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EXPERIMENTAL PATHOPHYSIOLOGY

GUIDE FOR PRACTICAL CLASSES IN GENERAL PATHOPHYSIOLOGY

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CONTENT

LIST OF ACRONYMS

Ab – antibody
ACO – average cardiac output
ADCC – antibody-dependent cell-mediated cytotoxicity
Ag – antigen
AP – arterial pressure
ASV – poorly regulated ventilation
BAS – biological active substances
BB – basic basis
BP – blood pressure
BR – breathing rate
CO – cardiac output
2,3, DPG – 2,3 diphosphoglycerate
ECF – extracellular fluid
ICF – intracellular fluid
GABA – gamma-aminobutyric acid
GSB – general circulating blood
HR – heart rate
LPO – lipid peroxidation
SV – stroke volume
TAC – tricarboxylic acids cycle
TPR – total peripheral resistance
TCA – tricarboxylic acid cycle

INTRODUCTORY LESSON

The purpose of the practical class: To argue the fundamental role of the subject in the formation of medical thinking. To learn the principles of differentiation of pathological and protective-adaptive reactions. To study the basics of modeling and experimental therapy of pathological processes.

The student should know:

1. Subject and tasks of pathological physiology. Its place among the other medical sciences, importance for the clinic (table 1).

2. Main compartments of pathological physiology: general nosology, typical pathological processes, pathological physiology of the body systems. Their characteristics.

3. Basic stages of pathophysiology history. The leading role of scientists in the development of pathological physiology.

4. Methods of pathophysiology. The significance of the experiment. General principles of modeling of biomedical experiments and interpreting their results. Moral and ethical aspects of animal experimentation.

5. Basic concepts of general nosology. Normal state, health, pre-illness, disease.

6. Disease as a dialectical unity of damage and protective-adaptive reactions of the organism. Stages of the disease. Outcomes. Complete and incomplete convalescence.

PRACTICAL WORK

Experiment 1. Breathing and arterial blood pressure disorders within the experimental plethora (hypervolemia)

The experimental animal (rabbit) is fixed on the surgery table. Under the local anesthesia an incision of skin on the median line of the thigh is made and the femoral artery is taken off. After this it is canullated and tied. On the peripheral ends of the vessels the ligatures are applied to avoid bleeding. The initial values of arterial blood pressure and breathing rate are recorded on kymograph tape. 20 ml of physiological isotonic solution are introduced into the vein of the ear and are accompanied with monitoring of arterial blood pressure and breathing disorders.

The student should be able to analyse the observed disorders and adaptive-compensatory mechanisms oriented to reestablish normal blood volume.

Experiment 2. Breathing and arterial blood pressure disorders due to painful excitation

After recording the initial values of arterial blood pressure and breathing rate, the same animal is induced a painful shock. The rabbit tail is compressed tightly with forceps. The modeled experiment results in disorders of arterial blood pressure and breathing rate.

The student should be able to describe the pathogenic mechanisms of the observed disorders.

Experiment 3. Breathing and arterial blood pressure disorders within intake of exogenous adrenaline.

To prove the adrenergic component involvement in the mechanism responsible for high arterial blood pressure due to painful excitation, the following experiment is done. After recording the initial values of arterial blood pressure and breathing rate, in the marginal vein of the same rabbit 1:10 000 solution of adrenaline is administered. This is followed the deviations of arterial blood pressure and breathing rate and the mechanisms of the followed disorders and adaptive-compensatory reactions in similar diseases are analyzed.

The student should be able to describe the pathogenic mechanisms of the observed disorders.

Table 1

SECTIONS OF PATHOPHYSIOLOGY AND ITS TASKS

I. GENERAL NOSOLOGY
1. The essence of the disease
2. Pre-illness
3. Mechanisms of appearance, development, and outcomes of the diseases
4.1. Pathological process
4.2. Pathological reaction
4.3. Pathological state
5. Nomenclature and classification of the diseases
6. Etiology
6.1. Classification of the disease factors:
1) mechanical 4) biological 2) physical 5) social 3) chemical
6.2. Conditions for the disease occurrence:

6.2.1. External
a) unfavorable climatic and geographic factors b) malnutrition
c) overwork d) physical inactivity e) bad habits
6.2.2. Internal
a) hereditary predisposition b) constitution
c) hyperergia d) hypergia e) dysergia

7. Pathogenesis

7.1. Mechanisms of damages
a) cause-effect relations
b) leading link
c) vicious circle
d) specific and non-specific
e) local and general
f) structure and function

7.2. Protective-adaptive mechanisms:
a) emergent
b) delayed

II. TYPICAL PATHOLOGICAL PROCESSES

1. Adaptation and stress 2. Cellular lesions
3. Local microcirculatory disorders
4. Inflammation 5. Fever 6. Immunopathology
7. Disorders of metabolic processes (carbohydrates, protein, lipids, acid-base, water-electrolytes) 8. Hypoxia 9. Extreme states
10. Tumor growth

III. TYPICAL DISORDERS OF ORGANS AND SYSTEMS

1. Nervous disorders
2. Endocrine disorders
3. Cardio-vascular disorders
4. Blood disorders
5. Hemostasis disorders
6. External breathing disorders
7. Kidneys disorders
8. Liver disorders
9. Gastro-intestinal disorders

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ETIOLOGY AND PATHOGENESIS. THE ROLE OF REACTIVITY IN PATHOLOGY

The purpose of the practical class: To understand the basic mechanisms of specific reactivity of the organism. To be able to explain the influence of endogenous and endogenous factors on reactivity; evaluate reactivity and resistance of the organism according to clinical and laboratory researches (nervous system state, non-specific barriers, hormonal background, immune system and others).

Basic questions the student should know:

1. Factors that ensure the integrity of the organism. Barriers of the external and internal environment of the organism (skin, mucous membranes, histohematological and blood-brain barriers) and their physical-chemical and physiological features.
2. Immunity, its types. Immunocompetent cells, their cooperation in the immune response. Neurohumoral regulation of immune response. Immunity as a regulatory system. Immune systems of different organs.
3. Protective reflexes. Protective behavior of animals and humans. Functional system to ensure the integrity of the body tissues.
4. Resistance. Notion of cross-resistance and sensitization.

The student should know:

1. Notion of etiology. The role of causes and conditions in the occurrence of diseases.
2. Injury as the initial link of pathogenesis. Injury levels: submolecular, molecular, subcelullar, cellular, organ-tissue, systemic, whole organism. Injuries manifestations at the different levels of the organism.
3. Cause-effect relationships in pathogenesis. Primary and secondary injuries.
4. Localization and generalization of injuries. Local and general reactions to injuries, their interrelations.
5. Reactivity and resistance. Definition. Notion.
6. Types, forms of reactivity, their features.
7. Factors determining reactivity: role of genotype, age, gender, constitution.

8. The importance of anatomical and physiological systems (nervous, endocrine, immune and others), their functional state and specific features of metabolism in the mechanisms of reactivity formation.

9. Indicators of reactivity, their features.

10. Influence of environmental factors on the reactivity of the organism. Features of human reactivity; the role of social and environmental factors.

11. Pathological reactivity. Definition of the concept. Features.

12. Directed change of individual and group reactivity as the most important means of disease prevention and therapy.

PRACTICAL WORK

Experiment 1. Pathogenic action of low atmospheric pressure

A rat is placed under the glass bell of Komovsky apparatus connected to a barometer. Initially the breathing rate is recorded. The volume of the abdomen, color of the mucous and skin are recorded. Using the Komovsky pump, atmospheric pressure is progressively reduced to the simulated level of (0.8-(–1) atmospheres). Hypobaria is accompanied by hypoxia. As the atmospheric pressure decreases, adaptive reactions cannot ensure the normal development of metabolic processes. The animal exhibits dyspnea, cyanosis of skin and mucous membranes, increased HR and BR, neuromuscular excitability, flatulence. The death of the animal can be preceded by generalized seizures. The responsible factors for triggering the death are hypobaria and hypoxia, which lead to an increased rate of oxygen consumption related to the increased activity of muscles.

Make conclusions, answering the following question:

1. What is the direct cause of pathological processes with the death outcome: low partial pressure of O_2 in the inspired air or low atmospheric pressure?

Experiment 2. Pathogenic action of exogenous normobaric hypoxia in laboratory animals

A mouse is placed in a glass jar, which is closed hermetically. On the bottom of the bowl there is CaCO3, that absorbs O_2. Initially the HR and BR are recorded followed by the record of the volume of the abdomen, color of the mucous and skin. After a short time of normobaric hypoxia the mouse has a pale skin and compensatory increase in the HR and BR. Long-term normobaric hypoxia causes the death of the mouse due to hypoxemia and systemic hypoxia due to exhaustation of the compensatory mechanisms.

Make conclusions, answering the following questions:

1. What is the direct cause of pathological processes with the death – exogenous normobaric hypoxia?
2. What kinds of metabolic disorders occur due to deficiency of O_2?

Experiment 3. Pathogenic action of hypobaric hypoxia via different endogenous conditions in laboratory animals

The experiment is modeled in two rats of the same age and the weight of 120-150 g. Rat I is given 0.3 ml of caffeine solution intraperitoneally to trigger excitation of the CNS. Rat II is given 1 ml of chloral hydrate to inhibit the CNS activity. Both rats are placed in the terrarium under hypobaric hypoxic conditions and their behavior is monitored. Rat I with caffeine administration is more active than Rat II. In both rats the HR, BR and rate of metabolic processes are increased due to compensatory reactions.

Make conclusions, answering the following question:

1. What are the direct causes of pathological processes- low partial pressure of O_2 in the inspired air or low atmospheric pressure via different endogenous conditions?

Experiment 4. Pathogenic action of hypobaric hypoxia on the reactivity in laboratory animals depending on the age

The experiment is modeled in two rats: a newborn and an adult. Both of them are placed under the glass bell of Komovsky apparatus connected to a barometer. Initially the breathing rate is recorded followed by the record of volume of the abdomen, color of the mucous and skin. Using the Komovski pump, atmospheric pressure is progressively reduced to the simulated level of (0.8-(-1) atmospheres). Hypobaria is accompanied by hypoxia. Both rats become excited, but first seizures develop in the adult rat. The animal rests under supervision.

Make conclusions, answering the following questions:

1. What are the direct causes of such a pathological process as hypobaric hypoxia depending on the age?

TESTS FOR KHOWLEDGE CONTROL IN SELF-TRAINING

1. What are the manifestations of biological (specific) reactivity?

1) seasonal anabiosis;
2) zoonoses;
3) inflammation;
4) allergy;
5) anthroponoses;
6) seasonal migration of animals.

2. What are the systems which determine the reactivity?

1) immune;
2) cardiovascular;
3) nervous;
4) blood;
5) endocrine;
6) excretory,
7) non-specific barriers.

3. What are the indices of reactivity that characterize the state of the nervous system?

1) chronaxy;
2) complement titer;
3) ratio of hormones ACTH/STH;
4) speed and force of unconditioned reflexes;
5) concentration of pituitary hormones;
6) speed and force of conditioned reflexes;
7) excitability;
8) concentration of pyrogens into the blood.

4. What are the indices of reactivity that characterize the state of endocrine system?

1) concentration of hormones into the blood;
2) excitability;
3) concentration of hormones into the urine;
4) number of receptors to hormones on target cells;
5) concentration of pyrogens into the blood;
6) ratio of hormones ACTH/STH;
7) complement titer.

5. What are the indices of reactivity that characterize the state of the immune system?

1) number of lymphocytes;
2) ratio of hormones ACTH/STH;
3) number and ratio of populations and subpopulations of lymphocytes;
4) concentration of pyrogens into the blood;
5) bactericidal properties of the skin;
6) Ig concentration;
7) activity of blast transformation reaction with mitogens.

6. The indices of reactivity that do not characterize the state of non-specific barriers are:

1) Ig concentration;
2) bactericidal properties of the skin;
3) composition and acidity of gastric juice;
4) concentration of lysozyme in biological fluids;
5) phagocytic activity of neutrophils.

7. What are the manifestations of non-specific physiological reactivity?

1) shock;
2) coma;
3) seasonal anabiosis;
4) immunity;
5) allergy;
6) seasonal disorders of organs and systems functions.

8. What are the manifestations of specific physiological reactivity?

1) shock;
2) coma;
3) immunodeficiency;
4) seasonal anabiosis;
5) congenital immunity;
6) acquired immunity;
7) allergy.

9. What are the manifestations of increased specific pathological reactivity?

1) allergy of humoral type;
2) immunity;
3) shock;
4) immunodeficiency;
5) immunosuppression;
6) coma;
7) allergy of cellular type.

10. What are the manifestations of decreased specific pathological reactivity?

1) allergy of humoral type;
2) immunity;
3) shock;
4) immunodeficiency;

5) immunosuppression;
6) allergy of cellular type;
7) coma;
8) anabiosis.

11. When does secondary damage occur?
1) normoergic reaction;
2) hyperergic reaction;
3) hypergias;
4) anergic reaction;
5) dysergia.

ANSWER KEYS:

1.	1, 2, 5, 6	**5.**	1, 3, 6, 7	**9.**	1, 7
2.	1, 3, 5, 7	**6.**	1	**10.**	4, 5
3.	1, 4, 6	**7.**	3, 6, 7	**11.**	2, 5
4.	1, 3, 4, 6	**8.**	5, 6		

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CELLULAR INJURY AND DEATH

The purpose of the practical class: To explain the basic mechanisms of cellular injury and death.

The student should know:

1. To identify the causes of cellular injury.
2. To describe three types of reversible cell changes that can occur with cell injury.
3. To define free radical and reactive oxygen species.
4. To relate oxidative stress to cell injury and death.
5. To describe cell changes that occur within ischemic and hypoxic cell injury.
6. To state the effects of impaired calcium homeostasis to cell injury and death.
7. To differentiate cell death associated with necrosis and apoptosis.
8. To relate local and systemic outcomes of cellular injury and death. To identify the indices of cellular injuries: hyperpotassemia, cytokinemia, enzymemia and organic or tissue specific biomarchers.

TESTS FOR KHOWLEDGE CONTROL IN SELF-TRAINING

1. What is the effect of ATP depletion?

1) increased protein synthesis;
2) decreased protein synthesis;
3) intracellular acidosis;
4) extracellular acidosis;
5) intracellular alkalosis.

2. What intracellular enzymes are activated by increased calcium in the cytoplasm?

1) ATP-ases;
2) Krebs cycle enzymes;
3) glycolytic enzymes;
4) glucose-6-phosphatase;
5) proteases.

3. What is the effect of increased sodium level in the cell hyaloplasm?

1) cell membrane depolarization;
2) cell membrane hyperpolarization;
3) reduced intracellular pH;
4) intracellular hypoosmolarity;
5) increased intracellular pH.

4. What pathological processes lead to generation of reactive oxygen species?

1) hypoxia;
2) arterial hyperemia;
3) hyperthermia;
4) hypothermia;
5) ionizing radiation.

5. What is the effect of K+ ions efflux?

1) inhibition of resting membrane potential;
2) hyperpolarization of cytoplasmatic membrane;
3) inhibition of active membrane potential;
4) hypernatremia;
5) activation of resting membrane potential.

6. How is apoptosis manifested in the initial period?

1) nucleus condensation;
2) cell membrane disintegration;
3) mitochondria disintegration;
4) karyorrhexis,
5) intercellular communication structures disorganization.

7. How is apoptosis manifested in the execution phase?

1) nucleus condensation;
2) nuclear structural proteins destruction;
3) cell membrane disintegration;
4) cytoskeleton proteins destruction;
5) nuclear regulatory proteins destruction.

8. What are the manifestations of reversible cellular injury?

1) cellular swelling,
2) decreased intracellular sodium;
3) fatty infiltration;
4) kariolysis;
5) non-selective permeability.

ANSWER KEYS:

1. 2, 3 **2.** 1, 5 **3.** 1, 3 **4.** 1, 5 **5.** 1 **6.** 1, 5 **7.** 2, 4, 5 **8.** 1, 3

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2. Carol Matson Porth, Glenn Matfin. Pathophysiology. Concepts of Altered Health States (eighth edition), 2011, p. 94.

DISORDERS OF LOCAL MICROCIRCULATION

The purpose of the practical class: To be able to differentiate the forms of local microcirculation disorders due to external manifestations and features of blood flow into the blood vessels and to identify the mechanisms of their development and consequences.

Basic questions the student should know:

1. Central and peripheral circulation control mechanisms, in particular neuroendocrine regulation of microcirculation.

The student should know:

1. Types of peripheral microcirculation disorders (table 2).
2. Arterial hyperemia. Neurogenic and humoral mechanisms of local vasodilatation; neuro myoparalytic mechanism of arterial hyperemia. Disorders of microcirculation in arterial hyperemia. Types, symptoms and significance of arterial hyperemia (table 3).
3. Ischemia. Reasons for the increased resistance to blood flow in the arteries. Vascular compression, angiospasm, thrombosis, embolism (types, significance in development of others pathological processes), sclerotic changes in artery walls. The significance of tissue and organ functioning level, shunting and collateral circulation in the result of ischemia. Heart attack as a consequence of ischemia (table 6).
4. Venous hyperemia, its causes. Microcirculation in the region of venous stasis. Manifestations and significance of venous hyperemia (table 4).
5. Stasis. Ischemic, venous and "true" capillary stasis. Experimental modeling of local microcirculatory disorders (table 7).
6. Typical forms of disorders of microcirculation and lymph: intravascular, transmural, extravascular. Their reasons, possible mechanisms of manifestation and consequences. Concept of capillarotrophic insufficiency.
7. Disorders of the rheological properties of blood as a cause of microcirculation disorders. Disorders of blood viscosity. Hemoconcentration. Suspension stability and deformability of erythrocytes, aggregation and agglutination of platelets and erythrocytes, "slaj" phenomenon. Disorders of blood flow at level of microcirculation. Syndrome of non-specific hemorheological disorders.

TESTS FOR KHOWLEDGE CONTROL IN SELF-TRAINING

1. What are the intravascular microcirculatory disorders?

1) cells injuries of connective tissue and parenchyma, surrounding microvessels;
2) disorders of the rheological properties of the blood;
3) reaction of mast cells;
4) injury of vascular endothelial cells;
5) difficulty in lymph circulation;
6) involvement of microvessels in neurodystrophic processes;
7) thrombosis;
8) embolism;
9) disorders of vascular permeability;
10) disorders of blood flow velocity.

2. What are the vascular microcirculatory disorders?

1) cells injuries of connective tissue and parenchyma, surrounding microvessels;
2) disorders of the rheological properties of blood;
3) reaction of mast cells;
4) injury of vascular endothelial cells;
5) difficulty in lymph circulation;
6) involvement of microvessels in neurodystrophic processes;
7) thrombosis;
8) embolism;
9) disorders of vascular permeability;
10) disorders of blood flow velocity.

3. What are the extravascular microcirculatory disorders?

1) cellular injuries of connective tissue and parenchyma, surrounding microvessels;
2) disorders of the rheological properties of blood;
3) reaction of mast cells;
4) injury of vascular endothelial cells;
5) difficulty in lymph circulation
6) involvement of microvessels in neurodystrophic processes;
7) thrombosis;
8) embolism;
9) disorders of vascular permeability;
10) disorders of blood flow velocity.

4. What are the consequences of arterial hyperemia?

1) increased blood flow;
2) decreased blood flow;
3) partial or total occlusion of micro vessels;
4) activation of specific and non-specific tissue function;
5) inhibition of specific and non-specific tissue function;
6) dystrophy;
7) micro- and macrobleeds;
8) necrobiosis;
9) necrosis;
10) edema;
11) heart infarction.

5. What are the consequences of venous hyperemia?

1) increased blood flow;
2) decreased blood flow;
3) partial or total occlusion of micro vessels;
4) activation of specific and non-specific tissue function;
5) inhibition of specific and non-specific tissue function;
6) dystrophy;
7) micro- and macrobleeds;
8) necrobiosis;
9) necrosis;
10) edema;
11) heart infarction;
12) proliferation of connective tissue.

6. What are the consequences of ischemia?

1) increased blood flow;
2) decreased blood flow;
3) partial or total occlusion of micro vessels;
4) activation of specific and non-specific tissue function;
5) inhibition of specific and non-specific tissue function;
6) dystrophy;
7) micro- and macrobleeds;
8) necrobiosis;
9) necrosis;
10) edema;
11) heart infarction;
12) proliferation of connective tissue.

7. What are the consequences of stasis?

1) increased blood flow;
2) decreased blood flow;
3) partial or total occlusion of micro vessels;
4) activation of specific and non-specific tissue function;
5) inhibition of specific and non-specific tissue function;
6) dystrophy;
7) micro- and macrobleeds;
8) necrobiosis;
9) necrosis;
10) edema;
11) heart infarction;
12) proliferation of connective tissue.

8. What are the basic mechanisms of thrombosis?

1) increase in volume and linear velocity of blood flow;
2) decrease of linear velocity of blood flow;
3) activation of blood coagulation system;
4) activation of blood anticoagulation system;
5) inhibition of blood anticoagulation system;
6) change of vessels walls;
7) thrombembolism.

9. What are the consequences of thrombosis?

1) increased blood flow;
2) decreased blood flow;
3) partial or total occlusion of micro vessels;
4) activation of specific and non-specific tissue function;
5) inhibition of specific and non-specific tissue function;
6) dystrophy;
7) micro- and macrobleeds;
8) necrobiosis;
9) necrosis;
10) edema;
11) heart infarction;
12) proliferation of connective tissue.

10. What are the consequences of embolism?

1) increased blood flow;
2) decreased blood flow;

3) partial or total occlusion of micro vessels;
4) activation of specific and non-specific tissue function;
5) inhibition of specific and non-specific tissue function;
6) dystrophy;
7) necrosis.

ANSWERS KEYS:

1. 2, 7, 8, 10
2. 4, 9
3. 1, 3, 5, 6
4. 1, 4, 7
5. 2, 5, 6, 7, 10, 12
6. 2, 5, 6, 8, 9, 11, 12
7. 2, 5, 6, 8, 9, 10, 12
8. 2, 3, 5, 6
9. 2, 3, 5, 6, 8, 9, 11, 12
10. 2, 3, 5, 6, 7

Table 2

DISORDERS OF MICROCIRCULATION

Types of disorders	Causes
vascular	● changes in vascular walls permeability; ● endothelial damage; ● adhesion of blood cells to endothelium; ● diapedesis of blood cells; ● microbleeds
intravascular	● rheological disorders, slag phenomenon, increased blood viscosity; ● hypercoagulation of blood; ● decrease in the rate of blood flow and tissue perfusion; ● lesions of cellular membranes; ● formation of aggregates from blood cells; ● ischemia of tissues and organs
extravascular	● isolation of biologically active substances from connective tissue cells and parenchymal organs, degranulation of mast cells; ● neurodystrophic changes in tissue; ● disorders of lymph circulation

Table 3

PATHOPHYSIOLOGY OF ARTERIAL HYPEREMIA

Mechanisms	neurogenic	● neurotonic-with the predominance of para-sympathetic effects on the walls of blood vessels; ● neuroparalytic -with a decrease or absence of sympathetic influences on arteries and arterioles;

	humoral	● with an increase in vasodilators (adenosine, nitric oxide, kinins, prostaglandins);
	neuro myoparalytic	● depletion of catecholamine stocks; ● decrease in the tone of smooth muscle cells of arterial vessels;
Manifestations		● diffuse redness; ● increased local temperature; ● increased tissue turgor; ● increase in volume of hyperemic part; ● increased pressure in the arteries, capillaries and venules; ● an increase in the number and diameter of arterioles, capillaries and venules; ● pulsation of small arteries and capillaries; ● increase in blood flow velocity; ● reduction of the diameter of the axial cylinder
Consequences		● activation of specific organ or tissue functions and potentiation of non-specific functions; ● maintenance of hypertrophy and hyperplasia of the structural elements of tissues through substrates and oxygen; ● overstretching and micro-rupture of vessels with bleeding in the tissue or bleeding (external and internal)

Table 4

PATHOPHYSIOLOGY OF VENOUS HYPEREMIA

Causes	● compression or obturation of veins; ● heart failure; ● infringement of elasticity of venous walls
Mechanisms	impaired venous outflow
Manifestations	● lowering the temperature of an organ or tissue site; ● cyanosis; ● edema; ● increase in the number and diameter of capillaries; ● retardation of outflow of venous blood; ● significant expansion of the axial cylinder; ● a pendulum movement of blood

Consequences	hypoxia and edema of tissue result in: ● inhibition of specific and non-specific tissue function; ● hypotrophy and hypoplasia of cellular and tissue structure elements; ● proliferation of connective tissue (sclerosis, cirrhosis); ● dystrophy; ● necrobiosis; ● necrosis

Table 5

PATHOPHYSIOLOGY OF STASIS

Causes	● ischemia; ● venous hyperemia; ● factors causing aggregation and agglutination of cells
Mechanisms	● aggregation of blood cells due to agglutination under the influence of: - proagregants(ADP, thromboxane, prostaglandins E and F, catecholamines, agglutinins); - ions excess (K^+, $Ca^{2+,}$ Na^+, Mg^{2+}); - protein adsorption in cells; ● changes in rheological properties of blood (dysproteinemia, hemoconcentration); ● pathological changes in capillaries
Types	●real; ●ischemic; ●venous
Manifestations	●cessation of blood flow; ● considerable extension of the lumen of the capillaries (stagnant-venous stasis) or reduction of their lumen in ischemic; ● slag-phenomenon (a large number of aggregates in the lumen of the vessels and on their walls); ● microbleedings (more frequently in stasis form)
Consequences	●dystrophy; ●heart infarction

Table 6

PATHOPHYSIOLOGY OF ISCHEMIA

Causes	● compression of vessels from the outside; ● spasm of blood vessels under the influence of physical (low temperature), chemical (nicotine, ephedrine, mezaton), biological (BAS-catecholamines, angiotensin, vasopressin, prostaglandins of the F group); ● stasis, thrombosis, embolism
Mechanisms	● decrease in blood flow due to nervous and humoral effects or mechanical obstruction to blood flow through arterioles (compression, obturation, neurogenic spasm); ● increase in oxygen consumption and tissue metabolism substrates
Manifestations	● reduction in the diameter and number of arterioles, capillaries; ● decrease in pulsation of arterial vessels; ● slowing of blood flow; ● expansion of the axial cylinder; ● pain; ● pallor of tissue; ● low temperature; ● decreased lymphogenesis; ● decrease in volume and in turgor of tissues
Consequences	● reduction of specific tissue function; ● reduction of nonspecific function and processes (local protective reactions, proliferation and differentiation of cells); ● dystrophy, hypotrophy and atrophy of tissues and organs; ● infarction of tissue or organ

PRACTICAL WORK

Experiment 1. Arterial hyperemia in frog's tongue

A frog is immobilized through the destruction of spinal cord without decapitation. The immobilized frog is fixed with belly down on a board that has a rectangular inlet. The frog's mandible is fixed on the board with two pins. With a small clip the tongue is extended and fixed on the perimeter of the rectangular

inlet. The preparation must be done in such a way to avoid excessive stretching of the frog's tongue, which should be in the same plane with the board. Otherwise, circulatory disorders may occur. The preparation is ready. For the study under a microscope, examining the local microcirculation in the lingual vessels of the frog, estimating the number of functioning capillaries, their caliber, the speed of blood flow. Then, the tongue is rubbed with a cotton ball wetted with 0.65% solution of sodium chloride. Finally, the microcirculatory disorders in the frog's tongue in arterial hyperemia are followed.

Make conclusions, answering the following questions:

1. What are the microscopic manifestations of arterial hyperemia?
2. What are pathogenetic mechanisms of arterial hyperemia?

Experiment 2. Venous hyperemia in frog's tongue

Venous hyperemia can be modeled by ligation of the main venous vessels of the tongue's root. The mucosa of the tongue is stretched with the use of anatomic clip. The vein is located laterally to the artery and nerve. A ligature is applied on the vein. The tongue's preparation is studied under a microscope. The disorders of blood flow are examined after binding of the vein, and the results are noted.

Make conclusions, answering the following questions:

1. What are the microscopic manifestations of venous hyperemia?
2. What are pathogenetic mechanisms of venous hyperemia?

Experiment 3. Ischemia of swimming membrane in frog

A frog is immobilized by the destruction of spinal cord, without decapitation. After this the swimming membrane is stretched and is fixed with pins on a triangular orifice. Then the normal circulation (counting the functional capillaries, their caliber, the speed of blood flow) is examined under a microscope. On the swimming membrane 1-2 drops of 1:5000 adrenaline solution are dropped. Applied adrenaline causes ischemia.

Make conclusions, answering the following questions:

1. What are the microscopic manifestations of ischemia?
2. What are pathogenetic mechanisms of ischemia?

Experiment 4. Formation of white thrombus in mesentery vessels of frog's intestine

A frog is immobilized by the destruction of spinal cord, without decapitation and it is fixed with the belly down on a board that has a round inlet such as the right side of the abdomen joins the round inlet. The skin is cut with scissors layer after layer, the muscles and peritoneum in the right side of the abdomen are cut too. An intestinal loop of mesentery is taken off without excess from

abdominal cavity, not damaging the bowels. The preparation is examined under a microscope. After this, a crystal of salt is applied with eye of a needle. During 30-40 min. the disorders of blood flow and formation process of white parietal thrombus occur.

Make conclusions, answering the following questions:

1. What events are observed in thrombogenesis and what is their succession?
2. What is the trigger moment of the thrombogenesis in this experiment?
3. How does thrombogenesis depend on the speed of blood flow?

Experiment 5. Fat embolism in frog's vessels

The immobilized frog is fixed on a board with the belly up. With the anatomic forceps a triangular flap on the sternum is cut. The ribcage is opened. 0.65% solution of sodium chloride is applied on the discovered heart. The frog is flipped with the back up. After this, the frog's tongue is prepared. 0.1 ml of oil emulsion is introduced into the ventricle cavity. The frog's tongue, the moving of embolus into vessels lumen and the disorders of blood flow are examined. The results of the experiment are analyzed.

Make conclusions, answering the following question:

1. What are the pathogenetic mechanisms of ischemia?

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INFLAMMATION

The purpose of the practical class: To study etiology and pathogenesis of inflammation. To be able to determine the stage of microcirculation disturbance the inflammatory focus. To explain its pathogenesis. To be able to explain pathogenesis of the local signs of the inflammation.

Basic questions the student should know:

1. Local microcirculatory disorders (arterial and venous hyperemia, thrombosis, embolism and stasis).

The student should know:

1. Inflammation. Definition of the notion. Etiology. The role of exogenous and endogenous factors (table 7).
2. Pathogenesis of inflammation: the main components of the inflammatory processes (fig. 1).
3. Alteration. Disorders of functions, metabolism, the state of cell membranes and cellular organelles (table 8).
4. Release and activation of biological active substances-mediators of inflammation; their types, origin and significance in the dynamics of development and ending of the inflammation. Interrelation of different mediators (table 9). Primary and secondary alteration (table 8).
5. Exudation. Reaction of microcirculatory vessels. Change in tone, vascular wall permeability and blood flow; their stages and mechanisms.
6. Changes in the rheological properties of the blood into inflammatory focus; protein composition and physical-chemical properties of the plasma.
7. Intensification of filtration, diffusion, osmosis and microvesicle as the basis of the process of exudation, the importance of physical-chemical shifts into the focus of the inflammation (fig. 2).
8. Types of exudates.
9. Inflammatory edema, its pathogenetic links.
10. Stages and mechanisms of phagocytosis. Its role in the pathogenesis of inflammation.
11. Cardinal (local) manifestations of inflammation, their pathogenesis.
12. Proliferation, mechanisms of formation. Stimulatory and inhibitors of proliferation.

TESTS FOR KHOWLEDGE CONTROL IN SELF-TRAINING

1. What are the causes of aseptic inflammation?

1) venous thrombosis;
2) transient hyperoxia of tissues;
3) tissue necrosis;
4) hemorrhage into the tissue;
5) surgical intervention performed in strictly aseptic conditions;
6) parenteral administration of a foreign sterile protein;
7) enteral administration of foreign non-sterile protein.

2. What are the cardinal signs of the inflammation?

1) short-term artery spasm;
2) pain;
3) redness;
4) exudation;
5) fever;
6) proliferation;
7) tumor (swelling);
8) formation of bradykinin;
9) disorder of function;
10) alteration.

3.a. What are cellular-derived mediators of inflammation?
3.b. What are plasma-derived mediators of inflammation?

1) serotonin;
2) kinin;
3) lymphokines;
4) histamine;
5) compliment;
6) lysosomal enzymes;
7) lysosomal cationic proteins;
8) prostaglandins;
9) coagulation factors.

4. What mediators are obtained from arachidonic acid due to lipoxygenase pathway?

1) thromboxanes;
2) leukotrienes;
3) prostaglandin E_2;
4) prostacyclin;
5) prostaglandin F_{2a}.

5. What mediators are obtained from arachidonic acid due to cyclooxygenase pathway?

1) thromboxanes;
2) leukotrienes;
3) prostaglandin E_2;
4) prostacyclin;
5) prostaglandin F_{2a}.

6. Which mediators cause short-term spasm of arteries into the focus of the inflammation?

1) histamine;
2) bradykinin;
3) adrenaline;
4) neural- reflex mechanisms;
5) prostaglandin E_2;
6) prostaglandin F_{2a};
7) thromboxanes.

7. Who does arterial hyperemia provoke in the inflammatory focus?

1) neural-reflex mechanisms;
2) prostaglandin E_2;
3) prostaglandin F_{2a};
4) adrenaline;
5) bradykinin;
6) histamine.

8. Who does venous hyperemia provoke in the inflammatory focus?

1) prostaglandin F_{2a};
2) prostaglandin E_2;
3) neuroreflex mechanisms;
4) adrenaline;
5) bradykinin;
6) histamine.

9. What factors can cause pain?

1) adrenaline;
2) thromboxanes;
3) leukotrienes;
4) kinins;
5) histamine;
6) hyperpotasemia;

7) acidosis;
8) increased temperature into inflammatory focus;
9) mechanical excitation of nervous ends;
10) prostaglandins.

10. What are the features of bradykinin:
1) it causes a drop in blood pressure;
2) it contracts smooth muscles;
3) it increases permeability of micro vessels;
4) it irritates the end of pain nerves;
5) it is a chemoattractant for leukocytes.

11. What are the features of histamine:
1) it belongs to the preformed mediators of inflammation;
2) it causes dilation of microvessels;
3) it increases permeability of vessels;
4) it excites nerve endings of pain;
5) it is a chemoattractant.

12. What mediators cause increased permeability of blood vessels into inflammation?
1) heparin;
2) histamine;
3) bradykinin;
4) interferon;
5) serotonin;
6) leukotrienes.

13. What kinds of substances stimulate leukocytes migration in the inflammatory focus?
1) bacterial lipopolysaccharide;
2) leukotriene B_4;
3) interleukin 8;
4) fragment of complement C5a;
5) thromboxanes;
6) interleukin 12.

14. What kinds of factors cause edema in the inflammatory focus?
1) increased oncotic pressure of the blood;
2) increased oncotic pressure of the intercellular fluid;
3) decreased oncotic pressure of the intercellular fluid;
4) increased permeability of vessels walls;

5) decreased osmotic pressure of the intercellular fluid;
6) increased pressure in the venous section of the capillaries and venules;
7) increased osmotic pressure of the intercellular fluid.

15. What are physico-chemical changes typical for the site of acute inflammation?

1) hyperonkia;
2) hyperosmia;
3) hypoosmia;
4) acidosis;
5) increased concentration of potassium ions outside cells;
6) hypoonkia.

16. What are properties of purulent exudates are different from those of transudation?

1) large number of blood cells (leukocytes);
2) single blood cells;
3) large number of destroyed and damaged tissue elements;
4) small amount of protein;
5) large amount of protein.

17. What are the cells that ensure the elimination of tissue defects in inflammation?

1) T-lymphocytes;
2) B-lymphocytes;
3) fibroblasts:
4) monocytes;
5) histiocytes;
6) parenchymal cells.

18. Which factors stimulate the cell proliferation in inflammation?

1) cheylons;
2) inhibitors of cheylons;
3) mineralcorticoids;
4) sexual hormones;
5) glucocorticoids.

ANSWERS KEYS:

1. 1, 3, 4, 5, 6	**5.** 1, 3, 4, 5	**10.** 1, 3, 4	**15.** 1, 2, 4, 5
2. 2,3,5,7,9	**6.** 3, 4	**11.** 1, 2, 3, 4	**16.** 1, 3, 5
3. a) 1, 3, 4, 6, 7, 8	**7.** 2, 5, 6	**12.** 2, 3, 5, 6	**17.** 3, 4, 5, 6
b) 2, 5, 9	**8.** 1, 5, 6	**13.** 1, 2, 3, 4	**18.** 2, 3, 4
4. 2	**9.** 4, 5, 6, 7, 9, 10	**14.** 2, 4, 6, 7	

Table 7

ETIOLOGY OF INFLAMMATION (PHLOGOGENIC FACTORS)

Exogenous	Endogenous
Mechanical: trauma, foreign bodies Physical: burn, frostbite, ionizing radiation, ultraviolet irradiation Chemical: acids, bases, substances of irritating action (mustard gas, carrageenan, turpentine) Biological: bacteria, rickettsia, spirochetes, viruses, fungi, protozoa, helminths, insect toxins, plants	Hemorrhage Ischemia Thrombosis Complexes antigen+antibodies Decay products Calculous processes of the biliary and urinary tract

Table 8

Differences in primary and secondary alteration in the focus of inflammation

Primary alteration	Secondary alteration
Cause	*Cause*
Etiological factor of inflammation (phlogogenic factors)	Physicochemical, metabolic disorders in site of primary alteration; action of inflammatory mediators (phagocytic enzymes)
Localization	*Localization*
Place of direct action of the damaging agent	The periphery of the site of the phlogogenic agent, the region around the zone of primary alteration
Mechanism of formation	*Mechanism of formation*
Specific damage and destruction of cell membranes, their metabolic disorders (predominance of catabolism), significant physicochemical disorders	Disorders of nervous regulation, axonal transport, trophic and plastic factors, vascular wall tone and blood flow; action of inflammatory mediators
Time of formation	*Time of formation*
Immediately after the action of the damaging factor	On the background of active exudation
Reactivity of the organism	*Reactivity of the organism*
Normal, hyperergic, anergic, dysergic	Hyperergic, dysergic

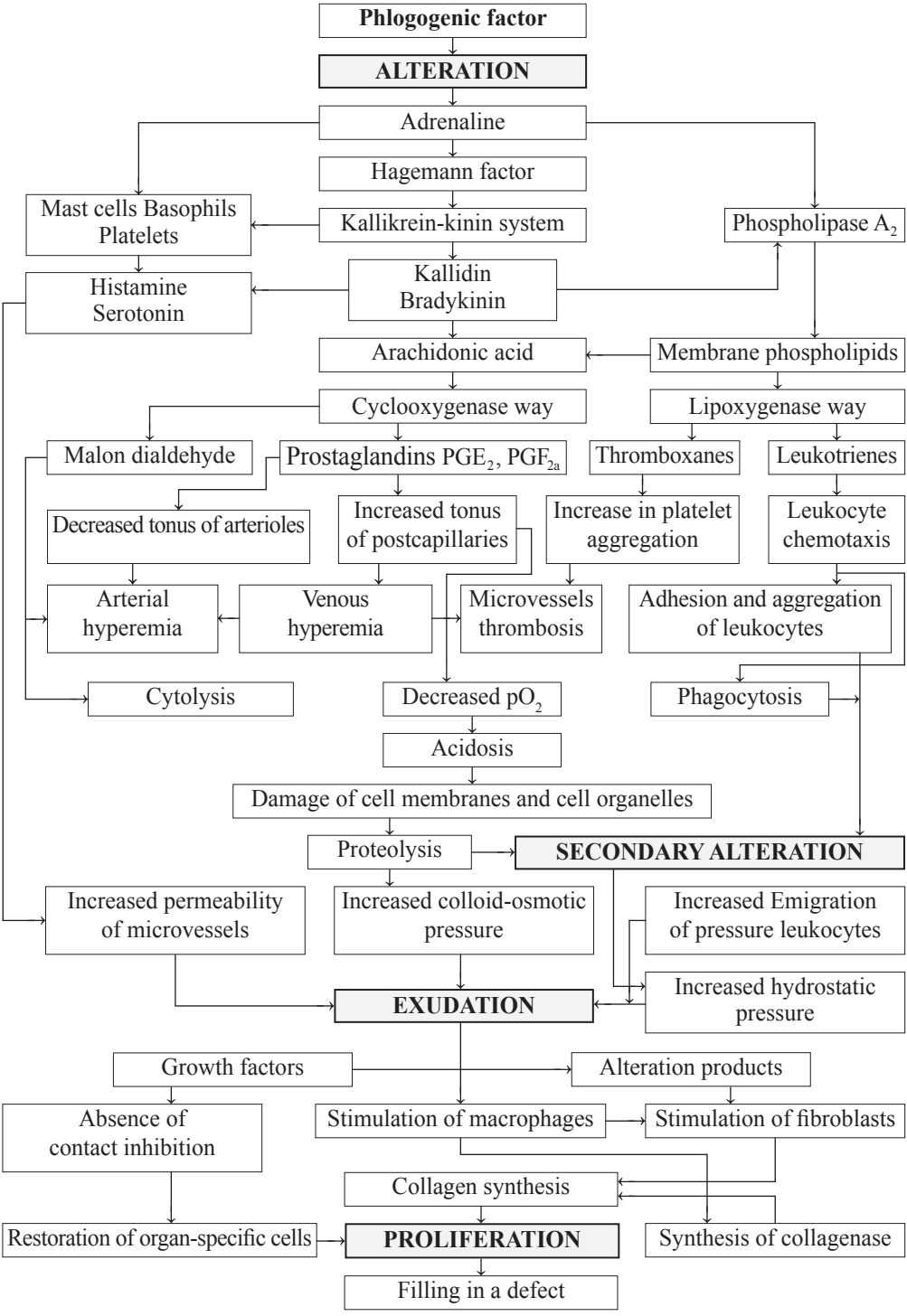

Figure 1. **PATHOGENESIS OF INFLAMMATION**

Table 9

MEDIATORS OF INFLAMATION

Basic groups	Basic mediators	Main sources	Main effects
I. Plasma-derived mediators			
Complement derivatives	C_{5b}-C_9 C_{5a}, C_{3a}	Plasma Tissue fluid	Tissue destruction (C_{5b}-C_9) Leukocytes activation Increased permeability of vessels (C_{5a},C_{3a}) Degranulation of mast cells (C_{5a},C_{3a}) Spasm of smooth musculature
Kinins	Bradykinin Kallidin	Plasma Tissue fluid	Vasodilatation Increased permeability of vessels Spasm of smooth musculature Inhibition of granulocytes Stimulation of lymphocytes and fibroblasts Pain
Factors of the blood coagulation system	Fibrinopeptides Fibrin degradation products	Plasma	Activation of leukocytes Enhanced phagocytosis
II. Cell-derived mediators ***1. Pre-existing mediators***			
Vasoactive amines	Histamine	Basophils Mast cells	Vasodilatation Increased permeability of vessels Spasm of smooth musculature Pruritus

	Serotonin	Platelets	Pruritus Inhibition of granulocytes Stimulation of monocytes, macrophages and fibroblasts
Lysosomal factors	Proteinases	Granulocytes Monocytes-macrophages	Tissue destruction Enhanced emigration and phagocytosis Stimulation of monocytes, macrophages and fibroblasts Proliferation and activation of lymphocytes
	Non-enzymatic cationic proteins	Granulocytes	Microbicide Increased permeability of vessels Degranulation of mast cells Adhesion and aggregation of leukocytes
Neuromediators	Acetylcholine	Cholinergic neurons	Vasodilatation Spasm of smooth musculature Leukocytes activation
2. Newly formed mediators			
Arachidonic acid derivatives	Prostaglandins E_2, F_{2b}	Monocytes-macrophages Granulocytes Platelets	Decreased tonus of precapillary sphincters, increased tonus of postcapillary sphincters Hyperergic effect
	Thromboxanes		Aggregation of platelets Spasm of smooth musculature Granulocytes activation

	Leukotrienes		Leukocytes activation Increased permeability of vessels (LTC_4, D_4,E_4) Vasodilatation Spasm of smooth musculature (LTC_4, D_4,E_4, lipoxine)
Active forms of oxygen	Superoxide anion, hydroxyl anion, perhydroxyl anion, singlet oxygen, hydrogen peroxide, hypochloride	Monocytes-macrophages Granulocytes	Tissue destruction Granulocytes activation Stimulation of phagocytosis Inhibition of monocytes

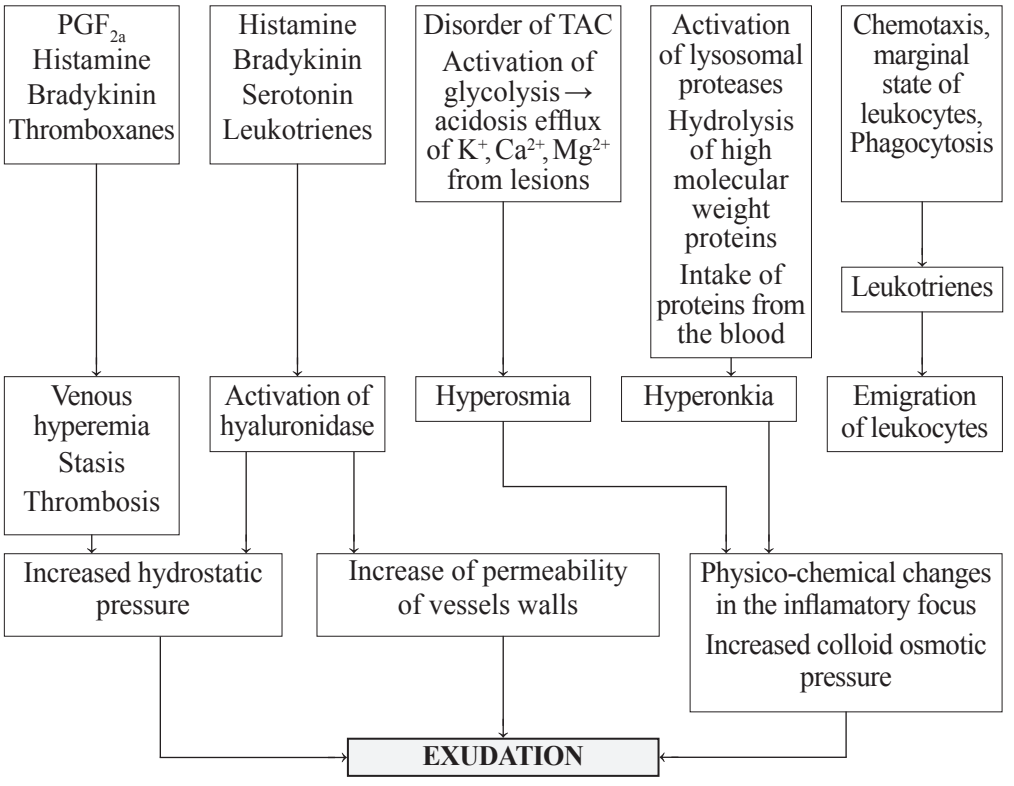

Figure 2. **MECHANISMS OF EXUDATION**

Table 10

MICRICIRCULATORY DISORDERS INTO INFLAMMATORY FOCUS

	STAGIES	MEDIATORS	EFFECT
1	Short-term vasospasm	Axon reflex	Vasospasm
2	Arterial hyperemia	PGE_2	Decreased tonus of precapillary sphincters
		Bradykinin	Decreased tonus of vessels
		Histamine	Spasm of sphincter of arteriolo-venular shunt
3	Venous hyperemia	$PGF_{2\alpha}$	Decreased tonus of postcapillary sphincters
		Bradykinin	Vasodilatation
		Bradykinin Histamine	Increased permeability of vessels walls→plasma leakage→ increase in blood viscosity
4	Stasis		Cessation of blood flow
5	Thrombosis	Thromboxanes	Adhesion and aggregation of platelets
		Hageman (XII) factor	Activation of blood coagulation system

PRACTICAL WORK

Experiment 1. Vascular reaction to inflammation of the frog intestine (Conheim's experiment)

The immobilized frog is pinned to the cork board with the abdomen upward so that the right side is on the edge of the round hole. The skin is cut with scissors on the right, along the anterior axillary line, on the segment of the middle third of the trunk, then the muscles and peritoneum are cut too.

Carefully remove the loop of the small intestine. The mesentery is fixed with pins that stick into the free edge of the intestinal wall.

The preparation is examined under a microscope at low magnification.

After the marginalization of leukocytes, one should go on to the examination under a large magnification. It is necessary to trace all the stages of local circulatory disorders and those of emigration of leukocytes.

Make conclusions, answering the following questions:

1. What factors did the inflammatory reaction trigger in the frog's mesentery?
2. What kinds of local disorders of blood flow were observed in the inflammation evolution and what is their sequence?
3. What stages of leukocytes migration were observed in the experience?

Experiment 2. Alteration to the inflammation of the frog's tongue

The frog is fixed with the belly down on a board. The frog's tongue is taken off, is extended and fixed on the perimeter of the rectangular inlet. A crystal of lunar caustic is applied on the tongue's mucosa during 2 seconds. Then the tongue is plentifully washed with distilled water. After 3-5 min., 1-2 drops of 1% methylene blue solution are applied, washed after 2min with water.

The degree of alterative processes is estimated according to the intensity of necrotic area and adjacent tissues.

Make conclusions, answering the following questions:

1. What are the microcirculatory disorders in inflammation?
2. What are pathogenetic mechanisms of these disorders?

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HYPERSENSITIVITY DISORDERS

The purpose of the practical class: To understand the main causes of occurrence, mechanisms of development and manifestations of humoral type of allergy. To be able to explain the similarities and differences between allergy and immunity.

Basic questions the student should know:

1. Body reactions to antigen stimulation.
2. Humoral and cellular immunity.
3. Functional characteristics of the cells involved in immunogenesis, types of specific immunopathology.

The student should know:

1. Allergy. Definition of a concept and general characteristics of allergy.
2. Relationships between allergy and immunity, allergy and inflammation.
3. Allergens. Classification. Nature of allergens. Value of hereditary predisposition to allergy.
4. Types of allergic reactions, their classification.
5. Stages of allergic reactions.
6. Features of allergens, mediators and mechanisms of development of type I allergic diseases (table 11). Clinical forms.
7. Features of allergens, mediators and mechanisms of development of type II allergic diseases (table 12). Clinical forms.
8. Features of allergens, mediators and mechanisms of development of type III allergic diseases (table 13). Clinical forms.
9. Pseudoallergy. Clinical manifestations, pathogenetic differences from true allergies.
10. Methods of diagnostics, prevention and treatment of allergic diseases.

TESTS FOR KHOWLEDGE CONTROL IN SELF-TRAINING

1. What allergens cause anaphylactic forms of type I allergic reactions?

1) pollen of plants;
2) therapeutic serum;
3) novocaine;
4) penicillin;
5) protein components of the blood;
6) house dust.

2. Where does the formation of Ag-Ab complexes occur?
1) in blood serum;
2) on the surface of mast cells;
3) on the surface of membranes of erythrocytes, leukocytes, platelets;
4) on the surface of macrophages;
5) on the lymphocyte membrane;
6) on the surface of basophils.

3. What does passive sensitization cause in allergic reactions?
1) suspension of lymphocytes;
2) suspension of foreign erythrocytes;
3) serum immunoglobulins;
4) suspension of neutrophils;
5) allergens.

4. Antibody –dependent cell-mediated cytotoxicity occurs:
1) in serum;
2) on the surface of basophils;
3) on the membranes surface of target cells (endoallergens);
4) on the surface of macrophages;
5) on the lymphocyte membrane.

5. Where do immune Complex-Mediated Disorders occur?
1) in serum;
2) on the surface of basophils;
3) on the membranes surface of target cells (endoallergens);
4) on the surface of macrophages;
5) on the lymphocyte membrane;
6) on the walls of microvessels.

6. What does histamine cause?
1) increased permeability of vessels walls;
2) proteolysis;
3) pain, itching;
4) smooth muscles spasm of the bronchi, intestine, uterus;
5) spasm of the sphincter of the hepatic veins.

7. What does activated complement cause?
1) increased permeability of vessels walls;
2) proteolysis;
3) pain, itching;
4) smooth muscles spasm of the bronchi, intestine, uterus;
5) spasm of the sphincter of the hepatic veins.

8. What does bradykinin cause?
1) increased permeability of vessels walls;
2) proteolysis;
3) pain, itching;
4) smooth muscles spasm of the bronchi, intestine, uterus;
5) spasm of the sphincter of the hepatic veins.

9. What does leukotrien D_4 cause?
1) increased permeability of vessels walls;
2) proteolysis;
3) pain, itching;
4) smooth muscles spasm of the bronchi, intestine, uterus;
5) spasm of the sphincter of the hepatic veins.

10. What do cellular lesions cause in the focus of allergic inflammation?
1) lysosomal enzymes;
2) LPO metabolites;
3) histamine;
4) clotting factors;
5) bradykinin.

11. What are mediators with vasodilatory effect?
1) histamine;
2) lysosomal enzymes;
3) bradykinin;
4) prostaglandin E_2 ;
5) activated components of the complement system.

12. What mechanisms occur in type II hypersensitivity disorders?
1) direct damaging effect of antibodies on cells;
2) complement activation;
3) degranulation of mast cells;
4) activation of phagocytosis;
5) vascular injury by micro-precipitates.

13. What mechanisms occur in type II (cell-mediated cytotoxicity) hypersensitivity disorders?
1) direct damaging effect of antibodies on cells;
2) complement activation;
3) degranulation of mast cells;
4) activation of phagocytosis;
5) vascular injury by micro-precipitates.

14. What mechanisms occur in type III, immune complex-mediated disorders?

1) direct damaging effect of antibodies on cells;
2) complement activation;
3) degranulation of mast cells;
4) activation of phagocytosis;
5) vascular injury by micro-precipitates.

15. What are manifestations of anaphylactic reaction?

1) angioedema;
2) collaps;
3) skin erythema;
4) bronchospasm;
5) fibrillation.

16. What kinds of events are the manifestations of anaphylaxis?

1) anaphylactic shock;
2) bronchial asthma;
3) Shvartsman phenomenon;
4) food allergy;
5) Arthus phenomenon;
6) serum sickness of immediate type;
7) pollinosis (hay fever);
8) serum sickness of delayed type.

17. What kinds of events are attributed to atopy ?

1) anaphylactic shock;
2) bronchial asthma;
3) Shvartsman phenomenon;
4) food allergy;
5) Arthus phenomenon;
6) serum sickness of immediate type;
7) pollinosis (hay fever);
8) serum sickness of delayed type.

18. What are the clinical manifestations of type II hypersensitivity?

1) angioedema;
2) autoimmune hemolytic anemia;
3) pollinosis (hay fever);
4) myocarditis;
5) serum sickness;
6) glomerulonephritis;

7) autoimmune form of agranulocytosis;
8) urticaria:
9) Arthus phenomenon
10) rheumatoid arthritis.

19. What are the clinical manifestations of type III (immune complex-mediated disorders)?

1) angioedema;
2) autoimmune hemolytic anemia;
3) pollinosis (hay fever);
4) myocarditis
5) serum sickness;
6) glomerulonephritis;
7) hepatitis;
8) urticaria:
9) Arthus phenomena
10) rheumatoid arthritis.

20. What are the indices of peripheral blood smear in type II (antibody-mediated disorders)?

1) leukocytosis;
2) aneosinophilia ;
3) eosinophilia ;
4) neutrophilia ;
5) lymphocytosis;
6) lymphocytopenia;
7) leucopenia.

21. How is the specific hyposensitization achieved in type II allergic reactions?

1) administration of small doses of an allergen;
2) administration of glucocorticoids;
3) avoiding an allergen;
4) administration of antihistaminic drugs;
5) after anaphylactic shock.

22. How is non-specific hyposensitization achieved in humoral allergic reactions?

1) administration of small doses of an allergen;
2) administration of glucocorticoids;
3) avoiding an allergen;
4) administration of antihistaminic drugs;
5) after anaphylactic shock.

ANSWERS KEYS:

1. 3, 4	**5.** 1, 6;	**9.** 1, 4	**13.** 2, 4	**17.** 2, 4, 7	**21.** 1
2. 1, 2, 6	**6.** 1, 3, 4, 5	**10.** 1, 2	**14.** 2, 3, 4, 5	**18.** 2, 4, 6, 7	**22.** 1
3. 3	**7.** 2	**11.** 1, 3, 4	**15.** 2, 4	**19.** 5, 6, 9, 10	
4. 3	**8.** 1, 3	**12.** 3	**16.** 1, 5, 6, 8	**20.** 1, 3, 5	

Table 11

TYPE I (IMMEDIATE) HYPERSENSITIVITY DISORDERS (ANAPHYLACTIC, ATOPIC)

ALLERGENS – exogenous

Atopic (local): food allergens, chemicals like antibiotic penicillin, protein in pollen, house dust mites, animal dander

Anaphylactic (systemic): presence of antigen introduced by injection, insect sting, or absorption across the epithelial surface of the skin or gastrointestinal mucosa

STAGE OF IMMUNE REACTIONS

a) sensitization phase (initial antigen contact):
- phagocytosis of antigen by macrophage, refining and its presentation;
- reaction of cell cooperation;
- synthesis of Ig: atopic forms –Ig E, anaphylactic- IgG;
- fixation of antibodies on the membranes surface of target cells (basophils; mast cells);

b) second antigen contact:
formation of the antigen -antibody complex on the membranes surface of the target cells (basophils; mast cells) and into the blood;

I. PATHOCHEMICAL STAGE

Cell-derived mediators:

● ***basophils, mast cells:***

- Release of preformed mediators (histamine, heparin, chemotactic factor of eosinophils, chemotactic factor of neutrophils, basophilic kallikrein);
- Newly synthesized mediators (prostaglandins D_2, leukotriens C_4, E_4, D_4, factor of platelet activation, thromboxane A_2;

● ***neutrophils****:*

- Release of preformed mediators (cationic proteins, lysosomal enzymes, peroxidase);

● ***eosinophils:***

- Release of preformed mediators (histaminase, arylsulfatase);

● **platelets:**

- Release of preformed mediators (serotonin, histamine);
- Newly synthesized mediators (prostaglandins, leukotriens, thromboxanes, metabolites).

Plasma-derived mediators:

Kinin system (bradykinin, kallidin); Clotting system (Hageman factor); Complement proteins.

II. PATHOPHYSIOLOGICAL STAGE

a) Primary (early-phase response):

● increased permeability of capillaries (occurs within 5 to 30 minutes, it is mediated by mast cell degradation and the release of preformed mediators-histamine, acetylcholine, adenosine, chemotactic mediators, and enzymes such as chymase and trypsin) → edema of tissue;

● dilation of arterioles and capillaries (histamine, bradykinin) → local hyperemia;

● irritation of pain receptors → pain, itching;

● smooth muscle spasm (histamine, leukotrien D_4, prostaglandin D_2, factor of platelet activation, thromboxan A_2, prostaglandin $F_{2\alpha}$) → bronchial constriction; histamine → spasm of the sphincter of the hepatic veins → abnormal blood deposition → hypovolemia → BP reduction;

● increased secretion of mucus (histamine);

● cellular damage (arachidonic acid metabolites, lysosomal enzymes).

b) Secondary late response (occurs about 2 to 8 hours later and lasts several days): It results from the action of lipid mediators and cytokines; the lipid mediators are derived from mast cell membrane phospholipids, which are broken down to form arachidonic acid. Arachidonic acid is the parent of leukotriens and prostaglandins:

● mucosal edema ● mucus secretion ● leukocyte infiltration
● epithelial damage ● bronchospasm

CLINICAL MANIFESTATIONS

Atopic forms: atopic forms of asthma, urticaria (hives), allergic rhinitis, atopic dermatitis.

Anaphylactic forms: anaphylactic shock.

Table 12

TYPE II HYPERSENSITIVITY DISORDERS

(COMPLEMENT-AND ANTIBODY-MEDIATED CELL DESTRUCTION, COMPLEMENT-AND ANTIBODY-MEDIATED INFLAMMATION, ANTIBODY-MEDIATED CELLULAR DYSFUNCTION)

ALLERGENS – endogenous

primary (natural) – brain, crystalline, testicles, colloid of the thyroid gland (within damage to the histohematological barriers;

secondary (acquired) – components of cellular and basal membranes, modified by the action of drugs, chemical substances, physical (cold, heat, radiation) factors: fixed on the cell foreign substance (haptene).

I. STAGE OF IMMUNE REACTIONS

a) sensitization phase (formation autoallergens):

- antigen refining by macrophage;
- cellular reaction;
- synthesis of autoantibodies (Ig M, Ig G);

b) second antigen contact:

The formation of an antigen-antibody complex on the membranes surface of the target cells

II. PATHOCHEMICAL STAGE

plasma- derived mediators:

- complement system components (C_{4b}, C_{2a}, C_{3a}, C_{5a});

cell-derived mediators:

- lysosomal enzymes;
- metabolites of LPO (superoxide-anion, hydrogen peroxide, singlet oxygen, hydroxyl radical).

III. PATHOPHYSIOLOGICAL STAGE

1. complement-and antibody-mediated cell destruction can occur by way of either the compliment system or by antibody-dependent cell-mediated cytotoxicity (ADCC).
2. complement-and antibody-mediated inflammation
3. antibody-mediated cellular dysfunction

CLINICAL MANIFESTATIONS

Autoimmune hemolytic anemia, leukopenia (autoimmune form of agranulocytosis), thrombocytopenia, glomerulonephritis, vascular rejection of organ grafts,

Goodpasture syndrome, Graves disease, myasthenia graavis.

Table 13

TYPE III HYPERSENSITIVITY DISORDERS
(IMMUNE COMPLEX-MEDIATED DISORDERS)

ALLERGENS – exogenous

Soluble protein, injected parenterally in large quantities (therapeutic serum, blood plasma, vaccines).

I. STAGE OF IMMUNE REACTIONS

a) sensitization phase (initial antigen contact):
- antigen refining by macrophage;
- reaction of cell cooperation;
- synthesis of precipitating antibodies, predominantly IgG, IgM

b) second antigen contact:
- formation of large-molecule free-circulating complexes

II. PATHOCHEMICAL STAGE

plasma- derived mediators:
- complement system components (C_3, C_4, C_5);
- proteins of clotting system (Hageman factor, fibrinogen)

cell-derived mediators:
- ***mast cells:***

- release of preformed mediators (histamine, heparin, chemotactic factor of eosinophils, chemotactic factor of neutrophils, basophilic kallikrein;
- ***neutrophils****:*

- release of preformed mediators (cationic proteins, lysosomal enzymes, peroxidase);
- ***eosinophils:***

- release of preformed mediators (histaminase. arylsulfatase);

platelets:
- release of preformed mediators (serotonin, histamine);
- newly synthesized mediators (prostaglandins, leukotriens, thromboxanes, LPO metabolites, IL_1, IL_6)

III. PATHOPHYSIOLOGICAL STAGE

- damage of cells (vascular endothelium, synovial membranes, mast cells, thrombocytes, leucocytes) activated by complement system complexes, lysosomal enzymes, LPO metabolites;
- development of allergic inflammation with severe microcirculation disorders, increased blood clotting, fever.

CLINICAL MANIFESTATIONS

● serum sickness; ● vasculitis-nodal periarteritis, hemorrhagic vasculitis, nodal erythema, glomerulonephritis; ● Arthus reaction; ● rheumatoid arthritis; ● CID-syndrome; ● pancytopenia, granulocytopenia.

PRACTICAL WORK

Experiment 1. Modeling of anaphylactic shock

A dose of antigen (0.1 ml of native horse serum) is injected to an active sensitized rabbit into the marginal vein of the ear. The sensitization is made by the following method: a rabbit is administered subcutaneously 1 ml of native horse serum within 10 days with intervals of 5-6 days. The evolution of anaphylactic shock is followed up. Within 1-2 min. after the administration of the serum excitation, cries, uncoordinated movements appear, followed by generalized seizures. The relaxation of sphincter with incontinence of feces and urine occur often in the animal.

Make conclusions, answering the following questions:

1. What type of hypersensitivity disorders does anaphylactic shock refer to?
2. What types of Ig are involved in type I hypersensitivity?
3. What is the organ of shock in rabbit?
4. In which clinical states can such complications occur?

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TYPE IV, CELL-MEDIATED HYPERSENSITIVITY DISORDERS (DELAYED)

The purpose of the practical class: To understand the main causes of occurrence, mechanisms of development and manifestations of cellular type of allergy. To be able to differentiate allergic reactions of cellular types according to clinical and laboratory investigations.

The student should know:

1. Type IV, Cell-Mediated Hypersensitivity Disorders (delayed type). Classification and their features (table 14).
2. Etiology of type IV, Cell-Mediated Hypersensitivity Disorders.
3. Stages of type IV, Cell-Mediated Hypersensitivity Disorders:

a) immunological; b) pathochemical: lymphokines, kinds, mechanisms of action; c) pathophysiological.

4. Autoimmune disorders. Etiology, pathogenesis, clinical forms.
5. Role of external and internal factors in pathogenesis of autoimmune disorders.
6. Principles of diagnosis, prevention and treatment of autoimmune disorders.

TESTS FOR KHOWLEDGE CONTROL IN SELF-TRAINING

1. How is the passive sensitization achieved in Cell-Mediated Hypersensitivity Disorders?

1) by administration of serum;
2) by administration of lymphocyte suspension;
3) by administration of neutrophils suspension;
4) by administration of washed red blood cells with fixed antibodies on them;
5) by transplant.

2. Where does the formation of Ag+Ab complex occur in Cell-Mediated Hypersensitivity Disorders?

1) on the mast cells membrane surface;
2) into the blood plasma;
3) In the intercellular fluid;
4) on the lymphocytes membrane surface;
5) on connective tissue fibers.

3. What are the mediators of Cell-Mediated Hypersensitivity Disorders?

1) histamine;
2) bradykinin;
3) lymphokines;
4) leukotrienes;
5) interleukins.

4. What lymphokines act on lymphocytes?

1) lymphotoxins;
2) interferon;
3) transfer factor;
4) mitogenic factor;
5) helper-suppressor factors;
6) skin-reactive factor;
7) chemotactic factor;
8) factors of migration inhibition;
9) activating factors.

5. What lymphokines act on phagocytes?

1) lymphotoxins;
2) interferon;
3) transfer factor;
4) mitogenic factor;
5) helper-suppressor factors;
6) skin-reactive factor;
7) chemotactic factor;
8) factors of migration inhibition;
9) activating factors.

6. What lymphokines act on target-cells?

1) lymphotoxins;
2) interferon;
3) transfer factor;
4) mitogenic factor;
5) helper-suppressor factors;
6) skin-reactive factor;
7) chemotactic factor;
8) factors of migration inhibition;
9) activating factors.

7. How does cytolytic action of sensitized lymphocytes on the target-cells occur?

1) through the action of activated complement on the membrane;
2) through the action of membrane associated phospholipases on the membrane;
3) via damage of membrane by Ag+Ab complex;
4) in the result of significant increase of vessels permeability;
5) in the result of cellular ischemia.

8. How does the deterioration of the vision of the intact eye occur after the trauma of one eye?

1) change in Ag composition of tissue under the influence of a damaging factors (mechanical, thermic, chemical);
2) damage of the histohematological barrier;
3) ingress of Ag into damaged tissue from the outside;
4) neural-reflex mechanism;
5) activation of phagocytosis.

ANSWERS KEYS:

1. 2 **2.** 4 **3.** 3 **4.** 3, 4, 5 **5.** 7, 8, 9 **6.** 1, 2, 6 **7.** 2 **8.** 2

Table 14

TYPE IV, CELL-MEDIATED HYPERSENSITIVITY DISORDERS

Allergens ● exogenous: transplant; ● endogenous: - primary (native) – brain, lens, testicles, colloid of the thyroid gland (damage of the histohematological barriers); - secondary (acquired) – components of cellular and basal membrane, modified by drugs, chemical substances, physical (cold, warm, irradiation), biological (tuberculosis agent, brucellosis, salmonellosis, herpes viruses, measles, mushrooms) factors; foreign substance fixed on the cell (haptene); tumor, old cells.
I. IMUNOLOGICAL STAGE **a) sensitization stage (**initial Ag contact with organism): ● Ag processing cells; ● cellular reaction; ●formation of sensitized clone to T-cells allergen; **b) resolution phase** (repeated Ag contact): ● interaction of sensitized T-cells with allergen.

II. PATOCHEMICAL STAGE

Mediators- lymphokines

● lymphokines, acting on lymphocytes:

- transfer factor
- blast transforming factor, mitogenic factor (determine blast- and mitogenic activity);
- immune-regulatory factors (helper-suppressor factors);

● lymphokines, acting on phagocytosis:

- chemotactic factors (attraction in the focus of micro-and macrophages);
- factor, inhibiting the phagocytes migration (contributes to the accumulation of macrophages in the focus of allergic reaction);

● lymphokines, acting on target-cells:

- lymphotoxin (cytotoxic effect);
- interferon (antiviral activity, increase of lymphocytes cytotoxicity, activation of phagocytes);
- skin-reactive factor.

III. PATHOPHYSIOLOGICAL STAGE

1) infiltration of the focus of allergic inflammation by lymphocytes, monocytes;
2) microcirculatory disorders in the focus, increased vascular permeability(kinines, hydrolytic enzymes, permeability factor)→edema;
3) cellular damage;
4) direct cytotoxic action of sensitized T-lymphocytes;
5) cytotoxic effect of lymphotoxins
6) lysosomal enzymes.

CLINICAL MANIFESTATIONS:

Tuberculin reaction, infectious-allergic disorders, contact dermatitis, eczema, rejection of transplant, antitumor immunity.

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HYPOXIA

The purpose of the practical class: To understand the general patterns of occurrence, development and outcome of hypoxic conditions. To be able to find signs of disorders and compensation from the oxygen budget systems and determine the type of hypoxia.

Basic questions the student should know:

1. Functional system for the consistency of the gas composition of blood.
2. Transport of gases (O_2, CO_2) by blood. Hemoglobin and its forms. Myoglobin. Factors affecting the formation and dissociation of oxyhemoglobin. Gas exchange between blood and tissues. O_2 and CO_2 content in arterial and venous blood. Oxygen capacity of the blood.
3. Electron transfer chain as a part of the respiratory system. Coefficient of O2 utilization in different conditions.
4. Functional system for the consistency of the gas composition of blood.
5. Transport of gases (O_2, CO_2) by blood. Hemoglobin and its forms. Myoglobin. Factors affecting the formation and dissociation of oxyhemoglobin. Gas exchange between blood and tissues. O_2 and CO_2 content in arterial and venous blood. Oxygen capacity of the blood.
6. Electron transfer chain as a part of the respiratory system. Coefficient of O_2 utilization in different conditions.

The student should know:

1. Hypoxia as a state of absolute or relative insufficiency of biological oxidation. The role of hypoxia in the development of various pathological processes and diseases. Stability of individual organs and tissues to oxygen starvation.
2. Principles of classification of hypoxic states. Types of hypoxia (fig. 3).
3. Etiology and pathogenesis of main types of hypoxia: exogenous, respiratory, circulatory, hemic, tissue. Indicators of gas composition of arterial and venous blood for individual types of hypoxia (fig. 4).
4. Emergency and long-term adaptive reactions for hypoxia and their mechanisms (fig. 5).
5. Disorders of metabolic processes, functions and morphology of cells and physiological functions for acute and chronic hypoxia. Reversibility of hypoxia. Hypoxia – general mechanism of cells damage and death.
6. Pathophysiological basis of prevention and therapy of hypoxic states.

7. Hyperoxia and its role in pathology. Hyperoxigenation and free radicals processes. Hyperoxia as a cause of hypoxia. Therapeutic effect of hyperoxygenation: hyper- and normobaric oxygenation and their use in medicine.
8. Features of hypoxia development in altitude.

TESTS FOR KHOWLEDGE CONTROL IN SELF-TRAINING

1. What are the causes of physiological hypoxia?
1) rise to a height;
2) rest in hermetically sealed space;
3) respiratory failure;
4) anemia;
5) hypobaria;
6) cardiovascular failure.

2. What are the causes of respiratory hypoxia?
1) emphysema;
2) right ventricular heart failure;
3) collapse;
4) hypovolemia;
5) anemia;
6) carbon monoxide poisoning;
7) pneumosclerosis;
8) pneumonia.

3. What are the causes of circulatory hypoxia?
1) collapse;
2) hypovolemia;
3) rise to height;
4) infarct;
5) pneumonia;
6) bronchial asthma;
7) heart failure;
8) anemia.

4. What are the causes of hemic hypoxia?
1) acute bleeding;
2) poisoning with nitrates and nitrites;
3) barbiturate poisoning;
4) myocardium infarction;

5) collapse;
6) anemia;
7) heart failure;
8) respiratory failure.

5. What are the causes of histotoxic hypoxia?

1) vitamins deficiency of B group;
2) heart failure;
3) hyperthyroidism;
4) pneumonia;
5) anemia;
6) bronchial asthma;
7) cyanide poisoning;
8) collapse.

6. What is the main indicator of respiratory hypoxia?

1) arterial hypoxemia;
2) venous hypoxemia;
3) decrease in oxygen blood capacity;
4) decrease in oxygen arterio-venous difference;
5) increase in oxygen arterio-venous difference;
6) decrease of CO;
7) hypovolemia;
8) decrease in volume blood flow;
9) increase in volume blood flow.

7. What is the main indicator of circulatory hypoxia?

1) arterial hypoxemia;
2) venous hypoxemia;
3) decrease in oxygen blood capacity;
4) decrease in oxygen arterio-venous difference;
5) increase in oxygen arterio-venous difference;
6) decrease of CO;
7) hypovolemia;
8) increase in volume blood flow.

8. What is the main indicator of hemic hypoxia?

1) arterial hypoxemia;
2) venous hypoxemia;
3) decrease in oxygen blood capacity;

4) decrease in oxygen arterio-venous difference;
5) increase in oxygen arterio-venous difference;
6) decrease of CO;
7) hypovolemia;
8) decrease in volume blood flow;
9) increase in volume blood flow.

9. What is the main indicator of histotoxic hypoxia?

1) arterial hypoxemia;
2) venous hypoxemia;
3) decrease in oxygen blood capacity;
4) decrease in oxygen arterio-venous difference;
5) increase in oxygen arterio-venous difference;
6) decrease of CO;
7) hypovolemia;
8) decrease in volume blood flow;
9) increase in volume blood flow.

10. What are the mechanisms of emergent adaptation to hypoxia?

1) centralization of blood circulation;
2) increasing the volume of alveolar ventilation:
3) erythropoiesis stimulation;
4) increase in 2,3 diphosphoglycerate in erythrocytes;
5) mobilization of deposited blood;
6) hypertrophy of myocardium;
7) intensification of mitochondriogenesis;
8) tachypnea;
9) tachycardia;
10) increased anaerobic glycolysis;
11) activation of LPO.

11. What are the mechanisms of long-term adaptation to hypoxia?

1) intensification of mitochondriogenesis;
2) tachypnea;
3) tachycardia;
4) increased anaerobic glycolysis;
5) activation of LPO;
6) hypertrophy of myocardium;
7) mobilization of deposited blood;

8) increase in 2,3 diphosphoglycerate in erythrocytes;
9) erythropoiesis stimulation;
10) increasing the volume of alveolar ventilation;
11) centralization of blood circulation.

12. What are the main indicators of energetic metabolism disorders in hypoxia?

1) increase in extracellular K;
2) metabolic acidosis;
3) hyperlactacidemia;
4) hyperaemia;
5) negative nitrogen balance;
6) hyperketonemia;
7) excess of ADP, AMP;
8) deficit of macroergists;
9) hypoglycemia.

13. What are the main indicators of protein metabolism disorders in hypoxia?

1) hypoglycemia;
2) hyperlactacidemia;
3) deficit of macroergists;
4) excess of ADP, AMP;
5) dysproteinemia;
6) hypoalbuminemia;
7) hyperketonemia;
8) hyperaemia;
9) hypocholesterolemia;
10) negative nitrogen balance.

14. What are the mechanisms of acid-basic imbalances in hypoxia?

1) oxygen deficiency;
2) hyperketonemia;
3) activation of glycolysis;
4) metabolic alkalosis;
5) excess of ADP, AMP;
6) deficit of macroergists;
7) disorders of lactate resynthesis;
8) metabolic acidosis;
9) increase in extracellular K;
10) hyperlactacidemia.

15. What are the main indicators of lipid metabolism disorders in hypoxia?

1) increase in extracellular K;
2) hyperaemia;
3) hypocholesterolemia;
4) negative nitrogen balance;
5) hypoglycemia;
6) hyperketonemia;
7) hyperlactacidemia;
8) excess of ADP, AMP;
9) deficit of macroergists.

16. What are the main indicators of carbohydrate metabolism disorders in hypoxia?

1) hyperaemia;
2) hypocholesterolemia;
3) hyperlactacidemia;
4) hypoalbuminemia;
5) dysproteiemia;
6) hyperketonemia;
7) deficit of macroergists;
8) excess of ADP, AMP;
9) hypoglycemia.

ANSWERS KEYS:

1. 1, 2, 5
2. 1, 7, 8
3. 1, 2, 4, 7
4. 1, 2, 6
5. 1, 3, 7
6. 1
7. 2, 5, 6, 8
8. 3
9. 4
10. 1, 2, 5, 8, 9, 10
11. 1, 6, 8, 9
12. 8
13. 5, 6, 8, 10
14. 1, 6, 5, 3, 7, 10, 2, 8, 9, 4
15. 3, 6
16. 3, 9

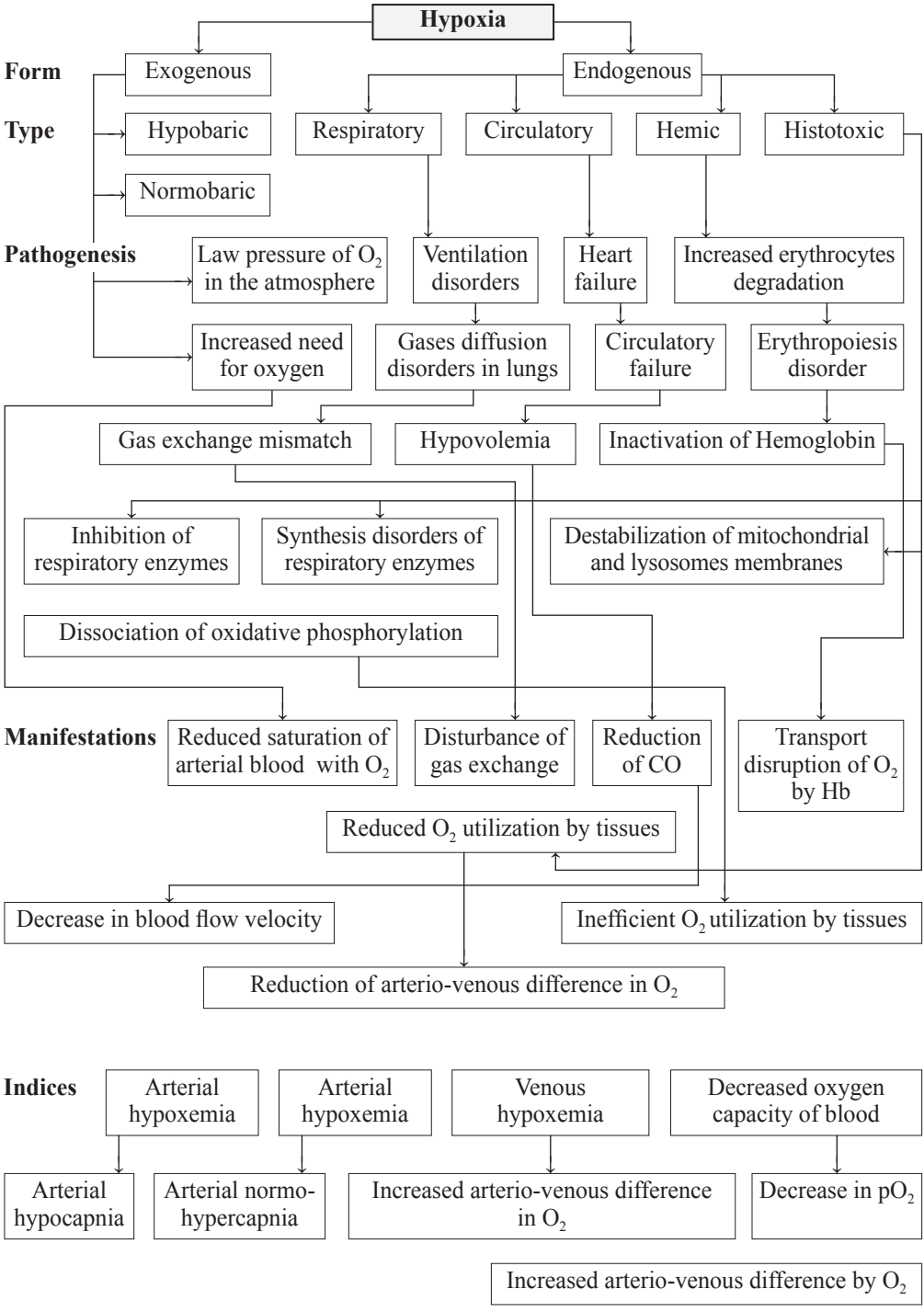

Figure 3. **TYPES OF HYPOXIA**

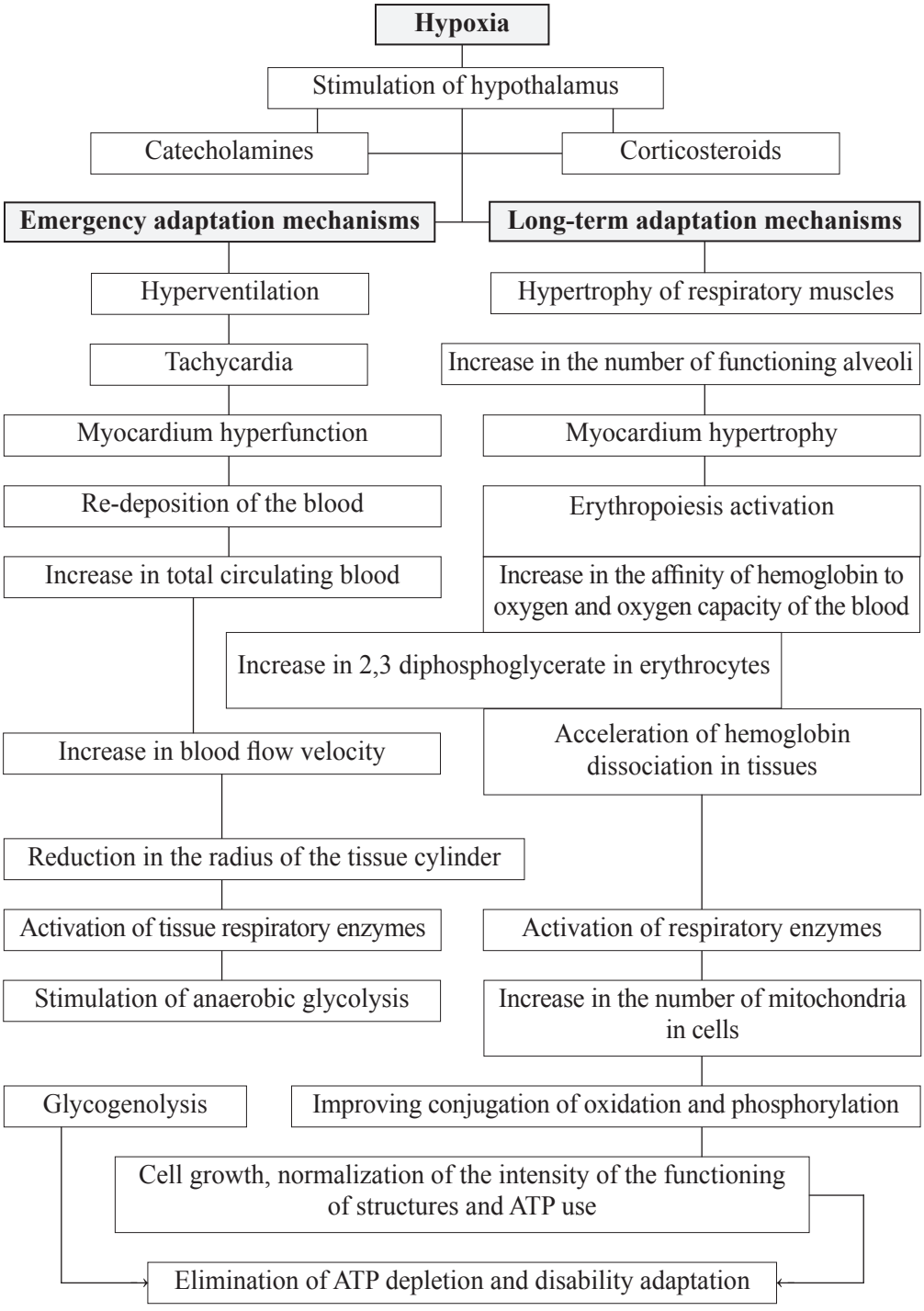

Figure 4. **THE MECHANISMS OF ADAPTATION TO HYPOXIA**

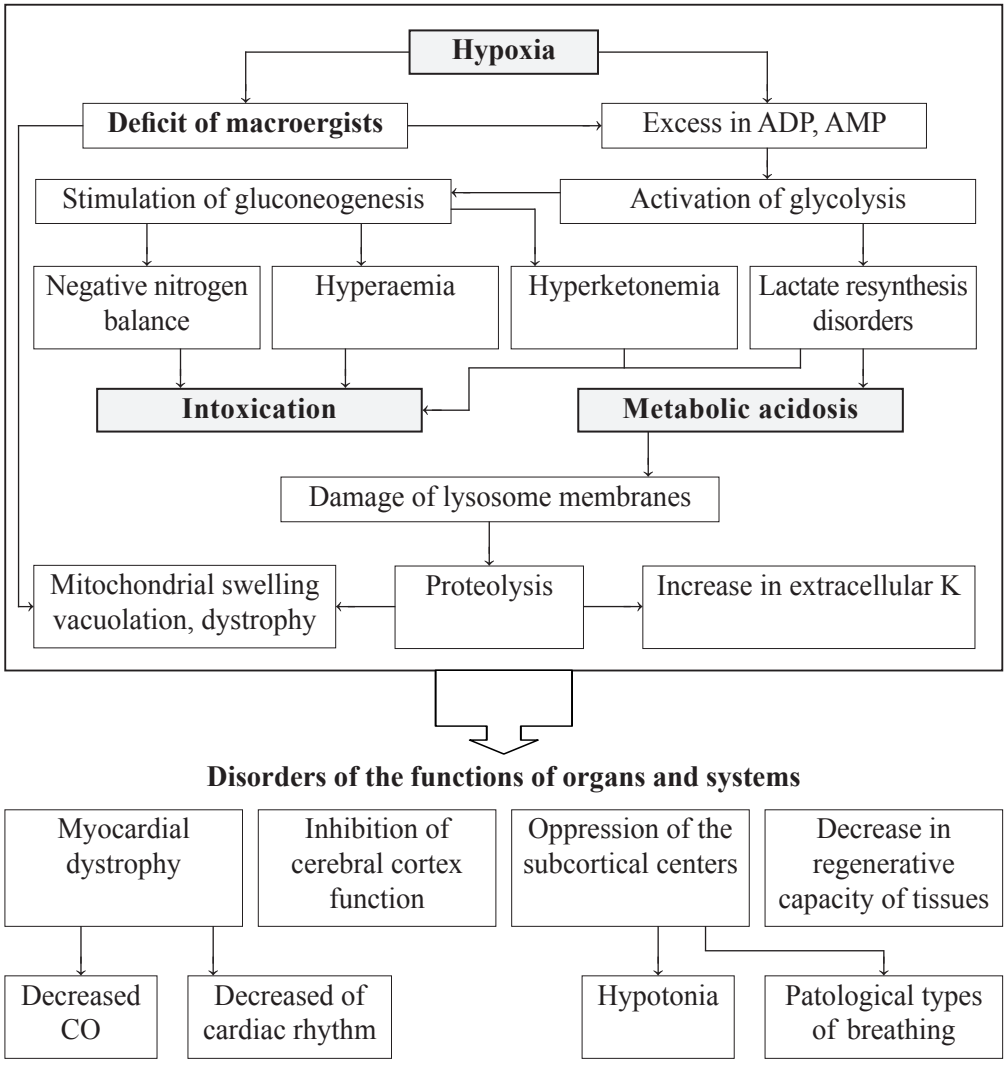

Figure 5. **MECHANISMS OF METABOLIC DISORDERS IN HYPOXIA**

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DISORDERS OF CARBOHYDRATE METABOLISM

The purpose of the practical class: should be able to:

- Determine the mechanisms of carbohydrate metabolism disorders;
- Describe the causes and the mechanisms of development, the pathogenesis of main manifestations and complications of diabetes mellitus;
- Differentiate the causes and the clinical manifestations of diabetic ketoacidosis, hyperosmolar hyperglycemic state and hypoglycemic coma.

Basic questions the student should know:

1. General scheme of sources and glucose utilization pathways in the body.
2. Glucose catabolism. Aerobic glycolysis-fundamental pathway of glucose catabolism in humans. Sequencing reactions of pyruvate formation (anaerobic glycolysis) as a specific pathway for glucose catabolism. Using glucose for fats synthesis in the liver and adipose tissue.
3. Anaerobic glycolysis. Distribution and physiological significance of anaerobic glycolysis.
4. Glucose biosynthesis (gluconeogenesis) from amino acids, glycerol and lactic acid. Interconnection between muscles glycolysis and hepatic gluconeogenesis.
5. Properties and distribution of glycogen as a reserve polysaccharide. Glycogen biosynthesis. Glycogen mobilization.
6. Glucose metabolism features in different organs and cells: red blood cells, brain, muscles, adipose tissue, liver.
7. Hereditary metabolic disorders of monosaccharides and polysaccharides: galactosemia, fructose intolerance, intolerance and malabsorption of disaccharides. Glycogenosis and aglycogenosis.
8. The role of insulin, glucagon and epinephrine in glucose metabolism, deposition and mobilization of fats in adipose tissue.
9. Ketone bodies. Biological significance, structure, formation and oxidation chemistry.
10. Regulation of energetic metabolism, the role of insulin and counter-regulatory hormones in ensuring homeostasis. The role of insulin and glucagon in the regulation of energetic metabolism in normal eating and in starvation.

The student should know:

1. Disorders of carbohydrates absorption, synthesis, deposition and glycogen broken, glucose uptake into the cells and its assimilation.

2. Hypoglycemic states, their types and mechanisms (table15).

3. Disorders of physiological functions of organism in hypoglycemia; hypoglycemic coma.

4. Hyperglycemic states, their types and mechanisms.

5. Diabetes mellitus, its types. Etiology and pathogenesis of different forms of diabetes mellitus. Mechanisms of insulin resistance.

6. Disorders of carbohydrates and other metabolic types in diabetes mellitus; disorders of physiological functions, their mechanisms.

7. Diabetic coma. Types. Causes. Pathogenesis. Manifestations.

Table 15

DISORDERS OF CARBOHYDRATE METABOLISM

TYPES	
HYPERGLYCEMIA	**HYPOGLYCEMIA**
ETIOLOGY	
1. Food consumption 2. Insulin insufficiency 3. Excess of counter-regulatory hormones 4. Neurogenic 5. Stress 6. Emotions 7. Pain 8. Seizures 9. Anesthesia with ether, and chloroform 10. Drugs (peroral contraceptive, adrenomimetics)	1. Starvation 2. Increased muscular activity 3. Prolonged psycho-emotional tension 4. Hyperinsulinism 5. Deficiency of glucose counter-regulatory hormones 6. Liver failure 7. Glycogenosis 8. Hypoxia 9. Enterites 10. Nephrosis 11. B_1 vitamin deficiency
PATHOGENESIS	
1. Increased absorption in the intestine 2. Excitation of sympathetic centers 3. Inhibition of glycogenogenesis 4. Stimulation of gluconeogenesis 5. Stimulation of glycogenolysis 6. Inhibition of carbohydrates oxidation 7. Inhibition of glucose uptake by the cells	1. Deficient intake from intestine 2. Increased excretion of glucose with urine 3. Stimulation of glycogenogenesis 4. Inhibition of gluconeogenesis 5. Stimulation of glycogenolysis 6. Activation of carbohydrates oxidation

MANIFESTATIONS	
1. Glycemia > 5.5 mmol / L 2. Glucozuria 3. Polyuria 4. Polydipsia 5. Polyphagia 6. Dry skin and mucous membranes	1. Glycemia < 3.3 mmol / L 2. Tremor, muscles tremors 3. Dizzines 4. Sweating 5. Palpitation 6. Hunger 7. Nausea

TESTS FOR KHOWLEDGE CONTROL IN SELF-TRAINING

1. What are the mechanisms of hyperglycemic effects due to STH action?

1) activation of phosphorylase in liver and in myocardium;
2) activation of phosphorylase in liver and in skeletal muscles;
3) stimulation of glycogenolysis;
4) inhibition of glucose uptake by the cells;
5) stimulation of gluconeogenesis from amino acids and lactate;
6) stimulation of lipolysis;
7) stimulation of ketonegenesis in the liver;
8) suppression of insulin secretion;
9) stimulation of glucagon secretion;
10) stimulation of liver insulinase;
11) inhibition of hexokinase.

2. What are the mechanisms of hyperglycemic effects due to thyroxine action?

1) activation of phosphorylase in the liver;
2) stimulation of glycogenolysis;
3) inhibition of glucose uptake by the cells;
4) stimulation of gluconeogenesis from amino acids and lactate;
5) stimulation of lipolysis;
6) stimulation of ketonegenesis in the liver;
7) suppression of insulin secretion;
8) stimulation of glucagon secretion;
9) stimulation of liver insulinase;
10) stimulation of glycogenolysis;
11) inhibition of hexokinase.

3. What are the mechanisms of hyperglycemic effects due to glucocorticoids action?

1) activation of phosphorylase in liver and in myocardium;
2) activation of phosphorylase in liver and in skeletal muscles;
3) stimulation of glycogenolysis;
4) inhibition of glucose uptake by the cells;
5) stimulation of gluconeogenesis from amino acids;
6) stimulation of lipolysis;
7) stimulation of ketonegenesis in the liver;
8) suppression of insulin secretion;
9) stimulation of glucagon secretion;
10) stimulation of liver insulinase;
11) inhibition of hexokinase.

4. What are the mechanisms of hyperglycemic effects due to adrenaline action?

1) activation of phosphorylase in the liver and in the skeletal muscles;
2) stimulation of glycogenolysis;
3) inhibition of glucose uptake by the cells;
4) stimulation of gluconeogenesis from amino acids and lactate;
5) stimulation of lipolysis;
6) stimulation of ketonegenesis in liver;
7) suppression of insulin secretion;
8) stimulation of glucagon secretion;
9) stimulation of liver insulinase.

5. What are the mechanisms of hyperglycemic effects due to glucagon action?

1) activation of phosphorylase in liver and in myocardium;
2) activation of phosphorylase in skeletal muscles;
3) stimulation of glycogenolysis;
4) inhibition of glucose uptake by the cells;
5) stimulation of gluconeogenesis from amino acids and lactate;
6) stimulation of lipolysis;
7) stimulation of ketonegenesis in liver;
8) suppression of insulin secretion;
9) stimulation of liver insulinase;
10) inhibition of hexokinase.

6. What are the causes of hyperglycemia?

1) lack of glucose counterregulatory hormones;
2) hyperinsulinism;

3) stress;
4) emotional stress;
5) prolonged mental stress;
6) skeletal muscles work overload;
7) excess of glucose counterregulatory hormones;
8) lack of insulin;
9) starvation.

7. What are the causes of hypoglycemia?

1) starvation;
2) lack of insulin;
3) excess of glucose counterregulatory hormones;
4) overload of skeletal muscles;
5) stress;
6) hyperinsulinism;
7) lack of glucose counterregulatory hormones;
8) enteritis;
9) nephrosis;
10) glycogenoses.

8. What are the mechanisms of hyperglycemia?

1) activation of carbohydrates oxidation in tricarboxylic acid cycle (CTCA);
2) inhibition of glucose uptake by cells;
3) stimulation of glucolysis;
4) inhibition of the carbohydrates oxidation in three carbonic acids cycle (CTCA);
5) stimulation of glycogenolysis;
6) inhibition of glycogenolysis;
7) stimulation of gluconeogenesis;
8) inhibition of gluconeogenesis;
9) stimulation of glycogenogenesis;
10) inhibition of glycogenogenesis.

9. What are the mechanisms of hypoglycemia?

1) inhibition of glycogenogenesis;
2) stimulation of glycogenogenesis;
3) inhibition of gluconeogenesis;
4) stimulation of gluconeogenesis;
5) inhibition of glycogenolysis;
6) stimulation of glycogenolysis;

7) stimulation of glucolysis;
8) inhibition of glucose uptake by cells;
9) alimentary carbohydrates deficiency;
10) malabsorption of carbohydrates;
11) increased excretion of glucose in urine.

10. What are the manifestations of hypoglycemia?
1) dry skin and mucosa;
2) seizures;
3) polyphagia;
4) sweating;
5) hunger;
6) polydipsia;
7) weaknesses;
8) poliuria;
9) tremor, muscle tremors;
10) glucosuria.

11. What are the manifestations of hyperglycemia?
1) tremor, muscle tremors;
2) polyuria;
3) weaknesses;
4) polydipsia;
5) hunger;
6) sweating;
7) polyphagia;
8) seizures;
9) dry skin and mucosa;
10) glucosuria.

12. What are the causes of insulin-depending diabetes mellitus?
1) increased secretion of prostaglandins A and E;
2) blocking of insulin receptors by antibodies;
3) congenital defects of insulin biosynthesis;
4) disorders of hormone receptor interaction;
5) damages of glucose receptors;
6) disorders of insulin receptors biosynthesis;
7) deficiency of zinc and copper;
8) autoimmune damages of beta-cells;
9) inactivating of self-antibodies against insulin receptors;
10) ischemia of pancreas.

13. What are the causes of insulin-independing diabetes mellitus?

1) excess of glucose counterregulatory hormones;
2) chronic pancreatitis;
3) activation of liver insulinase;
4) tumors of pancreas;
5) blocking of insulin by sinalbumin;
6) hemochromatosis;
7) inactivation of insulin by fatty inhibitors;
8) ischemia of pancreas;
9) disorders of the hormone receptor interaction;
10) congenital defects of insulin biosynthesis;
11) blocking of insulin receptors by antibodies.

14. What are the pathogenestic mechanisms of hyperglycemia in diabetes mellitus?

1) inhibition of carbohydrates oxidation in tricarboxylic acid cycle;
2) stimulation of lipolysis;
3) stimulation of gluconeogenesis from lactate and amino acids;
4) stimulation of glycolysis;
5) stimulation of glycogenogenesis;
6) stimulation of the glucose uptake by cells;
7) inhibition of glycogenogenesis;
8) inhibition of glycogenolysis;
9) inhibition of gluconeogenesis.

15. What are the mechanisms of hypercholesterolemia in diabetes mellitus?

1) inhibition of glucose uptake by cells;
2) stimulation of glucose uptake by cells;
3) stimulation of glycogenogenesis;
4) stimulation of glycogenolysis;
5) stimulation of gluconeogenesis from lactate and amino acids;
6) inhibition of carbohydrates oxidation in tricarboxylic acid cycle;
7) stimulation of lipolysis;
8) inhibition of glycogenogenesis;
9) inhibition of glycogenolysis;
10) inhibition of gluconeogenesis.

16. What are mechanisms of hyperlipidaemia in diabetes mellitus?

1) stimulation of glycogenogenesis;
2) stimulation of glycogenolysis;
3) stimulation of gluconeogenesis from lactate and amino acids;

4) stimulation of lipolysis;
5) inhibition of the carbohydrates oxidation in tricarboxylic acid cycle;
6) inhibition of gluconeogenesis;
7) inhibition of glycogenolysis;
8) inhibition of glycogenogenesis;
9) inhibition of the glucose uptake by cells;
10) stimulation of the glucose uptake by the cells.

17. What are the mechanisms of hyperlactataemia in diabetes mellitus?
1) stimulation of glycogenolysis;
2) stimulation of gluconeogenesis from lactate and amino acids;
3) stimulation of lipolysis;
4) inhibition of carbohydrates oxidation in tricarboxylic acid cycle (CTCA);
5) stimulation of glucose uptake by the cells;
6) stimulation of glycogenogenesis;
7) inhibition of glucose uptake by cells;
8) inhibition of glycogenogenesis;
9) inhibition of glycogenolysis;
10) inhibition of gluconeogenesis.

18. What are the pathogenestic mechanisms of hyperazotaemia?
1) stimulation of glucose uptake by cells;
2) stimulation of glycogenogenesis;
3) stimulation of glucolysis;
4) stimulation of gluconeogenesis from lactate and amino acids;
5) stimulation of lipolysis;
6) inhibition of carbohydrates oxidation in tricarboxylic acid cycle (CTCA);
7) inhibition of gluconeogenesis;
8) inhibition of glucolysis;
9) inhibition of glycogenogenesis;
10) inhibition of glucose uptake by cells.

19. What are the types of microangiopathies?
1) polyneuropathy;
2) atherosclerosis of coronary arteries;
3) atherosclerosis of cerebral arteries;
4) atherosclerosis of the arteries of inferior legs;
5) diabetic retinopathy;
6) diabetic nephropathy;
7) diabetic dermatopathy.

20. What are the types of macroangiopathies?

1) furunculosis;
2) immunodeficiency;
3) diabetic dermatopathy;
4) diabetic nephropathy;
5) diabetic retinopathy;
6) polyneuropathy;
7) atherosclerosis of coronary arteries;
8) atherosclerosis of cerebral arteries;
9) atherosclerosis of the arteries of inferior legs.

21. What are the mechanisms of diabettis insipidus?

1) decreased secretion of ADH;
2) disorders of carbohydrates metabolism;
3) increased secretion of ADH;
4) decreased secretion of aldosterone;
5) increased excretion of sodium in urine.

22. What are the basic metabolic signs of ketoacidotic coma?

1) ketoacidosis and hyperglycemia;
2) hypernatremia and ketoacidosis;
3) lactate acidosis and hypernatremia;
4) hyperosmolarity and lactateacidosis;
5) hyperglycemia and hyperosmolarity;
6) hypernatremia and hyperosmolarity;
7) lactate acidosis and hyperpotassaemia.

23. What are the basic metabolic signs of hyperosmolar coma?

1) lactate acidosis and hyperpotassaemia;
2) hypernatremia and hyperosmolarity;
3) hyperglycemia and hyperosmolarity;
4) hyperosmolarity and lactate acidosis;
5) lactate acidosis and hypernatremia;
6) hypernatremia and lactate acidosis;
7) ketoacidosis and hyperglycemia.

24. What are the basic metabolic signs of hyperlactatemic coma?

1) hyperosmolarity and lactate acidosis;
2) lactate acidosis and hypernatremia;
3) hypernatremia and ketoacidosis;
4) ketoacidosis and hyperglycemia;

5) lactate acidosis and hyperpotassaemia;
6) hypernatremia and hyperosmolarity;
7) hyperglycemia and hyperosmolarity.

ANSWERS KEYS:

1. 9, 10
2. 1, 10
3. 4, 5, 11
4. 1, 2, 3, 5, 7, 7
5. 1, 3, 4, 5,6, 7
6. 3, 4, 7, 8, 10, 12
7. 1, 4, 6, 7, 8, 9, 10
8. 2, 4, 5, 7, 10
9. 2, 3, 5, 7, 9, 10, 11
10. 2, 4, 5, 7, 9
11. 2, 4, 7, 9, 10
12. 1, 3, 5, 8, 10
13. 1, 3, 5, 7, 9, 11
14. 1, 3, 7
15. 1, 6, 7
16. 4, 5, 9
17. 1, 4, 7, 8
18. 4, 6, 10
19. 1, 5, 6, 7
20. 7, 8, 9
21. 1
22. 1
23. 2, 3
24. 5

Table 16

PATHOGENESIS OF HYPEROSMOTIC COMA

Causes: Diseases and disorders triggering hyperglycemia, insulin deficiency and dehydration

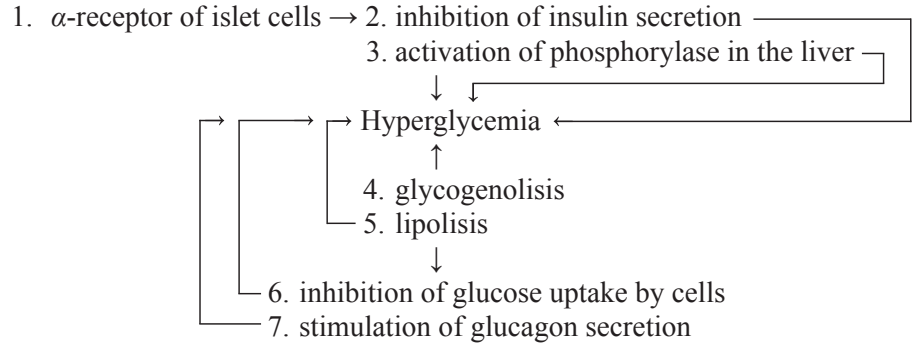
1. Massive hyperglycemia → inhibition of ketonegenesis in liver
2. Glucosuria → osmotic dieresis
   a) Progressive intracellular dehydration
   b) Polycythemic hypovolaemia
   c) Hyperaldosteronism → hypernatriemia
   d) Increase of blood osmolarity
   e) Haemoconcentration → CID-syndrome
3. Hypotension → collapse
   a) kidneys ischemia → oligo-, anuria
   b) hyperazotaemia
   c) brain microcirculatory disorders, micro focal hemorrhages
   d) neurons dehydration → hypertermia
   e) drop of CSF pressure
   f) loss of consciousness, coma

I. GLUCAGON

1. activation of phosphorylase in the liver
↓
2. glycogenolisis
3. gluconeogenesis from amino acids and lactate
4. lipolisis
↓
5. inhibition of glucose uptake by cells
6. stimulation of ketogenesis

→ Hyperglycemia

II. EPINEPRINE



III. STH

1. hyperplasia of islet α-cells
2. stimulation of glucagon secretion → Hyperglycemia
3. stimulation of liver insulin-ase

IV. GLUCOCORTICOIDS

1. catabolism of proteins
2. gluconeogenesis from glucagon
3. inhibition of hexokinase → Hyperglycemia
4. inhibition of glucose uptake by cells

V. TIROXINE

1. activation of phosphorylase in the liver
2. glicogenolysis → Hyperglycemia

The mechanisms of hyperglycemic actions of glucose counterregulatory hormones

Table 17

PATHOGENESIS OF KETOACIDOTIC COMA

Progressive insulin deficiency

1. Inhibition of hexokinase → inhibition of glucose uptake by cells → energy deficiency in cells
2. Stimulation glucose counterregulatory hormones secretion
   a) increase of glycogenolisis
   b) stimulation of gluconeogenesis
   c) activation of lipolysis
   d) steatosis of the liver
   e) activation of glycolysis → lactacidosis
   f) decompensation of metabolic acidosis → inhibition of insulin synthesis → → progressive insulin deficiency

3. Decompensation of metabolic acidosis → efflux of intracellular K^+, Mg^{++} → rapid inhibition of tricarboxylic acid cycle
4. Poor use of acetyl-Co A → increase of ketonemia and cholesterolemia
5. Increase of blood osmolarity
   a) dehydration of cells
   b) increase of osmotic diuresis
   c) polycytemic hypovolemia
6. Loss of electrolytes and phosphorus
   a) decrease of 2,3 diphosphoglycerate (DPG)
   b) increase of glycosylated hemoglobin
   c) worsening of HbO_2 dissociation → hemic hypoxia → worsening acidosis
7. Hyperventilation (Kussmaul breathing) → hypocapnia → fall in vascular tonus → hypo tension
8. Mechanisms of CNS injury
   a) hyperketonemia
   b) decompensation of metabolic acidosis
   c) hyperazotemia
   d) deposition of sorbitol and fructose inside neurons → significant increase of osmotic pressure → marked availability to edema
   e) decrease of neurotransmitters synthesis
   f) intracellular proteolysis
   g) suppression of aerobic glucose conversion
   h) ATP depletion, acid-basic and electrolytes imbalances
   i) blackouts, coma

Table 18

PATHOGENESIS OF HYPERLACTACIDEMIC COMA

Coma is an anticipated disease and disorder, accompanied by hypoxia, also biguanide, which stimulates glycolysis

1. Inhibited conversion of pyruvate into acetyl-Co A
2. Excessive accumulation of pyruvate and lactate
3. Mobilization of glucose counterregulatory hormones
4. Stimulation of anaerobic glycolysis
5. Decompensated metabolic acidosis and suppressed insulin synthesis
6. Hyperpotassiemia, hypercalcaemia
   a) blocking of the heart and vessels adrenergic receptors
   b) cardiac arrhythmias
   c) disorders of myocardial contractility
   d) arterial hypotension
   e) acute heart failure
   f) kidneys ischemia → anuria → hyperazotemia

7. Kussmaul breathing
8. Encephalopathy as a result of hyperlactateacidemia, hyperazotemia, progressive hypoxia

Table 19

HYPOGLYCEMIC COMA

ETIOLOGY
1. Hyperinsulinism 2. Inappropriate glucose-lowering therapy 3. Impaired diet on the background of insulin therapy 4. Hunger 5. High physical activity 6. Mental trauma 7. Liver failure 8. Lack of glucose counterregulatory hormones 9. Alcohol intoxication (stimulates insulin release, inhibits glycogenolysis)
PATOGENESIS
1. Acute onset of hypoglycemia a) energy deficiency of neurons b) compensatory activation of sympathoadrenal system and release of glucose counterregulatory hormones in the blood c) stimulation of glycogenolysis d) stimulation of gluconeogenesis 2. Hyperadrenalinemia a) sweating b) tremor c) tachycardia, arrhythmia d) tonic and clonic seizures e) hyperphrenia, malice, aggression, inadequate behavior 3. Pale, wet skin, preserved turgor 4. Preserved tonus of eyeballs 5. Increased muscles tonus and tendon , periosteal reflexes 6. Acute hypoxia of brain a) hunger f) aphasia b) headache g) seizures c) stupor h) fall of AP d) inadequate behavior i) hypertemia e) hallucinations j) blackouts

TYPES

Insulindependent (I type) — *Insulinindependent (II type)*

ETIOLOGY

1. Chronic pancreatitis
2. Tumors
3. Hemochromatosis
4. Ischemia of pancreas
5. Insulin autoantibodies
6. Zink and copper deficiency
7. Decrease of cellular sensitivity to insulin
8. Increased secretion of prostaglandins A, E

1. Excessive concentration of counterregulatory hormones
2. Activation of liver insulin-ase
3. Sinalbumin insulin blockage
4. Insulin inactivation by inhibitors of fats (atherosclerosis, hypertonic disease)
5. Autoimmune injures of β cells
6. Injuries of glucoreceptors
7. Congenital defect of insulin biosynthesis
   a) degradation of insulin receptors
   b) disorders of their biosynthesis
   c) disorders of receptor phosphorylation
   d) disorders of hormone receptor interaction
   e) receptor blockage by antibodies

PATHOGENESIS

1. Insufficient secretion of insulin by *β* cells
1. Insulin or receptors blockage at normal or increased level of hormone
2. Insulin deficiency at level of receptors → **Hyperglycemia** → glusosuria
3. Inhibition of glucose uptake by cells
4. Inhibition of glicogenogenesis
5. Stimulation of glicogenolysis
6. Stimulation of gluconeogenesis
   a) negative nitrogen balance

→ polyuria → polydipsia → hyperazotaemia → immune suppression → loss of body weight

7. Lipolysis → polyphagia → hypercholesterolaemia → hyperlipidaemia

8. Inhibition of carbohydrates oxidation → hyperketonaemia → ketonuria → hyperlactacidemia

Figure. 8. Diabetes mellitus

Table 20

LATE COMPLICATIONS OF DIABETES MELLITUS

1. Diabetic microangiopathy (accumulation of glycosylated proteins in the basic membrane of arterioles)
   a) diabetic retinopathy
   b) nephroangiopathy
2. Diabetic macroangiopathy (atherosclerosis of large vessels)
   a) coronary arteries
   b) cerebral arteries
   c) arteries of feet ("diabetic foot ulcers" –pain, gangrene)
3. Diabetic polyneuropathies (demyelinating of peripheral nerves in the result of chronic vascular insufficiency)-pain, paresthesia, loss of all types of sensitivity, trophic ulcers, gangrene.
4. Diabetic dermatopathies as a result of hyperlipidemia
   a) lipoid necrosis
   b) rash xanthomas
5. Immunodeficiency

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DISORDERS OF ACID-BASE BALANCE

The purpose of the practical class: Based on the blood and urine indicators you should be able to differentiate the form and the development mechanisms of acid-base imbalance, to determine the compensatory reactions and damages in these disorders.

Basic questions the student should know:

1. Body fluids Buffer Systems: bicarbonate buffer system, phosphate buffer system, protein buffer systems, and hemoglobin buffer system. The mechanisms of buffer systems action and their quantitative characteristics. The concept of body acid-basic states.
2. Synthesis and dissociation of bicarbonates. The importance of carbonic anhydrase.
3. The role of kidneys in maintaining the pH of blood. Glutaminase of kidneys; Formation and excretion of ammonium salts. The activation of kidneys glutaminase in acidosis.

The student should know:

1. Basic disorders of acid-basic states. Classification (tabl. 22).
2. Metabolic Acidosis. Etiology. Pathogenesis. Compensatory mechanisms. Disorders of organs and systems. Basic laboratory tests of acid-basic states (tabl. 23).
3. Respiratory Acidosis. Etiology. Pathogenesis. Compensatory mechanisms. Disorders of organs and systems. Basic laboratory tests (tabl. 24).
4. Metabolic Alkalosis. Etiology. Pathogenesis. Compensatory mechanisms. Disorders of organs and systems. Basic laboratory tests (tabl. 25).
5. Respiratory Alkalosis. Etiology. Pathogenesis. Compensatory mechanisms. Disorders of organs and systems. Basic laboratory tests (tabl. 26).
6. Mixed forms of acid-basic imbalances. Etiology. Pathogenesis. Compensatory mechanisms. Disorders of organs and systems. Basic laboratory tests.

TESTS FOR KHOWLEDGE CONTROL IN SELF-TRAINING

1. What are the compensatory mechanisms of respiratory acidosis?

1) stimulation of acido- and ammoniumgenesis in the kidneys;
2) blockade of acido- and ammoniumgenesis in the kidneys;
3) hyperventilation;

4) hypoventilation;
5) hyperkalemia;
6) hypokalemia;
7) hypercalcemia;
8) increased excretion of sodium and bicarbonate in urine;
9) increased reabsorption of bicarbonates in renal tubules.

2. What are the compensatory mechanisms of respiratory alkalosis?

1) stimulation of acido- and ammoniumgenesis in kidneys;
2) blockade of acido- and ammoniumgenesis in kidneys;
3) hyperventilation;
4) hypoventilation;
5) hyperkalemia;
6) hypokalemia;
7) hypercalcemia;
8) increased excretion of sodium and bicarbonate in urine;
9) increased reabsorption of bicarbonates in renal tubules.

3. What are the compensatory mechanisms of metabolic acidosis?

1) stimulation of acido- and ammoniumgenesis in kidneys;
2) blockade of acido- and ammoniumgenesis in kidneys;
3) hyperventilation;
4) hypoventilation;
5) hyperkalemia;
6) hypokalemia;
7) hypercalcemia;
8) increased excretion of sodium and bicarbonate in urine;
9) increased reabsorption of bicarbonates in renal tubules.

4. What are the compensatory mechanisms of metabolic alkalosis?

1) stimulation of acido- and ammoniumgenesis in kidneys;
2) blockade of acido- and ammoniumgenesis in kidneys;
3) hyperventilation;
4) hypoventilation;
5) hyperkalemia;
6) hypokalemia;
7) hypercalcemia;
8) increased excretion of sodium and bicarbonate in urine;
9) increased reabsorption of bicarbonates in renal tubules.

5. What are the disorders of the cardiovascular system in the metabolic acidosis?

1) arteriolar spasm;
2) vasodilation;
3) bradycardia;
4) fibrillation;
5) increase of blood pressure;
6) reduction of blood pressure;
7) dilation of cerebral vessels.

6. What are the disorders of the cardiovascular system in respiratory acidosis?

1) arteriolar spasm;
2) vasodilation;
3) bradycardia;
4) fibrillation;
5) increase of blood pressure;
6) reduction of blood pressure;
7) dilation of cerebral vessels.

7. What are the functional disorders of external respiration in respiratory acidosis?

1) Kussmaul breathing ;
2) Cheyne-Stokes breathing;
3) Biota breathing;
4) broncho-constriction;
5) re-irritation and decrease in excitability of the respiratory center;
6) increased secretion of bronchial glands.

8. What are functional disorders of external respiration in metabolic acidosis?

1) Kussmaul breathing ;
2) Cheyne-Stokes breathing;
3) Biota breathing;
4) bronchoconstriction;
5) re-irritation and decrease of excitability of the respiratory center;
6) increased secretion of bronchial glands.

9. How is the impaired renal function in respiratory acidosis?

1) hypertension;
2) hypotension;
3) kidneys ischemia;

4) reduced filtration;
5) oliguria;
6) polyuria.

10. Impaired renal functions in metabolic acidosis are:
1) hypertension;
2) hypotension;
3) kidneys ischemia;
4) reduced filtration;
5) oliguria;
6) polyuria.

11. What are the disorders of respiratory alkalosis?
1) reduction of vascular tone;
2) dehydration;
3) seizures;
4) polyuria;
5) collapse;
6) increase of vascular tone.

12. What are the disorders of metabolic alkalosis?
1) reduction of vascular tone;
2) dehydration;
3) seizures;
4) polyuria;
5) collapse.

13. What is the etiology of respiratory alkalosis?
1) hyperaldosteronism;
2) dyspnea;
3) excess alkali intake;
4) loss of hydrochloric acid in vomiting;
5) altitude hypoxia;
6) poorly regulated ventilation (ASV).

14. What is etiology of metabolic alkalosis?
1) hyperaldosteronism;
2) dyspnea;
3) excess alkali intake;
4) loss of hydrochloric acid in vomiting;
5) altitude hypoxia;
6) poorly regulated ventilation (ASV).

15. What is the etiology of metabolic acidosis?

1) disorders of gases diffusion in the alveoli;
2) starvation;
3) hypoxia;
4) renal failure;
5) hypoventilation;
6) diabetes mellitus;
7) heavy physical activity.

ANSWERS KEYS:

1. 1, 5, 7, 9
2. 2, 6, 8
3. 1, 3, 5, 7, 9
4. 2, 4, 6, 8
5. 2, 4, 6
6. 1, 3, 5, 7
7. 4, 6 (2, 3)
8. 1, 5
9. 1, 3, 4, 5
10. 2,3,4,5
11. 1, 2, 3, 4, 5
12. 2, 3, 4
13. 2, 5, 6
14. 1, 3, 4
15. 2, 3, 4, 6, 7

Table 22

DISORDERS OF ACID-BASE BALANCE

	Acidosis	Alkalosis
compensated	pH 7.35-7.40	7.40-7.45
subcompensated	pH 7.34-7.20	7.46-7.55
decompensated	pH 7.19-6.80	7.56-7.80

Table 23

RESPIRATORY ACIDOSIS

Etiology	1. Hypoventilation 2. Disorders of infusion ventilation relationships 3. Disorders of gas diffusion 4. Mixtures gas breathing with a high CO_2 content
Pathogenesis	Disorders of pulmonary gas exchange-hypercapnia
Indices	↓pH, ↑pCO_2(primary), ↑SB (standart bicarbonate; HCO_3^-; compensatory)

Disorders	1. Spasm of arterioles - increases the total peripheral vascular resistance (TPVR) - increases arterial pressure (AP) - ischemia of kidneys - reduction of filtration - oliguria 2. Dilation of cerebral blood vessels - increased CRL formation - intracranial hypertension - headache 3. Increased excitability of vagus nerve - bradycardia, possible cardiac arest - spasm of bronchioles - increased secretion of bronchial mucus 4. Increased secretion of catecholamines 5. Coma due to the narcotic effect of hypercapnia
Compensatory mechanisms	1. Acido- and ammonium genesis 2. Increased reabsorption of bicarbonates in tubules 3. Hypernatremia

Table 24

METABOLIC ACIDOSIS

Etiology	1. Hypoxia 2. Starvation 3. Diabetes mellitus 4. Renal failure 5. Liver failure 6. Hard physical work 7. Acid poisoning
Pathogenesis	1. Increased concentration of non-volatile acids 2. Insufficient renal excretion of non-volatile acids 3. Loss of bicarbonates 4. Excess of H^+, deficit of bases
Indices	$\downarrow$pH, $\downarrow$SB; $\downarrow HCO_3^-$(primary), $\downarrow pCO_2$(compensatory)

Disorders	1. Hyperventilation → Kussmaul breathing → hypocapnia - decreased muscle tone - decreased cardiac output (CO) - decreased arterial pressure (AP) 2. Hyperexcitation of respiratory center and decrease in its excitability 3. Hypotension - ischemia - reduced filtration in the kidneys - oliguria 4. Low pH - hyperadrenalemia - hyperkalemia - fibrillation 5. Acidosis - increased osmotic pressure of extracellular fluid - cell dehydration 6. Decalcification of bones 7. Suppression of neuromuscular excitability
Compensatory mechanisms	1. Hyperventilation – ↓ pCO_2 decrease, ↓ SB 2. Acido- and ammonium genesis 3. Hyperkalemia 4. Hypercalcemia

Table 25

METABOLIC ALKALOSIS

Etiology	1. Excess alkali intake 2. Loss of hydrochloric acid in vomiting 3. Chlorine loss (taking hypothiazide) 4. Hyperaldosteronism 5. Intensive treatment of glucocorticosteroids
Pathogenesis	↑pH, excess of base; ↑HCO_3^- (primary), lack of H^+, ↑pCO_2 (compensatory)

Indices	Excess of base (+BE, ↑SB)
Disorders	1. Loss of sodium - increased water removal - dehydration 2. Decrease in the concentration of calcium in the blood - increased neuromuscular excitability - convulsions 3. Reduction of contractile function of myocardium
Compensatory mechanisms	1. Hypoventilation - increased pCO_2 into the blood and its interaction with excess of sodium (↑ pCO_2, ↑SB) 2. blockade of ammonium and acidogenesis 3. Excretion of sodium excess by the kidneys

Table 26

RESPIRATORY ALKALOSIS

Etiology	1. Altitude hypoxia 2. Dyspnea 3. Overheating 4. Overdose of salicylates 5. Poorly adjusted modes of artificial ventilation (ASV)
Pathogenesis	Hyperventilation → hypocapnia
Indices	↑pH, ↓pCO_2(primary), ↓HCO_3^-(compensatory)
Disorders	1. Hypocapnia - reduction of vascular tone - blood pressure drop - decrease of cardiac output (CO) - collapse 2. Increased sodium excretion - loss of water in the urine - dehydration 3. Hypocalcemia - convulsions

Compensatory mechanisms	1. Blockade of ammonium and acidogenesis 2. Increased sodium excretion in the urine

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DISORDERS OF FLUIDS AND ELECTROLYTES

The purpose of the practical class: To learn the role of hydrostatic state changes, of colloid osmotic pressure of blood and tissues, permeability of vascular wall in the pathogenesis of edema and to be able to determine the significance of these factors in the development of edema in various pathological processes. To be able to determine the form of disturbance of water-electrolyte exchange and to explain the mechanism of its development, to carry out a comparative analysis of the pathogenesis of various types of edema.

Basic questions the student should know:

1. The importance of water for the body. Factors that determine the distribution and movement in the body. Concept of water balance.
2. Regulation of water-salt metabolism. Structure and function of aldosterone and vasopressin. RAAS.
3. Biochemical mechanisms of edema and dehydration.
4. Water and mineral metabolism in hot weather conditions.

The student should know:

1. Disorders of external water balance and distribution of water in the internal environment of the body. Their classification.
2. Dehydration. Hyper-, iso- and hypotonic dehydration. Etiology. Pathogenesis (tabl. 27).
3. Overhydration in the body (tabl. 28).
4. Edemas. Definition. Classification.
5. Pathogenetic factors of edemas. The value of the gradients of hydrodynamic, osmotic and oncotic pressure in blood and tissues, state of vascular tissue membranes. The role of neuro-humoral mechanisms in the development of edema.
6. Etiology and pathogenesis of cardiac edemas.
7. Pathogenesis of nephrotic edema (fig. 6).
8. Pathogenesis of edema in acute nephritis (fig. 7).
9. Pathogenesis of edema in liver cirrhosis (fig. 8).

TESTS FOR KHOWLEDGE CONTROL IN SELF-TRAINING

1. What are the causes of hypertonic dehydration?

1) restrictions of water intake;
2) loss of liquid through the skin;

3) hyperventilation;
4) non-diabetes mellitus;
5) Ist stage of acute bleeding;
6) Ist stage of acute bleeding;
7) diabetes mellitus;
8) hypoaldosteronism;
9) hyperaldosteronism;
10) intake of saluretikov.

2. What are the causes of isotonic dehydration?

1) recovering of liquid losses by drinking water without salt ;
2) hyperventilation;
3) Ist stage of acute bleeding;
4) II stage of acute bleeding;
5) hypoaldosteronism;
6) hyperaldosteronism;
7) diabetes mellitus;
8) insipidous diabetes;
9) intake of saluretikov;
10) restrictions of water intake.

3. What are the causes of hypotonic dehydration?

1) compensated fluid loss after drinking water without salt;
2) overdoses of saluretics;
3) insipidous diabetes;
4) I stage of acute bleeding;
5) II stage of acute bleeding;
6) hyperaldosteronism;
7) hypoaldosteronism;
8) diabetes mellitus;
9) hyperventilation;
10) exceed sweating.

4. What are the features of hypertonic dehydration?

1) deficiency of water without deficiency of electrolytes in the blood;
2) equal deficiency of water and electrolytes in the blood;
3) deficiency of electrolytes into the blood;
4) deficiency of water without deficiency of electrolytes in ECF;
5) deficiency of water without deficiency of electrolytes in ICF.

5. What are the features of isotonic dehydration?

1) deficiency of water without deficiency of electrolytes into the blood;
2) equal deficiency of water and electrolytes into the blood;
3) deficiency of electrolytes into the blood;
4) deficiency of water without deficiency of electrolytes in ICF;
5) deficiency of electrolytes in ICF.

6. What are the features of hypotonic dehydration?

1) deficiency of water without deficiency of electrolytes into the blood;
2) equal deficiency of water and electrolytes into the blood;
3) deficiency of electrolytes into the blood;
4) deficiency of water without deficiency of electrolytes in ICF;
5) deficiency of electrolytes in ICF.

7. What are the manifestations of hypertonic dehydration?

1) thirst;
2) fever;
3) delirium coma;
4) hyperosmolality of the blood (Na concentration above 145 mmol/L);
5) absent of the thirst;
6) soft eyeballs.

8. What are the manifestations of hypotonic dehydration?

1) thirst;
2) soft eyeballs;
3) cerebral edema, seizures, coma;
4) hypoosmolality of the blood);
5) absence of thirst;
6) fever.

9. What are the causes of hypertonic overhydration?

1) acute glomerulonepritis;
2) excessive introduction of hypertonic salt solutions;
3) primary hyperaldosteronism;
4) nephrotic syndrome;
5) heart failure;
6) liver cirrhosis.

10. What are the causes of hypotonic overhydration?

1) increased secretion of ADH;
2) acute glomerulonepritis;
3) heart failure;

4) acute renal failure;
5) heart failure;
6) primary hyperaldosteronism;
7) liver cirrhosis;
8) overdoses of saluretikov.

11. What are the pathogenic factors of cardiac edema?

1) increased hydrostatic pressure in the venous compartment of the vascular bed;
2) increased permeability of cellular membrane;
3) decreased oncotic blood pressure;
4) activation of RAA system;
5) lymphodynamic disorder.

12. What are the pathogenic mechanisms of nephrotic edema?

1) increased hydrostatic pressure in the venous part of the vascular bed;
2) increased permeability of glomerular capillaries;
3) decreased oncotic blood pressure;
4) activation of RAA system;
5) lymphodynamic disorder.

ANSWERS KEYS:

1. 1, 2, 3, 4, 6, 7
2. 3
3. 1, 2, 7
4. 4
5. 2
6. 3
7. 3, 4, 5
8. 3, 4, 5
9. 1, 2, 3, 5, 6
10. 1, 4
11. 1, 2, 3, 4
12. 3, 6

Table 27

TYPES OF DEHYDRATION

	Hypotonic	Isotonic	Hypertonic
Extracelullar fluid:			
osmolarity	↓	N	↑
volume	↓↓	↓	↓
Intracelullar fluid:			
osmolarity	N	N	N
volume	↑	N	↓↓
Water movement direction	Into the ICF	No movement	From the ICF

Thirst	Absent	May be	Expressed
Central venous pressure (CVP)	↓	↓	N
Hemodynamic disorders	Are present	Are present	Are absent
Tone of CNS	↓	↓	↑
Diuresis	↓	↓	↓
Total blood protein	↑	N	↑
Erythrocyte and hemoglobin content	↑	↑	↑
Hematocrit	↑	↑	↑N
Mean corpuscular volume (MCV)	↑	N (80-100 fL)	↓
Mean hemoglobin concentration in erythrocyte (MCHC)	↓	N (80-100 fL)	↑
Basic disorder	hypovolemia	hypovolemia	tissue hypoxia

Table 28

TYPES OF OVERHYDRATION

	Hypotonic	Isotonic	Hypertonic
Extracelullar fluid: osmolarity volume	 ↓ ↑	 N ↑	 ↑ ↑↑
Intracelullar fluid: osmolarity volume	 N ↑↑	 N N	 N ↓
Direction of water movement	Into the ICF	No movement	From the ICF
Thirst	Absent	Absent	Expressed
Edema	present	present	present
Central venous pressure (CVP)	↑	↑	↑
Hemodynamic disorders	present	present	present

Tone of CNS	↓↓	↓	N
Diuresis	↓	N	↓
Total blood protein	↑	↓	↓
Erythrocyte and hemoglobin content	↓	↓	↓
Hematocrit	N	↓	↓
Mean corpuscular volume (MCV)	↑	N (80-100 fL)	↓
Mean hemoglobin concentration in erythrocyte (MCHC)	↓	N (80-100 fL)	↑
Basic disorder	Cerebral edema	HF, pulmonary edema	Pulmonary edema

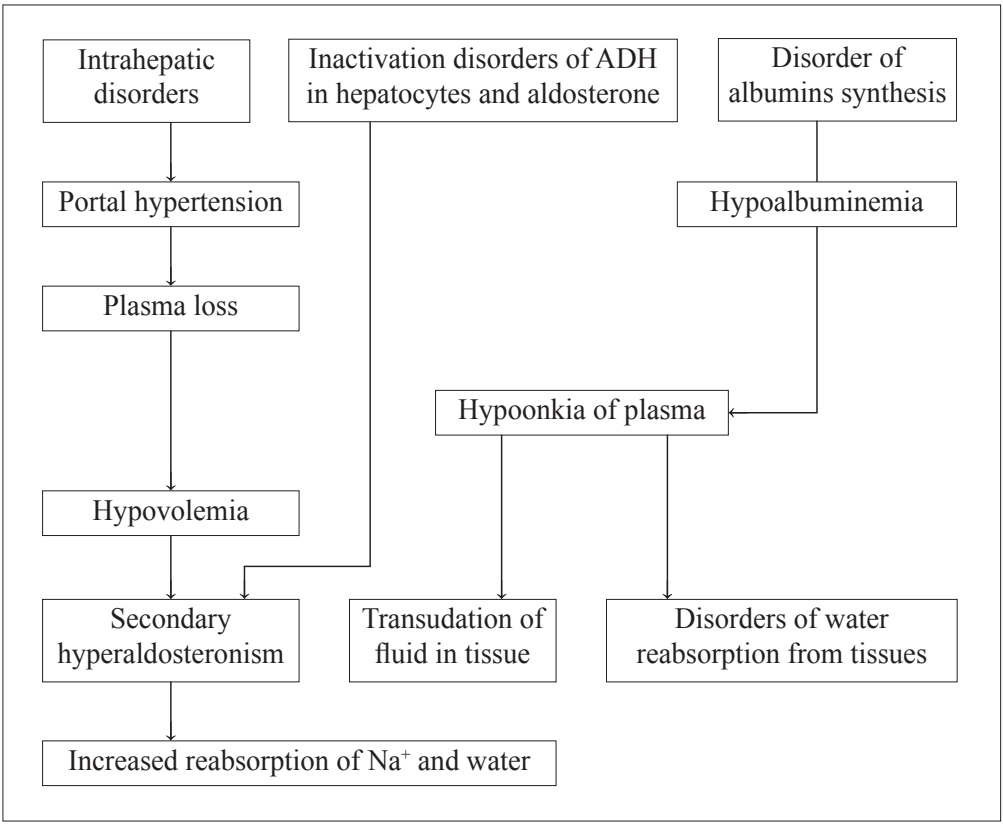

Figure 6. **PATHOGENESIS OF EDEMA IN LIVER CIRRHOSIS**

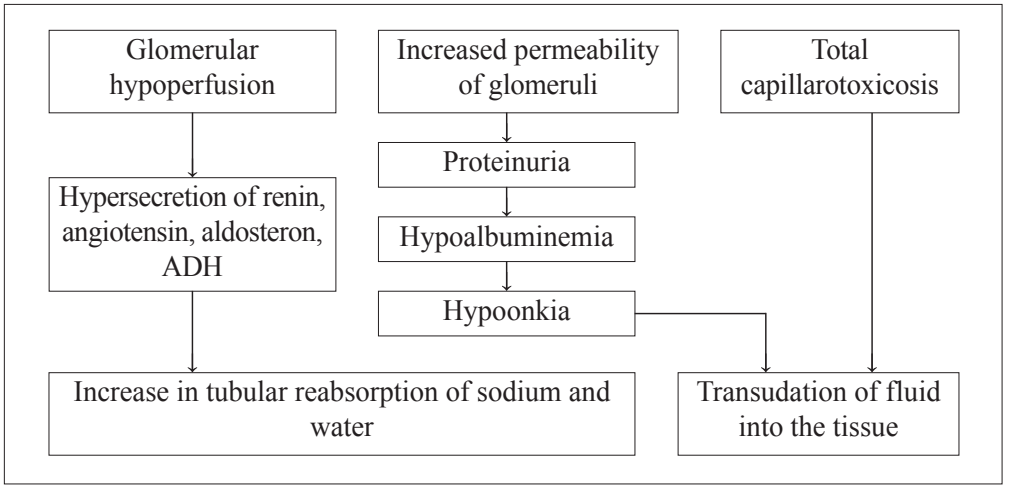

Figure 7. **PATHOGENESIS OF EDEMA IN ACUTE GLOMERULONEPHRITIS**

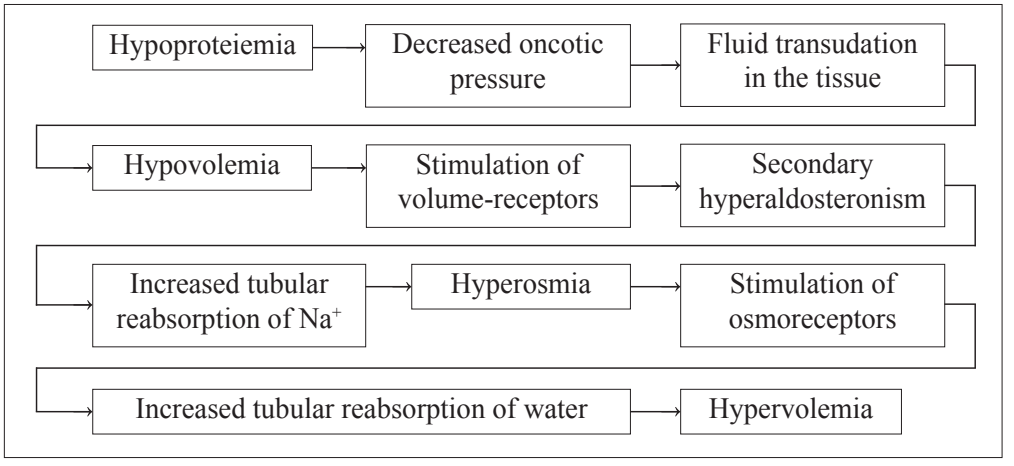

Figure 8. **PATHOGENESIS OF HYPOONCOTIC EDEMA**

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