tapeworm infection

– Bacterial overgrowth in blind loops and diverticula of bowel

– Increased requirement

Pregnancy, hyperthyroidism, disseminated cancer

• Folic Acid Deficiency

– Decreased intake

Inadequate diet—alcoholism, infancy

– Impaired absorption

Malabsorption states

Intrinsic intestinal disease

Anticonvulsants, oral contraceptives

– Increased loss

Hemodialysis

– Increased requirement

Pregnancy, infancy, disseminated cancer, markedly increased hematopoiesis

– Impaired use

Folic acid antagonists

Unresponsive to Vitamin B_{12} or Folic Acid Therapy

Metabolic inhibitors, e.g., mercaptopurines, fluorouracil, cytosine

Unexplained disorders

Clinical Course. Pernicious anemia is characteristically insidious in onset, so that by the time the patient seeks medical attention, the anemia is usually marked. The usual course is progressive unless it is halted by therapy.

Diagnostic features include:

(1) a moderate to severe megaloblastic anemia;

(2) leukopenia with hypersegmented granulocytes;

(3) mild to moderate thrombocytopenia;

(4) neurologic changes related to involvement of the posterolateral spinal tracts;

(5) achlorhydria even after histamine stimulation;

(6) inability to absorb an oral dose of cobalamin (assessed by urinary excretion of radiolabeled cyanocobalamin given orally, called the Schilling test);

(7) low serum levels of vitamin B_{12};

(8) excretion of methylmalonic acid in the urine; and

(9) a striking reticulocytic response and improvement in hematocrit levels after parenteral administration of vitamin B_{12}.

Serum antibodies to IF are highly specific for pernicious anemia. Their presence attests to the cause of B_{12} deficiency, rather than the presence or absence of cobalamin deficiency.

Anemia of Folate Deficiency

A deficiency of folic acid, more properly pteroylmonoglutamic acid, results in a megaloblastic anemia having the same characteristics as those encountered in vitamin B_{12} deficiency. However, the neurologic changes seen in vitamin B_{12} deficiency do not occur.

IRON DEFICIENCY ANEMIA

An iron deficiency may result from

(I) dietary lack,

(2) impaired absorption,

(3) increased requirement,

(4) chronic blood loss.

Dietary lack is a rare cause of iron deficiency in industrialized countries having abundant food supplies (including meat) *and* where about two thirds of the dietary iron is in the readily assimilable heme form. The situation is different in developing countries, where food is less abundant and diets are predominantly vegetarian, containing poorly absorbable inorganic iron. Despite the availability of iron, dietary inadequacy is still encountered in privileged societies under the following circumstances:

• *The elderly* often have restricted diets with little meat for economic reasons or because of poor dentition.

• *The very poor,* often minority group individuals, are at risk for obvious reasons.

• *Infants* are also at high risk because the diet, predominantly milk, contains very small amounts of iron. Human breast milk, for example, provides only about 0.3 mg/liter of iron, which, however, has better bioavailability than cow's milk, which contains about twice as much iron but has poor bioavailability.

• *Children,* especially during the early years of life, have a critical need for dietary iron to accommodate growth and expansion of the blood volume.

Impaired absorption is encountered in sprue, other causes of intestinal steatorrhea, and chronic diarrhea. Gastrectomy impairs iron absorption by decreasing hydrochloric acid and transit time through the duodenum. Specific items in the diet, as is evident from the preceding discussion, may also affect absorption.

Increased requirement is an important potential cause of iron deficiency. Growing infants and children, adolescents, and premenopausal (particularly pregnant) women have a much greater requirement for iron than do non-menstruating adults. Particularly at risk are economically deprived women having multiple, frequent pregnancies.

Chronic blood loss is the most important cause of iron deficiency in the Western world. Bleeding within the tissues or cavities of the body may be followed by total recovery and recycling of the iron. However, external hemorrhage depletes the reserves of iron. Such depletion may occur from the gastrointestinal tract (e.g., peptic ulcers, hemorrhagic gastritis, gastric carcinoma, colonic carcinoma, hemorrhoids, or hookworm or pinworm disease), from the urinary tract (e.g., renal, pelvic, or bladder tumors), or from the genital tract (e.g., menorrhagia, uterine cancer).

When all the potential causes of an iron deficiency are taken into consideration, deficiency in adult men and postmenopausal women in the Western world should be considered to be caused by gastrointestinal blood loss until proven otherwise. To prematurely ascribe an iron lack in such individuals to any of the other possible origins is to run the risk of missing an occult gastrointestinal cancer or other bleeding lesion.

Whatever the basis, iron deficiency induces a hypochromic microcytic anemia. Simultaneously, depletion of essential iron-containing enzymes in cells throughout the body may cause other changes, including koilonychia, alopecia, atrophic changes in the tongue and gastric mucosa, and intestinal malabsorption. These changes are seen in patients with severe and long-standing iron deficiency.

Uncommonly, esophageal webs may appear, to complete the triad of major findings in the *Plummer-Vinson syndrome:*

(1) microcytic hypochromic anemia,

(2) atrophic glossitis,

(3) esophageal webs.

ANEMIA OF CHRONIC DISEASE

The chronic illnesses associated with this form of anemia can be grouped into three categories:

- Chronic microbial infections, such as osteomyelitis, bacterial endocarditis, and lung abscess
- Chronic immune disorders, such as rheumatoid arthritis and regional enteritis
- Neoplasms, such as Hodgkin disease and carcinomas of the lung and breast

APLASTIC ANEMIA

This somewhat misleading term is applied to pancytopenia characterized by

(1) anemia,

(2) neutropenia,

(3) thrombocytopenia.

The basis for these changes is a failure or suppression of multipotent myeloid stem cells, with inadequate production or release of the differentiated cell lines.

MAJOR CAUSES OF APLASTIC ANEMIA

- Acquired
- Idiopathic

Primary stem cell defect
Immune mediated

- Chemical agents

Dose related
Idiosyncratic
Physical agents (e.g., whole-body irradiation)

- Viral infections

Non-A, non-B hepatitis
Cytomegalovirus infections
Epstein-Barr virus infections
Herpes varicella-zoster

- Miscellaneous

Infrequently, many other drugs and chemicals

Inherited – Fanconi anemia

Aplastic anemia may occur at any age and in either sex. The onset is usually gradual, but in some cases the disorder strikes with suddenness and great severity. The initial manifestations vary somewhat, depending on the cell line predominantly affected. Anemia may cause the progressive onset of weakness, pallor, and dyspnea. Petechiae and ecchymoses may herald thrombocytopenia. Granulocytopenia may manifest itself only by frequent and persistent minor infections or by the sudden onset of chills, fever, and prostration. *Splenomegaly is characteristically absent, and if it is present, the diagnosis of aplastic anemia should be seriously questioned.* The red cells are typically normocytic and normochromic, although slight macrocytosis is occasionally present; *reticulocytosis is absent.*

Hemolytic Anemias

The hemolytic anemias are characterized by the following features:

- Shortening of the normal red cell life span, that is, premature destruction of red cells
- Accumulation of the products of hemoglobin catabolism
- A marked increase in erythropoiesis within the bone marrow, in an attempt to compensate for the loss of red cells

These and some other general features are briefly discussed before we describe the features of specific hemolytic anemias.

As is well known, the physiologic destruction of senescent red cells takes place within the mononuclear phagocytic cells of the spleen. In hemolytic anemias, too, the premature destruction of red cells occurs predominantly within the mononuclear phagocyte system (extravascular hemolysis). In only a few cases does lysis of red cells within the vascular compartment (intravascular hemolysis) predominate.

Intravascular hemolysis occurs when normal erythrocytes are damaged by mechanical injury, complement fixation to red cells, or exogenous toxic factors. Trauma to red cells may be caused by mechanical cardiac valves or by thrombi within the microcirculation. Complement fixation may occur on antibody-coated cells during transfusion of mismatched blood. Toxic injury is exemplified by falciparum malaria and clostridial sepsis.

Whatever the mechanism, *intravascular hemolysis is manifested by*

(1) hemoglobinemia,

(2) hemoglobinuria,

(3) methemalbuminemia,

(4) jaundice,

(5) hemosiderinuria.

When hemoglobin escapes into the plasma, it is promptly bound by an α_2-globulin (haptoglobin) to produce a complex that prevents excretion into the urine, since the complexes are rapidly cleared by the reticuloendothelial system. A *decrease in serum haptoglobin level is characteristically seen in all cases of intravascular hemolysis.*

HEREDITARY SPHEROCYTOSIS (HS)

This inherited disorder is characterized by an intrinsic defect in the red cell membrane that renders erythrocytes spheroidal, less deformable, and vulnerable to splenic sequestration and destruction. The spheroidal shape of the erythrocyte appears to result from a fundamental defect in the skeleton of the red cell membrane.

Clinical Course. The characteristic clinical features are anemia, splenomegaly, and jaundice. In a minority of patients, HS presents at birth with marked jaundice, requiring exchange transfusion. In 20 % to 30 % of patients, the disease is largely asymptomatic because the mild red cell destruction is readily compensated for by increased erythropoiesis. In most, however, this compensatory reaction is outpaced and hence the patients have a chronic hemolytic anemia, usually of mild to moderate severity. This more or less stable clinical course may be punctuated by an *aplastic crisis*. It is characterized by temporary suppression of red cell production, manifested by sudden worsening of the anemia and the disappearance of reticulocytes from the peripheral blood. Transfusions may be necessary to support the patient, but eventually the crisis remits in most instances. A "hemolytic crisis" resulting from accelerated red cell destruction is seen in some patients, but clinically it is less significant than the aplastic crisis. Gallstones, found in many patients, may also produce symptoms. Diagnosis of HS is based on family history, hematologic findings, and laboratory evidence of spherocytosis manifested by osmotic fragility. In two thirds of the patients, the spherocytes are particularly vulnerable to *osmotic lysis*, induced in vitro by solutions of hypotonic salt, since there is little margin for expansion of red cell volume without rupture. Cellular dehydration, resulting perhaps from membrane injury, is manifested by increased mean cell hemoglobin concentration.

SICKLE CELL DISEASE

Sickle cell disease is the prototype of *hereditary hemoglobinopathies, characterized by the production of a structurally abnormal hemoglobin.* Hemoglobin, as you recall, is a tetramer of four globin chains comprising two pairs of similar chains, each with its own heme group.

Clinical Course.

From the description of the disease to this point, it is evident that these patients are beset with problems stemming from

(1) severe anemia,

(2) vaso-occlusive complications,

(3) chronic hyperbilirubinemia. Increased susceptibility to infections is another threat, the basis of which is multifactorial:

(1) splenic function is impaired because erythrophagocytosis interferes with the ability of the spleen to clear bacteria;

(2) in later stages, total splenic fibrosis removes an important filter of blood-borne microorganisms;

(3) defects in the alternative complement pathway impair opsonization of encapsulated bacteria such as pneumococci and *Haemophilus influenzae.* Septicemia and meningitis caused by these two organisms are the most common causes of death in children with sickle cell anemia.

Diagnosis is usually readily made from the clinical findings and the appearance of the peripheral blood smear. It can be confirmed by various tests for sickling that, in general, are based on mixing a blood sample with an oxygen-consuming reagent, such as metabisulfite, to induce sickling.

THALASSEMIA SYNDROMES

The thalassemia syndromes are a heterogeneous group of mendelian disorders, all characterized by a lack of or decreased synthesis of either the α- or β-globin chain of HbA ($\alpha_2\beta_2$). β-Thalassemia is characterized by deficient synthesis of the β chain, whereas α-thalassemia is characterized by deficient synthesis of the α chain. The hematologic consequences of diminished synthesis of one globin chain derive not only from the low intracellular hemoglobin (hypochromia) but also from the relative excess of the other chain. For example, in β-thalassemia, there is an excess of α chains. As a consequence, free α chains tend to aggregate into insoluble inclusions within erythrocytes and their precursors, causing premature destruction of maturing erythroblasts within the marrow (ineffective erythropoiesis) as well as lysis of mature red cells in the spleen (hemolysis).

IMMUNOHEMOLYTIC ANEMIA

Hemolytic anemias in this category are caused by extra-corpuscular mechanisms. Although these disorders are commonly referred to as auto-immune hemolytic anemias, the designation *immunohemolytic anemias* is preferred because in some instances the immune reaction is initiated by drug ingestion.

CLASSIFICATION OF IMMUNE HEMOLYTIC ANEMIAS

Warm Antibody Type

The antibody is of the IgG type, does not usually fix complement, and is active at 37 °C.

- *Primary* or idiopathic
- *Secondary* to

Lymphomas and leukemias

Other neoplastic diseases

Autoimmune disorder (particularly systemic lupus erythematosus)

Drugs

Cold Agglutinin Type

The antibodies are IgM and are most active in vitro at 0 to 4 °C. Antibodies dissociate at 30 °C or above. The antibody fixes complement at warmer temperatures, but agglutination of cells by IgM and complement occurs only in the peripheral cool parts of the body.

Acute (mycoplasmal infection, infectious mononucleosis)

Chronic

Idiopathic

Associated with lymphoma

Cold Hemolysins (Paroxysmal Cold Hemoglobinuria)

Setting up the experiment. Discussion of results and formulation of conclusions

- **Calculation of the number of erythrocytes in experimental hemolytic anemia**

Take two rabbits before practical lesson daily one of them under control of hemoglobin was injected under skin 1% sol. phenylhydrasin in increased dose: 1 injection – 0,25 ml; 2 – 0,5 ml; 3 – 0,75 ml; 4 – 1 ml.

Take 0,02 ml of blood by micropipete from marginal vein of ear and blow off into Vidal's tube with 3,98 ml one per cent of hydrochloric natrium solution.

After 3 times the washing of pipet shake up mixture carefully. By pipet for distill water from hemometer get the drop of mixture into calculating chamber. Calculate erythrocytes in 5 big (that is in 80 small) squares of Goryajev' net. By number of erythrocytes in 5 big squares calculate their numbers in 1 mkl of blood. Use the formula for calculation

$$X = \frac{A \times 4000 \times B}{C},$$

Where X – the number of erythrocytes;

A – the sum of erythrocytes, calculated in 5 big squares;

C – the number of calculated small squares (80);

B – the blood dilution (in 200 times);

4000 – multiplier, which brings the volium of the liquid in limits of small square (1/4000 mkl) to 1 mkl.

Calculate the number of erythrocytes for 1 L.

Compare the amount of erythrocytes of experimental and normal rabbits.

• **The definition of hemoglobin amount in experimental hemolytic anemia**

Investigate experimental and normal rabbits. Pour 0,1 N of hydrochloric acid into a middle tube of hemometer to the mark of 2 on the scale × 10 g/l. Then by the pipete from the hemometer fill 0,02 ml blood, wipe the end by cotton with great care, gently blow the blood into the tube, wash the pipete by solution twice. After 5 min. dilute the mixture by distill water till the color of solution in the tube will not corresponde with the colour of standart hydrochloric hematin solution.

Mark the figure on the lower level of meniskas on the tube which then must be multiplied by 10 to define hemoglobin in g/l.

Define the colour index according to the formula:

$$C.I. = \frac{\text{founded amount of hemoglobin}}{\text{normal amount of hemoglobin}} : \frac{\text{ounded amount of erythrocytes}}{\text{normal amount of erythrocytes}}$$

Compare the amount of hemoglobin and colour index in anemia and normal rabbits.

Discussion of the results of the experiment

Changes on the part of blood in anemia include: a possible change in blood volume, a decrease in erythrocytes, a change in the composition of erythrocyte forms in connection with a possible compensatory change in erythropoiesis, changes in the quality of erythrocytes themselves; decrease in hemoglobin content, its qualitative changes.

Formulation of conclusions based on the experiment

Hemolytic anemias are erythroblastic, regenerative, normo- or hypochromic (rarely hyperchromic). Degenerative and regenerative forms are revealed. In hereditary forms of anemia, enhanced regeneration of the erythrocyte sprout is noted, but often with ineffective erythropoiesis, when the nuclear forms of erythrocytes are destroyed in the bone marrow. Hyporegenerative anemia may develop with frequent hemolytic crises.

Tasks for independent work on the topic " Anemia, witch duo to disturbances of erythropoiesis. Hemolytic anemia."

The student is offered to investigate the results of a clinical blood analysis of a patient with a disorder in the blood system. It is necessary to determine the signs and type of violation. Be able to explain the mechanism of occurrence. Analysis of errors with an explanation of the correct answers.

List of questions and works to be studied:

1. Iron deficiency anemia. Etiology, pathogenesis, leading clinical syndromes.
2. B_{12}-and anemia of folic acid deficiency. Etiology, pathogenesis, leading clinical syndromes.
3. Hypoplastic (aplastic) anemias. Etiology, pathogenesis, leading clinical syndromes.
4. Haemolytic anemias. Classification. Main clinical syndromes.

5. Intravascular hemolysis of erythrocytes. Causes, mechanisms. The changes developing in an organism owing to an intravascular hemolysis. Clinical and laboratory signs of an intravascular hemolysis.

6. Intracellular hemolysis of erythrocytes. Reasons, mechanisms. The changes developing in an organism owing to an intracellular hemolysis. Clinical and laboratory signs of an intracellular hemolysis.

7. Hereditary haemolytic anemias. Fermentopathy. Hemoglobinopathy. Membranopathy.

8. The acquired haemolytic anemias. Causes and mechanisms of development.

List of practical skills that must be mastered:

1. Definition of hemoglobin amount in experimental hemolytic anemia.
2. Calculation of the number of erythrocytes in experimental hemolytic anemia.
3. Determination of anemia in a patient based on symptoms and data hemogram, description of peripheral blood smear.
4. Determination of anemia in a patient based on symptoms and data hemogram, description of peripheral blood smear.

Situational tasks KROK-1 to determine the final level of knowledge

1. A 58-year-old female patient complains of rapid fatigability, performance decrement, sleepiness, dyspnea during fast walking. In blood: RBCs – $4{,}0 \times 10^{12}$/l, Hb – 80 g/l, CI – 0,6; alurge number of annulocytes and microcytes. What anaemia are these presentations typical for?

A. Iron-deficient. *C. Sickle-cell.* *E. Haemolytic.*
B. Posthemorrhagic. *D. Pernicious.*

2. A 15 year old girl has pale skin, glossitis, gingivitis. Blood count: erythrocytes – $3{,}3 \times 10^{12}$/l, hemoglobin – 70 g/l, colour index – 0,5. Examination of blood smear revealed hypochromia, microcytosis, poikilocytosis. What type of anemia is it?

A. B_{12}-folic acid-deficient. *C. Iron-deficient.* *E. Thalassemia.*
B. Sickle-cell. *D. Hemolytic.*

3. Patient with hypochromic anemia has splitting hair and loss of hair, increased nail brittling and taste alteration. What is the mechanism of the development of these symptoms?

A. Deficiency of iron-containing enzymes.
B. Deficiency of vitamin B_{12}.
C. Decreased production of parathyrin.
D. Deficiency of vitamin A.
E. Decreased production of thyroid hormones.

4. 2 years ago a patient underwent resection of pyloric part of stomach. He complains of weakness, periodical dark shadows beneath his eyes, dyspnea. In blood: Hb – 70 g/l, erythrocytes – $3{,}0 \times 10^{12}$/l, colour index – 0,7. What changes of erythrocytes in blood smears are the most typical for this condition?

A. Megalocytes. *C. Schizocytes.* *E. Macrocytes.*
B. Microcytes. *D. Ovalocytes.*

5. A patient is diagnosed with iron-deficiency sideroachrestic anemia, progression of which is characterized by skin hyperpigmentation, pigmentary cirrhosis, heart and pancreas affection. Iron level in the blood serum is increased. What disorder of iron metabolism causes this disease?

A. Excessive iron intake with food.
B. Disorder of iron absorption in bowels.
C. Failure to assimilate iron leading to iron accumulation in tissues.
D. Increased iron assimilation by body.
E. –.

6. A 37-year-old female patient complains of headache, vertigo, troubled sleep, numbness of limbs. For the last 6 years she has been working at the gas-discharge lamp-producing factory in the lead-processing shop. Blood test findings: low hemoglobin and RBC level, serum iron concentration exceeds the norm by several times. Specify the type of anemia:

A. Iron-deficiency anemia. *D. Iron refractory anemia.*
B. Minkowsky-Shauffard disease. *E. Metaplastic anemia.*
C. Hypoplastic anemia.

7. A year after subtotal stomach resection on account of ulcer of lesser curvature the following blood changes were revealed: anemia, leukocytopenia and thrombocytopenia, color index – 1,3, megaloblasts and megalocytes. What factor deficiency caused the development of those pathology?

A. Castle's factor. *C. Mucin.* *E. Gastrin.*
B. Hydrochloride acid. *D. Pepsin.*

8. Blood test of a patient suffering from atrophic gastritis gave the following results: RBCs – $2,0 \times 10^{12}$/l, Hb – 87 /l, colour index –1,3, WBCs – $4,0 \times 10^{9}$/l, thrombocytes – 180×10^{9}/l. Anaemia might have been caused by the following substance deficiency:

A. Vitamin K. *B. Iron.* *C. Vitamin A.* *D. Zinc.* *E. Vitamin B_{12}.*

9. A 50-year-old patient has been examined by a dentist and found to have crimson smooth tongue. Blood analysis revealed a decrease in RBC level and hemoglobin concentration, colour index of 1,3, symptoms of megaloblastic hematopoiesis, degenerative changes in WBCs. What blood disorder was found in this patient?

A. . Hemolytic anemia *D. Iron deficiency anemia.*
B. B_{12}-folic-acid-deficiency anemia. *E. Aplastic anemia.*
C. Myeloid leukemia.

10. A 56 year old man was taken to the hospital with complaints of general weakness, pain and burning in the region of tongue, extremity numbness. In the past, he had resection of cardiac part of ventricle. Blood test: Hb – 80 g/L; RBC – $2,0 \times 10^{12}$/L; colour index of blood – 1,2; leukocytes – $3,5 \times 10^{9}$/L. What type of anemia is it?

A. B_{12} folic-deficient. *C. Posthemorrhagic.* *E. Iron-deficient.*
B. Hemolytic. *D. Aplastic.*

11. A 56 year old patient came to a hospital with complaints about general weakness, tongue pain and burning, sensation of limb numbness. In the past, he underwent resection of fore stomach. In blood: Hb – 80 g/l; erythrocytes – $2,0 \times 10^{12}$/l; colour index – 1,2, leukocytes – $3,5 \times 10^{9}$/l. What anemia type is it?

A. B_{12}-folate deficient. *C. Posthemorrhagic.* *E. Iron-deficient.*
B. Hemolytic. *D. Aplastic.*

12. Examination of a 52-year-old female patient has revealed a decrease in the amount of red blood cells and an increase in free hemoglobin in the blood plasma (hemoglobinemia). Color index is 0.85. What type of anemia is being observed in the patient?

A. Acquired hemolytic. *D. Chronic hemorrhagic.*
B. Hereditary hemolytic. *E. Anemia due to diminished erythropoiesis.*
C. Acute hemorrhagic.

13. A 19 year old patient was diagnosed with chronic acquired hemolytic anemia. What is the leading pathogenetic mechanism of this pathology's development?

A. Toxic hemolysis. *D. Hyposmolarity of plasma.*
B. Intracellular hemolysis. *E. Osmotic hemolysis .*
C. Autoimmune hemolysis.

14. Substitution of the glutamic acid on valine was revealed while examining initial molecular structure. For what inherited pathology is this typical?

A. Sickle-cell anemia. *D. Favism.*
B. Thalassemia. *E. Hemoglobinosis.*
C. Minkowsky-Shauffard disease.

15. A 19-year-old female patient has had low haemoglobin rate of 90–95 g/l since childhood. Blood count results obtained after hospitalization are as follows: erythrocytes – $3,2 \times 10^{12}$/l, Hb – 85 g/l, colour index – 0,78; leukocytes – $5,6 \times 10^{9}$/l, platelets – 210×10^{9}/l. Smear examination revealed anisocytosis, poikilocytosis and target cells. Reticulocyte rate is 6 %. Iron therapy was ineffective. What blood pathology corresponds with the described clinical presentations?

A. Membranopathy. *C. Sickle-cell anemia.* *E. Enzymopathy.*
B. Favism. *D. Thalassemia.*

16. A 25 year old Palestinian woman complains of weakness, dizziness, dyspnea. In anamnesis: periodically exacerbating anemia. In blood: Hb – 60 g/l, erythrocytes – $2,5 \times 0^{12}$/l, reticulocytes – 35 ‰, anisocytosis and poikilocytosis of erythrocytes, a lot of target cells and polychromatophils. What type of anemia is it?

A. Sickle-cell anemia. *D. Addison-Biermer disease .*
B. Thalassemia. *E. Glucose 6-phosphate dehydrogenase-defi-cient anemia.*
C. Minkowsky-Shauffard disease.

17. A 34 year old woman was diagnosed with hereditary microspherocytic hemolytic anemia (Minkowsky-Shauffard disease). What mechanism caused haemolysis of erythrocytes?

A. Membranopathy.
B. Enzymopathy.
C. Hemoglobinopathy.
D. Autoimmune disorder.
E. Bone marrow hypoplasia.

18. As a result of increased permeability of the erythrocyte membrane in a patient with microspherocytic anaemia (Minkowsky-Shauffard disease) cells receive sodium ions and water. Erythrocytes take form of spherocytes and can be easily broken down. What is the leading mechanism of erythrocyte damage in this case?

A. Calcium.
B. Acidotic.
C. Protein.
D. Electrolytic osmotic.
E. Nucleic.

Standards of correct answers to the task KROK-1

1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
A	*C*	*A*	*B*	*C*	*D*	*A*	*E*	*B*	*A*	*A*	*A*	*C*	*A*	*D*	*B*	*A*	*D*

Recommendations for registration of work results

1. Written answer to test tasks (initial level of knowledge).
2. The results of the experiment are drawn up in the form of an experiment protocol with the determination of relevant conclusions.
3. Protocol for the study of the results of the patient's clinical blood analysis.
4. Protocol for solving situational tasks with an explanation of the correct answers.

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Topic 4. Leukocytosis. Leukopenia

Justification of the topic: Idea of quantity of leukocytes, a ratio of their separate forms in peripheral blood, and also features of their qualitative changes has huge diagnostic value for the doctor of any profile. First of all, it concerns the symptomatic changes of leucocyte composition of peripheral blood studying of which is an integral part of laboratory researches at any pathology. The accounting of these indicators in dynamics of development of a disease and its treatment very often plays an important role in determination of efficiency of treatment and the forecast of a disease. Thus, knowledge of the causes, mechanisms of emergence and development of symptomatic changes of leucocyte composition of blood, their features at different pathological processes and diseases are necessary for the doctor of any specialty.

Purpose of the lesson:

General – to be able to understand the main symptomatic quantitative and qualitative changes of leucocyte composition of blood in the conditions of pathology, to know the possible causes and mechanisms of their emergence and development, to interpret changes of these data in diagnostic and predictive aspects of different types of pathology.

Specifically:

Know:

1. To distinguish from pathological positions symptomatic changes of leucocyte composition of peripheral blood at system forms of its pathology.
2. To give the characteristic to forms of changes of leucocyte composition of blood of symptomatic character, to explain their causes, the mechanism of development and to give classification.
3. To estimate data of changes of quantity of leukocytes and a leucocyte formula at various pathological processes and diseases, to be able to prove their diagnostic and predictive value.

Be able to:

1. To know the main stages of a leucopoesis and to have idea about normal leukocyte formula.
2. To make calculation of quantity of leucocytes and to know limits of normal fluctuations of this indicator in blood at the human.
3. To prepare and paint blood dab according to Romanovsky-Giemsa, nobility and distinguish (at its microscopy) different forms of leukocytes, to be able to count them and to count absolute number of each type of leucocytes.

Practical experience:

1. To prepare and color a blood smear according to Romanovsky-Giems, to know and recognize (with its microscopy) different forms of leukocytes, to be able to count them and calculate the absolute number of each type of leukocytes.
2. Count the number of leukocytes and know the limits of normal fluctuations of this indicator in the blood of a person.
3. Distinguish symptomatic changes in the leukocyte composition of peripheral blood from general pathological conditions in systemic forms of its pathology.

4. To characterize the forms of symptomatic changes in the leukocyte composition of blood, to explain their causes, the mechanism of development, and to give a classification.

5. To evaluate data on changes in the number of leukocytes and leukocyte formula in various pathological processes and diseases, to be able to justify their diagnostic and prognostic value.

The graphological structure of the topic "Leukocytosis. Leukopenia." is attached.

Material and methodological support of the topic " Leukocytosis. Leukopenia.":

1. Lectures;
2. Methodical instructions for teachers;
3. Methodical instructions for students;
4. Set of test tasks to determine the basic level of knowledge;
5. Set of situational tasks to determine the final level of knowledge;
6. Set of KROK-1 tasks;
7. Set of schemes and tables (presentation);
8. Set of forms with a clinical blood test
9. Video films;
10. For the experiment (experimental animals – white rat, micropipette (capilary tube) from haemometer, test-tubes, injection needles, pipettes, counting came-ras, 5 % solution of acetic acid, blood smears of sick people with different types of leukocytosis, microscopes with immersion objectives, immersion oil.).

Oriented map of students' work on the topic "Leukocytosis. Leukopenia"

No	Stage of lesson	Academic time, min	Educational guide		Place holding a class
			Educational tools	Equipment	
1	Determination of the initial level of knowledge	10	Written answer to test tasks	Test tasks	Study room
2	Analysis of theoretical material	35	Analysis of theoretical material based on control questions of the topic, situational tasks, tasks of KROK-1	Topic control questions, KROK-1 tasks, situational tasks	
3	Practical part (conduct experiment)	30	Introduction and preparation for setting up the experiment. Setting up the experiment. Discussion of the results of the experiment and formulation of conclusions	White rat, micropipette (capilary tube) from haemometer, test-tubes, injection needles, pipettes, counting came-ras, 5 % solution of acetic acid, blood smears of sick people with different types of leukocytosis, microscopes with immersion objectives, immersion oil	

No	Stage of lesson	Academic time, min	Educational guide		Place holding a class
			Educational tools	Equipment	
4	Determination of the final level of knowledge and skills. Summarizing the results	15	Determination of the final level of knowledge and skills. Summarizing the results	KROK-1 tasks, situational tasks	

Pathologic changes in leukocytes may be quantitative and qualitative.

Quantitative Changes in Leukocytes. These include leukocytosis and leukopenia.

Leukocytosis is an increase in the leukocyte count in the blood above 9×10^9/l.

Leukopenia is a decrease in the number of leukocytes in the blood below 4×10^9/l.

LEUKOCYTOSIS

Mechanisms of leukocytosis:

1) increased leukopoiesis,

2) increased efflux of leukocytes from the bone marrow into the blood,

3) redistribution of leukocytes as a result of their mobilisation from the marginal pool into circulating one (injection of adrenaline, emotional stress, influence of endotoxins) or as a result of redistribution of blood in shock, collapse - distributive leukocytosis.

Leukocytosis may be physiologic and pathologic.

Physiologic leukocytoses include:

1) leukocytosis of the new-borns (the number of leukocytes in the first 2 days is $15–20 \times 10^9$/l),

2) alimentary (digestive) leukocytosis – it develops in 2–3 hours after eating,

3) myogenic – in strenuous muscular work,

4) emotional – in psychic excitement,

5) leukocytosis in pregnant women (from the 5–6 months of pregnancy). Leukocytosis of the new-born and pregnant is longer and stipulated by the increased leukopoiesis, digestive and myogenic leukocytosis is due to reflex redistribution of blood in circulation and efflux of the blood from its depots.

Pathologic leukocytoses:

1) infectious,

2) inflammatory,

3) toxicogenic (in various exogenic intoxications and endogenic ones – uremia, diabetic coma),

4) posthemorrhagic,

5) "neoplastic" – in destruction of tumors,

6) "leukemic" – in leukemias.

These leukocytoses are due to increased leukopoiesis.

Besides, leukocytosis arises in the primary injury of the central nervous system (trauma or irritation of the intermediate brain), in shock, epilepsy, agony. It is distributive one.

Leukocytosis may arise in the disturbed function of thyroid and hypophysis.

The following forms of leukocytosis are distinguished:

1) neutrophilic one (neutrophilia, neutrophilosis) – increased number of neutrophils above 65 %. It occurs in acute infectious diseases and purulent inflammatory processes, in tissue destruction (myocardial infarction, acute hemolysis, malignant tumors, leukemias), in action of the toxic metabolites (uremia, hepatic coma), physical (cold, heat) and psychic factors, in hemorrhage, etc.

In evaluation of neutrophilia it is also necessary to take into account the so-called nuclear shift in the leukocytic formula (see below).

2) eosinophilic one (eosinophilia) – increased number of eosinophils above 5 %. It is observed in various allergic diseases, in certain infectious diseases, especially in those characterised by phenomena of an allergic character, as in scarlet fever, chronic sepsis, rheumatism, etc., in some skin diseases (psoriasis, eczema), in chronic myeloleukemia, lymphogranulomatosis, in certain endocrinopathias (hypophyseal cachecsia, myxedema, etc.), in use of some drugs (antibiotics, sulpha drugs, etc.). It is especially characteristic of helminthic and other parasitic diseases.

3) basophilic one (basophilia) occurs rather rarely – in chronic myeloleukemia, hemolytic anemias, erythremia, hemophilia, myxedema, ulceric colitis, after removing of the spleen.

4) lymphocytic one (lymphocytosis) – increased number of lymphocytes above 44 %. Physiologic lymphocytosis is observed in children in the first 10 years of life, as well as in vegetarians and in strenuous muscular work (myogenic lymphocytosis). Lymphocytosis can be absolute (an increase in lymphocytes with normal or increased total number of leukocytes in the blood) and relative (an increase in lymphocytes and a decrease in other cells, though the absolute number of lymphocytes is normal). Lymphocytosis is characteristic of chronic lympholeukemia. It is also developed in virus infections (infectious mononucleosis, hepatitis, measles, influenza) and bacterial infections (hooping-cough, tuberculosis, syphilis, abdominal typhus, malaria, brucellosis). It is observed in disturbances of nutrition (alimentary dystrophy), in bronchial asthma, some endocrine disorders (thyroidism, acromegaly, neurasthenia and certain other diseases of the central nervous system. Protozoan diseases involving enlargement of the spleen are not infrequently accompanied by lymphocytosis.

In experiment it is possible to cause lymphocytosis by irritation of the intermediate brain and the area of the III ventricle.

5) monocytic one (monocytosis) – an increased number of monocytes above 8 %. In certain acute infections (typhus, chicken-pox, measles, German measles, diphtheria, mumps, etc.) monocytosis usually denotes the termination of the disease. Prolonged monocytosis is characteristic of chronic processes and protozoan diseases (septic endocarditis, malaria, infectious mononucleosis, leishmaniosis, collagenoses). Monocytosis is observed in lymphogranulomatosis and Banti's syndrome (considerable chronic enlargement of the spleen accompanied by slowly developing anemia. Its later stage includes cirrhosis of the liver and ascites).

LEUKOPENIA

It is observed leukopenia with uniform reduction of number all of the cells of the white blood and leukopenia with predominant reduction of quantity of the separate leukocytes (neutropenia, eosinopenia, lymphocytopenia, etc.).

The most frequently leukopenia is due to neutropenia. Mechanisms of leukopenia (neutropenia):

1) redistribution of leukocytes in the vascular system, their delay in the blood depots;

2) destruction of leukocytes in hemopoietic organs and in vessels;

3) inhibition of leukopoiesis;

4) increased excretion of leukocytes from the organism (purulent endomethritis, cholecystoangiocholitis).

The kinds of leukopenia (neutropenia):

1) Distributive neutropenia is observed in shock, neuroses, inflammatory diseases, malaria. The ratio between the circulating and marginal pools of leukocytes is changed as a result of congestion of leukocytes in dilated capillaries of the blood depots (lung, liver, intestine). This leukopenia is temporary and is usually replaced by leukocytosis.

2) Neutropenia owing to intensive destruction of neutrophils. It is observed: a) under influence of antibodies leukoagglutinins, which are formed in blood transfusions, under influence of some drugs, which are allergens-haptens (sulpha drugs, amidopyrin, etc.); b) in diseases accompanied by increased number of the circulating immune complexes (autoimmune diseases, tumors, leukemias); c) in action of toxins (the toxic forms of typhoid fever, influenza, dysentery, the extensive inflammatory processes, the poisoning with benzene, arsenic, sulphonamides); d) in the enlarged spleen (collagenoses, liver cirrhosis, hemolytic anemia, etc.).

3) Neutropenia owing to disturbed or inhibited leukopoiesis. It is observed in action of various toxic substances and drugs, ionising radiation, in replacement of the bone marrow by leukemic or tumor tissue, in protein and vitamin starvation, etc.

Sometimes leukopenia is manifested in the form of agranulocytosis which is characterised by a strong decrease or even absence of neutrophils and other granulocytes in the blood, when the number of granulocytes is below $0{,}75 \times 10^9$/l or the total number of leukocytes is below 1×10^9/l.

Eosinopenia is observed in increased production of corticosteroids (stress, Cushing's disease), acute infections.

Lymphocytopenia occurs in immunodeficit conditions, stress, irradiation, lymphogranulomatosis, milliar tuberculosis, pneumonia, sepsis, collagenoses and some other diseases.

Monocytopenia is developed in radiation sickness, severe septic conditions, agranulocytosis.

The Qualitative Changes of Leukocytes

It is necessary to account the degree of lobation of the neutrophil nuclei.

After the degree of nuclear shift in the leukocytic formula the following kinds of neutrophilic leukocytoses are distinguished:

1) with any nuclear shift – an increased number of mature segmented neutrophils on the background of leukocytosis as a whole;

2) with a hyporegenerative nuclear shift to the left – an increased number of band forms of neutrophils (above 5%), it is characteristic of a slight course of several infections and inflammation;

3) with the regenerative nuclear shift to the left which indicates the reactive activation of granulocytopoiesis. On the background of neutrophilia and increased number of band forms metamyelocytes and sometimes individual myelocytes occur. It is characteristic of the purulent septic processes;

4) with the hyperregenerative nuclear shift to the left which reflects the excessive hyperplasia of leukopoietic tissue with disturbance of maturation of the cells and expressed rejuvenation of the blood. The quantity of band neutrophils and metamyelocytes is strongly increased, the younger forms occur (myelocytes and even individual promyelocytes and myeloblasts). The total number of leukocytes can be increased, nonchanged or even decreased because of exhausted myelopoiesis. The absence of eosinophils (aneosinophilia) is often observed. This shift is met in adversely proceeding infectious and purulent septic processes;

5) with the degenerative nuclear shift which testifies to an inhibition of the bone marrow. On the background of leukopenia the number of band neutrophils is increased, there are a lot of destructed segmented forms, metamyelocytes are absent. It is characteristic of severe infections, endogenic intoxications, etc.

In hyperproduction of pathologically chanced leukocytes and disturbance of their maturation the regenerative-degenerative shift is observed. Thus leukocytosis is marked, and the number of band neutrophils, metamyelocytes and myelocytes with the attributes of degeneration is increased;

6) with the nuclear shift to the right which is characterized by occurrence of hypersegmented (5 segments) neutrophils and testifies to an inhibition of granulocytopoiesis. It is found out in radiation sickness, pernicious anemia, however can be observed in a healthy man.

In various diseases the change in the total number of leukocytes is accompanied by the occurrence in the blood of the pathologic leukocytes, which are classified into regenerative (they are found out in norm only in the bone marrow) and degenerative (destructed) forms. The attributes of degeneration are: toxicogenic granularity, vacuolisation, hypochromatosis, anisocytosis, fragmentation, picnosis and rexis of the nucleus, hypersegmentation, etc.

Setting up the experiment. Discussion of results and formulation of conclusions

- **Differential Leukocyte count (Leukocyte formula)**

From your teacher, collect a numbered blood smear with the amount of leukocytes in a unit volume indicated. Determine the differential leucocyte count and crosscheck with the standard figures Determine the kind of leukocytosis. Write the results in the table below:

Total of leucocytes	Basophils	Eosinophils	Neutrophils				Lymphocytes	Monocytes
			Mielocytes	Young	Band neutrophils	Segment neutrophils		

- **Count the number of white blood cells during experimental postradiational leukopenia.**

Take two rats, one of which five days Before the experiment was subjected to general X-ray radiation in doses of 600 roentgen. Study the external signs of radiation syndrome, noting haemorrhage of the eyes, nose, changes in the fur, diarrhea, weight loss, change in general state (languitidy). Count the number of white blood cells of the experimental and intact rats. Place the rat in a camera, lower the tail in water with a temperature of 38 °C, there by causing hyperemy. Wipe the tail with cotton balls, place. Pierce one of the tail veins with an injection needle. Wipe away the first drop of blood, the second collect to the marked point in a measuring pipette from a haemometer. Blow the blood from the pipette to the bottom of the test-tube, where earlier was poured of 0,38 ml of a 3 % solution of acetic acid, dyed in hencianviolet. Rinse the pipette three times. Shake the mixture energetically for 3 minutes, transfer to the counting camera with the pipette for distelled water from a haemometer. Count the white blood cells in 100 big squares of Gorev's camera. The amount of white blood cells in 1 mkl of blood. Calculate by the formula:

$$X = \frac{A \times 4000 \times B}{C},$$

where X – unknown number of white blood cells

A – sum of white blood cells, counted in 100 big squares

B – sum of counted small squares (1600)

C – dilution of the blood (20 times)

The volume of the small square = 1/4000 mcl (microlitre), therefore to transfer to 1 mkl, the formula has a multiplier of 4000. The amount of white blood cells calculate in 1l. Compare the amount of white blood cells of the radiated rat and the control rat.

Discussion of the results of the experiment

During the discussion, indicate the reasons that cause the corresponding shifts in the leukocyte formula. Point out the features of the leukocyte shift in acute infectious diseases.

The research carried out in this lesson shows that ionizing treatment affects cells more strongly, the more their ability to reproduce, than a long path of the mitotic process, than cells are younger and less differentiated. In the discussion, pay attention to the appearance of immature forms of leukocytes in the peripheral blood.

The action of radiation is accompanied, in particular, by damage to hematopoietic organs, primarily bone marrow, as a result of which a hypoplastic state of hematopoiesis develops.

Formulation of conclusions based on the experiment

In the set of smears there are drugs with neutrophilia, eosinophilia, lymphocytosis and indicate the reasons that cause the corresponding shifts in the leukocyte formula. Point out the features of the leukocyte shift in acute infectious diseases.

In the irradiated rat, the number of leukocytes decreases sharply compared to the control. Violation of hematopoiesis appears soon after exposure. The appearance of immature leukocytes in the peripheral blood, which are found in places of hematopoiesis, indicates a deep qualitative violation of the process of hematopoiesis, leukemia is an independent disease characterized by systemic damage to hematopoietic organs.

Tasks for independent work on the topic "Leukocytosis. Leukopenia."

The student is offered to investigate the results of a clinical blood analysis of a patient with a disorder in the blood system. It is necessary to determine the signs and type of violation. Be able to explain the mechanism of occurrence. Analysis of errors with an explanation of the correct answers

List of questions and works to be studied:

1. Leukocytosis. Emergence mechanisms, classification.
2. Physiological leukocytosis.
3. Pathological leukocytosis. Causes and mechanisms of development.
4. Jet and redistributive leukocytosis. Causes and mechanisms of development.
5. Types of a leukocytosis depending on a type of leucocytes.
6. Leucocyte formula. Relative and absolute leukocytosis and leucopenia.
7. Nuclear shift of neutrophile leucocytes. Types, causes, their predictive value.
8. Leucemoid reactions, their causes and hematologic characteristic.
9. Leucopenia, principles of classification.
10. Pathogenesis of the main clinical manifestations of leucopenia.
11. Leucopenia owing to reduction of time of stay of leukocytes in peripheral blood and redistributive leucopenia. Causes and mechanisms of development.
12. Leucopenia due to violation of receipt of leukocytes from red bone marrow in blood. Causes, development mechanisms.
13. Agranulocytosis. Causes and mechanisms of development.

List of practical skills that must be mastered:

1. Explain the causes of leukopoiesis disorders.

2. Explain the concepts of "physiological", "pathological", "reactive" and "redistributive" leukocytosis.

3. Determine changes in the leukocyte formula, relative and absolute leukocytosis and leukopenia.

4. Analyze the results of clinical blood analysis (standards and criteria disorders of leukocytes and their individual types).

5. Define leukocytosis and leukopenia and their separate types in blood analysis, explain possible causes and mechanisms of their development.

6. To be able to determine the nuclear shift in a blood test for various pathologies.

7. Determine the signs of agranulocytosis, explain its causes and mechanism development

Situational tasks KROK-1 to determine the final level of knowledge

1. Two hours after an exam a student had a blood count done and it was revealed that he had leukocytosis without significant leukogram modifications. What is the most probable mechanism of leukocytosis development?

A. Redistribution of leukocytes in the organism.
B. Leukopoiesis intensification.
C. Deceleration of leukocyte lysis.
D. Deceleration of leukocyte migration to the tissues.
E. Leukopoiesis intensification and deceleration of leukocyte lysis.

2. Examination of a patient admitted to the surgical department with symptoms of acute appendicitis revealed the following changes in the white blood cells: the total count of leukocytes is 16×10^9/l. Leukocyte formula: basophils – 0, eosinophils – 2 %, juvenile forms – 2 %, stabnuclear – 8 %, segmentonuclear – 59 %, lymphocytes – 25 %, monocytes – 4 %. The described changes can be classified as:

A. Neutrophilia with right shift.
B. Neutrophilia with degenerative left shift.
C. Neutrophilic leukemoid reaction.
D. Neutrophilia with hyperregenerative left shift.
E. Neutrophilia with regenerative left shift.

3. 24 hours after appendectomy blood of a patient presents neutrophilic leukocytosis with regenerative shift. What is the most probable mechanism of leukocytosis development?

A. Redistribution of leukocytes in the organism.
B. Amplification of leucopoiesis.
C. Decelerated leukocyte destruction.
D. Decelerated emigration of leukocytes to the tissues.
E. Amplification of leukopoiesis and decelerated emigration of leukocytes to the tissues.

4. After an attack of bronchial asthma a patient had his peripheral blood teste d. What changes can be expected?

A. Eosinophilia. *C. Erythrocytosis.* *E. Leukopenia.*
B. Lymphocytosis. *D. Thrombocytopenia.*

5. A 3-year-old child had eaten some strawberries. SeSon he developed a rash and itching. What was found in the child's leukogram?

A. Hypolymphemia. *C. Eosinophilia.* *E. Neutrophilic leukocytosis.*
B. Lymphocytosis. *D. Monocytosis.*

6. A 5 year old child is ill with measles. Blood analysis revealed increase of total number of leukocytes up to 13×10^9/l. Leukogram: basophils – 0, eosinophils – 1, myelocytes – 0, juvenile neutrophils – 0, band neutrophils – 2, segmented neutrophils – 41, lymphocytes – 28, monocytes – 28. Name this phenomenon:

A. Agranulocytosis. *C. Monocytosis.* *E. Neutropenia.*
B. Lymphocytosis. *D. Eosinopenia.*

7. As a result of a road accident a 26-year-old man is in the torpid phase of shock. Blood count: leukocytes – $3{,}2 \times 10^9$/l. What is the leading mechanism of leukopenia development?

A. Faulty release of mature leukocytes from the bone marrow into the blood.
B. Leukocyte destruction in the hematopietic organs.
C. Leukopoiesis inhibition.
D. Leukocyte redistribution in the bloodstream.
E. Increased excretion of the leukocytes from the organism.

8. A 26-year-old man is in the torpid shock phase as a result of a car accident. In blood: $3{,}2 \times 10^9$/l. What is the leading mechanism of leukopenia development?

A. Disturbed going out of mature leukocytes from the marrow into the blood.
B. Leukopoiesis inhibition.
C. Lysis of leukocytes in the blood-forming organs.
D. Redistribution of leukocytes in bloodstream.
E. Intensified elimination of leukocytes from the organism.

9. Parents of a 3-year-old child have been giving him antibiotics with purpose of preventing enteric infections for a long time. A month later the child's condition changed for the worse. Blood examination revealed apparent leukopenia and granulocytopenia. What is the most probable mechanism of blood changes?

A. Myelotoxic. *C. Redistributive.* *E. Hemolytic.*
B. Autoimmune. *D. Age-specific.*

10. A patient with atrophic gastritis developed a vitamin B_{12} deficiency. What change in the leukocyte formula is the most typical for hypovitaminosis B_{12}?

A. Hyperregenerative shift to the left.
B. Degenerative shift to the left.
C. Nuclear shift to the right.
D. Regenerative-degenerative nuclear shift to the left.
E. Regenerative nuclear shift to the left.

Standards of correct answers to the task KROK-1

1	2	3	4	5	6	7	8	9	10
A	*E*	*B*	*A*	*C*	*C*	*D*	*D*	*A*	*C*

Recommendations for registration of work results

1. Written answer to test tasks (initial level of knowledge).
2. The results of the experiment are drawn up in the form of an experiment protocol with the determination of relevant conclusions.
3. Protocol for the study of the results of the patient's clinical blood analysis.
4. Protocol for solving situational tasks with an explanation of the correct answers.

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Topic 5. Leukemia

Justification of the topic: Being a kind of hemoblastoses, leukosis represent the group of diseases of system of blood of tumor character and they are, as well as malignant tumors of other localization, one of the most dangerous forms of pathology of the human, agricultural animals and pets. Despite the fact that for the last decades the medical science made the significant contribution to the solution of questions of an etiology, pathogenesis, diagnostics and treatment of leukosis, they continue to take the first place in the list among the most difficult diseases of the human, having big mortality percentage, in particular at children's and young age.

The beginning of leukosis can be followed by such changes in an organism concerning which patients can address to the doctor of any profile. Therefore the knowledge of symptoms of these diseases, mechanisms of their development, features of a hematologic state at their different forms is necessary for each doctor.

Purpose of the lesson:

General – to be able to give the characteristic to leukosis as kinds of hemoblastoses, to classify them, to explain blood formation violation mechanisms, quantitative and qualitative changes in composition of peripheral blood, to give the characteristic of leukosis at different forms of this disease. To be able to interpret the modern ideas of an etiology and pathogenesis of leukosis.

Specifically:

Know:

1. To characterize a leucosis as a system disease of the hematogenic system.
2. To give modern classification of leukosis by the hystogenetic principle, a course and a state of peripheral blood.
3. To characterize the main techniques of the hematologic researches which are used at diagnosis of leukosis.
4. To decide the possibility of a leucosis by hematograms data.
5. To understand a state of change of peripheral blood at a leucosis and to distinguish different forms of leukosis.
6. To call the main cytochemical indicators used for differential diagnosis of leukosis and to give by them the characteristic of the main forms of leukosis.
7. To explain mechanisms of changes of erythrocyte and platelet composition of blood at leukosis.
8. To explain mechanisms of violations of functions of organs and systems at leukosis.

Be able to:

1. To characterize the main stages of a haemopoesis.
2. To distinguish at blood dab microscopy forming elements of granulocyte, lymphocyte, monocyte and erythrocyte ranks.

Practical experience:

1. To characterize the violation of the qualitative and quantitative composition of "white blood" according to the leukogram of a patient with chronic myeloid leukemia.

2. Demonstrate immature granulocytes in a peripheral blood smear of a patient with chronic myeloid leukemia, interpret their presence in the blood.

3. To characterize the violation of the qualitative and quantitative composition of "white blood" in the leukogram of a patient with chronic lymphocytic leukemia.

4. To identify degeneratively changed lymphocytes in the peripheral blood smear of a patient with chronic lymphocytic leukemia.

5. Based on the study of the hemogram, characterize changes in the qualitative and quantitative composition of blood in patients with acute leukemia.

The graphological structure of the topic "Leukemia" is attached.

Material and methodological support of the topic "Leukemia":

1. Lectures;
2. Methodical instructions for teachers;
3. Methodical instructions for students;
4. Set of test tasks to determine the basic level of knowledge;
5. Set of situational tasks to determine the final level of knowledge;
6. Set of KROK-1 tasks;
7. Set of schemes and tables (presentation);
8. Set of forms with a clinical blood test
9. Video films;
10. For the experiment (Blood smears of the sick, microscopes with immersion objectives, immersion oil.).

Oriented map of students work on the topic "Leukemia"

No	Stage of lesson	Academic time, min	Educational guide		Place holding a class
			Educational tools	Equipment	
1	Determination of the initial level of knowledge	10	Written answer to test tasks	Test tasks	Study room
2	Analysis of theoretical material	35	Analysis of theoretical material based on control questions of the topic, situational tasks, tasks of KROK-1	Topic control questions, KROK-1 tasks, situational tasks	
3	Practical part (conduct experiment)	30	Introduction and preparation for setting up the experiment. Setting up the experiment. Discussion of the results of the experiment and formulation of conclusions	Blood smears of the sick, microscopes with immersion objectives, immersion oil	
4	Determination of the final level of knowledge and skills. Summarizing the results	15	Determination of the final level of knowledge and skills. Summarizing the results	KROK-1 tasks, situational tasks	

The leukemias are malignant neoplasms of cells originally derived from hematopoietic stem cells. They are characterized by diffuse replacement of bone marrow with unregulated, proliferating, immature neoplastic cells. In most cases, the leukemic cells spill out into the blood, where they are seen in large numbers. The term *leukemia* (*i.e.*, "white blood") was first used by Virchow to describe a reversal of the usual ratio of red blood cells to white blood cells. The leukemic cells may also infiltrate the liver, spleen, lymph nodes, and other tissues throughout the body, causing enlargement of these organs.

Epidemiology

1. Malignant diseases of bone marrow stem cells that may involve all cell lines
2. Risk factors
   a. Chromosomal abnormalities
   - Examples-Down syndrome, chromosome instability syndromes
   b. Ionizing radiation
   c. Chemicals
   d. Alkylating agents
3. Age ranges for common leukemias
   a. Newborn to 14 years old
   - Acute lymphoblastic leukemia (ALL)
   b. Persons 15 to 39 years old
   - Acute myelogenous leukemia (AML)
   c. Persons 40 to 60 years old
   - Chronic myelogenous leukemia (CML)
   d. Persons over 60 years of age
   - Chron ic lymphocytic leukemia (CLL)

Oncogenes are cellular genes homologous to retroviruses that cause malignant tumors in experimental animals.

According to their functional activity, oncogenes can be divided into 4 groups:

• oncogenes, the products of which are growth factors;

• oncogenes responsible for the expression of growth receptors factors;

• oncogenes that produce proliferative mediators

signal from the cell surface through the cytoplasm to the nucleus;

• oncogenes that form DNA-binding proteins that regulate

DNA replication and enhance the expression of other oncogenes. Activation of oncogenes of any of the listed species is associated with by increasing the production of oncoproteins, can lead to strengthening proliferation, disconnection of normally linked proliferation processes and differentiation.

Normal stimulators of proliferation are various growth factors which interact with specific receptors on the cell membrane. To such growth factors include:

• insulin,

• insulin-like growth factor or somatomedin,

• growth factor released by platelets,

• T-cell growth factor or interleukin-2,

• epidermal growth factor.

An important property of proteins reproduced under the influence of oncogenes transformation of cells, is their ability to replace normal growth factors in themstimulating effect on the cell.The main mechanisms of oncogene activation include translocations and deletions chromosomes, point mutations.

The main chromosomal mutations include:

• translocation (exchange of sections between non-homologous chromosomes),

• deletion (loss of chromosome section),

• duplication (doubling of the area),

• inversion (rotation of the site by 180 degrees),

• insertion (insertion of a chromosome section in a new place),

• amplification (multiplication of individual sections).

A wide range of chromosome changes can be detected in tumor cells, but some reconstructions naturally accompany certain nosological forms tumor diseases, including leukemias, and are specific for these forms. In the manifestation of GL, infiltration of the bone marrow by leukemic cells is total. The number of leukemic clone is at the same time about 10^{12} cells (or 1 kg). The smallest number of leukemic diagnoses blasts 1–10 % corresponds to 10^{10}–10^{11} cells. Calculation of the time required for the manifestation of GL: the minimum time for the development of a leukemic clone, which is detected by diagnostic methods research – 1 year, maximum – 10 years, and on average – 3.5 years (Mauer1973).

Classification

The leukemias commonly are classified according to their predominant cell type (*i.e.,* lymphocytic or myelogenous) and whether the condition is acute or chronic. Biphenotypic leukemias demonstrate characteristics of both lymphoid and myeloid lineages. A rudimentary classification system divides leukemia into four types: acute lymphocytic (lymphoblastic) leukemia, chronic lymphocytic leukemia, acute myelogenous (myeloblastic) leukemia, and chronic myelogenous leukemia.

The *lymphocytic leukemias* involve immature lymphocytes and their progenitors that originate in the bone marrow but infiltrate the spleen, lymph nodes, CNS, and other tissues.

The *myelogenous leukemias,* which involve the pluripotent myeloid stem cells in bone marrow, interfere with the maturation of all blood cells, including the granulocytes, erythrocytes, and thrombocytes.

Leukemias were originally termed acute or chronic based on life expectancy but now are classified according to cellular maturity.

Acute leukemias consist of predominantly immature, poorly differentiated cells (usually blast forms). Acute leukemias are divided into lymphocytic and myelocytic types, which may be further subdivided by the French-American-British classification.

Chronic leukemias have more mature cells than do acute leukemias. Chronic leukemias are described as lymphocytic or myelocytic.

Myelodysplastic syndromes involve progressive bone marrow failure but with an insufficient proportion of blast cells for making a definite diagnosis of AML; 40 to 60 % of cases evolve into AML.

A **leukemoid reaction** is marked granulocytic leukocytosis produced by normal bone marrow in response to systemic infection or cancer. Although not a neoplastic disorder, a leukemoid reaction with a very high WBC count may require testing to distinguish it from CML.

Leukemoid reaction

a. Absolute leukocyte count usually above 50,000/μL.
   - May involve neutrophils, lymphocytes, or eosinophils

b. Etiology
   - Perforating appendicitis (neutrophils)
   - Whooping cough (lymphocytes)
   - Cutaneous larva migrans (eosinophils)

c. Pathogenesis
   - Exaggerated response to infection
   - Leukoerythroblastic reaction

d. Immature bone marrow cells enter the peripheral blood

e. Pathogenesis
   - Bone marrow infiltrative disease
   - Examples-fibrosis, metastatic breast cancer

Peripheral blood findings (myeloblasts, progranulocytes)

Pathogenesis

1. Block in stem cell differentiation

Monoclonal proliferation of neoplastic leukocytes behind the block

2. Leukemic cells
   a. Replace the bone marrow
      - Replace normal hematopoietic cells
   b. Enter the peripheral blood
   c. Metastasize throughout the body

Clinical findings of leukemia

1. Abrupt onset of signs and symptoms
2. Fever (infection), bleeding (thrombocytopenia), fatigue (anemia)
3. Metastatic disease
   a. Hepatosplenomegaly
   b. Generalized lymphadenopathy
   c. Central nervous system involvement (especially in ALL)
   d. Skin involvement (especially T-cell leukemias)
4. Bone pain and tenderness
   a. Due to bone marrow expansion by leukemic cells

Manifestations of leukemia are due to suppression of normal blood cell formation and organ infiltration by leukemic cells. Inhibitory factors produced by leukemic cells and replacement of marrow space may suppress

normal hematopoiesis, with ensuing anemia, thrombocytopenia, and granulocytopenia. Organ infiltration results in enlargement of the liver, spleen, and lymph nodes, and occasional kidney and gonadal involvement. Meningeal infiltration results in clinical features associated with increasing intracranial pressure (eg, cranial nerve palsies).

A definitive diagnosis of acute leukemia is based on blood and bone marrow studies; it requires the demonstration of leukemic cells in the peripheral blood, bone marrow, or extramedullary tissue. Laboratory findings reveal the presence of immature (blasts) white blood cells in the circulation and bone marrow, where they may constitute 60 to 100 % of the cells. As these cells proliferate and begin to crowd the bone marrow, the development of other blood cell lines in the marrow is suppressed. Consequently, there is a loss of mature myeloid cells, such as erythrocytes, granulocytes, and platelets. Anemia is almost always present, and the platelet count is decreased. Bone marrow specimens are used to determine the molecular characteristics of the leukemia, the degree of bone marrow involvement, and the morphology and histology of the disease. Immunophenotyping is performed to determine the lineage subtype of the leukemic cells. In ALL, the staging always includes a lumbar puncture to assess CNS involvement. Imaging studies that include CT scans of the chest, abdomen, and pelvis may also be obtained to identify additional sites of disease.

Both CLL and CML have a more insidious onset than acute leukemias and may be discovered during a routine medical examination by a blood count. The two types of chronic leukemias differ, however, in their manifestations and clinical course. CLL typically follows a slow and indolent course. The clinical signs and symptoms are largely related to the progressive infiltration of neoplastic lymphocytes in the bone marrow and extramedullary tissue and to secondary immunologic defects. Often affected persons are asymptomatic at the time of diagnosis, and lymphocytosis is noted on a complete blood count obtained for another, unrelated disorder. Fatigue, reduced exercise tolerance, enlargement of superficial lymph nodes, or splenomegaly usually reflects a more advanced stage. As the disease progresses, lymph nodes gradually increase in size, and new nodes are involved, sometimes in unusual areas such as the scalp, orbit, pharynx, pleura, gastrointestinal tract, liver, prostate, and gonads. Severe fatigue, recurrent or persistent infections, pallor, edema, thrombophlebitis, and pain are also experienced. As the malignant cell population increases, the proportion of normal marrow precursors is reduced until only lymphocytes remain in the marrow. Typically, CML follows a triphasic course:

(1) a chronic phase of variable length,

(2) a short accelerated phase,

(3) a terminal blast crisis phase.

The onset of the chronic phase is usually slow with nonspecific symptoms such as weakness and weight loss. The most characteristic laboratory finding

at the time of presentation is leukocytosis with immature granulocyte cell types in the peripheral blood.

Anemia and, eventually, thrombocytopenia develop. Anemia causes weakness, easy fatigability, and exertional dyspnea. Splenomegaly is often present at the time of diagnosis; hepatomegaly is less common; and lymphadenopathy is relatively uncommon. Although persons in the early chronic phase of CML generally are asymptomatic, without effective treatment most will enter the accelerated phase within 4 years. The accelerated phase is characterized by enlargement of the spleen and progressive symptoms. Splenomegaly often causes a feeling of abdominal fullness and discomfort. An increase in basophil count and more immature cells in the blood or bone marrow confirm transformation to the accelerated phase. During this phase, constitutional symptoms such as low-grade fever, night sweats, bone pain, and weight loss develop because of rapid proliferation and hypermetabolism of the leukemic cells. Bleeding and easy bruising may arise from dysfunctional platelets. Generally, the accelerated phase is short (6 to 12 months). The terminal blast crisis phase of CML represents evolution to acute leukemia and is characterized by an increasing number of myeloid precursors, especially blast cells. Constitutional symptoms become more pronounced during this period, and splenomegaly may increase significantly. Isolated infiltrates of leukemic cells can involve the skin, lymph nodes, bones, and CNS.

Findings at Diagnosis in the Most Common Leukemias				
Feature	Acute Lymphocytic	Acute Myelocytic	Chronic Lymphocytic	Chronic Myelocytic
Peak age of incidence	Childhood	Any age	Middle and old age	Young adulthood
WBC count	High in 50 % Normal or low in 50 %	High in 60 % Normal or low in 40 %	High in 98 % Normal or low in 2 %	High in 100 %
Differential WBC count	Many lymphoblasts	Many myeloblasts	Small lymphocytes	Entire myeloid series
Anemia	Severe in > 90 %	Severe in > 90 %	Mild in about 50%	Mild in 80 %
Platelets	Low in > 80%	Low in > 90 %	Low in 20 to 30%	High in 60% Low in 10 %
Lymphadenopathy	Common	Occasional	Common	Infrequent
Splenomegaly	In 60 %	In 50 %	Usual and moderate	Usual and severe
Other features	Without prophylaxis, CNS commonly involved	CNS rarely involved. Sometimes Auer rods in myeloblasts	Occasionally hemolytic anemia and hypogammaglobulinemia	Low leukocyte alkaline phosphatase level. Philadelphia chromosome – positive in > 90 %

Treatment

- Chemotherapy
- Sometimes stem cell transplantation or radiation therapy

The 4 general phases of chemotherapy for ALL include

- Remission induction
- CNS prophylaxis

- Postremission consolidation or intensification
- Maintenance

Setting up the experiment. Discussion of results and formulation of conclusions

- **Microscopy of preparations of blood during aqute myeloid (myeloblastic) leukemia.**

Count the different forms of leukocytes. Pay attention to the absence of transition forms between young (blastic) and matured neutrophils.

- **Microscopy of preparations of blood during chronic myeloid (myelocytic) leukemia.**

Count the different forms of leukocytes. Pay attention that during clinical form leucosis in blood smear at great quantity meats the cells of mieloid types at all stadies of development.

- **Microscopy of preparations of blood during chronic lymphoid leukemia.**

While counting different forms of leukocytes, pay attention to the predominance of young lymphocyte forms (prolymphocytes, lymphoblasts).

Discussion of the results of the experiment

Examine the blood smear and pay attention to the impossibility of differentiation of leukocytes according to morphological features. Note the absence of transitional forms between immature cells (blast forms) and mature segmented neutrophils. Pay attention to the fact that with this myeloid form of leukemia in a blood smear, there are a large number of myeloid cells at all stages of development.

Formulation of conclusions based on the experiment

The appearance in the peripheral blood of immature leukocytes, which in physiological conditions are found in places of hematopoiesis, indicates a deep a qualitative violation of the process of hematopoiesis characteristic of leukemia. In contrast to pathological leukocytosis, which is a symptom of diseases (infections, intoxication, malignant neoplasms) leukemias are independent a disease characterized by a systemic lesion of the hematopoietic organs.

Tasks for independent work on the topic "Leukemia"

The student is offered to investigate the results of a clinical blood analysis of a patient with a disorder in the blood system. It is necessary to determine the signs and type of violation. Be able to explain the mechanism of occurrence. Analysis of errors with an explanation of the correct answers

List of questions and works to be studied:

1. Leucosis. Etiology and pathogenesis.
2. Modern classification of leukosis.
3. Acute leucosis. Clinical manifestations. Pathogenesis of the main clinical syndromes.
4. Chronic leucosis. Clinical manifestations.
5. Stages of an acute and chronic leucosis. Principles of diagnostics and treatment.

6. Changes in a hemogram and a myelogram in leukosis.

List of practical skills that must be mastered:

1. To characterize the violation of the qualitative and quantitative composition of "white blood" according to the leukogram of a patient with chronic myeloid leukemia.

2. Demonstrate immature granulocytes in a peripheral blood smear of a patient with chronic myeloid leukemia, interpret their presence in the blood.

3. To characterize the violation of the qualitative and quantitative composition of "white blood" in the leukogram of a patient with chronic lymphocytic leukemia.

4. To identify degeneratively changed lymphocytes in the peripheral blood smear of a patient with chronic lymphocytic leukemia.

5. Based on the study of the hemogram, characterize changes in the qualitative and quantitative composition of blood in patients with acute leukemia.

Situational tasks KROK-1 to determine the final level of knowledge

1. A 23 y.o. patient complains of weakness, temperature rise up to 38–40 °C. Objectively: liver and spleen are enlarged. Hemogram: Hb – 100 g/l, erythrocytes –- $2{,}9 \times 10^{12}$/l, leukocytes – $4{,}4 \times 10^{9}$/l, thrombocytes – 48×10^{9}/l, segmentonuclear neutrophils – 17 %, lymphocytes – 15 %, blast cells – 68 %. All cytochemical reactions are negative. Make a hematological conclusion:

A. Undifferentiated leukosis.
B. Chronic myeloleukosis.
C. Acute myeloblastic leukosis.
D. Acute lymphoblastic leukosis.
E. Acute erythromyelosis.

2. The total number of leukocytes in patient's blood is 90×10^{9}/1. Leukogram: eosinophils – 0 %, basophils – 0 %, juvenile – 0 %, stab neutrophils –2 %, segmentonuclear cells – 20 %, lymphoblasts – 1 %, prolymphocytes – 2 %, lymphocytes – 70 %, monocytes – 5 %, Botkin-Gumprecht cells. Clinical examination revealed enlarged cervical and submandibular lymph nodes. Such clinical presentations are typical for the following pathology:

A. Chronic myeloleukosis.
B. Acute lympholeukosis.
C. Chronic lympholeukosis.
D. Lymphogranulomatosis.
E. Infectious mononucleosis.

3. A patient suffering from chronic myeloleukemia has got the following symptoms of anemia: decreased number of erythrocytes and low haemoglobin concentration, oxyphilic and polychromatophilic normocytes, microcytes. What is the leading pathogenetic mechanism of anemia development?

A. Substitution of haemoblast.
B. Reduced synthesis of erythropoietin.
C. Intravascular hemolysis of erythrocytes.
D. Chronic haemorrhage.
E. Deficiency of vitamin B_{12}.

4. A 39-year-old patient underwent hematologic tests. The following results were obtained: RBC – $2{,}8 \times 10^{12}$/L, Hb – 80 g/L, color index – 0,85, reticulocytes – 0,1 %, platelets – 160×10^{9}/L, WBC – 60×10^{9}/L. Basophils – 2,

eosinophils – 8, promyelocytes – 5, myelocytes – 5, immature neutrophils – 16, stab neutrophils – 20, segmented neutrophils – 34, lymphocytes – 5, monocytes – 5. What form of blood pathology are these results indicative of?

A. Chronic myeloid leukemia. *D. Acute myeloid leukemia.*

B. Undifferentiated leukemia. *E. Hypoplastic anemia.*

C. Hemolytic anemia.

5. A patient who had a tooth removed due to acute purulent periostitis had long-term bleeding from the socket that did not stop with conventional methods. In the blood: erythrocytes – 2.9×10^{12}/l, Hb – 90 g/l; color index – 0.9; clot. – 60×10^{9}/l; leukocytes – 52×10^{9}/l; basophils – 0, eosinophils – 1 %, monocytes – 0, neutrophils: young – 0, Band nuclear – 2 %, segmentonuclear – 18 %, lymphocytes – 8 %, monocytes – 1 %, myeloblasts – 70 %. What blood disease does the patient have?

A. Undifferentiated leukemia. *D. Erythromyelosis.*

B. Promyelocytic leukemia. *E. Acute myeloid leukemia.*

C. Chronic myeloid leukemia.

6. During the examination, leukocytosis, lymphocytosis, Botkin-Gumprecht cells against the background of anemia were found in the patient's blood. What disease should we think about?

A. Chronic lymphocytic leukemia. *D. Lymphogranulomatosis.*

B. Myeloma disease. *E. Infectious mononucleosis.*

C. Acute myeloid leukemia.

7. Hematologic study shows the following pattern: erythrocytes – $2{,}8 \times 10^{12}$/L, Hb – 80 g/L, color index – 0.85, reticulocytes – 0.1 %, platelets – 160 thousand per microliter, leukocytes – 60×10^{9}/L. Basocytes – 2 %, eosinophils – 8 %, promyelocytes – 5 %, myelocytes – 5 %, juvenile – 16 %, stab neutrophils – 20 %, segmented neutrophils – 34 %, lymphocytes – 5 %, monocytes – 5 %. This clinical presentation indicated the following blood pathology:

A. Undifferentiated leukemia. *D. Hemolytic anemia.*

B. Chronic myeloleukemia. *E. Hypoplastic anemia .*

C. Acute myeloleukemia.

8. In the patient's leukogram: leukocytes – 14×10^{9}/l; myeloblasts – 71 %, promyelocytes, myelocytes, metamyelocytes – 0 %, rod neutrophils – 6 %, segmentonuclear – 13 %; lymphocytes – 7 %, monocytes – 3 %. What pathology of the blood in sick?

A. Myeloblastic leukemia. *D. Lymphoblastic leukemia.*

B. Neutrophil leukocytosis. *E. Chronic lymphocytic leukemia.*

C. Chronic myeloleukosis.

9. Over the past year, the patient began to notice increased fatigue, general fatigue weakness Blood analysis: Er – 4.1×10^{12}/l, Hb – 119 g/l, CP – 0.87, leukocytes – 57×10^{9}/l, leukocyte formula: y – 0, p – 0, c – 9 %, e – 0, b – 0, lymphoblasts – 2 %, prolymphocytes – 5 %, lymphocytes – 81 %, m – 3 %,

platelets – 160 × 10^9/l. In the smear: normochromia, large number of Botkin-Gumprecht shadows. What kind of pathology does the blood system indicate this hemogram?

A. Chronic myeloid leukemia. *D. Acute myeloblastic leukemia.*

B. Acute lymphoblastic leukemia. *E. Chronic monoleukosis.*

C. Chronic lymphocytic leukemia.

10. Patient P. has the following changes in peripheral blood: Er. – 3.0 × 1/l, Hemoglobin – 80 g/l, Leukocytes – 21 × 1/l. Leukocyte formula: basophils – 0 %, eosinophils – 0 %, myeloblasts – 54 %, promyelocytes – 1 %; myelocytes – 0 %, metamyelocytes – 0 %, stab – 1 %, segmented – 28 %, lymphocytes – 13 %, monocytes – 3 %. Determine the most likely pathology according to the given description blood pictures:

A. Acute myeloid leukemia. *D. Leukemoid reaction.*

B. Chronic myeloid leukemia. *E. Undefined leukemia.*

C. Erythromyelosis.

Standards of correct answers to the task KROK-1

1	2	3	4	5	6	7	8	9	10
A	*C*	*A*	*A*	*E*	*A*	*B*	*A*	*C*	*A*

Recommendations for registration of work results

1. Written answer to test tasks (initial level of knowledge).
2. The results of the experiment are drawn up in the form of an experiment protocol with the determination of relevant conclusions.
3. Protocol for the study of the results of the patient's clinical blood analysis.
4. Protocol for solving situational tasks with an explanation of the correct answers.

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Topic 6. Disturbances in hemostasis.
Changes in the physical and chemical properties of blood

Justification of the topic: The aggregation is one of the most ancient and extremely important manifestations of a homeostasis and represents the sum of the processes leading to a thrombogenesis. In activity of an organism the trombogenesis can have double value. On the one hand, formation of blood clot protects an organism from blood loss, with another – conducts to violation of a blood-groove and trophic of organs and tissues that is the important mechanism of pathogenesis of many diseases. In clinic doctors of almost all specialties face violations of an aggregation (because they complicate the course of surgical, obstetric and gynecologic, therapeutic, oncological, stomatologic, infectious and other diseases). Thus the range of manifestations of coagulapatias is extremely wide, from the hidden latent forms to life-threatening manifestations.

It is difficult to call a pathological state, process or a disease which wouldn't be followed by change of physical and chemical properties of blood. Despite the fact that in most part of change of different indicators of physical and chemical properties of blood have nonspecific character, date about some of them, along with data of other laboratory researches, help a doctor make a diagnose, and also at judgment about efficiency of cure. In some cases detailed studying of changes of some of these indicators is obligatory for statement of the correct diagnosis (some types of disproteinemia and the anemia, coagulopathy). One of the most widespread indicators of change of physical and chemical properties of whole blood is the Erythrocyte Sedimentation Rate (ESR), and in hema-tologic practice and toxicology – osmotic resistance of erythrocytes.

Purpose of the lesson:

General – to be able to characterize a condition of the coagulation system of blood by coagulogram indicators. To be able to interpret changes of ESR and osmotic resistance of erythrocytes at different pathological processes and diseases as the data of additional methods at diagnosis of diseases and criterion of efficiency of treatment.

Specifically:

Know:

1. To define the term "system of a hemostasis".
2. To characterize the mechanisms providing a stop of bleeding and restoration of integrity of the vascular course.
3. To define changes of ESR and osmotic resistance of erythrocytes.
4. To connect these changes with possible violations of physical and chemical properties of blood at pathology.
5. To explain mechanisms of change of ESR and osmotic resistance of erythrocytes at different pathological processes and diseases.

Be able to:

1. To characterize coagulation mechanisms.
2. To explain participation of a liver in coagulation mechanisms.
3. To characterize the main physical and chemical properties of blood and erythrocytes, to explain, than they are caused.

4. What shows the ESR indicator, what factors it depends on?
5. To determine value of ESR and to know normal borders of its fluctuations.
6. To characterize the cause of the osmotic and oncotic pressure of plasma of blood.
7. Know that represent iso-, hypo- and hypertensive solutions to characterize influence of these solutions on a cell.
8. To give definitions of the terms "maximum" and "minimum" resistance of erythrocytes, to specify normal borders of fluctuations of these sizes.
9. To explain, what properties of erythrocytes and plasma the size of osmotic resistance depends on.
10. To perform and consider reaction of determination of osmotic resistance of erythrocytes.

Practical experience:

1. Based on the study of the patient's hemogram, characterize changes in the number of thrombocytes and state the cause of this disorder
2. Based on the study of the patient's hemogram, characterize changes in ESR and state the cause of this disorder
3. To define changes of ESR and osmotic resistance of erythrocytes.
4. To perform and consider reaction of determination of osmotic resistance of erythrocytes.

The graphological structure of the topic "Disturbances in hemostasis. Changes in the physical and chemical properties of blood" is attached.

Material and methodological support of the topic "Disturbances in hemostasis. Changes in the physical and chemical properties of blood":

1. Lectures;
2. Methodical instructions for teachers;
3. Methodical instructions for students;
4. Set of test tasks to determine the basic level of knowledge;
5. Set of situational tasks to determine the final level of knowledge;
6. Set of KROK-1 tasks;
7. Set of schemes and tables (presentation);
8. Set of forms with a clinical blood test
9. Video films;
10. For the experiment (experimental animals – rabbit, sets of hypotonic solutions of table salt with different concentrations (from 0,60–0,32 %), 1 ml. pipettes, micropipettes (capillary tubes), injection needles, centrifuge, Panchenkov's apparatus, porcelain (china) crucibles, injection needles).

Oriented map of students' work on the topic "Disturbances in hemostasis. Changes in the physical and chemical properties of blood"

No	Stage of lesson	Academic time, min	Educational guide		Place holding a class
			Educational tools	Equipment	
1	Determination of the initial level of knowledge	10	Written answer to test tasks	Test tasks	Study room

No	Stage of lesson	Academic time, min	Educational guide		Place holding a class
			Educational tools	Equipment	
2	Analysis of theoretical material	35	Analysis of theoretical material based on control questions of the topic, situational tasks, tasks of KROK-1	Topic control questions, KROK-1 tasks, situational tasks	Study room
3	Practical part (conduct experiment)	30	Introduction and preparation for setting up the experiment. Setting up the experiment. Discussion of the results of the experiment and formulation of conclusions	Rabbit, sets of hypotonic solutions of table salt with different concentrations (from 0,60–0,32 %), 1 ml. pipettes, micropipettes (capillary tubes), injection needles, centrifuge, Panchenkov's apparatus, porcelain (china) crucibles, injection needles	
4	Determination of the final level of knowledge and skills. Summarizing the results	15	Determination of the final level of knowledge and skills. Summarizing the results	KROK-1 tasks, situational tasks	

DECREASED BLOOD CLOTTING (HYPOCOAGULATION)

A diminution in or slowing of blood clotting leads to hemorrhagic diatheses and syndroms. They may be hereditary, inherent and acquired, and are divided into:

1) coagulopathias (disturbances in blood clotting and fibrinolysis);

2) thrombocytic disturbances – thrombocytopenias, thrombocytopathias and thrombocytemias;

3) vasopathias or angiopathias (disorders of the vascular wall).

In specific group hemorrhagic diatheses are included stipulated by the same cause and simultaneous disturbances in the different links of hemostasis – hereditary Willebrand's disease (disturbed production of the large-molecular component of the VIII factor of the blood clotting by endothelium – Willebrand's factor), syndrome of disseminated intravascular clotting (DICS).

• Causes and mechanisms of coagulopathias:

1) hereditary and acquired decrease or perversion of synthesis of plasmatic and thrombocytic factors of the blood clotting and components of kallikrein-kinin system;

2) inhibition or increased expedinture of these factors;

3) increased release of endogenic anticoagulants;

4) activation of fibrinolytic system;

5) excessive administration of anticoagulants, fibrinolytic and defibrinated drugs.

These factors disturb various phases of the blood clotting and retraction of the clot or induce the combined their changes.

Causes and Mechanisms of Thrombocytic Disturbances

Thrombocytopenias

1) intensified destruction of thrombocytes (immune – in measles, German measles, action of sulpha drugs, chronic lymphoid leukemia, diffusive diseases of the connective tissue, etc.; in scarlet-fiver, sepsis, increased function of the mononuclear phagocytic system);

2) insufficient production of thrombocytes (irradiation, poisoning by the chemical substances, metaplasia of the bone marrow, deficit of vitamin B_{12} and folic acid, hereditary disturbances);

3) increased expenditure of thrombocytes (in local and generalized intravascular blood clotting);

4) redistribution of thrombocytes (in trauma, epylepsia, anaphylactic shock, etc.).

As a result there are the following mechanisms of hemorrhage:

1) increased vascular permeability and destruction of the vascular wall due to dystrophia of the vascular wall (elimination of the angiotrophic function of thrombocytes);

2) decreased the adhesive-aggregative function of thrombocytes;

3) decreased release of ADP, serotonin, adrenalin, antiheparinic factor from thrombocytes which results in disturbed formation of the thrombocytic thrombi, absence of the vascular spasm and slowing of the blood clotting;

4) decreased retraction of the blood clot due to reduced activity of the contractilic thrombocytic protein – thrombostenin (factor 8 of thrombocytes).

Thrombocytopathias

They arise in action of toxic substances and drugs (alcohol, pyrymidines, NSAIDs, etc.), endogenic metabolites (in uremia, cirrhosis, parasitary diseases of the liver, malignant tumors, leukemias), B12-deficient anemia, radiation sickness, myxedema, hereditary defects in thrombocytes.

As a result the capacity of thrombocytes to agglutination is lost and retraction of the blood clot is happened.

Disorders of the Vascular Wall

They include increased vascular permeability and destruction of the vascular wall and arise as a result of disturbed collagen synthesis (deficit of vitamin C, hereditary defects), action of biologically active substances (allergy), radiotoxin (radiation sickness), immune hemorrhagic vasculites, decreased the angiotrophic function of thrombocytes (thrombocytopenias and thrombocytopathias), destruction of the vascular wall by leukemic infiltrates; decreased production of the Willebrand's factor; increased peroxidation of membrane phospholipids, which results in increased synthesis of prostacyclin – potent inhibitor of thrombocyte aggregation – by endothelium; disturbances of neurohumoral regulation of the vascular tone.

INCREASED BLOOD CLOTTING (HYPERCOAGULATION)

It is a result of:

1) activation of blood clotting in excitement of sympathetic system (pain, stress) and in increased influx into the blood procoagulants and activators of blood clotting (traumatic or burn shock, inflammation, etc.);

2) decreased anti-thrombotic properties of endothelium in disturbance of their metabolism, mechanical or immune injury;

3) increased amount of thrombocytes in the blood;

4) increased aggregation and adhesity of thrombocytes;

5) injury to the vessels and slowing of the blood current;

6) excessive administration of vitamin K, which produces hyperthrombinemia;

7) increased tolerance of fibrin clot to plasmin;

8) decreased capacity of fibrinolytic system to fibrin lysis;

9) deficit of antithrombin in the plasma – hereditary ("thrombophilia") and acquired (in atherosclerosis, ischemic disease of the heart, diabetes, nephritis, etc.).

Hypercoagulation is manifested by increased intravascular blood clotting – local (thrombosis) and generalized (DICS).

CHANGES IN THE PHYSICOCHEMICAL PROPERTIES OF THE BLOOD

The **specific gravity of the blood** (normally 1.050–1.060) depends mainly on the number of erythrocytes, amount of proteins and content of sodium chloride. It increases as a result of hemoconcentration, erythremia and increased content of proteins, and decreases in blood dilution (hydremia), anemia and qualitative starvation.

The **surface tension of the blood** is reduced in accumulation of the capillary-stimulating substances (bile acids, soaps and certain metabolites). It also decreases in eclampsia, uremia and asphyxia when the amount of such substances noticeably increases. Contrariwise, protein deficiency and hydremia increase the surface tension.

The **osmotic pressure of the blood** (normally 7.7–8.1 atm.) increases (*hyperosmia*) in dehydration, consumption a lot of sodium, retention of sodium in the organism, increased content of carbon dioxide in the blood because of increased dissociation of salts. Hyperosmia results in *dehydration of cells and decomposition of cell proteins*. A decrease of the osmotic pressure (*hypoosmia*) can be connected with redundant consumption of water, retention of water in the organism, a loss of sodium. It is accompanied by redundant receipt of water into cells and leads to *water poisoning and hemolysis*.

The **colloid osmotic, or oncotic, pressure** depends on the content of albumins in the blood.

The osmotic and oncotic pressure are important in the pathogenesis of edemas.

The Viscosity of the Blood. If we assume the viscosity of water at 37° C to be unity, the viscosity of the blood in relation to water will normally be 4.5–5. The viscosity depends on the amount and sizes of formed elements, the ratio of leukocytes and erythrocytes, carbon dioxide saturation, concentration of proteins and proportion of their various fractions in the blood and partly the mineral composition. In pathology it may vary between 2 and 20. The viscosity increases in anhydremia (polycythemia and leukemia), accumulation of carbon dioxide because of the increased viscosity of proteins, in hyperfunction of the thyroid owing to slight hemoconcentration, in hyperproteinemia and the increased content of globulins and fibrinogen (inflammation and certain infections). It decreases in anemias and hydremias, decreased hemocoagulation, myxedema, hypoproteinemia.

With the increased viscosity of the blood the peripheral resistance of the vessels increases, *work of the heart and circulation are hindered*. With the decreased viscosity *circulation is accelerated.*

The Erythrocyte Sedimentation Rate (ESR; normally 1–10 mm/h in man and 2–15 mm/h in women). It depends on the various factors:

- ✓ on the changed ratio between proteins of the blood. The increased content of the high dispersed proteins (globulins, fibrinogen) in inflammation and certain infections leads to acceleration of ESR, as far as these proteins absorbed on the negative charged erythrocytes reduce their surface charge and thus promote their agglutination and sedimentation;
- ✓ on the number of erythrocytes. The increased their number (polycythemia, shock) reduces ESR, and the decreased number (anemia) accelerates ESR;
- ✓ on the content of cholesterol and lecitine in the blood. Cholesterol absorbed on erythrocytes accelerates and lecitine, on the contrary, decreases ESR;
- ✓ on the changed relative density of erythrocytes. In hypercapnia (asphyxia, cardiac insufficiency) ESR decreases owing to increased diameter of erythrocytes and reduced their relative density;
- ✓ on viscosity of the blood. Hydremia accelerates ESR and the increased viscosity (anhydremia) reduces ESR.

ESR also can be accelerated in intensive physical work.

The osmotic resistance of erythrocytes (ORE) is their stability in hypotonic solutions. There are ***minimum and maximum ORE***. The normal minimum implies the hypotonicity of a solution in which the least resistant erythrocytes are hemolysed (0.42–0.44 % sodium chloride solution), and the normal maximum is the concentration of a solution in which the most resistant cells (i.e. all of the cells) are hemolysed (0.32–0.34 %). ORE depends on their maturity, form, and composition of plasma. The form of erythrocyte is characterized by a ratio between its thickness and diameter. This ratio is called index of sphericity (normally 0.27–0.28).

The reduced ORE (increase of parameters minimum and maximum) is observed in hereditary microspherocytic anemia by Minkovsky and Shoffar

which is characterised by the increased index of sphericity of erythrocytes, in hemolytic jaundice, toxicoses, bronchopneumonias, leukemias, cirrhosis of the liver, etc.

The increased ORE takes place in mechanical jaundice; in several cases of polycythemia, massive hemorrhages and iron-deficiency anemia because of stimulated erythropoiesis (the less mature cells possessing the disk form and the small index of sphericity are more resistant).

CHANGES IN THE BIOCHEMICAL COMPOSITION OF THE BLOOD

Changes in protein content in the blood include *hypoproteinemia, hyperproteinemia and dysproteinemia.*

Hypoproteinemia is a decreased concentration of proteins in the blood plasma. It arises mainly at the expense of a decreased content of albumins and may be *acquired* and *hereditary*. Its causes are: starvation, cachexia, certain affections of the liver and digestive system, pathology of the kidneys accompanied by proteinuria, following hemorrhages, and formation of extensive transsudates and exudates. A content of fibrinogen is decreased in severe liver diseases.

One of the manifestations of hypoproteinemia is *hydremia* (diluted blood) and *decreased colloid osmotic pressure of the plasma* which is normally maintained mainly by albumins.

Hyperproteinemia is an increased concentration of proteins in the blood plasma. It may be absolute and relative. The *relative* one occurs more often and is a result of hemoconcentration (anhydremia), i.e. as a result of a loss of water. The *absolute* one is usually connected with hyperglobulinemia, as a rule, at the expense of γ-globulins in infectious diseases, allergy, and chronic liver diseases. An increased content of fibrinogen is observed in acute and chronic inflammations and infections, nephrosis, some tumours, stress.

It is very important to determine a *ratio of albumins to globulins* which in norm is equal 1.5–2.3. It is increased in acute and chronic infections, and decreased in liver, nervous and cardiac diseases, in cachexia.

Dysproteinemia is a changed ratio between the separate kinds of globulins. It may be acquired and hereditary and is divided into *dysglobulinemias and dysgammaglobulinemias (dysimmunoglobulinemias).*

Causes of ***dysglobulinemias*** are: acute inflammation, diffuse diseases of the connective tissue, autoimmune diseases, and hepatic dysfunctions. A deficit of haptoglobin (α_3-globulin) leads to disturbance of binding and transportation of hemoglobin which is released in normal hemolysis; a decreased synthesis of the antihemophilic globulin (β_2-globulin) leads to hemorrhages; a deficit of transferrin (β_1-globulin) leads to disturbance in iron metabolism.

Causes of ***dysgammaglobulinemias*** are: myeloma disease, when malignant cells produce abnormal globulins (M-protein and/or Bens-Johns' proteins), Waldenstrem's macroglobulinemia (tumour from B-lymphocytes which produce immunoglobulin M), diffuse diseases of the connective tissue with

appearance of cryoglobulins [proteins which are observed in malignant and autoimmune diseases and can precipitate in action of cold (hypothermia)].

Dysproteinemia leads to disturbance of immunity.

Paraproteinemia is an appearance in the blood plasma of qualitatively changed γ-globulins. Its causes are the same as the causes of dysgammaglobulinemias.

Setting up the experiment. Discussion of results and formulation of conclusions

• **Determination of the osmotic resistance of erythrocytes in experimental haemolitic anemia.**

Take two rabbits, in one of which experimentally was caused haemolytic phenylhydrase anemia. With the help of a pipette, transfer different concentrations of 1ml. solutions of table salt. Carry out the transfer, beginning with lower concentrations and ending with the highest. Then add 0,02 ml. of blood taken from the marginal vein of the ear into the test-tubes. Addition of the blood should begin from the highest concentration to the lowest. The capillary for taking blood should be rinsed twice with the same solution to ensure complete removal of blood. In half an hour all the test-tubes should be centrifuged at a speed of 3000 RPM/min for 5 minutes. Estimate the degree of haemolysis. Note the maximum (complete haemolysis) and the minimum (traces of haemolysis) osmotic resistance of erythrocytes in the blood of the control rabbit and experimental rabbit.

• **Studing of reticylocytes in experimental hemolytic anemia**

Rinse the capillary tube from Panchenkov's apparatus with 5 % solution of sodium citrate. Then fill the tube with the same solution to the point "P" (50 mm) and blow into the crucible. From the marginal ear vein take blood twice till point "K" (100 mm), blow into the crucible and mix throughly. By doing this the blood becomes stabilized . Fill up the capillary tube with the stabilized blood till point "O" and place it strictly upright in Panchenkov's apparatus. In an hour's time count in ml the height of the formed column of plasma. Compare the ESR of the anemic and control rabbit.

Discussion of the results of the experiment

A rabbit with hemolytic anemia has a decrease in the osmotic resistance of erythrocytes (maximum – up to 0.48, minimum – up to 0.60), compared to a control rabbit (maximum 0.32–0.34, minimum – 0.44–0.46).

The rate of sedimentation of erythrocytes in a rabbit with hemolytic anemia is significantly accelerated (10–12 mm/h), while in a control rabbit – 1–2 mm/h.

Formulation of conclusions based on the experiment

Indicate that the osmotic resistance of erythrocytes depends on the degree of their maturity, shape and on changes in plasma composition; young erythrocytes are more stable than mature ones; erythrocytes with a spherical shape are less resistant (normal sphericity index – 0.27–0.23).

In experimental animals, a decrease in the osmotic resistance of erythrocytes is noted, which is explained by a violation of erythrocyte production.

The rate of sedimentation of erythrocytes depends on changes in the protein fractions of blood, changes in blood viscosity, changes in the number of erythrocytes, the difference in the specific weights of erythrocytes and plasma, etc. In this case, with hemolytic phenylhydrazine anemia, ESR is accelerated due to a change in blood viscosity, a decrease in the number of erythrocytes.

Tasks for independent work on the topic "Disturbances in hemostasis. Changes in the physical and chemical properties of blood"

The student is offered to investigate the results of a clinical blood analysis of a patient with a disorder in the blood system. It is necessary to determine the signs and type of violation. Be able to explain the mechanism of occurrence. Analysis of errors with an explanation of the correct answers

List of questions and works to be studied:

1. Violations of total amount of blood. Normovolemia. Types of a normovolemia, causes of their development.
2. Hypervolemia. Types of a hypervolemia, causes and mechanisms of development. Pathogenetic value of a hypervolemia.
3. Hypovolemia. Types of a hypovolemia, causes and mechanisms of development. Pathogenetic value of a hypovolemia.
4. Definition of the terms "blood loss", "bleeding", "hemorrhage", "hematoma". Etiology and classification of blood loss.
5. Acute blood loss. Pathogenesis. The pathological changes happening at blood loss. Protective and compensatory reactions at blood loss.
6. Qualitative changes of erythrocytes, their causes.
7. Qualitative changes of leukocytes, their causes.

List of practical skills that must be mastered:

1. Hemostasis. The structurally functional components enabling the realization of mechanisms of a hemostasis.
2. Violations of vascular platelet hemostasis. Causes, pathogenesis. Clinical manifestations, their pathogenesis.
3. Main mechanisms and pathological manifestations of vascular platelet hemostasis (primary hemostasis).
4. Main mechanisms and pathological manifestations of a plasma hemostasis (secondary hemostasis).
5. Groups of hemorrhagic diseases. Criteria of diagnostics of mechanisms of violation of a hemostasis.
6. Bleeding types, their main manifestations.
7. Coagulopathy due to the excess of anticoagulants and acute stimulation of a fibrinolisys.
8. Hereditary coagulopathy. Pathogenesis, manifestations. Hemophilia. Clinical and laboratory criteria.

9. Thrombocytopenia. Etiology, pathogenesis.
10. Clinical and laboratory criteria idiopathic trombocytepenic purple.
11. Thrombocytopathy. Mechanism of violations of adhesion, aggregation of platelets, releases of platelets granules.
12. Vazopathy: types, Causes, development mechanisms, pathogenesis of the main clinical manifestations.
13. Hyper coagulation. Thtombocytic syndrome (trombophylia).
14. Syndrome of a disseminated intravascular coagulation (DIC-syndrome).
15. Osmotic and oncotic pressure of blood. Causes of disorders.
16. Osmotic resistance of erythrocytes. Causes of disorders.
17. Speed of subsidence of erythrocytes. Causes of disorders.
18. Violations of proteinaceous composition of blood, their causes.

Situational tasks KROK-1 to determine the final level of knowledge

1. A patient with tissue trauma was taken a blood sample for the determination of blood clotting parameters. Specify the right sequence of extrinsic pathway activation.

A. III–IV – Xa. *C. IV–VIII: TF – Xa.* *E. III–VIII: TF – Xa.*
B. III–VIIa – Xa. *D. IV–VIIa – Xa.*

2. A patient is diagnosed with hereditary coagulopathy that is characterized by factor VIII deficiency. Specify the phase of blood clotting during which coagulation will be disrupted in the given case:

A. Thrombin formation. *C. Fibrin formation.* *E. –.*
B. Thromboplastin formation. *D. Clot retraction.*

3. A 3-year-old boy with pronounced hemorrhagic syndrome doesn't have antihemophilic globulin A (factor VIII) in the blood plasma. Hemostasis has been impaired at the following stage:

A. External mechanism of prothrombinase activation.
B. Conversion of prothrombin to thrombin.
C. Internal mechanism of prothrombinase activation.
D. Conversion of fibrinogen to fibrin.
E. Blood clot retraction.

4. A 12-year-old patient has been admitted 3 a hospital for hemarthrosis of the knee Dint. From early childhood he suffers from frequent bleedings. Diagnose the boy's disease:

A. B_{12} (folic acid)-deficiency anemia. *D. Thrombocytopenic purpura.*
B. Hemolytic anemia. *E. Hemorrhagic vasculitis.*
C. Hemophilia.

5. Tooth extraction in a patient with chronic persistent hepatitis was complicated by a prolonged bleeding. What is the cause of hemorrhagic syndrome?

A. Decreased production of thrombin. *D. Increased fibrinolysis.*
B. Decreased production of fibrin. *E. Increased production of thromboplastin.*
C. Increased synthesis of fibrinogen.

6. A patient underwent a surgery for excision of a cyst on pancreas. After this he developed haemorrhagic syndrome with apparent disorder of blood coagulation. Development of this complication can be explained by:

A. Insufficient fibrin production. *D. Activation of Christmas factor.*
B. Reduced number of thrombocytes. *E. Activation of fibrinolytic system.*
C. Activation of anticoagulation system.

7. After a tourniquet application a patient was found to have petechial haemorrhages. The reason for it is the dysfunction of the following cells:

A. Neutrophils. *C. Monocytes.* *E. Lymphocytes.*
B. Platelets. *D. Eosinophils.*

8. A 43-year-old patient has thrombopenia, reduction of fibrinogen, products of degradation of fibrin presented in the blood, petechial haemorrhage along with septic shock. What is the most likely cause of the changes?

A. Autoimmune thrombocytopenia. *D. Disorder of thrombocytes production.*
B. DIC-syndrome. *E. Exogenous intoxication.*
C. Haemorrhagic diathesis.

9. A patient was ill with burn disease that was complicated by DIC syndrome. What stage of DIC syndrome can be suspected if it is known that the patient's blood coagulates in less than 3 minutes?

A. Hypercoagulation. *C. Hypocoagulation .* *E. Terminal.*
B. Transition phase. *D. Fibrinolysis.*

10. A patient, who had been working hard under conditions of elevated temperature of the environment, has now a changed quantity of blood plasma proteins. What phenomenon is the case?

A. Absolute hyperproteinemia. *D. Paraproteinemia.*
B. Absolute hypoproteinemia. *E. Relative hyperproteinemia.*
C. Dysproteinemia.

Standards of correct answers to the task KROK-1

1	2	3	4	5	6	7	8	9	10
B	*B*	*C*	*C*	*A*	*E*	*B*	*B*	*A*	*E*

Recommendations for registration of work results

1. Written answer to test tasks (initial level of knowledge).
2. The results of the experiment are drawn up in the form of an experiment protocol with the determination of relevant conclusions.
3. Protocol for the study of the results of the patient's clinical blood analysis.
4. Protocol for solving situational tasks with an explanation of the correct answers.

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Main

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Topic 7. Pathophysiology of the systemic blood circulation. Insufficiency blood circulation. Cardiac insufficiency

Justification of the topic. Heart failure – one of the main causes of incapacitation, disability and death in patients which suffering from diseases of the cardiovascular system. The study of the etiology and pathogenesis of these menacing forms of disease necessary for practice physician, as heart failure is due to different causes and mechanisms. In connection with this knowledge of the causes and mechanisms of this disease will promote the development of clinical, optionally rational approaches to the treatment of each patient. Studying in experiment on animals' heart failure can reveal the mechanisms of its development.

Purpose of the lesson:

General – to be able to characterize heart failure, and explain the main causes and mechanisms of development.

Specifically:

Know:

1. The concept of heart failure. Reasons, types.
2. Compensatory and adaptive mechanisms of heart failure. Violation of hemodynamics.
3. Clinical manifestations of heart failure.
4. Tonogenic and myogenic dilatation of the heart. Mechanisms of long-term adaptation of the heart to overloads. Myocardial hypertrophy.

Be able to:

1. To reveal the essence of the concept of "heart failure".
2. Classify the causes and mechanisms of heart failure
3. Identify the main manifestations of heart failure, and explain the mechanisms of their occurrence and development.Graph of the logical structure of the topic "**Pathophysiology of the systemic blood circulation. Insufficiency blood circulation. Cardiac insufficiency**" – added.

Graphological structure of the topic "Pathophysiology of the systemic blood circulation. Insufficiency blood circulation. Cardiac insufficiency" is added.

Material and methodological support of the topic " Pathophysiology of the systemic blood circulation. Insufficiency blood circulation. Cardiac insufficiency ".

1. Lectures;
2. Methodical instructions for teachers;
3. Methodical instructions for students;
4. Set of test tasks to determine the basic level of knowledge;
5. Set of situational tasks to determine the final level of knowledge;
6. Set of KROK-1 tasks;
7. Set of schemes and tables (presentation);
8. Set of forms with a clinical blood test;
9. Video films.

Oriented map of student work topics
«Pathophysiology of the systemic blood circulation.
Insufficiency blood circulation. Cardiac insufficiency»

No	Stage of lesson	Academic time, min	Educational guide		Place holding a class
			Educational tools	Equipment	
1	Determination of the initial level of knowledge	10	Written response to test tasks	Test tasks	Learning room
2	Analysis of theoretical material	45	Analysis of the theoretical material is carried out on the basis of control questions of the topic and "KROK 1" tasks	Control questions of the topic, task " KROK 1"	
3	Determination of the final level of knowledge and skills. Summa-rizing the results	35	Determination of the final level of formation of knowledge and skills	KROK 1 tasks, situational tasks	

PATHOPHYSIOLOGY OF THE SYSTEMIC BLOOD CIRCULATION. INSUFFICIENCY BLOOD CIRCULATION. CARDIAC INSUFFICIENCY

The cardiovascular system ensures all metabolic processes in the human body and is a component of various functional systems that determine homeostasis. Heart activity is the basis of blood circulation.

Circulatory insufficiency (CI) is a typical form of pathology, in which the circulatory system does not provide adequate (their functions and the level of plastic processes in them) blood supply to the needs of organs and tissues. This leads to a violation of their provision of oxygen, nutrients and removal of end products of metabolism.

Forms of CI according to the mechanism of development and clinical manifestations:

- Heart failure caused by weakening of the heart as a pump.
- Vascular insufficiency of blood circulation, associated with a violation of the tone of blood vessels and the physical and mechanical properties of their walls.
- Mixed (cardiovascular) circulatory failure.

Forms of CI according to the nature and speed of development:

Acute circulatory failure:

- vascular (shock, collapse, fainting);
- cardiac, due to acute weakening of the contractile function of the myocardium.

Chronic insufficiency of blood circulation (atherosclerosis, coronary insufficiency, hypertension, heart defects).

Degrees of chronic circulatory failure:

- The first degree (compensated, hidden, latent) is not detected at rest, but after exercise, shortness of breath, tachycardia, and fatigue are characteristic.

- IIA degree – shortness of breath, tachycardia, fatigue appear at rest.
- IIB degree – congestion develops in both circles of blood circulation.
- III degree (decompensated or clear, terminal) - the development of significant changes in the function a and structure of organs and tissues.
- II and III degrees are mainly of cardiac origin and develop into the corresponding stages of heart failure.

Heart failure (HF) is a syndrome of ventricular dysfunction. Left ventricular failure causes shortness of breath and fatigue, and right ventricular failure causes peripheral and abdominal fluid accumulation; the ventricles can be involved together or separately.

Causes of heart failure

Two main groups of reasons lead to the development of HF:

- have a direct harmful effect on the heart,
- cause functional overload of the heart.

I. Damage to the heart Factors that directly damage the heart can be physical, chemical and biological in nature.

Physical factors:

• compression of the heart (exudate, blood, emphysematous lungs, tumor),

• exposure to electric current (in case of electrocution, defibrillation of the heart),

• mechanical injury (in case of blows to the chest, penetrating wounds, surgical manipulations).

Chemical factors:

• non-medicinal chemical compounds (for example, oxidative phosphorylation uncouplers, calcium and heavy metal salts, enzyme inhibitors, lipid hydroperoxides),

• Medicines in inadequate dosage (for example, calcium antagonists, cardiac glycosides, adrenoblockers),

• deficiency of O_2,

• lack of chemical compounds necessary for metabolism (for example, glucose, O_2, etc.).

Biological factors.

• High levels of BAR (catecholamines, T4).

• Deficiency or absence of BARs necessary for metabolism (for example, enzymes, vitamins, etc.).

• Prolonged ischemia or myocardial infarction. Causes cessation of myocardial contractions in the area of damage. This is accompanied by functional overload of the myocardium outside the zone of ischemia or infarction.

Cardiomyopathies (CMP) – damage to the myocardium, mainly of a non-inflammatory nature. They are characterized by significant structural and functional changes in the heart.

Cardiac contractility (force and velocity of contraction), ventricular performance, and myocardial O_2 requirements are determined by preload, afterload, substrate availability (eg, O_2, fatty acids, glucose), heart rate and rhythm, and amount of viable myocardium. Cardiac output (CO) is the product of

stroke volume and heart rate; it is also affected by venous return, peripheral vascular tone, and neurohumoral factors.

Preload is the loading condition of the heart at the end of its relaxation phase (diastole) just before contraction (systole). Preload represents the degree of end-diastolic fiber stretch and end-diastolic volume, which is influenced by ventricular diastolic pressure and the composition of the myocardial wall.

Afterload is the force resisting myocardial fiber contraction at the start of systole; it is de-termined by chamber pressure, volume, and wall thickness at the time the aortic valve opens.

Classification of types of heart failure (HF)

- based on criteria of origin (myocardial and congestive),
- speed of development (acute and chronic),
- predominant damage to the heart (left ventricular and right ventricular),
- predominant insufficiency of the cardiac cycle phase (systolic and diastolic)
- primary lesion (cardiogenic and non-cardiogenic).

The myocardial overload and mixed forms of HF are distinguished

- **Myocardial** form of HF develops mainly as a result of direct damage to the myocardium.
- **Congestive** heart failure occurs mainly as a result of cardiac overload (increased preload or afterload).
- **The mixed** form of HF is the result of a combination of direct damage to the myocardium and its overload.

Types of heart failure by speed of development. According to the speed of development of symptoms of HF, acute and chronic forms are distinguished.

- **Acute** (develops in a few minutes or hours). It is the result of a myocardial infarction, acute insufficiency of the mitral and aortic valves, rupture of the walls of the left ventricle.
- **Chronic** (formed gradually, over weeks, months, years). It is a consequence of arterial hypertension, chronic respiratory failure, long-term anemia, heart defects. The course of chronic heart failure can be complicated by acute heart failure.

Types of CH according to the primacy of the mechanism of development

Primary (cardiogenic) and secondary (non-cardiogenic) forms of heart failure are distinguished by a decrease in the contractile function of the myocardium or a decrease in venous blood flow to the heart.

I. Primary (cardiogenic). It develops as a result of a predominant decrease in the contractile function of the heart with a venous blood flow to it that is close to normal. It is most often observed in:

- CHD (may be accompanied by myocardial infarction, cardiosclerosis, myocardial dystrophy),
- myocarditis (for example, with inflammatory lesions of the heart muscle or pronounced and long-lasting endotoxinemia),
- cardiomyopathies.

II. Secondary (non-cardiogenic). It arises as a result of a primary preferential decrease in venous inflow to the heart with near-to-normal myocardial function. It is most often found in:

- acute massive blood loss,
- violation of diastolic relaxation of the heart and filling of its chambers with blood (for example, when the heart is compressed by liquid that accumulates in the pericardial cavity with blood, exudate),
- pisodes of paroxysmal tachycardia (which leads to a decrease in cardiac output and the return of venous blood to the heart),
- collapse (for example, vasodilatory or hypovolemic).

Depending on the predominant lesion of the left or right part of the heart, left ventricular and right ventricular HF are distinguished.

- **LV failure.** In failure due to LV dysfunction, CO decreases and pulmonary venous pressure increases. When pulmonary capillary pressure exceeds the oncotic pressure of plasma proteins (about 24 mm Hg), fluid extravasates from the capillaries into the interstitial space and alveoli, reducing pulmonary compliance and increasing the work of breathing. Lymphatic drainage increases but cannot compensate for the increase in pulmonary fluid. Marked fluid accumulation in alveoli (pulmonary edema) significantly alters ventilation-perfusion (V/Q) relationships: Deoxygenated pulmonary arterial blood passes through poorly ventilated alveoli, decreasing systemic arterial oxygenation (PaO_2) and causing dyspnea., because of elevated pulmonary venous pressure and increased work of breathing;
- **RV failure**: In failure due to RV dysfunction, systemic venous pressure increases, causing fluid extravasation and consequent edema, primarily in dependent tissues (feet and ankles of ambulatory patients) and abdominal viscera. The liver is affected most, but the stomach and intestine also become congested; fluid accumulation in the peritoneal cavity (ascites) can occur. RV failure commonly causes moder-ate hepatic dysfunction, with usually modest increases in conjugated and unconjugated bilirubin, PT, and hepatic enzymes (eg, alkaline phosphatase, AST, ALT). The impaired liver breaks down less aldosterone, further contributing to fluid accumulation. Chronic venous congestion in the viscera can cause malabsorption of nutrients and drugs, protein-losing enteropathy (characterized by diarrhea and marked hypoalbuminemia).
- **Total heart failure.** In this form, both left ventricular and right ventricular heart failure is expressed.

In HF, the heart may not provide tissues with adequate blood for metabolic needs, and cardiac-related elevation of pulmonary or systemic venous pressures may result in organ congestion. This condition can result from abnormalities of systolic or diastolic function or, commonly, both.

Systolic dysfunction: In systolic dysfunction, the ventricle contracts poorly and empties inadequately, leading initially to increased diastolic volume and pressure and decreased EF. Many defects in energy utilization, energy supply, electrophysiologic functions, and contractile element inter-

action occur, with abnormalities in intracellular Ca modulation and cAMP production.Predominant systolic dysfunction is common in HF due to MI, myocarditis, and dilated cardiomyopathy. Systolic dysfunction may affect primarily the LV or the right ventricle (RV); LV failure often leads to RV failure.

Diastolic dysfunction: In diastolic dysfunction (also called HF with preserved systolic function or HF with preserved/normal EF), ventricular filling is impaired, resulting in reduced ventricular end-diastolic volume, increased end-diastolic pressure, or both. Contractility and hence EF remain normal; EF may even increase as the poorly filled LV empties more completely to maintain CO. Markedly reduced LV filling can cause low CO and systemic symptoms. Elevated left atrial pressures can cause pulmonary hypertension and pulmonary congestion.

Mechanisms of emergency compensation of reduced contractile function of the heart

The pathogenesis of heart failure is associated with the features of the development of compensatory mechanisms when the functional load on the myocardium increases. There are 4 main compensation mechanisms for HF:

• Heterometric (Frank-Starling mechanism) – compensation due to lengthening of muscle fibers.

• homeometric – strengthening of cardiac activity without changing the length of muscle fibers.

• Bain-Bridge reflex (increased cardiac activity due to an increase in the diameter at the mouth of the vena cava and the right atrium).

• Strengthening of sympathetic-adrenal effects on the heart

Increase in contractility of the myocardium when it is stretched by inflowing blood (Frank-Starling mechanism)

The **Frank-Starling** principle describes the relationship between preload and cardiac performance. It states that, normally, systolic contractile performance (represented by stroke volume or CO) is proportional to preload within the normal physiologic range. Contractility is difficult to measure without cardiac catheterization but is reasonably reflected by the ejection fraction (EF), which is the percentage of end-diastolic volume ejected with each contraction; Cardiac reserve is the ability of the heart to increase its performance above resting levels in response to emotional or physical stress; body O_2 consumption may increase from 250 to ≥ 1500 mL/min during maximal exertion. Mechanisms include increasing heart rate, systolic and diastolic volume, stroke volume, and tissue extraction of O_2 (the difference between O_2 content in arterial blood and mixed venous or pulmonary artery blood).

An increase in the strength of myocardial contractions in response to an increased load. Occurs with unchanged myocyte length.

- Such a mechanism is called homeometric, since it is implemented without a significant change in the length of muscle fibers.
- Bain-Bridge reflex – increased cardiac activity due to an increase in diameter at the mouth of the vena cava and the right atrium.

- An increase in the contractility of the heart as a result of an increase in sympathetic-adrenal effects is characterized by an increase in the frequency and force of contractions.
- Sympathetic innervation of the myocardium is carried out by axon endings of adrenergic neurons of the upper cervical, middle cervical and stellate (cervicothoracic) ganglia.
- Activation of sympathetic nerves causes a positive inotropic effect. The frequency of spontaneous depolarization of pacemaker membranes increases, impulse conduction in Purkinje fibers is facilitated, and the frequency and force of contraction of typical cardiomyocytes increase.

Compensatory hypertrophy of the heart

Myocardial hyperfunction determines the expression of certain cardiomyocyte genes. It is manifested by an increase in the intensity of the synthesis of nucleic acids and proteins. Acceleration of the synthesis of nucleic acids and proteins of the myocardium leads to an increase in its mass – hypertrophy.

The biological significance of compensatory hypertrophy of the heart is that the increased function of the organ is performed by its growing mass.

Hypertrophy of the heart can be physiological or pathological.

Physiological hypertrophy occurs as a result of increased muscle work. Its characteristic feature is an increase in heart contractions, a uniform increase in the volume of muscle fibers in all parts of the heart, increased vascularization of the myocardium, and preservation of proportionality between the volume of the heart and all other muscle mass of the body. The efficiency of the heart muscle increases.

Pathological hypertrophy develops in pathological conditions with long-term excessive work of the heart and is characterized by an increase in the minute volume due to an increase in the blood filling of the heart cavities or an increase in the resistance to their emptying. At the same time, the blood supply to the heart muscle increases and its metabolism increases, however, with strong pathological hypertrophy, oxygen deficiency may occur in the myocardium. With this hypertrophy, the mass of the heart muscle increases regardless of the increase in the volume of skeletal muscles.

Mechanisms of decompensation in cardiac hypertrophy

The potential possibilities of the hypertrophied myocardium to increase the strength and speed of contraction are not unlimited. If the heart continues to be subjected to an increased load or it is additionally damaged, the force and speed of its contractions decrease, and their energy "cost" increases: decompensation of the hypertrophied heart develops.

The basis of decompensation of long-term hypertrophied myocardium is a violation of the balanced growth of its various structures. 1). These changes, along with others, ultimately cause a decrease in the force of heart contractions and the speed of the contractile process, that is, the development of HF.

Manifestations of heart failure

Depression of strength and speed of contraction, as well as relaxation of the myocardium in HF is manifested by deviations from the norm of indicators of heart function, central and organ tissue (peripheral) hemodynamics.

1. Reduction of the percussive and minute output of the heart

It develops as a result of depression of the contractile function of the myocardium.

- In most cases, cardiac output is below normal (as a rule, less than 3 l/min).
- In some conditions, the cardiac output preceding the development of HF is higher than normal.

This is observed, for example, in patients with thyrotoxicosis, chronic anemia, and arteriovenous shunts, after infusing excess fluid into the vascular bed. When heart failure develops in these patients, the cardiac output remains above the normal range (for example, more than 7–8 l/min). However, even in these conditions, the insufficient blood supply to organs and tissues is noted, since the cardiac output remains below the required value. Such conditions are known as heart failure with high blood output.

2. An increase in the residual systolic volume of blood in the cavities of the ventricles of the heart

It is a consequence of the so-called incomplete systole.

Incomplete emptying of the ventricles of the heart is the result of excess blood flow to it (for example, in valvular insufficiency), excessively increased OPSS (for example, in arterial hypertension, aortic stenosis), direct damage to the myocardium.

3. An increase in end-diastolic pressure in the ventricles of the heart

It is caused by an increase in the amount of blood accumulating in their cavities, a violation of the relaxation of the myocardium, dilation of the heart cavities due to an increase in the volume of blood in them, and stretching of the myocardium.

4. Increase in blood pressure in vessels that bring blood to the heart

An increase in blood pressure in venous vessels and heart cavities from where blood flows to the mainly affected parts of the heart. Thus, with left ventricular heart failure, the pressure in the left atrium, the small circle of blood circulation, and the right ventricle increases. With right ventricular heart failure, the pressure increases in the right atrium and in the veins of the great circle of blood circulation.

5. Decrease in the rate of systolic contraction and diastolic relaxation of the myocardium

It is manifested mainly by an increase in the duration of the period of isometric tension and systole of the heart as a whole.

6. Manifestations of acute heart failure – pulmonary edema

As a rule, pulmonary edema develops quite quickly. In this connection, it is fraught with general acute hypoxia and significant disorders of the central nervous system.

The initial and main pathogenetic hemodynamic factor, which characterized by:

- Decreased LV myocardial function.
- An increase in residual systolic blood volume in the LV.
- An increase in end-diastolic volume and end-diastolic pressure in the LV.
- An increase in blood pressure in the vessels of the small circulatory circle (pulmonary capillary wedge pressure) above 25 mm Hg.
- An increase in the effective hydrodynamic pressure. When it exceeds the effective oncotic suction power, the transudate enters the intercellular space of the lungs (interstitial edema develops).
- Interstitial pulmonary edema – swelling of the parenchyma of the lungs without the release of transudate into the lumen of the alveoli. Clinical manifestations:
- shortness of breath,
- cough without sputum.

As the process progresses, alveolar edema occurs. When a large amount of edematous fluid accumulates in the interstitium, it penetrates between the cells of the endothelium and the epithelium of the alveoli, filling the cavities of the latter (alveolar edema develops). In this connection, gas exchange in the lungs is disturbed, and respiratory hypoxia and acidosis develop.

Clinical manifestations:

- cough with frothy sputum,
- suffocation,
- first dry and then moist rales are heard in the lungs.

Chronic heart failure is most often a complication and consequence of some cardiovascular diseases. It is the most common and often occurs asymptomatically for a long time. Any disease of the heart eventually leads to a decrease in its contractile function.

Usually, chronic heart failure develops against the background of myocardial infarction, coronary heart disease, cardiomyopathy, arterial hypertension, or heart valve defects.

As statistics show, untreated heart failure is the most common cause of death in patients with heart disease. In patients with chronic heart failure, left ventricular and right ventricular (more common) insufficiency, and systolic and diastolic dysfunction of the myocardium can be observed. Manifestations of chronic HF depend on the cause, the mechanism of its development, and the stage of HF. This information is presented above.

Tasks for independent work on the topic «Pathophysiology of the systemic blood circulation. Insufficiency blood circulation. Cardiac insufficiency»

The student is offered 2-3 ECGs with signs of heart failure. It is necessary to determine ECG signs of acute and chronic heart failure. Be able to explain the electrophysiological mechanisms of their occurrence. Analysis of errors with an explanation of the correct answers

List of questions and works to be studied:

1. The concept of heart failure. Reasons, types.
2. Compensatory and adaptive mechanisms.
3. Violation of hemodynamics.
4. Manifestations of heart failure.
5. Tonogenic and myogenic dilation of the heart.
6. Mechanisms of long-term adaptation of the heart to overloads.
7. Myocardial hypertrophy.

List of practical skills that must be mastered:

1. Explain compensatory reactions in heart failure.
2. Compare the features of systolic and diastolic dysfunction.
3. Identify on the ECG signs of accompanying disorders of systemic hemodynamics and heart function in acute and chronic heart failure,
4. Describe signs reflecting the presence of systolic and diastolic dysfunction, compensatory hypertrophy, nomotopic and heterotopic arrhythmias, conduction, excitability and contractility.

Situational tasks KROK-1 to determine the final level of knowledge

1. ECG of a 44-year-old patient shows signs of hypertrophy of both ventricles and the right atrium. The patient was diagnosed with the tricuspid valve insufficiency. What pathogenetic variant of cardiac dysfunction is usually observed in case of such insufficiency?

A. Heart overload by volume.
B. Heart overload by resistance.
C. Primary myocardial insufficiency.
D. Coronary insufficiency.
E. Cardiac tamponade.

2. In course of a preventive examination of a miner a doctor revealed changes of cardiovascular fitness, which was indicative of cardiac insufficiency at the compensation stage. What is the main proof of cardiac compensation?

A. Tachycardia.
B. Myocardium hypertrophy.
C. Rise of arterial pressure.
D. Dyspnea.
E. Cyanosis.

3. Dystrophic changes of the heart muscle are accompanied with cardiac cavity enlargement, decrease of the strength of heart contraction, increased amount of blood, which remains in the heart during systolic phase, overfilled veins. For what state of heart is it characteristic?

A. Myogenic dilatation.
B. Tonogenic dilatation.
C. Tamponade of the heart.
D. Cardiosclerosis.
E. Emergency stage of hyperfunction and hypertrophy.

4. A patient has a history of chronic heart failure. Which of the following hemodynamic parameters is a major symptom of cardiac decompensation development?

A. Tonogenic dilatation.
B. Decreased stroke volume.
C. Tachycardia development.
D. Increased peripheral vascular resistance.
E. Increased central venous pressure.

5. An animal with aortic valve insufficiency got hypertrophy of its left heart ventricle. Some of its parts have local contractures. What substance accumulated in the myocardiocytes caused these contractures?

A. Potassium. *C. Calcium.* *E. Sodium.*
B. Lactic acid. *D. Carbon dioxide.*

6. A patient with mitral valve insufficiency developed hypertrophy of the left ventricle of the heart. What is the starting mechanism in the development of hypertrophy?

A. Activation of the genetic apparatus.
B. Increasing consumption of fatty acids.
C. Increasing the intensity of cellular respiration.
D. Activation of glycolysis.
E. Increase in Ca_2+ influx into the cell.

7. A patient who suffers from severe disorder of water-salt metabolism experienced cardiac arrest in diastole. What is the most probable mechanism of cardiac arrest in diastole?

A. Hyperkaliemia. *C. Organism dehydratation.* *E. Hyponatremia.*
B. Hypernatremia. *D. Hypokaliemia.*

8. In order to reproduce heart failure, the frog's heart was perfused with a solution of cadmium bromide, a blocker of sulfhydryl groups. What variant of heart failure occurs in this case?

A. Mixed form.
B. From volume overload.
C. From toxic damage to the myocardium.
D. Caused by a violation of coronary blood circulation.
E. From resistance overload.

9. Transmural myocardial infarction in the patient was complicated with progressive acute left ventricle insufficiency. What is the most typical for this state?

A. Edema of the lungs. *C. Cyanosis.* *E. Arterial hypertension.*
B. Edema of the extremities. *D. Ascites.*

10. A patient with extensive myocardial infarction has developed heart failure. What pathogenetic mechanism contributed to the development of heart failure in the patient?

A. Pressure overload.
B. Acute cardiac tamponade.
C. Myocardial reperfusion injury.
D. Volume overload.
E. Reduction in the mass of functioning myocardiocytes.

Standards of correct answers to the task KROK-1

1	2	3	4	5	6	7	8	9	10
A	*B*	*A*	*C*	*C*	*A*	*A*	*C*	*A*	*E*

Recommendations for registration of work results

1. Written answers to test tasks (initial level of knowledge).
2. Protocol of ECG analysis with acute and chronic heart failure/
3. Protocol for solving situational tasks with an explanation of the correct answers.

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Topic 8. Heart arrhythmia

Justification of the topic. Diseases of the cardiovascular system, according to the World Health Organization, currently hold the first place in structure of morbidity of people of the world and are the most frequent cause of death. Many of them are often accompanied by changes in heart rhythm, which lead to important hemodynamic disturbances in the body of patients to disability, and sometimes in the death. The doctor needs to know the etiology and pathogenesis of arrhythmias, ECG changes, the principles of etiologic and pathogenic therapy. Modelling of arrhythmias in animals allows studying some of the etiological factors that cause arrhythmias, and find out some mechanisms of arrhythmias.

Purpose of the lesson:

General – to be able to reproduce the model of the main forms of cardiac rhythm disturbances caused by dysfunction of the pathways of the heart, to explain the causes and mechanisms of their occurrence in order to develop the ability to use etiotropic and pathogenetic treatment of arrhythmias.

Specifically:

Know:

1. Give the definition of "cardiac arrhythmia" and classify them.
2. In the experiment on the frog modulate violations of automatism, excitability and conduction of the heart.
3. Write down kymograms arrhythmias and compare them with the normal rhythm to determine the main features of arrhythmias.
4. Be able to explain the mechanisms of arrhythmias appearance, their main manifestations on ECG and hemodynamic disturbances in the organism during arrhythmia.

To be able to:

1. Explain the basic properties of the heart muscle (automatism, excitability, conductivity and contractility).
2. Explain the ECG of a healthy person in the standard leads.
3. To determine the main ECG signs in cardiac arrhythmias caused by a violation of the function of automatism, excitability and conduction of the heart. Explain the mechanism of their occurrence.
4. Explain the mechanisms of neural and humoral regulation of cardiac activity.

Practical experience:

Determination of signs of heart rhythm disorders on the ECG:

1. Nomotopic rhythms (sinus tachycardia, sync bradycardia, sinus arrhythmia);
2. Heterotopic rhythms (atrial, nodal, ventricular, pacemaker migration);
3. Extrasystole, flutter and fibrillation of atria and ventricles;
4. Slowing down or blockage of conduction of impulses to the heart;
5. Syndrome of premature excitation of the ventricles.

The graph of the logical structure of the topic "Heart Arrhythmia" is attached

Material and methodological support of the topic "Heart Arrhythmia".

1. Lectures;
2. Methodical instructions for teachers;
3. Methodical instructions for students;
4. Set of test tasks to determine the basic level of knowledge;
5. Set of situational tasks to determine the final level of knowledge;
6. Set of KROK-1 tasks;
7. Set of schemes and tables (presentation);
8. Set of forms with a clinical blood test;
9. Video films;
10. For the experiment (experimental animals – frogs; kymograph, tripod, cork board for fixing the frog, device for recording heart contractions, tweezers, scissors, Ringer's solution, ligatures)

Oriented map of students' work on the topics «Heart Arrhythmia»

No	Stage of lesson	Academic time, min	Educational guide		Place holding a class
			Educational tools	Equipment	
1	Determination of the initial level of knowledge	10	Written response to test tasks	Test tasks	Learning room
2	Analysis of theoretical material	35	Analysis of the theoretical material is carried out on the basis of control questions of the topic and "KROK 1" tasks	Control questions of the topic, task " KROK 1" situational tasks, ECG set	
3	Practical part (carrying out experiment	30	Introduction and preparation for setting up the experiment. Setting up the experiment. Discussion of experiment results and formulation of conclusions	Kymograph, tripod, cork board for frog fixation, device for recording heart contractions, tweezers, scissors, Ringer's solution, ligatures	
4	Determination of the final level of knowledge and skills. Summa-rizing the results	15	Solution of situational tasks to determine the final level of knowledge and skills of the student.	KROK-1 tasks, situational tasks	

HEART ARRHYTHMIA.

Arrhythmia – a typical form of heart pathology - is characterized by a violation of the frequency and periodicity of excitation generation and/or the sequence of excitation of the atria and ventricles.

The main causes of arrhythmias:

1. Inflammatory, ischemic or toxic damage to the myocardium.

2. Violation of the balance between the content of intracellular and extracellular potassium, sodium, calcium and magnesium.

3. Hormonal dysfunctions.

4. Violation of the interaction of sympathetic and parasympathetic innervation of the heart.

The presence of paths with different speeds of conduction of excitation (in the form of a certain structural anomaly or as a result of a focal pathological process), which create conditions for the continuous circulation of an excitation wave

Functional disorders of MS are characterized by:

- no signs of heart damage,
- absence of hemodynamic disorders,
- transitory (non-permanent) character,
- the absence of subjective sensations or their minimal expression,
- benign course.

It is typical for organic disorders of MS presence of signs of heart damage:

- hemodynamic disturbances are possible,
- permanent character,
- presence of complaints and clinical symptoms,
- progressive or relapsing course.

Automatism is the ability of heart tissue to spontaneously generate an action potential

1. The change in normal automatism is due to:

• violation of the functions of the sinus-atrial node (sinus node – SU),

• pace drivers of the second and third orders.

The emergence of pathological automatism (ectopic activity) can be observed:

• atrial tissue,

• in the tissues of the ventricles,

• in the bundle of His,

• in Purkinje fibers during partial depolarization of cardiomyocytes.

Depending on the place (topography) of the generation of the abnormal excitation pulse, nomotopic and heterotopic arrhythmias are distinguished.

They arise in the sinus-atrial node. These include:

• sinus tachycardia,

• sinus bradycardia,

• sinus arrhythmia,

• syndrome of weakness of the sinus-atrial node.

Heterotopic arrhythmias. These are ectopic rhythms. They arise outside the SU and are due to the predominance of automatism below the lying centers of rhythmogenesis.

Manifestations of these arrhythmias:

- supraventricular pacemaker migration,
- atrial slow rhythm,
- atrioventricular rhythm (AV rhythm) (nodal rhythm),
- idioventricular rare (ventricular) rhythm (heterotopic heart rhythm, in which the pacemaker – the pacemaker – is located in the myocardium of the ventricles),

o idioventricular accelerated heart rhythm – heart rate 60–120 per minute (occurs with pathological circulation of excitation through the myocardium of the ventricles),

o atrioventricular dissociation (AV-dissociation) – complete cessation of excitation from the atria to the ventricles; at the same time, the atria and ventricles contract independently of each other (complete transverse block), impulses "jump out".

1.1. Pathogenesis and manifestations of nomotopic arrhythmias Sinus Node Arrhythmias

In a healthy heart driven by sinus node discharge, the heart rate ranges between 60 and 100 beats per minute. On the ECG, a P wave may be observed to precede every QRS complex. Historically, normal sinus rhythm has been considered the "normal" rhythm of a healthy heart. In normal sinus rhythm, a P wave precedes each QRS complex, and the RR intervals, which are used to measue heart rate, remain relatively constant over time. Alterations in the function of the SA node lead to changes in rate or rhythm of the heartbeat.

Respiratory sinus arrhythmia is a cardiac rhythm characterized by gradual lengthening and shortening of RR intervals. This variation in cardiac cycles is related to intrathoracic pressure changes that occur with respiration and resultant alterations in autonomic control of the SA node. Inspiration causes acceleration of the heart rate, and expiration causes slowing. Respiratory sinus arrhythmia accounts for most heart rate variability in healthy individuals. Decreased heart rate variability has been associated with altered health states, including myocardial infarction, congestive heart failure, hypertension, diabetes mellitus, and prematurity in infants.

Sinus Bradycardia. Sinus bradycardia describes a slow (< 60 beats per minute) heart rate. In sinus bradycardia, a P wave precedes each QRS. A normal P wave and PR interval (0.12 to 0.20 second) indicate that the impulse originated in the SA node rather than in another area of the conduction system that has a slower inherent rate. Vagal stimulation decreases the firing rate of the SA node and conduction through the AV node to cause a decrease in heart rate. This rhythm may be normal in trained athletes, who maintain a large stroke volume, and during sleep. Sinus bradycardia may be an indicator of poor prognosis when it occurs in conjunction with acute myocardial infarction, particularly if associated with hypotension.

The main ECG signs of sinus bradycardia:

• Heart rate below the lower limit of the age norm (the RR interval is prolonged).

• The same distance between R teeth (RR interval).

• The driver of the rhythm is the SU: positive wave P in leads I, II, aVF, V4-V6, negative wave P in lead aVR, the same duration of the PQ interval.

Sinus Tachycardia. Sinus tachycardia refers to a rapid heart rate (> 100 beats per minute) that has its origin in the SA node. A normal P wave and PR interval should precede each QRS complex. The mechanism of sinus tachycardia is enhanced automaticity related to sympathetic stimulation or with-

drawal of vagal tone. Sinus tachycardia is a normal response during fever and exercise and in situations that incite sympathetic stimulation. It may be associated with congestive heart failure, myocardial infarction, and hyperthyroidism. Pharmacologic agents such as atropine, isoproterenol, epinephrine, and quinidine also can cause sinus tachycardia.

The main ECG signs of sinus tachycardia:

• Heart rate exceeds the upper limit of the age norm (RR interval is shortened).

• Equal distance between R teeth (RR interval).

• The driver of the rhythm is the SU: positive wave P in leads I, II, aVF, V4-V6, negative wave P in lead aVR, the same duration of PQ.

Sinus Arrest. Sinus arrest refers to failure of the SA node to discharge and results in an irregular pulse. An escape rhythm develops as another pacemaker takes over. Sinus arrest may result in prolonged periods of asystole and often predisposes to other arrhythmias. Causes of sinus arrest include disease of the SA node, digitalis toxicity, myocardial infarction, acute myocarditis, excessive vagal tone, quinidine, acetylcholine, and hyperkalemia or hypokalemia.

Sick Sinus Syndrome. Sick sinus syndrome is a term that describes a number of forms of cardiac impulse formation and intra-atrial and AV conduction abnormalities. The syndrome most frequently is the result of total or subtotal destruction of the SA node, areas of nodal–atrial discontinuity, inflammatory or degenerative changes of the nerves and ganglia surrounding the node, or pathologic changes in the atrial wall. In addition, occlusion of the sinus node artery may be a significant contributing factor. Approximately 40 of adults with sick sinus syndrome also have coronary heart disease. In children, the syndrome is most commonly associated with congenital heart defects, particularly following corrective cardiac surgery.

The main ECG signs of SSS (may be one or more of the following):

• Persistent sinus bradycardia or atrial pacemaker migration. In the test with physics. there is no adequate increase in heart rate with exercise or atropine.

• Periodic disappearance of sinus rhythm and its replacement for a short time by other ectopic rhythms.

• Tachycardia-bradycardia syndrome (alternating periods of tachycardia and bradycardia).

• Periodic occurrence of sinoatrial blockade (suspension of SU).

II. Arrhythmias as a result of conduction disturbances

Conductivity – the ability of cardiomyocytes to conduct excitation. Violations of conduction of excitation are manifested by various heart blocks or arise as a result of the mechanism of reentry arrhythmias.

Types of impulse conduction disorders in the heart:

According to the change in the pulse conduction speed:

• Slowdown,

• Blockade.

• Acceleration.

According to the duration of the conduction disorder:

• Temporary.

• Permanent.

According to the location of the violation:

• sinoatrial.

• intraatrial.

• atrioventricular.

• intraventricular.

Sinoatrial blockade

Inhibition or blockade of the transmission of the excitation impulse from the LV to the atria causes the failure of individual heart contractions. As a result, there is a slowing down of the frequency and violation of the regularity of heart contractions.

As a permissible variant of CA, blockade can be observed in infants when crying, restlessness, during night sleep. At an older age, it is found in people with high lability of the central nervous system. However, it is most often observed in diseases.

Incomplete CA blockades are most common. In case of complete CA blockade, ectopic contractions from the atria, AV junction, or ventricles are registered on the ECG.

The main ECG signs of CA blockade:

• Periodic loss of individual heart cycles (P waves and QRST complexes) after 1, 2, 3 or more normal cycles.

• An increase at the time of falling of cardiac cycles of the pause between two adjacent P or R waves by almost 2 times (rarely 3 or 4) in comparison with the usual PP or RR intervals.

Intraatrial blockade

Due to the asymmetric location of the LV in relation to the atria, their excitation normally occurs non-simultaneously (at first - the right and with some delay - the left). An increase in the heterochromia of atrial excitation in conditions of pathology can lead to varying degrees of intraatrial inhibition or blockade of conduction of sinus impulses. Incomplete blockade is most common.

Heart block refers to abnormalities of impulse conduction. It may be normal, physiologic (*e.g.*, vagal tone), or pathologic. It may occur in the AV nodal fibers or in the AV bundle, which is continuous with the Purkinje conduction system that supplies the ventricles. The PR interval on the ECG corresponds with the time it takes for the cardiac impulse to travel from the SA node to the ventricular pathways. Normally, the PR interval ranges from 0.12 to 0.20 second.

First-Degree AV Block. First-degree AV block is characterized by a prolonged PR interval (exceeds 0.20 second). The prolonged PR interval indicates delayed AV conduction, but all atrial impulses are conducted to the ventricles. This condition usually produces a regular atrial and ventricular rhythm. Clinically significant PR interval prolongation can result from con-

duction delays in the AV node itself, the His-Purkinje system, or both. When the QRS complex is normal in contour and duration, the AV delay almost always occurs in the AV node and rarely in the bundle of His. In contrast, when the QRS complex is prolonged, showing a bundle branch block pattern, conduction delays may be in the AV node or the His-Purkinje system. First-degree block may be the result of disease in he AV node such as ischemia or infarction, or of infections such as rheumatic fever or myocarditis.48–50 Isolated first-degree heart block usually is not symptomatic, and temporary or permanent cardiac pacing is not indicated.

Second-Degree AV Block. Second-degree AV block is characterized by intermittent failure of conduction of one or more impulses from the atria to the ventricles. The nonconducted P wave can appear intermittently or frequently. A distinguishing feature of second-degree AV block is that conducted P waves relate to QRS complexes with recurring PR intervals; that is, the association of P waves with QRS complexes is not random. Second-degree AV block has been divided into two types: type I (*i.e.*, Mobitz type I or Wenckebach's phenomenon) and type II (*i.e.*, Mobitz type II).

Third-Degree AV Block. Third-degree, or complete, AV block occurs when the conduction link for all impulses from the SA node and atria through the AV node is blocked, resulting in depolarization of the atria and ventricles being controlled by separate pacemakers. The atrial pacemaker can be sinus or ectopic in origin. The ventricular pacemaker usually is located just below the region of the block. The atria usually continue to beat at a normal rate, and the ventricles develop their own rate, which normally is slow (30 to 40 beats per minute). The atrial and ventricular rates are regular but dissociated. Third-degree AV block can result from an interruption at the level of the AV node, in the bundle of His, or in the Purkinje system. Third-degree blocks at the level of the AV node usually are congenital, whereas blocks in the Purkinje system usually are acquired. Normal QRS complexes, with rates ranging from 40 to 60 complexes per minute, usually are displayed on the ECG when the block occurs proximal to the bundle of His. Complete heart block causes a decrease in cardiac output with possible periods of syncope (fainting), known as a *Stokes-Adams attack.* Other symptoms include dizziness, fatigue, exercise intolerance, or episodes of acute heart failure. Most persons with complete heart block require a cardiac pacemaker.

The main ECG signs of complete AV block:

• PP intervals are the same, P waves are not changed, they are layered on different sections of the cardiac cycle.

• QRS complexes in atrioventricular rhythm are usually unchanged, in left ventricular rhythm they are expanded and deformed.

• RR intervals are prolonged, ventricular rhythm is always less than atrial rhythm: RR intervals < RR intervals (in contrast to AVD).

Blockade of the legs of the bundle of His (intraventricular) conduction disorders)

- Intraventricular blockade consists in inhibition or blockade of the propagation of excitation along the legs of the bundle of His, its branches and along the Purkinje fibers. Most often, there is a violation of conduction in one of the legs of the bundle of His. Then it spreads along the undamaged system of bundle legs and only after that to the other ventricle (mainly through the interventricular septum). This route of excitation causes nonsimultaneity, discordant contractions of the ventricles.
- If conduction is completely absent, it is said about complete blockade or simply about blockade (the word "complete" is not written in confinement). In the case of partial, slow conduction of the excitation impulse, one speaks of incomplete blockade.

General ECG signs of bundle branch block:

• Deformation of the QRS complex (jaggedness, M-shaped, and other forms of splitting) is best expressed in the right or left chest leads.

• Widening of the QRS complex.

• Discordant (difference) of the largest teeth of the QRS complexes in the right and left chest leads, as well as in I and III standards.

• Discordant waves of T and ST interval in relation to the largest wave of the QRS complex in the left or right chest leads.

Excitability is the ability of cells to perceive a signal and respond to it with an excitation reaction. The excitability of the heart muscle is expressed in the ability to generate PD.

Causes of excitability disorders

• Functional disorders of the nervous system (neurosis, stress, vagotonia).

• Organic lesions of the nervous system (brain tumors, skull injuries, impaired cerebral circulation).

• Myocardial lesions (dystrophies, myocarditis, cardiosclerosis, cardiomyopathies, myocardial infarction).

• Violation of the electrolyte balance (changes in the content of potassium, calcium, magnesium ions in the blood).

• Exposure to toxic substances (carbon monoxide, bacterial toxins, nicotine, alcohol, industrial toxic substances). Drug intoxication (anti-arrhythmic drugs, β-adreno-mimetics, cardiac glycosides).

• Hypoxemia (with heart failure, "pulmonary heart").

Types of combined arrhythmias

Rhythm disorders caused by a combination of changes in the properties of excitability, conduction and automatism are divided into several groups.

• Extrasystole: sinus, atrial (supraventricular), from the atrioventricular node (nodal, atrioventricular), ventricular.

• Paroxysmal tachycardia (atrial, from the atrioventricular junction, ventricular, fluttering and flickering of the atria).

• Fluttering and flickering of the ventricles.

Extrasystole is a premature out-of-order excitation and contraction of the heart and its parts. The excitation impulse usually comes from different areas of the conducting system of the myocardium.

Extrasystole is one of the most frequent heart rhythm disturbances and can occur both in healthy, as well as with diseases.

The main causes of extrasystole:

• organic lesions of the heart (carditis, cardiosclerosis, cardiomyopathy, etc.);

• functional disorders (somatic and infectious diseases, vegetative dysfunction syndrome, metabolic disorders of the myocardium, etc.).

Depending on the place of origin of impulses for premature contractions, ECs are divided into groups:

• atrial;

• from the atrioventricular connection;

• ventricular.

Depending on the number of ECS, the following are distinguished:

• single ECs,

• multiple ECs (more than 5 ECS in 1 minute),

• group extrasystole (if 3 or more ECS follow in a row).

Depending on the sequence of normal contractions with ECS:

Allorhythmia – a certain sequence of alternation of ECS and normal contractions:

• bigeminy – every normal contraction is followed by ECS.

• trigeminy – every 2 normal contractions are followed by an ECS or after each normal contraction two ECs are followed in a row;

• quadrigeminy – after every 3 normal contractions there is ECS or after every normal contraction there are three ECS in a row, etc.

• couplet – occurrence of two ECS in a row.

• three or more ECs in a row – a run of supraventricular tachycardia.

The main ECG signs of atrial extrasystole:

• Premature out-of-order appearance of the extrasystolic P wave and the unchanged QRST complex following it.

• Deformation and/or change in polarity of the P wave.

• Incomplete compensatory pause.

The main ECG signs of ventricular extrasystole:

• Premature out-of-order occurrence of extrasystolic altered ventricular QRST complex.

• Absence of a tooth.

• Significant expansion and deformation of the extrasystolic QRS complex, increase in its voltage.

• ST segment and T wave extrasystoles of the discordant direction of the main wave of the QRS complex, the ST segment may be absent altogether.

• Complete compensatory pause.

The main ECG signs of parasystole:

• Two independent rhythms are registered.

• An ectopic rhythm resembles EC, but the distance from the normal complex to EC changes all the time.

• ECs follow each other for different periods of time because parasystolic cells also have outlet blockade.

Paroxysmal tachycardia

• Paroxysmal tachycardia (PT) is an attack-like sharp increase in heart rate lasting from a few seconds to several hours or even days.

• A paroxysm of tachycardia is said to occur when the number of ectopic impulses exceeds 3–5, and their frequency varies from 160 to 220 per minute (when the heterotopic focus is located in the atrium) or from 140 to 200 per minute (when located in the ventricles).

Paroxysmal supraventricular tachycardia is sometimes referred to as paroxysmal atrial tachycardia. This term includes all tachyarrhythmias that originate above the bifurcation of the bundle of His and have a sudden onset and termination. They may be the result of AV nodal reentry, Wolff-Parkinson-White syndrome (caused by an accessory conduction pathway between the atria and ventricles), or intraatrial or sinus node reentry. Paroxysmal supraventricular tachycardias tend to be recurrent and of short duration.

Setting up the experiment. Discussion of results and Formulation of conclusions

Modeling of cardiac automatism disorders:

1. **Sinus tachycardia** – irrigate the heart with 1–2 ml of Ringer's solution, heated to 30–35 °C, and observe how quickly the frequency of heart contractions occurs;

2. **Reflex sinus bradycardia** – several blows are applied to the frog's stomach with tweezers; at the same time, there is a short-term stop or a sharp slowing of heart contractions; the activity of the heart is soon restored.

3. **Simulation of extrasystole**: after turning on the current, touch the end of the electrode to the ventricles of the heart during diastole. Electrical irritation causes an additional contraction (extrasystole), followed by a prolonged pause (compensatory).

4. **Simulation of heart block**: the recording of atrial contractions is set up simultaneously with the recording of ventricular contractions. After recording the curve of normal contractions of the atria and ventricles, apply a ligature on the border between the atria and the ventricle and tighten it. After the complete cessation of conduction, the atria continue to contract in the former rhythm. The contractions of the ventricles first stop, and then they begin to contract, but at a much slower rate.

Discussion of the results of the experiment

• As the first experience shows, the effect of heat (heated Ringer's solution) on the heart causes an increase in its contractions (tachycardia).

• Bradycardia, which was observed when the animal was tapped on the stomach, occurs reflexively. Irritation is perceived by the receptors of the organs of the abdominal cavity, comes along the precentral fibers to the center of the vagus nerve in the medulla oblongata, and from there is transmitted along the branches of the vagus nerve to the heart.

A similar stoppage or slowing down of heart activity in humans can be observed with injuries.

• Additional contraction of the heart (extrasystole) occurs in connection with the occurrence of an additional source of excitation in any part of the conduction system of the heart. The extended pause (compensatory) observed after extrasystole is explained by the fact that another normal impulse coming from the sinus node finds the heart muscle in the refractory phase of extrasystole. Therefore, the next contraction of the heart falls out and the ventricle remains at rest until the next normal impulse reaches it from the sinus node.

• Imposition of a ligature in our experience caused a violation of the conduction between the atria and the ventricles (atrioventricular block) (Stannius experiment). If you gradually tighten the ligature, you can sometimes observe incomplete blockade: for two or three contractions of the atria, one contraction of the ventricles is necessary. With the stronger tightening of the ligature, a complete blockade of the atrium is obtained, and the ventricles contract independently of each other. At the same time, the atria continue to receive impulses from the sinus node and contract in the same rhythm. The ventricle receives impulses from the lower parts of the conduction system. Due to the fact that the automatism of these departments is less pronounced than the automatism of the sinus node, the contractions of the ventricles occur at a much slower rate.

• Conduction disorders can occur as a result of changes of both functional and organic nature in the conducting system of the heart. For the first time, Pavlov experimentally induced neurogenic atrioventricular heart block by stimulating the heart's accelerating nerves. When the heart's reinforcing nerves were irritated, this phenomenon was eliminated.

Formulation of conclusions based on the experiment

1. **Sinus tachycardia**. As a result of applying heated Ringer's solution to the heart, an increase in heart rate occurs – sinus tachycardia. Mechanism: direct effect of the temperature factor on the sinus node.

2. **Sinus bradycardia.** As a result of blows to the stomach, damage to heart contractions occurs – sinus bradycardia. Mechanism: irritation of the vagus nerve, which in turn causes hyperpolarization, that is, there is a significant increase in the maximum diastolic potential.

3.**Ventricular extrasystole.** When an electric current is applied to the heart muscle, an extraordinary contraction occurs – extrasystole. Mechanism: additional contraction of the heart occurs due to the appearance of an additional source of excitation in the area of the heart's conduction system. An increased (prolonged) compensatory pause is observed after extrasystole and is explained by the fact that another normal impulse coming from the sinus node catches the heart muscle in the reflex phase of extrasystole.

4. **Complete atrioventricular block**. The imposition of a ligature caused a violation of conduction between the atria and ventricles (atrioventricular block). At the same time, the atria continue to receive impulses from the sinus node and contract in the former rhythm. The ventricles receive impulses from the lower parts of the conduction system. Because the automatism of these departments is less pronounced than the automatism of the sinus node, the contraction of the ventricles occurs in a more rarefied mode.

Tasks for independent work on the topic "Arrhythmias of the heart"

The student is offered 2–3 ECGs with rhythm and conduction disturbances. It is necessary to determine the ECG signs and the type of rhythm and conduction disturbance. Be able to explain the mechanism of occurrence. Analysis of errors with an explanation of the correct answers.

List of questions and works to be studied:

1. Definition of the term "arrhythmia". The main causes of arrhythmias. Signs of functional and organic heart rhythm disorders.
2. Arrhythmias caused by a violation of automatism. Reasons, types. ECG signs
3. Sinus node weakness syndrome. Causes, electrophysiological mechanism, main ECG signs.
4. Heterotopic heart rhythm disorders. Types of ectopic rhythms.
5. Migration of the rhythm driver. Reasons, main ECG signs.
6. Arrhythmias as a result of impaired conduction of impulses to the heart. Kinds
7. Arrhythmias as a result of slowing down or blocking the conduction of impulses to the heart. Reasons, types.
8. Syndrome of premature excitation of the ventricles. Reasons. Manifestations. Basic ECG signs.
9. Combined heart rhythm disorders. Causes, mechanisms, types.

List of practical skills that must be mastered:

Determination of signs of heart rhythm disorders on the ECG:

1. Nomotopic rhythms (sinus tachycardia, sync bradycardia, sinus arrhythmia, SNWS);
2. Heterotopic rhythms (atrial, nodal, ventricular, pacemaker migration);
3. Extrasystole, flutter and fibrillation of atria and ventricles;
4. Slowing down or blockage of conduction of impulses to the heart;
5. Syndrome of premature excitation of the ventricles

Situational tasks KROK-1 to determine the final level of knowledge

1. Processes of repolarisation are disturbed in ventricular myocardium in examined person. It will cause amplitude abnormalities of configuration and duration of the wave:

A. T. *B. Q.* *C. R.* *D. S.* *E. P.*

2. Person has stable HR, not more than 40 bpm. What is the pacemaker of the heart rhythm in this person?

A. Atrioventricular node. *C. Purkinye' fibers.* *E. His' bundle.*
B. Sinoatrial node. *D. Branches of His' bundle.*

3. A patient has a first-degree atrioventricular block accompanied by the prolongation of P-Q interval up to 0,25 s. Under such conditions the following myocardial function will be disturbed:

A. Excitability. *C. –.* *E. Contractibility.*
B. Conduction. *D. Automatism.*

4. A patient has extrasystole. ECG shows no P wave, QRS complex is deformed, there is a full compensatory pause. What extrasystoles are these?

A. Atrial. *C. Atrioventricular.* *E. –.*
B. Ventricular. *D. Sinus.*

5. A 45-year-old patient was admitted to the cardiological department. ECG data: negative P wave overlaps QRS complex, diastolic interval is prolonged after extrasystole. What type of extrasystole is it?

A. Sinus. *C. Atrioventricular.* *E. Bundle-branch.*
B. Atrial. *D. Ventricular.*

6. A 67-year-old patient complains of periodic heart ache, dyspnea during light physical activities. ECG reveals extraordinary contractions of heart ventricles. Such arrhythmia is called:

A. . Bradycardia *C. Flutter.* *E. Fibrillation.*
B. Tachycardia. *D. Extrasystole.*

7. Analysis of the ECG revealed the missing of several PQRST cycles. The remaining waves and complexes are not changed. Specify the type of arrhythmia:

A. Sinoatrial block. *C. Atrioventricular block.* *E. Atrial premature beat.*
B. Atrial fibrillation. *D. Intra-atrial block.*

8. In a 45-year-old patient on ECG it was revealed: sinus rhythm, the number of auricular complexes exceeds number of ventricular complexes; progressing extension of the P-Q interval from complex to complex; fallout of some ventricular complexes; P waves and QRST complexes are without changes. Name the type of heart rhythm dysfunction.

A. Synoauricular block. *C. Atrioventricular blockade of the I degree.*
B. Intraatrial block. *D. Complete atrioventricular block.*
E. Atrioventricular block of the II degree.

9. A 49 y.o. woman consulted a doctor about heightened fatigue and dyspnea during physical activity. ECG: heart rate is 50/min, PQ is extended, QRS is unchanged, P wave quanity exceeds quantity of QRS complexes. What type of arrhythmia does the patient have?

A. Extrasystole. *C. Ciliary arrhythmia.* *E. Atrioventricular block.*
B. Sinus bradycardia. *D. Sinoatrial block.*

10. ECG of a patient shows such alterations: P-wave is normal, P-Q-interval is short, ventricular QRST complex is wide, R-wave is double-peak or two-phase. What form of arrhythmia is it?

A. WPW syndrome (Wolff-Parkinson-White).
B. Frederick's syndrome (atrial flutter).
C. Atrioventricular block.
D. Ventricular fibrillation.
E. Ciliary arrhythmia.

Standards of correct answers to the situational tasks

1	2	3	4	5	6	7	8	9	10
A	*A*	*B*	*B*	*C*	*D*	*A*	*E*	*E*	*A*

Recommendations for registration of work results

1. Written answer to test tasks (basic level of knowledge).
2. The results of the experiment are drawn up in the form of an experiment protocol with the determination of relevant conclusions.
3. Protocol of ECG analysis with heart rhythm disturbance.
4. Protocol for solving situational tasks with an explanation of the correct answers.

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Topic 9. Coronary damage of the myocardium. Coronary insufficiency. Coronary heart disease. Myocardial infarction. Cardiogenic shock

Justification of the topic. Heart failure – one of the frequent causes incapacitation, disability and death of patients which suffering from diseases of the cardiovascular system. The study of the etiology and pathogenesis of these menacing disease forms necessary for practice doctor, as heart failure arises from different causes and mechanisms. In connection with this knowledge of the causes and mechanisms of this pathology will facilitate the development of clinical thinking, rational choice approaches to the treatment of each patient. Studying in the experiment on the animal heart failure can reveal the mechanisms of its development.

Purpose of the lesson:

General – be able to characterize heart failure, to explain main causes and mechanisms of development.

Specifically:

Know:

1. Disclose the essence of the notion of «heart failure».
2. To classify the causes and mechanisms of heart failure.
3. Allocate the main manifestations of heart failure, to explain the mechanisms of their appearance and development.
4. Model the on rat acute heart failure, to explain the mechanisms of compensation and decom-pensation during the experiment.

To be able to:

1. Explain the mechanism of heart rate.
2. Explain the role of cardiac and extracardiac mechanisms in the regulation of the heart function.
3. Interpret the main indicators of the heart function.
4. Explain the effect of a change heart rate and stroke volume values of the efficiency of the heart function.

Practical experience:

1. Determination of signs of ischemia, damage, necrosis of the myocardium on the ECG.
2. Determination on the ECG of signs of acute coronary insufficiency.
3. Myocardial infarction, its stage of development, depth, localization.

The graphological structure of the topic "Coronary damage of the myocardium. Coronary insufficiency. Coronary heart disease. Myocardial infarction. Cardiogenic shock." is attached.

Material and methodical support of the topic "Coronary damage of the myocardium. Coronary insufficiency. Coronary heart disease. Myocardial infarction. Cardiogenic shock.".

1. Lectures;
2. Methodical instructions for teachers;
3. Methodical instructions for students;

4. Set of test tasks to determine the basic level of knowledge;
5. Set of situational tasks to determine the final level of knowledge;
6. Set of KROK-1 tasks;
7. Set of schemes and tables (presentation);
8. Set of forms with a clinical blood test;
9. Video films;
10. For the experiment experimental animal – rats, electrocardiograph, adrenaline, syringe.

Oriented map of students' work on the topic "Coronary damage of the myocardium. Coronary insufficiency. Coronary heart disease. Myocardial infarction. Cardiogenic shock"

No	Stage of lesson	Academic time, min	Educational guide		Place holding a class
			Educational tools	Equipment	
1	Determination of the initial level of knowledge	10	Written answer to test task	Test task	Learning room
2	Analysis of theoretical material	35	Analysis of theoretical material based on control questions of the topic, situational tasks, tasks of KROK-1	Control questions of the topic, task " KROK 1". Situational tasks	
3	Practical part (carrying out experiment)	30	Introduction and preparation for setting up the experiment. Setting up the experiment. Discussion of the results of the experiment and formulation the conclusions	Electrocardiograph, adrenaline, syringe. The experimental animal is rats	
3	Determination of the final level of knowledge and skills. Summariz-ing the results	15	Determination of the final level of knowledge and skills. Summarizing the results	KROK-1 tasks, situational tasks	

CORONARY DAMAGE OF THE MYOCARDIUM. CORONARY INSUFFICIENCY. CORONARY HEART DISEASE. MYOCARDIAL INFARCTION. CARDIOGENIC SHOCK.

Coronary insufficiency is a typical form of heart pathology, characterized by an excess of the myocardium's need for oxygen and metabolic substrates over their inflow through the coronary arteries, as well as a violation of the outflow from the myocardium of metabolic products, BAV, ions, and other agents.

The leading pathogenetic factor of coronary insufficiency is myocardial ischemia.

Clinically, coronary insufficiency manifests itself as coronary heart disease (CHD). Coronary artery damage may develop:

- angina pectoris,
- myocardial infarction,
- sudden cardiac death.

Causes of coronary insufficiency

1. **Coronarogenic causes of coronary insufficiency:**

Reduce and/or stop blood flow to the myocardium through the coronary arteries.

2. **Non-coronary causes of coronary insufficiency:**

• Increase consumption of O2 and/or metabolic substrates by the myocardium.

• The content of O2 and/or metabolic substrates in the blood and myocardium will be reduced.

3. Factors that reduce and/or stop blood flow to the myocardium through the coronary arteries

4. Factors that lead to an absolute decrease in blood flow to the myocardium through the coronary arteries (in the clinic, they occur most often): atherosclerotic lesions of the coronary arteries, aggregation of formed blood elements, spasm of the coronary arteries, a decrease in blood flow to the heart and a decrease in the perfusion pressure in the coronary arteries arteries

5. Atherosclerotic lesion of coronary arteries - local narrowing of the lumen of at least one of the coronary arteries of the heart.

6. Aggregation of formed blood elements

• atherosclerotic changes in vessel walls;

• turbulent nature of blood flow in coronary vessels;

Increasing the content and activity of blood coagulation factors released from damaged blood cells and the vascular wall. Spasm of coronary arteries.

Catecholamines are of decisive importance in the development of coronary spasm.

Arguments in favor of the sympathergic (catecholamine) mechanism of arteriolar spasm in coronary insufficiency:

• Development of episodes of coronary insufficiency in stressful situations.

• Frequent attacks of angina pectoris with pheochromocytoma.

• Development of coronary insufficiency with intra-arterial injection of adrenaline.

• An increase in the content of catecholamines in the blood before and at the height of an episode of coronary insufficiency.

In real life, coronary insufficiency is the result of a complex of interrelated factors:

• reduction of smooth cells of coronary arteries and reduction of their lumen under the influence of catecholamines, thromboxane A2, PgF2α and other vasoconstrictors;

• reduction of the internal diameter of the lumen of the coronary arteries due to thickening of their walls (due to atherosclerotic changes, hypertrophy of the muscular membrane, fibrous changes, edema, etc.);

• narrowing and closing of the vessel lumen by aggregates of formed blood elements.

A decrease in blood flow to the heart and a decrease in perfusion pressure in the coronary arteries lead to:

• significant bradycardia or tachycardia,

• fluttering and flickering of the atria and / or ventricles of the heart,

• insufficiency of aortic valves,

• acute arterial hypotension,

• compression of the coronary arteries of the heart (by a tumor, scar, foreign body).

Mechanisms of disorders of energy supply of cardiomyocytes in coronary insufficiency:

In aerobic languages, the main substrates for ATP synthesis are fatty acids (65–70 %), glucose (15–20 %) and lactic acid (10–15 %). The role of amino acids, ketone bodies and pyruvate in the energy supply of the myocardium is relatively small.

In conditions of increasing ischemia:

• In the myocardium, depletion of the O_2 reserve associated with myoglobin and a decrease in the intensity of oxidative phosphorylation develop.

• As a result of these changes, the content of ATP and creatine phosphate in cardiomyocytes decreases.

• Violation of aerobic ATP synthesis leads to activation of glycolysis and accumulation of lactate in the myocardium. At the same time, glycogen reserves are rapidly decreasing.

• Activation of glycolytic metabolism of carbohydrates determines the development of acidosis.

• The development of intra- and extracellular acidosis significantly changes the permeability of membranes for metabolites and ions, suppresses the activity of enzymes of energy supply, synthesis of cellular structures, transport of metabolic substrates and cations.

Damage to cardiomyocyte membranes and enzymes

The main properties of the myocardium (automatism, excitability, conduction, contractility), as well as their regulation, largely depend on the condition of the membranes and enzymes of cardiomyocytes. In conditions of ischemia, their damage is the result of a number of common factors

Ion and fluid imbalance in coronary insufficiency

• The total content of ions in the cells of the ischemic myocardium increases significantly.

• Intra- and extracellular ratio and distribution of individual ions, as well as fluid in cardiomyocytes changes significantly:

- An increase in the concentration of K+ outside the cells.
- An increase in the concentration of Na+ and Ca_2+ in cells.
- Accumulation of fluid in the cells.

An imbalance of ions and fluid causes a number of processes occurring in myocardial cells (membrane electrogenesis: excitability of myocardial

cells, automatism of rhythmogenesis and conduction of excitation impulses) leading to heart arrhythmia.

Coronary insufficiency is characterized by stage changes in the activity of sympathetic and parasympathetic regulation mechanisms.

• At the initial stage of myocardial ischemia, as a rule, there is activation of the SAS with an increase in the content of noradrenaline and especially adrenaline in the myocardium. As a result, tachycardia develops, cardiac output increases, and as a rule, decreases immediately after the onset of an episode of coronary insufficiency.

• At later stages of coronary insufficiency (after several tens of minutes, sometimes - hours), a decrease in the content of norepinephrine in the myocardium and the preservation of an elevated level of acetylcholine are often registered. At the same time, bradycardia, a decrease in cardiac output, the rate of contraction and relaxation of the myocardium are noted.

In conditions of coronary insufficiency (especially with prolonged ischemia and at the initial stage of myocardial reperfusion), the phenomenon of **hormononeuromediatornoy dissociation of catecholamines (the ratio of the neurotransmitter norepinephrine and the hormone adrenaline) develops.** This phenomenon is characterized by:

• a significant increase in the concentration of adrenaline in the ischemic myocardium and the realization of its cardiotoxic effects;

• a simultaneous decrease in the content of norepinephrine. The phenomenon of hormone-neuromediated dissociation of catecholamines is accompanied by potentiation of ischemic and focal fusion damage of the myocardium.

Myocardial reperfusion

Angina is characterized by a spontaneous or drug-induced change of a more or less prolonged period of myocardial ischemia with a period of restoration of coronary blood flow - reperfusion, the most effective way to stop the action of pathogenic factors of myocardial ischemia and eliminate the consequences of their impact on the heart.

Reperfusion:

• prevents the development of myocardial infarction;

• prevents aneurysm formation in the previously ischemic area of the heart;

• contributes to the formation of connective tissue in the aneurysm wall, if it has developed;

• potentiates the recovery of the contractile function of the heart.

However, post-occlusion reperfusion of coronary vessels and myocardium is often accompanied by significant heart function disorders:

- development of arrhythmias, including ventricular fibrillation.
- short-lived destabilization of indicators of central and organ tissue blood circulation,
- mbalance of biochemical and electrophysiological parameters of the heart.

In this regard, the position was formulated that coronary insufficiency is a combination of two syndromes: ischemic and reperfusion, and not just one – ischemic, as was believed earlier.

The main mechanisms of reperfusion damage to myocardial cells:

Strengthening of disruption of the energy supply of cells by myocardial reperfusion at the stages of resynthesis, transport, utilization of ATP energy.

• Suppression of ATP resynthesis. The main reasons:

• hyperhydration, swelling and destruction of mitochondria during myocardial reperfusion (result of osmotic swelling of organelles, overstretching and rupture of their membranes due to excessive accumulation of Ca_2+ and fluid in them),

• dissociative effect of excess Ca_2+,

• release of ADP, AMP and other purine compounds from the mitochondria of cardiomyocytes into the intercellular fluid.•

Violation of the ATP energy transport mechanism in myocardial cells and a decrease in the efficiency of ATP energy utilization mechanisms.

✓ Potentiation of the degree of damage to membranes and enzymes of cells and myocardium. Reasons: reperfusion (oxygen) intensification of the lipoperoxide process, calcium activation of proteases, lipases, phospholipases and other hydrolases, as well as osmotic swelling and rupture of the membranes of myocardial cells and their organelles.

✓ Increasing imbalance of ions and fluid in cardiomyocytes. Causes: reperfusion disorders of energy supply processes and damage to membranes and enzymes. This leads to the accumulation of excess Na+ and Ca_2+ in myocardial cells and, as a result, fluid in them.

✓ Reduction in the effectiveness of regulatory (nervous, humoral) effects on myocardial cells (normally they contribute to the integration and normalization of intracellular processes).

✓ Increasing expression of hormone-neuromediator dissociation.

Angina Pectoris is a clinical syndrome of precordial discomfort or pressure due to transient myocardial ischemia without infarction. It is typically precipitated by exertion or psychologic stress and relieved by rest or sublingual nitroglycerin. Diagnosis is by symptoms, ECG, and myocardial imaging.

Etiology

✓ Angina pectoris occurs when cardiac workload and resultant myocardial O_2 demand exceed the ability of coronary arteries to supply an adequate amount of oxygenated blood, as can occur when the arteries are narrowed. Narrowing usually results from atherosclerosis but may result from coronary artery spasm or, rarely, coronary artery embolism. Acute coronary thrombosis can cause angina if obstruction is partial or transient, but it usually causes MI.

✓ Because myocardial O_2 demand is determined mainly by heart rate, systolic wall tension, and contractility, narrowing of a coronary artery typically results in angina that occurs during exertion and is relieved by rest.

✓ In addition to exertion, cardiac workload can be increased by disorders such as hypertension, aortic stenosis, aortic regurgitation, or hypertrophic cardiomyopathy. In such cases, angina can result whether atherosclerosis is present or not. These disorders can also decrease relative myocardial perfusion because myocardial mass is increased (causing decreased diastolic flow).

✓ A decreased O_2 supply, as in severe anemia or hypoxia, can precipitate or aggravate angina**.**

Acute Coronary Syndromes (ACS) (Unstable Angina; Acute MI)

Acute coronary syndromes (ACS) result from acute obstruction of a coronary artery. Consequences depend on degree and location of obstruction and range from unstable angina to non–ST-segment elevation MI (NSTEMI), ST-segment elevation MI (STEMI), and sudden cardiac death. Symptoms are similar in each of these syndromes (except sudden death) and include chest discomfort with or without dyspnea, nausea, and diaphoresis. Diagnosis is by ECG and the presence or absence of serologic markers.

Etiology These syndromes usually occur when an acute thrombus forms in an atherosclerotic coronary artery. Atheromatous plaque sometimes becomes unstable or inflamed, causing it to rupture or split, exposing thrombogenic material, which activates platelets and the coagulation cascade and produces an acute thrombus. Platelet activation involves a conformational change in membrane glycoprotein (GP) IIb/IIIa receptors, allowing cross-linking (and thus aggregation) of platelets. Even atheromas causing minimal obstruction can rupture and result in thrombosis; in > 50 % of cases, stenosis is < 40 %. The resultant thrombus abruptly interferes with blood flow to parts of the myocardium. Spontaneous thrombolysis occurs in about two thirds of patients; 24 h later, thrombotic obstruction is found in only about 30 %. However, in virtually all cases, obstruction lasts long enough to cause tissue necrosis.

Pathophysiology Initial consequences vary with size, location, and duration of obstruction and range from transient ischemia to infarction. Measurement of newer, more sensitive markers indicates that some cell necrosis probably occurs even in mild forms; thus, ischemic events occur on a continuum, and classification into subgroups, although useful, is somewhat arbitrary. Sequelae of the acute event depend primarily on the mass and type of cardiac tissue infarcted.

Myocardial dysfunction: Ischemic (but not infarcted) tissue has impaired contractility, resulting in hypokinetic or akinetic segments; these segments may expand or bulge during systole (called paradoxical motion). The size of the affected area determines effects, which range from minimal to mild heart failure to cardiogenic shock. Some degree of heart failure occurs in about two thirds of hospitalized patients with acute MI. It is termed ischemic cardiomyopathy if low cardiac output and heart failure persist. Ischemia involving the papillary muscle may lead to mitral valve regurgitation.

MI: MI is myocardial necrosis resulting from abrupt reduction in coronary blood flow to part of the myocardium. Infarcted tissue is permanently dysfunctional; however, there is a zone of potentially reversible ischemia adjacent to infarcted tissue.

Risk factors:

- Age – people whose age varies between forty and fifty years are more likely than others to become "hostages" of this pathology.
- Atherosclerosis is the main risk factor for the development of the disease. Atherosclerosis of coronary arteries can lead to spasm of coronary arteries and thrombosis.
- Smoking – smokers have a stronger narrowing of the coronary heart vessels, which contributes to poor blood supply.
- Arterial hypertension – is the cause of thickening of the heart walls, thereby increasing the heart's need for blood. The heart does not receive enough oxygen, its endurance is significantly reduced.
- Diabetes.
- Obesity – contributes to the faster development of not only hypertension, but also diabetes, as well as atherosclerosis.
- Sedentary and emotionally stressful lifestyle.
- Gout.

Etiology and pathogenesis. The reason for the development of a myocardial infarction is the rapid cessation or critical reduction (by more than 80 %) of blood flow in the coronary artery.

- At the heart of the etiology of myocardial infarction is stenosing atherosclerosis of the coronary artery. However, the degree of previous myocardial infarction and narrowing of the coronary artery is not a determining mechanism of the development of the acute process, affecting the severity and outcome of the disease.
- Regardless of the specific reason that led to absolute or relative insufficiency of coronary vessels, (E. I. Chazov, F. Z. Meerson, E. Braunvald) single out the following.

4 stages of development of ischemic damage to the myocardium:

1. In the first stage, ischemic factors cause local hypoxia of the myocardium and shutdown of the respiratory chain of mitochondria, accumulating in the area of ischemia, metabolites determine the occurrence of anginal pain. if the sanogenetic mechanisms or the applied therapy do not block the further development of the pathological process, it occurs

2. the second stage, characterized by suppression of the main metabolic pathways. As a result of exclusion of the respiratory chain of mitochondria at this stage of the process, a deficiency of macroergic phosphorus compounds (CF and ATP) develops. These changes cause the activation of glycolysis and an increase in the concentration of lactic acid in the cells. Acidosis inhibits glycolysis, and the developing inhibition of β-oxidation of fatty acids leads to their accumulation in cardiomyocytes. During the entire second, patho-

logical changes are reversible, but they lead to the possibility of serious damage to the membranes of both the cardiomyocytes themselves and their subcellular structures.

3. It is these injuries, or rather their depth, that is the starting factor of the transition of the process to the third, already irreversible, stage of pathological changes. Under the influence of an excess of catecholamines and fatty acids, the lipid layer of biological membranes is destroyed. This leads to the labilization of lysosomal membranes, the release of their enzymes into the cell, as well as to a change in the permeability of the membranes of the sarcolemma, sarcoplasmic reticulum, and mitochondria for Ca++. An excess of calcium, on the one hand, causes myofibril contracture, and on the other hand, increases further destruction of the lipid bilayer.

4. Necrosis of the cells of the ischemic area of the myocardium completes the fourth, final, stage of the pathological process

MI affects predominantly the left ventricle (LV), but damage may extend into the right ventricle (RV) or the atria. RV infarction usually results from obstruction of the right coronary or a dominant left circumflex artery; it is characterized by high RV filling pressure, often with severe tricuspid regurgitation and reduced cardiac output. An inferoposterior infarction causes some degree of RV dysfunction in about half of patients and causes hemodynamic abnormality in 10 to 15 %. RV dysfunction should be considered in any patient who has inferoposterior infarction and elevated jugular venous pressure with hypotension or shock. RV infarction complicating LV infarction may significantly increase mortality risk. Anterior infarcts tend to be larger and result in a worse prognosis than inferoposterior infarcts. They are usually due to left coronary artery obstruction, especially in the anterior descending artery; inferoposterior infarcts reflect right coronary or dominant left circumflex artery obstruction.

Transmural infarcts involve the whole thickness of myocardium from epicardium to endocardium and are usually characterized by abnormal Q waves on ECG. Nontransmural or subendocardial infarcts do not extend through the ventricular wall and cause only ST-segment and T-wave (ST-T) abnormalities. Subendocardial infarcts usually involve the inner one third of myocardium, where wall tension is highest and myocardial blood flow is most vulnerable to circulatory changes. These infarcts may follow prolonged hypotension. Because the transmural depth of necrosis cannot be precisely determined clinically, infarcts are usually classified by the presence or absence of ST-segment elevation or Q waves on the ECG. Volume of myocardium destroyed can be roughly estimated by the extent and duration of CK elevation.

Electrical dysfunction: Ischemic and necrotic cells are incapable of normal electrical activity, resulting in various ECG changes (predominantly ST-T abnormalities), arrhythmias, and conduction disturbances. ST-T abnormalities of ischemia include ST-segment depression (often downsloping from the J point), T-wave inversion, ST-segment elevation (often referred to as injury current),

and peaked T waves in the hyperacute phase of infarction. Conduction disturbances can reflect damage to the sinus node, the atrioventricular (AV) node, or specialized conduction tissues. Most changes are transient; some are permanent.

Classification is based on ECG changes and presence or absence of cardiac markers in blood. Distinguishing NSTEMI and STEMI is useful because prognosis and treatment are different.

Unstable angina (acute coronary insufficiency, preinfarction angina, intermediate syndrome) is defined as:

• Rest angina that is prolonged (usually > 20 min)

• New-onset angina of at least class III severity in the Canadian Cardiovascular Society (CCS) classification Increasing angina, ie, previously diagnosed angina that has become distinctly more frequent, more severe, longer in duration, or lower in threshold (eg, increased by ≥ 1 CCS class or to at least CCS class III). Also, ECG changes such as ST-segment depression, ST-segment elevation, or T-wave inversion may occur during unstable angina but are transient. Of cardiac markers, CK is not elevated but troponin I or T may be slightly increased. Unstable angina is clinically unstable and often a prelude to MI or arrhythmias or, less commonly, to sudden death.

Non–ST-segment elevation MI (NSTEMI, subendocardial MI) is myocardial necrosis (evidenced by cardiac markers in blood; troponin I or T and CK will be elevated) without acute ST-segment elevation or Q waves. ECG changes such as ST-segment depression, T-wave inversion, or both may be present.

ST-segment elevation MI (STEMI, transmural MI) is myocardial necrosis with ECG changes showing ST-segment elevation that is not quickly reversed by nitroglycerin or showing new left bundle branch block. Q waves may be present. Both troponin and CK are elevated.

By stages of development:

1. The most acute period lasts 2 hours.
2. The acute period lasts 10 days.
3. The subacute period lasts from 10 days to 4–8 weeks.
4. The period of scarring lasts from 4–8 weeks.

According to the anatomy of the lesion:

1. Transmural
2. Intramural
3. Subendocardial
4. Subepicardial

By extent of damage:

1. Large focal (transmural), Q-infarction
2. Small focal non-Q heart attack

According to the localization of the focus of necrosis:

1. Myocardial infarction of the left ventricle (front, side, bottom, back).
2. Isolated myocardial infarction of the apex of the heart.
3. Myocardial infarction of the interventricular septum (septal).
4. Myocardial infarction of the right ventricle.

Symptoms and Signs of ACS depend somewhat on the extent and location of obstruction and are quite variable. Except when infarction is massive, recognizing the amount of ischemia by symptoms alone is difficult.

After the acute event, many complications can occur. They usually involve:

- electrical dysfunction (eg, conduction defects, arrhythmias),
- myocardial dysfunction (eg, heart failure, interventricular septum or free wall rupture, ventricular aneurysm, pseudoaneurysm, mural thrombus formation, cardiogenic shock),
- valvular dysfunction (typically mitral regurgitation).
- Electrical dysfunction can be significant in any form of ACS, but usually, large parts of myocardium must be ischemic to cause significant myocardial dysfunction. Other complications of ACS include recurrent ischemia and pericarditis. Pericarditis that occurs 2 to 10 wk after an MI is known as post-MI syndrome or Dressler's syndrome.

Unstable angina: Symptoms are those of angina pectoris, except that the pain or discomfort of unstable angina usually is more intense, lasts longer, is precipitated by less exertion, occurs spontaneously at rest (as angina decubitus), is progressive (crescendo) in nature, or involves any combination of these features.

In RV infarction, signs include elevated RV filling pressure, distended jugular veins, clear lung fields, and hypotension.

Diagnosis

• Serial ECGs

• Serial cardiac markers

• Immediate coronary angiography for patients with STEMI or complications (eg, persistent chest pain, markedly elevated cardiac markers, unstable arrhythmias)

• Delayed angiography (24 to 48 h) for patients with NSTEMI or unstable angina. ACS should be considered in men > 30 yr and women > 40 yr (younger in patients with diabetes) whose main symptom is chest pain or discomfort.

Pain must be differentiated from the pain of pneumonia, pulmonary embolism, pericarditis, rib fracture, costochondral separation, esophageal spasm, acute aortic dissection, renal calculus, splenic infarction, or various abdominal disorders. In patients with previously diagnosed hiatus hernia, peptic ulcer, or a gallbladder disorder, the clinician must be wary of attributing new symptoms to these disorders.

The approach is the same when any ACS is suspected: initial and serial ECG and serial cardiac marker measurements, which distinguish among unstable angina, NSTEMI, and STEMI. Every emergency department should have a triage system to immediately identify patients with chest pain for rapid assessment and ECG. Pulse oximetry and chest x-ray (particularly to look for mediastinal widening, which suggests aortic dissection) is also done.

Forms of myocardial infarction

• **Abdominal form** – symptoms of MI are represented by pain in the upper abdomen, hiccups, abdominal distension, nausea, vomiting. In this case, the symptoms of MI may resemble the symptoms of acute pancreatitis.

• **Asthmatic form** – MI symptoms are represented by increasing shortness of breath. The symptoms of a heart attack resemble the symptoms of a cardiac asthma attack.

• **Atypical pain syndrome in MI** can be represented by pain localized not in the chest, but in the arm, shoulder, lower jaw, and iliac fossa.

• **Painless form of MI** is rarely observed. This development of MI is most typical for patients with diabetes, in whom impaired sensitivity is one of the manifestations of the disease (diabetes).

• **Cerebral form** – MI symptoms are represented by dizziness, disturbances of consciousness, neurological symptoms.

• **Arrhythmic variant** or disturbance of rhythm and conduction**.**

The ECG changes depending on the time that has passed since the onset of the myocardial infarction.

Complications of myocardial infarction:

Early:

• acute heart failure

• cardiogenic shock

• pulmonary edema

• rhythm and conduction disturbances (sinus bradycardia, atrioventricular (AV) blockade, ventricular heart rhythm disturbances, supraventricular heart rhythm disturbances (including atrial fibrillation))

• thromboembolic complications

• myocardial rupture with the development of cardiac tamponade

• pericarditis

Late:

• post-infarction syndrome (Dresler's syndrome – a combination of pericarditis with pleurisy, less often pneumonia and eosinophilia, which develops in the 3–4th week after the onset of MI; due to sensitization of the body to destructively changed proteins of the myocardium)

• thromboembolic complications

• chronic heart failure

• heart aneurysm

Cardiogenic shock is the extreme degree of left ventricular failure, characterized by a sharp decrease in the contractility of the myocardium (a drop in stroke and minute output), which is not compensated by an increase in vascular resistance and leads to inadequate blood supply to all organs and tissues.

Mechanisms causing CSH:

• Disorder of the pumping function of the heart muscle.

• Severe heart rhythm disturbances.

• Ventricular tamponade with effusion or bleeding into the pericardial sac.

• Shock due to massive embolism of the pulmonary artery, as a special form of CHD.

Causes of CSH:

• Acute myocarditis.

• Pronounced, acute aortic or mitral stenosis.

• Pronounced, acute aortic or mitral insufficiency.

• Rupture of the interventricular septum.

• Arrhythmias

Classification of CSH

Currently, the classification of cardiogenic shock proposed by E.I. is generally accepted. Chazov (1969).

1. **True cardiogenic shock** – develops when the size of the lesion exceeds 40 % of the mass of the LV myocardium (more often with anterolateral and repeated heart attacks, in people over 60 years old, against the background of arterial hypertension and diabetes). It is characterized by an extensive picture of shock resistant to therapy, often combined with congestive left ventricular failure; mortality rates of 80–100 %.

2. **Reflex shock** (pain collapse) – it is based on a pain syndrome, the intensity of which is quite often unrelated to the extent of myocardial damage. This type of shock can be complicated by a violation of vascular tone, which is accompanied by the formation of a deficiency of BCC. It is characterized by a quick response to analgesic therapy; lack of signs of congestive heart failure, deterioration of tissue perfusion (in particular, gray cyanosis); pulse pressure usually exceeds the critical level. It is quite easily corrected with painkillers, vascular means and infusion therapy.

3. **Arrhythmic shock** – it is based on disturbances of rhythm and conduction, which causes a decrease in blood pressure and the appearance of signs of shock. After stopping the rhythm disturbance, adequate hemodynamics is restored quite quickly.

4. **Reactive shock** – can develop even against the background of a small lesion of the LV myocardium. It is based on a violation of the contractile ability of the myocardium, caused by a violation of microcirculation, gas exchange, and the addition of DIC syndrome. Characteristic for this type of shock is the complete absence of a corresponding reaction to the introduction of pressor amines.

The main symptoms of cardiogenic shock:

- With the development of coronary artery disease on the background of myocardial infarction - a typical clinic of acute myocardial infarction with characteristic ECG signs.
- Confused consciousness.
- Fear of death.
- Progressive weakness, adynamia.

- The skin is grayish-pale, covered with cold, sticky sweat.
- Shortness of breath.
- The pulse is accelerated, with weak filling and tension.
- Tachycardia.
- Significant hypotension (drop in blood pressure) combined with a decrease in pulse pressure.
- High risk of heart rhythm disorders.
- Abdoinal bloating.
- Oligoanuria.

Degrees of cardiogenic shock

1. **The first degree** – blood pressure in the range of 90/50 – 60/40 mm Hg, pulse pressure is 40–25 mm Hg, there is no loss of consciousness, symptoms of heart failure (edema, shortness of breath) are weakly expressed.
2. **The second degree** – blood pressure 80/50 – 40/20 mm Hg, pulse pressure up to 30–15 mm Hg, collapse is weakly expressed (a sharp drop in blood pressure and a decrease in blood supply to vital organs), acute heart failure.
3. **The third degree** – severe progressive collapse during a pain attack lasting several hours, blood pressure is sharply reduced, pulse pressure is below 15 mm Hg, symptoms of acute heart failure increase, pulmonary edema develops.

Setting up the experiment.
Discussion of results and formulation of conclusions

Induction of myocardial necrosis in the rat.

1. Fix the rat .
2. Strengthen the electrodes connected to the electrocardiograph through the transition bar.
3. Record the electrocardiogram in standard leads.
4. Administer intraperitoneally a 0.1 % solution of adrenaline at the rate of 300 μg per 100 g of body weight.
5. Record the electrocardiogram after 15, 30, 45 minutes. after the injection of adrenaline.
6. Compare electrocardiograms with the original data. Pay attention to the change in the QRS complex, confusion of the S-T segment, the peculiarities of the T wave, as well as the change in the rhythm of cardiac activity.

Discussion of the results of the experiment. One of the models of noncoronary myocardial necrosis is epinephrine. Noncoronarogenic experimental necrosis also includes hypoxic necrosis, electrolyte-steroid cardiopathy, immune and neurogenic heart damage.

Formulation of conclusions from the experiment.

1. Myocardial necrosis. Myocardial necrosis developed as a result of the introduction of adrenaline in the rat. Mechanism: cardiotoxic effect of catecholamines on the myocardium (increased myocardial oxygen demand due to positive chronotropic and inotropic effects, decrease in coronary blood flow, disruption of ATP resynthesis mechanisms, prooxidant effect).

2. ECG signs of damage (necrosis) of the myocardium are manifested by a shift in the ST segment, a change in the T wave and the ventricular QRS complex (decrease in its amplitude), as well as heart rhythm disturbances.

Tasks for independent work on the topic "Coronary damage of the myocardium. Coronary insufficiency. Coronary heart disease. Myocardial infarction. Cardiogenic shock.":

The student is offered 2–3 ECGs with coronary damage of the myocardium. It is necessary to determine the ECG signs and the type of damage to the myocardium in case of coronary heart disease (ischemia, damage, necrosis, cardiosclerosis). To be able to explain the mechanism of the occurrence. Analysis of errors with an explanation of the correct answers

List of questions and works to be studied:

Coronary heart damage.

1. Ischemic heart disease, myocardial infarction.
2. Pathogenesis of electrocardiogram changes.
3. Coronary insufficiency. Definition of the concept. Reasons.
4. Myocardial reperfusion.
5. Reversible and irreversible disorders of coronary blood flow.
6. Cardiogenic shock. Pathogenesis.
7. Experimental models of myocardial necrosis.

List of practical skills that must be mastered:

1. Identify the main manifestations of heart failure,
2. Explain the mechanisms of their occurrence and development.
3. Determination of signs of ischemia.
4. Necrosis of the myocardium on the ECG.
5. Determination on the ECG of signs of acute coronary insufficiency – myocardial infarction, its stage of development, depth, localization.

Situational tasks KROK-1 to determine the final level of knowledge

1. After a serious psycho-emotional stress a 45-year-old patient suddenly felt constricting heart pain irradiating to the left arm, neck and left scapula. His face turned pale, the cold sweat stood out on it. The pain attack was stopped with nitroglycerine. What process has developed in this patient?

A. Myocardial infarction.
B. Stenocardia.
C. Stroke.
D. Psychogenic shock.
E. Stomach ulcer perforation.

2. After a serious psychoemotional stress a 48 year old patient suddenly developed acute heart ache irradiating to the left arm. Nitroglycerine relieved pain after 10 minutes. What is the leading pathogenetic mechanism of this process development?

A. Spasm of coronary arteries.
B. Dilatation of peripheral vessels.
C. Obstruction of coronary vessels.
D. Compression of coronary vessels.
E. Increase in myocardial oxygen consumption.

3. After a psychoemotional stress a 48 year old patient had a sudden attack of acute heart pain with irradiation to the left hand. Nitroglycerine suppressed pain in 10 minutes. What pathogenetic mechanism is principal for the pain development?

A. Spasm of coronary vessels.
B. Dilatation of peripheral vessels.
C. Coronary vessel occlusion.
D. Embarrassment of coronary vessels.
E. Increased need of myocardium in oxygen.

4. A patient is 59 years old and works as director of a private enterprise. After the inspection by tax authorities he developed intense burning retrosternal pain radiating to the left arm. After 15 minutes the patient returned to normal. What is the leading mechanism for the development of stenocardia in this patient?

A. Functional overload of heart.
B. Increased level of blood catecholamines.
C. Coronary thrombosis.
D. Coronary atherosclerosis.
E. Intravascular aggregation of blood corpuscles.

5. A patient suffering from stenocardia was taking nitroglycerine which caused restoration of blood supply of myocardium and relieved pain in the cardiac area. What intracellular mechanism provides restoration of energy supply of insulted cells?

A. Reduction of ATP resynthesis.
B. Increased permeability of membranes.
C. Intensification of ATP resynthesis.
D. Intensification of oxygen transporting into the cell.
E. Intensification of RNA generation.

6. During fighting a man had a cardiac arrest as a result of a hard blow to the upper region of anterior abdominal wall. Which of the described mechanisms might have provoked the cardiac arrest?

A. Sympathetic unconditioned reflexes.
B. Peripheric reflexes.
C. Parasympathetic unconditioned reflexes.
D. Sympathetic conditioned reflexes.
E. Parasympathetic conditioned reflexes.

7. A 59 year old patient is a plant manager. After the tax inspection of his plant he felt intense pain behind his breastbone irradiating to his left arm. 15 minutes later his condition came to normal. Which of the possible mechanisms of stenocardia development is the leading in this case?

A. Coronary atherosclerosis.
B. Intravascular aggregation of blood corpuscles.
C. Coronary thrombosis.

D. High catecholamine concentration in blood.

E. Functional heart overload.

8. The patient with acute myocardial infarction was given intravenously different solutions during 8 hours with medical dropper 1500 ml and oxygen intranasally. He died because of pulmonary edema. What caused the pulmonary edema?

A. Decreased oncotic pressure due to hemodilution.

B. Allergic reaction.

C. Neurogenic reaction.

D. Inhalation of the oxygen.

E. Volume overload of the left ventricular.

9. Since a patient has had myocardial infarction, atria and. ventricles contract dependently from each , other with a sequence of 60–70 and 35–40 per minute. Specify the type of heart block in this case:

A. Sino-atrial. *D. Complete atrioventricular.*

B. Intraventricular. *E. Partial atrioventricular.*

C. Intra-atrial.

10. A 47 year old man with myocardium infarction was admitted to the cardiological department. What changes of cellular composition of peripheral blood are induced by necrotic changes in the myocardium?

A.. Neutrophilic leukocytosis *C. Monocytosis.* *E. Lymphopenia.*

B. Eosinophilic leukocytosis. *D. Thrombocytopenia.*

Standards of correct answers to situational problems

1	2	3	4	5	6	7	8	9	10
B	*A*	*A*	*B*	*C*	*C*	*D*	*E*	*D*	*A*

Recommendations for registration of work results.

1. Written answer to test tasks (initial level of knowledge)

2. The results of the experiment are drawn up in the form of an experiment protocol with the determination of relevant conclusions.

3. Protocol for the ECG analysis with coronary myocardial damage.

4. Protocol for solving situational tasks with an explanation of the correct answers.

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Topic 10. Pathophysiology of blood vessels. Arterial hypertension and hypotension. Vascular insufficiency. Atherosclerosis

Justification of the topic: Studying the causes and mechanisms of regulation of vessels tone is an actual for theoretic and clinic medicine, because those disorders are basis of hypertonic disease and symptomatic hypertension, observed in different diseases. Knowing the causes and mechanisms of disorders is important for understanding the hypotension, especially of acute vascular insufficiency.

Making of adequate models is important for identification of causes and mechanisms of those disorders in human, and so that for improving the prophylactic measures and curing the hyper- and hypotension.

This pathology leads (avg 60 %) between all causes of death in different countries. Analyzing the causes of origins of cardio-vascular diseases, we can state that atherosclerosis is the basis almost of 90 % of them.

So studying of the pathogenesis and outcomes of atherosclerosis is very actual problem for modern medicine.

Purpose of the lesson:

General – to study common laws and features of different forms of disorders of vascular tone, particularly etiological different types of hypertension; – to study the common laws of beginning, development and results of atherosclerosis.

Specifically:

Know:

1. To determine the blood pressure in rabbits.
2. To explain the mechanisms of centrogenic, reflexogenic and renal hypertension.
3. Differ the hyper- and hypotension states, and acute vascular insufficiency.
4. Form the knowledge about atherosclerosis.
5. Explain the mechanisms of atherosclerosis development.
6. Know the morphological characteristic, results and value atherosclerosis in pathology.

To be able to:

1. Classify the division of vessels by function.
2. Explain the neurohumoral regulation of vascular tone
3. Classify the division of vessels by function.
4. Explain the neurohumoral regulation of vascular tone

Practical experience:

1. To analyze the mechanisms of regulation of vascular tone and the mechanisms of impaired regulation.
2. To find out the pathogenesis of hypotensive and hypertensive conditions.
3. To analyze the consequences of a persistent increase in blood pressure.

The graphological structure of the topic "Pathophysiology of blood vessels. Arterial hypertension and hypotension. Vascular insufficiency. Atherosclerosis " is attached.

Material and methodical provision of the topic "Pathophysiology of blood vessels. Arterial hypertension and hypotension. Vascular insufficiency. Atherosclerosis":

1. Lectures;
2. Methodical instructions for teachers;
3. Methodical instructions for students;
4. Set of test tasks to determine the basic level of knowledge;
5. Set of situational tasks to determine the final level of knowledge;
6. Set of KROK-1 tasks;
7. Set of schemes and tables (presentation);
8. Set of forms with a clinical blood test;
9. Video films;
10. For the experiment: an experimental animal – a rabbit (intact, with experimental renal and reflexogenic hypertension), a device for measuring blood pressure.

Oriented map of students' work on the topic "Pathophysiology of blood vessels. Arterial hypertension and hypotension. Vascular insufficiency. Atherosclerosis"

No	Stage of lesson	Academic time, min	Educational guide		Place holding a class
			Educational tools	Equipment	
1	Determination of the initial level of knowledge	10	Written answer to test tasks	Test task	Learning room
2	Analysis of theoretical material	35	Analysis of theoretical material based on control questions of the topic, situational tasks, tasks KROK 1	Control questions of the topic, task "KROK 1"	
3	Practical part (conduct experiment)	30	Introduction and preparation for setting up the experiment. Setting up the experiment. Discussion of experiment results and formulation of conclusions	Rabbit, device for measuring blood pressure)	
4	Determination of the final level of knowledge and skills. Summarizing the results	15	Determination of the final level of knowledge and skills. Summarizing the results	KROK-1 tasks, situational tasks	

PATHOPHYSIOLOGY OF BLOOD VESSELS. ARTERIAL HYPERTENSION AND HYPOTENSION. VASCU LAR INSUFFICIENCY. ATHEROSCLEROSIS

Vascular tone – this is the main function of the smooth muscles of the vascular walls, which is characterized by their constant tension, which counteracts stretching under blood pressure.

Components of vascular tone:

Basal component. Defined:

• structural features of the vascular wall

• myogenic factor

The vasoconstrictor component is part of the contraction of the vessel wall, which is determined by the α-adrenergic effect of catecholamines.

When assessing the tone of various blood vessels, the following terms are used:

- "arterial tone",
- "venous tone",
- "lymphatic tone".

Violation of vascular tone

Vascular dystonia, or angiodystonia, refers to various disorders of vascular tone due to a violation of the adaptive tonic function of vessels.

Types of vascular dystonias according to the nature of changes in vascular tone

- vascular dystonia of the hypertensive type corresponds to an increase in the resistance of the walls to stretching, pathologically restricts the blood flow.
- vascular dystonia of the hypotonic type – a decrease in resistance, which causes excess blood flow.

Types of vascular dystonia according to the predominant origin

Vascular dystonias of a myogenic nature occur with organic lesions of the vascular wall (arteritis, atherosclerosis, varicose veins, etc.), as well as with its damage (angiodystrophy) as a result of acute or chronic intoxication, radiation exposure, etc.

Dysregulatory vascular dystonia includes various disorders of neurohumoral regulation, which consist in excessive or insufficient production of vasoactive substances of a hormonal or metabolic nature.

Types of vascular dystonia according to causes and mechanisms of development

- Neurogenic (or primary),
- Symptomatic (secondary).

I. Primary vascular dystonia – neurocirculatory (vegetative-vascular) dystonia.

II. Symptomatic (secondary) vascular dystonia (endocrine, infectious-toxic, toxic, allergic, etc.).

Types of vascular dystonias by type and location

- Hyper- or hypotonia of arteries (arterioles).
- Hypotension of veins (venules).
- Hypotension of the sphincters of arteriovenous anastomoses.

Types of vascular dystonias by prevalence

- **Systemic** (common). is a symptomatic form of vascular dystonia in acute or chronic vascular insufficiency.
- **Localized** (monoregional) form such important clinical symptoms as acrocyanosis (with local hypotonia of skin venules and small veins in the distal parts of the body), varicose veins, headaches (with insufficient tone of intracranial veins).
- **Dystonia of regional veins**

Hypertension of arteries of different caliber (large, medium and small) with arterial hypertension and angiospasm.

Hypotension of regional arteries is characterized by excessive arterial inflow to a limited area of the body – arterial hyperemia, which leads to an increase in the amplitude of pulsation of the arterial wall, an increase in the speed of blood flow in the capillary network, and an increase in tissue temperature in the area of arterial hyperemia.

Types of vascular dystonias downstream

• Permanent, i.e. persistent (with symptomatic forms).

• Angiodystonic crises.

Hypertensive conditions are characterized by an increase in blood pressure above the norm.

These include hypertensive reactions and arterial hypertension.

Hypotensive conditions are manifested by a decrease in blood pressure below the norm. Include hypotensive reactions and arterial hypotension.

The terminological element **"tension"** is used to indicate the pressure of liquids in cavities and vessels, including blood vessels.

Hypertension means an increase, and hypotension means a decrease in pressure in the body cavities, its hollow organs and vessels.

Arterial hypertension is sustained elevation of resting systolic BP (≥ 140 mm Hg), diastolic BP (≥ 90 mm Hg), or both. Hypertension with no known cause (primary; formerly, essential hypertension) is most common. Hypertension with an identified cause (secondary hypertension) is usually due to chronic kidney disease or primary aldosteronism. Usually, no symptoms develop unless hypertension is severe or long-standing. Diagnosis is by sphygmomanometry. Tests may be done to determine cause, assess damage, and identify other cardiovascular risk factors.

Classification JNC Joint National Committee of High Blood Pressure.

Normal < 120/80 mm Hg, Prehypertension 120–139/80–89 mm Hg,

Stage 1 140–159 mm Hg (systolic) or 90–99 mm Hg (diastolic),

Stage 2 ≥ 160 mm Hg (systolic) or ≥ 100 mm Hg (diastolic).

BP increases with age. About two thirds of people > 65 have hypertension, and people with a normal BP at age 55 have a 90 % lifetime risk of developing hypertension. Because hypertension becomes so common with age, the age-related increase in BP may seem innocuous, but higher BP increases morbidity and mortality risk. Hypertension may develop during pregnancy.

Primary hypertension: Hemodynamics and physiologic components (eg, plasma volume, activity of the renin-angiotensin system) vary, indicating that primary hypertension is unlikely to have a single cause. Even if one factor is initially responsible, multiple factors are probably involved in sustaining elevated BP (the mosaic theory). In afferent systemic arterioles, malfunction of ion pumps on sarcolemmal membranes of smooth muscle cells may lead to chronically increased vascular tone. Heredity is a predis-

posing factor, but the exact mechanism is unclear. Environmental factors (eg, dietary Na, obesity, stress) seem to affect only genetically susceptible people at younger ages; however, in patients > 65, high Na intake is more likely to precipitate hypertension.

Secondary hypertension: Causes include primary aldosteronism, renal parenchymal disease (eg, chronic glomerulonephritis or pyelonephritis, polycystic renal disease, connective tissue disorders, obstructive uropathy), renovascular disease (see Hypertension: Renovascular Hypertension), pheochromocytoma, Cushing syndrome, congenital adrenal hyperplasia, hyperthyroidism, myxedema, and coarctation of the aorta. Excessive alcohol intake and use of oral contraceptives are common causes of curable hypertension. Use of sympathomimetics, NSAIDs, corticosteroids, cocaine, or licorice commonly contributes to worsening of BP control.

Manifestations of target organ damage in hypertension:

Manifestations of heart damage in hypertension:

• hypertrophy of the left ventricle, angina pectoris, myocardial infarction,

• heart failure, sudden cardiac death.

Manifestations of brain damage:

• thrombosis, hemorrhages, hypertensive encephalopathy, ● cerebral lacunae.

Manifestations of kidney damage:

• microalbuminuria, proteinuria, chronic renal failure.

Manifestations of damage to vessels:

• the involvement of retinal vessels in the process, involving the carotid arteries in the process, involving the aorta (aneurysm) in the process.

Types of arterial hypertension

1. The initial link of the development mechanism

General (systemic) hypertension. It is divided into:

• **Neurogenic** hypertension: centrogenic and reflex (reflexogenic).

● **Endocrine** (endocrinogenic, hormonal) hypertension. It develops as a result of endocrinopathies of the adrenal glands, thyroid gland, and pituitary gland.

• **Hypoxic** (metabolic, ischemic) hypertension. Ischemic (renal-ischemic, cerebro-ischemic), venous-congestive and hypoxic (without primary hemodynamic disturbance in organs and tissues) hypertension are distinguished.

• **Hemic** ("blood") hypertension. It develops as a result of an increase in blood volume and/or viscosity.

• **Local** (regional) AG. It is, as a rule, the result of a significant narrowing of the area of the arterial vessel.

2. Change in cardiac output

▪ **Hyperkinetic hypertension**. Increased cardiac output (with normal or reduced total peripheral vascular resistance - **TPVR**).

▪ **Hypokinetic hypertension**. Decreased cardiac output (with significantly increased OPSS).

▪ **Eukinetic hypertension**. Normal cardiac output and increased **TPVR**.

3. Type of blood pressure increase

- Systolic hypertension.
- Diastolic hypertension.
- Mixed (systolic-diastolic) hypertension.

4. Nature of the clinical course of hypertension

▪ **Benign hypertension.** With slow development, an increase in both systolic and diastolic blood pressure; usually eukinetic.

▪ **Malignant hypertension.** A rapidly progressive course, with a predominant increase in diastolic blood pressure; as a rule, hypokinetic, less often – hyperkinetic

Risk factors for hypertension

➢ family history, adiposity, alcohol abuse, excessive use of table salt, stress, hypodynamia, smoking

1. Neurogenic hypertension is characterized either by an increase in hypertensive neurogenic effects, or by a weakening of hypotensive neurogenic effects, or (more often) by a combination of both. It is divided into reflex (reflexogenic) and centrogenic

2. Centrogenic hypertension Cortical and subcortical neurons are a complex functional system consisting of pressor hypertensive and depressor hypotensive subsystems with the predominance of pressor hypertensive mechanisms. The main structure regulating systemic blood pressure is the cardiovasomotor (vascular) center. Its efferent effects change both vascular tone and heart function.

3. Arterial hypertension caused by disorders of higher nervous activity (neurosis)

Repeated and prolonged stress reactions with a negative emotional color

1. **Reflex hypertension** – can develop on the basis of conditioned and unconditional reflexes ("white coat" hypertension). It is characterized by an increase in blood pressure in the medical institution, while blood pressure outside it is normal.

The causes of conditioned reflex hypertension are the combination of indifferent signals (for example, information about an upcoming public speech, an important competition or event) with the action of agents that cause an increase in blood pressure (for example, caffeine, adrenomimetics, psychostimulants, alcohol or drugs).

Causes of unconditional reflex hypertension – develops as a result of chronic irritation of extero- and interoreceptors, nerve trunks and nerve centers or as a result of cessation of "depressive" afferent impulses.

Endocrine hypertension – (develops as a result of the hypertensive effect of a number of hormones).

Hypertension in adrenal endocrinopathy

- Adrenal hypertension is divided into catecholamine and corticosteroid, and the latter into mineralocorticoid and glucocorticoid.

● Catecholamine hypertension is the result of an increase in the content of catecholamines – adrenaline and noradrenaline in the blood. In 99 % of all cases, such hypertension is detected as a pheochromocytoma.

The mechanism of the hypertensive effect of an excess of catecholamines consists in simultaneously increasing the tone of blood vessels and stimulating the work of the heart.

● Norepinephrine stimulates mainly α-adrenoceptors and to a lesser extent – β-adrenoceptors. This leads to an increase in blood pressure due to the vasoconstrictor effect.

● Adrenaline affects both α- and β-adrenoceptors. In this connection, there is vasoconstriction (both arterioles and venules) and an increase in the work of the heart (due to positive chrono- and inotropic effects) and the release of blood into the vascular bed.

Manifestations of pheochromocytoma are nonspecific: arterial hypertension (in 90 % of cases), headache (in 80 % of cases), orthostatic arterial hypotension (in 60 % of cases), sweating (in 65 % of cases), palpitations and tachycardia (in 60 % of cases) and others

Corticosteroid hypertension

1. Mineralocorticoid hypertension Excess synthesis of aldosterone (primary and secondary hyperaldosteronism) is of primary importance in the pathogenesis of hypertension. Cortisol, 11-deoxycortisol, 11-deoxycorticosterone, corticosterone, although they have little mineralocorticoid activity, are considered glucocorticoids.

Primary aldosteronism. There are several etiological forms:

● Conn's syndrome (aldosterone-producing adenoma), adrenocortical carcinoma, primary adrenal hyperplasia, idiopathic bilateral adrenal hyperplasia.

Secondary aldosteronism. It develops with heart, kidney, and liver failure. With these forms of pathology, hyperproduction of aldosterone can be observed in the glomerular zone of the cortex of both adrenal glands.

2. **Glucocorticoid hypertension** is the result of hyperproduction of cortisol (17-hydrocortisone, hydrocortisone). Practically all variants of AG of glucocorticoid genesis develop in Itsenko-Cushing's disease and syndrome.

Hypertension in the pathology of the thyroid gland

AH in hyperthyroidism. It is characterized by an increase in heart rate and cardiac output, systolic hypertension with low (normal) diastolic BP.

Hypertension in hypothyroidism. High diastolic blood pressure is characteristic. Other manifestations from the side of the cardiovascular system are a decrease in heart rate and cardiac output. The basis of the development of hypertension is the cardiotonic effect of T3 and T4. It is characterized by a significant increase in cardiac output due to pronounced tachycardia (positive chronotropic effect) and an increase in shock output (due to the positive inotropic effect of thyroid hormones).

Hypertension in disorders of the endocrine function of the hypothalamic-pituitary system

Pathogenesis of hypertension with hyperproduction of ADH

● Activation (under the influence of ADH) of fluid reabsorption from primary urine. Increase in BCC (hypervolemia). This can lead to an increase in blood pressure. Increase in cardiac output.

Caused by increased blood flow to the heart due to hypervolemia. An excess of blood, stretching the myocardium, increases (Frank-Sterling's law) the strength of its contractions and the amount of cardiac output and blood pressure.

Hypertension with hyperproduction of ACTH (Itsenko-Cushing's disease).

Hypertension caused by hypoxia of organs (especially the brain and kidneys) is designated as "hypoxic" (metabolic, organoischemic). At the heart of the pathogenesis of hypertension are disorders of the metabolism of substances with hypo- and hypertensive effects.

Hypertension due to the action of hypotensive and hypertensive metabolites occurs as a result of increased effects on target cells and organs of hypertensive (pressor) metabolites or a decrease in the effects of hypotensive (depressor) metabolites.

Metabolites with hypertensive (pressor) action:

▪ angiotensin (mostly angiotensin II), biogenic amines (serotonin, histamine),

▪ prostaglandins (PGF), thromboxane A2, endothelin, cyclic nucleotides (mainly cAMP).

Metabolites with hypotensive (depressant) effect:

• kinins (especially bradykinin), prostaglandins of groups E and I, adenosine, acetylcholine, natriuretic factors (including atriopeptin), gamma-aminobutyric acid (GABA), nitric oxide (NO).

Clinical varieties of hypoxic (metabolic) hypertension are vasorenal and renoparenchymal hypertension.

Vasorenal hypertension (renovascular, renal-ischemic) hypertension – symptomatic, caused by ischemia of the kidney (kidneys) due to occlusion of the renal arteries.

Pathogenesis Activation of the renin-angiotensin system due to hypoperfusion of the kidney (kidneys) leads to vasospasm, increased synthesis of aldosterone, retention of sodium and water ions, increased intravascular volume and stimulation of the sympathetic nervous system. Key factors in the development of hypertension are angiotensin II and aldosterone.

Symptomatic (secondary) renoparenchymal hypertension caused by congenital or acquired kidney disease.

• Bilateral kidney damage: glomerulonephritis, diabetic nephropathy,

• Tubulointerstitial nephritis, polycystosis.

• Unilateral kidney damage: pyelonephritis, tumor, trauma, single kidney cyst, hypoplasia, tuberculosis.

Pathogenesis. Hypervolemia, hypernatremia, increased OPSS with normal or reduced cardiac output are important.

1. Mixed hypertension In addition to the types mentioned above, hypertension can develop as a result of the simultaneous inclusion of several mechanisms. For example, hypertension with brain damage or the development of allergic reactions is formed with the participation of neurogenic, endocrine and renal pathological factors.

2 Medicinal hypertension. Vasoconstriction due to stimulation of the sympathetic-adrenal system or direct effect on the smooth muscle cells of blood vessels, increased blood viscosity, stimulation of the renin-aldosterone-angiotensin system (RAAS), retention of sodium ions and water can be important in the pathogenesis of hypertension caused by LZ .

A hypertensive crisis is an acute increase in systolic and/or diastolic blood pressure, accompanied by deterioration of cerebral, coronary, or renal blood circulation, as well as pronounced autonomic symptoms.

Causes of hypertensive crisis:

▪ incorrect intake of sympathomimetics, glucocorticoids, oral and contraceptives, alcohol, anorexants; use of narcotic substances (for example, cocaine, amphetamine), cancellation of hypotensive drugs (especially clofelin),stopping taking drugs that depress the central nervous system; eclampsia and preeclampsia, pheochromocytoma, essential arterial hypertension, kidney disease, severe burns, postoperative hypertension.

Etiology of symptomatic hypertension

– ***Kidney lesions:*** acute and chronic glomerulonephritis and pyelonephritis, obstructive nephropathy, polycystic kidney disease, kidney connective tissue disease, diabetic nephropathy, hydronephrosis, congenital hypoplasia of the kidney, kidney injury, renin-secreting tumor, primary salt retention (for example, Liddle's syndrome).

– ***Drugs and exogenous substances*** (for example, oral contraceptives, glucocorticoids, antidepressants, sympathomimetics, alkaloids of horns, lithium preparations, NSAIDs, cyclosporine, erythropoietin, alcohol, cocaine, food products with tyramine in cmbination with monoamine oxidase inhibitors).

– ***Endocrine diseases:*** acromegaly, hypothyroidism, hypercalcemia, hyperthyroidism, Itsenko-Cushing syndrome, aldosteronism, congenital adrenal hyperplasia, pheochromocytoma.

Etiology of HD

The main cause of HD: repeated, as a rule, prolonged psycho-emotional stress. The stress reaction has a pronounced negative emotional character.

• An excess of Na+ determines two important effects: (increased transport of liquid into cells, their swelling, increased sensitivity of myocytes of vessel walls and heart to vasoconstrictor factors.

• Disorders of the functions of membrane receptors, which perceive neurotransmitters and BAS, which regulate blood pressure, leads to the dominance of the effects of hypertensive factors.

• Violation of the expression of genes that control the synthesis of vasodilating agents (nitric oxide, prostacyclin, PGE) by endothelial cells.

• Environmental factors. The most important are occupational hazards, intoxication (alcohol, nicotine, drugs), brain injuries (blows, shocks, electric shock, etc.).

• Individual characteristics of the organism. (Age after 40 years, increased body weight, high level of cholesterol in the blood, excessive production of renin).

Forms of essential hypertension:

• **Border.** It is observed in young and middle-aged people, characterized by blood pressure fluctuations from normal to 140/90–159/94 mm Hg. There are no signs of target organ damage.

• **Hyperadrenergic.** It is characterized by sinus tachycardia, unstable blood pressure with hyperemia of the face, a feeling of anxiety, throbbing headaches.

• **Hyperhydration** (sodium-, volume-dependent). Manifested by swelling of the face and paraorbital areas, fluctuations in diuresis with temporary oliguria; pale skin; constant throbbing headache.

• **Malignant** – a progressive disease with an increase in blood pressure to high values with impaired vision, development of encephalopathy, pulmonary edema, kidney failure.

Pathogenesis of HD Stage I hypertensive disease

The initial factor in the pathogenesis of GB is the development of a neurotic state. It is characterized by the activation of the centrogenic neurogenic link of the pathogenesis of GB

The centrogenic neurogenic mechanism includes:

• **Formation of the cortical-subcortical complex** of persistent disturbance (sympathetic nuclei of the hypothalamus, vascular center, etc.)

• **Strengthening of pressor (hypertensive) effects** on the cardiovascular system. It is implemented by two interdependent channels (nervous and humoral).

• **Neurogenic hypertensive effects** consist in the activation of sympathetic nervous effects on the wall of arterioles, venules, veins and on the heart.

Stage II of hypertensive disease. Stabilization of blood pressure at an elevated level is provided by reflexogenic, endocrine, hemic mechanisms.

• **Reflexogenic (baroreceptor)** – an increasing decrease in afferent depressor impulses from the baroreceptors of the aortic arch, sinoacarotid and other zones to the vascular (pressor) center.

• **Endocrine factor** – stimulation of the production and secretion of hormones with hypertensive effect into the blood.

• **Metabolic** (hypoxic, organ ischemic). Includes renal hypertensive mechanisms (vasorenal and renoparenchymatous) and organoischemic (excess BAS with hypertension, reduction of BAS with hypotension).

• **Chemical**. It consists in the development due to chronic hypoxia of polycythemia (due to significant erythrocytosis), increased blood viscosity (due to polycythemia)

Stage III of hypertensive disease is characterized by damage to structural elements, gross disorders of the functions of tissues and organs with the development of multiple organ failure.

Arterial hypotension

Arterial hypotension – blood pressure drop below 100/60 mm Hg. in men and 95/60 mm Hg. in women (normal limits with good health and full capacity for work).

I. Physiological hypertension

• Individual version of the norm.

• Arterial hypotension of high training (sports).

• Adaptive (compensatory) arterial hypotension (for residents of the highlands).

• **II. Pathoogical arterial hypotension**

• Collapse - acute circulatory failure resulting from an acute decrease in heart function, a drop in vascular tone and/or a decrease in BCC (acute myocardial infarction, PE, arrhythmias, blockages, blood loss)

• Long-term decrease in systolic blood pressure below 90 mm Hg, which is accompanied by anuria, impaired blood circulation and consciousness.

• Chronic arterial hypotension

• Chronic primary arterial hypotension.

• Arterial hypotension is neurocirculatory

• Orthostatic idiopathic arterial hypotension

• Chronic secondary (symptomatic) arterial hypotension with or without orthostatic syndrome.

Neurogenic arterial hypotension

Centrogenic arterial hypotension is the result of a functional disorder of higher nervous activity (VND) or organic damage to brain structures involved in the regulation of blood pressure.

Arterial hypotension as a result of VND violations

Mechanism of development:

• Overstrain (and disruption) of higher nervous activity - neurosis.

• Neurosis is characterized by the formation of a cortical-subcortical excitation complex. It extends to the parasympathetic nuclei of the anterior hypothalamus and other structures

• Activation of parasympathetic effects on the cardiovascular system results in a decrease in the contractile function of the myocardium, cardiac output of blood, and the tone of resistive vessels. Arterial hypotension develops.

• brain injuries (with its concussion or blows),

• violation of cerebral circulation (ischemia, venous hyperemia),

• degenerative changes in the substance of the brain,

• violation of release of catecholamines into the blood during physical exertion, changing the position of the body from horizontal to vertical

Centrogenic arterial hypotension

The reason: violation of the conduction of efferent hypertensive impulses from the vascular center of the medulla oblongata to the walls of

vessels and the heart in (neurosyphilis, amyotrophic lateral sclerosis, syringomyelia, peripheral neuropathies of diabetic, infectious, neurotoxic origin).

The mechanism of development is a significant reduction or cessation of the tonic effects of the sympathetic nervous system on the walls of blood vessels and the heart. This leads to a decrease in TPVR and diastolic blood pressure, a decrease in the contractile function of the heart, the amount of cardiac output and systolic blood pressure.

Endocrine arterial hypotension (adrenal, pituitary, hypothyroid genesis).

Causes of hypotension of adrenal origin:

• hypotrophy of the adrenal cortex,

• tumor of the cortex of the adrenal glands with destruction of the parenchyma,

• hemorrhage in the adrenal gland (one or both),

• tuberculous lesion of the adrenal glands,

• destruction of the adrenal glands as a result of reactions of immune autoaggression,

• destruction of the adrenal glands as a result of trauma, which leads to damage or destruction of the adrenal glands.

Pathogenesis. Deficiency of catecholamines, mineralo- and glucocorticoids and/or insufficiency of their effects cause hypotonus of arteriolar walls, OPSS, BCC and cardiac output. The causes of hypotension with damage to the pituitary gland are hypofunction of the pituitary gland.

Arterial hypotension in pituitary insufficiency is the result of an insufficient effect of vasopressin, ACTH, TSH, THG, which leads to a decrease in the tone of arterioles and TPVR, BCV, cardiac output. The causes of hypotension in hypothyroid conditions are deficiency of T3 and T4 and/or their effects.

Mechanisms of development:

• Bradycardia. It develops as a result of a decrease or lack of a positive chronotropic effect of thyroid hormones due to their deficiency, a decrease in the activity of the SAS.

• Decrease in cardiac output.

• Decrease in the tone of the vessel walls due to their dystrophic changes and as a result – a decrease in OPSS.

Possible causes of metabolic hypotension

• Dystrophic changes in organs and tissues (intoxications, infections, starvation), which cause a decrease in the production and/or effects of endothelin, PGE, thromboxane A2, etc., hypotonus of the myocytes of the arteriole walls, ↓ myocardial function.

• Hypohydration of the body. It is caused by a decrease in the volume of liquid in the body due to a decrease in the intensity of metabolism.

The main links of the pathogenesis are a decrease in the tone of the smooth muscle cells of the vessel walls and, as a result, OPSS, a decrease in the contractile function of the heart, which leads to a decrease in cardiac output of blood, a decrease in the volume of circulating fluid.

Atherosclerosis is a type of arteriosclerosis or hardening of the arteries. The term *atherosclerosis,* which comes from the Greek words *atheros* (meaning "gruel" or "paste") and *sclerosis* (meaning "hardness"), denotes the formation of fibro fatty lesions in the intimal lining of the large and medium-sized arteries, such as the aorta and its branches, the coronary arteries, and the large vessels that supply the brain.. The major complications of atherosclerosis, including ischemic heart disease, stroke, and peripheral vascular disease, account for more than 40 % of the deaths in the United States. Atherosclerosis begins as an insidious process, and clinical manifestations of the disease typically do not become.

Risk Factors The cause or causes of atherosclerosis have not been determined with certainty. Epidemiologic studies have, however, identified predisposing risk factors. In terms of health care behaviors, some of these risk factors can be affected by a change in behavior, and others cannot. The major risk factor for atherosclerosis is hypercholesterolemia. Nonlipid risk factors, such as increasing age, family history of premature CHD, and male sex, cannot be changed. The tendency to the development of atherosclerosis appears to run in families. Persons who come from families with a strong history of heart disease or stroke due to atherosclerosis are at greater risk for developing atherosclerosis than those with a negative family history.

Endothelial dysfunction may be worsened by cigarette smoke, which is why cessation of smoking by high-risk individuals often is followed within a few years by reduced risk for ischemic heart disease. Obesity, type 2 diabetes, high blood pressure, and high blood cholesterol levels often can be controlled with a change in health care behaviors and medications. There is evidence that elevated serum cholesterol not only contributes to development of atherosclerotic lesions that block arteries but also interferes with vessel relaxation.

The optimal level of total cholesterol in the blood is 5.2–6.0 mmol/l (200–230 mg%). With a normal diet, about 500 mg of cholesterol enters the body every day, and the same amount is formed in the liver.

In all European countries, a total cholesterol level of up to 250 mg % (6.5 mmol/l) is considered moderate hypercholesterolemia, from 250 to 300 mg% (7.8 mmol/l) pronounced hypercholesterolemia – more than 300 mg%

Coefficient of atherogenicity (Ka) is an estimated indicator of the degree of risk of developing atherosclerosis in a person. It is determined by the amount of low-density lipoprotein (LDL), high-density lipoprotein (HDL), and total cholesterol in the blood. In healthy people, the value of this coefficient does not exceed 2–3 (maximum 3.5), with the progression of atherosclerosis it can increase to 4, and sometimes even more than 6–7 units. The calculation of the coefficient is the ratio of the content of LDL cholesterol and HDL cholesterol to the content of HDL cholesterol.

Ka = (LDL cholesterol + LDL cholesterol) / HDL cholesterol.

Often the calculation is also carried out according to the formula:

Ka = (total cholesterol - HDL cholesterol) / HDL cholesterol.

The general scheme of the pathogenesis of atherosclerosis

The main links in the pathogenesis of atherosclerosis are the alteration of the vascular endothelium, the local inflammatory process, a change in the properties of LDL (peroxide modification), the accumulation and destruction of foam cells in the subendothelium, the formation of an atherosclerotic plaque and its destruction.

Risk factors

• uncontrollable risk factors (heredity, age, gender)

• managed risk factors (hypertension, stress, hormonal disorders, unhealthy diet, obesity, hypodynamia, etc.).

In the formation of atherosclerotic plaque – the morphological basis of atherosclerosis – both lipid metabolism disorders (dyslipoproteinemia) and the condition of the vascular wall play an important role. Plaques can grow along the vessel, then they develop slowly, over time and are less dangerous, but they can also be located across the vessel – such plaques are often called "lethal", since even single formations of this type can lead to a vascular catastrophe.

Setting up the experiment.
Discussion of results and formulation of conclusions

Mastering the method of determining blood pressure according to the Grand Rothschild method.

1. Put a cuff on the central artery of the rabbit's ear so that the artery crossing the cuff in its central part is clearly visible through the outer surface of the cuff.

2. Connect the cuff with the injection balloon and the device for measuring blood pressure.

3. With the fingers of the left hand, fix the cuff, with the right hand, squeezing the balloon, inject air into the system until the blood flow stops in the center of the artery.

4. At this moment, note the value of the blood pressure according to the manometer reading (measure the pressure at least three times and calculate the average value).

5. Set the value of blood pressure in the rabbit in the norm.

6. Blood pressure on the day of the class is _____ mmHg**.**

Study of blood pressure in experimental renal hypertension.

1. Before the lesson, an incision was made in the skin and subcutaneous adipose tissue in the place of the projection of the left kidney in a rabbit under general anesthesia (mask ether anesthesia).

2. Tissue stratification up to the paranephric tissue was produced by a blunt method.

3. The kidney is brought out into the operating hole.

4. The renal pedicle is compressed by muscles on both sides.

5. The wound is sutured in layers.

6. Blood pressure on the day of the class is _____ mmHg.

7. Draw a diagram of the pathogenesis of renal (renovascular) hypertension**.**

Studing of blood pressure in experimental reflexogenic hypertension.

1. Before the lesson, an incision was made in the skin and subcutaneous fascia of the rabbit under local anesthesia (10 ml of 0.25 % novocaine solution) along the middle line of the neck.
2. Bluntly selected vascular-nerve bundle.
3. The depressor nerve is taken with ligatures and brought out into the operating hole.
4. Two ligatures are placed on the nerve at a distance of 1 cm from each other and tightened tightly.
5. We dissect the nerve between these ligatures.
6. The area of the carotid sinus is treated with ethyl alcohol.
7. The wound is sutured in layers.
8. Blood pressure on the day of the class is _____ mmHg.
9. Draw a scheme of pathogenesis of reflexogenic hypertension.

Discussion of the results of the experiment

There are various methods of causing a persistent increase in blood pressure – hypertension in an experiment by influencing the animal's nervous system. Such experimental neurogenic hypertension includes reflexogenic hypertension. Receptors of blood vessels, in particular, receptors in the ascending part of the aortic arch and in the region of the carotid sinus, are important in the reflex regulation of blood circulation. In these places of the vascular system, there are sensitive endings of afferent nerves – the depressor (in the arch of the aorta) and the sinus nerve (in the carotid sinus). Bilateral transection of these nerves has an inhibitory effect on the vascular-motor center and causes a long-term increase in blood pressure in the animal. The second type of experimental neurogenic hypertension demonstrated in this session is caused by a direct effect on the animal's central nervous system. For this purpose, a suspension of kaolin (20 mg/kg) is injected into the cysterna cerebello-medularis, as a result of which an inflammatory process develops, which leads to difficulty in draining the cerebrospinal fluid and increasing intracranial pressure. It is believed that hypertension develops as a result of brain ischemia.

Formulation of conclusions based on the experiment.

1. Experimental renal hypertension is caused by applying clamps to both renal arteries, due to which their lumen is narrowed. Kidney ischemia leads to the appearance of renin in the blood, under the influence of which angiotensinogen is split into the decapeptide angiotensin I, which, interacting with enzymes of the lungs and other tissues, turns into the octapeptide angiotensin II, which is the most powerful of the known pressor substances.

2. Experimental reflexogenic hypertension (refers to neurogenic hypertension) is caused by bilateral cutting of the afferent nerves of the aortic arch and carotid sinus, which has an inhibitory effect on the vasomotor center and causes a long-term increase in blood pressure in the animal.

3. Experimental hypertension is important for studying the pathogenesis of neugenic (reflexogenic) and renal (nephrogenic) hypertension in humans.

Tasks for independent work on the topic "Pathophysiology of blood vessels. Arterial hypertension and hypotension. Vascular insufficiency. Atherosclerosis"

The student needs to determine the signs of arterial hypertension and is asked to explain the mechanism of increased blood pressure during stenosis of the renal arteries. Analysis the errors with an explanation of the correct answers.

List of questions and works to be studied:

1. Definition of the concepts "hypertension", "hypotension".
2. Classification of disorders of vascular tone.
3. Hypertensive disease, its etiology and pathogenesis.
4. Symptomatic hypertension, their types, pathogenesis.
5. Experimental models of hypertension.
6. Acute and chronic vascular insufficiency, its types.
7. Shock. Causes, pathogenesis, stages, changes in the body.
8. Collapse. Reasons, mechanism of development.

List of practical skills that must be mastered:

1. Explain the mechanisms of centrogenic, reflexogenic hypertension.
2. Describe the mechanisms of renal hypertension
3. Determine hypo- and hypotonic states; acute vascular insufficiency

Situational tasks KROK-1 to determine the final level of knowledge

1. A 43-year-old-patient has arterial hypertension caused by an increase in cardiac output and general peripheral resistance. Specify the variant of hemodynamic development of arterial hypertension in the given case:

A. Hyperkinetic. B. Hypokinetic. C. –. D. Combined. E. Eukinetic.

2. Prophylactic medical examination of a 36-year-old driver revealed that his AP was 150/90 mm Hg. At the end of working day he usually hears ear noise, feels slight indisposition that passes after some rest. He was diagnosed with essential hypertension. What is the leading pathogenetic mechanism in this case?

A. Neurogenic. B. Nephric. C. Humoral . D. Endocrinal. E. Reflexogenic.

3. Arterial pressure of a surgeon who performed a long operation rised up to 140/110 mm Hg. What changes of humoral regulation could have caused the rise of arterial pressure in this case?

A. Activation of formation and excretion of aldosterone
B. Activation of sympathoadrenal system
C. Activation of renin angiotensive system
D. Activation of kallikrein kinin system
E. Inhibition of sympathoadrenal system

4. A patient has the following diagnosis: renal hypertension. What is the initial pathogenetic factor of arterial hypertension development in this case?

A. Hypernatremia.
B. Renal ischemia.
C. Hyperaldosteronism.
D. Intensified renin synthesis.
E. Intensified angiotensin synthesis.

5. A patient with constant headaches, pain the occipital region, tinnitus, dizziness has in admitted to the cardiology department, objectively: AP – 180/110 mm Hg, heart rate 5/min. Radiographically, there is a stenosis one of the renal arteries. Hypertensive condition in this patient has been caused by in activation of the following system:

A. Renin-angiotensin. *C. Kinin.* *E. Hemostatic.*
B. Sympathoadrenal. *D. Immune.*

6. Arterial hypertension is caused by the stenosis of the renal arteries in the patient. Activation of what system is the main link in the pathogenesis of this form of hypertension?

A. Sympathoadrenal. *C. Renin-angiotensin.* *E. Hypothalamic-pituitary.*
B. Parasympathetic. *D. Kallikrein-kinin.*

7. A month after surgical constriction of rabbit's renal artery the considerable increase of systematic arterial pressure was observed. What of the following regulation mechanisms caused the animal's pressure change?

A. Serotonin. *C. Angiotensin-II.* *E. Vasopressin.*
B. Noradrenaline. *D. Adrenaline.*

8. A patient ill with essential arterial hypertension had a hypertensic crisis that resulted in an attack of cardiac asthma. What is the leading mechanism of cardiac insufficiency in this case?

A. Heart overload caused by increased blood volume.
B. Heart overload caused by high pressure.
C. Absolute coronary insufficiency.
D. Myocardium damage.
E. Blood supply disturbance.

9. A 50 year old patient suffers from essential hypertension. After a physical stress he experienced muscle weakness, breathlessness, cyanosis of lips, skin and face. Respiration was accompanied by distinctly heard bubbling rales. What mechanism underlies the development of this syndrome?

A. Acute left-ventricular failure. *D. Collapse.*
B. Chronic right-ventricular failure. *E. Cardiac tamponade.*
C. Chronic left-ventricular failure.

10. An 18-year-old patient complains of general weakness, fatigue, low spirits. The patient is of the asthenic constitution type. Ps – 68/min., AP – 90/60 mm Hg. She has been found to have primary neurocirculatory hypotension. What is the leading factor of the arterial pressure drop in this patient?

A. Decreased minute blood volume.
B. Hypovolemia.
C. Decreased tonus of resistive vessels.
D. Deposition of blood in the veins of the systemic circulation.
E. Decreased cardiac output.

Standards of correct answers to the situational tasks

1.	2.	3.	4.	5.	6.	7.	8.	9.	10.
E	*A*	*B*	*B*	*A*	*C*	*C*	*B*	*A*	*C*

Recommendations for registration of work results

1. Written answer to test tasks (basic level of knowledge).

2. The results of the experiment are drawn up in the form of an experiment protocol with the determination of relevant conclusions.

3. Protocol for the study of the results determining blood pressure in experimental renal hypertension and experimental reflexogenic hypertension

4. Protocol for solving situational tasks with an explanation of the correct answers (final level of knowledge).

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Topic 11. Pathophysiology of external respiration. Respiratory failure

Justification of the topic. Expiratory system is one of the main systems of life support systems of organisms. The main aim is to provide the tissues by oxygen and raising of carbon acid from organism. Studying the etiology and pathogenesis of disorders of expiration is required for practice of doctor, because the breathing insufficiency appears in different sicknesses of breathing system, and it can be the result of disorders of different functions of other organs and systems. So knowing of causes and mechanisms of disorders of expiration will lead to the development of clinical thinking and choosing the rational cure of this pathology. Studying in experiment on animals the disorders of expiration allows to understand the mechanisms of those development and manifestations, especially dyspnea.

Purpose of the lesson:

General – to be able to characterize the dyspnea as a manifestation of expiration, explain the common causes and mechanisms of its development.

Specifically:

Know:

1. Define the “pathological breathing”, “dyspnea”.
2. Classify the pathological types of breathing, types of dyspnea.
3. To model the different types of dyspnea on rabbits.
4. Show the role of reflect influences and disorders of functions of upper respiratory trance in forming of the dyspnea.
5. To distinguish the main signs and manifestations of dyspnea, explain the main mechanisms of those forming and development.

To be able to:

1. Explain the role of mechanoreceptors (Hering-Beuer reflex) in expiration regulation
2. Interpret chemoreceptor regulation of expiration.
3. Explain the influence of changes of frequency and depth of expiration on its effectiveness.

The graphological structure of the topic "Pathophysiology of external respiration. Respiratory failure" is attached.

Material and methodological support of the topic “Pathophysiology of external respiration. Respiratory failure”.

1. Lectures.
2. Methodical instructions for teachers.
3. Methodical instructions for students.
4. Set of test tasks to determine the basic level of knowledge.
5. Set of situational tasks to determine the final level of knowledge.
6. Set of KROK-1 tasks.
7. Set of schemes and tables (presentation).
8. Set of forms with a clinical blood test.

9. Video films.

10. For the experiment: a board for animal's fixing, a pneumograph, a kymograph, a tripod, a device for recording respiratory movements, scissors, tweezers, surgical needles, threads, ether, a syringe, 20 % sodium nitrite solution. Experimental animals – rabbit, mice.

Oriented map of students' work on the topic "Pathophysiology of external respiration. Respiratory failure"

No	Stage of lesson	Academic time, min	Educational guide		Place holding a class
			Educational tools	Equipment	
1	Determination of the initial level of knowledge	10	Written answer to test tasks	Test task	Learning room
2	Analysis of theoretical material	35	Analysis of the theoretical material is carried out on the basis of control questions of the topic and situational tasks, tasks of KROK-1	Topic control questions, KROK-1 tasks, situational tasks	
3	Practical part (carrying out experiment)	30	Introduction and preparation for setting up the experiment. Setting up the experiment. Discussion of experiment results and formulation of conclusions	Board for fixation of animals, pneumograph, kymograph, tripod, device for recording of breathing move-ments, scissors, tweezers, surgical needles, threads, ether, syringe, 20 % Na nitrite solution	
4	Determination of the final level of knowledge and skills. Summariz-ing the results	15	Determination of the final level of knowledge and skills. Summarizing the results	KROK-1 tasks, situational tasks	

PATHOPHYSIOLOGY OF EXTERNAL RESPIRATION. RESPIRATORY FAILURE

Respiratory failure is a pathological condition characterized by one of two types of disorders:

1. The external breathing system cannot ensure the normal gas composition of the blood,

2. The normal gas composition of the blood is ensured due to increased work of the external respiratory system.

The main causes of respiratory failure

I. Pulmonary (intrapulmonary) causes:

• disorders (partial and mixed) of the gas exchange function of the lungs:

• violation of ventilation, perfusion, ventilation-perfusion ratios,

• violation of diffusion of gases through the alveolar-capillary membrane.

II. Extrapulmonary (extrapulmonary) causes:

• disorders of mechanisms of neurogenic regulation of external breathing (for example, in case of injuries, strokes, brain tumors);

• violation of the implementation of efferent regulatory influences in the neuromuscular synapses of the intercostal muscles and the diaphragm (for example, in poliomyelitis, myasthenia, polyneuritis); respiratory muscle function disorders (for example, with myalgias and myodystrophy of the intercostal muscles);

• violation of respiratory excursions of the chest (for example, with injuries to the ribs or spine, ankylosis of the rib joints);

• systemic insufficiency of blood circulation in the lungs (for example, with heart disease.

Typical disorders of external breathing:

1. Violation of alveolar ventilation:

a) alveolar hypoventilation;

b) alveolar hyperventilation.

2. Violation of lung perfusion.

3. Violation of ventilation and perfusion relations.

4. Violation of the diffusion capacity of the lungs.

5. Mixed forms.

1.1. Alveolar hypoventilation

The obstructive type (lat. obstructio – barrier) of breathing disorders is characterized by a decrease in the patency of the airways. The pathological basis of this type of pathology is the growth of the so-called "resistive" (inelastic) air flow resistance. In this regard, the volume of ventilation of the corresponding areas of the lungs decreases, the work of the respiratory muscles increases, and the energy supply (energy consumption) of the external breathing apparatus increases.

The reason for the violation of the patency of the upper respiratory tract:

• their partial or complete obturation (tongue depression in sleep, under anesthesia, in a comatose state);

• getting food or foreign bodies into the trachea;

• obstruction of the respiratory tract by sputum, vomitus, mucus or meconium in newborns;

• thickening of the mucous membranes of the trachea and bronchi during inflammation and swelling of the larynx;

• compression of the upper respiratory tract by a tumor, etc.

Causes of impaired patency of the lower respiratory tract: bronchospasm and bronchiolospasm;

• decline of small bronchi when the lungs lose their elastic properties;

• narrowing of the lumen of the airways due to the development of edematous and inflammatory changes in the bronchial wall;

• obturation of bronchioles with pathological contents (blood, exudate, etc.);

• compression of small bronchi in conditions of increased transmural pressure (when coughing).

Alveolar hypoventilation of the obstructive type often occurs when the lungs lose their elastic properties, since the lumen of the airways largely depends on the elasticity of the lung tissue. Overfilling of the lungs with air can be acute (an attack of bronchial asthma, astmoid bronchitis) or be chronic (various types of emphysema of the lungs).

Restrictive disorders (lat. restrictio – restriction, reduction) include hypoventilation disorders arising as a result of restriction of lung expansion. Two groups of factors are distinguished – intrapulmonary and extrapulmonary, which lead to restrictive violations of lung ventilation.

The pathogenetic basis of the pulmonary form of restrictive disorders is an increase in the elastic resistance of the lungs. The magnitude of this resistance depends on the extensibility of the lung parenchyma. Distensibility refers to changes in lung volume per unit change in transpulmonary pressure.

Clinical forms of restrictive alveolar hypoventilation include:

• apneic breathing,
• difficult breathing
• periodic forms of breathing.

1.2. Alveolar hyperventilation

Causes of alveolar hyperventilation:

• Inadequate mode of mechanical ventilation (anesthesia, transfer of the patient to artificial respiration in case of brain injury or coma);
• stress reactions, neurotic states (hysteria or phobias);
• organic brain damage (hemorrhage, ischemia, intracranial tumors, bruises and concussion);
• hyperthermic conditions (fever, heat stroke, etc.);
• exogenous hypoxia
• various intoxications
• effects on DC of analeptic drugs.

Manifestations of alveolar hyperventilation:

▪ hypocapnia (potentiates the inhibition of 02 utilization by tissues, reduces coronary and cerebral blood flow due to a decrease in the tone of the arteriole walls and the development of arterial hypotension);
▪ respiratory alkalosis (as a result of alveolar hyperventilation);
▪ decrease in oxygen consumption by tissues and organs (can lead to tissue hypoxia);
▪ ion imbalance in blood plasma and interstitial fluid (hypernatremia, hypokalemia, hypocalcemia, hypomagnesemia);
▪ muscle spasms (hypocalcemia and other manifestations of ion imbalance);
▪ paresthesias (as a result of brain ischemia and ionic imbalance).

1. Violation of lung perfusion

Normally, the amount of total blood flow in the lungs is equal to the minute blood volume of the heart (MI) and is 4.5–5 l/min.

The driving force of pulmonary blood flow (lung perfusion) is the pressure gradient in the right ventricle and in the left atrium, and the main regulatory mechanism is pulmonary vascular resistance.

Inadequacy of the pulmonary capillary blood flow to the level of alveolar ventilation most often occurs with the development of hyper- and hypotension of the small circle of blood circulation. Primary or secondary damage to the pulmonary blood flow not only causes respiratory failure due to ventilation and perfusion disorders, but also leads to a restrictive mechanism of respiratory failure due to alveolar tissue ischemia, BAR release, increased vascular permeability, interstitial edema, decreased surfactant formation, atelectasis, etc.

2. Violation of ventilation and perfusion relations

For the normal course of gas exchange in the lungs, the correct ratio of ventilation and blood flow is very important. At rest, the effective alveolar ventilation (AV) of a healthy person is 4–5 L, the minute volume of blood is about 5 L, and the ratio of alveolar ventilation/minute blood volume (AV/MO) is 0.8–1 (ventilation-perfusion indicator). It is this ratio that ensures the normal gas composition of the blood flowing from the alveoli.

Two variants of violation of ventilation-perfusion relations are possible:

– ventilation of non-perfused areas of lung tissue,

– perfusion of non-ventilated areas of lung tissue.

3. Violation of the diffusion capacity of the lungs

The thickness of the alveolar-capillary membrane varies from 0.3 to 2.0 microns. Its basis is alveolar epithelium and capillary endothelium. Between them there is an interstitium, which includes a gel-like main substance and bundles of connective tissue fibers.

The diffusion capacity of the lungs depends mainly on the thickness of these layers, as well as on the degree of their permeability to gases. In addition, the total area of the membranes through which O_2 and CO_2 pass and the contact time of blood with alveolar air are important for the normal course of diffusion. A change in one of these factors can lead to the development of respiratory failure.

Dyspnea

Shortness of breath is one of the most important manifestations of insufficient external breathing.

Shortness of breath or dyspnoea is difficulty breathing, characterized by a violation of the rhythm, frequency and depth of respiratory movements and is accompanied by a subjective feeling of lack of air.

The mechanism of shortness of breath is a change (disruption) in the activity of the respiratory center. However, it should be noted that the feeling of shortness of breath appears when there is a discrepancy between the

requirements for increasing the volume of ventilation and the capabilities of the external breathing apparatus to their satisfaction due to damage to the latter. And if these possibilities do not allow to increase the volume of ventilation, then no actions on the respiratory center can cause this increase. Shortness of breath can be recreated by arbitrarily holding the breath.

Objective manifestations of shortness of breath, i.e. changes in breathing, generally appear in the form of the above-mentioned disorders of breathing regulation, i.e. tachypnea, bradypnea, hyperpnea, etc. We emphasize once again that in this case they are combined with a subjective feeling of lack of air. The nature of breathing is different depending on the cause and mechanism of shortness of breath (frequent, deep, rare and deep breathing).

With shortness of breath, not only the nature of breathing itself can change, but also the ratio between the phases of inhalation and exhalation. Exhalation can become active and take place with the participation of expiratory muscles. Shortness of breath, in which difficulty in breathing prevails, is called inspiratory, difficulty in exhaling is called expiratory. Mixed shortness of breath is also distinguished.

Violation of external breathing can manifest itself in the form of so-called periodic breathing. Intermittent breathing is defined as the occurrence of short-term periods of altered breathing rhythm, replaced by a temporary stoppage of it, which is designated as apnea. Cheyne-Stokes and Biot's breathing are part of periodic breathing.

Kussmaul's pathological breath ("big breath") is a pathological form of breathing that occurs in severe pathological processes (pre-terminal stages of life). Periods of stopping respiratory movements alternate with rare, deep, convulsive, noisy breaths.

Asphyxia

If respiratory failure occurs acutely or subacutely and has reached such a degree that oxygen stops flowing into the blood, and carbon dioxide is not removed from the blood, asphyxia develops. The term "asphyxia" literally means the absence of a pulse.

Asphyxia is a condition characterized by insufficient supply of oxygen to the tissues and the accumulation of carbon dioxide in them, which occurs as a result of the lack of ventilation exchange of gases in the lungs, more precisely between the blood and the external environment, that is, it is one of the manifestations of impaired external breathing.

Causes of asphyxia:

- compression of the respiratory tract from the outside
- the presence of liquid in the respiratory tract and alveoli (in case of drowning, aspiration of vomitus, pulmonary edema).
- bronchospasm (with anaphylactic shock)
- lung expansion disorder (bilateral pneumothorax),
- suppression of the respiratory center,

• violation of the innervation of the respiratory muscles,
• sharp restriction of chest mobility.

The mechanism of asphyxiation consists in the reflex and direct effect on the central non-trivial system, on the respiratory center of an excess of carbon dioxide, as well as a lack of oxygen.

Peculiarities of pathology of external breathing in children

The most common cause of acute respiratory failure in children is acute obstruction of the upper respiratory tract due to pathological processes that lead to narrowing of the larynx and bronchi. The severity of the process is determined by the following factors: the respiratory tract of the child; loose fiber of the subligamentous space of the larynx; susceptibility of children to laryngospasm; relative weakness of respiratory muscles.

Setting up the experiment. Discussion of the results and formulation of conclusions.

Causing breathing disorders with gradual narrowing of the upper respiratory tract.

1. The rabbit is tied to the machine.
2. The sensors of the pneumograph are attached to the chest and the recording of respiratory movements is set up on the kymograph tape.
3. Observe the nature of breathing in the initial state.
4. Observe the nature of breathing at different degrees of closure of the nasal passages, paying attention to changes in the frequency and depth of respiratory movements.

Causing breathing disorders with a sharp narrowing of the upper respiratory tract (asphyxia).

1. The mouse is fixed to the board on the back.
2. An incision of 1 cm length is made along the midline of the neck, the muscles are bluntly pushed aside and the trachea is exposed.
3. Carefully place a silk thread under the trachea with tweezers.
4. The board with the mouse is fixed on a tripod.
5. I apply a small clamp connected to a pen to the skin of the chest.
6. Adjust the recording on the kymograph drum.
7. Record the initial respiratory movements.
8. Bandage the trachea and observe the nature of changes in breathing during asphyxia.
9. After stopping breathing, open the thorax, expose the heart of the animal and observe heart contractions.

Discussion of the results of the experiment.

Discussing the results of the experiments, remind the students of the main mechanisms of breathing regulation. Explain the features of stenotic breathing and the mechanism of its occurrence. It should be noted that with slight narrowing of the upper airways, the increase in the volume of pulmonary ventilation occurs due to an increase in the depth of breathing, and a

sharper stenosis is accompanied by a decrease in the depth of respiratory movements, which remain rare. In the explanation of the mechanism of stenotic breathing, note the delay of the Hering-Breuer reflex.

Identify 3 periods of asphyxia. Explain the mechanism of changes in breathing, blood circulation and heart activity during asphyxia. Explain the mechanism of terminal respiratory movements. Note the importance of maintaining cardiac activity after respiratory arrest.

Point out the importance of the research of domestic scientists in the development of the main issues of respiratory pathology (I. M. Sechenov, V. V. Pashutin, N. M. Syrotinin, etc.).

Formulation of conclusions from the experiment

1. With a gradual narrowing of the upper respiratory tract (incomplete closure of the rabbit's nasal passages), an increase in the volume of pulmonary ventilation is observed due to an increase in the depth of breathing while simultaneously slowing it down (stenotic breathing). Mechanism: delay of the Hering-Breyer reflex and associated inhibition of inhalation.

2. With rapid narrowing of the upper respiratory tract (asphyxia), 3 periods of breathing disturbance are observed:

1) excitement, characterized by increased frequency and deepening of breathing with a predominance of the inhalation phase over the exhalation phase (inspiratory dyspnea);

2) depression, characterized by a decrease in the frequency and depth of breathing with difficult exhalation (expiratory dyspnea);

3) terminal, characterized by agonal or terminal breathing after short-term apnea (gasping breathing) and preservation of cardiac activity after stopping breathing.

Tasks for independent work on the topic «Pathophysiology of external respiration. Respiratory failure»

The student is invited to determine the causes of violations of the external respiration system and identify possible consequences. To be able to explain the mechanism of occurrence. Analysis of errors with an explanation of the correct answers

List of questions and works to be studied:

1. Definition of the concepts of "breathing", "external breathing", "cellular (tissue) breathing. Factors determining the effectiveness of the external breathing system.

2. Indicators of the functional state of the external breathing system (lung volumes and capacities) and their changes in the pathology of external breathing.

3. Respiratory insufficiency. Types. Causes. Typical disorders of external breathing.

4. Alveolar hypoventilation. Definition of the concept. The main reasons. Pathogenesis. Forms Manifestations

5. Alveolar hyperventilation. Reasons. Forms Manifestations

6. Impaired lung perfusion. Pulmonary hypertension: forms, main causes, pathogenesis. Pulmonary hypotension: forms, main causes, pathogenesis.

7. Violation of ventilation-perfusion ratios. Reasons, options.

8. Violation of the diffusion capacity of the lungs. Reasons. Mechanisms.

9. Manifestations of insufficiency of external breathing. Shortness of breath: types, mechanisms. Periodic breathing: types, mechanisms. Asphyxia: causes, mechanisms, types, mechanisms.

10. Features of the pathology of external breathing in children.

List of practical skills that must be mastered:

1. Explain the role of reflex effects and disorders of the function of the upper respiratory tract in the origin of shortness of breath.

2. Identify the main signs and manifestations of shortness of breath.

3. Explain the main mechanisms of their occurrence and development.

Situational tasks KROK-1 to determine the final level of knowledge

1. An unconscious young man with signs of morphine poisoning entered admission office. His respiration is shallow and infrequent which is caused by inhibition of respiratory centre. What type of respiratory failure is it?

A. Ventilative dysregulatory. *D. Perfusive.*
B. Ventilative obstructive. *E. Diffusive.*
C. Ventilative restrictive.

2. A patient with bronchial asthma has developed acute respiratory failure. What kind of respiratory failure occurs in this case?

A. Obstructive disturbance of alveolar ventilation.
B. Restrictive ventilatory defect.
C. Perfusion.
D. Diffusion.
E. Dysregulation of alveolar ventilation.

3. A 12 y.o. boy who suffers from bronchial asthma has an acute attack of asthma: evident expiratory dyspnea, skin pallor. What type of alveolar ventilation disturbance is it?

A. Restrictive. *C. Central.* *E. Obstructive.*
B. Throracodiaphragmatic. *D. Neuromuscular.*

4. A patient has a history of chronic obstructive bronchitis. Blood gas analysis revealed the development of hypoxemia and hypercapnia on the background of dyspnea, tachycardia and cyanosis. What disorder of external respiration is observed in the patient?

A. Hyperperfusion. *C. Hyperdiffusion.* *E. Hypoventilation.*
B. Hyperventilation. *D. Hypoperfusion.*

5. A patient with marked pneumofibrosis that developed after infiltrating pulmonary tuberculosis has been diagnosed with respiratory failure. What is its pathogenetic type?

A. Restrictive. *C. Obstructive.* *E. Apneustic.*
B. Dysregulatory. *D. Reflex.*

6. A patient with evident pneumosclerosis that developed after infiltrative pulmonary tuberculosis presents with respiratory failure. What is its pathogenetic type?

A. Restrictive. *C. Obstructive.* *E. Dysregulative.*
B. Apneustic. *D. Reflectory.*

7. A 50-year-old male patient suffers from chronic bronchitis, complains about dyspnea during physical activity, sustained cough with sputum. After examination he was diagnosed with pulmonary emphysema. This complication is caused by:

A. Ventilation-perfusion disbalance. *D. Decrease in lung elasticity.*
B. Decrease in lung perfusion. *E. Decrease in lung compliance.*
C. Decrease in alveolar ventilation.

8. Examination of a miner revealed pulmonary fibrosis accompanied by disturbance of alveolar ventilation. What is the main mechanism of this disturbance?

A. Constriction of superior respiratory tracts.
B. Disturbance of neural respiration control.
C. Limitation of breast mobility.
D. Limitation of respiratory surface of lungs.
E. Bronchi spasm.

9. A patient staying in the pulmonological department was diagnosed with pulmonary emphysema accompanied by reduced elasticity of pulmonary tissue. What type of respiration is observed?

A. Expiratory dyspnea. *D. Infrequent respiration.*
B. Inspiratory dyspnea. *E. Periodic respiration.*
C. Superficial respiration.

10. A 23-year-old patient has been admitted to a hospital with a craniocerebral injury. The patient is in a grave condition. Respiration is characterized by prolonged convulsive inspiration followed by a short expiration. What kind of respiration is it typical for?

A. Apneustic. *C. Kussmaul's.* *E. Biot's.*
B. Gasping breath. *D. Cheyne-Stokes.*

11. A 23 year patient was admitted to the hospital in grave condition with craniocerebral trauma. His respiration is characterized by a spasmodic long inspiration interrupted by a short expiration. What respiration type is it typical for?

A. Gasping. *D. Cheyne-Stokes respiration.*
B. Kussmaul's respiration. *E. Biot's respiration.*
C. Apneustic.

12. A 62-year-old patient was admitted to the neurological department due to cerebral haemorrhage. Condition is grave. There is observed progression of deepness and frequency of breathe that turnes into reduction to apnoea,

and the cycle repeates. What respiration type has developed in the patient?

A. Kussmaul's respiration. *D. Gasping respiration.*

B. Biot's respiration. *E. Apneustic respiration.*

C. Cheyne-Stockes respiration.

13. A 62-year-old patient with cerebral haemorrhage was admitted to the neurological department in grave condition. Objectively: increase of respiration depth and rate with its following reduction to apnoea, thereafter respiration cycle restores. What respiration type is it?

A. Cheyne-Stokes. *C. Gasping.* *E. Kussmaul's.*

B. Biot's. *D. Apneustic.*

14. A patient with a craniocerebral injury presents with respiration characterized by progressively deeper respiratory movements followed by a gradual decrease that results in a temporary stop in breathing. What pattern of abnormal respiration are these features typical for?

A. Cheyne-Stokes. *C. Kussmaul's.* *E. Apneustic.*

B. Biot's. *D. Gasping.*

15. While having the dinner the child choked and aspirated the food. Meavy cough has started, skin and mucosa are cyanotic, rapid pulse, rear breathing, expiration is prolonged. What disorder of the external breathing developed in the child?

A. Stage of inspiratory dyspnea on asphyxia. *D. Alternating breathing.*

B. Stage of expiratory dyspnea on asphyxia. *E. Biot's breathing.*

C. Stenotic breathing.

16. A 30-year-old man has sustained an injury to his thorax in a traffic incident, which caused disruption of his external respiration. What type of ventilatory difficulty can be observed in the given case ?

A. Restrictive extrapulmonary ventilatory impairment.

B. Obstructive ventilatory impairment.

C. Impair ventilation regulation dysfunction.

D. Restrictive pulmonary ventilatory impairment.

E. Cardiovascular collaps.

Standards of correct answers to the situational tasks

1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
A	*A*	*E*	*E*	*A*	*A*	*D*	*D*	*A*	*A*	*C*	*C*	*A*	*A*	*B*	*A*

Recommendations for registration of work results

1. Written answer to test tasks (basic level of knowledge).

2. The results of the experiment are drawn up in the form of an experiment protocol with the determination of relevant conclusions.

3. Protocol for solving situational tasks with an explanation of the correct answers (final level of knowledge).

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Topic 12. Pathophysiology of the digestive system. Insufficiency of digestion. Pathophysiology of the liver. Liver failure

Justification of the topic: Diseases of the stomach and digestion are constantly increasing, which leads to a decrease in work capacity and disability. Quite often, these diseases become the cause of death. One of the most important and earliest disorders of the stomach functions is a disorder of gastric secretion, which can develop as a result of a violation of neuroendocrine regulation, with pathological processes in the stomach, in other organs and systems, with various external influences on the body. Gastrointestinal secretion disorders are characterized by both quantitative and qualitative changes. Knowledge of the basic patterns of gastric secretion disorders, quantitative and qualitative changes in gastric juice thus makes it possible to correctly carry out prevention and rational therapy of gastric secretion disorders. Violation of the biliary function of the liver, accompanied by the development of jaundice, is a pathological syndrome that can be observed in diseases of the liver and biliary tract of a therapeutic, infectious and surgical profile, and a number of diseases. Hemolytic situations of hereditary, immune and toxic nature. Knowledge of the etiology and pathogenesis of various types of jaundice, the basics of their clinical and laboratory differential diagnosis are necessary in the general theoretical training of a general practitioner. In addition, many clinical manifestations of diseases of the liver and biliary tract of various etiologies are based on the development of cholemia.

Purpose of the lesson:

General – to be able to determine and characterize the acidity of gastric juice in various disorders of gastric secretion, the essence of jaundice as a pathological syndrome, which is a consequence of impaired bile formation and bile secretion, to interpret the main laboratory parameters. Differential diagnosis of various types of jaundice. To be able to interpret the cholemic syndrome as a set of functional changes in the body in diseases of the liver and biliary tract, accompanied by mechanical or parenchymal jaundice..

Specifically:

Know:

1. Explain normal and pathological types of gastric secretion.

2. To analyze the mechanism of hypo- and hypersecretion, hypo- and hyperacidity. 3. Explain the effect of secretion disorders on the mechanism of gastric motor function disorders.

4. Use the knowledge of these mechanisms to correctly understand their role in the pathogenesis of diseases of the digestive tract.

5. Define the concept of jaundice as a pathological syndrome.

6. Classify jaundice taking into account their etiology and pathogenesis.

7. To justify the use of the used laboratory indicators, the study of which is necessary for the differential diagnosis of jaundice.

8. Carry out a qualitative determination of direct and indirect bilirubin in blood serum.

9. Conduct differential diagnosis of various types of jaundice, using knowledge of the mechanisms of biochemical disorders.

10. List the main symptoms of cholemic syndrome.

11. Explain the mechanism of emergence and development of the main manifestations of cholemic syndrome.

Be able:

1. Describe the content and acidity of gastric juice.

2. Interpret and explain the mechanisms of gastric secretion regulation.

3. To analyze the mechanism of development of hypo- and hypersecretion.

4. To explain the effect of secretory disorders on the mechanism of disturbances in the motor function of the stomach.

5. To apply the received ideas about the mechanisms of digestive disorders in the stomach for a correct understanding of their role in the pathogenesis of diseases of the gastrointestinal tract (GI).

6. Visualize the anatomical and histological structure of the liver and biliary tract.

7. To know the main stages of the exchange of bile pigments in the human body.

8. Explain the main physiological mechanisms of the biliary function of the liver.

9. Characterize the processes of bile formation and bile secretion and the chemical composition of bile.

10. Explain the importance of bile in the digestion process.

Practical experience:

1. Define the terms "digestion", "digestive insufficiency", "dyspepsia syndrome", "dyspepsia".

2. Determine the main causes of taste disturbance, appetite, thirst. Types. Causes.

3. Find out what are the signs of the type of esophageal dysfunction, their causes.

4.Kokava reasons for the development of dyspepsia in the stomach. What is a violation of the secretory function of the stomach.

5. Explain what is a violation of the digestive function of the intestine.

6. Name the signs of malabsorption syndrome, the main causes and manifestations. Nonspecific ulcerative colitis. Causes, manifestations

7. Name the main pathological syndromes of liver damage, their biochemical markers.

8. Explain the consequences of functional liver failure.

9. Define the concept of "jaundice". Types of jaundice. Hemolytic jaundice. Causes, pathogenesis and manifestations

The graphological structure of the topic "Pathophysiology of the digestive system. Insufficiency of digestion. Pathophysiology of the liver. Liver failure" is attached.

Material and methodological support of the topic "Pathophysiology of the digestive system. Insufficiency of digestion. Pathophysiology of the liver. Liver failure".

1. Lectures.
2. Methodical instructions for teachers.
3. Methodical instructions for students;
4. Set of test tasks to determine the basic level of knowledge.
5. Set of situational tasks to determine the final level of knowledge.
6. Set of KROK-1 tasks.
7. Set of schemes and tables (presentation).
8. Set of forms with a clinical blood test.
9. Video films.
10. For the experiment (experimental animals – rabbit, microscopes, immersion oil, subject slides, polish slides, hydrochloric acid solution, distillates for painting of smears, injector, pins, Petri-dish.

Oriented map of students' work on the topic "Pathophysiology of the digestive system. Insufficiency of digestion. Pathophysiology of the liver. Liver failure"

No	Stage of lesson	Academic time, min	Educational guide		Place holding a class
			Educational tools	Equipment	
1	Definition of initial knowledge	20	Control of theoretical training of students programmable by using structural answers to the issue of tickets	Test control issue tickets	Study room
2	Analysis of theoretical material	45	Analysis of theoretical material on the basis of control conduct by question topic	Control question topic	Study room
3	The experiment	5	Introduction to the formulation and preparation of the experiment. Setting experiment	Burettes, pipettes, erlenmeyerovskie cones, 1 % phenolphthalein alcohol solution, 0.5 % alcohol solution dimetilamid 0,1 N sodium hydroxide solution	Study room
4	The final stage of determining the level of knowledge and skills. Summing up	20	Determining the source of formation of knowledge and skills	The decision of situational problems	Study room

THEORETICAL MATERIAL FOR LESSON PREPARATION

PATHOPHYSIOLOGY OF THE DIGESTIVE SYSTEM. INSUFFICIENCY OF DIGESTION. PATHOPHYSIOLOGY OF THE LIVER. LIVER FAILURE

DISTURBANCES IN DIGESTION IN THE ORAL CAVITY

They include:

- disorders of mastication;
- disturbances in salivary secretion;
- disorders of the tonsils.

Disturbances in Mastication

They arise as a result of:

- affections of teeth (the absence of a large number of teeth, caries, pulpitis, periodontitis, parodontosis);
- stomatitides and gingivitides;
- disturbances of the masticative muscles (traumas, inflammation);
- disturbances of the masticative nerves;
- lesions of the temporal-mandibular joint;
- lesions of masticative apparatus as a whole;
- bulbar paralyses.

The results of disturbed mastication: traumatisation of the mucosa of the mouth, gums, esophagus and stomach, infecting, inflammation, affection of the gastric and pancreatic secretion (normally mastication of food reflexly causes secretion of gastric and pancreatic juices) and, thus, of functions of the lower parts of the digestive tract.

Disturbances of the Secretory Function

Gastric hypersecretion and hyposecretion are distinguished (in norm the quantity of gastric juice is 2–2.5 litres a day).

Achlorhydria has been defined by multiple separate systems in reference to gastric acid secretion.

First, achlorhydria has been defined by a peak acid output in response to a maximally effective stimulus that results in an intragastric pH of greater than 5.09 in men and greater than 6.81 in women.

Second, achlorhydria has been defined by a maximal acid output of less than 6.9 m/mole/h in men and less than 5.0 m/mole/h in women.

Third, achlorhydria has been defined as a ratio of serum pepsinogen I.

Pathophysiology Acid secretion by gastric epithelial cells is related to the physiologic function of oxyntic cells, which are called parietal cells. Parietal cells are mainly present in the gastric corpus and fundus, although complete mapping in the human stomach is not fully known. Parietal cells are responsible for secretion of hydrochloric acid and also produce intrinsic factor. Parietal cells have large mitochondria with short microvilli and a cytoplasmic canaliculi system in contact with the lumen. The H^+/K^+ -ATPase responsible for acid secretion resides in the apical microvillus membrane.

The relationship between parietal cell function and achlorhydria is illustrated using genetic knockout mice models, as follows: The absence of the H^+/K^+ -ATPase is chronically associated with achlorhydria and mucosal hyperplasia but with no histological evidence for neoplasia.

In a gastrin knockout model, achlorhydria is present because of the inactivation of enterochromaffin like (ECL) cells and parietal cells. This model leads to intestinal metaplasia, bacterial overgrowth, and, in some instances, gastric tumors.

Chronic inflammatory changes related to gastric Helicobacter pylori infection can also induce parietal cell changes.

Among the origins of achlorhydria that are related to medical care, medications that block H+/K+ -ATPase activity can induce achlorhydria.

Motor Dysfunctions of the Stomach

Disorders of the motor activity of the stomach may manifest themselves as changes in muscular tone and changes in peristalsis.

The changed muscular tone is manifested in gastric hypertonia and hypotonia (atonia).

Gastric hypertonia is observed in ulcer disease, in the beginning of acute gastritis, under reflex influences (renal or hepatic colics, etc.), neurosis. Hypotonia, or relaxation of the stomach, may arise in splanchnoptosis, gastroptosis, paresis of the muscular layer, reflexly – when obstruction to the movement of the chyme toward the pyloric end of the stomach appear locally (neoplasm, scars), infectious diseases of the gastrointestinal tract, action of psychic factors (various emotions).

ACUTE GASTRITIS

Acute gastritis is a term covering a broad spectrum of entities that induce inflammatory changes in the gastric mucosa. The different etiologies share the same general clinical presentation. However, they differ in their unique histologic characteristics. The inflammation may involve the entire stomach (eg, pangastritis) or a region of the stomach (eg, antral gastritis). Acute gastritis can be broken down into 2 categories: erosive (eg, superficial erosions, deep erosions, hemorrhagic erosions) and nonerosive (generally caused by *Helicobacter pylori*).

Other symptoms include nausea, vomiting, loss of appetite, belching, and bloating. Occasionally, acute abdominal pain can be a presenting symptom. This is the case in phlegmonous gastritis (gangrene of the stomach) where severe abdominal pain accompanied by nausea and vomiting of potentially purulent gastric contents can be the presenting symptoms. Fever, chills, and hiccups also may be present.

CHRONIC GASTRITIS

Chronic gastritis is a histopathologic entity characterized by chronic inflammation of the stomach mucosa. Gastritides can be classified on the basis of the underlying cause.Chemical or reactive gastritis is caused by injury to the gastric mucosa resulting from reflux of bile and pancreatic

secretions into the stomach. These chemicals cause epithelial damage, erosions, and ulcers that are followed by regenerative hyperplasia detectable as foveolar hyperplasia, and damage to capillaries, with mucosal edema, hemorrhage, and increased smooth muscle in the lamina propria.*H pylori* gastritis is a primary infection of the stomach and is the most frequent cause of chronic gastritis. Cases of histologically documented chronic gastritis are diagnosed as chronic gastritis of undetermined etiology or gastritis of undetermined type when none of the findings reflect any of the described patterns of gastritis and a specific cause cannot be identified.

Etiology

Chronic gastritis may be caused by either infectious or noninfectious conditions. Infectious forms of gastritis include the following:

- Chronic gastritis caused by *H pylori* infection – This is the most common cause of gastritis
- Gastritis caused by *Helicobacter heilmannii* infection
- Granulomatous gastritis associated with gastric infections in mycobacteriosis, syphilis, histoplasmosis, mucormycosis, South American blastomycosis, anisakiasis, or anisakidosis
- Chronic gastritis associated with parasitic infections. Non-infectious forms of gastritis include the following:
- Autoimmune gastritis
- Chemical gastropathy, usually related to chronic bile reflux or NSAID and aspirin intake
- Uremic gastropathy

Chronic non-infectious granulomatous gastritis – This may be associated with Crohn disease, sarcoidosis, Wegener granulomatosis, foreign bodies, cocaine use, isolated granulomatous gastritis, chronic granulomatous disease of childhood, eosinophilic granuloma, allergic granulomatosis and vasculitis, plasma cell granulomas, rheumatoid nodules, tumoral amyloidosis and granulomas associated with gastric carcinoma, gastric lymphoma, or Langerhans cell histiocytosis

- Lymphocytic gastritis, including gastritis associated with celiac disease (also called collagenous gastritis)
- Eosinophilic gastritis
- Radiation injury to the stomach
- Graft-versus-host disease (GVHD)
- Ischemic gastritis
- Gastritis secondary to drug therapy
- Some patients have chronic gastritis of undetermined etiology or gastritis of undetermined type (eg, autistic gastritis).

Pathophysiology

The pathophysiology of chronic gastritis complicating a systemic disease, such as hepatic cirrhosis, uremia, or another infection, is described in the articles specifically dealing with these diseases. The pathogenesis of the most common forms of gastritis is described below.

PEPTIC ULCER DISEASE

Gastric and duodenal ulcers usually cannot be differentiated based on history alone, although some findings may be suggestive. Epigastric pain is the most common symptom of both gastric and duodenal ulcers. It is characterized by a gnawing or burning sensation and occurs after meals—classically, shortly after meals with gastric ulcer and 2–3 hours afterward with duodenal ulcer.

In most patients with uncomplicated PUD, routine laboratory tests usually are not helpful; instead, documentation of PUD depends on radiographic and endoscopic confirmation. Testing for H pylori infection is essential in all patients with peptic ulcers. Rapid urease tests are considered the endoscopic diagnostic test of choice. Of noninvasive tests, fecal antigen testing is more accurate than antibody testing and is less expensive than urea breath tests. A fasting serum gastrin level should be obtained in certain cases to screen for Zollinger-Ellison syndrome.

Etiology

Peptic ulcer disease (PUD) may be due to any of the following:

- H pylori infection
- Drugs
- Lifestyle factors
- Severe physiologic stress
- Hypersecretory states (uncommon)
- Genetic factors

DISORDERS OF INTESTINAL DIGESTION

The disorders of intestinal digestion include those of secretion, motorium, excretion, absorption and intestinal fermentation and putrefaction (changes in the microbial flora).

Secretory Dysfunction of the Intestines

Secretory disorders in the intestinum depend on disturbed secretion of bile, pancreatic and intestinal juices.

Causes of absence or *insufficient delivery of bile to the duodenum* and appropriate disturbances of intestinal digestion will be considered in the next chapter.

Digestive disorders associated with an *absence or deficiency of pancreatic juice* may be observed in calculi, tumours, inflammation, atrophy, disturbed innervation, etc.

Disorders in the secretion of bile and pancreatic juice *are manifested* by disturbed cavital and membrane intestinal digestion and absorption of fats (*steatorrhea*), proteins, carbohydrates, nucleic acids, vitamins.

Motor Dysfunction of the Intestines

It consists in excessive or diminished peristalsis.

Excessive peristalsis arises as a result of inflammatory processes in the intestinal mucosa (enteritis, colitis), mechanical or chemical irritations by coarse and barely digestible parts of food, accumulated decomposition

products, acids and toxic substances, dysfunction of the nervous system (for example, in strong emotions – fear – and in hypersensitivity of the receptor apparatus. It *results* in *diarrhea* – increased frequency of the stool. *Frequent diarrheas lead* to deep disturbances of intestinal secretion, digestion, absorption, insufficiency of digestion, dehydration, hypovolemia, collapse, starvation, general nutritional disturbances.

Diminished peristalsis causes *constipation* which may be atonic and spastic. Its *causes* are: inherent spasms of intestines in Hirschsprung's disease, acquired spasms in plumbum poisoning, psychic influences, atonia of the intestinum in quantitative and qualitative food insufficiency – deficit of cellulose, potassium, calcium, vitamin B_1, etc., stimulation of the nervus vagus, action of glucagon, etc. *Constipation leads* to putrefaction, accumulation of gases, intoxication, meteorism, ileus.

Diarrhea

Overview. Diarrhea is the frequent passage of loose, watery, soft stools with or without abdominal bloating, pressure, and cramps commonly referred to as gas. Diarrhea can come on suddenly, run its course, and be helped with home care to prevent complications such as dehydration.

Diarrhea is one of the most common illnesses in all age groups and ranks along with thecommon cold as a main cause of lost days of work or school.

People of all ages can suffer from diarrhea, and the average adult has one episode of acute diarrhea per year, and young children average two acute episodes per year.

Diarrhea and related complications can cause severe illness. The most significant cause of severe illness is loss of water and electrolytes. In diarrhea, fluid passes out of the body before it can be absorbed by the intestines. When the ability to drink fluids fast enough to compensate for the water loss because of diarrhea is impaired, dehydration can result. Most deaths from diarrhea occur in the very young and the elderly whose health may be put at risk from a moderate amount of dehydration.

Pathophysiology of the liver. Liver failure.

The main functions of the liver are the digestive and homeostatic which, in turn, supported by such private functions such as:

1) the formation and secretion of bile,

2) participation in all types of metabolism,

3) and neutralize the barrier function,

4) the formation and secretion of cholesterol, biliary excretion of metabolites, and toxic drugs,

5) the deposit of blood, the maintenance of vascular tone,

6) participation in the processes of blood

7) the synthesis of components of coagulation and anticoagulation systems, etc.

All the functions of the liver are complex (multicomponent) and interconnected.

Acute Liver Failure

Acute liver failure (ALF) is an uncommon condition in which the rapid deterioration of liver function results in coagulopathy and alteration in the mental status of a previously healthy individual. Acute liver failure often affects young people and carries a very high mortality.

The term acute liver failure is used to describe the development of coagulopathy, usually with an international normalized ratio (INR) of greater than 1.5, and any degree of mental alteration (encephalopathy) in a patient without preexisting cirrhosis and with an illness of less than 26 weeks' duration.

Acute liver failure is a broad term that encompasses both fulminant hepatic failure (FHF) and subfulminant hepatic failure (or late-onset hepatic failure). Fulminant hepatic failure is generally used to describe the development of encephalopathy within 8 weeks of the onset of symptoms in a patient with a previously healthy liver. Subfulminant hepatic failure is reserved for patients with liver disease for up to 26 weeks before the development of hepatic encephalopathy.

The outcome of acute liver failure is related to the etiology, the degree of encephalopathy, and related complications (see Prognosis). Although mortality from FHF remains significantly high, improved intensive care and use of orthotopic liver transplantation have improved survival from less than 20 % to approximately 60 %.

BASIC PATHOPHYSIOLOGY OF LIVER DISEASE

The basic pathophysiology of all forms of liver disease represents failures of the numerous and complex hepatic metabolic functions. Although there is some variability in basic pathophysiology from one type of liver disease to another, all forms of liver disease can reasonably be called hepatic failure. The signs and symptoms, the natural history, and the rationale of treatment for all forms of liver disease derives from certain relatively simple basic pathophysiologic concepts.

LIVER DISEASE - PRIME CLINICAL FEATURES

Acute Viral Hepatitis

Acute viral hepatitis is a systemic infection which affects the liver. Two viruses have been identified (A and B). The third type is referred to as non A, non B.

It is recognized that a distinction between hepatitis A and B cannot be made solely by clini-cal features or by epidemiologic features because ways of transmission overlap. The distinction must be made by specific serologic testing.

Hepatitis compromises hepatic function. With hepatic function impaired, hepatocyte formation and excretion of bile are also impaired. Since bile salts are necessary for the degradation of foodstuffs in the gut, particularly of fatty foodstuffs, obvious gastrointestinal signs and symptoms are likely to develop early.

The clinical course of acute viral hepatitis has three major phases: the preicteric stage, the icteric stage, and the recovery stage. The signs and symptoms tend to vary considerably from one stage to the next. The first symptoms

that appear in the preicteric phase are vague constitutional symptoms and, usually, symptoms directly referable to the G.I. tract. Thus, this infectious disease is heralded by fatigue, malaise, and anorexia. There may be fever, with hepatitis A, there may be upper respiratory symptoms, which are unusual in hepatitis B. During the course of the first week or so, the patient's anorexia is likely to become nausea, possibly with vomiting and diarrhea. During the pre-icteric stage, a mild polyarthritis may develop. In other words, during the pre- icteric stage both hepatitis A and B may resemble a "flu-like" illness.

Cirrhosis

Many of the physical signs encountered in cirrhosis are difficult to describe and must be seen to be appreciated. Some are poorly understood. With regard to symptoms in cirrhosis, it is fair to say that, except in far-advanced disease, there are no symptoms directly attributable to the hepatic dysfunction present. The reason for this is that very little normal hepatic function is required for successful carrying- on of everyday activities.

As cirrhosis progresses, and as fatty infiltration continues, there is a tendency for the liver to enlarge. This may continue slowly and steadily for many years. Because there is persistent necrosis, there is a steady accumulation of fibrous scar tissue within the organ, and so, as the organ enlarges, it tends to become firmer than normal. Eventually, necrosis and fibrosis supersede fatty enlarge-ment, and the liver begins to shrink under the influence of fibrotic retraction.

During the period of enlargement the lower border may also become palpable, and is usually firmer than normal. As diffuse interstitial fibrosis progresses, the liver edge is often felt to be much firmer than normal and may become quite hard. If fibrotic retraction shrinks the organ to such an extent that the lower border is far above the right costal margin, then the edge is no longer palpable.

Thus, there are really only two safe rules of thumb with regard to liver size and consistency:

1) hepatic enlargement strongly suggests ongoing pathologic processes,

2) a liver size definitely less than normal strongly suggests late pathologic changes.

Portal hypertension, a serious consequence of advanced liver disease, often exists for years before evidence of its presence is observed. The usual evidence of portal hypertension, ascites, the caput medusae and hemorrhoids, are late findings that develop after the gastrointestinal vasculature is no longer able to compensate for the persistent increase in venous pressure.

Pathophysiology of portal hypertension

In a healthy individual, the liver is a very low resistance organ which passively receives whatever blood flow is coming from the mesenteric bed, a value that changes over the course of the day. The liver is able to accommodate these changes in blood flow without an increase in portal pressures by decreasing the resistance n the liver through the recruitment of additional

hepatic sinusoids. Thus, the ΔP does not change despite an increase in Q because the R is reduced. One needs to understand how changes in both the resistance to blood flow in the portal system and volume of blood flow in the portal system in patients with cirrhosis combine to produce portal hypertension.

ASCITES

Pathophysiology

There is considerable evidence which suggests that ascites is related to an increase in hepatic sinusoidal pressure rather than an increase in splanchnic capillary pressure. Patients with pre-sinusoidal portal hypertension rarely develop ascites while those with post-hepatic portal hypertension have ascites as a prominent feature of their illness. An increase in the hepatic sinusoidal pressure in combination with a decreased oncotic pressure results in the increased production of hepatic lymph. When the production of lymph exceeds the ability of the lymphatics and the thoracic duct to return the lymph of the general circulation, ascites results.

Symptoms in Cirrhosis

Patients with various kinds of cirrhosis tend to have many kinds of symptoms simultaneously. Most of them are not directly referable to the liver and suggest extensive multisystem disease. The alcoholic, for example, with advanced portal cirrhosis is very likely to have the symptoms of a peripheral neuropathy, such as numbness and tingling (paraesthesia) as well as impairment of the sense of touch and of the vibratory sense, usually in all four extremities but more often in the feet and hands.

Patients with biliary cirrhosis are most likely to present with generalized, intractable pruritus. Although there are not many definitive signs and symptoms, pale-colored stools, dark urine, Uterus and melanosis of exposed skin frequently accompany pruritus of biliary cirrhosis. Signs of early liver failure are few. Although pruritus may be the only symptom, xanthalasmas, xanthomas, hepatomegaly, splenomegaly and clubbing of the finger may be noted.

Setting up the experiment. Discussion the results and formulation the conclusions

Experiment 1 Determination of the acidity of gastric juice of patients with hypo-, hyper- and normo-secretion.

1. Fill burettes with 0.1 N caustic sodium solution.

2. Pour 5 ml of gastric juice into an Erlenmeyer flask with a pipette, add 1–2 drops of a 0.5 % alcoholic solution of dimethylamidoazobenzene and 1–2 drops of a 1 % alcoholic solution of phenolphthalein. The juice turns crimson.

3. Note the initial level of alkali in the burette and titrate the juice until the appearance of a brick color, which corresponds to the end of neutralization of free hydrochloric acid with caustic soda.

4. Determine the number of milliliters of caustic soda solution that was needed to neutralize free hydrochloric acid, and continue the titration until the appearance of a persistent pink color, which corresponds to the neutrali-

zation of all acids of the gastric juice with alkali, that is, the total acidity. Note once again the amount of spent caustic soda solution.

5. Calculate the total and free acidity of gastric juice in milliliters of caustic soda solution required for titration of 10 ml of gastric juice, as well as in mmol/l.

6. Determine the content of hydrochloric acid in gastric juice by multiplying the amount of free hydrochloric acid by 0.00365.

7. Using the obtained experimental data and applying knowledge of the theoretical material, formulate and record the conclusions of the conducted experiment. Enter the obtained results in the table.

Discussion of the results of the experiment

With gastric hypersecretion, there is an increase in the amount of gastric juice both after eating and on an empty stomach, correspondingly, an increase in total acidity and the content of free hydrochloric acid in gastric juice.

Formulation the conclusions based on the experiment.

Based on the experiment, it can be explained that gastric hypersecretion can be simulated in the experiment a) by stimulating mucosal receptors; b) a decrease in the inhibitory effect of the cerebral cortex on the vagus centers; c) electrical stimulation of the centers of the vagus nerve or its efferent fibers innervating the stomach; d) the introduction of histamine or pharmacological agents that stimulate its formation in the gastric mucosa.

Tasks for independent work on the topic "Pathophysiology of the digestive system. Insufficiency of digestion. Pathophysiology of the liver. Liver failure"

The student is invited to examine the results of the content of gastric juice to determine the violation of its formation in the gastric mucosa. It is necessary to determine the signs and type of violation. Be able to explain the mechanism of occurrence. Analysis of errors with an explanation of the correct answers.

List of questions and works to be studied:

1. Definition of the terms "digestion", "digestive insufficiency", "syndrome of insufficiency of digestion", "dyspepsia". Main reasons for insufficiency of digestion.
2. Violations of taste, appetite, feeling of thirst. Types. Reasons. Consequences.
3. Violation of digestion in oral cavities and violations of swallowing. Types. Reasons. Consequences.
4. Gullet dysfunction. Types. Reasons. Consequences.
5. Violations of digestion in a stomach. Disorders of secret, motor, absorptive, barrier and protective function of a stomach.
6. Violation of digestion in intestines. Disorders of the digesting, motor, barrier and protective function of intestines.
7. Stomach ulcer of a stomach and duodenum. Etiology. Pathogenesis. Manifestations. Complications.

8. Malabsorption syndrome. Main reasons and manifestations. Coeliacs disease. Nonspecific ulcer colitis. Reasons. Manifestations.

9. Violation of excretory function of a liver. Frustration of a bile production and bile excretion. Reasons. Manifestations.

10. Jaundice. Definition of concept. Types of jaundice. Haemolytic jaundice. Reasons. Pathogenesis. Manifestations.

11. Parenchymatous (hepatic) jaundice. Reasons. Pathogenesis. Manifestations.

12. Mechanical (subhepatic) jaundice. Reasons. Holemic syndrome. Pathogenesis. Manifestations.

13. Violation of haemodynamic function of a liver. Syndrome of portal hypertensia. Etiology. Pathogenesis. Manifestations.

14. Hepatic coma. Etiology. Pathogenesis.

List of practical skills that must be mastered:"Pathophysiology of the digestive system. Insufficiency of digestion. Pathophysiology of the liver. Liver failure"

1. Explain the types of gastric secretion, hypo- and hypersecretion, hypo- and hyperacidity.

2. Determine the mechanism of disruption of the motor function of the stomach, understanding their role in the pathogenesis of diseases of the digestive tract

3. Define the concept of jaundice as a pathological syndrome, classify jaundice according to their etiology and pathogenesis.

4. Justify the use of laboratory parameters, the study of which is necessary for the differential diagnosis of jaundice.

5. Explain the mechanism of occurrence and development of manifestations of cholemic syndrome. List the main symptoms of cholemic syndrome. List the main symptoms of cholemic syndrome.

6. Determine direct and indirect bilirubin in blood serum.

Situational tasks KROK-1 to determine the final level of knowledge

1. A 42-year-old patient complains of pain in the epigastral area, vomiting; vomit masses have the colour of “coffee-grounds”, the patient has also melena. Anamnesis records gastric ulcer. Blood formula: erythrocytes – $2{,}8\times10^{12}$/l, leukocytes – 8×10^{9}/l, Hb – 90 g/l. What complication is it?

A. Pyloric stenosis. *C. Penetration.* *E. Perforation.*
B. Haemorrhage. *D. Canceration.*

2. During an acute experiment some of diluted solution of hydrochloric acid was injected into the duodenal cavity of an experimental animal. This will result in hypersecretion of the following hormone:

A. Motilin. *C. Neurotensin.* *E. Gastrin.*
B. Histamine. *D. Secretin.*

3. A 57-year-old patient was admitted to the gastroenterological department with suspicion on Zollinger-Ellison syndrome because of rapid increase of gastrin level in the blood serum. What disorder of the secretory function of the stomach is the most likely?

A. Hyperacid hyposecretion.
B. Achylia.
C. Hypoacid hyposecretion.
D. Hypoacid hypersecretion.
E. Hyperacid hypersecretion.

4. Roentgenologically confirmed obstruction of common bile duct resulted in preventing bile from inflowing to the duodenum. What process is likely to be disturbed?

A. Fat emulgation.
B. Hydrochloric acid secretion in stomach.
C. Carbohydrate hydrolysis.
D. Protein absorption.
E. Salivation inhibition.

5. Hepatitis has led to the development of hepatic failure. Mechanism of edemata formation is activated by the impairment of the following liver function:

A. Barrier.
B. Chologenetic.
C. Antitoxic.
D. Glycogen-synthetic.
E. Protein-synthetic.

6. A tooth extraction in a patient with chronic persistent hepatitis was complicated with prolonged hemorrhage. What is the reason for the haemorrhagic syndrome?

A. Decrease in thrombin production.
B. Increase in fibrinogen synthesis.
C. Increase in thromboplastin production.
D. Fibrinolysis intensification.
E Decrease in fibrin production.

7. As a result of dysfunction of protein synthesis in liver a patient with hepatic insufficiency has disturbed synthesis of procoagulants, prothrombin, fibrinogen. Which of the listed syndromes can be expected in this patient?

A. Acholia syndrome.
B. Portal haemorrhagic syndrome.
C. Hepatolienal syndrome.
D. Haemorrhagic.
E. Cholaemia syndrome.

8. A patient who has been treated for viral hepatitis B developed symptoms of hepatic insufficiency. What changes indicating disorder in protein metabolism are likely to be observed in this case?

A. Absolute hyperalbuminemia.
B. Absolute hypoalbuminemia.
C. Absolute hyperfibrinogenemia.
D. Absolute hyperglobulinemia.
E. Protein rate in blood will stay unchanged.

9. A patient being treated for viral hepatitis type B got symptoms of hepatic insufficiency. What blood changes indicative of protein metabolism disorder will be observed in this case?

A. Absolute hyperalbuminemia.

B. Absolute hyperfibrinogenemia.

C. Absolute hypoalbuminemia.

D. Proteinic blood composition is unchanged.

E. Absolute hyperglobulinemia.

10. A patient presents with icteritiousness of skin, scleras and mucous membranes. Blood plasma the total bilirubin is increased, stercobilin is increased in feces, urobilin is increased in urine. What type of jaundice is it?

A. Haemolytic. *C. Parenchymatous.* *E. Cholestatic.*

B. Gilbert's disease. *D. Obturational.*

11. A patient with jaundice has high total bilirubin that is mainly indirect (unconjugated), high concentration of stercobilin in the stool and urine. The level of direct (conjugated) bilirubin in the blood plasma is normal. What kind of jaundice can you think of?

A. Parenchymal (hepatic). *D. Hemolytic.*

B. Mechanical. *E. Neonatal jaundice.*

C. Gilbert's disease.

12. Examination of a chemical plant worker who had had a poisoning revealed an increase in total bilirubin concentration at the expense of indirect fraction. Feces and urine are characterized by high stercobilin concentration. The level of direct bilirubin in blood plasma is normal. What type of jaundice is the case?

A. Mechanical. *C. Obstructive.* *E. Hemolytic.*

B. Parenchymatous. *D. Hepatic.*

13. A 53-year-old male patient complains of acute pain in the right hypochondrium. Objective examination revealed scleral icterus. Laboratory tests revealed increased ALT activity, and stercobilin was not detected in the stool. What disease is characterized by these symptoms?

A. Hemolytic jaundice. *C. Chronic colitis.* *E. Chronic gastritis.*

B. Hepatitis. *D. Cholelithiasis.*

14. An infectious disease unit admitted a patient with signs of jaundice caused by hepatitis virus. Select an indicator that is specific only for parenchymatous jaundice:

A. Increase in ALT and AST rate. *D. Cholaemia.*

B. Hyperbilirubinemia. *E. Urobilinuria.*

C. Bilirubinuria.

15. A 48 y.o. patient was admitted to the hospital with complaints about weakness, irritability, sleep disturbance. Objectively: skin and scleras are yellow. In blood: conjugated bilirubin, cholalemia. Feces are acholic. Urine is of dark colour (bilirubin). What jaundice is it?

A. Hemolytic. *D. Gilbert's syndrome.*
B. Parenchymatous. *E. Crigler-Najjar syndrome.*
C. Mechanic.

16. Blood analysis of a patient with jaundice reveals conjugated bilirubinemia, increased concentration of bile acids. There is no stercobilinogen in urine. What type of jaundice is it?

A. Hepatocellular jaundice. *D. Hemolytic jaundice.*
B. Obstructive jaundice. *E. Cythemolytic jaundice.*
C. Parenchymatous jaundice.

17. A patient ill with jaundice has increased content of conjugated bilirubin and bile acids in blood, no stercobilinogen in urine. What jaundice are these symptoms typical for?

A. Hepatic. *C. Hemolytic.* *E. Cythemolytic.*
B. Hepatocellular. *D. Obstructive.*

18. A patient with a pronounced icteritiousness of skin, sclera and mucous membranes has urine of dark beer colour and colourless feces. Direct bilirubin in blood is elevated, urine contains bilirubin. What type of jaundice is it?

A. Hemolytic. *C. Excretory.* *E. Obstructive.*
B. Parenchymatous. *D. Conjugation.*

19. A coprological survey revealed light-colored feces containing drops of neutral fat. The most likely reason for this condition is the disorder of:

A. Bile inflow into the bowel. *D. Intestinal absorption.*
B. Pancreatic juice secretion. *E. Gastric juice acidity.*
C. Intestinal juice secretion.

20. A 35-year-old man with peptic ulcer disease has undergone antrectomy. After the surgery secretion of the following gastrointestinal hormone will be disrupted the most:

A. Gastrin. *C. Secretin.* *E. Histamine.*
B. Cholecystokinin. *D. Neurotensin.*

21. A 43-year-old patient suffers from acute pancreatitis with disrupted common bile duct patency. What condition can develop in this case ?

A. Hepatocellular jaundice. *D. Hemolytic jaundice.*
B. Portal hypertension. *E. Hepatic coma.*
C. Mechanical jaundice.

22. A 50-year-old man, who has been suffering from chronic hepatic failure for several years, has developed ascites. What is the main mechanism of this disorder development ?

A. Decrease of albumin and globulin synthesis in liver.
B. Neurotoxins appearing in blood.
C. Increased pressure in portal vein system.
D. Increased content of low-density and very low-density lipoproteins in blood.
E. Increase of blood oncotic pressure.

23. A patient visited a dentist to extract a tooth. After the tooth had been extracted, bleeding from the tooth socket continued for 15 minutes. Anamnesis states that the patient suffers from active chronic hepatitis. What phenomenon can extend the time of hemorrhage ?

A. *Thrombocytopenia.*

B. Decrease of fibrinogen content in blood.

C. Decrease of albumine content in blood.

D. Increased activity of anticoagulation system.

E. Hypocalcemia.

Standards of correct answers to the task КROК-1

1	2	3	4	5	6	7	8	9	10	11	12	13
B	*D*	*E*	*A*	*E*	*A*	*D*	*B*	*A*	*A*	*D*	*E*	*D*

14	15	16	17	18	19	20	21	22	23
A	*C*	*B*	*D*	*E*	*A*	*A*	*C*	*C*	*B*

Recommendations for registration of work results

1. Written answer to test tasks (initial level of knowledge).

2. The results of the experiment are drawn up in the form of an experiment protocol with the determination of relevant conclusions.

3. The protocol of the experiment analysis of various forms of impaired vascular tone, in particular, hypertensive disease

4. Protocol for solving situational tasks with an explanation of the correct answers.

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Topic 13. Pathophysiology of the kidneys. Renal failure

Justification of the topic: The kidneys are the main effector organ of the water-electrolyte and acid-base homeostasis systems of the body. The functions of the kidneys include: maintaining the stability of the volume of circulating blood, ensuring the stability of the osmotic pressure of the blood, maintaining a constant concentration of ions in the blood, in particular hydrogen ions (acidic and secretory function). In addition, the kidneys are involved in the removal of end products of metabolism from the body (excretory function), in the exchange of vitamin D, carbohydrates and low molecular weight proteins. Renin, prostaglandins, kinin, erythropoietin and inhibitors of erythropoiesis are formed in the kidneys, which determines the influence of the kidneys on the regulation of blood pressure and erythropoiesis. These functions are provided by a limited number of kidney processes: filtration, reabsorption, secretion and incretion. Violation of any of them inevitably leads to violation of others. Since the kidneys are very sensitive to blood circulation disorders and the action of toxic substances, kidney diseases of different etiologies cause similar pathological processes and the same clinical manifestations (syndromes) in them, which often lead to a violation of the body's activity. Therefore, there is a need to study the basic patterns of renal process disorders and related mechanisms of renal failure.

Purpose of the lesson:

General - to be able to characterize the main causes and mechanisms of urinary disorders and the urinary function of the kidneys, the pathogenesis of changes in diuresis and urine composition.

Specifically:

Know:

1. To characterize the main causes and pathogenetic mechanisms of impaired filtration, reabsorption and secretion, their manifestations.
2. Explain the mechanism of changes in the qualitative composition of urine.
3. Using biochemical methods of research, explain the pathological components of urine: protein, glucose, acetone, bilirubin to interpret their diagnostic value.

Be able:

1. Explain the mechanism of urine formation
2. To evaluate the main indicators characterizing urine production and the urinary function of the kidneys.
3. Determine the procedure for carrying out qualitative reactions on the content of protein, sugar, bile pigments, acetone in urine, as well as be able to determine the specific gravity of urine
4. Quantitative and qualitative changes in urine can be characterized in case of kidney damage.

Practical experience:

1. Explain the main functions of the kidneys. Causes of kidney disease.
2. Describe the violations of glomerular filtration, reabsorption, secretion.
3. Determine changes in the relative density and composition of urine.
4. Explain the causes and pathologies of the kidneys in which they are observed.
5. Analyze extrarenal manifestations of renal dysfunction. Types of kidney pathology by origin.
6. Give a classification and manifestations of acute glomerulonephritis.
7. Explain the causes of chronic glomerulonephritis.
8. Determine risk factors for pyelonephritis. Pathogenesis and manifestations.
9. Definition of the concept of "nephrotic syndrome".
10. Definition of the concept. kidney failure. Acute renal failure. Causes. Pathogenesis. manifestations
11. Criteria for the diagnosis of chronic renal failure.
12. Determination of the mechanism of uremia formation. The main factors of tissue and organ damage in uremia and renal coma.
13. Find out the basic principles of the treatment of renal dysfunction. lusion about violation of the quantitative composition of "red" blood.

The graphological structure of the topic " Pathophysiology of the kidneys. Renal failure" is attached.

Material and methodological support of the topic "Pathophysiology of the kidneys. Renal failure"

1. Lectures;
2. Methodical instructions for teachers;
3. Methodical instructions for students;
4. Set of test tasks to determine the basic level of knowledge;
5. Set of situational tasks to determine the final level of knowledge;
6. Set of KROK-1 tasks;
7. Set of schemes and tables (presentation);
8. Set of forms with a clinical blood test;
9. Video films;
10. For the experiment. Microscopes, immersion oil, glass slides, cover slip, Pasteur pipette, test strips (determination of sugar concentration in urine), hydrometer and hydrometer (determination of urine density), urometer (determination of specific gravity of urine), distillates for staining smears, injector, pins.

Oriented map of students' work on the topic "Pathophysiology of kidneys. Renal failure"

No	Stage of lesson	Academic time, min	Educational guide		Place holding a class
			Educational tools	Equipment	
1	Definition of initial knowledge	10	Control of theoretical training of students programmable by using structural answers to the issue of tickets	Test control issue tickets	Study room

No	Stage of lesson	Academic time, min	Educational guide		Place holding a class
			Educational tools	Equipment	
2	Analysis of theoretical material	45	Analysis of theoretical material on the basis of control conduct by question topic	Control question topic	Study room
3	The experiment	20	Introduction and preparation for setting up experiments. Setting experiment	Samples of patients, measuring cylinders, urometr, vidalevski tubes, Pasteur pipettes, concentrated nitric acid, supports a set of chemical test tubes and pipettes, reagent Benedict microscope, subject and cover glass	Study room
4	The final stage of determining the level of knowledge and skills. Summing up	15	Determining the source of formation of knowledge and skills	The decision of situational problems	Study room

PATHOPHYSIOLOGY OF KIDNEYS. RENAL FAILURE

Control of Renal Function

The kidneys are remarkable organs. Each is smaller than a person's fist, but in a single day, the two organs process approximately 1700 L of blood and combine its waste products into approximately 1.5 L of urine. As part of their function, the kidneys filter physiologically essential substances, such as sodium and potassium ions, from the blood and selectively reabsorb those substances that are needed to maintain the normal composition of internal body fluids. Substances that are not needed for this purpose or are in excess pass into the urine. In regulating the volume and composition of body fluids, the kidneys perform excretory and endocrine functions. The renin-angiotensin mechanism participates in the regulation of blood pressure and the maintenance of circulating blood volume, and erythropoietin stimulates red blood cell production. The discussion in this chapter focuses on the structure and function of the kidneys, tests of renal function, and the physiologic action of diuretics.

Elimination functions of the kidney

Renal Clearance

Renal clearance is the volume of plasma that is completely cleared each minute of any substance that finds its way into the urine. It is determined by the ability of the substance to be filtered in the glomeruli and the capacity of the renal tubules to reabsorb or secrete the substance. Every substance has its own clearance rate, the units of which are always in volume of plasma cleared per unit of time. It can be determined by measuring the amount of a substance that is excreted in the urine and dividing by its plasma concentration. Inulin, a large polysaccharide, is freely filtered in the glomeruli and neither reabsorbed nor secreted by the tubular cells. After intravenous injection, the amount that appears in the urine is equal to the amount that is filtered in the glomeruli

(i.e., the clearance rate is equal to the GFR). Because of these properties, inulin can be used as a laboratory measure of the GFR. Some substances, such as urea, are freely filtered in the glomeruli, but the volume that is cleared from the plasma is less than the GFR, indicating that at least some of the substance is being reabsorbed. At normal plasma levels, glucose has a clearance of zero because it is reabsorbed in the tubules and none appears in the urine.

Urinalysis

Urine is a clear, amber-colored fluid that is approximately 95 % water and 5 % dissolved solids. The kidneys normally produce approximately 1.5 L of urine each day. Normal urine contains metabolic wastes and few or no plasma proteins, blood cells, or glucose molecules. Urine tests can be performed on a single urine specimen or on a 24-hour urine specimen. First-voided morning specimens are useful for qualitative protein and specific gravity testing. A freshly voided specimen is most reliable. Urine specimens that have been left standing may contain lysed red blood cells, disintegrating casts, and rapidly multiplying bacteria. Table describes urinalysis values for normal urine. Casts are molds of the distal nephron lumen. A gellike substance called Tamm-Horsfall mucoprotein, which is formed in the tubular epithelium, is the major protein constituent of urinary casts. Casts composed of this gel but devoid of cells are called hyaline casts. These casts develop when the protein concentration of the urine is high (as in nephrotic syndrome), urine osmolality is high, and urine pH is low. The inclusion of granules or cells in the matrix of the protein gel leads to the formation of various other types of casts. Because of the glomerular capillary filtration barrier, less than 150 mg of protein is excreted in the urine over 24 hours in a healthy person. Qualitative and quantitative tests to determine urinary protein content are important tools to assess the extent of glomerular disease. pH-sensitive reagent strips are used to test for the presence of proteins, whereas immunoassay methods are used to test for microalbuminuria. The specific gravity (or osmolality) of urine varies with its concentration of solutes. Urine specific gravity provides a valuable index of the hydration status and functional ability of the kidneys. Although there are more sophisticated methods for measuring specific gravity, it can be measured easily using an inexpensive piece of equipment called a urinometer. Healthy kidneys can produce a concentrated urine with a specific gravity of 1.030 to 1.040.

Acute renal failure

Acute renal failure represents a rapid decline in renal function sufficient to increase blood levels of nitrogenous wastes and impair fluid and electrolyte balance. Unlike chronic renal failure, acute renal failure is potentially reversible if the precipitating factors can be corrected or removed before permanent kidney damage has occurred. Acute renal failure is a common threat to seriously ill persons in intensive care units, with a mortality rate ranging from 40 % to 75 %. Although treatment methods such as dialysis and renal replacement methods are effective in correcting life-threatening fluid and electrolyte disorders, the mortality rate from acute renal failure has not

changed substantially since the 1960s. This probably is because acute renal failure is seen more often in older persons than before, and because it frequently is superimposed on other life-threatening conditions, such as trauma, shock, and sepsis. The most common indicator of acute renal failure is *azotemia*, an accumulation of nitrogenous wastes (urea nitrogen, uric acid, and creatinine) in the blood. In acute renal failure, the glomerular filtration rate (GFR) is decreased. As a result, excretion of nitrogenous wastes is reduced, and fluid and electrolyte balance cannot be maintained.

Types of acute renal failure

Acute renal failure can be caused by several types of conditions, including a decrease in blood flow without ischemic injury; ischemic, toxic, or obstructive tubular injury; and obstruction of urinary tract outflow.

The causes of acute renal failure commonly are categorized as **prerenal, intrinsic, and postrenal.**

Prerenal Failure

Prerenal failure, the most common form of acute renal failure, is characterized by a marked decrease in renal blood flow. It is reversible if the cause of the decreased renal blood flow can be identified and corrected before kidney damage occurs.

Causes of prerenal failure include profound depletion of vascular volume (*e.g.,* hemorrhage, loss of extracellular fluid volume), impaired perfusion due to heart failure and cardiogenic shock, and decreased vascular filling because of increased vascular capacity (*e.g.,* anaphylaxis or sepsis). Elderly persons are particularly at risk because of their predisposition to hypovolemia and their high prevalence of renal vascular disorders. Some vasoactive mediators, drugs, and diagnostic agents stimulate intense intrarenal vasoconstriction and induce glomerular hypoperfusion and prerenal failure.

Postrenal failure

Postrenal failure results from obstruction of urine outflow from the kidneys. The obstruction can occur in the ureter (*i.e.,* calculi and strictures), bladder (*i.e.,* tumors or neurogenic bladder), or urethra (*i.e.,* prostatic hypertrophy). Prostatic hyperplasia is the most common underlying problem. Because both ureters must be occluded to produce renal failure, obstruction of the bladder rarely causes acute renal failure unless one of the kidneys already is damaged or a person has only one kidney. The treatment of acute postrenal failure consists of treating the underlying cause of obstruction so that urine flow can be reestablished before permanent nephron damage occurs.

Intrinsic renal failure

Intrinsic or intrarenal renal failure results from conditions that cause damage to structures within the kidney—glomerular, tubular, or interstitial. The major causes of intrarenal failure are ischemia associated with prerenal failure, toxic insult to the tubular structures of the nephron, and intratubular obstruction. Acute glomerulonephritis and acute pyelonephritis also are intrarenal causes of acute renal failure. Injury to the tubules (acute tubular necrosis) is most common and often is ischemic or toxic in origin.

Acute Tubular Necrosis.

Acute tubular necrosis (ATN) is characterized by destruction of tubular epithelial cells with acute suppression of renal function. ATN can be caused by a variety of conditions, including acute tubular damage due to ischemia, the nephrotoxic effects of drugs, tubular obstruction, and toxins from a massive infection. Tubular epithelial cells are particularly sensitive to ischemia and also are vulnerable to toxins. The tubular injury that occurs in ATN frequently is reversible. The process depends on the recovery of the injured cells, removal of the necrotic cells and intratubular casts, and regeneration of renal cells to restore the normal continuity of the tubular epithelium. If, however, the ischemia is severe enough to cause cortical necrosis, irreversible renal failure occurs. Ischemic ATN occurs most frequently in persons who have major surgery, severe hypovolemia, overwhelming sepsis, trauma, and burns. Sepsis produces ischemia by provoking a combination of systemic vasodilation and intrarenal hypoperfusion. In addition, sepsis results in the generation of toxins that sensitize renal tubular cells to the damaging effects of ischemia. ATN complicating trauma and burns frequently is multifactorial in origin and due to the combined effects of hypovolemia and myoglobinuria or other toxins released from damaged tissue.

Diagnosis and treatment

Given the high morbidity and mortality rates associated with acute renal failure, attention should be focused on prevention and early diagnosis. This includes assessment measures to identify persons at risk for development of acute renal failure, including those with preexisting renal insufficiency and diabetes. These persons are particularly at risk for development of acute renal failure due to nephrotoxic drugs such as aminoglycosides and contrast agents, or to drugs such as the NSAIDs that alter intrarenal hemodynamics. Elderly persons are susceptible to all forms of acute renal failure because of the effects of aging on renal reserve. Careful observation of urine output is essential for persons at risk for development of acute renal failure. Urine tests that measure urine osmolality, urinary sodium concentration, and fractional excretion of sodium help differentiate prerenal azotemia, in which the reabsorptive capacity of the tubular cells is maintained, from tubular necrosis, in which these functions are lost. One of the earliest manifestations of tubular damage is the inability to concentrate the urine. Further diagnostic information that can be obtained from the urinalysis includes evidence of proteinuria, hemoglobinuria, and casts or crystals in the urine. Blood tests for BUN and creatinine provide information regarding the ability to remove nitrogenous wastes from the blood. It also is important to exclude urinary obstruction. A major concern in the treatment of acute renal failure is identifying and correcting the cause. Fluids are carefully regulated in an effort to maintain normal fluid volume and electrolyte concentrations. Adequate caloric intake is needed to prevent the breakdown of body proteins, which increases nitrogenous wastes.

Chronic renal failure

Unlike acute renal failure, chronic renal failure represents progressive and irreversible destruction of kidney structures. As recently as 1965, many patients with chronic renal failure progressed to the final stages of the disease and then died. The high mortality rate was associated with limitations in the treatment of renal disease and with the tremendous cost of ongoing treatment. Technologic advances in renal replacement therapy have improved the outcomes for persons with renal failure. The number of persons with kidney failure who are treated with dialysis and transplantation is projected to increase from 340,000 in 1999 to 651,000 in 2010. Chronic renal failure can result from a number of conditions that cause permanent loss of nephrons, including diabetes, hypertension, glomerulonephritis, and polycystic kidney disease.

Stages of progression

Regardless of cause, chronic renal failure results in loss of renal cells with progressive deterioration of glomerular filtration, tubular reabsorptive capacity, and endocrine functions of the kidneys. All forms of renal failure are characterized by a reduction in the GFR, reflecting a corresponding reduction in the number of functional nephrons. The rate of nephron destruction differs from case to case, ranging from several months to many years. The progression of chronic renal failure usually occurs in four stages: diminished renal reserve, renal insufficiency, renal failure, and end-stage renal disease. Typically, the signs and symptoms of chronic renal failure occur gradually and do not become evident until the disease is far advanced. This is because of the amazing compensatory ability of the kidneys. As kidney structures are destroyed, the remaining nephrons undergo structural and functional hypertrophy, each increasing its function as a means of compensating for those that have been lost. It is only when the few remaining nephrons are destroyed that the manifestations of renal failure become evident.

Renal Insufficiency

Renal insufficiency represents a reduction in the GFR to 20 % to 50 % of normal. The kidneys initially have tremendous adaptive capabilities. As nephrons are destroyed, the remaining nephrons undergo changes to compensate for those that are lost. In the process, each of the remaining nephrons must filter more solute particles from the blood.

Because the solute particles are osmotically active, they cause additional water to be lost in the urine. One of the earliest symptoms of renal insufficiency is **isosthenuria**, or polyuria with urine that is almost isotonic with plasma. It is during this stage that azotemia, anemia, and hypertension also begin to appear. Conservative treatment during this stage includes measures to retard deterioration of renal function and assist the body in managing the effects of impaired function. Urinary tract infections should be treated promptly, and medication with renal damaging potential should be avoided. Blood pressure control is important, as is control of blood sugar in persons with diabetes. Smoking cessation is recommended, particularly in persons with diabetic nephropathy. Because the kidneys have difficulty eliminating

the waste products of protein metabolism, a restricted-protein diet usually produces fewer uremic symptoms and slows progression of renal failure. The few remaining nephrons that constitute the functional reserve of the kidneys can be easily disrupted, after which renal failure progresses rapidly.

Setting up the experiment. Discussion the results and formulation the conclusions

The conduction of the experiment:

Experiment. 1. Investigation of the physical and chemical properties of urine and microscopy of urine sediment in case of impaired kidney function Determination of the specific gravity of urine: pour urine into a cylinder, then slowly immerse the urometer and note the number on the scale on the lower meniscus. The urometer should not come into contact with the walls of the cylinder.

2. Determination of protein: a reagent consisting of 1 volume of concentrated nitric acid and 4 volumes of a saturated solution of magnesium sulfate is poured into a narrow test tube. Carefully pour urine over the wall of the test tube so that it does not mix with the reagent. In the presence of protein in the urine, a grayish-white ring forms on the border of both liquids (Heller's test).

3. Determination of sugar: use a reagent containing sodium citric acid (17.3 %), sodium carbon dioxide 10 %, copper sulfate 1.73 %. Add 8 drops of urine to 5 ml of this reagent and boil for 1–2 minutes. Observe the color change during cooling. Pea-green color corresponds to 0.08–0.1 % sugar, brown-greenish 0.5%, brown – 0.5–0.6 %, yellow – 1 %, red – more than 2 %. (Benedict's trial).

4. Microscopy of urine sediment: pour urine into centrifuge tubes and centrifuge for 10 minutes. Drain the urine, the sediment remains on the narrow bottom of the test tube. Take a drop of sediment with a Pasteur pipette, transfer it to a glass slide and cover it with a cover glass, while avoiding air getting between the glass and cover glass. The sediment should be examined under a microscope first under low magnification, then under high magnification, with a narrowed aperture and lowered illuminator. Pay attention to organized (cylinders, fat droplets, erythrocytes, leukocytes, epithelial cells, etc.) and unorganized (different forms of uric acid crystals, urates, triple phosphates, calcium sulfate, calcium carbonate, triple phosphate crystals in the form of coffin lids and etc.) elements in urine sediment.

5. Make sketches and explain in which pathological conditions the specified changes can be detected.

6. Using the obtained experimental data and applying knowledge of the theoretical material, formulate and write down the conclusions of the conducted experiment.

Discussion of the results of the experiment.

The conduction of the experiment: Research of physical and chemical properties of urine and urinary sediment microscopy with impaired renal function. The specific gravity of urine, urine is poured into the cylinder, then slowly dip urometr and note the number on the scale at the bottom of the meniscus. Urometr should not collide with the walls of the cylinder.

Definition of protein, poured into a narrow tube reagent consisting of 1 part concentrated nitric acid and 4 volumes of a saturated solution of magnesium sulfate. Carefully pour urine on the wall of the tube so as not mixed with the reagent. In the presence of protein in urine on the border of the two fluids produced grayish-white ring. Determination of sugar, using a reagent containing sodium citrate (17.3 %), sodium carbonate 10 %, 1.73 % copper sernokysluyu. To 5 ml of this reagent add 8 drops of urine and boil for 1–2 minutes. Watch for the color change cooling. Pea green color corresponds 0,08–0,1 % sugar, brown-greenish 0.5 %, brown – 0,5–0.6 %, 1% – yellow, red-bolee – 2 %.

Formulation the conclusions based on the experiment

On the basis of the experiment, it can be explained that with normally functioning kidneys, there are wide fluctuations in the specific gravity of urine and a change in its concentration during the day, which is associated with periodic intake of food, water and fluid loss by the body (sweating, breathing). The kidneys under various conditions can excrete urine with a relative density of 1.001 to 1.040. Microscopy of the urinary sediment allows you to determine under the microscope the elements of the urinary sediment (cylinders, drops of fat, erythrocytes, leukocytes, epitheliocytes, etc.) and unorganized (various forms of uric acid crystals, urates, tripel phosphates, calcium sulfide, calcium carbonate, tripel phosphate crystals in grave covers and etc.).

Tasks for independent work on the topic "Pathophysiology of the kidneys. Renal failure"

The student is invited to examine the results of a clinical analysis of the urine of a patient with impaired renal function. It is necessary to determine the signs and type of violation. Be able to explain the mechanism of occurrence. Analysis of errors with an explanation of the correct answers.

List of questions and works to be studied:

1. Main functions of kidneys. The reasons of pathology of kidneys (by the nature, an origin, level of primary realization of action).
2. Violations of a glomerular filtration, reabsorption, secretion. Reasons.
3. Frustration of a urine production and urination. Manifestations.
4. Changes of relative density and composition of urine. The reasons and pathology of kidneys at which they are observed.
5. Extrarenal manifestations of disorders of function of kidneys.
6. Types of pathology of kidneys by origin. Standard forms of pathology of kidneys.
7. Sharp glomerulonephritis. Etiology. Pathogenesis. Classification. Manifestations.
8. Chronic glomerulonephritis. Etiology. Pathogenesis. Classification. Manifestations.
9. Pyelonephritis. Etiology. Risk factors. Pathogenesis. Manifestations.
10. Nephrotic syndrome. Definition of concept. Reasons. Pathogenesis. Manifestations.

11. Renal failure. Definition of concept. Sharp renal failure. Reasons. Pathogenesis. Manifestations. Criteria of diagnostics.

12. Chronic renal failure. Etiology. Pathogenesis. Manifestations.

13. Chronic Illness of Kidneys (CIK). Definition of concept. Modern criteria of CIK. Classification. Markers of injury of kidneys (laboratory, visual). Assessment of function of kidneys.

14. Uraemia. Definition of concept. Reasons. Major factors of damage of tissues and bodies at uraemia and a kidney coma.

15. Nephrolithiasis, urolithiasis. Definition of concepts. Reasons, conditions and mechanisms of development. Consequences.

16. Principles of treatment of disorders of functions of kidneys.

List of practical skills that must be mastered:

1. Explain what are the main causes and types of kidney pathology.

2. Find out the pathogenetic mechanisms of filtration, reabsorption and secretion disorders, their manifestations.

3. Determine the main mechanisms that underlie the violations of the formation and excretion of urine.

4. Explain what types of kidney pathology exist and how they affect the change in the qualitative composition of urine.

5. Justify the main factors that can cause an increase in glomerular filtration?

6. Identify the main methods by which kidney function can be assessed.

7. Explain what causes hematuria, leukocyturia, cylindruria?

8 Determine the most characteristic symptoms of pyelonephritis.

Situational tasks KROK-1 to determine the final level of knowledge

1. A man has a considerable decrease in diuresis as a result of 1,5 l blood loss. The primary cause of such diuresis disorder is the hypersecretion of the following hormone:

A. Parathormone. *C. Vasopressin.* *E. Natriuretic.*
B. Corticotropin. *D. Cortisol.*

2. Shock and signs of acute renal failure (ARF) developed in the patient due to permanent injury. What is the leading cause of development of ARF in the case?

A. Urine excretion violation. *D. Increased pressure in the renal arteries.*
B. Decreased oncotic BP. *E. Increased pressure in the nephron capsule.*
C. Decreased arterial pressure.

3. A child has an acute renal failure. What biochemical factor found in saliva can confirm this diagnosis?

A. Increase in urea concentration.
B. Increase in concentration of higher fatty acids.
C. Decrease in nucleic acid concentration.
D. Increase in glucose concentration.
E. Decrease in glucose concentration.

4. On the 6th day of treatment a patient with acute renal insufficiency developed polyuria. Diuresis intensification at the beginning of polyuria stage of acute renal insufficiency is caused by:

A. Volume expansion of circulating blood.
B. Renewal of filtration in nephrons.
C. Growth of natriuretic factor.
D. Reduction of aldosterone content in plasma.
E. *Reductio*n of vasopressin content in plasma.

5. Diabetic nephropathy with uremia has developed in a patient with pancreatic diabetes. The velocity of glomerular filtration is 9 ml/min. What mechanism of a decrease in glomerular filtration velocity and chronic renal failure development is most likely in the case of this patient?

A. Decrease in systemic arterial pressure.
B. Obstruction of nephron tubules with hyaline casts.
C. Tissue acidosis.
D. Arteriolar spasm.
E. Reduction of active nephron mass.

6. A patient with a history of chronic glomerulonephritis presents with azotemia, oliguria, hypo- and isosthenuria, proteinuria. What is the leading factor in the pathogenesis of these symptoms development under chronic renal failure?

A. Intensification of glomerular filtration.
B. Tubular hyposecretion.
C. Disturbed permeability of glomerular membranes.
D. Mass decrease of active nephrons.
E. Intensification of sodium reabsorption.

7. Injection of an anaesthetic before the tooth extraction resulted in development of anaphylactic shock accompanied by oliguria. What pathogenetic mechanism caused a decrease in diuresis in this case?

A. Decrease in hydrostatic pressure in the renal corpuscle capillaries
B. Increase in hydrostatic pressure in the Bowman's capsule.
C. Damage of glomerular filter.
D. Increase in vasopressin secretion.
E. Increase in oncotic pressure of blood plasma.

8. A driver who got a trauma in a road accident and is shocked has reduction of daily urinary output down to 300 ml. What is the main pathogenetic factor of such diuresis change?

A. Drop of oncotic blood pressure.
B. Drop of arterial pressure.
C. Increased vascular permeability.
D. Decreased number of functioning glomerules.
E. Secondary hyperaldosteronism.

9. A patient with massive burns developed acute renal insufficiency characterized by a significant and rapid deceleration of glomerular filtration. What is the mechanism of its development?

A. Damage of glomerular filter. *D. Rise of pressure of tubular fluid.*
B. Reduction of renal blood flow. *E. Reduction of functioning nephron number.*
C. Renal artery embolism.

10. Due to the use of poor-quality measles vaccine for preventive vaccination, a 1-year-old child developed an autoimmune renal injury. The urine was found to contain macromolecular proteins. What process of urine formation was disturbed?

. A. Filtration. *D. Reabsorption and secretion.*
B. Secretion and filtration. *E. Secretion.*
C. Reabsorption.

11. Chronic glomerulonephritis was diagnosed in a 34-year-old patient 3 years ago. Edema has developed in the last 6 months. What caused it?

. A. Hyperproduction of vasopressin. *D. Hyperosmolarity of plasma.*
B. Hyperaldosteronism. *E. Disorder of albuminous kidneys function.*
C. Proteinuria.

12. Two weeks after lacunar tonsillitis a 20-year-old man started complaining about general weakness, lower eyelid edemata. After examination the patient was diagnosed with acute glomerulonephritis. What are the most likely pathological changes in the urine formula?

A. Cylindruria. *C. Pyuria.* *E. Proteinuria.*
B. Presence of fresh erythrocytes. *D. Natriuria.*

13. A patient suffering from glomerulonephritis was found to have anasarca, AP of 185/105 mm Hg, anaemia, leukocytosis, hyperazotemia, hypoproteinemia. What factor indicates that glomerulonephritis has been complicated by the nephrotic syndrome?

A. . Hypoproteinemia *C. Arterial hypertension.* *E. Leukocytosis.*
B. Anaemia. *D. Hyperazotemia.*

14. A patient with primary nephrotic syndrome has the following content of whole protein: 40 g/l. What factor caused hypoproteinemia?

A. Transition of protein from vessels to tissues.
B. Proteinuria.
C. Reduced protein synthesis in liver.
D. Increased proteolysis.
E. Disturbance of intestinal protein absorption.

15. A patient with nephrotic syndrome has massive edemata of his face and limbs. What is the leading pathogenetic mechanism of edemata development?

A. Drop of oncotic blood pressure. *D. Lymphostasis.*
B. Increase of vascular permeability. *E. Increase of lymph outflow.*
C. Rise of hydrodynamic blood pressure.

16. A 30 year old woman has face edemata. Examination revealed proteinuria (5,87 g/l), hypoproteinemia, dysproteinemia, hyperlipidemia. What condition is the set of these symptoms typical for?

A. Nephritic syndrome. *D. Acute renal failure.*
B. Chronic pyelonephritis. *E. Chronic renal failure.*
C. Nephrotic syndrome.

17. Violation of safety rules resulted in calomel intoxication. Two days later the daily diuresis was 620 ml. A patient experienced headache, vomiting, convulsions, dyspnea, moist rales in lungs. What pathology is it?

. *A. Chronic renal insufficiency.* *D. Acute renal insufficiency.*
B. Uraemic coma. *E. Pyelonephritis.*
C. Glomerulonephritis.

18. 14 days after quinsy a 15-year-old child presented with morning facial swelling, high blood pressure, "meat slops" urine. Immunohistological study of a renal biopsy sample revealed deposition of immune complexes on the basement membranes of the capillaries and in the glomerular mesangium. What disease developed in the patient?

A. Necrotizing nephrosis. *D. Lipoid nephrosis.*
B. Acute interstitial nephritis. *E. Acute glomerulonephritis.*
C. Acute pyelonephritis.

19. A patient has insufficient blood supply to the kidneys, which has caused the development of pressor effect due to constriction of arterial resistance vessels. This condition results from the vessels being strongly affected by the following substance:

A. Norepinephrine. *C. Renin.* *E. Angiotensinogen.*
B. Angiotensin II. *D. Catecholamines.*

20. Poisoning caused by mercury (II) chloride (corrosive sublimate) occurred in the result of safety rules violation. In 2 days the patient's diurnal diuresis became 620 ml. The patient developed headache, vomiting, convulsions, dyspnea; moist crackles are observed in the lungs. Name this pathology:

A. Acute renal failure. *C. Glomerulonephritis.* *E. Pyelonephritis.*
B. Chronic renal failure. *D. Uremic coma.*

Standards of correct answers to the task KROK-1

1	2	3	4	5	6	7	8	9	10	11	12	13
C	*C*	*A*	*B*	*E*	*D*	*A*	*B*	*B*	*A*	*C*	*E*	*A*

14	15	16	17	18	19	20
B	*A*	*C*	*D*	*E*	*C*	*A*

Recommendations for registration of work results

1. Written answer to test tasks (initial level of knowledge).
2. The results of the experiment are drawn up in the form of an experiment protocol with the determination of relevant conclusions.
3. Protocol for the study of the results of the patient's clinical blood analysis.
4. Protocol for solving situational tasks with an explanation of the correct answers.

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Topic 14. Pathophysiology of the endocrine system

Justification of the topic: The works of G. Selye and numerous works of other scientists, the importance of the endocrine system, especially the hypothalamic-pituitary-adrenal system, protective and adaptive reactions of the body (general adaptation syndrome, or stress) has been shown.

A change in the activity of this system occurs in response to any physiological or pathological stimuli. It shows the dependence of any vegetative functions of the body on the functional state of the adrenal glands and pituitary gland. Hence, the role of hormones in the pathology of the pituitary gland and adrenal glands is extremely important. As regulators, they participate in the pathogenesis of diseases and pathological processes. With hypo- or hyperfunction, numerous pathologies on the part of the glands are possible. All this emphasizes the relevance of the topic.

Purpose of the lesson:

General – to know the main mechanisms of disruption of the functional activity of the endocrine glands, the importance of the hypothalamic-pituitary-adrenal system in the non-specific resistance of the body and its disorders, manifestations of hypo- or hyperfunction of these glands.

Specifically:

Know:

1. To characterize the endocrine system, to determine its place in the system of functional interaction of a whole organism
2. To interpret the principles of regulation of the functional activity of endocrine glands.
3. Describe the pituitary and parahypophyseal regulatory pathway and the principle of feedback.
4. Explain the physiological role of various adrenal hormones in the body.

Be able:

1. Describe the principles of regulation of the functional activity of endocrine glands.
2. Describe pituitary and parahypophyseal regulatory pathways and principles of feedback.
3. Explain the physiological role of various adrenal hormones in the body.

Practical experience:

1. Determine examples of modern hormone classification principles that are most relevant for practical use?
2. Explain the mechanisms of regulation of endocrine disorders.
3. Determine what principles of regulation underlie endocrine functions.
4. Substantiate the main reasons for the violation of hormone biosynthesis.
5. Explain what can cause a violation of hormone secretion.
6. Determine the main mechanism of hormone transport in the body, as well as endocrine dysfunction.

7. Explain the importance of the hypothalamus in the regulation of endocrine functions?

8. Describe what is the essence of the endocrine function of the pineal gland and what can be its violations?

The graphological structure of the topic "Pathophysiology of the endocrine system" is attached.

Material and methodological support of the topic "Pathophysiology of the endocrine system"

1. Lectures;
2. Methodical instructions for teachers;
3. Methodical instructions for students;
4. Set of test tasks to determine the basic level of knowledge;
5. Set of situational tasks to determine the final level of knowledge;
6. Set of KROK-1 tasks;
7. Set of schemes and tables (presentation);
8. Set of forms with a clinical blood test;
9. Video films;
10. Experimental part of the lesson.
11. For the experiment. For an experiment. Experimental animals – rats, microscope, tripod, glass slide, cover glass, test strips, Pasteur pipettes, blood smears stained according to Romanivsky-Giemz, smear distillate, injector, needles.

Oriented map of students' work on the topic "Pathophysiology of the endocrine system."

No	Stage of lesson	Academic time, min	Educational guide		Place holding a class
			Educational tools	Equipment	
1	Definition basic level of knowledge	10	Control of theoretical training of students programmable by using structural answers to the issue of tickets.	Test control issue tickets.	Study room
2	Analysis of theoreti-cal material	35	Analysis of theoretical material on the basis of control conduct by question topic	Situational tasks, tasks KROK-1	Study room
3	Practical part (conduct experiment)	30	Practical part (conduct experi-ment) 30 min. Introduction and preparation for productions experiment Setting experiment Discussion results e	Experimental animals are rats. Microscope, immersion oil, tripod, Blood smears stained according to Romanivskyi-Giemzi.	Study room
4	Determination of the final level of knowledge and skills. Beating results	15	Determining the source of formation of knowledge and skill	The decision of situational problems, tasks KROK-1	Study room

PATHOPHYSIOLOGY OF THE ENDOCRINE SYSTEM

Endocrine disorders

Endocrine disorders can result from dysfunction originating in the peripheral endocrine gland itself (primary disorders) or from understimulation or overstimulation by the pituitary (secondary disorders). The disorders can result in hormone overproduction (hyperfunction) or underproduction (hypofunction). Rarely, endocrine disorders occur because of abnormal tissue responses to hormones. Clinical manifestations of hypofunction disorders are often insidious and nonspecific.

Hyperfunction: Hyperfunction of endocrine glands may result from overstimulation by the pituitary but is most commonly due to hyperplasia or neoplasia of the gland itself. In some cases, cancers from other tissues can produce hormones (ectopic hormone production). Hormone excess also can result from exogenous hormone administration. In some cases, patients take hormones without telling the physician. Tissue hypersensitivity to hormones can occur. Antibodies can stimulate peripheral endocrine glands, as occurs in hyperthyroidism of Graves' disease.

Hypofunction: Hypofunction of an endocrine gland can result from understimulation by the pituitary. Hypofunction originating within the peripheral gland itself can result from congenital or acquired disorders (including autoimmune disorders, tumors, infections, vascular disorders, and toxins). Genetic disorders causing hypofunction can result from deletion of a gene or by production of an abnormal hormone. A decrease in hormone production by the peripheral endocrine gland with a resulting increase in production of pituitary regulating hormone can lead to peripheral endocrine gland hyperplasia. For example, if synthesis of thyroid hormone is defective, thyroid-stimulating hormone (TSH) is produced in excessive amounts, causing goiter.

Pathology of the pituitary gland

The pituitary gland is often called the “master gland” because it secretes many different hormones that affect other endocrine glands. The pituitary gland can be dysfunctional due to congenital conditions, tumors (benign or metastatic), and reaction to some drugs.

If the pituitary gland is overactive, the condition is hyperpituitarism, and depending upon which area of the pituitary is affected any one or more of the hormones can be increased. If growth hormone (HGH or GH) production is increased during childhood, gigantism is the result, and the patient’s bones could grow to be very long, making the person unusually tall. If this hormone is produced in excessive amounts in an adult, acromegaly is the result. In acromegaly, the bones grow thicker, but not longer.

PITUITARY GLAND DISORDERS HYPOPITUITARISM

Hypopituitarism – is a clinical syndrome of deficiency in pituitary hormone production. This may result from disorders involving the pituitary gland, hypothalamus, or surrounding structures.

Hypopituitarism resulting from pituitary adenomas is due to impaired blood flow to the normal tissue, compression of normal tissue, or interference with the delivery of hypothalamic hormones via the hypothalamus-hypophysial portal system.

In primary pituitary destruction, the anterior pituitary is destroyed, causing a deficiency in some or all pituitary hormones, including prolactin. Disease involving the hypothalamus or pituitary stalk may cause pituitary hormone deficiency with an elevated serum prolactin. Pituitary tumors, or adenomas, can be secretory or nonsecretory. Approximately 30% of all macroadenomas larger than 10 mm produce at least 1 hormone.

Hypothalamic disease involves destruction of the hypothalamus. This causes a deficiency or loss of hypothalamic regulatory hormone input to the pituitary, which leads to the loss of anterior pituitary hormone secretion, with an elevated serum prolactin level. Loss of antidiuretic hormone (ADH) may have concomitant diabetes insipidus.

HYPERPITUITARISM

Hyperpituitarism, or primary hypersecretion of pituitary hormones, is rare in children. It typically results from a pituitary microadenoma. The most frequently encountered adenoma in children is the prolactinoma, followed by corticotropinoma and somatotropinoma. Fewer than 20 cases of thyrotropinoma in children have been reported, all with onset after age 11 years. Pediatric gonadotropinoma has not been reported.

Hypersecretion of the secretory pituitary tumor hormone is suggestive of an adenoma. Another indication of a pituitary adenoma is a deficiency in some pituitary hormones with concomitant hyperprolactinemia. Normally, dopamine, produced in the hypothalamus, inhibits prolactin secretion by the anterior pituitary. Compressing the pituitary stalk decreases the inhibitory effect of dopamine and increases prolactin levels.

Another common intracranial tumor is craniopharyngioma, a squamous cell tumor that arises from remnants of the Rathke pouch. One third of these tumors extend into the sella, while approximately two thirds remain suprasellar.

Other causes of hypopituitarism include empty sella syndrome and infiltrative diseases. Empty sella syndrome occurs when the arachnoid herniates into the sella turcica through an incompetent sellar diaphragm and flattens the pituitary against bone, but resulting pituitary insufficiency is uncommon. Infiltrative diseases, such as Wegener granulomatosis and sarcoidosis, can cause destruction of the anterior pituitary. Lymphocytic hypophysitis is an autoimmune destructive disease that may be directed towards the pituitary or its stalk.

Pathophysiology

Hypothalamic dysfunction clearly may promote tumor growth, but overwhelming evidence indicates intrinsic pituicyte genetic disruption leads to pituitary tumorigenesis. Most pituitary adenomas are functional and secrete a hormone that produces a characteristic clinical presentation. Nonfunctioning pituitary adenomas are rare in children, accounting for only

3–6 % of all adenomas in 2 large series, whereas they comprise 30 % of adenomas in adults. In children, disruption of growth regulation and/or sexual maturation is common, either because of hormone hypersecretion or because of manifestations caused by local compression by the tumor.

Prolactinoma

Overall, prolactinoma is the most common pituitary adenoma encountered in childhood. Most pediatric cases occur in adolescence, more commonly in females than males. Boys tend to have larger tumors and higher serum prolactin (PRL) levels than girls. Females with these tumors present with amenorrhea, and males present with gynecomastia and hypogonadism. Prolactinomas arise from acidophilic cells that are derived from the same lineage as the somatotropes and thyrotropes. Hence, PRL-secreting adenomas may also stain for and secrete growth hormone (GH) and, occasionally, TSH.

PITUITARY HYPERCORTICISM (ITSENKO-CUSHING'S DISEASE)

Basophilic adenoma of the anterior lobe or interstitial-pituitary lesion is the basis of Itsenko-Cushing's disease (increased production of ACTH and, secondarily, glucocorticoids). It is characterized by obesity (face, neck and trunk, but not limbs), increased blood pressure, hyperglycemia and glycosuria. Increased excretion of 17-ketosteroids with urine.

PATHOLOGY OF THE NEUROPHYPOPHYSIS

Pathology of the neurohypophysis leads to violations of the water balance as a result of ADH-endocrinopathies (insufficiency or excess of ADH effects). These include central forms of diabetes insipidus (lack of ADH effects) and syndrome of inadequate ADH secretion (excessive ADH effects).

Diabetes insipidus Diabetes insipidus (non-sugar urinary incontinence) develops as a result of insufficient effects of ADH.

- Central (neurogenic);
- Hypothalamic-pituitary: violation of ADH synthesis, violation of ADH transport to the neurohypophysis, disorders of accumulation and release of ADH into the blood;
- Post-glandular: hyposensitization of ADH receptors in the kidney, increase in inactivation of ADH in tissues.

THYROID GLAND HYPERTHYROIS

Hyperthyroid conditions (hyperthyroidism) are characterized by excess effects of iodine-containing hormones in the body. Often these conditions are also called thyrotoxicosis. The term "thyrotoxicosis" is usually used to denote similar, but still different conditions: severe hyperthyroidism and hyperthyroidism caused by an excess of exogenous thyroid hormones. Causes of hyperthyroidism Factors cause damage at various levels of neuro-endocrine regulation (hypothalamic-pituitary-thyroid system), synthesis, transport and implementation of thyroid hormones. In this connection, the causes of primary, secondary and tertiary hyperthyroidism are highlighted.

Hyperthyroidism is a set of disorders that involve excess synthesis and secretion of thyroid hormones by the thyroid gland. The resulting elevation in levels of FT_4, free triiodothyronine (FT_3), or both leads to the hypermetabolic condition of thyrotoxicosis.

Thus, although many clinicians (endocrinologists excluded) use the terms hyperthyroidism and thyrotoxicosis interchangeably, the 2 words have distinct meanings. For example, both exogenous thyroid hormone intake and subacute thyroiditis can cause thyrotoxicosis, but neither constitutes hyperthyroidism, because the conditions are not associated with new hormone production.

Other causes of thyrotoxicosis

Several rare causes of thyrotoxicosis exist that deserve mention. Struma ovarii is ectopic thyroid tissue associated with dermoid tumors or ovarian teratomas that can secrete excessive amounts of thyroid hormone and produce thyrotoxicosis.

Iodide-induced thyrotoxicosis (Jod-Basedow syndrome) occurs in patients with excessive iodine intake The antiarrhythmic drug amiodarone, which is rich in iodine and bears some structural similarity to T_4, may cause thyrotoxicosis. Iodide-induced thyrotoxicosis also occurs in patients with areas of thyroid autonomy, such as a multinodular goiter or autonomous nodule.

Ophthalmopathy

The underlying pathophysiology of Graves ophthalmopathy (also called thyroid-associated orbitopathy) is not completely characterized. It most likely involves an antibody reaction against the TSH receptor that results in activation of T cells against tissues in the retro-orbital space that share antigenic epitopes with thyroid follicular cells.

Etiology

Genetic factors appear to influence the incidence of thyrotoxicosis. Autoimmune thyroid disease, including Hashimoto hypothyroidism and Graves disease, often occurs in multiple members of a family.

HYPOTHYROISIS

Hypothyroidism is a condition caused by insufficient secretion of thyroid hormones by the thyroid gland.

Hypothyroidism is a common endocrine disorder resulting from deficiency of thyroid hormone. It usually is a primary process in which the thyroid gland is unable to produce sufficient amounts of thyroid hormone.

Hypothyroidism can also be secondary—that is, the thyroid gland itself is normal, but it receives insufficient stimulation because of low secretion of thyrotropin (ie, thyroid-stimulating hormone from the pituitary gland. In tertiary hypothyroidism, inadequate secretion of thyrotropin-releasing hormone (TRH) from the hypothalamus leads to insufficient release of TSH, which in turn causes inadequate thyroid stimulation.

Primary hypothyroidism

Types of primary hypothyroidism include the following:

- Chronic lymphocytic (autoimmune) thyroiditis.
- Postpartum thyroiditis.
- Subacute (granulomatous) thyroiditis.
- Drug-induced hypothyroidism.
- Iatrogenic hypothyroidism.

For hypothyroidism, thyroid hormone is administered to supplement or replace endogenous production. In general, hypothyroidism can be adequately treated with a constant daily dose of levothyroxine (LT4). Congenital hypothyroidism, which affects 1 of every 4000 newborns, is due to congenital mal development of the thyroid.

Etiology

These disorders include the following: Familial gestational hyperthyroidism. One type of nonimmune hyperthyroidism. Congenital nongoiterous thyrotoxicosis. Toxic thyroid adenoma with somatic mutation.

Myxedema

Myxedema is a severe form of hypothyroidism that usually develops in adults and adolescents. A characteristic sign of myxedema is mucous swelling of the skin and subcutaneous tissue, in which there is no pit when pressed. The initial links of pathogenesis are insufficient effects of thyroid hormones, more often as a result of primary hypothyroidism (about 95 % of cases). Manifestations of hypothyroidism and their mechanisms The following signs are characteristic of all types of hypothyroidism. However, their combination and severity may be different in specific patients.

Graves disease

The most common cause of thyrotoxicosis is Graves disease (50–60 % of cases). Graves disease is an organ-specific autoimmune disorder characterized by a variety of circulating antibodies, including common autoimmune antibodies, as well as anti-TPO and anti-TG antibodies.

Thyroid hormone levels can be highly elevated in Graves disease. Clinical findings specific to Graves disease include thyroid ophthalmopathy (periorbital edema, chemosis [conjunctival edema], injection, or proptosis) and, rarely, dermopathy over the lower extremities. This autoimmune condition may be associated with other autoimmune diseases, such as pernicious anemia, myasthenia gravis, vitiligo, adrenal insufficiency, celiac disease, and type 1 diabetes mellitus.

PARATHYROID GLAND

Primary Hyperparathyroidism

Primary hyperparathyroidism is the unregulated overproduction of parathyroid hormone (PTH) resulting in abnormal calcium homeostasis.

Pathophysiology In primary hyperparathyroidism due to adenomas, the normal feedback on parathyroid hormone production by extracellular calcium seems to be lost, resulting in a change in the set point. However, this is not

the case in primary hyperparathyroidism from parathyroid hyperplasia. An increase in the cell numbers is probably the cause.

The chronic excessive resorption of calcium from bone caused by excessive parathyroid hormone can result in osteopenia. In severe cases, this may result in osteitis fibrosa cystica, which is characterized by subperiosteal resorption of the distal phalanges, tapering of the distal clavicles, salt-and-pepper appearance of the skull, and brown tumors of the long bones. This is not commonly seen now. In addition, the chronically increased excretion of calcium in the urine can predispose to the formation of renal stones.

Secondary Hyperparathyroidism

Definition of problem

Secondary hyperparathyroidism is the overproduction of parathyroid hormone secondary to a chronic abnormal stimulus for its production. Typically, this is due to chronic renal failure. Another common cause is vitamin D deficiency. A study by Bleskestad et al found that more than 50 % of patients who undergo kidney transplantation have elevated levels of intact PTH more than 1 year after transplantation.

Pathophysiology Chronic overproduction of parathyroid hormone in patients with renal failure contributes to the spectrum of bone disease observed in patients on dialysis (eg, osteitis fibrosa cystica and mixed uremic osteodystrophy). Nonskeletal consequences include cardiovascular calcification, soft tissue calcification, endocrine disturbances, compromised immune system, neurobehavioral changes, and altered erythropoiesis.

HYPOPARATHYROIDISM

Hypoparathyroidism is a condition of parathyroid hormone (PTH) deficiency.

Primary hypoparathyroidism is a state of inadequate PTH activity. In the absence of adequate PTH activity, the ionized calcium concentration in the extracellular fluid falls below the reference range. Primary hypoparathyroidism, the subject of this article, is a syndrome resulting from iatrogenic causes or one of many rare diseases.

Secondary hypoparathyroidism is a physiologic state in which PTH levels are low in response to a primary process that causes hypercalcemia.

Causes Most people have 4 parathyroid glands; consequently, primary hypoparathyroidism is uncommon. Hypocalcemia from hypoparathyroidism requires all 4 parathyroid glands to be affected.

ADRENAL GLAND

Addison disease (Primary or Chronic Adrenocortical Insufficiency)

Addison disease is an insidious, usually progressive hypofunctioning of the adrenal cortex. It causes various symptoms, including hypotension and hyperpigmentation, and can lead to adrenal crisis with cardiovascular collapse. Diagnosis is clinical and by finding elevated plasma ACTH with low plasma cortisol. Treatment depends on the cause but generally includes hydrocortisone and sometimes other hormones.

Addison disease develops in about 4/100,000 annually. It occurs in all age groups, about equally in each sex, and tends to become clinically apparent during metabolic stress or trauma. Onset of severe symptoms (adrenal crisis) may be precipitated by acute infection (a common cause, especially with septicemia). Other causes include trauma, surgery, and Na loss from excessive sweating. Even with treatment, Addison disease may cause a slight increase in mortality. It is not clear whether this increase is due to mistreated adrenal crises or long-term complications of inadvertent over-replacement.

Mineralocorticoid deficiency: Because mineralocorticoids stimulate Na reabsorption and K excretion, deficiency results in increased excretion of Na and decreased excretion of K, chiefly in urine but also in sweat, saliva, and the GI tract. A low serum concentration of Na and a high concentration of K result. Urinary salt and water loss cause severe dehydration, plasma hypertonicity, acidosis, decreased circulatory volume, hypotension, and, eventually, circulatory collapse. However, when adrenal insufficiency is caused by inadequate ACTH production (secondary adrenal insufficiency), electrolyte levels are often normal or only mildly deranged.

Glucocorticoid deficiency: Glucocorticoid deficiency contributes to hypotension and causes severe insulin sensitivity and disturbances in carbohydrate, fat, and protein metabolism. In the absence of cortisol, insufficient carbohydrate is formed from protein; hypoglycemia and decreased liver glycogen result. Weakness follows, due in part to deficient neuromuscular function. Resistance to infection, trauma, and other stress is decreased.

Cushing syndrome

Cushing syndrome is caused by prolonged exposure to elevated levels of either endogenous glucocorticoids or exogenous glucocorticoids.

Individuals with Cushing syndrome can develop moon facies, facial plethora, supraclavicular fat pads, buffalo hump, truncal obesity, and purple striae, as shown in the image below.

Individuals often complain of proximal muscle weakness, easy bruising, weight gain, hirsutism, and, in children, growth retardation. Hypertension, osteopenia, diabetes mellitus, and impaired immune function may occur.

In an emergency situation, remembering that the most common cause of Cushing syndrome is the use of exogenous glucocorticoids is important. Exogenous steroids may cause suppression of the hypothalamic-pituitary-adrenal (HPA) axis that can last for as long as a year after exogenous steroid administration has ended.

An individual with HPA-axis suppression cannot increase steroid production appropriately during a medical illness or other stress and would need to receive stress doses of steroids to avoid adrenal crisis. Thus, in an emergency, the potential for relative adrenal insufficiency should be considered in any patient with Cushing syndrome.

Primary aldosteronism (Conn Syndrome)

Primary aldosteronism is aldosteronism caused by autonomous production of aldosterone by the adrenal cortex (due to hyperplasia, adenoma, or carcinoma). Symptoms and signs include episodic weakness, elevated BP, and hypokalemia. Diagnosis includes measurement of plasma aldosterone levels and plasma renin activity. Treatment depends on cause. A tumor is removed if possible; in hyperplasia, spironolactone or related drugs may normalize BP and eliminate other clinical features.

Aldosterone is the most potent mineralocorticoid produced by the adrenals. It causes Na retention and K loss. In the kidneys, aldosterone causes transfer of Na from the lumen of the distal tubule into the tubular cells in exchange for K and hydrogen. The same effect occurs in salivary glands, sweat glands, cells of the intestinal mucosa, and in exchanges between ICFs and ECFs.

Reduction in blood volume and flow in the afferent renal arterioles induces secretion of renin. Renin transforms angiotensinogen from the liver to angiotensin I, which is transformed by ACE to angiotensin II. Angiotensin II causes secretion of aldosterone and, to a much lesser extent, secretion of cortisol and deoxycorticosterone; it also has pressor activity. Na and water retention resulting from increased aldosterone secretion increases the blood volume and reduces renin secretion.

Primary aldosteronism is caused by an adenoma, usually unilateral, of the glomerulosa cells of the adrenal cortex or, more rarely, by adrenal carcinoma or hyperplasia. Adenomas are extremely rare in children, but the syndrome sometimes occurs in childhood adrenal carcinoma or hyperplasia.

Secondary aldosteronism

Secondary aldosteronism is increased adrenal production of aldosterone in response to nonpituitary, extra-adrenal stimuli, including renal artery stenosis and hypovolemia. Symptoms are those of primary aldosteronism. Treatment involves correcting the cause.

Secondary aldosteronism is caused by reduced renal blood flow, which stimulates the renin-angiotensin mechanism with resultant hypersecretion of aldosterone. Secretion may be normal in heart failure, but hepatic blood flow and aldosterone metabolism are reduced, so circulating levels of the hormone are high.

Adrenal virilism (Adrenogenital Syndrome)

Adrenal virilism is a syndrome in which excessive adrenal androgens cause virilization. Diagnosis is clinical and confirmed by elevated androgen levels with and without dexamethasone suppression; determining the cause may involve adrenal imaging. Treatment depends on the cause.

Adrenal virilism is caused by an androgen-secreting adrenal tumor or by adrenal hyperplasia. Malignant adrenal tumors may secrete excess androgens, cortisol, or mineralocorticoids resulting in Cushing syndrome with suppression of ACTH secretion and atrophy of the contralateral adrenal as well as hypertension. Adrenal hyperplasia is usually congenital; delayed virilizing adrenal hyperplasia is a variant of congenital adrenal hyperplasia.

PHEOCHROMOCYTOMA

A pheochromocytoma is a catecholamine-secreting tumor of chromaffin cells typically located in the adrenals. It causes persistent or paroxysmal hypertension. Diagnosis is by measuring catecholamine products in blood or urine. Imaging tests, especially CT or MRI, help localize tumors. Treatment involves removal of the tumor when possible. Drug therapy for control of BP includes α-blockade, usually combined with β-blockade.

The catecholamines secreted include norepinephrine, epinephrine, dopamine, and dopa in varying proportions. About 90 % of pheochromocytomas are in the adrenal medulla, but they may also be located in other tissues derived from neural crest cells.

PATHOPHYSIOLOGY OF THE GENITAL GLANDS

Endocrine diseases associated with a violation of the hormonal activity of the gonads are caused by an increase or decrease (absence) of their hormonal activity. Hypofunction of the gonads is referred to as hypogonadism. Primary and secondary hypogonadism are distinguished. Primary hypogonadism is associated with direct damage to the gonads, secondary – with a violation of their regulation on the part of the hypothalamic-pituitary-adrenal system.

Causes of primary hypogonadism: injuries of the gonads, infectious and inflammatory processes, genetic disorders, embryonic disorders, tumors of the gonads, cryptorchidism, castration (surgical, radiation). Causes of secondary hypogonadism: stress, tumors and infections of the central nervous system, tumors of the hypothalamic-pituitary system, acromegaly, adipose-genital dystrophy, pituitary dwarfism, pituitary cachexia, Itsenko-Cushing disease, congenital and acquired myxedema, tumors of the adrenal cortex, diabetes, non-endocrine diseases

Causes of secondary hypogonadism: stress, tumors and infections of the central nervous system, tumors of the hypothalamic-pituitary system, acromegaly, adipose-genital dystrophy, pituitary dwarfism, pituitary cachexia, Itsenko-Cushing disease, congenital and acquired myxedema, tumors of the adrenal cortex, diabetes, non-endocrine diseases. The pathogenesis of hypogonadism consists in the loss of morphogenetic, anabolic and specific (androgenic and estrogenic) effects of sex hormones.

Hyperfunction of the gonads is referred to as hypergonadism. Causes of hypergonadism: hormonally active tumors of the hypothalamus and pituitary gland, virilizing tumors of the adrenal glands in boys, masculinizing tumors of the adrenal glands in girls, tumors of the gonads themselves. Manifestations of hypergonadism: In childhood, hypergonadism is manifested by premature puberty (appearance of secondary sexual characteristics in girls before 7.5 years, in boys – 9 years). In adults, hypergonadism is expressed in hypersexuality. In women, with increased production of estrogens, uterine bleeding occurs, with increased production of progesterone – amenorrhea, enlargement of the uterus and mammary glands, as in pregnancy.

Thymus Gland Pathology

The thymus is a primary lymphoid organ that manifests dynamic physiological changes as animals age in addition to being exquisitely sensitive to stress and toxic insult. It is typically the first lymphoid tissue to respond to immunotoxic xenobiotics, with the first change being loss of cortical lymphocytes by apoptosis. This is followed by removal of the apoptotic cellular debris and, in the absence of recovery, may lead to loss of the corticomedullary demarcation and organ atrophy. Nonneoplastic proliferative changes include focal lymphoid hyperplasia and proliferation of medullary epithelial cells, often with formation of ribbons, cords, or tubules. Thymomas are relatively rare tumors that exhibit a wide spectrum of morphologic types but do not metastasize. Thymic lymphomas are common in some mouse strains and can become leukemic with hematogenous spread throughout the body.

• Setting up the experiment

• Discussion the results and formulation the conclusions

The conduction of the experiment: Study of the functional state of the adrenal cortex by counting the number of eosinophils in peripheral blood under the influence of a stressor on the rat body.

To study the functional state of the adrenal cortex, it is necessary to determine the reaction of the stress factor on the rat's body. The number of eosinophils in the peripheral blood of a rat is determined with the help of the leukocyte formula, which is carried out by immersion microscopy of smears stained according to Romanivskyi-Giemz. Compare the number of eosinophils in the blood of a rat. Describe in detail and draw the slides.

• Discussion of the results of the experiment

The experimental rat showed a significant decrease in the number of eosinophils.

Make sketches and explain under what pathological conditions these changes can be detected. Using the obtained experimental data and applying the knowledge of theoretical material, formulate and write down the conclusions of the experiment.

•Formulation the conclusions based on the experiment

Based on the conducted experiment, it can be concluded that 1. A significant decrease in the number of eosinophils is found in the experimental rat. 2. In the development of the observed eosinopenia, the leading importance belongs to the breakdown of eosinophils under the influence of an excess of glucocorticoids. Make sketches and explain under which pathological conditions these changes can be detected.

Tasks for independent work on the topic "Pathophysiology of the endocrine system"

The student is invited to investigate laboratory tests, blood sugar level, biochemical blood test (with a complete lipid profile, determine the level of cholesterol, including high-density lipids, low-density lipids, triglyceride levels). When examining the concentration of hormones, it is recommended to conduct a blood test, determine the concentration of glycosylated hemoglobin, and

conduct a glucose tolerance test. It is necessary to determine the signs and type of hormonal disorders, to be able to explain the mechanism of occurrence.

List of questions and works to be studied:

1. Endocrine system. Definition of the concept. Hormones, their main functions. Variants of the effect of hormones on target cells. Causes of endocrine disorders.
2. Pathogenetic mechanisms of endocrine disorders.
3. Disorders of the hypothalamic-pituitary system.
4. Hypo- and hypopituitarism. Reasons. Kinds Pathogenesis. Manifestations.
5. Neurohypophysis pathology. Diabetes insipidus. Pathogenesis. Manifestations.
6. Typical forms of pathology of the adrenal glands.
7. Hyper- and hypofunctional states of the adrenal glands. Reasons. Pathogenesis.
8. Acute insufficiency of the adrenal cortex. Reasons. Manifestations
9. Typical forms of thyroid pathology. Assessment of thyroid status.
10. Hyper- and hypothyroidism. Kinds Reasons. Pathogenesis. Manifestations.
11. Mechanisms of calcium and phosphorus homeostasis regulation.
12. Typical forms of parathyroid gland pathology.
13. Pathophysiology of gonads.

List of practical skills that must be mastered:

1.Determine the main causes of endocrine disorders.
2. Explain the most typical forms of disorders of the hypothalamic-pituitary regulation.
3. Justify the classification of the pathogenesis of hypo- and hyperpituitarism.
4. Determine the pathogenesis and manifestations of the pathology of the neurohypophysis.
5. Explain the causes of the main most typical forms of adrenal pathology.
6. Explain the modern classification of acute adrenal insufficiency.
7. Perform an assessment of the condition in a typical form of thyroid disease.
8. Substantiate examples of evaluation of the mechanisms of development of endocrine disorders.

Situational tasks KROK-1 to determine the final level of knowledge

1. A patient complains of hydruria (7 liters per day) and polydipsia. Examination reveals no disorders of carbohydrate metabolism. These abnormalities might be caused by the dysfunction of the following endocrine gland:

A. Adenohypophysis. *D. Islets of Langerhans (pancreatic islets).*
B. Neurohypophysis. *E. Adrenal medulla.*
C. Adrenal cortex.

2. A woman after labor lost 20 kg of body weight, her hair and teeth fall out, she has muscle atrophy (hypophysial cachexia). Synthesis of what hypophysis hormone is disturbed?

A. Somatotropic. *C. Thyreotropic.* *E. Prolactin.*
B. Corticotrophic. *D. Gonadotropic.*

3. Examination of a patient revealed enlargement of some body parts (jaw, nose, ears, feet, hands), but body proportions were conserved. It might be caused by intensified secretion of the following hormone:

A. Somatostatin. *C. Somatotropin.* *E. Cortisol.*
B. Tetraiodothyronine. *D. Triiodothyronine.*

4. Examination of a 42 year old patient revealed a tumour of adenohypophysis. Objectively: the patient's weight is 117 kg, he has moon-like hyperemic face, red-blue striae of skin distension on his belly. Osteoporosis and muscle dystrophy are present. AP is 210/140 mm Hg. What is the most probable diagnosis?

A. Cushing's disease. *C. Conn's disease.* *E. Essential hypertension.*
B. Cushing's syndrome. *D. Diabetes mellitus.*

5. A 38-year-old female patient complains of general weakness, cardiac pain, increased appetite, no menstruation. Objectively: the height is 166 cm, weight 108 kg, the patient has moon-shaped face, subcutaneous fat is deposited mainly in the upper body, torso and hips. There are also blood-red streaks. Ps – 62/min, AP – 160/105 mm Hg. Which of the following diseases is the described pattern of obesity most typical for?

A. Alimentary obesity. *D. Cushing pituitary basophilism.*
B. Myxedema. *E. Babinski-Frohlich syndrome.*
C. Insulinoma.

6. A 46-year-old patient suffering from the diffuse toxic goiter underwent resection of the thyroid gland. After the surgery the patient presents with appetite loss, dyspepsia, increased neuromuscular excitement. The body weight remained unchanged. Body temperature is normal. Which of the following has caused such a condition in this patient?

A. Increased production of thyroxin.
B. Reduced production of parathormone.
C. Increased production of calcitonin.
D. Increased production of thyroliberin.
E. Reduced production of thyroxin.

7. A 5-month-old boy was hospitalized for tonic convulsions. He has a life-time history of this disease. Examination revealed coarse hair, thinned and fragile nails, pale and dry skin. In blood: calcium – 1,5 millimole/l, phosphor – 1,9 millimole/l. These changes are associated with:

A. Hypoaldosteronism. *C. Hypothyroidism.* *E. Hypoparathyroidism.*
B. Hyperparathyroidism. *D. Hyperaldosteronism.*

8. A child has abnormal formation of tooth enamel and dentin as a result of low concentration of calcium ions in blood. Such abnormalities might be caused by deficiency of the following hormone:

A. Thyroxin. *C. Parathormone.* *E. Thyrocalcitonin.*
B. Triiodothyronine. *D. Somatotropic hormone.*

9. A patient is followed up in an endocrinological dispensary on account of hyperthyreosis. Weight loss, tachycardia, finger tremor are accompanied by hypoxia symptoms – headache, fatigue, eye flicker. What mechanism of thyroid hormones action underlies the development of hypoxia?

A. Inhibition of respiratory ferment synthesis.
B. Disjunction, oxydation and phosphorylation.
C. Competitive inhibition of respiratory ferments.
D. Intensification of respiratory ferment synthesis.
E. Specific binding of active centres of respiratory ferments.

10. A 45-year-old woman has been diagnosed with endemic goiter. What mechanism has caused hyperplasia of thyroid gland in this patient?

A. Increased thyroxine production.
B. Increased thyrotropin production.
C. Increased catecholamine production.
D. Increased hydration of derma and hypodermic cellulose.
E. Increased iodine absorption.

11. A patient from Prykarpattia (at the foot of the Carpathian mountains) with endemic goiter consulted a doctor about suppuration of gingival angles and loosening of teeth. What is a major factor of periodontitis development in this case?

A. Endocrine disorders. *C. Violation of swallowing.* *E. Malnutrition.*
B. Hypersalivation. *D. Stress effects.*

12. A 29-year-old female patient has moon face, upper body obesity, striae on her anterior abdominal wall, hirsutism; urine shows an increased rate of 17-oxy ketosteroids. What disease are these presentations typical for?

A. Itsenko-Cushing syndrome. *D. Conn's syndrome.*
B. Secondary aldosteronism. *E. Pheochromocytoma.*
C. Primary aldosteronism.

13. A 44 year old woman complains of general weakness, heart pain, significant increase of body weight. Objectively: moon face, hirsutism, AP is 165/100 mm Hg, height – 164 cm, weight – 103 kg; the fat is mostly accumulated on her neck, thoracic girdle, belly. What is the main pathogenetic mechanism of obesity?

A. Reduced production of thyroid hormones.
B. Increased mineralocorticoid production.
C. Increased insulin production.
D. Reduced glucagon production.
E. Increased production of glucocorticoids.

14. To prevent the transplant rejection after organ transplantation it is required to administer hormonotherapy for the purpose of immunosuppression. What hormones are used for this purpose?

A. Mineralocorticoids. *C. Catecholamines.* *E. Thyroid.*
B. Sexual hormones. *D. Glucocorticoids.*

15. A 41-year-old male patient has a history of recurrent attacks of heartbeats (paroxysms), profuse sweating, headaches. Examination revealed hypertension, hyperglycemia, increased basal metabolic rate, and tachycardia. These clinical presentations are typical for the following adrenal pathology:

A. Hypofunction of the medulla. *D. Hypofunction of the adrenal cortex.*
B. Hyperfunction of the medulla. *E. Hyperfunction of the adrenal cortex.*
C. Primary aldosteronism.

16. A patient suffering from pheochromocytoma complains of thirst, dry mouth, hunger. Blood test for sugar revealed hyperglycemia. What type of hyperglycemia is it?

A. Hypercorticoid. *C. Adrenal.* *E. Hypoinsulinemic.*
B. Alimentary. *D. Somatotropic.*

17. A girl is diagnosed with adrenogenital syndrome (pseudohermaphroditism). This pathology was caused by hypersecretion of the following adrenal hormone:

A. Androgen. *B. Estrogen.* *C. Aldosterone.* *D. Cortisol.* *E. Adrenalin.*

18. A female patient presents with endocrine dysfunction of follicular cells of the ovarian follicles resulting from an inflammation. The synthesis of the following hormone will be inhibited:

A. Lutropin. *C. Follicle stimulating hormone.* *E. Estrogen.*
B. Follistatine. *D. Progesterone.*

19. A 40 year old man who took part in disaster-management at a nuclear power plant fell sick with paradontitis. What etiological agent is the most important for the development of this pathology?

A. Iron deficit. *C. Malnutrition.* *E. Increased load of dento-*
B. Emotional stress. *D. Streptococcus.* *alveolar apparatus.*

20. In course of an experiment a white rat was being stimulated with a stress factor (electric current). The researchers could observe muscle hypotonia, arterial hypotension, hypothermia. What period of general adaptation syndrome is it?

A. Exhaustion stage. *C. Antishock phase.* *E. –.*
B. Shock phase. *D. Resistance stage.*

21. Rats being under stress have muscular hypertonia and high arterial pressure, high glucose concentration in blood and intensified secretion of corticotropin and corticosteroids. In what stress phase are these animals?

A. Exhaustion. *C. Erectile.* *E. Terminal.*
B. Shock phase. *D. Antishock phase.*

22. A 41-year-old man has a history of recurrent attacks of heartbeats (paroxysms), profuse sweating, headaches. Examination revealed hypertension, hyperglycemia, increased basal metabolic rate, and tachycardia. These clinical presentations are typical for the following adrenal pathology:

A. Hypofunction of the medulla. *D. Primary aldosteronism.*
B. Hyperfunction of the adrenal cortex. *E. Hyperfunction of the medulla.*
C. Hypofunction of the adrenal cortex.

Standards of correct answers to the task KROK-1

1	2	3	4	5	6	7	8	9	10	11	12	13
B	*A*	*C*	*A*	*D*	*B*	*E*	*C*	*B*	*B*	*A*	*A*	*E*

14	15	16	17	18	19	20	21	22
D	*B*	*C*	*A*	*E*	*B*	*B*	*D*	*E*

Recommendations for registration of work results

1. Written answer to test tasks (initial level of knowledge).
2. The results of the experiment are drawn up in the form of an experiment protocol with the determination of relevant conclusions.

3. The protocol of the experiment analysis of various forms of impaired vascular tone, in particular, hypertensive disease

4. Protocol for solving situational tasks with an explanation of the correct answers.

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Topic 15. Pathophysiology of the nervous system

Justification of the topic: The nervous system is a higher regulatory system. It controls the functions of all its organs and systems, ensuring the perfect adaptation of the body to the environment. With the participation of the nervous system, numerous protective reactions are carried out, aimed at protecting the body from damage or compensating for those pathological changes that occur during diseases. Disorders of the nervous system can cause dysfunction of any other physiological system of the body, which becomes more sensitive to the action of pathogenic factors. Violation of higher nervous activity does not allow an individual to fully realize his social function. In the pathogenesis of any disease, at one or another stage of its development, it is possible to detect disturbances in the function of the nervous system. All this emphasizes the relevance of the topic.

Purpose of the lesson:

General – be able to describe disorders of higher nervous (conditional reflex) activity, motor and other functions of the nervous system, explain their causes, main forms and manifestations. The general goal is to be able to describe disorders of higher nervous activity, motor and other functions of the nervous system, to explain their causes, main forms and manifestations.

Specifically:

Know:

1. Describe the etiology and pathogenesis of disorders of higher nervous activity and neuroses.
2. Classify disorders of the motor function of the nervous system.
3. Describe the concepts of "hyperkinesis", "paralysis and paresis", "ataxia".
4. Explain the causes and mechanisms of hyperkinesis, paralysis and ataxia.
5. To reveal the main features and manifestations of disorders of the motor function of the nervous system in hyperkinesis, ataxia and paralysis, to explain the mechanism of their development.
6. Distinguish between central and peripheral paralysis.

Be able:

1. Describe the structure and functions of different departments of the central nervous system.
2. Explain the motor function of the nervous system, by which nervous structures it is carried out. What is a motor analyzer?
3. Describe the main motor nerve pathways
4. To assess the influence of the extrapyramidal system and the cerebellum on the body's motor function.
5. To evaluate the structural organization of connections of the spinal cord and other departments of the central nervous system

Practical experience:

1. Explain what is the main role of the nervous system and its main functions.
2. Justify the main risk factors for damage to the nervous system and the degree of its dysfunction.

3. Identify typical examples of various forms of disorders of the nervous system.

4. Explain the pathogenesis of neuronal dysfunctions and systemic pathological manifestations.

5. Justify the classification and main types of sensory disorders.

6. Substantiate the main mechanism of formation and development of pain, its causes and types of pain.

7. Explain the pathogenesis of the development of neurosis

The graphological structure of the topic "Pathophysiology of the nervous system" is attached

Material and methodological support of the topic "Pathophysiology of the nervous system".

1. Lectures;
2. Methodical instructions for teachers;
3. Methodical instructions for students;
4. Set of test tasks to determine the basic level of knowledge;
5. Set of situational tasks to determine the final level of knowledge;
6. Set of KROK-1 tasks;
7. Set of schemes and tables (presentation);
8. Set of forms with a clinical blood test;
9. Video films;
10. For the experiment (experimental animals – rabbit, microscopes, immersion oil, slides, polishing slides, distillates for staining smears, fixation, Romanovsky staining, injector, pins, Petri dish, 10 % camphor solution, 1 % amytal solution – sodium, syringes, injection needles, electric bell.

Oriented map of students' work on the topic "Pathophysiology of the nervous system"

No	Stage of lesson	Academic time, min	Educational guide		Place holding a class
			Educational tools	Equipment	
1	Definition of initial knowledge	10	Control of theoretical training of students programmable by using structural answers to the issue of tickets	Test control issue tickets	Study room
2	Analysis of theoretical material	35	Parsing theoretical material on based on control questions of the topic, situational tasks, tasks KROK-1	Control topic question, task KROK-1 situational tasks	Study room
3	Practical part (carrying out experiment)	30	Introduction and preparation for productions experiment Setting experiment Discussion results experiment and formulation of conclusions	10 % camphor solution, 1 % sodium amytal solution, syringes, injection needles; electric bell Experimental animals - white rats	Study room
4	Determination of the final level of knowledge and skills. Beating results	15	Determining the source of formation of knowledge and skills	Determination of the initial level of formation of knowledge and skills	Study room

PATHOPHYSIOLOGY OF THE NERVOUS SYSTEM.

Sensory Nervous System Disorders

The central nervous system (CNS) refers to the brain and spinal cord together. The peripheral nervous system refers to the cervical, thoracic, lumbar, and sacral nerve trunks leading away from the spine to the limbs. Messages related to function (such as movement) or dysfunction (such as pain) travel from the brain to the spinal cord and from there to other regions in the body and back to the brain again. The autonomic nervous system controls involuntary functions in the body, like perspiration, blood pressure, heart rate, or heartbeat. It is divided into the sympathetic and parasympathetic nervous systems. The sympathetic and parasympathetic nervous systems have links to important organs and systems in the body; for example, the sympathetic nervous system controls the heart, blood vessels, and respiratory system, while the parasympathetic nervous system controls our ability to sleep, eat, and digest food.

The peripheral nervous system also includes 12 pairs of cranial nerves located on the underside of the brain. Most relay messages of a sensory nature. Neuralgia, as in trigeminal neuralgia, is a term that refers to pain that arises from abnormal activity of a nerve trunk or its branches. The type and severity of pain associated with neuralgia vary widely.

The sensory nervous system is a major component of the body's overall nervous system function. It's a highly complex network of nerves, muscles and organs designed to delivery sensory input to the spinal cord and brain. Because of its complexity, diagnosing a disorder within this system can be a lengthy process.

Identification

The human body's central nervous system is made up of two subsystems – the peripheral system and the autonomic system. The brain and spinal cord are the components of the autonomic portion. The peripheral portion is made up of motor, sensory, autonomic and somatic systems. Sensory nervous system structures run along the skin in the form of receptors, in the muscles and other organs. Organs related to sight, sound and taste are also a part of this system. A disorder can develop within any one of these areas, and can affect other areas of the body as well.

Causes

Disorders can develop in the sensory nervous system when an injury occurs, when blood flow to a particular area is hampered, or as the result of a disease. Blood flow impairment can occur because of a tumor, a genetic defect, or a condition which causes the blood to clog, or clot inside blood vessels. Nutritional deficiencies, or metabolic imbalances can also work to alter the chemical make-up of the blood. Trauma related disorders may result from a blow to an area of the body where nerve damage is caused. Sensory receptors can also become damaged when an infection is present, or when nerve endings begin to deteriorate.

Types

Sensory nervous system disorders can affect large areas of the body, or localized regions. Pain, tingling, weakness and numbness are usually present in affected areas. Polyneuropathies involve nerve damage that's occurred in the long peripheral nerves of the body. Distal symmetric sensory-motor polyneuropathy is a disorder that involves the nerves that run from the bottom of the spinal cord to the feet. Carpal tunnel syndrome is a localized condition that develops in the wrist area. Multiple mononeuropathy is a disorder in which inflammation destroys the small blood vessels in an area like the hand or the foot.

Pathophysiology

Brown-Séquard syndrome results from damage to or loss of ascending and descending spinal cord tracts on 1 side of the spinal cord. Scattered petechial hemorrhages develop in the gray matter and enlarge and coalesce by 1 hour postinjury. Subsequent development of hemorrhagic necrosis occurs within 24–36 hours. White matter shows petechial hemorrhage at 3–4 hours. Myelinated fibers and long tracts show extensive structural damage.

Etiology

Traumatic causes

Brown-Séquard syndrome can be caused by any mechanism resulting in damage to 1 side of the spinal cord. Multiple causes of Brown-Séquard syndrome have been described in the literature. The most common cause remains traumatic injury, often a penetrating mechanism, such as a stab or gunshot wound or a unilateral facet fracture and dislocation due to a motor vehicle accident or fall.

More unusual etiologies that have been reported include assault with a pen, removal of a cerebrospinal fluid drainage catheter after thoracic aortic surgery, and injury from a blowgun dart.[4] Traumatic injury may also be the result of blunt trauma or pressure contusion.

Nontraumatic causes

Numerous nontraumatic causes of Brown-Séquard syndrome have also been reported, including the following:

- Tumor (primary or metastatic)
- Multiple sclerosis
- Disk herniation
- Cervical spondylosis
- Herniation of the spinal cord through a dural defect (idiopathic or post-traumatic)
- Epidural hematoma
- Vertebral artery dissection
- Transverse myelitis
- Radiation
- Intravenous drug use
- Tuberculosis

- Ossification of the ligamentum flavum
- Meningitis, Empyema
- Herpes zoster,Herpes simplex
- Syphilis
- Ischemia
- Hemorrhage – Including spinal subdural/epidural and hematomyelia
- Chiropractic manipulation – Rare, but reported.

Find out about pain

Pain is a feeling triggered in the nervous system. Pain may be sharp or dull. It may come and go, or it may be constant. You may feel pain in one area of your body, such as your back, abdomen or chest or you may feel pain all over, such as when your muscles ache from the flu.

Pain can be helpful in diagnosing a problem. Without pain, you might seriously hurt yourself without knowing it, or you might not realize you have a medical problem that needs treatment. Once you take care of the problem, pain usually goes away. However, sometimes pain goes on for weeks, months or even years. This is called chronic pain. Sometimes chronic pain is due to an ongoing cause, such as cancer or arthritis. Sometimes the cause is unknown.

Fortunately, there are many ways to treat pain. Treatment varies depending on the cause of pain. Pain relievers, acupuncture and sometimes surgery are helpful.

The Two Faces of Pain: Acute and Chronic

• **Acute pain**, for the most part, results from disease, inflammation, or injury to tissues. This type of pain generally comes on suddenly, for example, after trauma or surgery, and may be accompanied by anxiety or emotional distress. The cause of acute pain can usually be diagnosed and treated, and the pain is self-limiting, that is, it is confined to a given period of time and severity. In some rare instances, it can become chronic.

• **Chronic pain** is widely believed to represent disease itself. It can be made much worse by environmental and psychological factors. Chronic pain persists over a longer period of time than acute pain and is resistant to most medical treatments. It can—and often does—cause severe problems for patients. A person may have two or more co-existing chronic pain conditions. Such conditions can include chronic fatigue syndrome, endometriosis, fibromyalgia, inflammatory bowel disease, interstitial cystitis, temporomandibular joint dysfunction, and vulvodynia. It is not known whether these disorders share a common cause.

Pain Management: Neuropathic Pain

Introduction

Neuropathic pain is a complex, chronic pain state that usually is accompanied by tissue injury. With neuropathic pain, the nerve fibers themselves may be damaged, dysfunctional or injured. These damaged nerve fibers send incorrect signals to other pain centers. The impact of nerve fiber injury includes a change in nerve function both at the site of injury and areas around the injury.

One example of neuropathic pain is called phantom limb syndrome. This occurs when an arm or a leg has been removed because of illness or injury, but the brain still gets pain messages from the nerves that originally carried impulses from the missing limb. These nerves now misfire and cause pain. Neuropathic pain often seems to have no obvious cause; but, some common causes of neuropathic pain include:

- Alcoholism, Chemotherapy
- Back, leg, and hip problems
- Diabetes
- Facial nerve problems
- HIV infection or AIDS
- Multiple sclerosis
- Shingles
- Spine surgery

Symptoms may include:

- Shooting and burning pain
- Tingling and numbness

Unfortunately, neuropathic pain often responds poorly to standard pain treatments and occasionally may get worse instead of better over time. For some people, it can lead to serious disability.

THE PERCEPTION OF PAIN

Pain is an unpleasant yet important function for survival: warning system (but not all pain is needed for survival).

There are two different pathways to the brain on which pain can travel – information brought from free nerve endings in the skin to the brain via two different systems:

1) **fast pathways** – registers localized pain (usually sharp pain) and sends the information to the cortex in a fraction of a second. EX. – cut your finger with a knife.

2) **slow pathways** – sends information through the limbic system which takes about 1–2 seconds longer than directly to the cortex (longer lasting, aching/burning).

Factors in Pain Perception – not an automatic result of stimulation:

1) expectations – research shown that our expectations about how much something will hurt can effect our perception.

For example – study manipulated moods of subjects then asked them to complete questionnaires of pain perception. Those in negative mood group reported significantly more pain than other subjects. So, it seems that our brains can regulate, control, determine, and even produce pain.

Theories of pain perception

1) Gate Control Theory (Melzack & Walls, 1965) – incoming pain must pass through a "gate" located in the spinal cord which determines what information about pain will be sent to the brain. So, it can be opened to allow pain through or closed to prevent pain from being perceived.

The Gate – actually a neural network controlled by the brain. Located in an area of the spinal cord called the Substansia Gelatinosa. There are two types of nerve fibers in this area:

a) large – sends fast signals and can prevent pain by closing the gate.

b) small – sends slower signals which open the gate. So – when pain occurs it is because the large fibers are off and the small are on, opening the gate.

Since the gate is controlled by the brain, he factors discussed earlier (expectations, mood, personality) influence the functioning of the gate.

Contradiction to Gate Control Theory:

1) endorphins – the body's own pain killers (morphine-like). May explain acupuncture, acupressure, pain tolerance during last two weeks of pregnancy, etc.

BUT – endorphins may work with the gate control theory – maybe pain is perceived, endorphins are released, so the brain no longer needs the signals and closes the gate.

Phantom limbs

Ability to feel pain, pressure, temperature, and many other types of sensations including pain in a limb that does not exist (either amputated or born without).

The feelings and the pain are sometimes so life-like that person attempts to pick things up with phantom hand, step with phantom foot or leg, etc. Often person feels phantom moving in perfect coordination with the rest of the body – some report a missing arm extending outward at a 90 degree angle so they turn sideways when going through a doorway.

May occur right after amputation or not until years later.

Often felt as part of the body (belonging to the rest of the body). EX. – with a missing leg, some report having a phantom foot but not the rest of the leg. Still, the foot feels as though it is part of the body.

Explanations:

1) the neuroma explanation – remaining nerves in the stump grow into nodules (neuromas) at the end of the stump continue to fire signals. Signals follow the same pathways the brain as when the appendage existed.

2) the spinal cord explanation – neurons in the spinal cord that are no longer receiving information from the lost appendage continue to send information to the brain.

Problem – studies have shown that when areas in the spinal cord are severed often feelings still being perceived from areas that meet the spinal cord in lower areas (below separation in spinal cord).

3) the brain explanation – signals in the somatosensory circuits of the brain change when the limb is lost which produce the phantom...the brain compensates for the loss or altered signals. This has been expanded – brain contains a network of fibers that not only respond to stimulation but continually generates a pattern of impulses that indicate that the body is intact

and functioning. Thus, the brain creates the impression that the limb exists and is al right. This system may be prewired.

4) the hardwired explanation – we may have a biological makeup to be born with all of our appendages. So, when we are born w/o one or lose one, the nerves are still there and are still going to send the information.

Disorders of the nervous system and sensory disorders

Early recognition of drug-induced disorders of the nervous system is highly important because it can often prevent irreversible damage. **Drug-induced neurological disorders** (DINDs) can occur at initiation, during sudden withdrawal, or after many months or years of therapy.

Treatment is primarily concerned with controlled withdrawal, but some DINDs require urgent symptomatic treatment to avoid serious complications. Some DINDs can be reversed with certain vitamins and essential trace elements.

A chief mechanism in a number of DINDs is mitochondrial toxicity, a condition in which the "power plants" of certain cells become damaged or decline significantly in number. DINDs induced by statins (medications used to lower cholesterol levels) are more likely to become more prevalent. Increased use of newer humanized monoclonal antibodies may cause previously unrecognized DINDs. Antiretroviral agents are also commonly associated with DINDs. Drug interactions can also increase the toxicity of single agents.

Disorders of the nervous system and sensory disorders associated with the use of certain drugs include:

• Seizures – often seen in drug-induced encephalopathy (see below)

• Cerebrovascular disease – which can lead to stroke

• Headache – drugs that cause headaches often do so by exacerbating pre-existing migraine, chronic daily headache, or tension headache

• Encephalopathy – when drugs cause these diseases of the brain, they usually do so either by inducing metabolic disturbances, or by direct central nervous system toxicity

• Dementia – several drugs can cause a reversible condition resembling dementia

• Extrapyramidal disorders – symmetrical akinetic rigid syndromes, hyperkinetic syndromes acute dystonia-dyskinesia, choreo-athetosis, restless leg syndrome, and motor tics can all be caused by drugs

• Cerebellar disorders and tremor – these include postural, kinetic and resting tremor, and a host of drug-induced syndromes which are occasionally irreversible

• Myoclonus – this condition, in which muscles contract abnormally, may persist when the causative drug is withdrawn or reduced. This eventuality can be treated with other drugs, but alternative diagnoses should be considered

• Eye movement disorders -nystagmus, external ophthalmoplegia, and internuclear ophthalmoplegia are among eye movement disorders that can be caused by drugs

• Cranial neuropathies - several palsies have been shown to be drug-induced. Early withdrawal of the offending agent is critical

• Sensory disorders

o vision: while blurred vision is a common side effect of several medications, more serious, occasionally irreversible visual impairment is also possible. Examples include miosis, midriasis, refraction, cortical blindness, retinopathy, dyschromatopsia, xanthopsia and optic neuritis. Also of note is nonarteritic anterior ischemic optic neuropathy (NAION), which is likely caused by erectile dysfunction drugs.

o ototoxicity: by definition, damage to the hearing or balance functions of the inner ear by drugs or chemicals

o Disorders of the spinal cord and peripheral nervous system – drug-induced subacute myelo-opticoneuropathy is thought to occur by depletion of vitamins by the drug. Other than withdrawal, glutathione, B vitamin, and zinc supplements should be considered.

o Inflammatory demyelinating diseases of the central nervous system – these include multiple sclerosis, transverse myelitis, and Progressive Multifocal Leukoencephalopathy (PML).

o Inflammatory demyelinating diseases of the peripheral nervous system include aseptic meningitis, mononeuritis multiplex, polymyositis, vasculitis, bilateral anterior toxic optic neuropathy, orbital myositis, and CNS lupus, which may all be associated with anti-TNF treatment.

o Immune reconstitution inflammatory syndrome (IRIS) – a recognized complication of highly active antiretroviral therapy (HAART) in HIV.

o Propofol infusion syndrome – characterized by rhabdomyolysis, renal failure, bradyarrythmias, lipaemic plasma and metabolic acidosis, and is often fatal.

o Reye's syndrome – associated with the use of aspirin during acute viral illnesses.

Paralysis

Paralysis also called palsy, is defined as "loss or impairment of voluntary muscular power".

In general, diseases that produce paralysis can be divided into two groups; those that involve changes in the makeup of nervous or muscular tissue or those that are the result of metabolic disturbances in the function of nerves or muscles. Some diseases affect the entire body while others hit only a small area of the body.

At times, only one side of the body may be involved, producing a condition known as hemiplegia. In other instances both sides of the body may suffer the effects leading to diplegia or bilateral hemiplegia. When only the lower limbs are affected by paralysis it is called paraplegia. When all four limbs are affected, it is referred to as quadriplegia. How much of the body is affected depends on the site of the neurological damage. Strokes, brain

tumors, etc. classically cause such extensive loss of function. In instances of inflammation of nervous tissue such as occurs in polio, specific nerve cells are damaged leading to paralysis and muscle wasting.

Various diseases that affect muscle tissue are encountered much less often that those that affect nervous tissue. These are often hereditary, and due to a disturbance of muscle metabolism. Most cases of paralysis of muscular origin, therefore, usually begin early in life. However, other diseases can occur at any time of life, such as myasthenia gravis. Toxins such as alcohol can also affect muscle tissue, as well as abnormalities of hormonal production.

M**uscular disorders**

Movement disorders are a group of diseases and syndromes affecting the ability to produce and control movement. Though it seems simple and effortless, normal movement in fact requires an astonishingly complex system of control.

Disruption of any portion of this system can cause a person to produce movements that are too weak, too forceful, too uncoordinated, or too poorly controlled for the task at hand. Unwanted movements may occur at rest.

Intentional movement may become impossible. Such conditions are called movement disorders.

Types of Muscle disorders

Abnormal movements themselves are symptoms of underlying disorders. In some cases, the abnormal movements are the only symptoms. Disorders causing abnormal movements include:

- Parkinson's disease,
- Parkinson-plus syndromes (progressive supranuclear palsy, multiple system atrophy, and cortical-basal ganglionic degeneration),
- Huntington's disease,
- Wilson's disease,
- Inherited ataxias (Friedreich's ataxia, Machado-Joseph disease, and pinocerebellar ataxias),
- Tourette syndrome and other tic disorders,
- Essential tremor,
- Restless Leg Syndrome,
- Dystonia,
- Stroke,
- Cerebral palsy,
- Encephalopathies,
- Intoxication,
- Poisoning by carbon monoxide, cyanide, methanol, or manganese.

Movement is produced and coordinated by several interacting brain centers, including the motor cortex, the cerebellum, and a group of structures in the inner portions of the brain called the basal ganglia. Sensory information provides critical input on the current position and velocity of body parts,

and spinal nerve cells (neurons) help prevent opposing muscle groups from contracting at the same time.

To understand how movement disorders occur, it is helpful to consider a normal voluntary movement, such as reaching to touch a nearby object with the right index finger. To accomplish the desired movement, the arm must be lifted and extended.

The hand must be held out to align with the forearm, and the forefinger must be extended while the other fingers remain flexed.

The cerebellum

Once the movement of the arm is initiated, sensory information is needed to guide the finger to its precise destination. In addition to sight, the most important source of information comes from the "position sense" provided by the many sensory neurons located within the limbs (proprioception).

Proprioception is what allows you to touch your nose with your finger even with your eyes closed. The balance organs in the ears provide important information about posture. Both postural and proprioceptive information are processed by a structure at the rear of the brain called the cerebellum.

The cerebellum sends out electrical signals to modify movements as they progress, "sculpting" the barrage of voluntary commands into a tightly controlled, constantly evolving pattern. Cerebellar disorders cause inability to control the force, fine positioning, and speed of movements (ataxia). Disorders of the cerebellum may also impair the ability to judge distance so that a person under- or over-reaches the target (dysmetria). Tremor during voluntary movements can also result from cerebellar damage.

The basal ganglia

Both the cerebellum and the motor cortex send information to a set of structures deep within the brain that help control involuntary components of movement (basal ganglia). The basal ganglia send output messages to the motor cortex, helping to initiate movements, regulate repetitive or patterned movements, and control muscle tone.

Circuits within the basal ganglia are complex. Within this structure, some groups of cells begin the action of other basal ganglia components and some groups of cells block the action. These complicated feedback circuits are not entirely understood. Disruptions of these circuits are known to cause several distinct movement disorders.

A portion of the basal ganglia called the substantia nigra sends electrical signals that block output from another structure called the subthalamic nucleus. The subthalamic nucleus sends signals to the globus pallidus, which in turn blocks the thalamic nuclei. Finally, the thalamic nuclei send signals to the motor cortex. The substantia nigra, then, begins movement and the globus pallidus blocks it.

This complicated circuit can be disrupted at several points. For instance, loss of substantia nigra cells, as in Parkinson's disease, increases blocking of

the thalamic nuclei, preventing them from sending signals to the motor cortex. The result is a loss of movement (motor activity), a characteristic of Parkinson's.

In contrast, cell loss in early Huntington's disease decreases blocking of signals from the thalamic nuclei, causing more cortex stimulation and stronger but uncontrolled movements.

Disruptions in other portions of the basal ganglia are thought to cause tics, tremors, dystonia, and a variety of other movement disorders, although the exact mechanisms are not well understood.

Muscles tremor

Tremor is an unintentional (involuntary), rhythmical alternating movement that may affect the muscles of any part of the body. Tremor is caused by the rapid alternating contraction and relaxation of muscles and is a common symptom of diseases of the nervous system (neurologic disease).

Occasional tremor is felt by almost everyone, usually as a result of fear or excitement. However, uncontrollable tremor or shaking is a common symptom of disorders that destroy nerve tissue, such as Parkinson's disease or multiple sclerosis. Tremor may also occur after stroke or head injury. Other tremors appear without any underlying illness.

Causes and symptoms

Tremor may be a symptom of an underlying disease, and it may be caused by drugs. It may also exist as the only symptom (essential tremor).

Some types of tremor are signs of an underlying condition. About a million and a half Americans have Parkinson's disease, a disease that destroys nerve cells. Severe shaking is the most apparent symptom of Parkinson's disease. This coarse tremor features four to five muscle movements per second. The shaking is evident at rest but declines or disappears during movement.

Other disorders that cause tremor are multiple sclerosis, Wilson's disease, mercury poisoning, thyrotoxicosis, and liver encephalopathy.

A tremor that gets worse during body movement is called an "intention tremor." This type of tremor is a sign that something is amiss in the cerebellum, a region of the brain concerned chiefly with movement, balance and coordination.

Setting up the experiment. Discussion the results and formulation the conclusions

The conduction of the experiment:

Reproduction of camphor epilepsy.

1. Inject 0.5 ml of 10% camphor solution into the rat's abdominal cavity and observe the animal's condition.

2. Inject sodium amytal at the rate of 20 mg per 100 g of body weight under the skin of another rat.

3. After 10–15 minutes, when the animal becomes narcosis, inject 0.5 ml of 10 % camphor solution and observe the animal's condition.

4. Compare the condition of rats.

Reproduction of epilepsy caused by a strong audiogenic stimulus.

1. Place two previously selected rats with high audiogenic sensitivity in the cage.

2. After studying the initial state, turn on a strong electric bell for 3–5 minutes.

3. To note the phasic nature of the epileptoid response to a sound stimulus.

Study of the effect of sodium amytal on the convulsive state

1. Use rats from previous experience.

2. Inject sodium amytal at the rate of 15 mg per 100 g of body weight under the skin of one of the animals.

3. After 10 minutes, subject both animals to a sound stimulus according to the above method.

4. Describe the differences in condition

Discussion of the results of the experiment

For the first time, reproduction of conditioned reflexes to irritation of the central nervous system by toxic substances was obtained by Podkopaev (1914 – apomorphine) and V. A. Krylov. (1922 – morphine). The experience spent in this session proves that any indifferent stimulus can acquire the meaning of a disease-causing agent due to the formation of pathological conditional connections. This experience expands our ideas about the etiology of human diseases. In addition, this experience testifies to the powerful effect of the bark through the subcortical centers, on the vegetative processes in the body, and the possibility of the occurrence of various vegetative disorders when cortical activity changes.

Formulation the conclusions based on the experiment

1. An epileptic attack caused by the intra-abdominal injection of 0.5 ml of a 10 % camphor solution as an audiogenic stimulus manifested itself in the form of successive phases of harbingers, tonic convulsions and post-seizure catalepsy. The mechanism of the epileptic action of camphor: the direct effect of camphor on brain tissue and the flow of impulses from the peritoneum (from the site of initial injection) and from vascular receptors, which forms many foci of epileptic activity in the brain, which are accompanied by a violation of the functional balance of intracerebral systems and the development of the function of neurons in the focus of epileptic activity.

2. The phasic nature of an episeizure is caused by a sequential change in the bioelectric potentials of the brain: synchronous high-amplitude potentials (phase of tonic seizures) and the development of inhibition in the central nervous system (phase of post-seizure catalepsy).

3. In experimental rats, which were previously injected with sodium amytal (amobarbital), the action of camphor and a sound stimulus did not cause the development of a convulsive syndrome, which was due to the inhibitory effect of sodium amytal on the central nervous system, preventing the formation of foci of epileptic activity in the brain. Describe and draw the slides in detail.

Tasks for independent work on the topic "Pathophysiology of the nervous system".

The student is invited to familiarize himself with the results of the study of the pathological effect of rats on an epileptic attack caused by the intra-abdominal injection of a solution of 0.5 ml of a 10 % solution of camphor. The mechanism of the epileptic effect of camphor: the direct effect of camphor on the brain tissue and the flow of impulses. It is necessary to determine the signs and type of disorder. Be able to explain the mechanism of occurrence. Analysis of errors with an explanation of the correct answers. In experimental rats that were previously injected with sodium amytal (amobarbital), the action of camphor and a sound stimulus did not cause the development of a convulsive syndrome.

List of questions and works to be studied:

1. In contrast to physiological pain, what is pathological pain characterized.
2. What properties characterize epicritic pain.
3. Specify the features of protopathic pain.
4. What are the characteristic manifestations of central paralysis in the affected limbs.
5. What signs characterize peripheral paralysis.
6. State the signs of Brown-Sécart syndrome.
7. What is the characteristic development of syndromes for neuroses.
8. Specify the characteristic features of neurosis in a person.

List of practical skills that must be mastered:

1. Explain the method of experimental modulation of disturbances in motor functions of the nervous system.
2. Identify examples of the main syndromes that characterize disorders of the motor function of the nervous system.
3. Substantiate the causes and mechanisms of development of neuromuscular transmission disorders.
4. Explain the most effective methods used for experimental modeling of disorders of the autonomic nervous system.
5. Explain the causes and mechanisms of violations of electrophysiological processes in the central nervous system.
6. Determine the main mechanisms for the development of pathological excitation and inhibition in the nerve centers.
7. Formulate functional changes in the CNS that may be associated with the development of pathological excitation and inhibition.

8 Determine the mechanism of damage to brain neurons.

9. Explain the cause of intracranial hypertension and stroke.

Situational tasks KROK-1 to determine the final level of knowledge

1. A patient caught a cold after which there appeared facial expression disorder. He cannot close his eyes, raise his eyebrows, bare his teeth. What nerve is damaged?

A. Facial. *C. Trigeminus.* *E. Infraorbital.*
B. Vagus. *D. Glossopharyngeal.*

2. A 68-year-old woman can't move by the upper and lower right extremities due to insult. Muscle tone of these extremities and reflexes are increased. There are pathological reflexes. What form of the paralysis is it?

A. Paraplegia. *C. Monoplegia.* *E. Hemiplegia.*
B. Tetraplegia. *D. Dissociation.*

3. After a car accident a patient has been diagnosed with a fracture of spine. He is unable to move his lower extremities. This form of motor disorder is called:

A. Paralysis. *C. Hemiplegia.* *E. Quadriplegia.*
B. Paresis. *D. Paraplegia.*

4. After poisoning with an unknown drug a 37 year old patient has stereotypical face muscle contractions that imitate blinking and squinting. What form of motor function disorder of nervous system is it?

A. Hyperkinesia. *B. Hypokinesia.* *C. Akinesia.* *D. Ataxy.* *E. –.*

5. An experimental rat with extremity paralysis has no tendon and cutaneous reflexes, muscle tone is decreased, but muscles of the affected extremity maintain their ability to react with excitation to the direct action of continuous current. What type of paralysis is it?

A. Flaccid central. *C. Spastic peripheral.* *E. Extrapyramidal.*
B. Flaccid peripheral. *D. Spastic central.*

6. A patient complaining of pain in the left shoulder-blade region has been diagnosed with myocardial infarction. What kind of pain does the patient have?

A. Visceral. *B. Phantom.* *C. Protopathic.* *D. Radiating.* *E. Epicritic.*

7. After the traumatic tooth extraction a patient is complaining of acute, dull, poorly-localized pain in gingiva, body temperature rise up to 37,5 °C. The patient has been diagnosed with alveolitis. Specify the kind of pain in this patient:

A. Epicritic. *B. Visceral.* *C. Heterotopic.* *D. Protopathic.* *E. Phantom.*

8. A patient got a gunshot wound of hip which damaged the sciatic nerve. Any impact on the affected limb causes severe, excruciating pain. What mechanism of pain is most likely in this case?

A. Reflex. *C. Endorphin hypofunction.* *E. Causalgic.*
B. Phantom. *D. Enkephalin hypofunction.*

9. Four months ago a 43 year old patient had a traumatic amputation of his lower extremity. Now he complains of sensing the amputated extremity and having constantly grave, sometimes unbearable pain in it. What type of pain does he have?

A. Causalgia. *B. Phantom.* *C. Neuralgia.* *D. Thalamic.* *E. Reflex.*

10. A patient complains of toothache. On examination he has been diagnosed with pulpitis. Which factor played a main pathogenic role in the development of pain syndrome in this case?

A. Interleukin action.
B. Vasospasm.
C. Inadequate stimulation of a mandibular nerve branch.
D. Activation of one of the components of the complement system.
E. Increased intratissular pressure in the dental pulp.

11. A 28 year old man had a gunshot wound of shin that resulted in an ulcer from the side of the injury. What is the main factor of neurodystrophy pathogenesis in this case?

A. Traumatization of peripheral nerve.
B. Psychical stress.
C. Microcirculation disturbance.
D. Infection.
E. Tissue damage.

12. A patient who takes a blocker of membrane cytoreceptors of efferent conductor synapses of autonomic nervous system complains about dry mouth. What receptors are blocked?

A. Nicotinic cholinoreceptors.
B. H_2-receptors.
C. Alpha-adrenoreceptors.
D. Muscarinic cholinoreceptors.
E. Beta-adrenoreceptors.

Standards of correct answers to the task KROK-1

1	2	3	4	5	6	7	8	9	10	11	12
A	*E*	*D*	*A*	*B*	*D*	*D*	*E*	*B*	*E*	*A*	*D*

Recommendations for registration of work results

1. Written answer to test tasks (initial level of knowledge).
2. The results of the experiment are drawn up in the form of an experiment protocol with the determination of relevant conclusions.
3. Protocol for the study of the results of the patient's clinical blood analysis.
4. Protocol for solving situational tasks with an explanation of the correct answers.

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Topic 16. Pathophysiology of extreme conditions: Collapse, shock, coma. Pathophysiology of modern warfare injuries.

Justification of the topic: Extreme (critical, urgent) conditions are conditions that are caused by the impact on the body of pathogenic factors, expressed by the strength or duration of the impact, and which are characterized by a significant violation of metabolism and vital functions of the body. As a result, there is an immediate threat to life, which requires immediate medical assistance. Knowledge of the etiology and pathogenesis of extreme conditions is necessary for the treatment and prevention of these most dangerous phenomena.

In the conditions of wartime, it is advisable to pay attention to the study of pathological mechanisms of pathological conditions that quite often accompany the state of war – crunch syndrome, burn and traumatic disease, shock, coma, as well as wounded diseases of internal organs. An important role in the pathogenesis of internal pathology belongs to infection, anemia due to blood loss, changes in the general reactivity of the body under the influence of harmful effects caused by the combat environment (overfatigue, nervous tension, cooling, etc.).

Purpose of the lesson:

General - to study the main types of extreme conditions, their causes and mechanisms of their development, pathogenetic methods of treatment.

Specifically:

Know:

1. Concepts of "extreme states", "terminal state"; their criteria.
2. Types of extreme states, their features.
3. Collapse: definition, classification, etiology, pathogenesis, clinical manifestations.
4. Shock: definition, classification, etiology, pathogenesis, clinical manifestations.
5. Violations of hemodynamics and microcirculation in the pathogenesis of shock states.
6. Coma: definition, classification, etiology, pathogenesis, clinical manifestations.
7. Etiology and pathogenesis of hepatic, uremic, diabetic coma.
8. Principles of treatment of extreme conditions.
9. Definition, classification, pathogenesis of traumatic disease, burn disease, tranche syndrome; basic principles of their treatment.

Be able to:

1. Define the concept of "extreme states" and differentiate their individual types - collapse, shock, coma.
2. Explain the causes, conditions and mechanisms of the development of collapse, shock, coma in order to develop in clinical practice the ability to give a correct assessment of these phenomena.

3. Violations of hemodynamics and microcirculation in the pathogenesis of shock states.

4. Be able to explain the etiology and pathogenesis of various types of coma (hepatic, uremic, diabetic).

Practical experience:

1. Define the concept of "extreme states" and differentiate their individual types - collapse, shock, coma;

2. Explain the causes, conditions and mechanisms of the development of collapse, shock, coma, in order to develop in clinical practice the ability to give a correct assessment of these phenomena.

3. Violations of hemodynamics and microcirculation in the pathogenesis of shock states.

4. Be able to explain the etiology and pathogenesis of various comas (hepatic, uremic, diabetic).

The graphological structure of the topic "Pathophysiology of extreme conditions: Collapse, shock, coma. Pathophysiology of modern warfare injuries." is attached.

Material and methodological support of the topic "Pathophysiology of extreme conditions: Collapse, shock, coma. Pathophysiology of modern warfare injuries":

1. Lectures;
2. Methodical developments for teachers;
3. Methodical instructions for students;
4. A set of test tasks to determine the basic level of knowledge;
5. A set of situational problems to determine the final level of knowledge;
6. A set of "KROK-1" tasks;
7. A set of diagrams and tables (presentation);
8. Video films.
9. Experiment equipment: vector electrocardioscope, microscope, scissors, tweezers, clamps, napkins, capitals with a hole (viewing window) for fixing the animal, hexanal for anesthesia; the experimental animals are white rats.

Oriented map of students' work on the topic "Pathophysiology of extreme conditions: Collapse, shock, coma. Pathophysiology of modern warfare injuries"

No	Stage of lesson	Academic time, min	Educational guide		Place holding a class
			Educational tools	Equipment	
1	Determination of the basic level of knowledge	10	Written answer to test tasks	Test tasks	Study room
2	Analysis of theoretical material	35	Analysis of theoretical material based on control questions of the topic, situational tasks, tasks of KROK-1	Topic control questions, KROK-1 tasks, situational tasks	

No	Stage of lesson	Academic time, min	Educational guide		Place holding a class
			Educational tools	Equipment	
3	Practical part (conduct experiment)	30	Introduction and preparation for setting up the experiment. Setting up the experiment. Discussion of the results of the experiment and formulation the conclusions	Rabbit, microscopes, immersion oil, subject slides, polish slides, hydrochloric acid solution, distillates for painting of smears, fixation, Romanovsky staining, injector, pins, Petri-dish, solution of brilliant cresyl blue	Study room
4	Determination of the final level of know-ledge and skills. Summarizing the results	15	Determination of the final level of knowledge and skills. Summarizing the results	KROK-1 tasks, situational tasks	Study room

Extreme, critical, urgent conditions- general severe conditions of the body, which develop under the influence of extreme factors of the external or internal environment, characterized by significant disorders of the vital activity of the body, fraught with death.

From extreme conditions it is necessary to distinguish between terminal states, which are the final stages of an organism's life, a borderline state between life and death, usually a consequence of an unfavorable course of extreme states. If intensive medical assistance is not carried out in a terminal condition or they are ineffective, then clinical and then biological death occurs.

Extreme and terminal states have both similar and fundamentally different characteristics.

The similarity of extreme and terminal states: common causes, similar key links of pathogenesis, borderline position between life and death, fraught with the death of the organism, require urgent medical assistance.

Differences between terminal and extreme states

- Terminal conditions are based on much more severe prognostically unfavorable processes that, without emergency medical measures, acquire a progressive, irreversible course leading to death.
- With a developed terminal condition, the specificity of the cause loses its significance.
- *Small specificity and mechanisms* development of terminal states. The key links of pathogenesis are hypoxia, deviation of indicators of ABS, gas composition of blood, toxemia, etc.
- In extreme conditions, both the specificity of the pathogenic agent and the peculiarities of the mechanisms of their development are revealed. In this regard, carrying out specific etiotropic and pathogenetic therapy of extreme conditions allows blocking their development and normalizing the vital activity of the body.

Causes of extreme conditions

Extreme reasons – pathogenic agents that act in these specific conditions and when acting on this organism have an extremely high, very intense, often destructive effect.

Types of extreme factors. Extreme factors are divided into exogenous (physical, chemical, biological) and endogenous (adverse, severe course of diseases and painful conditions – severe insufficiency of the functions of organs and physiological systems, significant blood loss, massive hemorrhages in organs, excess of products of immune or allergic reactions, significant deficiency/excess BAS and/or their effects, mental overstrains, injuries).

Conditions contributing to the occurrence of extreme conditions. *Factors potentiating the effects of extreme agents* (sensitization of the body, consequences of blood loss, heart failure, etc.); reactivity of the body.

Pathogenesis of extreme conditions.

Extreme conditions are characterized by staged development: activation of adaptive mechanisms, their exhaustion and insufficiency, extreme regulation of the vital activity of the organism.

The most frequent and clinically significant emergency conditions include collapse, shock, coma and poisoning.

COLLAPSE – a general condition that occurs as a result of a significant discrepancy in the blood volume of the vascular bed and is characterized by insufficient blood circulation, primary circulatory hypoxia, a disorder of the functions of tissues, organs and their systems.

The direct cause of the collapse is the rapid development of a significant excess of the capacity of the vascular bed in comparison with circulating blood volume.

Types of collapse. Cardiogenic, hypovolemic and vasodilatory collapse. In practical medicine, varieties of collapse are often distinguished, taking into account its specific cause (posthemorrhagic, infectious, toxic, radiation, pancreatic, orthostatic, hypocapnic, etc.).

Causes of collapse

- **Cardiogenic collapse** – collapse that develops when the amount of blood ejected from the ventricles of the heart into the vascular bed is reduced in case of acute heart failure, heart defects (decompensation stage), etc.
- **Hypovolemic collapse** – collapse that develops when the circulating blood volume decreases due to: acute massive bleeding; rapid and significant dehydration of the body; loss of a large volume of blood plasma; redistribution of blood with deposition of a significant amount of it in venous vessels (shock).
- **Vasodilation collapse** – collapse that develops in case of severe infections, intoxications, hyperthermia, endocrinopathies, improper use of drugs (sympatholytics, ganglioblockers, calcium antagonists), hypocapnia, an excess of adenosine, histamine, kinins in the blood, deep hypoxia, and a number of others.

Pathogenesis of collapse. Peculiarities of the pathogenesis of various types of collapse.

Posthemorrhagic collapse. The initial pathogenetic factor is a rapid and significant decrease in circulating blood volume (hypovolemia). The increase in vascular tone does not eliminate the discrepancy in their capacity, which significantly decreased of circulating blood volume. As a result, hypoperfusion of organs and tissues develops, which leads to increasing, first circulatory, and then mixed (hemic, tissue) hypoxia. The consequence of hypoxia is a progressive disorder of the functions of the nervous system, lungs, kidneys, etc. It takes several days to replenish the lost blood (7–12 days in severe cases).

Orthostatic collapse. The initial links of pathogenesis are systemic vasodilation as a result of a sharp decrease in the tone of the walls of arterioles, when the body suddenly moves to a vertical position from a lying or sitting position. At the same time, the activation of cholinergic effects on the walls of blood vessels in connection with the irritation of the neurons of the vestibular centers with a sharp change in the position of the body. An important pathogenetic link is a decrease in the reactive properties of the walls of resistive vessels to vasopressor substances: catecholamines, angiotensin, etc. One of the leading reasons for this can be adrenal gland insufficiency, disorders of the functions of the cardiovasomotor center and hypothalamus, etc.

Toxic-infectious collapse. The reason of this is the pathogenic effect on the body of toxins of exo- and endogenous origin of an infectious or non-infectious nature. Toxins cause: direct neuro-, cardio- and myotropic damage; violation of metabolism and implementation of the effects of vasopressor and vasodepressor agents; disorders of the mechanisms of regulation of vascular tone and heart activity. As a result, a pronounced decrease in the tone of resistive vessels, cardiac output, of circulating blood volume develops in varying degrees. With a significant and progressive drop down of these indicators rapidly increasing disorders of the body's vital activity are observed, and, a threat to its life is created.

The main links of pathogenesis and general manifestations of collapse.

• ***Disturbance of the cardiovascular function*** is the initial and main pathogenetic link of collapse and is characterized by inadequate blood supply to organs and tissues.

Typical manifestations are circulatory disorders: decreased shock and cardiac output of blood; acute arterial hypotension; venous hyperemia; redistribution of blood flow; violation of microcirculation of blood and lymph; development of capillary-trophic insufficiency.

• ***Disorder of the function of the nervous system***. Manifestations: inhibition; apathy, indifference to events; tremor of the fingers; sometimes convulsions; hyporeflexia; fainting with significant hypoperfusion and hypoxia of the brain.

• ***Violation of the gas exchange function of the lungs*.** Manifestations: frequent and shallow breathing; hypoxemia; hypercapnia in the blood flowing from the lungs.

▪ ***Disorder of the excretory function of the kidneys***. Manifestations: acute systemic hypotension and, in connection with this, hypoperfusion of the kidneys (oliguria; hyperstenuria; hyperazotemia).

• ***Disorders of the blood and hemostasis systems.*** Manifestations: hypovolemia; increase in blood viscosity; hyperaggregation of platelets and erythrocytes; the formation of blood clots; development of the sludge phenomenon.

Clinical manifestations of collapse are caused by the development of hypoxia, initially circulatory, and later mixed (including respiratory, hemic, tissue, substrate). With increasing severity of hypoxia, significant disorders of the vital activity of the body may develop, fraught with death.

SHOCK is a conditional concept that means a number of syndromic-like clinical conditions characterized by a critical decrease in blood flow in tissues in combination with excessive straining of homeostasis regulation mechanisms.

Shock – a general, extremely severe condition of the body, which occurs under the influence of extreme extreme factors and is characterized by a stage-by-stage progressive disorder of the vital activity of the body as a result of increasing dysfunction of the nervous, endocrine, cardiovascular and other vital systems.

Clinical syndromes: acute circulatory failure, acute heart failure, acute vascular failure, fainting, collapse.

An important distinguishing feature of shock is that it is caused by an extreme factor of great force, which, as a rule, leads to varying degrees of destruction of structural elements of tissues and organs. The patient's exit from the state of shock is possible with the implementation of emergency and effective medical measures.

Causes of shock:

• Different types of injuries (mechanical damage; large burns, exposure to electric current, etc.).

• Massive blood loss (usually combined with trauma).

• Transfusion of a large volume of incompatible blood.

• Entry of allergens into the internal environment of a sensitized organism.

• Significant ischemia or extensive necrosis of organs (heart, kidneys, liver, intestines, etc.).

Types of shock. The criterion for differentiating shock states is their ***reason***: traumatic shock (wound, pain), burn, post-transfusion, allergic (anaphylactic), electric, cardiogenic, toxic, psychogenic (mental);

• ***blood circulation component:*** hypovolemic (posthemorrhagic) shock, cardiogenic shock, vascular shock (shock associated with reduced vascular resistance): septic, anaphylactic.

• severity of their course: shock I degree (mild), shock II degree (moderate severity), shock III degree (severe).

Pathogenesis of shock

1. In the pathogenesis of shock states, regardless of the type of shock, disturbances in the blood circulation system at the level of macrocirculation followed by microcirculation are recognized as primary; at the same time, the indisputable role of the central nervous system in the formation of shock, which acts as a trigger for the reaction of hypercatecholaminemia with the subsequent development of vasoconstriction, is not denied.

2. Metabolic disorders, ABS, endocrine and enzymatic disorders, etc. are recognized as secondary.

Stages of shock. Regardless of the severity of clinical manifestations, two step-by-step stages of shock are distinguished. First, the activation of specific and non-specific adaptive reactions is observed – the stage of generalized excitement, or erectile. In recent years, it has been called adaptive, compensatory, non-progressive or early stage. If the adaptation processes are insufficient, the second stage of shock develops – stage of general inhibition or torpid stage. Currently, it is called the stage of deadaptation or decompensation. At this stage, two substages are distinguished: progressive (which consists in exhaustion of compensatory reactions and tissue hypoperfusion) and irreversible (during which changes incompatible with life develop).

Stage of compensated shock.

The stage of shock adaptation (compensation) is the result of considerable severity and scale of damage to organs and tissues by an extreme factor, as well as secondary changes in the body arising under its influence.

I. Neuroendocrine link. Excessive generalized activation of the nervous and endocrine systems, which develops in connection with hyperafferentation of various modalities, is characterized by a significant increase in the effector effects on organs and tissues from the sympathoadrenal and hypothalamic-pituitary-adrenal systems, the release of hormones of the thyroid gland, pancreas and other endocrine glands into the blood.

The consequence of this is hyperfunction of the cardiovascular system and respiratory system, kidneys, liver, other organs and tissues. Manifestations: hypertensive reactions, tachycardia, increased and deepened breathing, redistribution of blood flow in different regions of the vascular bed, release of blood from the depot. Consciousness is not lost during shock. Nervous, mental and motor excitement is usually noted.

The specificity of shock states is revealed, as a rule, only at the initial stage of its development. In the future, the triad of interconnected and simultaneously acting pathogenic factors acquires leading pathogenetic significance: hemodynamic disorders, hypoxia and toxemia.

II. The hemodynamic link of the shock adaptation stage. Violations of hemodynamics during shock are the result of disorders of the heart, changes in the tone of resistive and capacitive vessels, reduction of circulating blood volume, changes in blood viscosity, changes in the activity of factors of the hemostasis system.

1. Disorders of cardiac activity.

Reasons: severe effect on the heart of an extreme factor and cardiotoxic effect of hypercatecholaminemia, high level of hormones of the adrenal cortex and thyroid gland in the blood. Manifestations: significant tachycardia, various disturbances of heart rhythm, reduction of shock and cardiac output, disturbance of central, organ-tissue and microhemocirculation, systemic venous blood stasis, slowing of blood flow in the vessels of the microcirculatory channel, most pronounced in the venules.

2. Change in the tone of resistive and capacitive vessels. Under the influence of a shockogenic factor, the tone of blood vessels initially, as a rule, increases. The main reason is an increase in the activity of the SAS and a significant increase in this connection of the level of KA in the blood. Over a period of time, the increased tone of the walls of resistive vessels (arterioles) contributes to the maintenance of systemic blood pressure. Manifestations: an increase in blood flow (in the arteries of the heart and brain; a simultaneous decrease in blood flow in the vessels of the skin, muscles, organs of the abdominal cavity, kidneys. This phenomenon was called the centralization of blood flow.

Manifestations of shock at the stage of compensation

• *Nervous and endocrine systems*: mental and motor excitement, activation of the sympathoadrenal system, activation of the hypothalamic-pituitary-adrenal system, activation of the thyroid gland, hyperreflexia.

• *Cardiovascular system :*tachycardia, hypertensive reactions, centralization of blood circulation, organ-tissue and microhemocirculation disorders, arrhythmias.

• *Lungs:*tachypnea with the development of hypocapnia.

• *System of blood and hemostasis:* decrease of circulating blood volume, increase of blood viscosity, disorders in the hemostasis system (hypercoagulation-thrombotic state).

• *Liver*: activation of glycogenolysis, reduction of detoxification function.

• *Kidneys:* oliguria, uremia.

Decompensation stage of shock.

The stage of shock decompensation - (irreversible, torpid) – the result of the action of both the extreme factor itself and the progressive insufficiency of the functions of tissues, organs, and their systems, as well as the exhaustion of the body's adaptive capabilities.

In contrast to the stage of shock compensation, the degree and scale of disorders are much more pronounced. Various pathological changes develop simultaneously and potentiate each other. Decompensation of kidneys, lungs, and liver functions is most often observed (syndromes of "shock kidneys", "shock lungs", etc.). Under these conditions, organ failure reaches its limits. This can cause the death of the patient.

1. Neuroendocrine link. Consciousness is not lost during the decompensation stage. At the same time, with a severe course of shock, signs of retardation and confusion of consciousness are noted. This is manifested by the fact that

the patient answers questions with delay and often incoherently, does not always orientate himself in the surrounding environment. The intensity of nervous influences and the level of hormones either decrease or remain at an elevated level. The effects of nervous and hormonal influences are progressively reduced, until they are absent. The combination of these changes leads to an imbalance of both the content of neurotransmitters and hormones in blood plasma and intercellular fluid, as well as their effects. This is the reason for the breakdown of the functional and physical systems of the body, which causes the discoordination and the tendency to minimize the functions of organs and tissues.

2. Hemodynamic link of shock decompensation. At this stage, the hemodynamic link of the pathogenesis of shock is of key importance. Manifestations of shock decompensation: total hypoperfusion of organs and tissues, significant microcirculation disorder, capillary trophic insufficiency. Consequences: DIC syndrome, tissue ischemia, dystrophic due to transformational changes in organs and tissues, tissue necrosis, hemorrhages in them.

3. Hypoxic link. *Reasons:* systemic disorders of hemodynamics, hypoventilation of the lungs, reduction of circulating blood volume, impaired kidney function, metabolic disorders. Consequences: the development of severe hypoxia of the mixed type, uncompensated acidosis. In such conditions, metabolic disorders increase, products of disturbed metabolism accumulate, and the functions of organs and tissues are even more suppressed.

4. Toxemic link of shock decompensation is characterized by an increase in the content in the blood and other biological fluids of the products of disturbed metabolism and physiologically active substances; accumulation in the blood of compounds that are released from damaged and destroyed cells (enzymes, denatured proteins, ions, various inclusions, etc.) and are formed in the body in connection with insufficiency of liver and kidney functions of indoles, phenol, skatole, urea, uric acid and a number of others.

These substances significantly increase organ damage.

5. Metabolic link of shock decompensation characterized by the dominance of the catabolism processes of proteins, lipids, carbohydrates, and their complex compounds; minimizing the intensity of metabolism and plastic processes in cells cells; hyperhydration of cells; accumulation of underoxidized substances in biological fluids; an increase in the level of lipoperoxidation products in the tissues.

6. Cellular link of shock decompensation characterized by: increasing inhibition of enzyme activity and cell vital activity; damage and destruction of membranes; violations of intercellular interactions.

COMATOSIS STATES.

Coma is not an independent disease, it always indicates the development of a severe, often life-threatening condition that requires urgent treatment.The general and main symptom of a comatose state of any origin is a profound loss of consciousness due to damage to vital parts of the brain.

Clasification of unconsciousness, recommended by the Ministry of Health.

- **Clear consciousness**.
- **Stun** – state of limited wakefulness; usually combined with drowsiness: moderate (I), deep (II).
- **Sopor** – a state of reactivity, from which the patient can be brought out only for a short time with intensive repeated stimulation.
- **Coma** – a state of reactivity from which the patient cannot be brought out by stimulation, in a deep coma, even primitive protective reflexes may be absent: moderate (I), deep (II), extramural (III).

Causes of coma

Exogenous factors of coma – pathogenic agents of the environment, as a rule, of extraordinary strength, toxicity and / or destructive nature.

Endogenous factors of coma, which lead to the development of a coma, are the result of severe disorders of the body's vital activity. They are observed during the unfavorable course of various diseases and painful conditions. These conditions lead to significant deviations from the norm of vital parameters and constants, an excess or deficiency of metabolic substrates and/or oxygen in the body.

More than 30 types of coma are described in classifications of coma according to the etiological principle.

Primary cerebral coma

This type of coma is based on inhibition of CNS functions due to primary brain damage: traumatic, epileptic, apoplectic, meningeal, apoplectiform, tumor.

Hypoxic coma(anoxic) – due to suppression of cellular respiration due to insufficient supply of O_2 to tissues or blocking of respiratory enzymes. They are distinguished: hypoxemic coma (associated with insufficient supply of O_2 from the outside), anemic (caused by severe anemia), respiratory (caused by insufficient external breathing), asthmatic (a consequence of an asthmatic condition).

Endocrine coma – coma caused by metabolic disorders due to insufficient synthesis of hormones, their excessive production or overdose of hormonal drugs.

Coma caused by lack of hormones: diabetic (insulin deficiency, which leads to hyperglycemia with plasma hyperosmosis and ketoacidosis, which is also hyperglycemic and ketoacidotic), hypocorticoid (adrenal cortex insufficiency), hypopituitary (reduced pituitary hormone secretion, synonym: pituitary coma), hypothyroid (reduced secretion or disposal of thyroid hormones, synonym: myxedematous coma).

Coma caused by an excess of hormones: *thyrotoxic*(by a sharp increase in the content of thyroid hormones), *hypoglycemic(sharp*decrease in blood glucose).

Toxic coma – comas caused either by the influence of exogenous poison or endogenous intoxication with liver or kidney failure, toxic infections, pancreatitis, various infectious diseases (alcohol, barbiturate, smoking, cholera, eclamptic, hyperosmolar, hyperketonemic, hyperlactacidemic, hepatic, uremic).

Coma associated with the loss of electrolytes, water and energy substances (hunger, hyponatremic, hemolytic, malarial, chlorpenic).

Pathogenesis of comatose states.

The pathogenesis of comatose states, regardless of their causes, includes several common key links. Hypoxia, disruption of the energy supply processes of cells, intoxication, ABS disorders, imbalance of ions and fluids, disruption of electrogenesis, imbalance of BAS content and their effects develop in all organs and tissues. However, to the greatest extent, they are expressed in *brain*, therefore a mandatory sign of coma is loss of consciousness. Damage to other tissues and organs, severe violations of the neuroendocrine regulation of their functions, lead to progressive multi-organ failure and increasing inhibition of the vital activity of the body as a whole.

Manifestations of coma.

1. Hyperthermia.

2. Changes in the skin and mucous membranes. When examining the mucous membranes, you should pay attention to the color, degree of moisture: **yellowness of the sclera is usually found in hepatic coma, anemia. When examining the tongue, the presence of fresh bites and scars from old bites should suggest epilepsy. Uremic coma is characterized by extreme dryness of the tongue. Pronounced edema of the subcutaneous tissue can be detected in uremic and liver worms.**

3. *Peculiarities of breathing* *with different types of coma.* A comatose state is characterized by a violation of the breathing rhythm: large, loud Kussmaul breathing is often observed in diabetic and hepatic coma. With a cerebral coma, snoring, Cheyne-Stokes breathing with a gradual increase and then a weakening of the depth of breathing movements until the appearance of a pause in breathing movements (a period of apnea) usually appears.

4. Determining the smell of the air exhaled by the sick person has important diagnostic value. Uremic coma is characterized by the smell of ammonia, sometimes so strong that it can be detected already upon entering the room where the patient is lying. With a diabetic coma, exhaled air is almost always determined by the smell of acetone, which resembles the smell of a slightly sour apple.

5. *Features of the cardiovascular system.* Great importance is the study of pulse and blood pressure in patients in a coma. Bradycardia with pulse tension and blood pressure is noted in eclampsia, in the initial stages of cerebral coma. High blood pressure is usually found in patients with uremic coma. Diabetic coma is characterized by low blood pressure and tachycardia. The detection of gross neurological symptoms in the form of hemiplegia or hemiparesis indicates an acute violation of cerebral circulation as a cause of coma. High BP values are registered in apoplectic coma. Bradycardia is observed in insects: apoplectic, traumatic, in coma that develops with a brain tumor, AV-blockade, in exotoxic insects associated with poisoning by β-adrenergic blockers, digitalis, in hyperkalemia of various origins.

6. *Organs of vision:* *mydriasis*is observed in coma associated with poisoning with cholinolytics, in asthmatic and alimentary-dystrophic coma;

miosis is characteristic of hyperglycemic (diabetic), uremic coma, coma with morphine and opiate poisoning; anisocoria is observed in destructive coma, apoplectic and traumatic.

7. ***Seizures*** are characteristic for epileptic as well as eclamptic coma.

8. ***Myoclonic twitching of muscles.*** Early tendinous areflexia.

9. ***There is also a vegetative state (apalic syndrome).*** If it lasts more than a month, it is designated as a chronic vegetative state. Usually, this is the result of a large lesion of the brain – the cortex, limbic system, basal nuclei with the preservation of the brain stem. Independent breathing and the function of the cardiovascular system are preserved in patients. Alternating periods of feigned wakefulness and sleep are characteristic. In the absence of motor activity, patients periodically open their eyes, although they are not aware of their surroundings and do not respond to speech stimuli. Recovery in a chronic vegetative state is extremely rare. Higher mental and social functions are irreversible.

Clinical manifestations and course.

Coma can develop suddenly, quickly (within a period of several minutes to 1–3 h) and gradually – within several hours or days (slow development of coma). From a practical point of view, there are certain advantages to the classification, which provides for the allocation of precoma and 4 degrees of severity (stages of development) of the comatose state.

Precoma

✓ Disorder of consciousness is characterized by confusion, moderate stupor.

✓ Inhibition, drowsiness or psychomotor excitement; psychotic conditions are possible (for example, with toxic, hypoglycemic coma).

✓ Purposeful movements are not sufficiently coordinated.

✓ Vegetative functions and somatic status correspond to the nature and severity of the main and accompanying diseases.

✓ All reflexes are preserved (their changes are possible in primary cerebral coma and coma caused by neurotoxic poisons).

Coma of the first degree.

✓ Pronounced stupor, sleep (hibernation), inhibition of reactions to strong stimuli, including painful ones

✓ The patient performs simple movements, can swallow water and liquid food, originals and turns in bed, but contact with him is significantly difficult;

✓ Muscle tone is increased.

✓ The reaction of the pupils to light is preserved, strabismus, pendulum-like movements of the eyeballs are often noted.

✓ Cutaneous reflexes are weakened, tendon reflexes are increased (decreased).

Coma II degree.

✓ Deep sleepsopor.

✓ Contact with the patient is not possible.

✓ Acute weakening of reactions to pain.

✓ Rare spontaneous movements are uncoordinated (chaotic).

✓ Pathological types of breathing are noted (loud, stridorous, Kussmaul, Cheyne-Stokes, etc., more often with a tendency to hyperventilation).

✓ Involuntary urination and defecation are possible.

✓ Pupil reaction to light is sharply weakened, miosis.

✓ Corneal and pharyngeal reflexes are preserved, skin reflexes are absent, pyramidal reflexes are found.

✓ Muscular dystonia, spastic contractions, fibrillation of individual muscles, hormetonia (a change in the sharp tension of the muscles of the limbs by their relaxation and the appearance of early muscle contracture).

Coma III degree (or "atonic").

➢ Consciousness, reaction to pain, corneal reflexes are absent.

➢ Pharyngeal reflexes are depressed.

➢ Miosis, lack of reaction of the pupils to light.

➢ Tendon reflexes and muscle tone are diffusely reduced (periodic local or generalized convulsions are possible).

➢ Urination and defecation are involuntary.

➢ Blood pressure is reduced.

➢ Breathing is arrhythmic, often suppressed to rare, shallow, body temperature is low.

IV degree coma.

- Complete areflexia, atony.
- Mydriasis.
- Hypothermia.
- Profound disturbance of medulla functions with cessation of spontaneous breathing, sharp drop in blood pressure.

Getting out of the comatose state.

✓ Recovery from a comatose state under the influence of treatment is characterized by a gradual recovery of CNS functions, usually in the reverse order of their suppression.

✓ First, corneal, then pupillary reflexes appear, the degree of autonomic disorders decreases.

✓ Recovery of consciousness goes through stages of stupor, confused consciousness, sometimes delusions and hallucinations are noted.

✓ Often, during the period of coming out of a coma, there is a sharp motor restlessness with chaotic, uncoordinated movements against the background of a state of stupor.

✓ Convulsive attacks with subsequent twilight state are possible.

Pathophysiology of modern combat trauma.

In the conditions of wartime, the pathological conditions that quite often accompany the state of war include crunch syndrome, burn and traumatic disease, various types of shock, coma, as well as diseases of the internal organs of the wounded. An important role in the pathogenesis of internal pathology belongs to infection, anemia due to blood loss, changes in the general reactivity of

the body under the influence of harmful effects of the external environment caused by the combat condition (overfatigue, nervous overstrain, cooling, etc.).

Special types of shock during hostilities.

During the war, very common complications of bleeding and injuries are shocks – painful, hypovolemic, tourniquet.

Painful shock – shock states, where the main pathogenetic link is pain (traumatic, burn shock), attention should be paid to the peculiarities of the realization of the feeling of pain, as a type of sensitivity (the main principle of the nocioceptive system, as well as the principle of the natural painkiller (antinocioceptive system). Yes, in pain shock (BS) the erectile stage is clearly distinguished, which is caused by excessive excitation of the central nervous system due to a large number of impulses from the nocioceptive system and the release of a large amount of endogenous adrenaline. The main principle of pathogenetic therapy in this stage of shock is the elimination of pain signaling through the use of narcotic analgesics.

The mechanism of development of the torpid stage of pain shock is associated with excessive activation of the antinociceptive system due to overloading of the CNS with pain impulses. Given that the mediators of the antinociceptive system (enkephalins, endorphins, endomorphins) realize their biological effect by influencing opiate receptors in the brain, under the conditions of their excessive production and release, suppression of breathing and heart activity is possible. Therefore, even in the torpid stage of pain shock, first of all, narcotic analgesics should be used, which on the one hand will reduce the intensity of impulses through the nocioceptive system, and on the other hand will create competition for opiate receptors between natural opiate ligands and synthetic ones.

Hypovolemic shock – there is hemorrhagic shock, which occurs as a result of rapid and massive blood loss and can accompany any gunshot injury. The main link in the pathogenesis of this type of shock is a decrease in BCC, as a result of which the venous return to the heart will decrease sharply, which will lead to a sharp decrease in blood pressure (according to the Frank-String law), loss of consciousness and death of the soldier from hypoxia of the brain. Therefore, the main principle of pathogenetic therapy under the conditions of the development of hypovolemic types of shock is to restore the volume of circulating blood, which, according to the pathogenesis, will restore cardiac activity.

Tourniquet shock is another type of shock that accompanies fighters on the battlefield. It occurs as a result of long-term application of a tourniquet (more than 3 hours). The pathogenesis of this type of shock has several key links:

• loosening of the tourniquet after 3 hours (from application) – there is a sharp activation of the nocioceptive system due to the activation of nociore-ceptors in the affected limb (this is pain shock in pathogenesis).

• prolonged ischemia leads to necrosis of the tissues of the limb and the release of the intracellular medium into the surrounding tissues, which increases further necrosis in the absence of blood flow (the tourniquet is not removed).

• entry of lysosomal proteolytic enzymes into the general circulation as a result of restoration of blood flow after removal of the tourniquet activates the kallikrein-kinin system, which leads to a sharp decrease in blood pressure and leads to the development of shock.

Special types of coma during hostilities. Comatose states are a common phenomenon in wartime. Given that a coma is a pathological condition accompanied by deep disturbances in the central nervous system, loss of consciousness and control over the body's vital functions, knowledge and understanding of the mechanisms of development and the principles of pathogenetic therapy of comatose states is necessary, especially during a state of war.

The reasons for its development in wartime are brain injuries, poisoning by combat poisons, the impossibility of rational therapy of chronic diseases (diabetes mellitus, etc.). The main link in the pathogenesis of comatose states is a violation of the energy supply processes of the brain. Therefore, pathogenetic therapy should be aimed at eliminating the cause of energy deficit and restoring the brain's energy supply. Most often, a traumatic coma occurs as a result of damage (concussion) to the brain after a bullet hits a protective helmet. The reason for the development of energy deficit of brain is thrombotic complications of such an injury, which lead to ischemia. Therefore, timely rational antithrombotic therapy can prevent the development of coma.

Long-term squeezing syndrome, crash syndrome – a pathological condition that arises as a result of long-term and severe mechanical damage to large volumes of muscle tissue with the development of muscle necrosis due to their ischemia in the development of a complex of specific pathological disorders that develops after the release of the wounded from the rubble, where they have been for a long time (for one hour or more) were crushed by heavy debris. The occurrence of STZ is associated with the restoration of blood circulation in damaged and long-term ischemia tissues.

In the conditions of war, the frequency of crash syndrome reaches 5–20 %. Damage to the limbs is noted in injured persons with crash syndrome (> 90 %), because compression of the head and trunk due to damage to internal organs is often fatal.

Pathogenesis of crash syndrome is multi-component and complex.

Recirculation syndrome develops after the restoration of a damaged artery of a long-term ischemic limb or removal of a long-term applied tourniquet. The basis of the pathogenesis of recirculation syndrome is endogenous intoxication by products of tissue ischemia and reperfusion. In squeezed tissues, together with areas of direct traumatic necrosis, zones of ischemia are formed, where acidic products of anaerobic metabolism accumulate.

Tissue reperfusion – restoration of blood and lymph circulation in ischemic tissues after release of the wounded from compression, characterized by increased permeability of capillaries. With:

• *toxic substances*(myoglobin, products of impaired lipid metabolism, potassium, phosphorus, polypeptides, tissue enzymes – histamine, bradykinin,

etc.) enter the general bloodstream, which causes toxic damage to internal organs, primarily the lungs, with the formation of acute respiratory failure (ARF).

• *Hyperkalemia* lead to acute heart failure.

• accumulation of underoxidized products of anaerobic metabolism (lactic acid, etc.) cause pronounced metabolic acidosis.

• large amounts of myoglobin, which is freely filtered in the renal glomeruli, but clogs the renal tubules, forming insoluble hydrochloric acid hematin in conditions of metabolic acidosis.

• *myoglobin*has a toxic effect on the epithelium of the kidney tubules, which leads to myoglobinuric nephrosis and acute renal failure.

• Rapidly developing postischemic edema of damaged and long-term compressed tissues causes acute hypovolemia with hemoconcentration (circulating blood volume decreases by ≥ 20–40 %), which is accompanied by clinical shock and contributes to the deterioration of kidney function.

The classification of STZ, depending on the prevalence and duration of tissue compression, involves the allocation of three degrees of severity of the course of the syndrome.

Recirculation syndrome of a light degree develops with a relatively small area and duration of compression (for example, compression of the forearm for 2–3 hours). Endogenous intoxication may be insignificant, oliguria regresses after a few days. The prognosis for recirculation syndrome of a mild degree with proper treatment is favorable.

Recirculation syndrome of medium degree develops with larger areas of extremity crushing for up to 6 hours. It is accompanied by endotoxicosis and kidney dysfunction within a week or more after the injury. The prognosis of recirculation syndrome of moderate severity is determined by the timeliness and quality of first aid, as well as further treatment with early application of extracorporeal detoxification.

Recirculation syndrome of a severe degree develops when crushing one or two limbs for more than 6 hours. With severe recirculation syndrome, endogenous intoxication rapidly increases, acute renal failure, multiple organ failure and other life-threatening complications develop. In the absence of timely intensive treatment using hemodialysis, the prognosis is unfavorable.

Factors involved in the development of recirculation syndrome : pain syndrome; plasma loss; toxemia

➢ ***Pain syndrome***. Prolonged pain causes complex pathological reactions both in the body of the victim as a whole and in the affected limb. This leads to spasm of blood vessels, which, in turn, causes disruption of tissue nutrition.

➢ ***Loss of plasma.*** It develops after removing the pressure of the limb and grows as the swelling increases, the liquid part of the blood comes out, and its coagulation increases.

➢ ***Toxemia***. It occurs when the breakdown products of damaged tissues enter the blood, the electrolyte composition of the blood is disturbed and the number of inflammatory enzymes increases.

3 periods are distinguished during r*ecirculation syndrome*: early, intermediate and late.

The early period of recirculation syndrome – these are the first 3 days after the injury. After the release of the limb, elimination of compression, the victim's condition improves, pain in the injured limb, restriction of movement in it are disturbing. A few hours after the release, swelling of the limb is formed, it becomes dense like a tree, bubbles with a bloody liquid appear in the places of greatest compression. Pulsation of the vessels of the limb is weakened. The extremity becomes cold to the touch, its sensitivity decreases. The general condition of the patient also worsens. Blood pressure decreases, excitement is replaced by lethargy, inhibition, the skin is gray-earthy, covered with cold, sticky sweat. Hypothermia. Excretory function of the kidneys suffers, signs of blood clotting appear. During this period, in the absence of adequate treatment, the victim may die within 1–2 days.

Intermediate period of recirculation syndrome begins to develop from the 3rd day after the injury. Signs of kidney failure develop slowly. The general condition worsens, dead skin and soft tissues begin to detach in the places of greatest compression, muscle tissue protrudes in the wound, which has the characteristic color of boiled meat. After the stage of relative stabilization of the condition, after 1–2 days, signs of kidney failure begin to increase, and by the 5–6th day, a uremic syndrome develops, the potassium content in the blood increases, which leads to interruptions in the work of the heart, bradycardia. By the 5–7th day, signs of pulmonary insufficiency appear. Within 2–3 weeks, the condition of the kidneys and changes in the blood are restored.

The late period of recirculation syndrome occurs in 1 month after the injury, it corresponds to the period of cessation of acute renal failure. The victim's condition is improving, body temperature is normalizing. Swelling and pain in the limb pass. Dead muscle tissue is replaced by connective tissue, which causes muscle atrophy. But purulent complications in the wound may also occur.

Traumatic disease (TD) is a set of general and local changes, pathological and adaptive reactions that occur in the body in the period from the moment of mechanical injury to its result.

***The reason for the development of* TD** – mechanical impact. In victims with the lightest injuries, TD does not have characteristic periods, phases and complications. Clinical experience allows us to distinguish individual uncomplicated fractures as mainly local suffering, sometimes accompanied by a transient acute reaction, and more significant damage causing TD. Such a distinction is quite conditional, since even so-called minor injuries can cause disruption of the vital activity of the body as a whole.

Morphological substrate of TD is damage to organs and tissues, differing in localization and nature, arising from excessive mechanical impact. The release of BAS, in particular proteolytic enzymes and biogenic amines, causes secondary damage to the functional elements of organs and tissues.

In the basis of the pathogenesis of TD lies a combination of various pathological processes, "damage reactions" and "defense reactions". Adaptive

reactions are aimed at ensuring the vital activity of the organism in extreme conditions with subsequent restoration of impaired functions and structures.

Three periods are conventionally distinguished, characteristic of all severe mechanical damage, regardless of the specific manifestations of injuries of different localizations:

- acute period
- the period of the developed clinical picture,
- rehabilitation period.

The development of all periods of the traumatic disease in each victim is absolutely optional.

First period (acute – characterizes the course of the disease from the moment of exposure to the damaging agent to the stable stabilization of vital functions. Three phases are conventionally distinguished:

- the phase of instability of vital functions,
- the phase of relative stabilization of vital functions,
- the phase of stable stabilization of vital functions.

The duration of the first phase is several hours, the moment of its end coincides with the completion of resuscitation measures. The main phase of the first period is the second. Its content is determined by the detailed clinical picture of traumatic shock or blood loss against the background of hemodynamic instability, provided that the anatomical integrity of the damaged organs and systems is restored. The first period of TD ends with a stable stabilization of the body's vital functions. The duration of the first period is up to 2 days. Even during this period, with a rather severe injury or lack of adequate treatment, a fatal outcome can occur. The clinical picture is dominated by general manifestations of the main pathological processes characteristic of this period: traumatic shock, acute blood loss, traumatic toxicosis, processes associated with primary organ damage.

The second period (the period of the developed clinical picture) – conditionally divided into phases: catabolic, anabolic (early stage, late stage).

The catabolic phase is characterized by lysis and subsequent evacuation of necrotized tissues. In the anabolic phase, plastic remodeling is carried out in two stages, which are based on proliferative processes and scarring, respectively. In the clinical picture of the disease, following the short-term predominance of local factors, manifestations of a general nature begin to dominate again, mechanisms of delayed adaptation are activated.

By the end of the early stage of the anabolic phase, there is a relative normalization of the state of the circulatory, respiratory, blood, etc. systems. This period is characterized by suppression of immunological reactivity, which leads to the development of purulent-inflammatory complications.

The late stage of the anabolic phase is characterized by the completion of plastic remodeling, which consists in the fibrosis of the granulation tissue, the formation of a scar and its epithelization. The end of the local process coincides with the end of anabolic processes. Dystrophic and sclerotic pro-

cesses develop in damaged organs. The same processes are observed in areas of pronounced hypocirculation, which persist for a long time in the acute period of TD. The duration of the stage is from several weeks to several months and even years. Disturbances in the function of various organs and systems, as well as complications, are characteristic.

The third period (rehabilitation) is characterized by physical and social, complete or incomplete recovery. The duration of the period can be many months and years, it is characterized by the transition of pathological processes that developed in previous periods into pathological states – contractures, shortening of limbs, sclerotic changes of the myocardium, which cause chronic insufficiency of blood circulation, etc.

Setting up the experiment. Discussion of results and formulation of conclusions.

1. Study of microcirculation disorders and heart rhythm during reproduction of hemorrhagic collapse.

1. The rat is previously anesthetized by intraperitoneal injection of hexenal at a dose of 10 mg/kg.
2. The rat is fixed in a supine position on a table with an opening (viewing window).
3. The abdominal cavity of the rat is opened on the lateral surface of the abdomen.
4. The small intestine is pulled out and the mesentery is fan-shaped above the inspection window (by pricking the intestine with pins).
5. Microcirculation vessels are looked for under the minimum magnification of the microscope and the movement of blood in the initial state is observed.
6. At the same time, the electrodes of the electrocardioscope vector are placed on the paws of the rat in standard leads and the nature of cardiac activity according to the data of the electrocardiogram (ECG) is observed on the oscilloscope screen.
7. Then the femoral artery is opened with scissors and acute blood loss is caused (blood loss is determined by the difference in the weight of the napkins that drain the place where the femoral artery is crossed).
8. Violations of hemodynamics in microvessels are observed.
9. At the same time, we register ECG changes on the oscilloscope.
10. The data are entered into the protocol and analyzed.

Discussion of the results of the experiment.

Collapse is a general condition that occurs as a result of a significant discrepancy in the circulating blood volume capacity of the vascular bed and is characterized by insufficient blood circulation, primary circulatory hypoxia, a disorder of the functions of tissues, organs and their systems. The direct cause of the collapse is the rapid development of a significant excess of the capacity of the vascular bed in comparison with circulating blood volume.

Hypovolemic collapse – collapse that develops when the circulating blood volume decreases due to: acute massive bleeding; rapid and significant

dehydration of the body; loss of a large volume of blood plasma; redistribution of blood with deposition of a significant amount of it in venous vessels (shock).

Posthemorrhagic collapse – one of the types of hypovolemic collapse. The initial pathogenetic factor is a rapid and significant decrease in circulating blood volume (hypovolemia). The increase in vascular tone does not eliminate the discrepancy in their capacity, which significantly decreased circulating blood volume. As a result, hypoperfusion of organs and tissues develops, which leads to the development of first circulatory, and then mixed (hemic, tissue) hypoxia. The consequence of hypoxia is a progressive disorder of the functions of the central nervous system, lungs, kidneys, etc., which led to the cessation of cardiac activity and the death of the animal.

Formulation of conclusions from the experiment.

1. In the experiment, after acute blood loss, a rat developed signs of a microcirculation disorder (slowing down of blood flow, pendulum-like oscillation, stasis in individual microcirculation vessels) and at the same time rhythm disturbances were registered on the ECG (at first tachycardia, then bradycardia and fibrillation followed by cardiac arrest).
2. All the mentioned violations indicated the development of posthemorrhagic (from etiology) hypovolemic (from pathogenesis).
3. Disturbance of the cardiac system function is the initial and main pathogenetic link of collapse and is characterized by inadequate blood supply to organs and tissues.

Tasks for independent work on the topic "Pathophysiology of extreme conditions: collapse, shock, coma. Pathophysiology of modern warfare injuries".

List of questions and works to be studied:

1. Extreme conditions. Similarities and differences of extreme and terminal states.
2. Etiology and pathogenesis of extreme conditions.
3. Collapse. Risk factors. Types. Reasons.
4. Peculiarities of the pathogenesis of various types of collapse.
5. General manifestations of collapse.
6. Shock. Reasons. Risk factors. Types of shock.
7. Pathogenesis and stages of shock. Clinical manifestations of shock
8. Coma. Changes and suppression of consciousness.
9. Causes of coma.
10. Classification of commas.
11. Pathogenesis of comatose states.
12. Clinical manifestations, course and exit from comatose states (hepatic, uremic, diabetic).
13. Principles of treatment of extreme conditions
14. Definition, classification, pathogenesis of traumatic disease, burn disease, trench syndrome; basic principles of their treatment.

List of practical skills that need to be explained:

1. Concepts of "extreme states", "terminal state"; their criteria.
2. Collapse: definition, classification, etiology, pathogenesis, clinical manifestations.
3. Shock: definition, classification, etiology, pathogenesis, clinical manifestations.
4. Coma: definition, classification, etiology, pathogenesis, clinical manifestations.
5. Etiology and pathogenesis of uremia, hepatic, hypoglycemic and diabetic tumors.

List of practical skills that must be mastered:

5. Define the concept of "extreme states" and differentiate their individual types – collapse, shock, coma;
6. Explain the causes, conditions and mechanisms of the development of collapse, shock, coma, in order to develop in clinical practice the ability to give a correct assessment of these phenomena.
7. Violations of hemodynamics and microcirculation in the pathogenesis of shock states.
8. Be able to explain the etiology and pathogenesis of various comas (hepatic, uremic, diabetic).

Situational tasks KROK-1 to determine the final level of knowledge

1. Patient with diabetes didn't get insulin injection in time that caused hyperglycemic coma (glucose in the blood 50 mmol/L). What mechanism is prevalent in the development of the coma?

A. Hyperosmia. *C. Hypoxia.* *E. Acidosis.*
B. Hypokaliemia. *D. Hyponatremia.*

2. A 12-year-old teenager has significantly put off weight within 3 months; glucose concentration rose up to 50 millimole/l. He fell into a coma. What is the main mechanism of its development?

A. Hyperosmolar. *C. Ketonemic.* *E. Hypoxic.*
B. Hypoglycemic. *D. Lactacidemic.*

3. An experimental rat got intra-abdominal injection of 10 ml of 40 % glucose solution. 60 minutes later the rat passed into a comatose state as a result of dehydratation. What is the mechanism of development of this state?

A. Rise of osmotic pressure of extracellular fluid.
B. Rise of oncotic pressure of extracellular fluid.
C. Reduction of vasopressin secretion.
D. Loss of salts and water.
E. Acid-base disbalance.

4. An unconscious patient had been delivered to a hospital by the ambulance. Objectively: absent reflexes, occasional convulsions, irregular breathing. After a laboratory examination he was diagnosed with hepatic coma. What metabolite accumulation is essential for the development of the central nervous system disorders?

A. Ammonia. *B. Urea.* *C. Glutamine.* *D. Bilirubin.* *E. Histamine.*

5. A 62-year-old patient has been hospitalized due to massive cerebral hemorrhage. Blood pressure is 70/30 mm Hg, heart rate is 120/min., respiratory rate is 4/min., unconscious, no response to external stimuli. Such condition can be determined as:

A. Collapse. B. Coma. C. Shock. D. Agony. E. Stress.

6. A patient with jaundice has high total bilirubin that is mainly indirect (unconjugated), high concentration of stercobilin in the feces and urine. The level of direct (conjugated) bilirubin in the blood plasma is normal.
What type of jaundice can be suspected ?

A. Gilbert's disease. C. Neonatal. E. Hemolytic.
B. Parenchymal (hepatic). D. Mechanical.

7. A patient complaining of pain in the left shoulder-blade region has been diagnosed with miocardial infarction. What kind of pain does the patient have?

A. Phantom. B. Visceral. C. Protopathic. D. Radiating. E. Epicritic.

8. On examination the patient presents with hirsutism, moon-shaped face, stretch marks on the abdomen. BP is 190\100 mm Hg, blood glucose is 17.6 mmol\l. What pathology is such clinical presentation characteristic of?

A. Hypothyroidism.
B. Hyperthyroidism.
C. Adrenocortical hyperfunction.
D. Hyperfunction of the insular apparatus.
E. Gonadal hypofunction.

9. A 38-year-old man, who has been suffering from systemic lupus erythematosus for 3 years, developed diffuse renal lesions accompanied by massive edemas, marked proteinuria, hyperlipidemia, and dysproteinemia. What is the most likely mechanism of proteinuria develoment in this case?

A. Morbid affection of the urinary tracts.
B. Ischemic damage to the tubules.
C. Autoimmune damage to the nephrons.
D. Inflammatory damage to the nephrons.
E. Increased blood proteins.

10. A 50-year-old inpatient during examination presents with glucosuria and blood glucose of 3,0 mmol/l, which are the most likely to be caused by:

A. Renal disorder. C. Pellagra. E. Essential hypertension.
B. Myxedema. D. Diabetes insipidus.

11. A 46-year-old woman suffering from cholelithiasis developed jaundice. Her urine became dark yellow, while feces are light – color. What substance will be the most increased in concentration in the blood serum in this case?

A. Conjugated bflirubin. C. Urobilinogen. E. Unconjugated bih'rubin.
B. Mesobilirubin. D. Biliverdine.

12. A 38-year-old man, who has been suffering from systemic lupus erythematosus for 3 years, developed diffuse renal lesions accompanied by massive edemas, marked proteinuria, hyperlipidemia, and dysproteinemia. What is the most likely mechanism of proteinuria develoment in this case?

A. Autoimmune damage to the nephrons.
B. Ischemic damage to the tubules.

C. Morbid affection of the urinary tracts.
D. Inflammatory damage to the nephrons.
E. Increased blood proteins.

13. A patient suffers from posttraumatic hemorrhage that resulted in development of hemorrhagic shock. What volume of circulating blood was lost by the patient?

A. 25–40 %. B. 40–50 %. C. 50–75 %. D. 12–25 %. E. 3–20 %.

14. On examination the patient presents with hirsutism, moon-shaped face, stretch marks on the abdomen. BP is 190/100 mm Hg, blood glucose is 17.6 mmol/L. What pathology is such clinical presentation characteristic of?

A. Adrenocortical hyperfunction.
B. Gonadal hypofunction.
C. Hyperfunction of the insular apparatus.
D. Hyperthyroidism.
E. Hypothyroidism.

15. A victim of a traffic accident was received by the intensive care unit. The patient is in a grave condition that can be characterized as a severe pathologic process that leads to exhaustion of vital functions and puts the patient into the marginal state between life and death due to critical reduction of capillary circulation in the affected organs. The patient is in the state of:

A. Shock. B. Collapse. C. Preagony. D. Coma. E. Agony.

16. During removal of the hyperplastic thyroid gland of a 47-year-old woman, the parathyroid gland was damaged. One month after the surgery the patient developed signs of hypoparathyroidism: frequent convulsions, hyperreflexia, laryngospasm. What is the most likely cause of the patient's condition?

A. Hypocalcemia. *C. Hyperchlorhydria.* *E. Hyperkalemia.*
B. Hyponatremia. *D. Hypophosphatemia.*

17. On clinical examination a woman presents with excessive sweating, tachycardia, loss of weight, and tremor. What endocrine pathology can cause these sings?

A. Hyperthyroidism. *C. Hypoaldosteronism.* *E. Hypogonadism.*
B. Hypergonadism. *D. Hypothyroidism.*

18. A patient with Cushing syndrome presents with persistent hyperglycemia and glycosuria. This patient is likely to have increased production and secretion of the following hormone:

A. Glucagon. B. Aldosteron. C. Adrenalin. D. Cortisol. E. Thyroxine.

19. A 50-year-old man, who has been suffering from chronic hepatic failure for years, developed ascites. What is the main mechanism of development of this new disorder in the patient?

A. Decreased hepatic synthesis of albumins and globulins.
B. Increased pressure in the portal venous system.
C. Increased oncotic blood pressure.
D. Appearance of necrotoxin substances in blood.
E. Increased blood levels of low density and very low density lipoproteins.

20. The doctor started the absence of respiration and cardiac activity in a traffic accident victim. This condition lasts for 1 minute already. This clinical presentation corresponds with the following terminal state:

A. Traumatic shock, torpid phase.
B. Clinical death.
C. Agony.
D. Traumatic shock, erectile phase.
E. Preagony.

Standards of correct answers to the task КROK-1

1	2	3	4	5	6	7	8	9	10	11	12
A	*A*	*A*	*A*	*B*	*E*	*D*	*C*	*C*	*D*	*A*	*A*

13	14	15	16	17	18	19	20				
A	*A*	*A*	*A*	*A*	*D*	*B*	*B*				

Recommendations for registration of work results

1. Written answer to test tasks (initial level of knowledge).
2. The results of the experiment are drawn up in the form of an experiment protocol with the determination of relevant conclusions.
3. Protocol for the study of the results of the patient's clinical blood analysis.
4. Protocol for solving situational tasks with an explanation of the correct answers.

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Subject plan

Навчальне видання

PATHOPHYSIOLOGY OF ORGANS AND SYSTEMS

Методичні вказівки
для практичних занять з підготовки іноземних студентів
(спеціальність «Медицина» та «Стоматологія»)

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Формат А5. Ум. друк. арк. 13,4. Зам. № 23-34336.

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Свідоцтво про внесення суб'єкта видавничої справи до Державного реєстру видавництв, виготівників і розповсюджувачів видавничої продукції серії ДК № 3242 від 18.07.2008 р.