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Department of pathological physiology

METHODOLOGICAL MATERIALS

for 3rd year students of the medical faculty
by academic discipline

Pathophysiology, clinical pathophysiology

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Part 3

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Content

HYPOXIA

Hypoxia a condition resulting from insufficient supply of tissues of the body with oxygen and / or violation of its assimilation during biological oxidation.

A synonym for "hypoxia" are "oxygen starvation" and "hypoxia."

In other cases terminological element *oxy* interpreted as referring to the oxidation (from the English oxydation - oxidation). In this embodiment, the term "hypoxia" is used in a broad sense:

Hypoxia a typical pathological process that develops as a result of failure of biological oxidation, which leads to disruption of energy supply functions and plastic processes in the body.

Such an interpretation of the term "hypoxia" refers to absolute or relative deficiency of the real level of energy compared to the level of functional activity and intensity of plastic processes in organs, tissues, body. This condition leads to disruption of vital activity of the whole organism, disorders of organs and tissues. Morphological changes in them have a different scope and degree, up to cell death and destruction of non-cellular structures.

Hypoxemia

Hypoxia (in any version of interpretation) is often combined with hypoxemia.

Hypoxemia - a decrease compared with the proper voltage levels and the oxygen content in the blood.

Anoxia and anoxemia

In connection with developing the problem of hypoxia in the experiment (e.g., when using preparations of isolated organs, tissue fragments or cells) commend anoxic - absence of oxygen and usually halting biooxidation - or anoxemia - lack of oxygen in the blood, used for perfusion individual organs, tissues, cells or subcellular structures. In a holistic living organism the formation of these states is impossible.

The criteria for classification of hypoxia

Hypoxic conditions are classified taking into account different criteria: the etiology, the severity of disorders, developmental rate and duration of hypoxia.

ETIOLOGY (Petrov)

According to the etiology identify several types of hypoxia, conditionally combined into two groups: exogenous (normo- and hypobaric hypoxia) and endogenous.

Exogenous be normobaric and hypobaric.

Endogenous can be tissue, breathing (respiratory), cardiovascular (circulatory), blood (hematic), reloading, substrate.

PATHOGENESIS (A.D. Ado)

1. Hypoxia associated with the violation of external respiration (exogenous hypoxic hypoxia and respiratory type of hypoxia)

2. Hypoxia associated with the violation of internal breathing (circulatory, hemic, tissue)

Severe disorders

On the criterion of the severity of disorders of vital activity distinguishes between the following types of hypoxia: an easy, medium (moderate), heavy, critical (life-threatening, lethal).

The main features of a particular expression (gravity) is used hypoxia following:

- the degree of violation of neuro-psychic activity,
- severity of disorders of the cardiovascular and respiratory systems,
- the amount of deviation indicators gas composition and acid base balance of blood, as well as some other factors.

Rate of occurrence and duration

According to the criteria of rate of occurrence and duration of hypoxic state allocate some of its varieties.

Lightning

Lightning hypoxia develops within a few seconds. Typically, after a few tens of seconds (within the first minute) after exposure to hypoxia causes of heavy patient's condition is detected, often serving as the reason for his death, for example, depressurization of aircraft on a large, over 9000-11 000 m altitude, or as a result of the rapid loss large amounts of blood, for example, in wounds or major arterial aneurysm rupture their walls.

Acute

Acute hypoxia develops within a few minutes (usually within the first hour) following exposure to hypoxia causes (e.g., as a result of acute blood loss or acute respiratory failure).

Subacute

Subacute hypoxia is formed within a few hours (but within the first day). Examples of such species may be hypoxic conditions, developing as a result of ingestion of methemoglobinoformation (nitrates, nitrogen oxides, and benzyl), venous bleeding slowly increasing respiratory or heart is not enough.

Chronic

Chronic hypoxia develops and / or lasts more than a few days (weeks, months, years), such as chronic anemia, cardiac or respiratory failure.

Etiology and pathogenesis of different types of hypoxia

Exogenous TYPES hypoxia

Exogenous types of hypoxia include normo- and hypobaric hypoxia, the reason for their development: reducing the partial pressure of oxygen (pO2) in the air enters the body.

- In the normal barometric pressure talk about exogenous normobaric hypoxia.
- With a decrease in barometric pressure known as hypobaric hypoxia exogenous.

Normobaric exogenous hypoxia

Normobaric hypoxia exogenous reasons: limiting intake of oxygen from air at normal barometric pressure. These conditions are formed when:

- Finding people in the small and / or poorly ventilated space (room, mine, well, the elevator).
- Violation of the regeneration air and / or supply oxygen mixture to breathe in deep and flying machines, self-contained suits (astronauts, pilots, divers, rescue workers, firefighters).
- Failure to observe ventilation techniques.

Hypobaric hypoxia exogenous

Reasons exogenous hypobaric hypoxia: reduced barometric pressure rise to the height (a 3 000-3 500 m, where pO2 air reduced to about 100 mm Hg) or in the pressure chamber. Under these conditions may develop either a mountain or altitude or decompression sickness.

Mountain sickness occurs when climbing into the mountains where the body is exposed not only to a reduced oxygen content in the air and reduced barometric pressure, but also more or less pronounced physical load, cooling, high insolation and other factors, medium and high altitudes.

Altitude sickness occurs in people, raised to great heights of public aircraft, on the chairs-lifts, and when the pressure in the chamber. In these cases, the body are substantially reduced pO2 in the inspired air and the barometric pressure.

Decompression sickness occurs when a sharp decrease in barometric pressure (eg due to depressurization of aircraft at an altitude of 10 000 -11 000 m). This forms a life-threatening condition characterized by mountainous and high-altitude sickness or acute fulminant.

The pathogenesis of exogenous hypoxia

The main pathogenesis of exogenous hypoxia (regardless of the cause) include arterial hypoxemia, hypocapnia, gas alkalosis acidosis alternated; hypotension, combined with hypoperfusion of organs and tissues.

Reduced oxygen tension in the plasma of arterial blood (arterial hypoxemia) – initial and the main link exogenous hypoxia. Hypoxemia leads to a decrease in oxygen saturation of Hb total oxygen content in the blood and as a result - a violation of gas exchange and metabolism in tissues.

Reducing the voltage levels of carbon dioxide (hypocapnia). It is the result of compensatory hyperventilation lungs (due to hypoxemia).

The gas is the result of alkalosis hypocapnia.

However, it should be remembered that the presence in the inhaled air of high carbon dioxide content (for example, when breathing in a confined space or in a production environment) exogenous hypoxemia can be combined with hypercapnia and acidosis. Moderate hypercapnia (unlike hypocapnia) does not aggravate hypoxia exogenous influences, but rather increases the blood circulation in the vessels of the brain and heart. However, a significant increase in the pCO2 in blood leads to acidosis, ion imbalance cells and biological fluids, hypoxemia, decrease in oxygen affinity of Hb and several other pathogenic effects.

Reducing systemic blood pressure (hypotension), combined with tissue hypoperfusion, largely a consequence of hypocapnia. CO2 is one of the main factors of the regulation of vascular tone brain. A significant decrease in PaCO2 is a signal to the narrowing of the lumen of arterioles of the brain, the heart and reduce their blood supply. These changes are the cause of significant disorders of vital activity, including the development of syncope and coronary insufficiency (angina manifested, and sometimes - myocardial infarction).

In parallel with these abnormalities are detected violations of the ion balance in cells and in body fluids: extracellular, plasma levels (hypernatremia, hypokalemia and hypocalcemia), lymph, cerebrospinal fluid. The above-described deviation can be reduced or eliminated by adding to the inspired air required (calculation) the amount of carbon dioxide.

Endogenous TYPES hypoxia

Endogenous hypoxic conditions in most cases are the result of pathological processes and diseases resulting in inadequate oxygen transport to the organs, the metabolism of substrates and / or the use of their tissues. Hypoxia of varying intensity and duration may also develop as a result of a sharp increase in the body's need for energy due to the significantly increased workload (eg, with a sharp increase in physical activity). However, even the maximum activation of oxygen transport and energy is produced systems are not able to eliminate the energy deficit (hypoxia overload).

Respiratory hypoxia

The cause respiratory (respiratory) hypoxia - lack of gas exchange in the lungs - respiratory failure.

Pathogenesis

The development of respiratory failure can be caused by alveolar hypoventilation, decreased blood perfusion lung violation of diffusion of oxygen through the air-blood barrier, the dissociation of ventilation-perfusion ratio. Regardless of the origin of respiratory hypoxia pathogenetic link is an initial arterial hypoxemia, is usually associated with hypercapnia and acidosis.

Alveolar hypoventilation characterized by the fact that the volume of mechanical ventilation per unit of time below the body's need for gas exchange at the same time. This state is the result of violations of the biomechanical properties of the respiratory system and the regulation of pulmonary ventilation disorders.

Violations of respiratory biomechanics can be obstructive and restrictive.

Causes of obstructive type: swelling of the walls of the bronchi and bronchioles, tumors, foreign bodies in the lumen of the airways.

Causes of restrictive (due to decreased lung elastic properties and extensibility): extensive pneumonia, atelectasis, edema and fibrosis of the lungs, pneumonia or hemothorax, stiffness osteoarticular apparatus of the chest, a significant amount of fluid in the pleural cavity.

Disorders of the mechanisms of regulation of breathing.

Causes of disorders: the direct effect of damaging factors on neurons of the respiratory center (eg, bleeding, swelling, edema, inflammation in the medulla oblongata or area of the bridge) and reflex influence in the form of deficiency afferentation excitatory neurons of the respiratory center (for example, drug poisoning); excess excitatory impulses, leading to frequent shallow breathing (for example, stress, neurosis, encephalitis); afferentation excess braking (for example, irritation of the nasal passages and trachea chemicals or mechanical, acute tracheitis and bronchitis).

Reduced perfusion lung blood.

Reasons: reduced BCC (hypovolemia); failure of the contractile function of the heart; an increase in resistance to blood flow in the pulmonary vascular bed (pre- and / or post-capillary hypertension); increasing the air pressure in the alveoli and / or the airways; the opening of arteriovenous anastomoses and discharge of blood for intra- and extrapulmonary shunts from right to left, bypassing the capillaries of the alveoli.

Violation of the diffusion of oxygen through the blood barrier

Reasons: thickening and / or thickening of the components alveolocapillary membrane This leads to a more or less pronounced dissociation of the gaseous medium alveolocapillary alveoli and blood capillaries. This phenomenon is observed when interstitial pulmonary edema, diffuse interstitial pulmonary fibrosis (for example, fibrosing alveolitis), pneumoconioses (a condition characterized by focal and diffuse overproduction of connective tissue in the lungs, such as silicosis, asbestosis, sarcoidosis).

Dissociation of ventilation-perfusion ratio

The reasons: violation of patency of the bronchi and / or bronchioles; reduction in tensile alveoli; Local reduction of blood flow in the lungs.

Such changes are observed, such as bronchospasm and pnevmoskleroze of various origins, pulmonary emphysema, embolism or thrombosis of the branches of the vascular bed. This leads to the fact that certain regions of the normal lung is ventilated, but not perfused with blood, which will on the contrary, is well perfused, but insufficiently ventilated. In this regard, the blood flowing from the lungs revealed hypoxemia.

Changes in the gas composition and the pH of the blood

- Reduced PaO 2 and pv02 (arterial and venous hypoxemia).
- Increase in PaCO2 (hypercapnia).
- Acidosis (early acute respiratory distress - gas, and then the non-gas).
- The decline in SaO2 and SVO2 (saturation of hemoglobin, respectively arteri¬alnoy and venous blood).

Circulatory hypoxia

The cause of cardiovascular (circulatory, hemodynamic) hypoxia: lack of blood supply to tissues and organs.

Pathogenesis. Insufficient blood supply is generated on the basis of hypovolemia, heart failure, reduce the tone of vascular walls, microcirculation disorders, disorders of diffusion of oxygen from the blood to cells of the capillary.

Hypovolemia - a decrease in the total volume of blood in the bloodstream and heart cavities. This is one of the important mechanisms of circulatory failure and circulatory hypoxia. Hypovolemia reasons: a large blood loss; hypohydration the body (eg, chronic diarrhea, burns, massive prolonged sweating).

Heart failure is manifested emission reduction of blood from the ventricles of the heart, and as a consequence - a decrease in the bcc. Causes: direct myocardial damage (eg cardiotropic toxins when infarction, diffuse cardiosclerosis); Overload infarction (eg, weight or blood vascular

resistance increased her current); violation of diastolic relaxation of the heart (for example, when compression of - tamponade exudate or blood, accumulated in the pericardial cavity).

Reduced tone of the vessel walls. Reduced tone of the vessel walls (both arterial and venous). This increases the capacity of the vascular bed and reduction of VCB. Reasons: reduced adrenergic effects on the walls of blood vessels (for example, adrenal insufficiency, damaged neurons cardio vasomotor center); dominance cholinergic effects (eg, in neurotic states on torpid phase of shock, with deviation of the electrolyte balance and acid-base balance); mineralocorticoid deficiency in the body. Hypotension vessel walls of all origins and causes a decrease in blood perfusion pressure, and volume of blood flow in the vessels of the tissues and organs.

Microcirculation disorders. These changes are considered in violation of the topics of regional circulation and microcirculation and pathophysiology of the heart and blood vessels.

Violation of the diffusion of oxygen through the wall of microvessels, in the interstitial fluid through plasmolemma and the cytosol to the mitochondria. Ultimately, this leads to a shortage of oxygen in the mitochondrial matrix and, consequently, to reduce the intensity of tissue respiration. Reasons: seal the walls of microvessels (eg dystrophy their walls, vasculitis, arteriolosclerosis, interstitial edema, myxedema); membranopatia cells (e.g., activation POL process of cellular degeneration, tumor growth).

Circulatory hypoxia is often the result of a combination of the above mechanisms (for example, collapse, shock, adrenal insufficiency and Cushing different genesis, arterial hyper- and hypotension).

Types of circulatory hypoxia

An important feature of hypoxia circulatory type is the possibility of the development of the local system and its forms.

1. Local hypoxia

The reasons: the local circulatory disorders (venous hyperemia, ischemia, stasis, regional disorders of the diffusion of oxygen from the blood to the cells and their mitochondria.

2. Systemic hypoxia

The reasons: hypovolemia; heart failure; generalized forms reduce vascular tone.

Changes in the gas composition and the pH of the blood

- Reduce pv02 (venous hypoxemia).
- Average (usually) PaO 2.
- Increased arteriovenous oxygen difference (with the exception of options to large-scale dumping of arteriovenous shunts blood, bypassing the capillary network).
- Non-gas acidosis.
- Reduce SVO2 (exception - hypoxia at the arteriovenous shunt).

Hematic type of hypoxia

Cause blood (hemic) hypoxia: oxygen reduction in the effective capacity of the blood and, therefore, it transports oxygen function.

Hb is the best carrier of oxygen. Transport of oxygen from the lungs to the tissues almost completely carried out with the participation of Hb. The highest amount of oxygen that is capable of transferring Hb well 1.39 ml of O2 gas per 1 g of Hb. Real transport capacity of hemoglobin is determined by the amount of oxygen bound to hemoglobin and the amount of oxygen, gives tissues. When the oxygen saturation of hemoglobin by an average of 96% capacity of the arterial blood oxygen (VaO2) reaches about 20% (by volume). In venous blood, this figure is closer to 14% (volumetric). Consequently, arteriovenous oxygen difference is 6%.

Pathogenesis. The main functioning mechanism of reducing the oxygen capacity of blood are reduction of hemoglobin per unit volume of blood (and, as a rule, in the body as a whole), and transport properties of hemoglobin disorders. In general hematic type of hypoxia is characterized by decreased ability of erythrocyte hemoglobin to bind oxygen (in the capillaries of the lung), to transport and deliver the optimum amount of it in the tissues. At the same time the real oxygen capacity of the blood can drop to 5-10% (by volume).

1. Reduction of hemoglobin per unit volume of blood

Leading to hypoxia reduction of hemoglobin per unit volume of blood in the body as a whole when there is: a very significant reduction in the number of red blood cells and / or reducing the amount of hemoglobin (sometimes up to 40-60 g / l), ie, when severe anemia; violations of the transport properties of hemoglobin

2. Violations of the transport properties of hemoglobin due to a change in its ability to oxygenation in the blood capillaries of the alveoli and capillaries deoxygenation in tissues. These changes (hemoglobinopathies) can be inherited or acquired.

a) Inherited hemoglobinopathies. The reason for reducing the properties inherited hemoglobin to transport oxygen to the tissues of most gene mutations are accompanied by violation of the amino acid composition of globins. There are many hereditary hemoglobinopathies.

b) Acquired hemoglobinopathies. The reason most often acquired hemoglobinopathies is elevated blood methemoglobinoformation, carbon monoxide, carbilaminhemoglobine, nitroxihemoglobine.

Methemoglobinoformation - a group of substances that determine the transition from I iron ion ferrous form (Fe2 +) in the oxide (Fe3 +). The latter form is typically in communication with OH- . By methemoglobinoformation include nitrates, nitrites, quinones, hypochlorous acid compounds, certain drugs (sulfonamides, phenacetin, aminopyrine), endogenous peroxides. The formation of methemoglobin (MetHb) - a reversible process. Elimination from the body is accompanied by methemoglobinoformation transition house (for several hours) of iron in the ferrous form of hemoglobin. Involved in this process to pyruvic MK dehydrated. MetHb is not capable to carry oxygen. In this regard, oxygen capacity of the blood is reduced. Given that the MetHb is dark brown in color, blood and tissues of the body also acquire the appropriate shade.

Carbon monoxide has a high affinity (about 300 times more than oxygen) to the hemoglobin. Carbon monoxide contained in high enough concentration in the exhaust gases of internal combustion engines, pabotayuschih gasoline or kerosene; a city gas; composed of many gases generated in foundries; during firing bricks; upon receipt of acetone, methanol, ammonia and other substances. In the reaction of carbon monoxide with hemoglobin forms carboxyhemoglobin (NSO), losing the ability to transport oxygen to the tissues. Number NSO generated is directly proportional to pCO and inversely proportional to the pO2 in the air. Marked disorders of vital activity developed with increasing content of NSO in the blood up to 50% (of the total concentration of hemoglobin). Raising the level up to 70-75% leading to severe hypoxemia and death. Elimination of CO from the inhaled air causes the dissociation of NSO, but this process is slow and takes several hours. NSO has a bright red color. In this regard, when the formation of excess body skin and the mucous membranes become red.

Other compounds of hemoglobin (eg carbilaminhemoglobine, nitroxihemoglobine), formed under the influence of strong oxidants also reduce the transport capacity of hemoglobin and cause the development of hemic hypoxia.

Education and dissociation of HbO2 is largely dependent on the physicochemical properties of the plasma. Changes in pH, osmolarity, the content of 2,3-diphosphoglycerate, rheological properties reduce transport and the ability of hemoglobin characteristics HbO2 oxygenate tissues.

Changes in the gas composition and the pH of the blood

- Reduced volume of oxygen in arterial blood (VaO2 normally equal to 19,5-21% by volume).

  Average (!) Partial pressure of oxygen in arterial blood.

- Reduce pv02 (venous hypoxemia).
- Reduce VVO2.
- non-gas acidosis.
- Reduction of arteriovenous oxygen difference.

Tissue hypoxia

Causes of tissue hypoxia: factors; reducing the efficiency of utilization of oxygen by cells of tissues and / or coupling of oxidation and phosphorylation.

Pathogenesis

1) Reducing the efficiency of oxygen uptake by cells most often the result of inhibiting the activity of enzymes of the biological oxidation, a significant change in the physico-chemical parameters in the tissues, inhibition of enzyme synthesis and biological oxidation damage to cell membranes.

Suppressing the activity of enzymes of the biological oxidation is observed at:

a) specific inhibition of enzymes. Examples are cyanide ions (CN ~), preventing oxidation of cytochrome. As a result of reduction of iron is blocked respiratory enzymes and oxygen transport to cytochrome. In this reaction, tissue respiration activated by other agents (containing no iron), are not inhibited. However, the effectiveness of these reactions is very low and does not prevent the development of hypoxia and disorders of life.

Similar effects cause blockage of active sites of enzymes of tissue respiration antimycin A, compounds containing sulfide ion S2 ~, and some other substances.

b) Non-specific inhibition of enzymes of the biological oxidation of metal ions (Ag2 +, Hg2 +, Cu2 +). Thus these metals reversibly react with SH-groups of the enzyme to form merkaptoidnoy its inactive form.

c) competitive inhibition of enzymes of the biological oxidation. It is to block the enzyme active agent having the structural analogy with the natural substrate of the reaction. The effect of competitive inhibition of the enzyme can be eliminated or reduced with the increase in the content of the real cell

substrate. In the role of competitive inhibitors can act oxalate and malonate, succinate block the interaction with the succinate dehydrogenase in the TCA cycle; phorlimonic acid compete for the active site of aconitase citrate.

Changes in physical and chemical parameters in the tissues (temperature, electrolyte composition, pH, the phase state of membrane components) in more or less pronounced extent reduce the effectiveness of biological oxidation. Abnormality of these and other parameters observed in many diseases and pathological conditions: hyperthermia and hypothermia, multiple organ failure (heart, kidney, liver), anemia and a number of others.

Inhibition of the synthesis of enzymes of the biological oxidation can be observed in the total or partial (especially protein) starvation: while the majority of hypo- and disvitaminosis; violation of mineral metabolism, required for the synthesis of enzymes.

Damage to the membranes. To the greatest extent it relates to the membranes of mitochondria.
Damage and destruction of membranes are a result of:

- Excessive intensification of free radical processes and lipoperoksidnyh.
- activation of lysosomal hydrolases.
- excess detergent action of amphiphilic compounds.
- hyperextension and tear swollen cells and their mitochondria.

These mechanisms damage cell membranes implemented in many pathological processes and diseases of non-infectious and infectious origin, accompanied by disorders of breathing, blood circulation, nutrition, development of immunopathological reactions and several other states. It is important that any type of severe hypoxia itself mno¬gie activates the mechanisms that lead to damage to the membranes of cells and enzymes to the development of tissue hypoxia.

2) Reducing coupling of oxidation and phosphorylation-rich compounds in the respiratory chain.

a) In these circumstances, increase tissue oxygen consumption rate and operation of the components of the respiratory chain. However, most of the energy of the electron transport is transformed into heat and is not used for resynthesis macroergs. The effectiveness of the biological oxidation is reduced. The cells do not get the energy supply. Therefore violated their functions and vital functions of the whole organism.

b) the expression capacity splits oxidation and phosphorylation have many endogenous agents (e.g., excess Ca2 +, H +, IVH iodinated thyroid hormones) as well as exogenous substance (2,4-dinitrophenol, bishydroxycoumarin, pentachlorophenol, gramicidin, etc.). .

Changes in the gas composition and the pH of the blood

An increase in the partial oxygen pressure in the venous blood.

- Increase oxygen saturation of hemoglobin in the venous blood.
- Increasing the volume of oxygen in the venous blood.
- Normal range pO2, SO2 and VO2 in the arterial blood (in typical cases).

- Reduce arteriovenous oxygen difference (exception - tissue hypoxia, which developed under the influence of oxidation and phosphorylation releasers).

- non-gas acidosis.

Substrate type of hypoxia

The reason: lack of substrates in the cells of biological oxidation. In clinical practice, it most often comes to glucose. Thus delivery of oxygen to the cells is not significantly impaired.

Pathogenesis substrate hypoxia is a progressive deceleration of biological oxidation. In this regard, the cells rapidly reduces the level of ATP and creatine phosphate, the amount of MP. Change and other electrophysiological parameters, violated various pathways and plastic processes.

Changes in the gas composition and the pH of the blood at the substrate hypoxia.

- An increase in the partial oxygen pressure in the venous blood.
- Increased red blood cell hemoglobin oxygen saturation of venous blood.
- Increased volume of oxygen in the venous blood.
- Reduce arteriovenous oxygen difference.
- Normal values pa02, SaO2, VaO2.

- Acidosis, developing as a result of metabolic disorders, hemodynamic, external respiration and other changes resulting from the disease or pathological process caused by hypoxia, substrate type. For example, in DM - deficiency of glucose in cells accumulate in the body CT, lactate, pyruvate (due to violation of lipid and carbohydrate metabolism), which results in metabolic acidosis.

Overload type of hypoxia

The reason for the overload of hypoxia: a significant and / or long-term increase in the function of tissues, organs or systems. This intensification of the delivery to them of oxygen and substrate metabolism, metabolism, conjugation reactions of oxidation and phosphorylation are not able to eliminate the deficit of energy compounds, which developed as a result of cell hyperfunction. Most often we are talking about situations of high and / or prolonged functioning of skeletal muscle and myocardium.

Pathogenesis. Over the level and / or duration of the load on the muscle (skeletal or cardiac)

stipulates:

- The relative (compared with a required function at a given level) insufficient blood supply to the muscles.

- Lack of oxygen in the myocytes. Last causing failure of processes of biological oxidation in them.

Changes in the gas composition and the pH of the blood during hypoxia overload.

- Reduction of the partial oxygen pressure in the venous blood (venous hypoxemia) flowing from hyperfunctioning muscle.

- Reduction of the degree of saturation of hemoglobin of red blood cells in the venous blood.

- Increased arteriovenous oxygen difference.

- Increasing the partial tension of carbon dioxide (hypercapnia) in the venous blood, which is the result of the activated metabolism in muscle tissue.
- Acidosis in samples of blood taken from a vein hyperfunctioning muscle.

Mixed hypoxia

Mixed hypoxia is the result of a combination of several types of hypoxia.

Causes:

actors for breaking two or more delivery mechanism and with use of oxygen and metabolic substrates during biooxidation.

Examples are drugs that can in high doses inhibits the function of the heart, the neurons of the respiratory center and the activity of enzymes of tissue respiration. As a result of developing hypoxia mixed haemodynamic, respiratory and tissue types.

Acute massive blood loss results in both a reduction of the oxygen capacity of the blood (due to the decrease in the amount of hemoglobin) and to circulatory disorders: developing hematic and hemodynamic types of hypoxia.

1) Consistent impact factors leading to damage to the various mechanisms of oxygen transport and metabolism of substrates and processes of biological oxidation. This pattern is observed in the development of severe hypoxia of any origin.

For example, acute massive blood loss leads to hemic hypoxia. Reduced blood flow to the heart leads to a decrease in blood output, hemodynamic disorders including coronary and cerebral blood flow. Ischemia can cause tissue brain function disorder of the respiratory center and cause respiratory type of hypoxia. Relative potentiation of hemodynamic and respiratory leads to significant deficit in the tissues of oxygen and metabolic substrates to gross damage cell membranes, enzymes and biological oxidation and as a result - a type of tissue hypoxia.

The pathogenesis of hypoxia include units of mixed type mechanisms of various types of hypoxia. Mixed hypoxia is often characterized by its individual vzaimopotentsirovaniem types with the development of severe, extreme and even terminal conditions.

Changes in the gas composition and the pH of the blood when mixed hypoxia determined by the dominant mechanisms of disorders oxygen transport and utilization, substrate metabolism, as well as the processes of biological oxidation in various tissues. The nature of the changes in this case may be different and very dynamic.

Adaptive response body by hypoxia

Action on the body factor causing hypoxia of any type, accompanied by the inclusion of two categories of interrelated processes: causes the development of hypoxia and providing adaptation to hypoxia and aimed at maintaining homeostasis in these conditions.

The processes of the first category described above. Below are characterized by general mechanisms of adaptation to hypoxia.

GENERAL DESCRIPTION OF adaptation to hypoxia

When exposed to even moderate hypoxia immediately formed behavioral response aimed at finding the existence of the environment, providing optimal levels of biological oxidation. A person can change the conditions of life directed to eliminate the state of hypoxia.

The resulting hypoxia is a factor which: the body formed dynamic functional system to achieve and maintain an optimal level of biological oxidation in cells.

The system realizes the effects due to activation of the delivery of oxygen and metabolic substrates to the tissues, and their inclusion in the biological oxidation reactions.

The structure of the system consists of the lungs, heart, vascular system, blood, biological oxidation system and regulatory system.

Conventionally, adaptive responses are divided into two groups: emergency and long-term adaptation.

ADAPTATION OF EMERGENCY

The reason for the activation mechanisms of urgent adaptation to hypoxia: lack of biological oxidation. As a consequence of reduced tissue ATP content required for optimum activity.

A key factor in the process of emergency adaptation to hypoxia - activation of O2 transport mechanisms and metabolic substrates to tissues and organs. These mechanisms are pre-exist in each organism. In this regard, they are activated immediately (emergency, urgent) in case of hypoxia and decrease the effectiveness of biological oxidation.

Increased oxygen transport systems function and metabolic substrates to the cells by intensive energy consumption and metabolic substrates. Thus, these mechanisms have a high "energy substrate and price." That it is (or can be) a limiting factor in the level and duration hyperfunctions.

The system of external respiration

Lack of biological oxidation in hypoxia leads to hyperventilation - increasing the volume of alveolar ventilation.

Reason: the activation of afferent impulses from chemoreceptors (aorta, carotid area of the carotid arteries, the brain stem and other parts of the body) in response to changes in blood gas parameters (reduction of PaO2, increased PaCO2, etc.).

Mechanism: an increase in the frequency and depth of breathing movements and the number of alveoli this attempted backup. As a result of minute volume of respiration (MOU) could increase by more than an order of magnitude: 5-6 l at rest to 90-110 liters under hypoxic conditions.

A heart

In acute hypoxia, heart function significantly intensified.

Reason: activation sympathetic-adrenal system.

Mechanisms

- Tachycardia.
- Increasing the stroke volume of blood from the heart.
- Increased integrative index of cardiac function - minute volume of blood flow (cardiac output of blood). When at rest it is 4-5 liters, that in hypoxia can reach 30-40 liters.
- Improved linear and volumetric blood flow in vessels.

Vascular system

Under the conditions of hypoxia develops the phenomenon of redistribution, or centralization of blood flow.

The causes and mechanisms of the phenomenon of centralization of blood flow

1) activation in hypoxia sympathetic-adrenal system and the release of catecholamines. Recent cause narrowing of arterioles and reduction of blood flow for him to most tissues and organs (muscles, abdominal organs, kidneys, subcutaneous tissue, and others.).

2) Fast and considerable accumulation in the myocardium and brain tissue metabolites with vasodilator effect: adenosine, prostacyclin, PGE, kinins and others. These substances not only impede the implementation of the vasoconstrictor action of catecholamines, but also ensure the expansion of arterioles and increased blood supply to the heart and brain in hypoxic conditions.
Effects

• Expansion of the arterioles and increase the blood supply to the brain and heart.

• Simultaneous narrowing of arterioles and reducing the volume of blood supply to other organs and tissues: muscle, subcutaneous tissue, blood vessels of the abdominal cavity, kidneys.

Blood System

Acute hypoxia of any origin accompanied by adaptive changes in the blood:

1. Activation of ejection of erythrocytes from bone marrow and depot (in the latter case - simultaneously with other blood corpuscles). The reason: high concentrations of catecholamines in the blood, thyroid and corticosteroid hormones. As a result, acute hypoxia develops polycythemia.

Impact: The increase in oxygen capacity of blood.

2. Increasing the degree of dissociation of HbO2 in the tissues. Causes:

• Hypoxemia, especially in the capillary and venous blood. In this regard, it is in the post-capillary venules and capillaries is an increase of the degree of oxygen release HbO2.
• Acidosis, growing naturally in any type of hypoxia.

Increased concentration in hypoxia erythrocyte 2,3-diphosphoglycerate and other organic phosphates: ADP, pyridoxal phosphate. These substances stimulate the elimination of oxygen from the HbO2.

2. Increasing the affinity of hemoglobin for oxygen in the capillaries of the lungs. This effect is realized with the assistance of organic phosphates, mainly 2,3-diphosphoglycerate. This important property of hemoglobin to bind a considerable amount of oxygen even in a significant decrease in pO2 in the capillaries of the lungs. When pO2 of 100 mmHg, produced 96% HbO2 at pO2 of 80 mm Hg and 50 - 90 and 81% respectively.

Systems biological oxidation

Activation of metabolism - an important link in the emergency adaptation to acute hypoxia.

This provides:

1. Improving the efficiency of the processes of assimilation of oxygen and substrate oxidation tissues of the body and deliver them to the mitochondria.
2. Activation of enzymes and oxidation phosphorylation, which occurs at moderate damage cells and their mitochondria.
3. Increasing the degree of coupling of oxidation and phosphorylation of adenine nucleotides ADP, AMP, and creatine.
4. The activation of the glycolytic pathway of oxidation. This phenomenon is registered in all types of hypoxia, particularly in its early stages.
The reasons for the activation of glycolysis:

• Reducing the level of intracellular ATP and the weakening of its inhibitory effect on the enzymes of glycolysis.

• An increase in the cells of the hydrolysis products of ATP (ADP, AMP, inorganic phosphate), activating the key glycolytic enzymes.

Long-term adaptation

The reason for the inclusion of mechanisms of long-term adaptation to hypoxia: repeated or continued failure of the biological oxidation of moderate severity.

Terms of incorporating long-term mechanisms of adaptation to hypoxia

1. Repeated or prolonged exposure to moderate hypoxia, which causes the activation of multiple urgent adaptation mechanisms. This ensures the formation of structural and functional bases for long-term adaptation to hypoxia. It is essential that the interval between episodes of moderate hypoxia was not too big or small.
• Large range will lead to the elimination of the structural (subcellular, cellular, organ and tissue) adaptive changes.

• Small spacing is insufficient for their development and consolidation.

2. Intensity of moderate hypoxia.

• Hypoxia little expression of activates mechanisms of urgent and long-term adaptation. Recorded a transient response in a range of physiological response to the decline of biological oxidation.
• Hypoxia causes excessive severity of the failure of the adaptation process, impairment of function, metabolism, and damage to structures of the body.
• The optimal functioning of the body condition. This allows you to develop the mechanisms of urgent adaptation and fix structural and functional changes that underlie long-term adaptation to hypoxia. The lack of any body systems (respiratory, cardiovascular system, blood, tissue metabolism) and / or plastic processes makes it impossible to implement adaptive processes to hypoxia (as well as other extreme factors).

Mechanisms of long-term adaptation

Long term adaptation to hypoxia is implemented at all levels of life: from the whole organism to the cellular metabolism.

Features of the mechanisms of long-term adaptation to hypoxia:

The process of adaptation to repeated and / or prolonged hypoxia formed gradually as a result of multiple and / or prolonged activation of urgent adaptation to hypoxia.

• The transition from the imperfect and unstable emergency adaptation to hypoxia to a sustainable and long-term adaptation has a significant biological (vital) importance: it creates the conditions for optimal functioning of the body in the new, often extreme conditions of existence.

• the basis of transition of an organism to a long-term adaptation to hypoxia is the activation of the synthesis of nucleic acids and proteins.
• Synthetic processes dominate bodies providing transport of oxygen and metabolic substrates, as well as tissues, intensively functioning in conditions of hypoxia.
• In contrast to the emergency adaptation to hypoxia, in which the leading role is the activation of O2 transport mechanisms and metabolic substrates to the tissues, the main link of long-term adaptation to hypoxia is a significant increase in the efficiency of the processes of biological oxidation in cells.

• Systems for the delivery of oxygen and metabolites to the tissues (external respiration and blood circulation), with a stable adaptation to hypoxia also acquire new qualities: increased power, efficiency and reliability of operation.

Systems biological oxidation

Systems biological oxidation in the tissues ensure optimum energy supply and the level of functioning structures of plastic processes them under hypoxic conditions. This is achieved by:

• Increased the number of mitochondria and mitochondrial cristae.
• Increase the number of enzyme molecules of tissue respiration in the mitochondria of each, as well as the activity of enzymes, especially cytochrome oxidase.
• improve the effectiveness of biological oxidation and pairing it with phosphorylation.

• The effectiveness of the mechanisms of anaerobic ATP re-synthesis in cells.

The system of external respiration

The system provides a level of external respiratory gas exchange sufficient for optimum flow metabolism and plastic processes in the tissues. This is achieved by:

• Hypertrophy of the lungs and increase in this connection: the square alveolar capillaries in between alveolar partitions, the level of blood flow in the capillaries.
• An increase in blood barrier diffusion capacity of the lungs.

• The efficiency ratio of alveolar ventilation and perfusion of blood (ventilation-perfusion ratio).

• hypertrophy and increase the power of the respiratory muscles.

• Increased vital capacity lungs (ZHËL).

A heart

When long-term adaptation to hypoxia increases the power and speed of the processes of contraction and relaxation of the myocardium. The result is an increase in the volume and speed of the ejected blood in the bloodstream - shock and cardiac (minute) emissions. These effects are made possible by:

• Moderate Balanced hypertrophy of all the structural elements of the heart: myocardial, vascular bed, the nerve fibers.
• increased number of functional capillaries to the heart.

• Reduce the distance between the capillary wall and sarcolemma of cardiomyocytes.

• Increased mitochondria in cardiomyocytes and the efficiency of the biological oxidation reactions. In this connection the heart consumes 30-35% less oxygen and metabolic substrates than unadapted to hypoxia condition.

• Improving the efficiency of transmembrane processes (transport of ions, substrates and products of metabolism, oxygen, and others.).
• Increased power and speed of the interaction of actin and myosin in myofibrils in cardiomyocytes.

• The effectiveness adren- and cholinergic systems of regulation of the heart.

Vascular system

In the adapted body vascular system is able to provide this level of tissue perfusion with blood, which is necessary to carry out their function even under hypoxic conditions. The basis of this based on the following mechanisms:

1. Increase in the number of functioning capillaries in tissues and organs.

2. Reduced myogenic tone of arterioles and reduction of reactive properties of the walls of resistance vessels to vasoconstrictor: catecholamines, ADH, leukotrienes, separate PG and others. This creates the conditions for sustainable development of arterial hyperemia in functioning organs and tissues.

Blood System

At steady adaptation to hypoxia significantly increase the oxygen capacity of blood, the dissociation rate of NO2, I desoxyhemoglobin affinity for oxygen in the capillaries of the lungs.

Increased blood oxygen capacity is the result of stimulation of erythropoiesis and erythrocytosis. Erythrocytosis mechanism: the activation of pop influence of ischemia and hypoxia formation of kidney erythropoietin stimulates erythropoiesis.

Metabolism

The metabolic processes in the tissues when the condition of a stable adaptation to hypoxia is characterized by:

• reduce their intensity.

• economical use of oxygen and metabolic substrates in the reactions of biological oxidation and plastic processes.
• High efficiency and lability reactions of anaerobic ATP resynthesis.

• Dominate anabolic processes in tissues compared to catabolic.

• High power and portability arrangements transmembrane ion transport. This is largely a consequence of increasing the efficiency of the membrane ATPase that provides the regulation of transmembrane ion distribution, myogenic tone of the arterioles, water-salt metabolism and other important processes.

Systems regulation

Systems of regulation adapted to hypoxia, the body provide sufficient effectiveness, efficiency and reliability of the control of his life. This is achieved thanks to the inclusion of mechanisms of nervous and humoral regulation of functions.

Nervous control

Significant changes in higher brain regions and in the autonomic nervous system to adapt to hypoxia body characterized by:

• increased resistance of neurons to hypoxia and a deficit of ATP, as well as some other factors (eg, toxins, lack of metabolic substrates).
• hypertrophy of neurons and an increase in the number of nerve endings in tissues and organs.

• increase the sensitivity of the receptor structure to neurotransmitters. The latter is usually associated with a decrease in the synthesis and release of neurotransmitters.

These and apparently and other changes in the nervous system is facilitated by:

• The development of mobile and effectively regulate the function of organs effects them.

• Rapid development of new and preservation of conditioned reflexes.

• Moving the acquired skills from short-term to long-term.

• Sustainability of the nervous system to pathogenic influences.

Humoral control

The restructuring of the functioning of the endocrine system in hypoxia causes:

• lesser extent stimulate the adrenal medulla, the hypothalamic-pituitary-adrenal and other systems. This limits the activation mechanisms of stress reaction and its possible pathogenic effects.

• Increased sensitivity to the hormone-receptor cells, which helps to reduce the volume of their synthesis in the endocrine glands.

In general, changes in regulation systems potentiate both system and organ adaptive response of the organism, which of life carried out in conditions of hypoxia.

Disorders in hypoxia

The nature, extent and dynamics of changes in functioning of the body depends on several factors: the type of hypoxia, its extent, the speed of development and the state of reactivity.

1. Acute (lightning) severe hypoxia leads to a rapid loss of consciousness, suppression of body functions and his death. Such a situation occurs, for example, by inhalation of gaseous mixtures not containing oxygen, or containing it in small quantities. This can be in case of accidents in a production environment (such as mines), in aircraft, in submarines, with damage suits. Lightning hypoxia develops as in ventricular fibrillation in acute massive (arterial) blood loss, cyanide poisoning and other similar situations.
2. Chronic (constant or intermittent) moderate hypoxia is accompanied, as a rule, the adaptation to hypoxia.

PRINCIPLES FOR THE PREVENTION AND ELIMINATION OF HYPOXIA

Etiotropic principle

Etiotropic treatment includes measures to eliminate; any reduction in the extent or duration of the effects on the causes of hypoxia. The therapy is carried out with the indispensable Registered type of hypoxia.

Hypoxia exogenous type

When hypoxia exogenous type is necessary to normalize the oxygen content in the inspired

air.

1. Hypobaric hypoxia.

• Restore the optimum partial pressure of oxygen in the inspired gas mixture (for example, depressurization of aircraft, individual suits, breathing apparatus, etc.).

• Ensure the restoration of normal barometric pressure, and as a consequence - the partial pressure of oxygen in the air. This is achieved by reducing the height of the flight restore integrity of aircraft and the necessary conditions for supply of breathing air in the suit, self-contained breathing apparatus, or the apparatus cabin.

2. Normobaric hypoxia.

• Provide normalization of oxygen in the inspired air by intensive airing the room or supply air into it with normal oxygen content.

• added into the inhaled air normoxic small amounts of carbon dioxide. The optimal increase in partial CO2 content up to 3-7%. It provides: stimulation of inspiratory neurons of the respiratory center and breathing aktiva¬tsiyu; dilation of arterioles brain and heart, normalizing the gas exchange therein, delivery substrates outflow CO2 and metabolic products; reducing the degree of hypercapnia and its pathogenic effects: circulatory disorders of the brain, myocardium and other organs, disorders of GNI, respiratory acidosis and others.

Endogenous types of hypoxia

When endogenous types of hypoxia should:

• Treatment of disease or the process leading to hypoxia.

• Provide the body optimal oxygen content in the inspired air.

This is achieved by breathing gas enriched with oxygen, under normal or elevated pressure (normobaric and hyperbaric oxygen therapy, respectively). These measures provide an increase in the partial pressure of oxygen in the inspired air, alveoli and hence - its voltage levels.

Hyperoxygenation

When normobaric oxygenation pO2 can reach 760 mm Hg (when breathing 100% oxygen) conditions, in a hyperbaric oxygenation - any desired value. It is important to know the possible reactions and consequences of developing conditions in hyperoxygenation.

Reaction to hyperoxygenation.

• Normalization (or tendency to) the volume of alveolar ventilation, mainly due to a decrease in respiratory rate.

• Optimizing cardiac output due to the slowing of the heart contracts.

• Reduce the BCC as a result of re-deposit facility blood.

Consequences of reactions to hyperoxygenation.

Elimination of hypoxia and its pathogenic effects. This is achieved by carrying out timely and adequate oxygen therapy and other therapeutic measures.

The development of pathogenic reactions, exacerbation of hypoxic conditions and disorders of the body's vital functions.

Reason: The toxic effects of excess oxygen. This results in an unjustified or improper conduct hyperoxygenotherapy.

Pathogenesis

• formation of an excess of reactive oxygen species and their direct damaging effect on cell membranes, enzymes, nucleic acids, proteins and their combinations with other substances.

• Excessive, uncontrolled intensification Spolli and other organic compounds.

• Direct and indirect inhibition of tissue respiration, aggravating violations energy cells.

Manifestations. The toxic effect of excess oxygen is manifested in three variants of pathological conditions:

• convulsive. The reason is the predominant damage to the brain and spinal cord, causes excessive excitation of neurons number of nerve centers, as well as motor neurons.
• Hypoventilation (characterized by respiratory failure. Reasons: atelectasis in the lungs, reducing the permeability of the blood barrier, lung edema.
• general toxicity. It is the development of multiple organ failure. Last often occurs in the absence of early convulsions and severe respiratory failure. If hypoxia continues, the patient has seizures and signs of asphyxiation.

Eliminating oxygen toxicity is achieved by switching to breathing air with normal oxygen content.

Pathogenetic PRINCIPLE

Pathogenic therapy aims to break the chain of pathogenesis of hypoxic conditions and / or elimination of its key elements. Pathogenetic treatment includes the following activities:

• Eliminating or reducing the degree of acidosis in the body.
• Reduction of the severity of the imbalance of ions in the cells, interstitial fluid, blood.

• Preventing or reducing the extent of damage to cell membranes.

• prevention or reduction of the severity of alterations in the enzymes in the cells and body fluids.

• Reduction of energy consumption of energy-rich compounds by limiting the intensity of the life of the organism.

Symptomatic PRINCIPLE

Purpose: removal or reduction of painful, aggravating the patient experiences as well as secondary symptoms associated with the consequences of the effects of hypoxia on the body. To eliminate these and other symptoms used anesthetics, analgesics, tranquilizers, cardiovascular and vasotropic and other drugs.

Pathophysiology of external breathing

Breath - gas exchange of oxygen, carbon dioxide and other gaseous substances - occurs by diffusion along their concentration gradient. The determining factor - the partial pressure of gases (eg, pO_2 and pCO_2). There are fabric and external respiration.

Tissue respiration - sided diffusion of gases between the lumen of the capillaries of the blood and internal organs cells (the term "tissue respiration" has a broader meaning - O_2 utilization in cell metabolism).

External respiration - sided diffusion of gases between the alveoli of the lung cavity and the lumen of the blood capillary walls interalveolare (blood barrier).

1) External breathing apparatus includes airways, respiratory department of lungs, thorax (including its osteochondral frame and neuromuscular system), as well as neural respiratory control centers.

2) External breathing apparatus provides alveolar ventilation (two-way diffusion of oxygen and carbon dioxide between the cavity of the alveoli and blood capillaries interalveolare across the alveolar-capillary membrane - blood barrier) and lung tissue perfusion (blood flow to the lungs).

Partial or combined disorders of functioning of the external breathing apparatus can lead to respiratory failure - a condition characterized by the development of hypoxia and, as a rule, hypercapnia as a result of violations of gas exchange function of the lungs.

External respiration involves the following steps:

1. The pulmonary ventilation, which results in the exchange of gases (oxygen and carbon dioxide) between atmospheric and alveolar air.

2. Perfusion of the lungs (pulmonary circulation).

3. Diffusion of gases (oxygen and carbondioxide) at the boundary of the lungs - the blood. At the same time the exchange of gases between the alveolar air and blood.

Spirometry

Spirometry (spirography) - VC measurement and other lung volumes - easy and affordable method for studying the function of the lungs.

Spirograph - a device for the continuous registration of the graphic changes inhaled volume and exhaled air.

Spirogram. Recording starts with the maximum deep inspiration, then the patient breathes quietly, and then repeats the last maneuver with maximum effort.

Application. Spirometry helps distinguish obstructive lung disease from restrictive, to assess the severity of respiratory failure and its dynamics during treatment.

RESPIRATORY FAILURE

Respiratory failure - a pathological condition that develops as a result of violations of the external breathing, in which either do not provide normal gas composition of arterial blood, or it is achieved as a result of compensatory mechanisms that control the reserve capacity of the organism, or maintained by artificial means.

Manifested respiratory (pulmonary) insufficiency of the development of hypoxemia and, as a rule, hypercapnia (but not always).

Extended description of the concept includes a provision that respiratory failure and include such conditions that the gas composition of the blood does not go beyond the normal range, but this is achieved at the expense of the external breathing apparatus hyperfunction. The latter reduces the

adaptive capacity of the organism, is fraught with their breakdown and the development of extreme condition.

Causes

Lung (intrapulmonalary) reasons. These are all options disorders (partial and mixed) gas exchange function of the lungs: ventilation, perfusion, ventilation-perfusion ratios, the diffusion of gases through the alveolar-capillary membrane.

1. extrapulmonary (extrapulmonary) causes.

- Disorders of neurogenic mechanisms of regulation of the external breathing (for example, with injuries, stroke, brain tumors).
- Violations of the implementation of the efferent regulatory effects in neuromuscular synapses intercostal muscles and the diaphragm (for example, polio, myasthenia gravis, polyneuritis).
- Disorders of the respiratory muscles functions (for example, myalgia and muscular dystrophy intercostal muscles).
- Violations of the chest respiratory excursions (for example, ribs or spine injuries, rib joints ankylosis).
- Systemic circulatory insufficiency in the lungs (for example, heart failure or anemia).

Classification of respiratory failure

Respiratory failure:

- Forms RF
- Species RF
- Stage RF
- Types RF

Forms respiratory failure

Depending on the rate of change of arterial blood gas analysis to distinguish between:

- acute respiratory failure - disorders arterial blood gases developed within a few days, hours (or even minutes) and require intensive care;
- chronic respiratory insufficiency - a violation of blood gas develops gradually, within a few days, months or years.

Acute respiratory failure

With the rapid development of respiratory failure do not have time to join the compensatory mechanisms of other organs and body systems, especially the kidneys, so characteristic feature otsroy respiratory failure are acute disorders of acid-base balance, in particular, respiratory alkalosis in the excessive excretion of carbon dioxide and respiratory acidosis due to delay carbon dioxide in the body.

Among the factors that provoke the exacerbation of respiratory failure leading role for respiratory infections, pulmonary embolism, uncontrolled appointment kilosloroda and certain drugs (sedatives, diuretics).

Causes of acute respiratory failure:

- spasm of the airways
- foreign body
- pneumothorax

Chronic respiratory failure

When chronic respiratory failure compensatory mechanisms are activated, normalize acid-base balance and improve the delivery of oxygen to the tissues:

- changes in the frequency and depth of breathing,
- mobilizing mechanisms of renal regulation of acid-base balance,
- acceleration of peripheral blood flow (tachycardia, increased cardiac output)
- Blood hemoglobin increase (secondary polycythemia)
- changes in oxyhemoglobin dissociation.

Pathological changes in patients with chronic respiratory insufficiency External usually irreversible. However, almost always under the influence of treatment there is a significant improvement in functional parameters.

Insufficiency compensatory mechanisms for respiratory insufficiency leads to the development of tissue (hypoxemic) hypoxia, most of which are sensitive to the cell cortex and attacks.

The degree of chronic respiratory insufficiency

1) Latent respiratory failure - alone all indicators are normal, under load - the inclusion of compensatory mechanisms can be shortness of breath.

2) Compensated stage - dyspnea at light load; compensatory mechanisms included in peace.

3) Decompensated stage - constant shortness of breath at rest; lack of oxygen in the body, compensatory mechanisms are insufficient.

Species of respiratory failure

Types of external respiratory failure are determined by the basic functional unit of the apparatus of external respiration, which revealed pathological changes:

- dysregulation of respiration,
- violations of ventilation,
- violation of the diffusion of gases through the alveolar-capillary membrane,
- violations of pulmonary blood flow (perfusion),
- changes in gas composition of the surrounding air.

The types of respiratory failure

1. Hypoxemic (parenchymal, type I). It is characterized by a decrease in the oxygen partial pressure in arterial blood (hypoxemia).

The main **reasons**: violation of the diffusion of gases through the alveolar-capillary membrane (the most common factor), perfusion lung disorder, disturbance of ventilation-perfusion ratios, exogenous hypoxia (hypo- and normobaric).

Hypoxemic form of respiratory failure occurs in severe lung parenchyma lesions - and this is determined by one of its names (for example, by generalized infection of, fluid aspiration, bronchiolitis and bronchitis, inhalation of toxic gases, pulmonary edema, shock).

2. Hypercapnia (gipoventilyatsionnaya, type II). It is characterized by hypoxemia and hypercapnia.

The main **reasons**: alveolar hypoventilation (the main factor) and violation of ventilation-perfusion ratios (due to insufficient ventilation of the alveoli).

Hypercapnic form of pulmonary insufficiency occurs in bronchitis, bronchopneumonia, asthma, tumors of the bronchi.

3. The mixed form. Characterized primary hypercapnia and hypoxemia.

Main **causes**: acute and chronic diseases of the lungs, leading to obstructive hypoventilation type (eg, bronchitis, bronchial asthma, obstructive pulmonary emphysema, bronchiectasis, pneumonia and lung abscess).

Typical forms of external breathing disorders

Typical forms of external breathing disorders include violations of ventilation (including alveolar), perfusion disorders, adequacy of ventilation and perfusion of the lungs (violations of ventilation-perfusion matching) and impaired diffusion of oxygen and carbon dioxide through the alveolar-capillary membrane.

DISORDERS OF VENTILATION

The reason for violations of exchange of oxygen and carbon dioxide in the alveoli of the lungs - alveolar ventilation disorders. There are alveolar hypo- and hyperventilation.

lveolar hypoventilation

Hypoventilation alveolar air (alveolar hypoventilation) - a standard form of violation of the external respiration, in which the actual volume of the alveolar ventilation per unit time is lower than the body under these conditions.

Causes.

Causes of alveolar hypoventilation

1. Disorders of the biomechanics of the external breathing. Among the disorders of external respiration biomechanics disorder distinguish obstructive and restrictive.
2. Infringement of the external breathing regulation mechanisms: centrogenic (neurogenic), afferent and efferent.

Obstructive alveolar hypoventilation.

Obstructive alveolar hypoventilation is to reduce airway. In connection with this increased resistance to movement of the air flow, reduces the volume ventilation respective areas of the lungs, increasing the work of the respiratory muscles, increased energy supply external breathing apparatus. Even a relatively small obstruction of the bronchial tubes can substantially increase their resistance to air flow and increase the work of the respiratory muscles (eg, reduction of bronchial diameter by 1/3 can lead to an increase in the movement of air resistance at 300-500%).

Main reasons.

1. obturation of the lumen of the upper and / or lower respiratory tract of food and other foreign bodies (eg, vomiting or breathing polluted air) sinks the language (for example, in a coma, during sleep, anesthesia), sputum, mucus, exudate, blood (for example, when tracheitis, bronchitis, cystic fibrosis, bronchiolitis, tumor growth), neoplasms airway.
2. bronchospasm and / or bronchial tubes (for example, asthma attack). Bronchospasm usually combined with mucosal edema and the formation of viscous mucus.
3. Spasm of the larynx (eg, inhaled irritants, or in neurotic states).
4. Compression (compression) of the respiratory tract from the outside (eg, a tumor, enlarged lymph nodes, thyroid gland).
5. The dynamic compression of the bronchi of small and medium diameter with increasing intrapulmonary pressure during exhalation (especially forced).

This phenomenon is known as "compression of the bronchi expiratory" (expiratory compression phenomenon hyperexcitability lung, bronchi expiratory collapse). It can be observed with a strong cough in patients with emphysema of the lungs, when forced breath during exercise.

Manifestations.

1. Reduction of indicators:
- The volume of forced vital capacity (FVC)
- Forced expiratory volume in 1 second (FVC1)

- Reducing the ratio of FVC / FVC1 (index Tiffno).

2. Increased performance:

- Residual lung volume (RLV)

- RLV relation to total lung capacity.

3. Save in the range of norm measure of total lung capacity.

Restrictive type of alveolar hypoventilation.

It is characterized by a decrease in (limited) degree of unfolding light. In this connection, reduced ventilation of the lungs, increasing the load on the respiratory muscles, increased energy "cost" of breathing.

Main reasons

1. intrapulmonary (parenchymal) reasons.

The main reason - the decline of lung tissue extensibility (change in lung volume, the value ascribed to the through pulmonary pressure). Observed in fibrosing processes in the lung tissue (eg,

as a result of diffuse inflammation or fibrosis), large and / or multiple pulmonary atelectasis, diffuse lung tumors.

2. extrapulmonary causes restrictive lung hypoventilation. Determining limit values breathing excursions easy. Most often this occurs when:

- Compression of the chest (like a corset, spacesuit, heavy objects with rubble earth, sand in the destruction of buildings).

- Decreased mobility of the joints of the chest and / or ossification of cartilage ribs ("gimp" hypoventilation of the lungs). Developed as a result of kyphoscoliosis, ankylosing spondylitis.

- Inflammation of the pleura. Severe pain causes the patient with pleurisy limit inspiratory volume.

- Pleural fibrosis.

- Congestion in the chest of blood, exudate, transudate, air. It results to more or less pronounced restriction of the unfolding light.

Manifestations of restrictive lung hypoventilation: reduction in overall capacity of the lungs, the residual lung volume, VC (this index directly reflects the degree of restriction of the lungs).

Disorders of the external breathing regulation mechanisms.

Respiratory disorders arise as a result of violations of the respiratory center, its afferent and efferent connections.

1. Disorders of the central regulation of the external breathing.

The most common **causes** are: trauma and tumors in the medulla oblongata, cerebral compression (if edema or inflammation, bleeding in the brain substance or ventricles), acute severe hypoxia of different genesis, intoxication (eg, ethanol, drugs, endotoxins produced during uremia or liver failure), destructive changes in the brain tissue (for example, encephalitis, multiple sclerosis, syringomyelia, syphilis).

Manifestations. To be clinically significant forms include apneusis breathing, shortness of breath and recurrent form of breathing.

Apneusis - temporary cessation of breathing, characterized by an elongated breath due to spasmodic contraction of the respiratory muscles and relatively brief exhalation. Apneusis breathing observed in myocardial bridge brain, acute severe hypoxia, poisoning by barbiturates.

Breathing such as "gasping" (from the English gasp - shortness of breath, choking). There in the agonal state. Characterized by deep convulsive short breaths, large gaps between them, lack of response to the afferent action (eg, pain, or elevated levels of carbon dioxide in the blood).

Recurrent respiratory forms are characterized by periods of strengthening of the respiratory movements and their subsequent weakening and apnea periods. These include breathing Biota, Cheyne-Stokes, Kussmaul.

Possible mechanisms of development of periodic breathing.

- Periodically increasing failure (up to critical) energy respiratory neurons.

- The consequent, as well as a violation of physico-chemical state of membrane disorder transmembrane ion distribution. This leads to disruption of the formation of PM and PD.
- Fluctuation of neuronal excitability of the respiratory center and because of this - change the frequency and depth of breathing.

2. Violations of the afferent regulation of the respiratory center function. Manifest lack or excess afferentation.

Lack exciting afferentation.

Causes.

- Poisoning by drugs or ethanol. Leads to a restriction of the respiratory center to excitatory stimuli.
- Low excitability chemoreceptors, sensing the oxygen content and / or carbon dioxide in the blood (seen, for example, premature infants or abnormalities of brain development).

Reduction of non-specific tonic activity of neurons in the reticular formation of the brain stem (inherited or acquired, for example, an overdose of opioids, barbiturates, tranquilizers and other neuro- and psychoactive substances).

Excess exciting afferentation.

Causes of stress reaction (accompanied by activation of the stimulating impulses to the respiratory center of the receptor vessels and bronchi), encephalitis, cerebral ischemia or in the medulla oblongata, neurotic states (for example, hysteria and phobia), excessive irritation noci-, chemo- and mechanoreceptors at injury, respiratory, abdominal, or burns the skin and mucous membranes.

Manifestations: frequent shallow breathing (tachypnea), hypoxia, hypercapnia, acidosis.

The excess braking afferentation.

The most common causes are: severe pain in the chest and / or respiratory tract (eg, trauma, burns, pleurisy), excessive irritation of the respiratory tract mucosa (when inhaled irritants such as ammonia, by inhalation of cold or hot air in acute bronchitis and / or trachea).

3. Violations of the efferent neural regulation of breathing.

Can occur as a result of damage to the various levels of effector pathways governing the respiratory muscles.

- Lesions of pathways of the respiratory center to the diaphragm (eg, ischemia or spinal cord injury, multiple sclerosis and polio) manifest loss of respiratory automatism and the transition to an arbitrary breath. It becomes irregular and ends with falling asleep ("Ondine curse" syndrome).

- Damage to the corticospinal tract to the respiratory muscles (for example, tumors, trauma or spinal cord ischemia, syringomyelia) results in the loss of any (conscious) breath control and switch to "automatic" breathing.

- The defeat of the descending spinal pathways of the spinal cord motor neurons, the nerve trunks to the respiratory muscles (eg, trauma or spinal cord ischemia, poliomyelitis, botulism, neuritis, blockade of neuromuscular conduction in infants or the use of curare drugs). Manifestations: reduced amplitude of respiratory movements and intermittent apnea.

Alveolar hyperventilation

Hyperventilation lungs (alveolar hyperventilation) - a standard form of violation of the external respiration, characterized by the excess of the actual lung ventilation per unit time in comparison with the body needs in these conditions.

Causes.

- Inadequate ventilation mode (eg during anesthesia, transfer the patient to the artificial respiration with brain injury or coma). Developing at the same time called passive hyperventilation.
- Stress reactions, neurotic states (for example, hysteria, or phobias).

- Organic brain damage (for example, as a result of hemorrhage, ischemia, intracranial tumors, injury and concussion).
- The state of hyperthermia (fever, heat stroke, etc.).

- Exogenous hypoxia.

Manifestations.

- Hypocapnia (potentiates the inhibition of O2 utilization tissues, reduces coronary and cerebral blood flow by reducing the tone of the walls of the arterioles and the development of arterial hypotension).

- Respiratory alkalosis (as a result of alveolar hyperventilation).

- Reduced oxygen consumption tissues and organs (which can lead to tissue hypoxia).

- An imbalance of ions in the blood plasma and interstitial fluid (characterized by hypernatremia, hypokalemia, hypocalcemia, hypomagnesemia).

- Muscle cramps (due to hypocalcemia and other manifestations of ionic imbalance).

- Paresthesia (as a consequence of cerebral ischemia and ionic imbalance).

CIRCULATORY DISORDER IN THE LUNGS

Significant violations of perfusion lung observed with hypo- and hypertension in the blood vessels of the pulmonary circulation (pulmonary hypo- and hypertension).

Pulmonary hypertension

There are three forms of pulmonary hypertension: precapillary, post-capillary and mixed.

1. precapillary hypertension. It is characterized by an increase in pressure in the capillaries and precapillaries above normal (more than 30 mm Hg systolic and 12 mm Hg diastolic).

The most common causes.

- Spasm of arterioles (for example, under stress, embolism pulmonary vascular release of catecholamines from pheochromocytomas, when acidosis, acute decrease in partial pressure of oxygen in the inhaled air). Hypoxia is the most powerful factor in vasoconstriction (the most important mediators of vasoconstriction: catecholamines, endothelin, thromboxane A2).

- Obturation lung microvascular (eg microthrombi, emboli, hyperplastic endothelium).

- Compression of the pulmonary arterioles (eg, a tumor, enlarged lymph nodes, increased air pressure in the alveoli and bronchi during an acute attack of coughing).

2. postcapillary hypertension. It is characterized by impaired blood outflow from the blood vessels into the left atrium and its excess accumulation in the lungs.

The most common causes: stenosis of the opening of the mitral valve (for example, as a result of endocarditis), compression of the pulmonary veins (eg, enlarged lymph nodes or tumors), the lack of contractile function of the left ventricle - left ventricular failure (eg, myocardial infarction, hypertension, myocardial).

3. The mixed form of pulmonary hypertension. Often the result of progression and complications of pre- or post-capillary hypertension. For example, the difficulty of outflow of blood from the pulmonary veins to the left atrium (typical of the post-capillary hypertension) leads to a decrease in reflex arteriolar lumen light (characteristic of precapillary hypertension).

Manifestations: signs of left ventricular and / or right ventricular heart failure (stagnation of blood in the venous blood vessels, edema, ascites, and others.), A decrease VC, hypoxemia and hypercapnia, acidosis (respiratory, the chronic course - mixed).

Hypotension in the vessels of the small circle

Pulmonary hypotension is characterized by a persistent reduction in blood pressure in the pulmonary vessels.

The most common causes.

- Heart disease with shunting of blood from right to left. Thus there is a venous blood into the arterial system reset (for example, tetralogy of Fallot, pulmonary artery valve insufficiency).
- Hypovolemia various origins (for example, during prolonged diarrhea, shock conditions, as a result of chronic blood loss).
- Systemic hypotension (eg, in the collapse or coma).

DISORDERS PERFUSION-VENTILATION RATIO.

Normally, the ratio between the values of ventilation and perfusion are associated in some areas, and in the lungs as a whole: the bloodstream is implemented in those areas of the lung, in which the ventilation. When this ratio is optimal ventilation and perfusion. It is in these areas of the lung gas exchange occurs between the alveolar air and the blood flowing through the capillaries interalveolar. This provides a ratio of CO2 to the lungs release of O2 consumption, which is adequate tidal coefficient, reflecting the intensity of metabolism (these factors - ventilation-perfusion and respiratory - normally equal to about 0.8).

Violation of conjugation of ventilation and perfusion of the lungs leads to the development of respiratory failure. The quantitative relationship between ventilation (V) and perfusion (Q) indicator light is expressed V / Q, which normally is in the range 0.8-1.0.

Main reasons:

The factors leading to local hypoventilation pulmonary (alveolar hypoventilation). They cause a regional reduction of air into the alveoli. The volume of the alveolar ventilation and the amount of blood flow in any region of lung becomes smaller than in the lungs in general.

Effect: increase of the functional dead space and reduced oxygenation of the blood flowing from the site hypoventilated lung.

1) Factors that lead to local hypoperfusion.

- Obturation branches of the pulmonary artery (eg, thrombus or embolus with disseminated blood coagulation, fatty embolism, aggregates of blood cells in sepsis or shock).
- Compression of the blood vessels of the pulmonary artery (eg, tumors, foreign body, scar tissue).

- Muscle spasm wall of a branch of the pulmonary artery.

- Shunting of blood in the lungs (alveoli passing). This occurs, for example, if communications between the branches of the pulmonary arteries and veins.

These circumstances are responsible for:

- Decreased perfusion of a section of the lung (resulting formed alveolar dead space - ventilated but not perfused).

- Uselessness alveolar ventilation (normal or even increased) level of lung perfusion.

- Reduction of the partial oxygen pressure in the blood flowing from the lungs (hypoxemia).

- Blood CO2 tension usually remains normal (eucapnia) since diffusion of gas is not reduced.

DISORDER DIFFUSION OF OXYGEN AND CARBON DIOXIDE

Reasons for reducing diffusion capacity

The main reasons.

1. Increasing the thickness of the membrane as a result of increasing the amount of liquid on the surface of the alveolar epithelium (eg, due to mucus or exudate in allergic alveolitis, or pneumonia), interstitial edema (accumulation of fluid between the basement membrane of endothelium and epithelium), increasing the thickness of the capillary endothelial cells and alveolar epithelial (for example, as a result of hyperplasia or hypertrophy, sarcoidosis development).

2. The increase in the density of the membrane due to calcification (eg, interstitial structures), increasing the viscosity of the gel interstitial space, increasing the amount of collagen, elastin fibers and reticular in interalveolar partitions.

Examples of pathological conditions that reduce the ability of the air-blood diffusion membrane:

- Pneumonia (especially chronic recurrent diffuse interstitial pneumonia).

- Pneumoconiosis. Being developed by inhalation of dust containing silica (silicosis), asbestos (asbestosis), beryllium (berylliosis).

- Fibrosing alveolitis (diffuse or focal).

- Allergic alveolitis (for example, hay fever).
- Heart failure.

Rhythm disorders of the respiratory movements.

Types of periodic breathing. These include breathing Cheyne-Stokes respiration and Biota. When breathing Cheyne-Stokes breathing pauses interspersed with movements that are growing in depth first, and then decrease. When breathing Biota pause alternate with respiratory movement's normal rate and depth. The pathogenesis of periodic breathing is a decrease in excitability of the respiratory center. It can occur when organic brain injuries - injuries, strokes, tumors, inflammatory processes with acidosis, diabetic and uremic coma at endogenous and exogenous intoxication. Possible shift in the types of terminal breath. Sometimes periodic breathing in children and elderly people during sleep. In these cases, normal breathing easily restored on waking.

The mechanism of periodic breathing. Against the background of low respiratory center excitability does not respond to normal concentrations of carbon dioxide and H + - ions in the blood. high concentrations are required to excite the respiratory center. Time accumulation of these

stimuli to the threshold dose determines the length of the pause. Respiratory movements create ventilation, CO2 is washed out of the blood, and respiratory motion freeze again.

Terminal types of breathing. These include Kussmaul breathing (big breath) apneusis breathing and gasping, breathing. There is reason to assume the existence of a fatal respiratory disorders specific sequence to a complete stop, first excitation (Kussmaul breathing), apneusis, gasping, breathing, paralysis of the respiratory center. If successful resuscitation is possible to reverse the development of respiratory disorders to its full recovery.

Kussmaul breathing - deep breathing noisy, typical of patients with impaired consciousness in diabetic, uremic coma. Kussmaul Breathing is the result of violations of excitability of the respiratory center in the brain against hypoxia, acidosis, toxic effects.

Apneusis breathing is characterized by prolonged convulsive breath enhanced, occasionally choking breath. This type of respiratory movements in the experiment occurs after section of both the animal and the trunk of the vagus nerves at the boundary between the upper and middle third of the bridge.

Gasping breath, it occurs most terminal phase asphyxia. This single, deep, rare, declining in strength "sighs". pulse source of a given form of the respiratory movements are cells of the caudal medulla oblongata at the termination of the functions of the overlying brain.

There are more varieties of dissociated breathing: paradoxical movement of the diaphragm, the asymmetry of movement of the left and right side of the chest. "Ataxic" is characterized by the dissociation of the respiratory movements of the diaphragm and intercostal muscles. It is observed in cerebrovascular disorders, brain tumors and other serious disorders of the nervous regulation of respiration.

Pathophysiology of kidney

The main idea of the function of kidneys

Kidney transformed with 1700 liters of blood passing through it per day, about 1 liter of highly concentrated urine. However, they perform the following functions:

- Participate in maintaining consistency and osmolarity of the extracellular fluid concentrations of various electrolytes in it (Na \ K +, Ca +, etc.);
- Excrete metabolic products and many exogenous compounds;
- Regulate systemic arterial pressure;
- It regulates the acid-base status, maintaining the consistency buffer bases plasma and H +;
- Secrete erythropoietin, which stimulates erythropoiesis;
- Form the active form of vitamin D3.

Adjusting the concentration of electrolytes, blood volume and blood pressure. This essential function of the kidneys allows the body to avoid fluid overload and dehydration if fluid intake changes

in the body. The kidneys have a huge reserve for the maintenance of electrolyte levels. For example, in the experiment 10-fold increase or decrease the intake of sodium through the kidney causes a significant change in blood plasma concentration. Also other concentrations are regulated electrolytes chloride, potassium, calcium, magnesium and phosphate ions.

A key role in this process is played by the juxtaglomerular apparatus (JGA) of the nephron.

By the juxtaglomerular apparatus include the following types of cells:

- Tight spot cell - sensors sodium ion concentration in the urine of the distal convoluted tubule; while reducing the concentration of sodium ions, they secrete more renin;
- Granular (juxtaglomerular) cells covering the afferent arterioles - pressure sensors in the afferent arterioles; with a decrease in her blood pressure granule cells secrete more renin;
- Mesanglial glomerular cells, forming a kind of "mesentery" for glomerular capillaries, evenly distributing the hydrostatic pressure of the blood along the entire length of the capillary glomerulus, which is necessary for unidirectional fluid flow from the capillaries into the Bowman's capsule.

JGA cells are both a kind of receptors (sensors concentration of ions Na + - and blood pressure in the glomerular afferent arterioles), and hormonally active cells - producers of renin.

Incentives to produce renin JGA cells are:

- Reduction of hydrostatic pressure & glomerular afferent arterioles
and / or

- Reducing the concentration of sodium ions in the lumen of a distal convoluted tubule.

Changing renin production runs produce angiotensin II (AT-II). Formed under the influence of first renin activity (in response to a decrease in blood pressure), and then angiotensin-convertase (ACE), locally in the capillaries of the glomerulus AT-II causes a spasm of efferent arterioles, which is important for maintaining the stability of the renal blood flow and glomerular filtration rate at blood vibrations pressures from 75 to 160 mm Hg. Art. AT-II produced by the action of renin into the systemic circulation, causing spasm of the arterioles of the systemic circulation and enhances the secretion of aldosterone glomerular zone of the adrenal cortex. Steroid hormone aldosterone, in turn, acts on cells of the distal tubules and collecting ducts of the nephron, increasing expression in these transport proteins that provide the reabsorption of sodium in exchange for potassium and hydrogen ions excretion.

The kidneys play an important role in the long-term mechanisms of systemic blood pressure regulation by removing different amounts of water and sodium. In this process, taking part of the renin-angiotensin-aldosterone system, as well as locally synthesized by cells of the South in response to pressure changes in the afferent arterioles of the glomerulus and the change in the concentration of sodium ions in the distal convoluted tubule vasoconstrictors (endothelin, thromboxane) and vasodilators {prostaglandins, kinins). These substances control the tone of the afferent and efferent arterioles and hence affect the maximum blood pressure value (norma - 160 mmHg), above which is included pressor diuresis and natriuresis pressor.

Blood pressure increase leads to a certain increase in the glomerular filtration rate. As a result, by increasing the current UF rate tubules. This reduces the reabsorption rate of the cells of the proximal convoluted tubule and the loop of Henle of sodium ions. As a result, the distal convoluted tubule sodium concentration is increased. It is recognized by the cells and release tight spots vasoconstrictors

(endothelin), causing a spasm of afferent arterioles, leading to normalization of pressure in the capillaries of the glomerulus and the glomerular filtration rate. Excess blood pressure critical level of 160 mm Hg. Art. the feed is not accompanied by a further spasm of afferent arterioles. As a result of increasing pressure in the glomerular capillaries. As a result, there is an increase in glomerular filtration rate, leading to an increased excretion of water and sodium organism (pressor diuresis and natriuresis pressor).

Regulation of acid-base balance is carried out through the allocation of non-volatile acids and maintain a constant buffer bases of plasma. Non-volatile acid such as sulfuric and phosphoric, are output only kidneys.

Excretory function primarily associated with excretion of metabolic products, are not used by the body. The kidneys excrete urea (formed by the metabolism of amino acids), creatinine (product of creatine metabolism), uric acid (the product of the metabolism of nucleic acids), conjugated bilirubin and derivatives thereof (final product breakdown of hemoglobin), metabolites of various hormones. In addition, most of the kidney is output through the consumption of natural toxins (produced by fungi, bacteria, etc.) And xenobiotics (drug substances, pesticides and others.).

Regulation of erythropoiesis associated with the development of erythropoietin by the kidneys in response to a chronic lack of oxygen in the kidney tissue.

The formation of vitamin D3. Kidneys inactive vitamin D is converted into the active form - vitamin D3 (1,25-dihydroxycholecalciferol hormone), which promotes absorption of calcium and phosphate ions in the intestines and their incorporation into the bone (promotes bone mineralization).

Gluconeogenesis. In the kidney, there is synthesis of glucose from amino acids and other non-sugar products.

Structural and functional unit is the nephron. Total nephrons (in the kidney weight of 150 g) is 1-1.2 million. Each nephron is made up of a glomerulus and the renal tubule. Within a few cortical tubules open into the collecting ducts. Kidney glomerulus beam formed capillaries, which are branching afferent arterioles. By the capillaries adjacent internal machine bilayer Bowman's capsule, formed by tubular epithelium. Between the two layers is a capsule space communicating with the lumen of the tubule exhaust capsules. All glomeruli are located in the cortex, but the ones that are located in the outer layers of the cortex are called cortical glomeruli, and those that are in the depths of the kidneys - on the border of cortical and medullary layers - are called glomeruli juxtamedullary. Depending on the name of the glomeruli corresponding nephrons also referred to as cortical or juxtamedullary.

Renal blood flow. Both kidneys are only 0.5% of total body weight, but they receive about 25% of cardiac output. Of the total amount of blood flowing through the kidneys approximately 90% from the cortical and only 10% - in the medulla. In conditions of ischemia possible redistribution of blood flow to increase it in the medulla.

Blood supply of the renal tubules and collecting ducts arranged on the principle of portal systems. A ball is formed by the capillary network formed of afferent arterioles. Hinges glomerular capillaries gather in one efferent arterioles. The lumen of efferent arterioles in the cortical nephrons slightly smaller than the lumen of afferent arterioles. In juxtamedullary nephrons inverse relationship. Abductor arterioles again breaks up into capillaries, forming a network around the convoluted proximal and distal tubules of the nephron corresponding. blood enters the capillary venules From

peritubular network. Abductor arterioles juxtamedullary glomerular capillary enters lumen wide, located along the hinge of nephrons and collecting ducts.

Due to the existing autonomous multi kidney renal blood flow autoregulation system less sensitive to variations in systemic arterial pressure ranging from 75 to 160 mm Hg. Art. Changes occur only when the pressure level deviation of the specified range. The pressure drop of less than

60 mm Hg. Article; lead to a sharp decrease, and lowers the 40mm. Hg. Art. - For a full cessation of glomerular filtration process due to the activation of CAS, causing spasm of renal arterioles by norepinephrine released from the synapses of the sympathetic nerve fibers innervating abundantly afferent and efferent glomerular arterioles.

In the formation of urine involves all departments of the nephron. This process begins in the glomerulus, where the glomerular filtration (ultrafiltration). Nephron glomerulus is a capillary network formed by afferent arterioles. The wall of the capillary, as opposed to normal tissue capillary consists of three layers: the endothelium, the basement membrane, and glomerular epithelial cells (podocytes) covering capillary loops. The capillary loops are connected to each other and hung like a mesentery to glomerular pole by means of the connective tissue of the glomerulus, or mesangium.

Endothelial system and then slit diaphragms and structural lattice form glomerular basement membrane barrier filter size albumin macromolecules (molecular weight above 70 000 with a radius above 3.6 microns). The system of legs and slit diaphragms podocytes helps evenly distribute hydraulic pressure to the capillary wall, providing a high permeability to plasma and its components. The negative charge of the glomerular capillary wall gives the filter also features a barrier filtration of negatively charged macromolecules.

The principal difference between the glomerular capillary from the tissue fluid flow is unidirectional - only from the capillary into the space of Bowman's capsule and into the tubules of the nephron. This is because in all the glomerular capillary network (and bringing near, and near the efferent arteriole) supported by the same filtration pressure. Therefore, all that portion of the blood plasma, which is the gradient of the filtration pressure enters the capsule Bowman of glomerular capillaries back into the capillaries of the glomerulus are not supplied. This part of the blood plasma is the primary urine or ultrafiltrate and is approximately 1/5 of the volume of plasma flowing through the capillaries of the glomerulus.

In the primary urine contains various low molecular substances. Almost all of the protein molecules remain, and blood capillaries due to the small size of the pores and the special structure of the wall of the renal capillary and glomerular basement membrane.

Glomerular filtration rate. Glomerular filtration rate (GFR) is the volume of ultrafiltrate generated per unit time. In males, GFR is about 125 ml / min, women - 110 ml / min (normal GFR typically taken as 100%).

GFR depends on the filtration pressure and filtration rate.

Normally, due to the mechanism of autoregulation of renal blood flow and glomerular filtration rate filtration pressure are maintained almost constant, despite the changes in systemic blood pressure from 75 to 160 mm Hg. Art. (Autoregulation of GFR).

The concept of renal clearance. The flow rate of plasma purification of a substance called the renal clearance of the substance. This is measured in ml / min. The clearance of a substance

quantitatively equal to plasma volume, is completely cleared of this substance for 1 minute by the kidneys.

Reducing the clearance of substances released by the kidneys, such as creatinine, urea and other nitrogen-containing substances leads to increased non-protein nitrogen concentration in the blood plasma, and suggests renal failure.

Creatinine is produced when muscle work and normally excreted by the kidneys by filtering only in the glomeruli. Therefore, the blood plasma volume, which over time is cleared of creatinine (creatinine clearance), corresponds to the rate of glomerular filtration.

The resulting ultrafiltrate subsequently passes through the renal tubules and collecting ducts. Its composition varies greatly with the result transtubular transport of water and solutes. This transport is carried out in two directions; depending on the transfer direction it is subdivided into tubular reabsorption and tubular secretion. During most of the tubular reabsorption in the primary filtrate. Specifically, water and most of the substances necessary for the organism) back into the blood capillaries peritubular. In tubular secretion process into the filtrate coming substances

contained in the blood of the capillaries (e.g., some organic acids) or formed in the tubular cells (e.g., hydrogen ions and ammonia).

Causes of kidney disease

The evaluation of various forms of renal disease produced by the nature of their causes: the nature, origin and level of implementation of the preferential action.

The nature of causal factors

The nature of the causative factors of renal disease may be infectious (e.g., bacteria, viruses, rickettsia) and noninfectious. Among the non-infectious causes distinguish the chemical, physical and biological factors.

1. Chemical (e.g., lead compounds, mercuric chloride, mercury, arsenic, some antibiotics, diuretics).
2. Physical (eg, penetrating radiation, radioactive decay products, low temperature, kidney injury).
3. Biological (eg antinephrotic AB, NK-cells, macrophages, immune complexes, allergens, excess or deficiency of catecholamines, endoperoxides, Pg, PTH and other biologically active substances).

The origin of the reasons

By origin distinguish primary (hereditary and congenital) and secondary (acquired) factors.

1. Primary. They constitute a disease caused by mutations in genes in the kidney and renal morphogenesis numerous defects. For diseases in this group include fermentopathy, polycystic membranopathy, dysplasia, renal diabetes insipidus, Pseudohypoaldosteronism, aminoaciduria, phosphaturia and others.
2. Secondary. Acquired diseases account for most of the kidney disease.

The level of implementation of the preferential action of the causal factor

In terms of pre-emptive effects of causal factors distinguish prerenal, renal and postrenal reasons.

1. Pre-renal causes.

- Neuropsychiatric disorders: prolonged stress, trauma, state, combined with severe pain (such as pain reflex anuria).
- Endocrinopathies (eg, excess or deficiency of ADH, aldosterone, thyroid hormone, insulin, catecholamines).
- Disorders of blood circulation in the form of a hypotensive and hypertensive states.

2. Renal reasons.

- Direct damage to the parenchyma, vascular, renal extracellular matrix component factors of infectious or non-infectious.
- Circulatory disorders in the kidneys in the form of ischemia, venous congestion, stasis.

- Mutations in genes in the kidney.

3. postrenal reasons. Disrupt the flow of urine for urinary tract. This is accompanied by an increase in intrarenal pressure (under stones and urinary tract tumors, their edema, prostate adenoma, ureter excesses, etc.).

Said causes kidney damage leads to various disturbances of kidney function. Many of them are mentioned in other chapters and annexes of this publication. This chapter discusses mocheobrazovatelnoy disorders and urinary (excretory ie in the broadest sense) of kidney function.

General mechanisms of occurrence and development of renal disease.

Disorders urine formation is the result of partial or, more often, combined filtration disorders (formation of primary urine in the kidney cells), reabsorption (ion transport, liquids, proteins, amino acids, glucose and other substances from the lumen of the renal tubules into the lumen of the capillaries of the secondary network) secretion (Transport ions, liquids and other substances in the tubule lumen).

In the early stages of renal damage typically occurs activation of any one of the below-described pathogenesis. and other connected with the development of the pathological process. That is why in clinical nephrology difficult to identify any specific characteristic only of one disease mechanisms and clinical manifestations. Many of renal syndromes and symptoms observed in varying degrees of severity and in different combinations in a variety of diseases and lesions of the kidney.

Disorders of glomerular filtration

Violations of glomerular filtration rate accompanied by a decrease or an increase in filtrate volume.

1. Reducing the volume of glomerular filtrate.

Causes.

- Lowering the effective filtration pressure in hypotensive states (arterial hypotension, collapse, etc.), Renal ischemia (renal), hypovolemic states.

- Reduced glomerular filtrate area. There necrosis in renal (kidney) or a part of, multiple myeloma, chronic glomerulonephritis, and other conditions.

- Reduction in permeability of the filtration barrier due to thickening of the basement membrane reorganization or other changes in her. There is a chronic glomerulonephritis, diabetes, amyloidosis, and other diseases.

2. The increase in the volume of glomerular filtrate.

Causes.

- Improving the efficiency of the filtration pressure by increasing the tone of the smooth muscle cell efferent arterioles (under the influence of catecholamines, Pg, angiotensin, ADH) or decreased tone smooth muscle cell bringing arteriol (exposed to kinins, Pg, and others.), And also because of the blood hypooncia (for example, liver failure , starvation, prolonged proteinuria).
- Increase filtration barrier permeability (eg, due to the disintegration of the basement membrane) under the influence of biologically active substances - mediators of inflammation or allergy (histamine, kinins, hydrolytic enzymes).

Disorders of tubular reabsorption

Reduced efficacy tubular reabsorption occurs at various defects and enzymopathies systems transepithelial transport of substances (e.g., amino acids, albumin, glucose, lactate, bicarbonate, etc.), And membranopatiyah epithelium and the basal membrane of the renal tubules.

It is important that the preferential damage proximal nephron broken reabsorption organic compounds (glucose, amine acids, protein, urea, lactate) and bicarbonates, phosphates, Cl, K, M for faults distal tubule upset processes reabsorption of Na +, K + , Mg2 +, Ca2 +, water.

Disorders secretion

Violations secretion develop mainly at gene defects and lead to cystinuria, aminoaciduria, phosphaturia, renal diabetes, bicarbonaturia, renal acidosis.

Manifestations of renal disease

Disorders of renal function are shown changes in blood and urine parameters, and the development of nephrogenic common syndromes.

Indicators changes in urine output, composition of urine and urination rate

Changes diuresis (urine output).

1. Polyuria - is characterized by the increase in the volume of daily urine output of more than 2000 ml regardless of the amount of fluid you drink. In the mechanism of the role played by polyuria increased glomerular filtration of blood plasma, and (or) a decrease in the tubule fluid reabsorption. The latter can be seen at the poliuric stage acute and chronic renal failure, as well as at the termination of the secretion of ADH. In a healthy person may be a temporary polyuria resulting

increased water load or into the blood and then a large number of glomerular filtrate osmotically active substances (salts, etc., and glucose.). Polyuria observed in newborns due to the inability to carry out tubule epithelial reabsorption of water in the normal size.

2. Oliguria - is characterized by a decrease in the daily urine output of up to 500 - 200 ml. The reasons for this may be the decrease in the volume of glomerular filtrate, increased water reabsorption in the kidney tubules or urinary outflow obstruction. In a healthy person oliguria occurs by limiting fluid intake.

3. Anuria - characterized by the cessation of urination or urine output of less than 200 ml / day. On the mechanism of development distinguish prerenal anuria, renal and postrenal. An example is the termination of pre-renal anuria urination due to reflex inhibition of renal function in severe pain. Injury, illness of one kidney or ureteral compression of a brake function and a second kidney also can cause anuria. In the mechanism of reflex anuria play the role of a spasm of afferent arterioles and glomeruli stimulate ADH secretion. Renal anuria occurs at a certain stage of acute renal failure due to a sharp decline in glomerular filtration and tubular obstruction. Postrenal anuria occurs when there is an obstruction to the flow of urine at any level of the urinary tract, as well as the paralysis of the bladder.

Changes in the relative density and the composition of urine.

Relative density of urine is an indicator of the concentration ability of the kidneys. In a healthy person, it varies from 1002 to 1035 depending on the number received in the body fluid. In the context of pathology relative density of urine can vary independently of the intake of liquid, it can be increased (baruria), decrease (hypostenuria) or match the relative density of the glomerular filtrate.

1. Hyperstenuria - increase of urine density above normal (more than 1,029- 1,030), due to increased water reabsorption process in the distal nephron (at suhoedeniem greater extrarenal losses of extracellular fluid). As a rule, due to the increased reabsorption.

2. Hypostenuria - decreased urine density is below normal (less than 1,009). There is a concentration in violation of kidney function.

3. Isostenuria - varies little during the day relative density of urine. Indicates a decrease in the efficiency of tubular reabsorption and reducing the concentration ability of the kidneys. This occurs when the renal form of acute renal failure in patients with chronic renal failure, when the adrenal hypofunction, in the absence of ADH, as well as hypercalcemia and potassium deficiency, which upset the normal action of ADH on the cells of the collecting ducts and distal convoluted tubules.

Changes in the composition of urine.

Changes in the composition of urine is characterized by the appearance of its protein (proteinuria), glucose (glycosuria), amino acids (aminoaciduria), blood (hematuria), leukocytes (leucocyturia), cylinders (cylindruria), epithelial cells of the renal tubules or urinary tract crystals of various salts or amino acids (crystalluria), microorganisms (bacteriuria).

Proteinuria. Normally, the penetration of plasma proteins into glomerular filtrate inhibit glomerular filter (endothelium, the basement membrane, podocyte) and these structures electrostatic

charge that repels the negatively charged molecules including albumin molecule. The charge of the glomerular filter due to the presence in it sialoglicoprotein and glycosaminoglycans.

In a healthy human plasma in the glomeruli of filtered 0.5 g of protein per day (mainly albumin). A large part of incoming protein in the glomerular filtrate is reabsorbed in the proximal tubules by means of pinocytosis. Some of the incoming protein in the urine is formed in the epithelium of Henle's loop and the distal tubule - a uroprotein Tamm-Horsfall is a complex glycoprotein. The total amount of protein released from the daily urine, normally about 50 mg, and can not be detected by conventional laboratory methods. Urinary excretion of more than 50 mg of protein per day called proteinuria. On the mechanism of development distinguish **glomerular** and **tubular** proteinuria.

Glomerular proteinuria is associated with increased permeability of the glomerular filter, tubular - in violation of the protein reabsorption in the proximal tubule epithelium due to lack of function or reduce the outflow of lymph from the kidney tissue. In the latter case, the protein accumulates in the interstitial tissue edema and causes renal parenchyma.

There are selective and nonselective proteinuria. Development of proteinuria is associated with **selective** loss of glomerular filter ability to repel negatively charged protein molecules and thereby inhibit their passage into the ultrafiltrate. Therefore, the filter pore diameter (70 nm) is greater than the size of molecules of albumin and transferrin, these proteins are freely unloaded through a filter and developed massive proteinuria. It is observed in the nephrotic syndrome with minimal changes, which are expressed in the loss of subtle intertwining legs podocytes islands.

Nonselective proteinuria occurs when the loss of glomerular filter's ability to regulate the passage of the protein molecules according to their size. In this regard, the ultrafiltrate coming not only albumin and transferrin, but coarser plasma proteins such as immunoglobulins and lipoproteins.

There are functional and pathological proteinuria. **Functional proteinuria** is observed in people with healthy kidneys. There are several varieties of functional proteinuria: orthostatic voltage proteinuria, feverish, and idiopathic congestive. Orthostatic proteinuria occurs in some people (often at a young age) with prolonged standing or walking; by changing the position of the body on the horizontal it disappears. Proteinuria voltage is observed in approximately 20% of healthy people after heavy physical exertion. The feverish proteinuria occurs more frequently in children and the elderly; normalization of body temperature when it disappears. Congestive proteinuria observed in congestive heart failure. Idiopathic proteinuria sometimes found in healthy people with a medical examination, it is transient. It should also be borne in mind the possibility of proteinuria in healthy women willows horse pregnancy.

A common feature of all types of functional proteinuria are its small size, usually less than 1 gram protein per day.

Pathological proteinuria is related to various diseases. It is divided into prerenal, renal and postrenal.

Prerenal proteinuria (or overload) occurs at elevated levels in blood plasma of low molecular weight proteins, such as immunoglobulin light chains (Bence Jones protein), myoglobin, hemoglobin, lysozyme. These proteins are easily pass through the glomerular filter, but not completely reabsorbed tubular epithelium. This form of proteinuria develops in multiple myeloma, monocytic leukemia, intravascular hemolysis and others. Size prerenal proteinuria can reach 20 grams of protein per day.

Renal pathological proteinuria may be related to the defeat as the glomeruli and tubules. It occurs in glomerulonephritis, interstitial nephritis, pyelonephritis, amyloidosis, acute tubular necrosis, tubulopathy, and some other diseases. Urinary excretion of protein in the range of 1-3 g of protein per day or higher. If it is greater than 3.0 grams of protein per day, develops a nephrotic syndrome.

Postrenal proteinuria (extrarenal) is observed in diseases of the urinary tract, it is due to entering into the urine exudates.

Cylindruria urine excretion from the cylinder, which are protein casts of distal renal tubular cylindrical shape.

Protein-based cylinders up uroprotein Tamm-Horsfall secreted in the ascending part of the loop of Henle and the distal tubule and aggregated whey proteins.

Precipitation of Tamm-Horsfall protein and plasma proteins in the gel, leading to cylindroformation promotes change in osmolarity, electrolyte concentration, pH of urine.

The size and shape corresponding to the shape of cylinders and the inner diameter of the renal tubules and collecting tubules. Most cylindroformation occurs in the lumen of the convoluted (the narrowest) part of the distal tubule.

Cylinders can be: pure protein (hyaline and waxy), and cellular.

Protein-based cellular cylinders covered with clinging red blood cells, white blood cells, epithelial cells. For protein based cylinders can also be connected mucus salt crystals.

All kinds of cylinders are identified and stored for a long time only in the acidic environment conducive to protein coagulation. they either do not form in alkaline reaction, or quickly destroyed.

Cylinders most easily identified in the first morning urine sample, while reducing the amount of urine (When edema).

The appearance of the cylinders in the urine indicates kidney damage, and their presence is of particular importance for the differential diagnosis of urinary tract diseases.

To differentiate tubular and glomerular lesions cylinders, in contrast, are of little use.

Different types of cylinders have different differential diagnostic value.

Hyaline casts consist largely of protein and Tamm-Horsfall protein are coagulated blood serum, which filtered in the glomerulus and reabsorbed in the proximal tubule, and passing through the distal their departments, took the form of tubular lumen, ie, cylindrical.

The larger protein is filtered in the glomeruli and it is reabsorbed less than in the proximal tubules (hence, the higher its concentration in the tubules), the more hyaline casts formed. Therefore, in patients with nephrotic syndrome, accompanied by the highest proteinuria, there is most pronounced cylindruria.

Hyaline casts a gentle homogeneous structure transparent. They are longer than other types of cylinders (from 0.1-0.3 to 1 mm), the ends of their rounded or irregular shape.

Because of the stickiness on the surface thereof is often deposited cells (renal epithelium, red blood cells, white blood cells), salt (amorphous urates, phosphates), mucus (called hyaline cylinders stratifications). However, between layers of homogeneous areas are free, and it allows to distinguish these cylinders from grainy. In hemorrhagic nephritis cylinders painted in brown color, and they are jaundiced urine greenish.

Hyaline cylinders detected at any renal pathology in healthy humans (in 1 to 50 ml of urine), especially in the morning concentrated portions, after exercise, dehydration.

Single hyaline cylinders may be general for any disease. they do not have in connection with this great diagnostic value.

The appearance of granular or waxy cylinders testifies to serious kidney damage.

Granular cylinders - opaque, rough, contain large amounts of granular granular inclusions, which are degenerative degenerated epithelial cells of the proximal tubule, granular inclusions of neutrophils and The precipitated serum proteins in the protein matrix-Tamm Horsfall. Cylinders are usually short, thick.

The presence of granular cylinders indicates degenerative processes in the tubules (tubulopathy, glomerulopathy, tubulointerstitial component, particularly with nephrotic syndrome, amyloidosis, diabetic glomerulosclerosis, etc.).

In addition to the diseases of the kidneys, granular casts are found in all serious diseases with secondary renal toxicity. There may be abundant granular casts with bacterial pneumonia; diabetic coma identified short "comatose" cylinders.

Waxy cylinders in its homogeneity similar to hyaline, but tougher because closely spaced protein, direct, much wider than hyaline have dull luster and yellowish color and is therefore similar to the wax.

Waxy cylinders are formed by massive proteinuria and long-term stay in the cylinder tubules (oliguria when edema). May result from changes in quality protein (amyloidosis).

The appearance of waxy cylinders indicative of severe kidney disease. They identified more frequently in chronic glomerulonephritis with nephrotic syndrome, but may also occur in acute glomerulonephritis, acute tubular necrosis. In the urine of healthy they are absent.

Cell cylinders are:

- Epithelial,
- Erythrocyte,

- Leukocyte.

Cell cylinders always indicate renal origin of their constituent cells.

Epithelial cylinders consist yl glued together lowered cell tubular epithelium, has not yet been subjected to decay, and testify about the defeat of the tubules.

Epithelial cylinders evidence of enhanced renal tubular epithelial desquamation, identified with tubulointerstitial kidney damage, especially in large amounts in acute tubular necrosis, as well as with leukocyte cylinders in pyelonephritis.

Erythrocyte (blood) consist of cylinders or cylindrical erythrocytes of blood clots, a characteristic pink color. Red blood cells in the blood cylinders are easily destroyed so that the outlines of the cells disappear, but the pink (sometimes brown) staining is retained due to the impregnation of hyaline matrix pigment (hemoglobin). Blood cylinders are often identified with hematuria associated with glomerular disease (glomerulonephritis, vasculitis), but can also occur when interstitial nephritis, tubular necrosis, renal infarction.

Leukocyte cylinders usually contain polymorphonuclear granulocytes, but may include other types of leukocytes (eosinophils, lymphocytes).

The leukocyte (neutrophil) cylinders are typical for pyelonephritis (acute or exacerbation of chronic), they are rarely detected in glomerulonephritis (with the inclusion of lymphocytes).

Eosinophilic cylinders can be detected in acute drug interstitial nephritis.

It can be mixed cellular cylinders containing renal tubular epithelium, red blood cells and (or) leukocytes.

Vacuolated cylinders - is epithelial cylinders conditions pronounced vacuolization. There are at severe renal lesions.

Brown-pigmented cylinders - is granular and epithelial cylinders, pigmented hemosiderin.

There are at glomerulopathy.

Fatty, fatty granular casts more or less densely covered with small fat droplets. There nephrotic syndrome.

Cylinders mostly hyaline necessary to distinguish them from similar formations mucous, so-called cylindroid.

Hematuria (red blood cell) - a pathological phenomenon, characterized by an excess (higher than normal) urinary excretion of red blood cells.

Red blood cells in urine may come from any portion of the urinary tract.

Being on microscopic examination of the urinary sediment after centrifugation of urine a red blood cell in the 10-12 field of view is not a pathology; finding at least a single red cell in each field of view - pathology.

Availability 2-3 erythrocytes in each field of view, or more than 1000 red blood cells in 1 ml of urine requires clarification of the pathological process nature.

Hematuria must be distinguished from hemoglobinuria, myoglobinuria, uroporfinuria, melaninuria.

Hemoglobinuria occurs in cases of massive hemolysis (hemolytic anemia, transfusion of incompatible blood).

Myoglobin appears in the urine in the decay of muscle tissue (crush syndrome, myocardial muscle with occlusion of a major artery, prolonged hyperthermia, especially in combination with cramps).

Uroporphyrin found in hemochromatosis; porphyrin melanin - with black cancer.

Urine can take a red color when taking certain foods (beetroot), drugs (phenolphthalein, Amidopyrine), with a large number of urate.

Depending on the intensity of excretion of red blood cells are distinguished microhematuria and gross hematuria.

When microhematuria number of red blood cells varies from individual to 10-100 in sight, and sometimes red blood cells under a microscope densely cover the entire field of view, but the color of the urine at the same time has not changed.

In gross hematuria red blood cells can not be under the microscope and counting the densely cover the entire field of view, and urine becomes the color of meat slops or becomes dark red.

Mechanism hematuria in various diseases of the kidneys and urinary tract are not the same.

1. Renal hematuria due to: a decrease in the negative charge of red blood cells of peripheral blood, damage (fragmentation) of red blood cells in patients with renal and generalized mikroapgiopatii, increased vascular permeability of glomerular capillaries and peritubular capillaries, reducing the electric charge of the basement membrane of glomerular capillaries, in hemorrhagic vasculitis, thrombocytopenia, hemophilia, overdose of anticoagulants reason hematuria- decrease clotting activity.
2. When urolithiasis occurrence of hematuria associated with damage to the mucosa of the ureter or bladder concrement, especially if it has an uneven surface.
3. In patients with tuberculosis, kidney tumors and bladder hematuria is caused by the destruction of tissues and damaged blood vessels in it.
4. urological pathology cause of hematuria can be venous hypertension.

In identifying the macro - or microscopic hematuria is necessary to decide whether it is renal (blood is released from the kidneys) or extrarenal (postrenal - blood mixed into the urine in the urinary tract).

Differential diagnosis of renal and extrarenal hematuria is conducted based on the following data:

1. When the glomerular (renal) hematuria more than 80% make up modified red blood cells, characterized by:
- Unequal size, -
Irregular shape.

- The presence of cytoplasmic inclusions, -
Deformation of the membrane,

- Low content or completely devoid of hemoglobin (red blood cells leached)
- And a small amount of red blood cells.

2. Nonglomerular hematuria is characterized by the prevalence (over 80%) of unchanged erythrocytes, characterized by:
- The correct form, -
The same size,

- Lack of fragmentation, and deformation of the membrane.

3. The mixed nature of hematuria can be observed in tuberculous lesions of the kidneys and urinary tract; hemorrhagic diathesis.
If a small quantity of erythrocytes (20-30 in the field of view) the amount of protein in the urine of more than 1 g / l, renal hematuria.

Conversely, when the amount of red blood cells with a substantial (50 to 100 field of view) the protein concentration is less than 1 g / l, no precipitate and cylinders, hematuria, most likely extrarenal.

Undoubted evidence of renal hematuria character is the presence in urinary sediment erythrocyte cylinders.

Since the cylinders are tubular molds urinary lumens, their presence indicates with certainty that the red blood cells derived from the kidneys.

Urine color:

- With renal hematuria is usually brownish-red,
- When extrarenal - bright red.

The presence of blood clots in the urine usually indicates that the blood comes from the bladder or pelvis.

Leucocytouria - selection with white blood cells in urine in excess of the norm.

Norma is considered the detection of no more than 3-4 in sight - men and women with 4-6 y indicative study of urinary sediment, with urine Nechiporenko study - to 2500 (according to some estimates, up to 4000 in 1 ml); and a sample Aleksander Addis-Kakowski - 4000000 to day.

Leucocytouria may be:

Small - 8-10; 20-40 in sight;

- Moderate - 50-100 in sight;

- Expressed - pyuria when leukocytes cover the entire field of view, or there are clusters. Piuria can be suspected even at the macroscopic study on diffuse clouding of urine or detect lumps and flakes, are not endangered by heating and adding a few drops of 10% acetic acid solution. This distinguishes turbidity, the turbidity caused by leukocytes associated with the presence of salts.

Urine contains a large number of white blood cells and bacteria, often has an alkaline reaction (as a result of bacterial fermentation, ammonia). Persistent leucocyturia with acidic urine suspected tuberculosis.

The treatment of any infectious leukocyturia may lead to errors in diagnosis and treatment strategy (in some cases, unjustified use of antibiotics).

Bacterial (infectious) leucocyturia common in microbial inflammation of the kidneys and urinary tract.

Bacteriuria - allocation of microbes in the urine in an amount of more than 1-105 in 1 ml (true bacteriuria). Normally, urine contained in the bladder, sterile. During urination pathogenic germs may enter from the lower end of the urethra, but their number is typically less than 1 1-104 ml (false bacteriuria).

In the presence of infection in the kidneys and other parts of the urinary tract bacteria entering the bladder and lingering there, multiply rapidly, as the urine is for them a good breeding ground.

Changes in urination rhythm.

Along with daily urine volume may vary urination frequency and distribution of urine during the day. In a number of kidney diseases, and certain disorders in the urinary tract observed prevalence of nocturnal urine on day - nocturia, while a healthy person the amount of daily urine output is 65-80% of the total daily urine. Reasons: renal blood supply, the development of BPH, renal disease (amyloidosis) and / or urinary tract (urethritis, cystitis).

Frequency urinary can be increased - thamuria - frequent urination. Causes: polyuria and / or irritation of the urinary tract (with the inflammation, the passage of small stones - "sand" and others.). And also can be reduced - ollacisuria.

The indicators of volume and composition of the blood changes

1. hypervolemia (renal dysfunction). Reasons: reduced glomerular filtration and / or an increase in tubular reabsorption.

2. Hypovolemia (renal origin). Reasons: as a rule, is the result of increasing the filtration and / or reduce the reabsorption.

3. azotemia (increased levels of non-protein nitrogen in the blood). Reason: violation of renal excretory function (glomerulonephritis, pyelonephritis, amyloidosis). More than half of urea nitrogen, about 25% - amino acid, the rest - of uric acid nitrogen (= 4%), creatine (= 5%), creatinine (= 2.5%) and other non-proteinaceous compound.

4. Hypoproteinemia (decreased protein level in the blood). Reason: violation of tubular reabsorption of albumin.

5. Dysproteinemia (disruption of the normal ratio of individual protein fractions in the blood - globulins, albumin). Reason: increased secretion of albumin in the urine.

6. Hyperlipoproteinemia. One of the most common causes - nephrotic syndrome.

7. Acidosis. Causes: loss of efficiency Acidogenesis, ammoniogeneza, ion exchange mechanism of Na + / K +, and excretion by the kidneys of compounds with "acidic" properties.
8. In various diseases of kidneys can develop as hyper (hypo) fosfatemia, hyper (hypo) potassium, hyper (hypo) natriemia, hyper (hypo) kaltsiemia, hyper (hypo) magniemia and other changes in the content of blood components.

Character is determined by the specific deviations of kidney disease and impaired filtration processes, reabsorption and secretion.

General nephrogenic syndrome

1. Arterial hypertension. The role of the kidney in the development of hypertension has been shown in experiments in dogs (narrowing of the renal artery) (Goldblatt, 1934). Then it turned out that the cause of hypertension is a special proteolytic enzyme renin, which is produced in the juxtaglomerular apparatus of the kidneys.

2. Violation of the coagulation - trombohemorragic syndrome. The kidneys play a role in blood clotting, especially fibrinolysis. The available human urine urokinase enzyme activating plasminogen. Formed this enzyme in the juxtaglomerular apparatus. It was shown that 94% of urokinase secreted into the blood, and only a small amount of urine comes in, so renal venous blood compared to the arterial has a higher fibrinolytic activity. In addition, data are available on the effect of the kidney to the process of blood coagulation due to the effect of some of the factors involved in blood coagulation.

Available currently few data on changes in blood coagulation and fibrinolysis in various kidney diseases show that acute and chronic glomerulonephritis, nephrotic syndrome and pyelonephritis increases of free heparin and also increase the time of fibrinolysis. Increased levels of free heparin in renal disease is associated with excessive production of its mast cells, release of heparin in violation of the affected kidney, slow inactivation of his kidney and heparinase antiheparine decrease in activity of the blood. Increasing the time of fibrinolysis and decreased fibrinolytic activity is probably due to reduced formation of urokinase in the juxtaglomerular apparatus and increase of antifibrinolytic activity of the blood. All this is of some importance in the development of hemorrhagic diathesis (nosebleeds, skin and intestinal hemorrhage).

3. Edema syndrome. When kidney disease often develop swelling. Pathogenesis of his rather complicated and consists of the interaction of different pathophysiological mechanisms. The main role is played by hypoproteinemia (reduction of protein concentration in serum), which develops due to the loss of protein in the urine. Hypoproteinemia accompanied by a decrease in oncotic pressure of blood plasma. This causes the liquid in the capillary filtration interstitium and edema formation. fluid transition from vascular causes a decrease in plasma volume, which in turn leads to increased secretion of aldosterone adrenal glands. Evolving hyperaldosteronism enhances sodium reabsorption in the ascending part of the direct tubule, which leads to sodium retention and increased plasma osmolarity. Increasing the osmotic pressure intravascular fluid activates the osmoregulation system; of the neurohypophysis in the blood to a greater number of antidiuretic hormone and collecting tubes enhanced reabsorption of water. Detained in body fluids due to the plasma oncotic pressure reduction is unable to stay in the bloodstream and re-enters the interstitium increasing swelling, and a decrease in intravascular volume is maintained.

Further, renal diseases increases vascular permeability. This is partly due to tissue hypoxia (as a result of anemia and reduction of blood volume) and the activation of proteolytic enzymes, as well as increased production of tissue acidosis with biologically active substances (histamine, serotonin,

bradykinin, prostaglandins). In glomerulonephritis there is a generalized damage to the capillaries, which also has a certain importance in the development of local edema (in the loose subcutaneous tissue of the face, under the eyes and so on. D.).

4. Anemia. The kidneys are one of the main bodies involved in the regulation of erythropoiesis. In animal experiments have shown that in the juxtaglomerular apparatus of the kidneys are formed erythropoietin influencing the proliferation and differentiation of bone marrow cells in the direction erythroblastic series. Fractionation kidney homogenates experimental animals succeeded in isolating two fractions, one of which stimulates a different inhibits erythropoiesis. In acute glomerulonephritis broken relationship factors regulating erythropoiesis - erythropoietin and erythropoiesis inhibitor towards increasing the latter activity. In chronic glomerulonephritis and chronic renal failure, reduced formation of erythropoietin. In addition, blood serum thus has an inhibiting effect on erythropoiesis. There is evidence that anemia in these diseases is associated

ith increased degradation of red blood cells. Haemolysis of erythrocytes is caused not only by the "hemolysing" factors in the blood plasma, and red blood cells is associated with impaired metabolism. Uremic intoxication and violation of protein metabolism also have a certain influence on the ability to regenerate bone marrow. Despite the absence of iron deficiency, a role in the pathogenesis of anemia in renal disease plays a violation of the synthesis of hemoglobin and watch at the same time the lack of the use of iron. All of the factors listed above are combined in the circuit of the pathogenesis of anemia in renal disease.

Types of renal disease

Currently there is no classification of renal disease, based on a unified approach. Various experts have developed and used the classification, readers, mostly morphological, etiology, pathogenesis, clinical and other criteria of differentiation nephropathy. However, in all classifications have focused on one or more attributes.

1. On the primary lesion of any structures (with the release of, for example, or glomerulopathy tubulopathy).
2. The causes of nephropathy.
3. On the mechanisms of development of nephropathy.
4. On the nature of the therapeutic effects ("surgical", "therapeutic" kidney disease), etc. Given these circumstances, considered below, and nephropathy are characterized by distinct groups of typical forms of renal disease with the obligatory indication of their origin and development mechanisms.

Types of renal pathology in origin

1. Primary (hereditary, congenital, genetically determined) forms of nephropathy.

- Anomalies of development of kidneys (the number, shape, macro and microstructure).
- Tubulopathy (mainly affecting the renal tubules: renal diabetes insipidus, renal Pseudohypoaldosteronism et al.).
- Enzimopaty tubular epithelium (eg, cystinuria, aminoaciduria).

- Nephropathy (kidney damage generalized).

2. Secondary (acquired, symptomatic) forms of nephropathy.

- Infectious origin - microbial, parasitic, fungal, protozoal (eg, nephritis, pyelonephritis, hydatid disease, kidney actinomycosis, nephrotic syndrome, renal failure).
- Immunoallergic genesis (nephritis, nephropathy and immunoallergic al.).

- Conditional direct renal damage factors of physical, chemical and biological nature (eg, trauma, radiation injuries; toxogenic, medicinal nephropathy).
- Related (satellite), nephropathy (in amyloidosis, endocrinopathy [for example, in diabetes], nephrolithiasis, renal migration, cardiovascular diseases [eg, atherosclerosis, hypertension] immunoaggression diseases [eg, SLE]).

- Tumor genesis.

Typical forms of renal disease

1. Nephritis

2. Pyelonephritis,

3. Nephrotic syndrome

4. Renal failure (acute and chronic) → Uremia → Renal coma,

5. Nephrolithiasis.

Characteristic of certain forms of kidney disease

For certain groups of kidney disease include nephritis (eg, acute post-streptococcal glomerulonephritis and nonstreptococcic, chronic glomerulonephritis, rapidly progressive glomerulonephritis), pyelonephritis, nephrotic syndrome, acute and chronic renal failure, nephrolithiasis.

NEPHRITIS

Nephritis - a group of diseases characterized by diffuse lesions kidney tissue inflammation and

/ or immunopathological origin, with involvement in the pathological process of all parts of the nephrons, interstitial tissue and blood vessels.

One of the most common forms of pathological processes in this category are glomerulonephritis.

Acute glomerulonephritis

Acute glomerulonephritis - a disease, as a rule, infectious-allergic or immunoaggression genesis.

Causes.

- Infectious agents: Streptococcus (often p-hemolytic streptococcus group A), pneumococcus, meningococcus, salmonella, pale treponema, viruses (causing hepatitis, infectious mononucleosis, smallpox, and others.), Plasmodium falciparum, Toxoplasma.

- Non-infectious factors. Autoaggressive most cases and / or cross-AT, complexes circulating in the blood Ar, Ig, complement factors, as well as foreign proteins (such as vaccines, serum or whole blood, proteins of tumor cells or damaged tissues).

Pathogenesis.

One of the most common form of glomerulonephritis - acute diffuse glomerulonephritis. The reason for it is the group A hemolytic streptococcus (strain 12).

- AT for Education Ar streptococcus.

- Impact on antistreptococcic AT streptococci (their destruction) and renal corpuscles structure (especially their membranes having Ar, Ar similar to hemolytic streptococcus).
- Protein denaturation appreciated in NBI system as foreign to the body.

- Direct damage to the structures of the nephron streptococcus toxins, leading to the formation of additional autoantigens.
- Development in response to the appearance in the blood of autoantibodies and autoantigens nephrotoxic lymphocytes. It potentiates kidney damage due to the development of immune reactions autoaggression, allergy, inflammation (in response to damage to renal tissue). This is evidenced by infiltration of kidney leukocytes (including lymphocytes) and macrophages, the presence of IgG, complement factor NW, Clq, C4 (detected by immunofluorescence) in the loops of capillaries in the kidney mesangial cells.
- The periodic activation immunoaggression process influenced by unspecific damaging - "permissive" (allergic reactions) - factors (for example, cooling the body intoxication, infection, getting into the blood protein-containing drugs, radiation). Thus formed immune complexes fixed on the glomerular basement membrane and microvascular, potentiating and expanding the scale of damage to the kidney tissue, making it diffuse (hence the name - "diffuse glomerulonephritis").

- Evidence of infectious genesis of acute diffuse glomerulonephritis (occurrence of disease following a streptococcal infection (sore throat, tonsillitis, pharyngitis, scarlet fever); detection in the body of foci of infection (in the tonsils, adenoids, the mucous membrane of the larynx and pharynx); blood detection antistreptococcic the AB; playback acute diffuse glomerulonephritis model in experimental animals by administering them to a mixture containing the killed culture hemolytic streptococcus and homogenized kidney tissue).
- Arguments immunoallergic presence and / or immunoaggression diffuse component of pathogenesis of acute glomerulonephritis (through the development of the disease 14-18 days after undergoing streptococcal infection (time required for the formation of AT, their complexes with Ar and mediators of allergy and their impact on glomerular membrane); detection of blood nephrotoxic autoantibodies, detection of non-specific "permissive" factors (cooling, intoxication, infection) detection in the walls glomerular capillaries complexes "a + aT + complement" (for example, by immunofluorescence reaction), experimental reproduction signs of disease after injection animals nephrotoxic serum).

Chronic diffuse glomerulonephritis

Chronic diffuse glomerulonephritis - one of the most common kidney diseases. In 10-20% of

patients it is the outcome of acute diffuse glomerulonephritis, and at 80-90% - the result of slow-

clinically poorly the manifested (hidden) course.

Causes.

1. Infectious agents (bacteria, viruses, and plasmodium al.).
2. Non-infectious factors.

- Endogenous (eg, Ag tumors [lung cancer, stomach, kidney), Ar, resulting from massive tissue damage (for example, burn disease, crush syndrome, tissue, etc.).
- Exogenous (e.g., lithium-containing drugs or gold, some antibiotics, non-narcotic analgesics, vaccines, serum, alcohol, organic solvents).

Pathogenesis.

- An initial factor - the development of AB to the causal agent and / or self antigens that appear when damaged kidney tissue.
- The formation of immune complexes «AG + AB + complement factors" and cytotoxic T lymphocytes.
- Effects of the immune complexes and T-lymphocytes to components of the basal membrane of cells, and renal cells and capillaries.
- Induction of inflammation and allergies.

- Potentiation immunoallergic reactions and inflammation. This leads to an increase in the degree and extent of damage of renal tissue, which makes the process a chronic, diffuse and potentially irreversible.

NEPHRITIC SYNDRONE

Nephritic syndrome is a typical pathological process, which is characterized by the following features:

1. hematuria

2. azotemia

3. hypertension

4. The tendency to kidney failure.

Acute nephritic syndrome:

1. Renal changes

Pat. anatomical aspects: inflammation of the kidney glomeruli and extra intracapillary type. Part of

the glomeruli is not functioning.

The pathophysiological aspects:

1. glomerular filtration ↓
2. tubular reabsorption of water ↑

3. tubular secretion ↓

4. The effective renal blood flow ↓

5. Since there is a disruption in the glomerular vessels, ↓ renal blood flow, so excited pressor kidney cycle and produces aldosterone (sodium retention, water). Depressor kidney cycle is inhibited.

2. urinary syndrome:

1. oliguria

2. baruria

3. selective proteinuria - albuminuria 1-2-2,5 g / l

4. cylindruria

5. Micro and macrohematuria

6. leucocyturia (10-25, etc.)

3. extrarenal changes:

1. hyperrvolemia

2. unexpressed azotemia (25-35-40 mg / dL)

3. eosinophilia

4. The protein in the low normal limits (60-80 g / l)
hypertension

5. edema - from unexpressed to hydrops

Mechanism edema - hypervolemia → ↑with aldosterone production in the tissues of ↑ sodium and ↑ osmotic pressure in the tissue → ↑ vascular permeability, since increased production of hyaluronidase, and other biologically active substances. Clinical outcome - more recovery, chronicity possible.

Chronic nephritic syndrome

1. renal changes

Pat. anatomical aspects: a gradual destruction of nephrons and their replacement by connective tissue. The number of nephrons is reduced - again the contracted kidney. The pathophysiological aspects:

- glomerular filtration ↓
- tubular reabsorption ↓ (epithelium decreases sensitivity to aldosterone and ADH occurs compensatory hypertrophy of the remaining nephrons → urine flows as if on one of the walls of the tubules)

- tubular secretion ↓

- effective renal blood flow ↓

- active pressor kidney loop. Depressor kidney cycle is inhibited.

2. urinary syndrome:

Stage 1 – renal failure - number of urine is normal, the proportion of 1024-1025
Stage 2 - chronic renal disease

- polyuria

- fluctuating gipostenuriya

- increased blood nitrogen (azotemia) - expanded tubular skylight **Stage 3**
– chronic renal failure - uremic (save 10% of existing nephrons)

- oliguria

- hypoisostenuria

urine

- A small proteinuria - 0,66g / l, 1.5 g / l in connection with violation of protein reabsorption
- cylindruria: hyaline, 2-3 in the stage of waxy, rarely – blood

- microhematuria

- leucocyturia (10-25, etc.) is not enough

3. extrarenal changes: -
hyperrvolemia

- severe azotemia –uremiya
- eosinophilia

- protein at low normal limits (60-80 g / l)
- hypertension

- overload heart failure
- swelling

Clinical outcome - peritoneal dialysis, "artificial kidney"

NEPHROTIC SYNDROME

Nephrotic syndrome - a condition that develops when the kidneys lesions of various origins, leading to defects in the glomerular capillaries. For nephrotic syndrome characterized by complex symptoms of nephrogenic: proteinuria (mainly albuminuria), hypoproteinemia (hypoalbuminemia), hyperlipoproteinemia, lipiduriya, edema. Some time ago, this state (nephrotic syndrome) was designated as nephrosis.

Causes

Generally, nephrotic syndrome - the final stage of the disease and pathological processes that lead to violations of glomerular filtration and tubular reabsorption of albumin, LP, ions, and other organic and inorganic substances.

1. kidney disease (primary nephrotic syndrome): acute and chronic glomerulonephritis (detected in 2/3 patients with nephrotic syndrome), glomerulosclerosis, lipoid nephrosis, membranous glomerulopathy.

2. extrarenal pathology (secondary nephrotic syndrome) chronic infections (eg osteomyelitis, tuberculosis, syphilis, malaria, viral hepatitis), destruction of the blood system (eg, lymphoma, leukemia, lymphoma), malignant neoplasms (bronchi, lung, stomach, colon ulcers, etc..), diabetes, diseases of the immune autoaggression (SLE, rheumatoid arthritis, scleroderma, vasculitis, and

others.), drug disease (eg, due to the use of drugs of gold, mercury, penicillin, X-ray contrast agents, antitoxins).

Pathogenesis

1. At the initial stage of development of nephrotic syndrome are the mechanisms that cause: - Damage to the membrane and glomerular cells (under the influence of the causal factor);

- Immunoallergic reaction (found in the blood increased content Ig, complement components, immune complexes, and the latter are determined in kidney tissue);

- Inflammation (in kidney tissue upset microcirculation, increases the permeability of the walls of microvessels, there is infiltration of leukocytes tissue proliferative processes develop).

2. The important pathogenetic links of nephrotic syndrome are: increased filtration barrier permeability, increased tubular reabsorption of proteins with its subsequent deterioration and activation of the LP synthesis by hepatocytes.

- Changes in protein reabsorption in the kidney tubules. Excess protein in the glomerular filtration combined with their increased reabsorption in the renal tubules. In chronic course, this leads to damage to the tubular epithelium, the development of degenerative changes in their processes and violation of reabsorption and secretion.

- Improving the permeability of the walls of the glomerular capillaries.
These filter changes and reabsorption lead to proteinuria.

The manifestations of nephrotic syndrome

The main manifestations of nephrotic syndrome are: hypoproteinemia (mainly due to hypoalbuminemia) and dislipoproteinemia, proteinuria, hyperlipoproteinemia, lipiduria, microscopic hematuria (usually membranous-proliferative disease nephron), edema, polyhypovitaminosis, hypercoagulation of blood proteins and thrombosis, reduced anti-infective resistance of the organism, anemia (microcytic, hypochromic), acidosis (secretory - kidney).

RENAL INSUFFICIENCY

Renal insufficiency - a syndrome that develops as a result of a significant reduction or termination of the excretory functions, as well as violations of other processes in the kidney.

For renal failure is characterized by a progressive increase in blood products of nitrogen metabolism (azotemia) and growing disorder organism.

Depending on the rate of occurrence and the development of further distinguish acute and chronic renal failure.

Acute renal failure

Acute renal failure occurs "suddenly" and progresses rapidly. This condition is potentially reversible. Often, however, acute renal failure leading to death of patients. Causes. There are prerenal, renal and postrenal causes of acute renal failure.

1. Prerenal. They cause a significant decrease in renal blood flow.

- The most frequent causes of prerenal acute renal failure: a massive blood loss, collapse, shock, congestive heart failure, renal artery thrombosis.
- The functions of the kidneys themselves under the influence of these causes in the initial stages of acute renal failure stored. However, they can not be realized mainly in connection with a significant decrease in blood flow to the kidneys. In terms of their effective hypoperfusion reduced glomerular filtration pressure and the products accumulate in the blood (including toxic), normally removed from the body, kidney involvement.

2. Renal. Factors of this kind have a direct damaging effect on renal tissue. These include:

- Necronephrosis. There is approximately 2/3 of the patients with acute renal failure. Often develops after kidney surgery.
- Acute significant local or total ischemia of the kidney.

- Nephrotoxic agents (eg, carbon tetrachloride, certain antibiotics, sulfonamides, organic solvents, cytostatics).
- Sharply current pathological processes affecting the kidney tissue: acute glomerulonephritis, vasculitis, pyelonephritis. Such conditions lead to acute renal failure in approximately 20% of patients.

3. postrenal. Lead to the violation (until the end) the outflow of urine for urinary tract. The most common are:

- Obturation of the urinary tract (kidney stones, tumors, foreign bodies [eg, long located in the ureteral catheters], blood clots, inflammatory edema).
- Compression of the urinary tract (eg, tumors of the abdominal organs, enlarged uterus, prostate adenoma tissue, ascites).
- Ureter inflection (for example, when migrating the kidney, its excess length).

Pathogenesis.

1. A significant and rapidly growing volume reduction in glomerular filtration.
Causes.
- Glomerular hypoperfusion resulting in ischemia of both kidneys prerenal origin (blood pressure is considered a critical level in the afferent arterioles of 40-60 mm Hg).

- Constriction of the renal arterioles, which develops due to hypotension and hypoperfusion of the kidneys.

- Microthrombi and / or aggregation of blood cells in the microvessels of kidney (at least the most recently observed in various types of shock, accompanied by the formation of excess blood coagulation factors).

2. The narrowing or obstruction of a large number of kidney tubules.
Causes.

- The accumulation of damaged cells in hydrophilic Ca2 +, edema and swelling of the epithelium. This reduces the lumen of the tubules.
- Closure of the lumen of the tubular cell detritus (due to damage and loss of epithelium) or cylinders composed of protein (with the development of inflammation and increase the glomerular filter permeability), myoglobin (in patients with muscle injuries), Hb (in patients with hemolysis of red blood cells).
3. Suppression of excretion and secretion processes in the epithelium of tubules nephrotoxic factors under the action (phosphorus preparations salts of heavy metals, phenols, arsenic compounds and

others.). The severity of acute renal failure is largely caused by the degree of alteration of the tubules and reduce glomerular filtration rate.

4. Additional (to the action of the above-mentioned mechanisms) damage to the glomeruli, tubules, interstitial tissue in connection with the development of inflammatory reactions and immunoallergic in response to the direct damage to these structures. This mechanism often results in a transition of acute renal failure in chronic.

Chronic renal failure

Chronic renal failure - a condition (syndrome) is caused by the increasing loss of life and significant decrease in the number of nephrons and is characterized by a significant, progressive (often irreversible) reduction in kidney function.

Typically, chronic renal failure, leads to the death of patients. The clinical manifestation of chronic renal failure begins with fewer nephrons to 30% of normal. Reducing their number to 15-10% accompanied by the development of uremia.

Causes.

As with acute renal failure, distinguish prerenal, renal and postrenal reasons.

- Prerenal: chronic hypertension, slowly progressive renal artery stenosis, bilateral renal artery embolism.
- Renal: chronic pathological processes in the kidney (such as glomerulonephritis, pyelonephritis, tubulointerstitial nephritis, polycystic, tubulopathy) and chronic pathology of other organs to warrant secondary renal disease (eg, diabetes, lupus, disproteinozy).

- Postrenal. Factors causing prolonged disturbance of outflow of urine (inside closing or squeezing the outside of the urinary tract).

Pathogenesis.

The pathogenesis of chronic renal failure is a progressive decline (until the end), glomerular filtration, tubular secretion and reabsorption. At the core of these processes is a progressive destruction of nephrons, their replacement by connective tissue (ie the development of nephrosclerosis). This leads to the increasing failure of kidney function. The final stage of chronic renal failure is uremia.

Uremia

Uremia - a syndrome comprising autointoxication organism products of metabolism (normal and impaired), "uremic toxins" and exogenous compounds normally excreted renally.

Causes.

The immediate cause of uremia is renal failure (acute or chronic).

The main factors of damage to tissues and organs in uremia and renal coma include:

- Intoxication organism excess ammonium compounds (ammonia, ammonium derivative) formed during the transformation of urea in the intestine.
- The toxic effect of the aromatic amino acid metabolic products: phenol, indole, skatole.

- Damage to these and other agents of cell membranes and enzymes. This is accompanied by a violation of the energy supply of cells.

- Increasing acidosis. It is the result of potentiation process of "accumulation of acid valences due to braking and atsido- ammoniogeneza, excretion of" acid "compounds kidneys, hemodynamic disorders (metabolic acidosis), and gas exchange in the lungs (respiratory acidosis).

- Imbalance in ion and fluid cells.

- Disorders electrogenesis in excitable cells, including brain and heart. This is the basis of loss of consciousness during coma, worsening disorders of the cardiovascular, respiratory and other physiological systems.

"Uremic toxins".

- Urea and its metabolism products, guanidine, aliphatic amines (such as dimethylamine).

- Parathyroid hormone. In chronic renal failure there is an excess of PTH, leading to the accumulation of Ca2 + ions in cells. And this, in turn, leads to dissociation of oxidation and phosphorylation, ATP deficiency disorders and energy-dependent processes.

- Inadequate concentration in blood, interstitial fluid, cells and microcells (Mg2 +, Zn2 +, Cu2 +, Cr2 +, etc.).

Uremia often ends renal coma. Like any other, renal coma is characterized by oppression and function of the nervous system is manifested by loss of consciousness, hypo- or areflexia, significant disorders of functions of organs and physiological systems of the body.

PRINCIPLES OF TREATMENT

Treatment of disorders of kidney function based on causal, pathogenetic and symptomatic principles.

Etiotropic. The aim is the elimination of (reduction in the degree of pathogenic action) causal factor. With this purpose, such as antibiotics, sulfonamides, and we treat other diseases caused by kidney disease.

Pathogenetic. It has the aim of breaking the pathogenesis of kidney diseases. To do this, use immunosuppressants, immunomodulators, anti-allergic drugs and carry out activities to "unload" the kidneys (hemodialysis, peritoneal, gastrointestinal dialysis).

The most effective way to eliminate toxic substances that accumulate in renal failure, dialysis is using a special device - the "artificial kidney" (hemodialyzer). The first such device used in the experiment! animal, was developed in 1913. In 1960, hemodialysis first used to treat patients with chronic renal failure.

Work "artificial kidney" apparatus based on the principle of the diffusion of blood into dialysate through special semi-permeable membrane of non-protein compounds. The use of "artificial kidney" to normalize a short time, a number of parameters of the body and relieve the patient's condition. However, hemodialysis is not a substitute for all renal function. In order to eliminate the radical pathology renal (kidney) transplant using a donor organ (kidney transplant).

Symptomatic. It is to eliminate (or facilitating) the secondary suffering and effects caused by kidney disease (anemia, edema, gastritis, enterocolitis, trombogemorragicheskih disorders, hypertension, and others.).

PATHOPHYSIOLOGY OF BLOOD

Blood system includes three components: the organs and tissues, which divide and mature blood cells - organs of blood formation (hematopoiesis); organs and tissues in which blood cells are destroyed – haemolysis organs (hemodieresis); the so-called peripheral blood: its circulating and deposited (in the organs and tissues) fraction.

Numerous forms of pathology and reactive changes in the blood system can be conditionally combined into five groups.

Typical forms of pathology and reactive changes in the blood system

1. Typical forms of disease and reactive changes in total plasma and the ratio of blood cells.
2. Typical forms of pathology and reactive changes in red blood cell system.
3. Typical forms of pathology and reactive changes in the platelet system.
4. Typical forms of pathology and reactive changes in leukocyte system.
5. Standard forms of pathology of coagulation, anticoagulation and fibrinolytic systems of blood (hemostasis disorders).

Typical forms of pathology and reactive changes of total, the ratio of plasma and blood corpuscles

The blood volume in adult humans is 6 - 8% by volume of the body, i.e. an average of about 5 liters. Thus 3.5 - 4 liters circulates in the bloodstream (circulating blood fraction), and 1.5 - 2 liters deposited in blood vessels of the abdominal cavity, lungs, subcutaneous tissue, and other tissues (deposited fraction). Shaped elements constitute 36 - 48% of the total volume of blood (hematocrit or hematocrit, - the ratio of the volume of blood cells to plasma volume).

In various pathological processes, diseases and disease conditions may vary as the total blood volume, and the ratio of its formed elements and plasma. In this case there are three main groups of typical forms of violations.

Normovolemia.

Normovolemia - conditions characterized by normal total blood volume, combined with decreased or increased Ht.

Oligocytemic normovolemia

Oligocytemic normovolemia - condition with normal total volume of blood in reducing the number of its formed elements (mainly red blood cells), accompanied by a drop below normal hematocrit values.

The main reasons:

- The massive hemolysis (eg, the formation of antierythrocyte Ig; action hemolytic substances - snake venom, lead compounds, arsenic, phenylhydrazide, etc.).

- Prolonged and pronounced inhibition of hematopoiesis, mainly erythropoiesis (for example, aplastic anemia).
- Conditions after acute blood loss. In this case, the total blood volume to normal relatively quickly as a result of transport fluid from the tissues into the bloodstream, and the number of blood cells is still reduced.

Manifestations:

- Anemia (due to reduced number of red blood cells), and as a consequence - hemic hypoxia.

- Thrombocytopenia (blood loss or immune reactions against autoaggression platelets).

- Reduced blood clotting, combined often with hemorrhagic syndrome.

- Leukopenia to warrant reduction of anti resistance.

- Reducing blood viscosity. Observed under conditions of recovery volume of the liquid part of blood with a significant decrease in the number of its formed elements (eg during hidremic compensation in acute blood loss).

Polycythemic normovolemia

Polycythemic normovolemia - a condition characterized by normal total volume of blood by increasing the number of its formed elements, which is accompanied by an increase in Ht above normal.

The most common reasons:

- Infusion patients fractions of blood cells (erythrocyte, leukocyte or platelet).

- Chronic hypoxia (polycythemia is due to the activation of erythropoiesis);

- erythema.

Manifestations:

- The increase of blood viscosity.
- Development of thrombotic syndrome.

- microcirculation disorders (slowing of blood flow in microvessels, stasis), which cause reduction of transcapillary exchange in tissues.
- Hypertension (eg, due to an increase in cardiac output).

Hypervolemia

Hypervolemia - conditions characterized by an increase in total blood volume and usually change Ht. Distinguish normocythemic, oligocythemic and polycythemic hypervolemia.

Normocythemic hypervolemia

Normocythemic hypervolemia (simple) - a condition manifested by an equivalent increase in the volume of formed elements and the liquid part of the volume circulating of blood. Ht thus remains within the normal range.

The main reasons: a large volume of blood transfusion, acute hypoxic state, accompanied by the ejection of blood from her custody, as well as significant physical activity, leading to hypoxia.

Oligocytemic hypervolemia

Oligocytemic hypervolemia (polyplasmia, hemodilution) - a condition characterized by an increase in total blood volume due to the increase of its liquid part. Ht index with below normal.

The main reasons:

- Excessive intake of fluid at a pathological thirst (for example, in patients with diabetes) and the introduction into the bloodstream of a large number of plasma expanders or blood plasma.
- Reduced excretion of body fluids as a result of failure of the excretory function of the kidney (eg, renal failure), overproduction of ADH hyperosmolatic plasma.

Polycythemic hypervolemia

Polycythemic hypervolemia - a condition manifested by an increase in total blood volume due to the preferential increase in the number of its formed elements. Therefore Ht exceeds the upper limit of normal.

The main reasons:

- Polycythemia (erythrocytosis) - a group of pathological conditions characterized by an increase in the number of erythrocytes (regardless of the number of white blood cells, platelets).
- Polycythemia vera (polycythemia vera, a disease Vaquez) - chronic leukemia with a lesion at the level of progenitor cells with characteristic myelopoietic unlimited proliferation of tumor cells retained the ability to differentiate four germs, especially the red. Erythremia accompanied by significant erythrocytosis and as a consequence - increased Ht.
- Chronic hypoxia of any type (hemic, respiratory, circulatory, tissue, etc.).

Polycythemia reflects hyperregeneratic state bone marrow, which is accompanied by increased proliferation of blood cells, especially red blood cells, and release them into the bloodstream. Polycythemic hypervolemia revealed in chronic heart failure, alveolar hypoventilation,

lowering blood oxygen capacity and efficiency of biological oxidation, when exogenous (norms and hypobaric) hypoxia.

Symptoms:

- The increase in cardiac output. Is the result of compensatory hyperfunction of the heart due to increased blood volume. However, decompensated heart failure and development of cardiac output, it is usually reduced.

- Increased blood pressure. Due mainly to an increase in cardiac output, as well as the volume circulating of blood and the tone of resistance vessels.
- Increased blood viscosity.

- Elevated aggregation and agglutination of blood cells.

- Disseminated thrombosis.

- microcirculation disorders.

Hypovolemia

Hypovolemia - states characterized by a decrease in the total blood volume, and generally the ratio of its breach formed elements and plasma. Distinguish normocytemic, oligocytemic polycythemic and hypovolemia.

Normocythemic hypovolemia

Normocythemic hypovolemia - a condition manifested by a decrease in total blood volume while maintaining Ht within normal limits.

The most common reasons:

- Acute hemorrhage.

- state of shock, vasodilatory collapse.

In the latter two cases normocythemic hypovolemia is caused deposition of a large volume of blood in the venous (capacitive) vessels and a significant reduction in connection with the VCB.

Manifestation:

Determined by the nature of the reasons that caused it (blood loss, shock, collapse), as well as the inclusion of compensatory mechanisms aimed at addressing the acute hypoxia.

Oligocythemic hypovolemia

Oligocythemic hypovolemia - a condition characterized by a decrease in total blood volume with a primary decrease in the number of its formed elements. Ht with below normal.

The most common reasons:

- Conditions after acute blood loss (at that stage, when the transport fluid from the tissues and blood output deposited in the bloodstream has not eliminate hypovolemia, and delivery of blood cells from hematopoietic organs - deficiency of red blood cells).

- erythropenia as a result of massive hemolysis of erythrocytes (eg, burns a large area of the body when combined with the loss of hemolysis body liquid part of blood in connection with plasmorrhages) and suppression of erythropoiesis (for example, aplastic or aregeneration states).

Manifestation:

- Reduction measure blood oxygen capacity (as a result eritropenia).

- signs of hypoxia (for example, lowering blood oxygen, acidosis, decrease venous blood PO2, etc.).

- Disorders organ-tissues circulation and microcirculation of varying degrees caused by, among other factors, a decrease in BCC.

Polycythemic hypovolemia

Polycythemic hypovolemia - a condition in which the lowering of total blood volume in the organism caused mainly by the decrease in plasma volume. Indicator Ht In this state above the normal range.

The most common reasons:

- Conditions causing increased loss of body fluids: repeated vomiting (for example, pregnant or as a result of exogenous intoxication), prolonged diarrhea (eg, breach of membrane digestion, intestinal poisoning), polyuria (eg, renal failure), elevated and prolonged sweating (for example, in hot climates or in hot shops in the workplace) and extensive skin burns (accompanied plasmorrhages).

- condition that prevents adequate intake of fluids in the body (water " starvation "): lack of drinking water and the impossibility of drinking water (for example, as a result of muscle spasms of tetanus or rabies).

Manifestation:

- organ-tissues microcirculation disorders due to hypovolemia and polycythemia.

- Increased blood viscosity, aggregation of blood cells in the microvasculature of organs and tissues and disseminated microtrombosis.
- Signs underlying pathology causing polycythemic hypovolemia (e.g. shock, diabetes insipidus, renal failure, burns, etc.).

Anemia

Anemia a typical pathological process of red blood cell system, which is found in a variety of diseases and is characterized by three interrelated features:

- Decrease in the number of red blood cells and hemoglobin per unit volume of blood;
- Qualitative changes in the red blood cells and hemoglobin;

- Damaged organs and systems as a result of hypoxia hemic.

Methods of study of anemia,

1. Determination of the number of red blood cells in the unit. blood volume.

In healthy men the number of red blood cells is 4.5 - 5.5 x 10^{12} / l or 4.5 -5.5 ter / L,
1 tera (trillion) = 10^{12}.

Women - 4- 5 x 10^{12} / liter. - 4.5 -5.5 ter / l

2. Determination of the amount of hemoglobin.

In healthy men the amount of hemoglobin of 130-170 g / l; Women 120-150 g / l.

3. Determination of the color indicator is performed by the formula:
CI = Hb (g / l) x 0, 03 / RBC (ter / L)
The color indicator shows the hemoglobin content in one erythrocyte. In a healthy person for the men and women he is 0.9-1.1 cu.

4. The biochemical method (enzymatic).

5. Immunological.

6. Clinical.

7. The method of microscopy stained smears of human blood in the usual way and in his lifetime.
The usual way of painting involves 3 steps:
a) preparing a smear;

b) fixing a smear or a mixture of methyl alcohol Nikiforov (1: 1 ethyl alcohol and ether);
c) The color of the stroke acidic and basic dyes.

Intravital method comprises two phases:
a) preparing a smear;

b) fixing the smear is not present;
c) The color of the basic dyes.

Blood smear microscopy is necessary for the detection of pathological forms of erythrocytes - the presence in the peripheral blood erythrocytes and unusual forms of development. These include:

I. Degenerative forms:

1. Changes in the color of red blood cells:
- hypochromia (CP <0.9);

- hyperchromia (CPU> 1.1);
- anisochromia.

2. Changes in the value of red blood cells - anisocytosis:
- Microcytosis - dominated microcytes (diameter less than 6.7 microns)
- Macrocytosis - dominated macrocytes (diameter from 7.7 to 9.5 microns)

- Megalocytosis - among the various values of red blood cells have megalocytes (diameter greater than 9.5 microns)
3. Change the shape of red blood cells

- Poikilocytosis;

- Isopoikilocytosis.

4. The presence in the blood smear of unusual forms of development:
- Megaloblasts;
- Megalocytes; -
Erythroblasts.

Degenerative forms of evidence of damage phenomena in the erythrocyte system (more about anemia).

II. Regenerative form

1. Regenerative form with signs of immaturity of nuclear origin:
- Pronormocyte;

- Normocytes basophilic, polychromatic, oxyphilous;
- Erythrocytes with Jolly corpuscles;

- Red blood cells with rings Cape.

2. Regenerative form with signs of immaturity cytoplasmic origin:
- Polychromatic erythrocytes
- Reticulocytes.

Normally, polychromatic erythrocytes 2-10 ‰. Increasing polychromatic erythrocytes in the peripheral blood is called polichromasia.

Normally reticulocytes 0-6 ‰. Increased reticulocytes in peripheral blood called reticulocytosis.

Regenerative forms show the protective bone marrow response to the body's red blood cells decline in anemia

When reading the blood test should take into account the presence of degenerative and regenerative forms of red blood cells that helps diagnose and differentiate anemia.

Classification of anemia.

According to the etiology:

1. Acquired

2. Hereditary.

According to the pathogenesis (M.P. Konchalovsky)

1. After blood loss - posthemorrhagic.

2. As a result of the destruction (hemolysis) of red blood cells - haemolytic.

3. As a result of violations of the formation of red blood cells.

By taking into account the pathogenesis of the main etiological factors (G.A.Alekseev):

1. hemorrhagic:

a) sharp (cause - acute blood loss);
b) chronic (reason - chronic blood loss).

2. Hemolytic:

a) with intravascular hemolysis (acquired);

b) with extravascular hemolysis (hereditary)

3. From the insufficient formation of red blood cells:

a) the functional bone marrow failure (iron deficiency, B12, folic acid, protein deficiency, eritropoetin deficiency);
b) mielotoxic - from depressed bone marrow toxicity (cause - exogenous and endogenous intoxication);
c) hypo-and aplastic anemia - bone marrow from the devastation causes (hereditary and acquired)

g) metaplastic (by substitution of foreign bone marrow tissue); reasons - leukemia, cancer metastasis to the bone marrow, etc.

According to the type of hematopoiesis.

1. Anemia with erythroblastic type hematopoiesis.

2. Anemia with megaloblastic type of blood formation.

On a functional state of the bone marrow (number of reticulocytes in peripheral blood).

1. Aregenerative anemia - bone marrow function is not available (reticulocytes: 2 -10 ‰ or <2 ‰).

2. Hyporegenerative anemia - insufficient bone marrow function (reticulocytes to 20 ‰).

3. Regenerative anemia - with sufficiently severe bone marrow function (reticulocytes -> 20 ‰ to 100 ‰).

4. Hyperregenerative anemia - anemia with overly pronounced bone marrow function (reticulocytes 100 ‰ and more).

Disregenerative anemia (anemia with megaloblastic type of blood formation). Relapse - no reticulocytes (representatives erythroblastic type hematopoiesis), there megalocytes, megaloblasts. Remission - appear reticulocytes (erythroblastic type hematopoiesis) -> 10 to 20% of may be megalocytes in a small amount.

According to the color index (a healthy person CI = 0.9-1.1)

1. normochromic anemia (CI = 0.9-1.1)

2. hypochromic anemia (CI <0.9)

3. hyperchromic anemia (CI> 1.1)

In most cases, accompanied by anemia and erythropenia. The exceptions are some iron deficiency and thalassemia, when the number of red blood cells may be normal or even increased.

It should be distinguished from anemias polyplasmia - condition caused by an increase in the liquid portion of blood (hemodilution) for a total content of normal hemoglobin in the body and erythrocytes. hemoglobin concentration per unit volume of blood thus reduced, which provides a formal pattern anemia. However, in this case one speaks of "false" anemia, because the total amount of hemoglobin in the blood is not reduced. "False" anemia observed in particular when large amounts of fluid infusion, blood plasma or serum. On the other hand, when the dehydration of patients with anemia (vomiting, diarrhea, intense and / or prolonged perspiration without replenish the lost volume of liquid) can be marked "thickening" of blood (hemoconcentration), wherein in one of its volume amount of hemoglobin may be normal or even increased despite reducing its total content in the body. Given these facts, it is necessary to conduct a thorough differential diagnosis, which will provide an opportunity to undertake a focused etiological and (or) the pathogenetic therapy of these conditions.

Anemia is often a symptom of some other disease, disease process or condition. Therefore strict nosological or pathogenetic classification (based on the underlying disease) absent anemia. However, there are common features that allow differentiation of anemia for a number of qualitative and quantitative criteria.

From a practical point of view, the basic and essential sign of anemia is to reduce the hemoglobin content per unit volume of blood. It follows that the essence of anemia and its importance for the organism is determined primarily by a decrease in the oxygen capacity of the blood, leading to hypoxia hematic type. It is associated with hypoxia main clinical symptoms and disorders of life in patients with anemia.

Hemolytic anemia

Hemolytic anemia (HA) are the result of the predominance of the intensity of the process of red blood cell hemolysis over their products. Erythrocyte life expectancy therefore reduced and no more than 90-100 days.

By HA origin are divided into secondary (acquired) and primary (hereditary or congenital).

Types of hemolytic anemias

1. Acquired (secondary)

2. Hereditary or congenital (primary):

1) due to membranopathy:
a) proteindependent:

- Microspherocytosis,

- Elliptocytosis (ovalocytosis) -
Stomathocytosis,

- Pyro poikilocytosis,

- Disease of «Rh-zero";

b) lipidodependent - acanthocytosis;

2) due to fermentopathy:
a) glycolysis,

b) the pentose phosphate shunt,

c) the glutathione system;

3) due to hemoglobinopathies:
a) in thalassemia,

b) with anemia in violation of the primary structure of globin chains (sickle cell, and others.).

Acquired hemolytic anemia

Causes. The reasons are various acquired HA agents of physical, chemical and biological nature.

Among the factors of a physical nature is of great importance mechanical damage of red blood cells: in patients with artificial heart valves, vascular prostheses or multiple underwent surgery and the use of cardiopulmonary bypass; at long crosswalks or running on hard ground ("march" hemoglobinuria due to intravascular hemolysis caused by injuries to their feet in the capillaries); with prolonged spasm of the small arterioles or thrombus formation in them (erythrocytes while injured, their plasma membrane is fragmented due to the compression of the cells or "cutting" them fibrin strands). Additionally, hemolysis may occur when exposed to high temperature (for burns), or with a significant reduction of the osmotic pressure of blood (for example, when a large volume of erroneous administration hypnotonic liquid, in particular distilled water).

Among the chemical factors haemolysis of red blood cells are the so-called "hemolytic poisons" - lead compounds, copper, arsenic, phosphorus, phenylhydrazine, nitrobenzene, certain medications that contain nitrites, sulfonamides, phenacetin.

Most hemolytic agent is a biological (plant, microbial or animal) origin: mushroom, snake, bee venoms; endo - and exotoxins of bacteria (hemolytic streptococci, staphylococci, anaerobic microbes); parasites metabolic products (Plasmodium falciparum, Leishmania); protivoeritrotsitarnye antibodies (autoantibodies, antibodies produced by transfusion of incompatible blood, antibodies with Rh-conflict mother and fetus). Cause hemolysis of erythrocyte deficiency may also be "membrane stabilizing" factors, such as vitamin E.

Among all causes acquired GA largest share of anemia associated with exposure to erythrocytes of autoantibodies. Autoimmune aggression may be exposed as a mature red blood cells of peripheral blood and erythrocyte germ cells in the bone marrow. The basis of the formation of autoantibodies against their own red blood cells may lie unaltered removal of immune tolerance. One of the main reasons is a violation of the ratio of lymphocyte pools. In particular, the lack or functional deficiency of T or B suppressor can remove the "veto" for production of autoantibodies or T cell-killers acting against its own erythrocytes.

Pathogenesis. The action sets the hemolytic factors of different origin mechanism of lysis of erythrocytes is disorganization phospholipid-protein structure of the membrane. The scale of damage it can vary over a wide range - from the micro-breaks to the decomposition of complex molecules and formation of pores. In the latter two cases, the semipermeable disrupted cell loses biomembranes and potassium cations, phosphate compounds, micro- and macromolecular organic materials, including enzymes. In the cell of sodium ions enter and calcium. In addition, it hyaloplasm out various ions, previously found in organelles: the mitochondria, sarcoplasmic reticulum. Increasing the intracellular concentration of fine organic compounds that accumulate as a result of violations of the metabolism of carbohydrates, proteins, lipids. This is accompanied by an increase in osmotic pressure within the erythrocyte. The cell directs the fluid, which also contributes to its damage plasmolemma. Red blood cells hyperhydrogenate, swell, lose their discoid shape and become round (spherocytes) and destroyed a large hydration in the lumen of blood vessels. Cells have less hydrated reduced elasticity of the cell membrane and its ability to deform. These erythrocytes are damaged or destroyed during passage through the capillaries of the tissues, the spleen and liver sinuses, exposed from the damaging effects of macrophages. Most of the hemoglobin is transformed into bilirubin, which circulates in the blood, into the tissue, and is excreted in the feces and urine, which manifests the development of hemolytic jaundice with its characteristic features disorders of physiological systems of the body.

Clinical picture of acquired hemolytic anemia

1. Current acute.
2. The obligatory picture of the disease hemolytic jaundice type (no bilirubin in urine, many urobilin in the blood and urine).
3. The blood is determined by the free hemoglobin.
4. Maybe hemoglobinuria (dark urine).
5. There renal hemosiderosis.
6. The liver and spleen are increased slightly, but painful.

Blood picture with acquired hemolytic anemia.

<u>Degenerative forms of red blood cells.</u>

1) normochromia, hypochromia;

2) Anisocytosis - macrocytosis (red blood cells);

3) poikilocytosis, spherocytosis (microcytosis);

4) can be isolated erythroblasts.

Regenerative form erythrocytes.

1. "nuclear": pronormotsity, normocytes - basophilic, polychromatic, oxyphilous; erythrocytes with Jolly corpuscles. Oxyphilous normocytes - 3-5 in sight, the same can be erythrocytes with Jolly corpuscles.

2. "cytoplasmic":
1) polihromasia -> 100 ‰ (up to 400-500 ‰)
2) Reticulocytosis -> 100 ‰.
Leukocytosis with a left shift.

Conclusion:

1) The etiology - acquired,
2) in the pathogenesis mainly with intravascular hemolysis,

3) the type of blood formation - with erythroblastic type of blood,

4) in the bone marrow - giperregeneratornaya,

5) on the color indicator - hyperchromic (free hemoglobin in the blood plasma).

Principles of therapy:

1. Causal therapy (removal of the causes, treatment of the underlying disease).
2. Pathogenetic therapy:

a) strengthening of erythrocyte membranes (donators of SH-groups, antioxidants, glucocorticoids)

b) immunosuppressants (to suppress immune processes).

c) blood transfusions (sometimes replace).

Hereditary hemolytic anemia

Hemolysis in hereditary HA due to a genetically programmed partial or combined defect:

1. Erythrocytopathia:

1) the structure of erythrocyte membranes (membranopathia),
2) their enzymes (fermentopathia),
2. Defect the hemoglobin molecule (hemoglobinopathia).

Hereditary HA, developing as a result of membranopathy. They are characterized by violation of the protein-lipid structure of erythrocyte membranes.

Causes. The reason the majority of hereditary GA caused membranopathy, a genetic defect, passed from parents to offspring in an autosomal dominant or autosomal recessive mechanism.

Pathogenesis. For hereditary HA, developing due to a defect lipoprotein membrane structure, characterized by the predominance in them or abnormal proteins (proteindependent membranopathy), or abnormal lipids (lipiddependent membranopathy). The former include hereditary microspherocytosis, elliptocytosis (ovalocytosis) stomatocytosis, pyropoikilocytosis illness «Rh-zero"; to the second - hereditary acanthocytosis, HA, due to deficiency of lecithin-

cholesterol acyltransferase, or caused by violation of fatty acid composition of erythrocyte membrane lipids. In humans, the most widely used is the first group of "membrandependent" hereditary HA.

Hereditary proteindependent membranopathy. Microspherocytosis (disease Minkowski's - Shaffar) inherited in an autosomal dominant manner. Membranopathia due to a significant reduction in the protein content of spectrin, a violation of the binding of the latter with other membrane proteins. Furthermore, the structure of spectrin in patients with microspherocytosis changed. All this leads to increased permeability of the erythrocyte plasmolemma for sodium ions, and calcium excess accumulation of them, as well as fluid in hyaloplasm. Hyperhydrogenate red blood cells become spherical. These changes reduce the ductility of erythrocyte membranes and their ability to deform in microvessels. Passing through the splenic sinuses and between sinus space, spherical erythrocytes with decreased elasticity plasmolemma can not change its shape sufficiently (deformed). They lose a part of their surface and become spherocytes small size (microspherocytes). Furthermore, the lifespan microspherocytes significantly reduced. It is 8-15 days, ie, about 10 times shorter than that of normal erythrocytes.

Elliptocytosis (ovalocytosis) also inherited in an autosomal dominant manner. Patients exhibit oval erythrocytes, the number of which can reach 25 - 75% of the total erythrocytes. In ovalocytes no more fractions of membrane proteins including spectrin. This is accompanied by a decrease in the resistance of red blood cells (especially osmotic) and increase their autohemolisis.

Hereditary stomathocytosis is transmitted in an autosomal dominant mechanism. Red blood cells have a distinctive appearance: unpainted strip in the center of a red blood cell is surrounded by dyed lateral portions that resembles a mouth (from the Greek stoma - mouth.). Development stomathocytosis also associated with conformational changes of proteins and as a result of lipoprotein complexes of erythrocyte membranes.

Hereditary lipiddependent membranopathy. Usually transmitted in an autosomal recessive mechanism. This is combined with a change in shape of red blood cells. In particular, they may have a toothed contour similar to the acanthus leaves (hereditary acanthocytosis) or target shape - a darker center and the periphery of the red blood cell with a light ring between them. The increased hemolysis of red blood cells and the development of HA are due to lowering their resistance to various factors (the change of osmotic pressure, temperature) and low deformability. This results in the reduction of red cell membranes of higher fatty acids, especially unsaturated phospholipids structure changes, significant accumulation of cholesterol on the surface of the cell membrane, disorders update membrane phospholipids.

Hereditary HA due fermentopathy. The **cause** of hereditary fermentdependent HA is a genetic defect that leads to shortages and (or) reduce the activity of erythrocyte enzymes involved in the process of energy supply. Defects are inherited by an autosomal recessive manner, or adhesion to the sex chromosomes.

Pathogenesis. To date, identified more than 20 different stages fermentdependent reactions in the metabolism of red blood cells, accompanied by their premature hemolysis. Most of these reactions are associated with glycolysis, the pentose phosphate cycle, systems and glutathione metabolism of adenine nucleotides. Most commonly defects found in the first three metabolic systems.

In humans, there are often hereditary defects in the activity of enzymes of glycolysis: pyruvate kinase, hexokinase, phosphofructokinase, 3-phosphoglycerate kinase. The red blood cells is almost the only significant by re-synthesis of ATP is glycolysis. The main share of the ATP energy is expended in them on the transport of ions and plastic processes. The lack of ATP energy leads to a violation of transmembrane ion transport. In connection with this imbalance develops them expressed in relation tackle various ions in the cells, and their content is within and erythrocytes. This is accompanied by swelling and overhydration, in connection with which this group HA with a large number of erythrocytes is usually increased size.

The most common genetic abnormality erythrocyte enzymes - reduction in the activity of enzymes of the pentose phosphate cycle. Last, along with glycolysis it is an important route of

metabolism of glucose in erythrocytes. In the course of its implementation is formed reduced form NADPH, which is used to restore glutathione. Reduced glutathione - a necessary component of erythrocyte antioxidant system. Hydrogen glutathione sulfhydryl group involving enzymes - peroxidases provides neutralizing organic and inorganic peroxides. In the course of these reactions is oxidized glutathione itself. Peroxides prevents the destruction of organic compounds involving membranes erythrocytes primarily by their lipid peroxidation reactions in free radical oxidation, accompanied by breach of unilateral destruction of permeability and membrane lipoprotein complexes.

The glutathione system deficit described three enzymes: gluconatesynthetase, glutathione reductase and glutathione peroxidase. These forms of disease are relatively rare. Anomalies enzymes glutathione systems are characterized by activation lipoperoxide reactions in erythrocytes, permeability and damage the integrity of their membranes.

Hereditary HA associated with the violation of the synthesis of the hemoglobin molecule. The molecules of hemoglobin healthy adult human are heterogeneous. The main ("standard") hemoglobin fraction indicated by the letter A (the first letter of the English word adult - adult). This fraction is about 95% of total hemoglobin. Approximately 3.5 - 4% is a fraction A2 and 1 - 1.5% - for hemoglobin F (the fetus from the word - the fruit). Each fraction consists of 574 amino acids constituting a polypeptide chain. The hemoglobin molecule consists of four polypeptide chains, which are denoted by the Greek letters: α, β, γ, δ. Hemoglobin A form two α- and two β-chains; A2 - a and 5 respectively; F - α and γ-chain. α-amino acid chains 141 are formed, and the other three -

146. Consequently, all types necessarily consist of hemoglobin α-chain and any other that is different from it in primary structure (arrangement of amino acids), and molecular weight. In this regard, the properties of various hemoglobin fractions are different from each other. In particular, hemoglobin F has greater stability in alkaline conditions and a greater affinity for oxygen than hemoglobin A last type, to some extent explains why the fetal tissue oxygenated greater than newborn and adult tissue.

HA may also be the result of hemoglobinopathies, most likely observed in thalassemia (hereditary anemias diserythropoietic under which disrupted the synthesis of globin individual targets), as well as anemia, due to changes in the primary structure of globin molecules.

When one of thalassemia globin chains synthesized in larger quantities and "unbalanced" its other chain (α, β, etc.). It precipitates and precipitates hyaloplasm erythrokaryocytes. This is accompanied by a violation of the synthesis of the required number of globin and formation of the hemoglobin molecule. These RBCs are less destroyed and life expectancy in the bone marrow and spleen (intracellular hemolysis).

In case the primary structure of the globin chains in connection with the replacement of one amino acid (usually glutamine) are broken to another physico-chemical properties of hemoglobin (in particular, the solubility, colloidal state), its conformation, increased ability to precipitate. This causes the change in shape and red blood cells (in particular, in sickle-cell anemia, they acquire S-shaped), a decrease in their resistance (such as hypoxia, a change in osmotic pressure of blood plasma), increased their destruction, shortening life expectancy. More questions about the etiology, pathogenesis and manifestations of this variety of anemias are analyzed in the section diserythropoietic anemia associated with violation of globin synthesis.

Typical clinical features of hereditary hemolytic anemia.

1. The course - a chronic, with exacerbations in the form of hemolytic crises.
2. The clinical picture is always present hemolytic jaundice (increase of indirect bilirubin in the blood, the absence - in the urine, the presence urobilinic bodies in blood and urine).
3. Free Hb blood there.
4. No renal hemosiderosis.
5. There hemosiderosis of the spleen and liver, and then a painless enlargement of the liver and spleen.

Typical blood picture with hereditary hemolytic anemia (during hemolytic crises).

Degenerative forms.

1. Normochromia, hypochromia.
2. Anisocytosis - microcytosis (spherocytosis).
3. poikilocytosis light:
4. Isopoikilocytosis - unidirectional change in the shape of red blood cells: codocyte, drepanocyte, spherocyte, ovalocytes etc.

Regenerative form.

"Nuclear": normocytes basophilic, polychromatic, oxyphilous, oxyphilous - 2-3 in sight; erythrocytes with Jolly calves - 2-3 in sight.

Cytoplasmic forms: polihromasia - 200-300 ‰

reticulocytosis - 300-400 ‰, it is possible and more significant reticulocytosis. Leukocytosis.

Principles of therapy:

1. The principle of causal therapy is not (a hereditary anemia).
2. Patogenetichechky principle - stabilization of the cell membrane (anti-oxidants, donator SH-gpypp).
In severe cases, surgical treatment - splenectomy (removal), up to date medical cause gel embolism plot splenic artery (preserved immune system).

Treatment for hemolytic anemia

Principles	Purpose	Methods and activities
A. Etiotropic treatment		
Eliminating (termination) causes of haemolysis of red blood cells	Decrease degree of hemolysis of red blood cells	1. Termination of the hemolytic factors of physical, chemical and biological nature 2. The introduction into the body of factors, the lack of which caused hemolysis (eg, riboflavin, glutathione, Flavinat)
B. Pathogenetic therapy		
I. Eliminating (reduction of power) erythropenia	Sequestration and prevent destruction of erythrocytes in the spleen, prolong the life of the erythrocytes	Splenectomy
II. Prevention (reducing power) hemosiderosis	To prevent (reduce the degree) damage to organs and tissues as a result of deposits in them an excess of iron (hemosiderin)	The use of "iron-binding" of drugs, substances that bring iron from the body (eg, desferola)
III. Eliminating (a decrease of) hypoxia	To prevent (reduce the degree) life of the organism disorders caused by the damaging action of hypoxia	1. Blood transfusions, RBC 2. Application antihypoxants 3. The use of antioxidants (such as vitamin E, C, dibunola)
IV. Correction of acid-	Eliminate the changes of	1. Blood transfusions, RBC

base status	acid-base status	2. Application antihypoxants 3. The use of antioxidants (such as vitamin E, C, dibunola) 4. Splenectomy 5. The introduction of "buffer" solutions

C. Symptomatic therapy

Eliminating (a decrease of) the consequences of hemolysis of red blood cells, hypoxia, hemosiderosis	Normalize the function of organs and tissue, disturbances which were caused by hemolysis of red blood cells, hemosiderosis	Correction of the cardiovascular system, kidneys, liver and other organs and tissues

Diserythropoietic anemia (DA)

Depending on the origin (or a strict nosological pathogenetic classification in this case is also difficult) diserythropoietic anemia can be divided into two main groups.

Types of anemia diserythropoietic

A. Conditional erythropoiesis violation in connection with primary damage of stem cells:

- Hypoplastic anemia.
- Aplastic anemia.

B. Conditional violation of erythropoiesis in connection with primary damage progenitor cells myelopoiesis and (or) erythropoietinsensitivity cells:

1. Due to the violation of the synthesis of nucleic acids erythrokaryocytes (megaloblastic):

a) vitamin B12 - and (or) folic acid deficiency anemia (pernicious, Addison-Birmera disease);
b) Vitamin B12 - and (or) folienondependent anemia.

3. As a result of violation of the synthesis of the theme:
a) iron-deficiency anemia;
b) porfirinodeficient (iron-refractory) anemia;

4. As a result of violations of globin synthesis:
- thalassemia;
- anemia caused by disturbance of the primary structure of globin chains;

4. As a result of violation of the regulation of division and maturation erythrokaryocytes.

Diserythropoietic anemia, developing as a result of the pre-emptive damage to stem cells

Etiology: etiology distinguish between hereditary and acquired aplastic anemia.

Causes of acquired aplastic anemia:

- Physical factors (ionizing radiation, overheating);

- Chemical:
- toxic - benzene, benzpyrene;
- cytostatic;

- toxic - allergic - sulfonamides, aminopyrine,

- Biological: hepatitis B virus, causative agents of brucellosis, typhoid fever, syphilis, sepsis. Causes of inherited aplastic anemia - mutagenic factors (physical, chemical, biological). **Pathogenesis** - is developing a devastating process in the bone marrow, resulting in the cell disappears semistem cell myelopoiesis that leads, ultimately, to the aplasia of germs:
- Erythroblastic (↓ Er.)

- Myeloblastic (decrease granular leukocytes)

- Megakarioblastic (platelets disappear)

- Monoblastic (decrease monocytes).

The process goes in stages:

Stage 1 - hypoplastic - these cells are gradually disappearing from the long bones, the bone marrow of flat bones are not affected.

Stage 2 - Aplastic - these progenitor cells disappear from the flat bones.

Stage 3 - panmieloftis ("consumption" of bone marrow) - progenitor cells disappeared from the tubular and flat bones. At the site of the bone marrow appear adipose tissue and large reticular cells.
Mechanisms of destruction semistem cell myelopoiesis.

- causal factors through germ cells, or hematopoietic cells through somatic mutations causing chromosomal (genomic, aberration and others.). This disturbed synthesis enzymes glucose-6-

phosphate dehydrogenase, resulting in cell membrane susceptibility to disturbance of the synthesis of enzymes involved in the assimilation of Fe and vitamin B12. These violations are transmitted 4th hemopoietic stem cells and its sprouts gradually die. Microenvironment impulses are not transmitted by the affected cells. Because colony stimulating factor (CSF) which is not formed, since stromal cells are transformed into fat cells. Perhaps initially defeated stromal cells, which reduces the production of CSF.

3. The second mechanism may be associated with autoimmune lesions semistem bone marrow cells.

Typical clinical features of hypo -, aplastic anemia.

1. adrift:

- Acquired - often chronic,
- Hereditary - sharp.

2) marked pancytopenia - reducing the amount of granular leukocytes, monocytes, platelets, red blood cells.
The clinical picture in the foreground anemia (weakness, paleness, dizziness). Complications in the form of neurotic tonsillitis, sepsis, a significant increase in body temperature, as well as the phenomenon of bleeding diathesis - bleeding, blood loss.

Blood picture with hypo -, aplastic anemia.

Degenerative forms of red blood cells.

3) Normochromia, hypochromia (when acquired anemia).
Normochromia, hyperchromia (for hereditary anemia).

4) Anisocytosis - macrocytosis, at least - Anisocytosis - microcytosis.

5) poikilocytosis not.
Regenerative form erythrocytes.

- Nuclear power - unit in preparation oxyphilous normocytes and erythrocytes with body Jolly.

- cytoplasmic form - in the first stage - polichromasia no, (2-6 ‰) reticulocytosis no (2-10 ‰).
In aplastic anemia 2nd stage of polychromatic erythrocytes no reticulocytes <2 ‰ or missing.
Thus, the data of anemia:

- Etiology can be acquired and hereditary;

- Pathogenesis - from a lack of red blood cell - hypo, aplastic (bone marrow depletion);
- By type of hematopoiesis - with erythroblastic type hematopoiesis;

- Bone marrow - aregenerative;

- A color indicator - normochromic, hypochromic, hyperchromic.

Principles of therapy.

- Causal - purchased for anemia - Treatment of the underlying disease.
- Pathogenic - blood transfusion (allogeneic - from relatives, syngeneic - from one of the twins), a bone marrow transplant.
For dentists it is important to:

- During the operation, and after the possible loss of blood.

- On examination of the oral cavity to draw attention to the presence of necrotic angina.

- The Permanent bleeding gums.

Diserythropoietic anemia, developing as a result of the pre-emptive damage to cells - precursors myelopoiesis and (or) erythropoietinsensitivity cells

These anemias are also among the syndromes which accompany other pathological processes and disease status.

Diserythropoietic anemia, developing as a result of violation of the synthesis of nucleic acids

A large group of hereditary, congenital and acquired anemias develops as a result of violation of the synthesis of DNA and RNA in nucleated cells erythrone.

With all these DA says the transition to pathological hematopoiesis, megaloblastic, type, and therefore they are called megaloblastic. In the bone marrow and blood along with normal cells appear megaloblasts and megalocytes.

Violation of the synthesis of nucleic acids, the transition to megaloblastic hematopoiesis and anemia are observed in hereditary and acquired deficiency of vitamin B12 and (or) folic acid, as well as in some hereditary diseases characterized by a decrease in enzyme activity, providing education coenzyme forms of folic acid (tetrahydrofolic), synthesis thymidine, uridine, orotic acid, and their incorporation into DNA.

Vitamin B12 deficiency anemia.

For the first time this kind of DA Addison described in 1849, and then in 1872 - Biermer, who called it "progressive pernicious" (fatal, malignant) anemia.

The **causes** of the development of this form of anemia can be divided into two groups:

- insufficient intake of vitamin B12 in the body with food;
- violation of the assimilation of vitamin B12 in the body.

Anemia arising for this reason, more severe, difficult to treat, it is in this connection referred to the form of megaloblastic DA called pernicious anemia, or Addison - Birmera.

Vitamin B12 (cyanocobalamin) is contained in animal products - meat, eggs, cheese, liver, milk, kidney. In these tissues, it is associated with the protein. When cooked, and stomach cyanocobalamin released from the protein (in this case - under the influence of proteolytic enzymes). In a free state Vitamin B12 forms a complex with the glycoprotein synthesized in the stomach and in this form is absorbed into the bloodstream. Lack of vitamin B12 in these foods, fasting or abstinence from animal food (vegetarian) often cause the development of vitamin B12 deficiency, megaloblastic DA. Vitamin B12 enters the body with food, at the suggestion of Kastla (1930) called the "external factor" of anemia.

Gastric parietal cells synthesize alkali-proof labile factor (it is referred to as "intrinsic factor" Kastla), which is a glycoprotein with a molecular mass of 50 000 - 60 000. The complex vitamin and glycoprotein binds to specific receptors on mucosal cells the middle and lower part of the ileum and then goes in blood. Minor amounts of vitamin B12 (about 1%) absorbed in the stomach without intrinsic factor. Stores of vitamin B12 in the body are large enough (about 2 - 5 mg). Basically, it is deposited in the liver. Because the body is derived from the daily excrement around 2 - 5 mg. In this

regard, a vitamin deficiency in a significant reduction of its receipt and (or) a developing uptake after 3 - 6 years.

Lack of vitamin B12 as a result of the violation and (or) reduce its absorption may be due to the reduction or termination of the synthesis of intrinsic factor; malabsorption complex "Vitamin B12 + glycoprotein" in the ileum; increased consumption of vitamin; "Competitive" the use of vitamin B12 in the gut microorganisms or parasites.

Pathogenesis. Lack of vitamin B12 results in violation of any origin nucleic acid synthesis in erythrokaryocytes and fatty acid metabolism in these cells and other tissues.

Vitamin B12 has two coenzyme forms: methyl-cobalamin and 5 deoxyadenosilcobalamin.

Methylcobalamin is involved in ensuring the normal erythroblastic, hematopoiesis.

Tetrahydrofolic acid, which is formed with the participation of methylcobalamin is needed for the synthesis of 5,10-metiltetrahydrofolic acid (coenzyme form of folate) involved in the formation of timidinfosfata. Last included in the DNA erythrokaryocytes and other rapidly dividing cells.

Lack thymidinephosphate, combined with the violation of uridine incorporation into DNA and orotic acid, causes a violation of the synthesis and structure of DNA, which leads to the breakdown of the processes of division and maturation of red blood cells. They increase in size (and megaloblasts megalocytes), in connection with which resemble erythrokaryocytes and megalocytes embryo. However, this similarity is only superficial. Red blood cells of the embryo to fully provide the oxygen transport function. Erythrocytes is formed in a vitamin B12 deficiency, megaloblastic result from abnormal erythropoiesis. They are characterized by a low mitotic activity and low

resistance, short life expectancy. Most of them (50%, normally about 20%) in the bone marrow is destroyed. In this regard, substantially reduced the number of erythrocytes in peripheral blood.

Manifestations. In the bone marrow revealed a greater or lesser amount megaloblasts (diameter over 15 microns) and megalokariocyte. Megaloblasts desynchronization characterized by ripening the nucleus and cytoplasm. The rapid formation of hemoglobin (in the megaloblasts) is combined with slow differentiation of the nucleus. These changes in erythrone cells combined with impaired differentiation of other cells, and myeloid series: megakaryoblasts, myelocytes, metamyelocytes, palochko- and segmented leukocytes are also increased in size, their nuclei are more delicate than normal, the structure of chromatin.

In peripheral blood erythrocyte count is significantly reduced, sometimes to -0.8 1012 0.7 / l. They are large - up to 10-12 microns, often oval, without a central illumination. As a rule, there are megaloblasts. In many red blood cells are found remnants of nuclear material (calf Jolly) and nucleolema (ring Kebota). Characterized Anisocytosis (dominated by macro and megalocytes) poikilocytosis, polychromatophilia, basophilic stippling of erythrocytes. Red blood cells are over-saturated hemoglobin. The color indicator is usually more than 1.1 - 1.3. However, the total hemoglobin content in blood significantly decreased (!) Due to a significant decrease in the number of erythrocytes. The number of reticulocytes usually reduced, at least - is normal. As a rule, there are leucopenia (by neutrophils), combined with the presence of giant macropolycyte and thrombocytopenia.

Due to increased hemolysis of erythrocytes (mainly in the bone marrow) develops bilirubinemia.

Significantly, vitamin B12 deficiency is usually accompanied by anemia and other vitamin deficiency symptoms: change in the gastrointestinal tract due to a violation of division (identified with atypical features mitosis) and cell maturation (presence megalocytes), especially at the mucosa. This is followed by the formation of glossitis and "polished" language (due to its atrophy papillae), stomatitis, gastroenterocolitis, exacerbating the anemia due to malabsorption of vitamin B12; neurological syndrome due to changes in developing neurons. These deviations largely result from metabolic disorders of higher fatty acids. The latter is due to the fact that the other metabolically active form of vitamin-B12-5-deoxyadenosilcobalamin (in addition to methylcobalamin) regulates the synthesis of fatty acid, succinic acid catalyzing the formation of methylmalonic. Deficiency 5 deoxyadenosilcobalamin causes a violation of the formation of myelin, has a direct damaging effect on the neurons of the brain and spinal cord (especially the rear and side of its pillars), which manifests itself mental disorders (delusions, hallucinations), signs funicular myelosis (staggering gait, paresthesia, pain, numbness and others.).

Folic acid deficiency anemia.

Folic acid - a complex compound. It consists of three components: glutamic acid, para-aminobenzoic acid and pteridine ring. folic acid compound (folates) are contained in large amounts in the liver, meat, yeast, spinach. However, when more than half of cooking it collapses. With a deficit of income in the body of its reserves are exhausted within 3 - 4 months. Folic acid is absorbed primarily in the upper small intestine.

Metabolically active (coenzyme) Folic acid is the form of tetrahydrofolic acid. Normally, the latter is required to regulate the formation of thymidine monophosphate, included in the structure of DNA, the synthesis of glutamic acid, purine and pyrimidine bases.

The **causes** of folic acid deficiency anemia (as well as vitamin B12-deficient) are divided into two groups: 1) causing failure of folic acid intake of food; 2) conditional on the assimilation of the violation of folic acid in the body and deliver its cells of hematopoietic tissue.

Pathogenesis. Deficiency of folic acid causes a violation of DNA synthesis and structure given that this acid in its metabolically active form - tetrahydrofolic acid in the form required for the synthesis of thymidine monophosphate, and the inclusion in a DNA molecule orotic acid and uridine. It is accompanied by a transition type normoblastic megaloblastic hematopoiesis on with all the ensuing consequences (see. The pathogenesis of vitamin B12-deficiency anemia).

Manifestations of this species diserythropoietic anemia are mostly the same as for vitamin

B12 deficiency. However, no gastroenterocolitic and neurological syndromes (caused by vitamin

B12 deficiency with low 5- deoxyadenosilcobalamin).

Concluding the discussion of the etiology, pathogenesis and manifestations of vitamin B12-and folic acid deficiency anemia, it must be emphasized that, as a rule, in different patients they develop in isolation and rarely - combination. In many ways, their pathogenesis is similar, but nevertheless has significant differences noted above. Therefore incorrect to equate these species megaloblastic anemia and designate it as a "vitamin B12 (folic acid) deficiency" anemia. This inaccuracy in the title and

classification in medical practice leads to the fact that patients with megaloblastic anemia often prescribe drugs simultaneously vitamin B12, and folic acid, although this is not necessary. In this regard, the top treatment should be preceded by careful differential diagnosis of these types of anemia.

Vitamin B12- and (or) folienondependent megaloblastic anemia.

Development of megaloblastic anemia is possible not only because of the deficit of vitamin B12 and (or) of folic acid, but also disorders resulting synthesis purine or pyrimidine bases needed for synthesis of nucleic acids.

The **cause** of anemia is usually inherited (usually recessive) violation of the activity of enzymes necessary for the synthesis of folic, orotic, adenyl, guanyl, and possibly some other acids.

The pathogenesis of the variety megaloblastic anemia is in violation of compounds involved in the biosynthesis of DNA, in particular timidinphosphate, uridinphosphate, orotic acid.

Diserythropoietic anemia, developing as a result of violation of the synthesis of heme

To this species include iron deficiency and DA porfirinodeficiency (iron refractory) anemia.

Iron deficiency anemia.

This is the most common anemia in humans. They account for about 2/3 of all varieties.

The **cause** of iron deficiency DA is excess loss of iron by the body in comparison with its receipt. This decreases the content of iron in the blood plasma, bone marrow and tissue depots.

In an adult weighing 70 kg contains 4 - 4.5 g of iron included mainly in the different proteins. The bulk of the iron (about 58%) in hemoglobin contained approximately 28% - muscle (composed of 21.9% and 68.1% of myoglobin - as ferritin), about 8% - in the liver as ferritin and hemosiderin. The remainder of the iron part of the enzyme molecules: cytochromes, catalases, glutathione peroxidases and others.

After the intestinal absorption (mainly in the duodenum and jejunum) iron enters the blood plasma where it binds to the protein - transferrin (β-globulin with a molecular weight of about 80,000 having two active sites, each of which connects one atom of trivalent iron). Transferrin delivers iron bone marrow erythrokaryocytes. This same protein transports iron to the bone marrow of parenchymal organs and macrophage cells. Iron is delivered to the mitochondria, where it connects with protoporphyrin and participates in the formation of heme.

In the body, there is also deposited iron. It is in the form of: 1) ferritin (water soluble ferric hydroxide complex, coupled with residual phosphoric acid and apoferritin protein). Ferritin has a normal plasma and in almost all cells of the body; 2) hemosiderin (iron-containing protein of a partially deproteinized and denatured ferritin) present in macrophages and Kupffer cells of the liver.

With food (Meat, apples, pomegranates, buckwheat, etc.) the body receives about 2 - 2.5 mg of iron per day. Deficit it develops when the iron losses exceed 2 mg / day. To this can cause the following reasons:

2) Reduction of intake of iron due to: 1) the total starvation or significant reduction in dietary foods containing iron; 2) disorders of iron absorption in the gastrointestinal tract (primarily in the duodenum and jejunum initial section). Of all types of iron compounds (bi-, trivalent) in the gastrointestinal tract is absorbed mostly ferrous iron, a part of the heme. Violation of this process develops in chronic gastritis, enteritis, gastric resection, and especially the small intestine.

 The increase in the loss and (or) consumption of iron organisms: 1) chronic, recurrent blood loss (gastric, intestinal, uterine, etc.), as well as hemorrhages, when a day lost more than 2 - 2.5 mg of iron;. 2) during pregnancy and the subsequent feeding of the child (lost during this period a total of 800 mg of iron), especially against the not yet manifested clinical iron deficiency.

These factors account for a substantial reduction of the iron content in the blood, macrophages, spleen, liver, lungs, and eventually - in the bone marrow.

Pathogenesis. Deficiency of iron in the blood cells of the body and the plasma causes a decrease in its content in the mitochondria of bone marrow erythrokaryocytes. It inhibits the synthesis of heme and its connection to the globin and therefore the formation of hemoglobin. Simultaneously, the synthesis is broken and other iron compounds in the erythrocyte (catalase, glutathione peroxidase) and in cells of parenchymatous organs (cytochrome, myoglobin, peroxidases, catalase, glutathione peroxidase). Lack of these enzymes in red blood cell reduction causes resistance to the damaging action of peroxide compounds, increased hemolysis, and shortening their life span.

Manifestations. The bone marrow is stored normoblastic type of blood, often (but not always) observed moderate hyperplasia of red sprout hematopoietic cells, increasing the number of basic and polychromatic erythrocytes with a decrease in the number of oxyphilous (a sign of maturation inhibition cells). Reduced maintenance sideroblasts - erythrokaryocytes with iron granules (about 20-40% of normal).

In the peripheral blood decreased number of red blood cells. Significantly reduced hemoglobin content (up to 30 - 40 g / l). Color index reduced to 0.6 or more. The number of reticulocytes is different from normal to reduced (anemia in chronic current) or increased (in the early stages of anemia). Characterized poikilocytosis, Anisocytosis (many microcytes), the existence of "shadow" of red blood cells (due to the reduced content of hemoglobin). iron levels in blood plasma is lowered (sideropenia) to 1.8 - 7.2 mol / l (at a rate of 12 - 30 mol / L).

Content leukocyte tends to decrease (by neutrophils), platelet count usually within normal limits.

With a significant deficiency of iron in the body there are a perversion of taste, muscle weakness, hair loss, brittle nails, cracked skin, atrophic gastritis, and others., As well as hemic and tissue hypoxia. In the latter case the development of hypoxia associated with dysfunction of the cells iron enzymes, especially cytochrome.

Porfirinodeficiency (iron refractory) anemia.

They develop a breach inclusion in heme iron (content in blood and plasma cells in connection with this increased). This type of anemia diserythropoetic is mainly due to decreased activity of the enzymes involved in the synthesis of porphyrins.

In the molecule of heme iron is associated with a form of the porphyrin - protoporphyrin. Porphyrins are synthesized in all cells of the body, but in the greatest amount - erythrokaryocytes in bone marrow and liver cells. Porphyrins are an essential component of iron-containing enzymes - catalase, peroxidases, cytochromes, and hemo and myoglobin.

By origin porfirinodeficiency DA divided into 1) hereditary (primary) and 2) acquired (secondary).

1. Hereditary DA due to shortage of porphyrins, first described in 1945 by Cooley.

The **reason** for them is an inherited recessive (is linked to the X chromosome and autosomes) violation of the synthesis of one or more enzymes involved in the formation of porphyrins.

Pathogenesis. Violations at any stage of the synthesis of protoporphyrin makes it impossible to iron binding and the formation of the heme molecule. In connection with this drop in red blood cells and hemoglobin content developed hypochromic anemia. In addition, excess iron accumulates in the tissues and blood plasma, leading to disruption of their function. The deposition of iron compounds in the liver tissue often causes the development of cirrhosis it, in the adrenal glands - their hormonal insufficiency, the pancreas - diabetes, in the testes - syndrome, etc.

A number of authors that form DA, characterized in violation of turn iron heme, an excess of it in the blood plasma and tissues, increase sideroblasts in the bone marrow, called iron refractory, sideroblastic or sideroahrestical (devoid of iron, from the Greek achrestos -. A useless, futile).

Manifestations. In the bone marrow revealed a large number of sideroblasts - erythrokaryocytes containing high amounts of iron pellets. These granules are usually ring surrounding a cell nucleus, mitochondrial cristae deposited between which normally occurs with the synthesis of heme iron and protoporphyrin. Characterized by an increase in the number of basophilic (ie, younger) erythrokaryocytes forms and reducing the amount of hemoglobinized.

In the peripheral blood of a moderately reduced content of red blood cells. hemoglobin decreases progressively and could reach 40 - 50 g / l. Color index is typically lower than 0.6. The number of reticulocytes, or normal or slightly reduced. Characterized Anisocytosis, poikilocytosis, target presence of red blood cells. Significantly (up to 80 - 100 mol / L) increased the content of serum iron.

3) Acquired DA, due to shortage of porphyrins. Most often **caused** by lead poisoning or deficiency of vitamin B6 (pyridoxine).

Pathogenesis. Lead poisoning their marked blockade sulfhydryl groups of enzymes protoporphyrins synthesis (in particular, dehydrogenases amino-levulinic acid, uroporphyrin decarboxylase gene hem synthetase) and as a consequence - heme.

At deficiency of vitamin B6 violated inclusion of iron present in the mitochondria eritrokarioblastov in the molecule heme and hemoglobin synthesis. In this regard, increased plasma cells and iron content of various organs.

Along with impaired heme synthesis often (especially when toxic lead compounds) globin synthesis rate decreases, especially the α-chain and the damaged membrane of erythrocytes. This is combined with depression of enzyme activity membranofixed K, Na-ATPase, resulting in the accumulation of sodium ions in the erythrocytes, their swelling and hemolysis. The lifespan of red blood cells at the same time significantly shortened.

Manifestations. When lead poisoning is usually observed changes in the blood system, and nervous system symptoms and gastrointestinal tract.

The marked increase in bone marrow proliferation activity erythrokaryocytes, increase their number. When painting on iron revealed a large number of its granules surrounding the nucleus eritrokarioblastov (these cells are called sideroblasts).

In the peripheral blood decreased number of red blood cells. They hypochromic, mishenevidnye with basophilic stippling cytoplasm (due to denaturation of the RNA). Reticulocyte count is usually higher than normal and can reach 30 - 80 ‰. The number of leukocytes and platelets usually does not differ from the normal range. The increased serum iron levels (60 - 80 mmol / l). It is also found in the cells of tissues, i.e. develop hemosiderosis. In urine significantly increased content of ALA, which is one of the most characteristic signs of lead poisoning (as a consequence of the blockade lead dehydrogenase aminolevulinic acid).

The defeat of the nervous system characterized by the development of encephalopathy (manifested by headache, memory loss, convulsions), polyneuritis (a disorder of movement and sensitivity), paresis.

Damage to the gastrointestinal tract is shown a sharp decrease in appetite, "lead colic" - cramping severe abdominal pain, constipation. X-ray examination revealed alternating areas of spasm and intestinal atony. On the gums, mainly front teeth visible narrow purple fringe, caused by the deposition of lead in the cells.

For vitamin B6 deficiency anemia is characterized by a slight in comparison with the rate of decline in the number of peripheral blood erythrocytes, expressed their hypochromia, Anisocytosis (macrocytosis) poikilocytosis, mishenevidnyh presence of single red blood cell. The increased serum iron content.

Diserythropoietic anemia, developing as a result of violations of globin synthesis

This group of anemia include:

thalassemia - anemia, decreased synthesis in which one of the two globin chains;

3. anemia caused by disturbance of the primary structure of globin chains.

Thalassemia

Thalassemia (from the Greek thalassa -. Sea + Greek haima -. Blood) - a large group of diseases.

The **cause** of thalassemia is a genetic defect inherited in most cases in an autosomal dominant, at least - recessive manner.

Pathogenesis. In most cases of thalassemia gene deletion is detected, determining a synthesis of globin chains. These genes are located in a pair of 11th chromosome (synthesis they encode α - chain) or 16 minutes (products encode β, γ- and δ - globin chains). Due to the fact that one of the globin chains synthesized in smaller amounts or not at all, disturbed balance rules for a regular two of its chains. "Unbalanced" (ie, not having pairs) chain aggregates and precipitates hyaloplasm erythrocytic nucleated bone marrow cell growth as well as reticulocytes and erythrocytes in peripheral blood. Nucleated erythroid cells containing the "unbalanced" aggregated chain break in the bone marrow and red blood cells and reticulocytes circulating in the blood, - in the spleen. Due to increased destruction of red blood cells anemia.

Anemia caused by disturbance of the primary structure of globin chains (haemoglobinopathies), are common clinical variant of DA.

The **reason** for this variety of anemias is the inheritance of a dominant or autosomal semidominant type mutated gene controlling the synthesis of the polypeptide chain of globin. In the case of the homozygous inheritance of developing clinically severe form of anemia, while heterozygous - easy or even non manifestation.

The most common anemia, developing as a result of the primary structure of globin disorders include sickle cell anemia, anemia caused by the presence of abnormal hemoglobins stable, anemia caused by abnormal synthesis of unstable hemoglobins.

Pathogenesis. Sickle cell disease is inherited in semidominant type and is the result of gene mutation resulting in substitution of glutamine to valine residue in the 6-position of N-end of the β-globin chain. Red blood cells containing the modified hemoglobin, have a form resembling the crescent. The phenomenon is caused by a decrease in hemoglobin camber solubility, who gave oxygen. In normal hemoglobin A deoxygenated, insoluble in 2-fold less than its oxiform. In sickle cell anemia, hemoglobin abnormal solubility decreases on the average by 100 times. He goes into a gel. Thus under light microscopy revealed an abnormal hemoglobin crystal size 1.5-1.8 microns.

Anemia, caused by the presence of abnormal hemoglobins.

Depending on the physicochemical state of hemoglobin, particularly high or low aggregation ability, it identified two types: volatile (composed of molecules in the erythrocyte aggregating) or stable (hemoglobin molecules do not aggregate or precipitate).

In the first case, the disease is inherited in a dominant mechanism and is caused by a single amino acid substitution in a molecule of the other globin. This leads to a disruption of communication with a globin gene, or α- and β-globin chains.

Stable abnormal hemoglobins are a consequence of their amino acid substitutions in the β-chain. The most common forms are stable hemoglobin C, D and E.

Diserythropoietic anemia is caused by dysregulation of division and maturation erythrokaryocytes

On the origin of species as mentioned anemia are hereditary or acquired.

Hereditary DA erythrokaryocytes **caused** by infringement of the fission process and often inherited in an autosomal recessive manner (sometimes in an autosomal dominant). In this case violated the regulation of division and maturation of bone marrow erythrokaryocytes.

Pathogenesis is defect mechanism to ensure the timely termination of the nuclear fission process hemoglobinised erythrokaryocytes. Characteristic of the normal state of "ban" on nuclear fission in the case of this type of anemia occurs.

Manifestations. In the bone marrow erythroid hyperplasia revealed significant growth. The erythroblasts morphological changes were detected. But of basophilic, polychromatic and oxyphilous erythroid cells there from 2 to 7-12 nuclei. Some of them are fragmented or destroyed completely. They are identified as megaloblasts megalocytes and a large number of nuclei. Many destroyed cells with signs karyorhexis. There is a decrease (by 25 - 50% compared with the norm) inclusion of iron in the red blood cells in its accumulation in the bone marrow, indicating that increased destruction of the bone marrow erythroid cells.

The recorded reduction of peripheral blood erythrocyte count (2 -3,5-1012 / l) and hemoglobin level (to 100 - 60 g / l). In this regard, this kind of anemia, usually normochromic. Number of reticulocytes at the upper limit of normal or increased to 12 - 18%. Characterized Anisocytosis (macrocytes a lot, and sometimes megalocytes), basophilic stippling red blood cells, the presence of fragmented cells. The content of white blood cells and platelets are usually normal.

The increased serum iron levels (60 - 70 mmol / l) and indirect bilirubin (a sign of increased hemolysis of erythrocytes).

Acquired DA associated with impaired erythrokaryocytes fission process, are obvious (the study of this issue continues), the result of a somatic mutation erythrokaryocytes. A number of patients are found division in the 20th pair of chromosomes erythrokaryocytes or extra chromosome in the 8th pair.

Pathogenesis completely unclear. It is assumed that somatic mutation causes a violation of the formation of the hemoglobin molecule, proliferation and maturation erythrokaryocytes. It is also possible depression mechanism to eliminate abnormal genes, ie, reparative DNA synthesis system.

Manifestations of acquired DA related with the violation of the division erythrokaryocytes, similar to those of hereditary Yes, but they are expressed to a much lesser extent. Furthermore, they are characterized by an increase in the quantity of bone marrow sideroblasts.

Treatment of anemia diserythropoietic

Methods of treatment of anemia diserythropoietic aimed at eliminating or termination of the causal factors that cause a violation of the proliferation and differentiation of cells erythrone gap pathogenetic mechanisms of development units anemic conditions, as well as the elimination of their consequences.

The principles, objectives and methods of treatment of anemia diserythropoietic

principles	purpose	Methods and activities
A. Etiotropic therapy		
Eliminating (termination) causes of the violation of division and maturation erythrokaryocytes	Eliminate (reduce the degree) violation of division and maturation erythrokaryocytes	1. The effects aimed at the termination of the factors causing hypo- and (or) bone marrow aplasia 2. Introduction into the organism "deficient" factors (vitamins B12, B6, folic acid, iron, enzyme synthesis of purines and pyrimidines, thiamine, uridine, etc.
B. Pathogenetic therapy		
I. Eliminating (reduction of power) hypoxia	To prevent (reduce the degree) life of the organism disorders caused by hypoxia	1. Application antihypoxants 2. The use of antioxidants (such as vitamin E, C, dibunola)
II. Предотвращение (уменьшение степени) гемосидероза	To prevent (reduce the degree) damage to organs and tissues as a result of deposition of excess iron in them (at porfirino deficient, iron refractory anemia)	
III. Correction of acid-base status	Eliminate the changes of acid-base status	1. Impact, aimed at correcting the function of the cardiovascular system, kidneys, liver and other organs and tissues 2. Introduction of "buffer" solutions
C. Symptomatic therapy		
Eliminating (a decrease	Normalize the function of	

of) the effects of hypoxia	organs and tissues, impaired hypoxia, hemosiderosis	

Blood loss

Blood loss - a condition that develops as a result of bleeding and leading to a more or less pronounced disorders of vital activity.

Etiology. Blood loss is a result of the bleeding - effusion of blood from blood vessels, and (or) the heart chambers to the external environment (external bleeding) or in the body cavity (inside, cavitary bleeding).

The presence of blood in the cavities of the body designated by special terms: hemothorax (accumulation of blood in the pleural cavity), hemoperikardium (pericardial), hemoperitoneum (abdominal), hemarthrosis (in the joint cavity), etc.

Bleeding should be distinguished from hemorrhage and hematoma. Under hemorrhage understand focal or diffuse impregnation of tissues (organs, subcutaneous tissue, muscle) blood under a hematoma - a local accumulation of blood, tissues limited. When hemorrhage and hematoma of the vascular bed beyond a relatively small volume of blood disorders and significant systemic circulation are not observed. Developing body disorders are mainly determined by the role of the organ or tissue in which there was bleeding or hematoma that formed (brain, liver, kidneys, muscles, subcutaneous tissue).

Cause bleeding may be:

- violation of the integrity of the walls of the blood vessels or heart. This may be the result of mechanical damage (trauma), purulent "melting" of the vessel wall tumor or its destruction due to the development of atherosclerosis, or break the atrial ventricular wall of the heart in myocardial and aneurysm etc .;
- a significant increase in the permeability of the vessel walls. The latter is often observed in the development of radiation sickness, gematosarkom, the presence of foci of extramedullary hematopoiesis in leukemia, certain infections (septicemia, typhus) or non-infectious (scurvy) processes;
- decrease in blood clotting (with the development of hemorrhagic diathesis).

The nature of the course and outcome of bleeding depends on the following conditions:

- characteristics of blood loss: a) the amount of blood lost. Out vasculature to 20 - 25% of circulating blood usually compensated and Low hazard due to the inclusion of emergency of adaptation mechanisms. Loss of 25 - 35% of circulating blood is associated with significant disorders of the central, organotissues and microcirculation. Loss of 50% or more of the total blood volume, particularly fast, is local; b) the rate of blood loss. The lower the rate of blood loss, the less pronounced disorders of vital activity. For example, the loss of even a half of the total volume of blood in a few days (with uterine, gastric, and other types of hemorrhoidal bleeding) generally does not lead to death; the ratio of activity of coagulation factors, anticoagulation and fibrinolytic systems of the body (decreased activity or content of coagulation factors and / or increasing the anticoagulant and fibrinolytic systems may lead to an increase in the speed and volume of blood loss, which contributes to its course and consequences); reactivity. Consequences of blood loss vary depending on gender (women are less "sensitive" for hemorrhage); age (adults suffer

blood loss more easily than children); "Current" state of the body (when overheating or cooling the body the effects of blood loss more severe than at the normal temperature, under deep anesthesia vital activity disorders are more pronounced than in the waking state); "Lessons learned" of the body (in particular, repeated loss of relatively small volumes of blood can increase the body's resistance to blood loss, ie, to provide "training effect").

Pathogenesis. At the initial stage of blood loss to a greater or lesser extent, decreased blood volume, while maintaining the normal hematocrit (developing "simple" hypovolemia). In this connection, reduced inflow of venous blood to the heart and its ejection stroke. This causes a drop in blood levels and as a consequence - the perfusion pressure in the blood vessels of organs and tissues. As a result of reduced transport of oxygen and metabolic substrates from the blood to the cells and from the latter - carbon dioxide and metabolic products. Develops kapillyarotroficheskaya failure, resulting in violation of turn energy supply of the cells, as well as the maintenance of plastic processes in them, disturbed the function of organs and tissues. It upsets the body's vital functions.

The main pathogenesis posthemorrhagic states.

Blood loss

↓

Reduced blood volume

↓

Reduction of venous blood flow to the heart

↓

Reducing the stroke volume of the heart

↓

Lowering blood pressure

↓

The decrease in perfusion pressure in the blood vessels of organs and tissues

↓

Violation microcirculation

↓

Upset transcapillary exchange of oxygen and carbon dioxide, the substrates and products of metabolism

↓

Hypoxia, acidosis, imbalance of ions in the cell and outside it

↓

Violation of energy and plastic to ensure the cells of organs and tissues

↓

Upset the body's vital functions (paralysis of the respiratory and vasomotor center)

↓

Death

Violation of systemic hemodynamics and reducing the intensity of biological oxidation in the cells are the inclusion of a signal or activation of adaptive mechanisms.

The main ones include the processes of activation of the hemostatic system; reaction cardiovascular compensation; increase blood volume by entering the blood vessels and lymph tissue fluid ("hidremic compensation"); recovery of the protein composition of blood ("protein compensation"); replenishment of the blood cell (cell, "bone marrow compensation"). Given that these mechanisms may be included at different times after hemorrhage, conventionally emit respective stage of the compensation process, "cardiovascular," "hidremic", "protein", "cell".

However, it should be understood that many processes are not sequentially (by stages), and in parallel, coinciding in time and usually potentiating each other.

From the first minutes after the start of bleeding is marked activation of the hemostatic reactions that raise the activity and concentration in blood plasma clotting factor. This increases the so-called haemostatic potential defect locations thrombosis of the vascular wall and reduce the intensity of or prevent bleeding.

Cardiovascular compensation of blood loss develops in the first few seconds after bleeding and is to stimulate the heart and increase cardiac output, mainly due to the increase in the frequency of its contraction (due to activation in conditions of hypoxia and reduction in cardiac output sympathoadrenal system). Simultaneously in different parts of the body varies arteriolar tone. Vessels such vital organs as the heart, brain dilate and blood flow in them increases. One of the main reasons for the decline arteriolar tone of these organs is rapid and significant accumulation of these vasoactive metabolites such as adenosine, prostacyclin, kinins. At the same time decrease in the ATP level, the activation of glycolysis, oxidation metabolites breach significantly alter the physical and chemical composition of these bodies, in particular in connection with the accumulation of hydrogen ions, the release of the potassium cations cells, the accumulation of oxidized products of metabolism. These changes also reduce arteriolar tone and increase blood supply to the heart and brain.

In parallel with this improved tone arterioles subcutaneous tissue, skin, kidney, abdominal organs (especially in connection with hypercatecholaminemia) and reduced blood flow in them. organotissues redistribution of blood flow described above is called "flow centralization phenomenon." Increased vascular tone in these organs and tissues and causes the release of deposited (not participated previously in circulation) of blood in the bloodstream and increase blood volume. At this stage, after the loss of blood is preserved normocytemic hypovolemia.

In the first hours after hemorrhage activated mechanisms for fluid flow from the tissues into the bloodstream. An initial factor "start" of these mechanisms is a reduction in circulating blood volume,

which activates the synthesis and incretion in the posterior hypothalamic nuclei factor that stimulates the production of aldosterone in the glomerular zone of the adrenal cortex. Increasing the level of aldosterone in the blood causes activation process reabsorption of sodium ions in the distal renal tubules and increasing therefore the osmotic pressure of blood plasma (said sequence of "events" is being volume reflex). Hyperospheresia blood "includes" osmoreflex: excitation osmoreceptors vascular activates neurosecretion antidiuretic hormone (ADH) in the hypothalamus and its transport to the pituitary back and forth - reaching the blood. ADH increases the permeability of the walls tubule fluid. The latter enters the blood capillaries by the osmotic pressure gradient (in connection with hypernatremia). This is the essence of "hidremic compensation" as a result of reduced blood loss of circulating blood volume. The latter also facilitates fluid flow from the cell into the extracellular space (along the gradient of osmotic pressure) into the lymph capillaries and further - into the blood. At this stage, there is the state of hemorrhagic oligocytemic normovolaemia or hypovolemia. Entering into the vascular tissue fluid is compared with the blood plasma of a lower content of proteins. This is followed by the activation of proteosynthesis in the liver, normalizing the level of protein in blood plasma, and the elimination of hypoproteinemia (protein compensation effects of blood loss). Activating proteosynthesis observed within a few hours after the bleeding and recorded over the next 1,5 - 3 weeks or more depending on the volume of blood loss and the state of reactivity.

Development in connection with blood loss hypoxia, which is mixed and is inherently hemic, circulatory and to some extent the respiratory (the latter develops due to the reduction of pulmonary perfusion volume), and the physical and chemical changes in the body stimulates the synthesis of substances that activate the proliferation bone marrow cells and lymphoid formations.

Primary importance among these substances is erythropoietin - sour, thermally stable, highly glycosylated protein with a molecular mass of about 34 kDa produced in various nephron cells, as well as in the liver and spleen. Erythropoietin stimulates proliferation, morphological and functional differentiation of erythroid cells. To detect the action of erythropoietin enough of its contact with

the surface of the target cell. Under the influence of erythropoietin erythropoetinsensitivity cells differentiate into erythroblasts and further - to the mature red blood cells, which go into the bloodstream and compensate for the lost cells when blood loss. In terms of blood loss also stimulated the proliferation, maturation and yield of hematopoietic tissue in the blood and other lymphocytic cells, myelocytic and platelet way hematopoietic (bone marrow compensation of blood loss).

Simultaneously with the above reactions are activated and compensatory mechanisms of adaptation to hypoxia, which are conventionally divided into urgent and long-term.

Types of blood loss.

Depending on the damaged vessel or heart card from which bleeding occurs, the lost volume of blood bleeding time after heart or vascular injury, hemorrhage blood loss place differentiated as follows.

Types of blood loss

I. In view of the damaged vessel or chamber of the heart:

5. Arterial,

6. Venous,

7. Capillary,

8. Mixed.

II. By the volume of blood lost:

3. Light (up to 20-25% of blood volume),
4. Average (25-35%),

5. Heavy (more than 35-40%).

- At the time of the onset of bleeding after heart injury or vessel: - Primary - bleeding starts immediately after injury;
- Secondary - dismissed the bleeding in time after the injury (in connection with the separation, lysis or destruction of a blood clot).

IV. In place of the outpouring of blood:

- External - bleeding into the environment;

- Internal (abdominal) - bleeding into the body cavity or organ.

Principles and methods for the treatment of blood loss.

All therapeutic interventions in haemorrhage are designed to stop bleeding and removal of the consequences of blood loss. Conventionally, these activities can be divided into three groups:

- designed to stop bleeding and removal of the causes of blood loss. These activities include methods of interim and final stop bleeding (by finger compression of the vessel and a tourniquet to vascular suture and prosthetic vascular), decreased vascular permeability (eg, using calcium supplements, as well as by the treatment of diseases and pathological conditions that caused increased permeability of the vessel walls: leukemia, gematosarkom, infectious diseases, scurvy, etc.), increase in blood clotting by blood transfusion or its components - formed elements, plasma, serum, coagulation factors;.
- with the aim of compensation amount of lost blood, stimulating hematopoiesis, the elimination of hypoxia, disorders of acid-base balance, protein and ion exchange;
- eliminate body waste disorder resulting from loss of blood.

The principles, objectives and methods of treatment for blood loss

Principles	Purpose	Methods and activities
A. Etiotropic therapy		
Elimination of causes blood loss	Stop blood loss or reduce its extent	1. Restore the integrity of the vessel wall and heart

		2. Increased blood clotting

B. Pathogenetic therapy

I. Restoring blood volume	Eliminate (reduce the degree) disorders of the central organ and tissue blood flow	Blood transfusion, plasma, plasma substituents
II. Normalization transcapillary exchange	Eliminate (reduce the degree) microcirculation disorders	The infusion of plasma substituents (eg, physiological sodium chloride solution, and others.)
III. Коррекция водного, белкового, ионного баланса	Eliminate (reduce the degree) changes of water, protein, ion balance	1. Blood transfusion, plasma, plasma substituents 2. The infusion of plasma substituents (eg, physiological sodium chloride solution, and others.) 3. Introduction of solutions containing proteins and ions in an amount and ratio of eliminating imbalance in the body
IV. Correction of acid-base status	Eliminate shifts acid-base status	1. Blood transfusion, plasma, plasma substituents 2. The infusion of plasma substituents (eg, physiological sodium chloride solution, and others.) 3. Maintain "buffer" solutions 4. Normalization (activate) the function of organs, compensating shifts the acid-base state

C. Symptomatic therapy

Clearing (a decrease of) the effects of blood loss and hypoxia	Normalize the function of organs and tissues, disturbed as a result of blood loss and hypoxia	Correction of cardiovascular function, respiratory system, kidneys, liver, etc..

Posthemorrhagic anemia

Posthemorrhagic anemia (PHA) develop as a result of a significant amount of blood loss.

Causes. The reason for the PHA is bleeding into the environment or in the body cavity (for more details in the "blood loss").

Pathogenesis. PHA leading pathogenetic link it is to decrease the total volume of blood, especially the circulating fraction, leading to hypoxia; shifts of acid-base, ion imbalance in cells and beyond.

Depending on the rate of blood loss secrete acute and chronic PHA.

Acute hemorrhagic anemia.

Etiology. The cause of acute post-hemorrhagic anemia (syndrome) is a disease - acute blood loss.

The **pathogenesis** of acute post-hemorrhagic anemia should be associated with the stages of compensation in case of acute blood loss.

In the first stage of cardiovascular compensation which lasts 1-3 hours after the blood loss, anemia laboratory is not determined, because there normocytemic hypovolemia.

In the second stage of compensation (hydremic) - its duration - 2-4 days - laboratory anemia can be defined as hypovolemia there first, and then normovolaemia oligocytemic.

According to this indicator, the color is a normochromic anemia, because red blood cells are the same as before the blood loss.

In the third stage of acute blood - bone marrow - anemia laboratory determined to 40-55 days depending on the size of blood loss. According to the color indicator, it is hypochromic, because in connection with the blood loss observed Fe deficiency.

By the 40th day restored the number of red blood cells in the unit. blood volume is restored to the 50-55 day white blood cell count, anemia liquidated. Mass recovered in circulating blood. There normovolemia oligocytemic first, then - normocytemic.

Blood picture in acute post-hemorrhagic anemia 9-10 days after acute blood loss (bone marrow stage).

Degenerative forms:

- normochromia (newly formed red blood cells)
- Anisocytosis (microcytosis - newly formed young red blood cells)
- poikilocytosis - Low to moderate, depending on the size of blood loss.

It reflects not only the violation of red blood cells function, but also the activation of the regeneration processes in the bone marrow (young forms).

Regenerative forms:

- Regenerative form with signs of immaturity of nuclear origin (nuclear): pronormocyte, normocytes basophilic, polychromatic normocytes, normocytes oxyphilous, erythrocytes with body Jolli;
- Regenerative form with signs of immaturity cytoplasmic nature (cytoplasmic)
- polichromasia - increasing the number of polychromatic erythrocytes from 40 to 60 ‰;
- reticulocytosis - increase in the number of reticulocytes from 20 to 100 ‰.

The blood picture is observed neutrophilic leukocytosis with a left shift.

Thus, acute hemorrhagic anemia

3. Acquired (after acute blood loss) - etiology
4. Pathogenesis - acute,
5. By type of hematopoiesis - type erythroblastic anemia with blood,
6. Bone marrow - regenerative,
7. The colored indicator - hypochromic.

Principles of therapy:

- Causal therapy - the fight against blood loss.
- Pathogenic - iron therapy.
- calorie diet, vitamin therapy.

Chronic hemorrhagic anemia

Etiology. The cause of chronic post-hemorrhagic anemia (CPHA) are chronic blood loss (women - uterine men - gastrointestinal, hemorrhoids, in the dental practice in chronic bleeding gums). The conditions for the emergence of CPHA are hemorrhagic diathesis, increased vascular permeability, the period of growth, lactation).

Pathogenesis. The total iron content is 4 g, of which 2.5 g of Fe-hemoglobin in the composition, 1.0 g of Fe-respiratory enzymes in the composition and myoglobin, 0.5 g - deposited iron. If a person loses 1 tea spoon of blood, he deprives himself of the daily iron needs, appears Fe deficiency, and because iron is part of hemoglobin and a stimulant of hematopoiesis, then eventually develops hyporegenerative hypochromic anemia.

Easy form is characterized by a decrease in hemoglobin in the blood up to 100 g/l and asymptomatic. This is due to a sufficiently high level of compensatory processes. Reducing blood viscosity with decreasing hematocrit enhances blood flow to organs and tissues, weakly expressed hypoxia significantly increases erythropoietin production that nonetheless stimulates the production colony formation erythrocyte units in the bone marrow, increases the weight of the erythroid and enhances access to the blood stream of young and qualitative changes in erythrocytes high content of 2,3 - diphosphoglycerate. In such cells, decreases the affinity of hemoglobin for oxygen and increases its ability to give the cells of organs and tissues. In addition, enhanced cardiac

sympathetic reflexes from the mouth of the vena cava, there is tachycardia, which increases the cardiac output of blood. At the same time due to a compensatory increase in the number of functioning alveoli increases respiratory lung surface, accelerates blood circulation and lymph flow in the lung tissue, supported by increased volume of venous return. Cellular metabolism is characterized by increased activity of the enzyme utilization of oxygen from the blood system and low compensatory activation of anaerobic glycolysis. As a result, compensation comes not lead to significant disturbances in the body.

Average form develops in lowering blood hemoglobin to 80 g / l. It has a more severe clinical manifestations. Patients with symptoms of dyspnea and failure of the cardiovascular system is mostly lacking exercise. When muscle activity appear weakness, fatigue. Therefore, the blood supply shortage, particularly coronary, requires a systematic pharmacological correction. The peculiarity of the middle forms of anemia, as well as an easy, practical loss is the stage of increased excitability of the nerve centers of stem and sympathetic-adrenal system in the slow development of hemoglobin deficit and reduce the oxygen capacity of the blood. Changes in blood rheology no longer provide adequate oxygen supply of the tissues. Lack of neurogenic mechanisms of compensation (gain of external breathing, increase blood flow to organs and tissues, etc.) Supports the long-term hypoxia, especially when exercising. This is facilitated by lack of erythropoietin production, activation of which is impossible without the involvement of the sympathetic nervous system. Tissue metabolism characterized by a deficiency of activation of oxidative processes in the cells, a compensatory gain anaerobic glycolysis, development of extra- and intracellular acidosis restriction recycling the ferrous form of iron in the gastrointestinal tract, the occurrence of negative iron balance, mobilizing it from the depot with subsequent depletion. Deficiency hemoglobinisation erythrocytes and the synthesis of iron disorders enzyme potentiates the oxidation processes in the tissues and inhibits proliferation of hematopoietic cells in the bone marrow tissue. Reducing the erythroid mass activation of ineffective erythropoiesis, violation of hemoglobin synthesis in the early forms of polychromatic tetraploid normoblasts combined with the acceleration of their maturing and becoming a oxyphilous normoblasts. This activates the terminal division and the release of these cells together with the degenerative forms of erythrocytes (aniso - and poikilocytosis). Products in the bone marrow red blood cells with defective expressed hypochromia normocytes by reducing the activity of enzyme systems of synthesis of heme and globin contributes to the progression of metabolic acidosis and tissue development dystrophies.

Severe (hemoglobin content of less than 80 g / l) is characterized by severe impairment of the cardiovascular system, even in a state of physiological dormancy. It is caused by imbalance of not only hematopoietic but also the functions of organs and tissues due to severe iron deficiency activity of enzymes and the violation of redox processes. These conditions contribute to the rapid development of degeneration of cells of organs and tissues.

Blood picture with CPHA

Degenerative forms:

- hypochromia - color index is sharply reduced (up to 0.5)
- Anisocytosis, microcytosis (microcytes appearance of having a higher specific surface area, many consider protective act)
- poikilocytosis little (few young forms)

Regenerative forms:

- nuclear - normocytes mainly oxyphilous - 1.2 in a preparation unit body Jolli with erythrocytes,
- cytoplasmic - polichromasia 11-15 ‰, reticulocytosis more than 10 ‰, and 20 ‰.
- there may be leukocytosis.

Thus, chronic hemorrhagic anemia:

- Acquired (after chronic blood loss) - etiology
- Pathogenesis - chronic hemorrhagic anemia,
- By type of hematopoiesis - type of anemia with erythroblastic hematopoiesis.
- Bone marrow - hyporegenerative,
- A color indicator - hypochromic.

Principles of therapy:

3. Causal - treatment of the underlying disease.
4. Pathogenic - iron supplementation, diet.

Pathophysiology of leukocytes system

The total number of leukocytes in the blood of healthy adult at rest and fasting ranges from $4x10^9$/L to $9x10^9$/L (4000-9000 in 1 mm). Violations of the quantitative composition of leukocytes in peripheral blood may wear jet (temporary) nature (leucocytosis, leukemoid reactions, and leucopenia) and have the nature of the tumor (leukemia, lymphoma). In some cases they are accompanied by a change in morphological and functional properties of leukocytes. In turn, defects in leukocytes quality can be formed not only on the number of leukocytes background changes, but wearing autonomous character. Their identification is crucial in the differential diagnosis of certain types of diseases of the blood system.

The qualitative composition of L bloodstream reflects WBC -% content of certain white blood cells (Kassirskiy IA).

eosinophils	basophils	neutrophils				lymphocyte	monocytes
		myelocyte	young	band	segment		

2-4	0-1	-	-	3-6	51-67	23-40	4-8

Pathological forms of leukocytes

Pathological forms of leukocytes are divided into regenerative (normally found in only in the bone marrow) and degenerative (destructive changes) form. Degenerative changes of leucocytes may be direct or indirect consequence of the damaging effects of harmful factors on mature blood cells and bone marrow hematopoietic dysregulated function resulting pathology of early hematopoietic microenvironment and hemopoietic progenitor cells. Signs of degeneration in the white blood cells can be detected in infections, inflammation, in terms of exogenous and endogenous intoxication, burns, ionizing radiation, vitamin B12 deficiency and folic acid, agranulocytosis, leukemoid reactions, leukemia, myelodysplastic syndrome, during treatment with cytotoxic drugs, corticosteroids and al.

Types of degenerative changes in white blood cells

Variant lesions leukocytes	Morphological characteristics
anisocytosis	Downsizing (microforms) and an increase in cell size (makropolitsity - giant white blood cells)
Pathology of nucleus:	
hypersegmentation	Increasing the number of segments in the nuclei of the neutrophil granulocytes (above 5 at a rate of 2-5), eosinophils (more than 3 at a rate of 2-3)
hyposegmentation	Violation of the segmentation of the nucleus of mature granulocytes - a decrease in the number of segments or no segmentation (nucleus round or elliptical, bean, peanut, gymnastic weights, pince-nez)
pyknosis	seal chromatin
rhexis	The disintegration of the nucleus into separate parts, the disappearance of intersegmental "threads" in mature granulocytes
fragmentation	The formation of fragments of nuclear chromatin (micronuclei)
lysis	Dissolution of the nuclear envelope
chromatinolysis	Liquefaction of chromatin
vacuolation	Colourless stains ("holes") in the chromatin
bare nucleus lymphocyte	Lymphocytes without cytoplasm

forms Ridder	dual-lymphocytes
body of Botkin-Gumpreht	The crushed lymphocyte nuclei
Pathology of the cytoplasm:	
"depletion" graininess	Deficiency or absence of specific granules

toxogenic grain	Large coarse basophilic granules
azurophilic grain	Multiple, overlapping nuclei of cells or single large azurophile granules in the cytoplasm of mature white blood cells
vacuolation	Colorless spots ("holes") in the cytoplasm
body Knyskova- Dele	Round or oval amorphous turn blue
Auer rods	Sticks cherry color (azurophilic agglomerated grain)

Furthermore, the morphology of leukocytes defects may be hereditary nature. An example is an autosomal dominant anomaly Pelgera-Hyueta characterized hyposegmentation nuclei of neutrophils due to a defect of genetic control postmitotic stage granulocyte maturation with the formation pseudomyelocyte (neutrophils with round large blocks, pycnotic nuclei) cells with nuclei in the form of "eyeglasses", "sticks " twosegmented cells. By the combined hereditary defects morphology, function, and the number of leukocytes include autosomal recessive syndrome Chediak-Higashi. In this disease in the early stages of blood marked neutropenia, subsequently - pancytopenia. In neutrophils, eosinophils, monocytes, lymphocytes found giant pellets (diameter greater than 5 microns), showing a positive reaction to peroxidase and conditional violation microbicidal chemotaxis and cell function. There is also a defect of dense granules in platelets. In the bone marrow - the signs of granulocytic hyperplasia germ.

Functional defects in leukocytes

Violations of the functional properties of leukocytes can be hereditary or acquired. They relate mainly to the defects of neutrophil granulocytes due to the violation of their margination, adhesion, migration and microbicidal properties.

Typical changes in the number of white blood cells per unit volume of blood

Typical changes in the number of leukocytes in a unit volume of blood include leucopenia and leucocytosis.

And leucopenia and leucocytosis, as a rule, are not independent diseases, but belong to the reactions developing in various diseases, pathologies and conditions. Cure disease, elimination of pathologic process or disease state leads to more or less rapid normalization of the total number of

individual shapes or leukocytes ratio of mature cells, disappearance of signs of degeneration and do not require special treatment.

Deviations are the number of leukocytes in peripheral blood, as well as qualitative changes in them to a certain extent make it possible to judge the presence of the pathological process and the dynamics of its flow, ie, have diagnostic value (in contrast to, for example, leukemia - independent diseases with specific causes, mechanisms of development, manifestations, which require special treatment).

Leucopenia

Leucopenia - conditions characterized by a decrease in the number of leukocytes in a unit volume of blood below normal (usually less than $4\text{-}10^9$ / L).

Classification of leucopenia.

By origin distinguish primary (congenital or hereditary) and secondary (acquired) leucopenia.

Primary leucopenia

The primary leucopenia (in most cases we are talking about neutropenia) are Kostmata disease syndromes Grischemi, "lazy" of leukocytes, Chediak-Higashi, congenital aleukia, family neutropenia, hereditary periodic neutropenia, chronic granulomatous disease.

Secondary leucopenia

Causes of secondary (acquired) leucopenia.

- Ionizing radiation. Chemicals (benzene, mustard gas), insecticides.
- Medicinal products (can lead to neutropenia and agranulocytosis even):
- Non-steroidal anti-inflammatory drugs, antimetabolites (methotrexate, fluorouracil, cytarabine), sulfonamides, barbiturates; diakarb, levamisole, tiamazol (Mercazolilum), chloramphenicol (chloramphenicol), isoniazid, methicillin, trimethoprim, hingamin, cyclophosphamide, antitumor antibiotics (doxorubicin).

3. Diseases of the immune autoaggression (eg, systemic lupus erythematosis), generalized infection (typhoid fever, paratyphoid fever, influenza, measles, rickettsiosis, hepatitis), cachexia.

According to the etiology of leucopenia can be:

- Physiological leucopenia - at 2-12% of healthy people of European race in the absence of immune suppression or leucopoiesis.

- Pathological leucopenia - a decrease in the absolute number of certain types of white blood cells.

According to the etiology:

Absolute leucopenia - a decrease in the absolute number of certain types of white blood cells
The relative leucopenia - a decrease in the percentage of certain types of white blood cells due to the increase of other species.

On the mechanism of occurrence:

1. True

- Related disorders leucopoiesis (aplasia, metaplasia, toxic and toxic-allergic effects on bone marrow, the effect on the hematopoietic tissue of physical factors, deficient)
- Related to the exit delay of neutrophils from the bone marrow (leukemia, hypersplenism)
- Due to increased destruction of white blood cells (immune leucopenia)
- Due to inefficient myelopoiesis ("shift to the right")

2. False or redistribution

- Conditioned reflex reactions and digestive redistributive
- The redistribution of white blood cells under the influence of substances vagotropic in shock, chills, collapse, various neurotic reactions
- Harmless leucopenia

According to the percentage of certain types of white blood cells in peripheral blood (in the leukocyte count):

Neutropenia. This leucopenia observed against acute radiation syndrome, viral diseases (influenza, hepatitis, infectious mononucleosis, HIV), bacterial infections (typhoid fever, brucellosis, miliary tuberculosis, fulminant sepsis), malaria, as well as on the background of autoimmune disease, hypersplenism, receiving cytotoxic drugs. It is typical for such blood diseases such as aplastic anemia, B12- and folic acid deficiency anemia, leukemia, myelodysplastic syndrome, and others.

Neutropenia may be associated with a degenerative left shift, which is characterized by a decrease in blood of segmented on the background of the increase of band neutrophils in the absence of younger predecessors and the presence of degenerative changes in the cells (toksogennaya grain, vacuolization of cytoplasm, nuclear structure abnormalities, and others.). There may be a shift of neutrophils to the right - against the background of the lack of band and segmented neutrophils decrease in blood neutrophils are large (macrocytosis) with polysegmented nuclei and vacuoles in the cytoplasm, which is most characteristic of megaloblastic anemia.

Agranulocytosis. Called agranulocytosis syndrome characterized granulocytopenia (less neutropenia ($0,8\text{-}1x10^9$ / l (800-1000 / ml) against severe leukopenia ($1 – 3x10^9$ / L).

The term agranulocytosis ("no granulocytes") reflects extreme deficiency of neutrophils in the peripheral blood, leading to a sharp weakening immunity and development of infection. It is an

infectious sick more often is a cause of the patient to see a doctor: heavily flowing necrotic angina, pneumonia, necrotizing bacterial or fungal stomatitis, candidiasis (fungal infections) other sites.

Typically, a bacterial infection is associated with neutrophil leukocytosis, which is secondary to disease. In agranulocytosis the infection is due to a lack of neutrophils.

In the pathogenesis of agranulocytosis may be immune or myelotoxic.

Immune agranulocytosis, including drug, is a consequence of the destruction of neutrophils (and often other granulocyte) cytotoxic (IgG, IgM) with the participation of activated components of the complement system. Other blood cells is not affected: no anemia, thrombocytopenia, observed relative lymphocytosis.

Myelotoxic agranulocytosis develops in the bone marrow damage. This affects all the blood shoots. Leucopenia (primarily granulocytopenia) combined with monocytopenia, trombocytopenic and aplastic anemia. Causes of myelotoxic agranulocytosis are the same as with hypo - and aplastic anemia. It is also characterized by a relative lymphocytosis. The absolute number of lymphocytes per unit volume of blood, or normal or reduced (e.g., with radiation sickness).

Clinical manifestations myelotoxic agranulocytosis pattern except infectious diseases (main manifestation) also include hypoxic syndrome, the severity of which depends on the degree of reduction of red blood cells and hemoglobin, as well as possible development hemorrhagic syndrome when the number of blood platelets decreases to critical numbers.

Eosinopenia. This form of leucopenia can be observed on the background of stress, glucocorticoid therapy, acute phase response, myelotoxic agranulocytosis, malignant tumors with disease and Cushing's syndrome, certain viral diseases, possibly due to a deficiency of interleukin-5.

Lymphopenia. This leukopenia develops under the influence of excess body glucocorticoids (stress, hypercortisolism, long-term steroid therapy), as well as radiation sickness or radiation therapy, lymphoma (Hodgkin's disease) and immunodeficiency syndromes (Louis-Bar, Wiskott-Aldrich syndrome, Di Giorgi). It is characteristic of many chronic diseases (congestive heart failure, systemic lupus erythematosus, tuberculosis of the lymph nodes, chronic renal failure in the stage of uremia, miliary tuberculosis, tumor metastasis, and others.). Lymphopenia causes immunosuppression antilymphocytic globulin or cyclophosphamide.

Monocytopenia. This type of result may be leucocytosis excess of glucocorticoids in the body, as well as a consequence of bone marrow damage (leukemia, aplastic anemia, Addison-Biermer anemia, radiation disease, cancer metastasis, and chemotherapy, etc.). Reduction in blood monocytes can be observed on a background of the height of acute infection (in conjunction with neutropenia), exacerbation of TB process, rheumatic heart disease (in combination with lymphocytosis).

The term "**bazopenia**" do not use as normal may not basophils in the peripheral blood.

Nuclear changes leukocyte leucopenia

• Degenerative nuclear shift to the left - an indicator of inhibition of functional activity of bone marrow, can occur in severe infectious diseases, endogenous intoxication, etc;

Eosinophil	Basophil	Neutrophils				Lymphocyte	Monocytes
		Myelocyte	Metamyelocytesband		segmented		
-	-	-	-	36	13	49	2

3) Degenerative nuclear shift to the right - in radiation sickness, pernicious anemia, Addison Birmera; in some cases, in healthy people.

Eosinophil	Basophil	Neutrophils				Lymphocyte	Monocytes
		Myelocyte	Metamyelocytesband		segmented		
-	-	-	-	2	53	42	3

Mechanisms of development of leucopenia

The development of leucopenia is a result of the violation and / or oppression leucopoiesis processes, Excessive destruction of white blood cells in the bloodstream and organs of hematopoietic, the redistribution of white blood cells in the bloodstream, the loss of white blood cells by the body, hemodilution.

4. Infringement and / or inhibition of the formation of white blood cells,

Causes.

2. The genetic defect leucopoiesis cells (eg, gene abnormalities that control the maturation of white blood cells).

3. Upset leucopoiesis neurohumoral regulation mechanisms (in particular, in hypothyroid states hypocorticism, reducing leukotrienes or sensitivity thereto leukocytic hematopoietic germ cells).

4. Lack of components needed to leucopoiesis (e.g., with a significant deficiency of proteins, phospholipids, amino acids, folic acid, cyanocobalamin).

Type. Upset leucopoiesis may concern all germs (eg, under the influence of high dose radiation), or preferably one or more of them (for example, chronic administration amidopirina, meprobamate, chloroquine, colchicine developed agranulocytosis, which is characterized by a significant reduction in the number of granulocytes: neutrophils, eosinophils and basophils and monocytes).

2. Excessive destruction of white blood cells in the bloodstream, or hematopoietic organs.

Causes: ionizing radiation and antileykotsitarnye antibodies. Antileukocytic antibodies can be generated due to mutations in the genome of B-lymphocytes producing Ig, in response to a transfusion of donor blood weight (formed against antigens of foreign antibodies leukocytes can have cross-damaging effect on the body's own cells), and by the use of drugs that act as haptens (Amidopyrine, sulfonamides, barbiturates). Haptens determine antibody causing agglutination and destruction of leukocytes.

Redistribution of white blood cells in different regions of the vascular bed (of a temporary nature).

Causes:

5. Shock (anaphylactic, traumatic, blood transfusion).

6. Severe and prolonged muscle work (when it is observed concentration of white blood cells in the capillaries of muscles, intestines, liver, lungs, and at the same time - a reduction in their numbers in other regions of the vascular bed).

7. The development of the phenomenon of the "edge standing" leukocyte adhesion is characterized by a large number of them on the walls of microvessels. This pattern often observed in the early stage of inflammation, covering a large area (eg, in erysipelas, cellulitis).

8. Out of a large number of massive damage in their white blood cells from the vascular tissue (eg, peritonitis, pleurisy, pneumonia, extensive mechanical damage to the soft tissues).

Increased loss of white blood cells by the body.

Causes: acute and chronic blood loss, as well as plasma- and lymphorrhage (for example, extensive burns, chronic purulent processes - osteomyelitis, endometritis, peritonitis).

5. Hemodilution leukopenia (relatively rare).

Causes: hypervolemia as a result of large volume transfusion of plasma or plasma substitutes and tissues liquid flow into the bloodstream by the gradient of osmotic or oncotic pressure (with hyperaldosteronism, hyperglycemia, hyperalbuminemia).

Manifestations of leukopenia

- Reduction of the content per unit volume of blood leukocytes of all areas of differentiation (leucopenia) or of one of them: lymphocytes, monocytes, neutrophils, basophils and eosinophils (lymphocyto-, monocyto-, eosino-, neutropenia, respectively).

- Reduce the number of predominantly young forms of neutrophils (stab, metamyelocytes) in the early stages of development leukocytopenic reaction. This is indicative of inhibition of regenerative capacity of hematopoietic tissue.

- Increase the number of young forms of neutrophils (a shift leukocyte left) at the termination of the causal factor. It is a sign of activation leucopoiesis.

- Signs of degeneration of leukocytes. They are often detected in neutrophils and monocytes.

- Degenerative changes are seen various changes leukocytes circuit (poikilocytosis), in particular subulate outgrowths cytolemma, the presence of different sized cells (Anisocytosis), shrinkage or swelling of the cells, the appearance of vacuoles, toxogenic grain and inclusions in the cytoplasm, hypersegmentation or pyknosis nuclei and their destruction (karyorhexis).
- A large number of degenerative forms of leukocytes in leucopenia is sometimes combined with a decrease in the number of leukocytes and segmented. a moderate increase in the content of band and even metamyelocytes (this blood picture is referred to as degenerative nuclear shift to the left).

• If an increasing number of segmented white blood cells with signs of degenerative changes in them without increasing the number of band cells, that indicate degenerative nuclear shift to the right.

Meaning leukopenia

In severe leucopenia observed decrease in resistance of the organism (mainly anti-infection and anti-tumor). This is because the leukocytes are involved in the implementation of humoral and cellular immunity and phagocytic reaction. When leucopenia frequently observed infection of the body (with the development of rhinitis, bronchitis, pleurisy, pneumonia, conjunctivitis and other forms of the infection process) may also develop tumors.

Leucocytosis

Leucocytosis - unstable temporary increase in the number of white blood cells per unit volume of blood, which is an indication of the physiological condition of the body or symptom of the disease.

Causes of leucocytosis

On the genesis of leucocytosis divided into endogenous and exogenous (and those, and others may be infectious and noninfectious). Causal factors leucocytosis may be physical, chemical and biological.

Physical factors (e.g., periodic influence of ionizing radiation on the body in small amounts).
Chemical (eg, alcohol, moderate deficiency of oxygen in the inspired air; receiving drugs that stimulate the proliferation of cells).

Biological factors. Their majority (for example, the waste products of the living and dead components of viruses, bacteria, Rickettsia, immune complexes antigen-antibody; elevated levels of BAC: leucopoetin, histamine, cell degradation products).

According to the etiology leucocytosis divided into physiological (sign of the physiological state of the body) and pathological (disease symptoms).

Physiological leucocytosis include alimentary (digestive), developing in 2-3 hours after a meal; myogenic when muscle tension; emotional - due to mental excitement, as well as leucocytosis neonates (within the first two days of life), pregnant women (growing from 5-6 th month of pregnancy) and pregnant women (celebrated on the second week after birth). Short-term physiological leucocytosis is redistributive in nature and linked to the mobilization of the reserve into the blood stream of mature white blood cells from the organs depot; long (newborns, pregnant women) - is due to activation of leukocytes formation processes in the bone marrow.

Among pathological leucocytosis distinguished:

• Infection - pneumonia, meningitis, scarlet fever, and a number of other infectious diseases;
• Inflammation (especially in purulent inflammation) - with various kinds of injuries: electrocution injury, operation of high and low temperature, etc;

• Toxogenic - under the action of harmful substances such as exogenous (benzene, arsenic, hydrogen, aniline, etc.) And endogenous (in uremia, diabetic coma);

osthemorrhagic - coming after acute blood loss;

4) New formation - the decay of tumors;

5) Leukemia in acute and chronic leukemia's. The mechanism of their occurrence is associated with increase leukopoietic bone marrow function, and only one kind of pathological leucocytosis - Centrogenic (when shock conditions, epilepsy, agony; postoperative) is redistributive.

Pathological leucocytosis.

All pathological leucocytosis % on the content of certain types of white blood cells in peripheral blood are divided into the following types:

• Neutrophil -% increase in neutrophils in the leukocyte formula;

• Eosinophilic -% increase in eosinophils in the leukocyte formula;

• Basophilic - Increase% basophils in the leukocyte formula;

• Monocytosis -% increase in monocytes in the leukocyte formula;

• Lymphocytosis -% increase in lymphocytes in the leukocyte count.

Pathological leucocytosis can be absolute and relative.

The relative and absolute changes in leukocyte formula

Relative leucocytosis - increase the percentage of this species of leukocytes in the leukocyte formula is not the result of this kind of absolute increase of leukocytes in a unit volume of blood, it is the result of an absolute decrease of another species of leukocytes in a unit volume of blood. Typically, when the total number of white blood cells per unit blood volume decreases.

When changes the relative (percentage) the content of a particular type of white blood cells in the leukocyte count say anything about the relative neutropenia, eosinopenia, lymphopenia, monocytopenia (by reducing the percentage of the respective type of white blood cells), or the relative neutrophils eosinophils, relative monocytosis, lymphocytosis (increasing their relative content).

Absolute leucocytosis - leucocytosis is such that the increase in the percentage of this species of leukocytes is the result of an absolute increase of leukocytes in the bloodstream while the total number of leukocytes in the blood volume unit is increased.

Changes in the absolute leukocyte content per unit volume of blood is referred to as absolute neutropenia, eosinophilia, lymphopenia, monocytopenia (with a decrease of the absolute number per unit volume of blood) or absolute neutrophils, eosinophils, absolute lymphocytosis monocytosis or (in the case of increasing the number of relevant varieties of white blood cells).

In characterizing the changes in the composition of leukocytes must be evaluated as a relative, and (necessarily) their absolute content.

This is determined by the fact that it is the absolute values reflect the true content of certain types of white blood cell count, and the relative ratio of only characterize different cells with each other in a unit volume of blood.

In many cases, the direction of change is the same. It often occurs, for example, the relative and absolute neutrophilia or neutropenia.

The deviation of the relative (percentage) cell content per unit volume of blood does not necessarily reflect a change in their true, the absolute number. Thus, the relative neutrophilia can be combined with the absolute neutropenia (a similar situation arises when there is relative neutrophilia in significant leucopenia conditions: for example, the content is 80% neutrophils and the total number of leukocytes is only $1,0\text{-}10^9$ / l).

To determine the absolute amount of a particular type of white blood cell count is necessary to calculate this value based on the total number of leukocytes and the knowledge of the percentage of the corresponding cells (in the above example, 80% of the $1.0\text{- }10^9$ / L will be $0.8\ 10^9$ / L. This more than half the $2.0\text{-}10^9$ / l - the lower limit of normal absolute neutrophil count).

On the mechanism of leucocytosis are true and false. If true leucocytosis absolute number of leukocytes in a unit of blood volume of the vascular region is increased; leucocytosis with a false number of white blood cells per unit volume - increased, but it is the result of blood clots.

Mechanisms of development of leucocytosis

The development is the result of leucocytosis; leucopoiesis stimulation and release of leukocytes from hematopoietic tissue in the peripheral blood redistribution of leukocytes in the bloodstream, tumor activation in leukemia and leucopoiesis hematosarcoma, hemoconcentration.

1. Reactive leucocytosis - increased normal leucopoiesis.

Causes: increase the level and / or activity of humoral leucopoiesis stimulants (e.g., growth factors), and the reduction and / or activity of cell proliferation leukopoietic inducers and inhibitors of their maturation. The result is an increase in the number of proliferating cells leukopoietic fabric, combined, usually with their differentiation into mature leukocytes. It is observed, for example, in inflammatory reactions and in the development of allergic processes.

Leucocytosis with development mechanism referred to as regenerative (true, absolute).

4. The redistributive leucocytosis - redistribution of white blood cells in the bloodstream.

3. Characterized by the accumulation of a large number of mature leukocytes into any body region, the absence of signs of hyperplasia leukopoietic tissue preservation total white blood cell count within the normal range.

4. Can be observed after considerable physical exertion ("myogenic leucocytosis"), traumatic, blood transfusion, anaphylactic shock (increased number of white blood cells in the blood microvessels of lung, liver, intestine wall).

The redistributive leucocytosis is temporary and not accompanied increase in the number of young forms of leukocytes. That is why leucocytosis with the development of a mechanism called the false or relative.

Hyperproduction leukocytes in tumor lesions of hematopoietic tissue (leukemia). It is the result of increasing the total number of white blood cells by activating the proliferation of leukemia (cancer) cells and stimulates division and maturation of normal white blood cells in the body due to the appearance of alien - tumor - antigens. Are formed in response to the increased number of normal white blood cells provides immune response.

Hemoconcentration leucocytosis.

Reason: hypohydration organism with the development of various origin hypovolemia (e.g., as a result of repeated vomiting, diarrhea, polyuria). With a total number of normal white blood cells count them per unit volume of blood increased. Simultaneously, blood and increased in the number of other blood cells.

Manifestations of leukocytosis

Increase in the number of white blood cells forms or their individual types (lymphocytes, monocytes, granulocytes different) is largely determined by the nature of the causal factors.

In allergic reactions tend to occur mainly an increase in the number of eosinophils in the blood (an allergen causes the release of lymphocyte stimulants eosinophilic leucopoiesis - IL-5, IL17, eosinophil chemotactic factor of the ECF, eotaxin).

Infectious processes caused by bacteria (such as streptococci, staphylococci), and stimulated emission in myelopoiesis blood granulocytes, mostly neutrophils.

At introduction into the body of many viruses (e.g., causative agents of whooping cough, hepatitis) and some microbes (e.g., causative agents of tuberculosis, syphilis, brucellosis) occurs mainly lymphopoiesis stimulation and increase in the number of lymphocytes in the peripheral blood.

Some viruses, bacteria and protozoa that cause infectious diseases (eg, infectious mononucleosis, rubella, brucellosis, malaria), also monocytopoiesis activate and mobilize monocytes from the bone marrow into the blood with the development monocytosis.

Changes in leukocyte counts with leucocytosis

True leucocytosis (regenerative, absolute), developing at the expense of the gain cell proliferation myelocytic series, accompanied by changes in leukocyte counts.

These changes are due to an increase or decrease in the blood of young forms of myelocytic cells and the appearance of forms, normally absent. In this case, they say, to change the ratio of mature and immature white blood cells - granulocytes of nuclear shift to the left or right. The use of these terms is associated with the location names of young forms of neutrophils (stab, metamyelocytes, myelocytes, promyelocytes) on the left side of the form of laboratory and mature - in their right-hand side.

Nuclear changes leukocytosis with leukocyte

Since the smear of blood the main criterion for identification of different forms of maturity granular leukocytes is the nature of the nucleus (shape, size, color intensity), leukocyte shift is referred to as nuclear.

Shift right

Often combined with the emergence of signs of degeneration of the white blood cells and a decrease in the content of band neutrophils.

Shift left

Since the time of the following types V.Shilling leucocytosis.

2 Leucocytosis without nuclear shift. Thus the total number of leukocytes leucocytosis slightly increased to 10-11 x 10^9/l. Marked increase in the total % of neutrophils due to segmented neutrophils. Such leucocytosis occurs in some physiological leucocytosis, with some forms of pulmonary infectious diseases, lung hemorrhages. It indicates process purity.

Eosinophil	Basophil	Neutrophils				Lymphocyte	Monocytes
		Myelocyte	Metamyelocytesband		segmented		
-	-	-	-	5	70	22	3

2. Leucocytosis with a hyporegenerative nuclear shift to the left. The total number of leukocytes in a unit volume of blood is increased (up to 11-12 x 10^9/l). There is increase in the percentage of neutrophils: the number of band neutrophils increased slightly and segmented neutrophils increased or is within a high rate. There occurring in benign infectious and parasitic diseases, catarrhal appendicitis, with superficial outflow of pus from abscesses, with moderate blood loss. It indicates most of purity of the process (1 degree).

Eosinophil	Basophil	Neutrophils				Lymphocyte	Monocytes
		Myelocyte	Metamyelocytesband		segmented		
-	-	-	-	8	69	21	2

- Leucocytosis with a regenerative nuclear shift to the left. Total leukocytes significantly increased to 15-20 x 10^9/l. There is a general significant increase in the percentage of neutrophils, the increase in the percentage of band neutrophils, neutrophils appear young (metamyelocytes), segmented neutrophils within high standards. Observed in severe forms of acute infectious and parasitic diseases - diphtheria, scarlet fever, dysentery, typhus when, lobar pneumonia, suppurative appendicitis, peritonitis, retropharyngeal abscess, severe blood loss. This shift is evidence of severe forms of the disease, and more sufficient resistance of the organism (2 degree shift).

Eosinophil	Basophil	Neutrophils				Lymphocyte	Monocytes
		Myelocyte	Metamyelocytesband		segmented		
-	-	-	6	12	54	23	5

3. Leucocytosis with a hyperregenerative nuclear shift to the left. Total leukocytes in a unit of blood volume is increased (to 20 x 10^9/l), but may tend to decrease. Increased overall percentage of neutrophils, increase of band neutrophils, there is a large percentage of young neutrophils and myelocytes appear, with segmented neutrophils are relatively and absolutely reduced. Typically, when these forms of shift no eosinophils. There is this form when very heavy infectious and parasitic diseases, lobar pneumonia with abscess formation process in phlegmonous appendicitis, heavy peritonitis, sepsis and other septic complications. The emergence of this shift with the downward trend in the total number of white blood cells indicates a violation of the process of proliferation and maturation of neutrophils violation processes in the bone marrow. pathological forms may occur with degenerative changes in the nucleus and cytoplasm. This type of leucocytosis reflects not only the severe form of the disease, but also the poor body resistance (in the terminology of the old doctors - "atonal syndrome").

Eosinophil	Basophil	Neutrophils				Lymphocyte	Monocytes
		Myelocyte	Metamyelocytesband		segmented		
-	-	3	8	16	54	17	2

Nuclear shift index

The above change in the balance of mature and immature forms of neutrophils can be quantified - by calculating the nuclear shift index. It reflects the ratio of the percentage of the sum of all the young forms of neutrophils (myelocyte, metamyelocytes, myelocytes, promyelocytes) to their mature forms.

$$SI = (M+MM+B) / S$$

In healthy adults, the nuclear shift index ranges from 0.05 to 0.10. Increasing evidence of his nuclear shift of neutrophils to the left, decrease - a shift to the right.

Redistributive and hemoconcentration (false) leucocytosis not accompanied by changes in leukocyte counts.

With significant leucocytosis In bone marrow and lymph nodes, signs of tissue hyperplasia lymphopoetic as increasing the size of lymphoid follicles and germinal centers.

Typical changes in leukocyte

Leukocytic formula - the ratio of different types of circulating leukocytes in the peripheral blood. Leukocyte changes are a consequence of increasing or decreasing the content of the individual types of leukocytes and thereby - changes the ratio between them.

The increase in excess of the number of certain types of white blood cells is termed neutrophilia, basophilia, eosinophilia, lymphocytosis, monocytosis.

Neutrophilia - increase of neutrophils more than 70% in the hemogram. It is noted in acute infectious diseases, purulent inflammation, myocardial infarction, bites of poisonous insects after acute blood loss, as well as alimentary and emotional physiological leucocytosis. Of great practical importance is the determination of the degree of nuclear shift in leukocyte formula. On this basis distinguish six kinds of neutrophilic leucocytosis.

Eosinophilia - increase of eosinophils in excess of 5% in the hemogram. According to modern concepts eosinophilia is a kind of reaction to foreign proteins, histamine, infestation by parasites and is associated with anti-toxic, anti-histamine (via histaminase - enzyme eosinophil granule), phagocytic (phagocytosis of immune complexes) and anthelmintic (exocytosis larvae, the destruction of the myelin nerve parasites fibers) function eosinophils.

The development of eosinophilia occurs in a variety of allergic diseases and syndromes (asthma, angioedema, urticaria, etc.); in parasitic diseases (opisthorchosis, ascariasis, giardiasis, and others.), certain skin diseases (psoriasis, eczema), collagen (rheumatism, dermatomyositis), hemoblastoses (chronic myelogenous leukemia, Hodgkin's disease), some endocrinopathy (pituitary

chexia, myxedema, and others.) infection number of diseases (scarlet fever, syphilis, tuberculosis), with the use of certain medications (antibiotics, sulfonamides, and others.); also described the hereditary form of eosinophilia.

Basophilia (more than 1% basophils in the hemogram) - a rare form of leukocytosis encountered in anaphylactic and reaginic allergic reactions (urticaria, angioedema, food and drug allergies, etc.), which is due to basophil ability to fix IgE and of IgG, releasing mediators granules (factors chemotaxis of neutrophils and eosinophils, heparin, histamine, serotonin and others.). Basophilia also found in vaccination, hemolytic anemia, hemophilia, endocrinopathy (diabetes, myxedema, etc.), chronic myeloid leukemia.

Lymphocytosis - increase in lymphocyte content of over 45% in the hemogram. Physiological lymphocytosis is characteristic of children during the first 10 years of life, and is seen in vegetarians and after physical activity (myogenic). In the context of pathology lymphocytosis developed in a number of infectious diseases (typhoid, mumps, whooping cough, malaria, brucellosis, infectious mononucleosis, tuberculosis, syphilis, and others.), Which is associated with the formation of anti-infective immunity, as well as malnutrition, asthma and some endocrine disorders (syndrome: myxedema, acromegaly).

Monocytosis - increase of monocytes over 9% in the hemogram. Revealed by persistent bacterial and viral infections (tuberculosis, infectious mononucleosis, measles, rubella, etc.), inflammatory diseases (ulcerative colitis, sprue, collagen, and others.), hemoblastosis, breast cancer and ovarian cancer, after splenectomy, and others.

Value

Analysis of leukocyte (detection of changes in the absolute content of neutrophils, eosinophils, and other leukocytes, estimate the direction and intensity of neutrophil shift) to determine the presence and type of leucocytosis or leucopenia on the cellular composition, the degree of changes in the content and proportion of individual forms of white blood cells, a possible mechanism of their occurrence.

Thus, the increase in the total number of white blood cells in combination with absolute neutrophilia shows regenerator (true) leucocytosis. If the increase in the total number of white blood cells accompanied by the absolute neutron and eosinophilia, holds regenerative mixed - neutrophilic-eosinophilic leucocytosis. Reducing total content of leukocytes in conjunction with absolute lymphopenia - flag true lymphocytic leucopenia, etc.

The presence of neutrophils expressed nuclear shift to the left with leucocytosis is usually indicative of the true (regenerative) nature of leucocytosis, and absence of such a shift is more common in redistributive mechanism of leucocytosis or leucopenia neutrophil.

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Leukemias

Leukemia - tumor disease of the blood system is characterized by three main features:

- **Hyperplasia -** proliferation of tumor, or a germ hematopoiesis in places where it should be in a normal state (in the bone marrow);
- **Anaplasia -** is when the processes of proliferation (cell proliferation) prevails over the differentiation process;
- **Metaplasia -** tumor proliferation, of any germ hematopoiesis in places where it should not be (inside the body, the brain, etc.), with an expanding germ hematopoiesis displaces local tissue elements, replacing them with a.

Currently, this process is called metastasis.

Unlike leucocytosis, leukemoid reactions and other reactive hematopoietic tissue growths at the base of leukemia is uncontrolled (unlimited) cell proliferation in violation of their ability to differentiation and maturation. Loss of ability to mature leukemia cells can take place much more than normal blood cells, the number of cycles of division, and that creates a huge cell production that characterizes leukemia.

The etiology of leukemia to date is not certain. On the tumor nature of leukemia indicated by the presence of the general laws that unite leukemias and tumors: a violation of the cell's ability to differentiate; morphological and metabolic anaplasia cells; common etiological factors contributing to the development of leukemia and tumors, and others.

The possible etiologic factors causing the development of leukemia, include ionizing radiation, a number of chemicals, viruses. Some importance in the development of leukemia is attached to genetic

factors, hereditary and acquired immune deficiency action blastomogenic metabolite of tryptophan and tyrosine.

Theories of the origin of leukemia.

Radiation theory. The role of ionizing radiation in causing leukemia was proved experimentally. As single (at a dose of 2 Gy or higher) and chronic (2-3 months) irradiating X-rays in low doses can induce leukemia in laboratory animals (rats, mice). It traces the increased incidence of acute and chronic myeloid leukemia among residents of Hiroshima and Nagasaki have Radiologists. The data on the increase in the frequency of leukemia in patients treated with high doses of X-rays, yttrium, radium for malignant neoplasms and ankylosing spondylitis, as well as in children who received irradiation of the thymus at an early age, and others. Described a higher incidence of acute leukemia among patients eritremii after treatment of radioactive phosphorus.

Chemical theory. Experimentally proved possible to induce leukemia in animals by administration of carcinogens (dimetilbenzantratsen, methylcholanthrene et al.). Also in experiment demonstrated the possibility of stimulation leukogenesis metabolites of tryptophan and tyrosine (ML Rauschenbach). However, the role of these substances has not been proven in human leukogenesis. At the same time, the accumulated data indicating an increased risk of leukemia disease (usually sharp) in people with long-term occupational exposure to benzene and volatile organic solvents (drivers, workers of the leather and footwear industry, etc.). In recent years there has been a marked increase in cases of acute leukemia in patients with malignant tumors treated with cytotoxic drugs such as tsiklosfosfan, hlorbutin, methotrexate, mielosan, adriamycin and others. The drugs capable of inducing leukemia are also phenylbutazone, chloramphenicol, and others.

Virus theory connects the occurrence of leukemia with the activation (under the influence of radiation and chemical factors) leukogenetic latent viruses. There is no doubt proved a viral origin of leukemia in many species of animals - birds, mice, rats, hamsters, cats, cattle. To date, isolated and thoroughly characterized by several types of viruses that cause different types of leukemia in animals. Typically, this RNA viruses and DNA viruses, which belong to the herpes virus.

The role of viruses in the origin of leukemia in humans remains largely controversial. Against viral etiology of human leukemia says, first of all, the fact of the impossibility of direct inoculation of leukemia Accidental transfusion of persons suffering from leukemia, and the lack of convincing

evidence of leukemia contagious. Do not also described cases of transmission of leukemia from the sick mother to the fetus and the newborn during breast-feeding.

Genetic theory has sufficiently convincing arguments, indicating the possibility of a genetic predisposition to leukemia. There are cases of family leukemia, proved the role of ethnic features in the development of lymphocytic leukemia. By the occurrence of leukemia predispose disease characterized by spontaneous chromosome breaks and nondisjunction somatic or sex chromosomes (Down syndrome, Fanconi anemia, Klinefelter syndrome, Turner et al.). Mice were obtained, in which the frequency of spontaneous leukemia is close to 100%.

The pathogenesis of leukemia. According mutationally-clonal theory of the origin of leukemia leukemic factor (ionizing radiation, chemical, virus, etc.) Causes a mutation (DNA damage, violation of the genetic code), one of the hematopoietic progenitor cells II-III classes. As a result, the

information is broken division and cell differentiation, observed their way out from under the control of the regulatory systems of the body. This leads to uncontrolled proliferation of certain cell varieties. Thus, the components of the substrate leukemia tumor cells are monoclonal offspring originally mutated cells and retain all the typical signs of it. In step monoclonic tumor cells sensitive to chemotherapy.

In favor of the clonal nature of leukemia are the following facts: the possibility of transplantation of leukemia in mice by administering a leukemia cells; Production of homogeneous immunoglobulin multiple myeloma and Waldenstrom's macroglobulinemia; the same type of leukemia cells (bearing surface immunoglobulins of a class and subclass) in chronic lymphocytic leukemia; the presence of specific chromosomal changes in cancer cells (for example, ring chromosomes as the radiation damage marker) in acute leukemia that occurred in patients with erythema treated with radioactive phosphorus, and others.

Convincing evidence of clonal origin of leukemia is to detect the vast majority of patients with chronic myeloid leukemia (80-90% of cases), abnormal (with a shortened long arms) a so-called Philadelphia (Ph1) chromosome in all myeloid cells, including granulocyte, erythroid and megakaryocytic sprouts, possibly except T lymphocytes. This fact is undeniable proof of the origin of chronic myeloid leukemia from one abnormal clone, which is the ancestor of pluripotent stem cell progenitor myelopoiesis (CFU-GEMM).

In the development of leukemia (tumor progression) qualitative changes constituting the substrate of the tumor cell due to the instability of their genetic apparatus. Activities of the latter, in turn, is subject to change under the influence violates the structure of chromosomes (changes in the structure, the appearance of aneuploid) and epigenetic, that is not associated with changes in gene structure, violations - the transition of the previously inactive in the cell genes in an active state (a phenomenon derepression genes). These changes of tumor cells leads to the appearance of new clones. As a result, developing polyclonal tumor becomes malignant. Individual clones of tumor cells out from under the control of regulatory systems of the body become resistant to the ongoing cytostatic therapy, metastasize to organs and tissues in normal hematopoiesis is not involved, forming foci of extramedullary hematopoiesis.

Classification of leukemia, particularly hematopoiesis and cellular composition of peripheral blood in different types of leukemia.

I. Morphogenetic classification of leukemia on AI Vorobiev, YI Lorna. (Similar to the burgeoning germ hematopoiesis).

- Acute and chronic plasmoblastic and plasmocytic leukemia.

Plasmoblast grows, proplasmocyte, plasmocyte.

- Acute lymphoblastic and chronic lymphocytic leukemia.

To grow different types of lymphocytes: lymphoblasts, according to them prolymphocytes and lymphocytes.

- Acute histiomonoblastic leukemia and chronic monocytic leukemia

Monoblast grows, promonocyte, monocytes, histiocytes.

- Acute myeloblastic leukemia and chronic myeloid leukemia.

Grow cells - myeloblasts, promyelocytes, myelocytes, young, band, segmented neutrophils.

A variety of acute myeloid leukemia is acute promyelocytic leukemia. Myeloblasts azurophilic grows with grit.

5. Acute erythroblastic and chronic erythrocytic leukemia

Grow cells red germ hematopoiesis - erythroblasts, pronormocyte, normocytes (basophilic, polychromatic, oxyphilic), polychromatic erythrocytes and mature red blood cells

6. Erythromyeloleukemia acute and chronic (mixed leukemia).

There is a proliferation of white granular germ hematopoiesis and red germ hematopoiesis. The cellular composition of bone marrow and peripheral blood mixed, there are all forms of granular white blood cells and red blood cells.

Grow cells - myeloblasts, promyelocytes, myelocytes, young, band, segmented neutrophils. Grow cells rad germ hematopoiesis - erythroblasts, pronormocyte, normocytes (basophilic, polychromatic, oxyphilic), polychromatic erythrocytes and mature red blood cells.

- Acute megakaryoblastic and chronic megakaryocytic leukemia - proliferation platelet hemopoietic stem - megakaryoblast, promegakaryocyte, megakaryocyte and platelets.
- Acute leukemia with morphologically undifferentiated cells.

Grow cells: first class - stem or second class - semistem or third class - unipotent.

All cells are morphologically similar to each other, reminiscent of mature lymphocyte or lymphoid cells young

II. Classification of leukemia in the clinical course. (Number of blasts in peripheral blood forms).

4. **Acute leukemias** are distinguished malignant course, high lethality, hit a young age. The leucocyte count tens of percent of blast forms (from 10 to 100%). Maybe leukemia hiatus leukemicus - the lack of intermediate forms between a large number of blast cells form and mature.

5. **Chronic leukemias** are more benign course, affects mature and old age can go into acute leukemia. The leucocyte count - a few percent of blast forms, there are intermediate and relatively large number of mature cells.

- Classification of leukemia in the number of white blood cells (cells) per unit volume of blood (Dameshek).

The number of leukocytes in the blood of a healthy person 4-9 x 10^9 / L (gig/l or 10^9/l).

1. Leukopenic - less than 4 gig / liter;

2. aleukemic leukemia - the number of white blood cells in the normal range (4-9 gig / liter);

3. subleukemic - the number of white blood cells from 9 to 100 gig / liter.

4. leukemic over 100 gig / l (blood takes a whitish hue).

According to pathogenetic principle, based on the characteristics of the morphological characteristics of the leukemia cells, leukemia is subdivided into acute and chronic. Acute leukemia tumor include a complete stop differentiation of hematopoietic progenitor cells at a certain level of maturation; Substrate tumor cells make up II, III and IV classes in modern scheme of hematopoiesis. The group includes chronic leukemia tumor cells with partial delay cell maturation and accumulation of a certain degree of ripeness.

Acute leukemia. Hematologic picture in the advanced stage of the disease is characterized by the classic triad - a change in the content of white blood cells (the total number of white blood cells is reduced, increased or remain normal), the emergence of a large number of blast cells in the blood and so-called leukemic hiatus (hiatus leukaemicus), when in the peripheral blood is dominated by blast cells, there is a small percentage of mature white blood cells and virtually no intermediate form of maturation. Already in the early stages of the disease observed normochromic anemia and thrombocytopenia, the development of which is due to inhibition of normal hematopoiesis due to leukemic transformation of hematopoiesis.

Components of tumor blasts substrate with various embodiments of acute leukemia are difficult to distinguish morphologically, but can be differentiated using cytochemical techniques on

the difference in enzyme content. Based on the characteristics of cytochemical properties of leukemia cells in most modern classification of acute leukemias are divided into myeloid, lymphocytic, promyelocytic (the term "acute promyelocytic leukemia" is largely conditional, since the tumor is not made up of promyelocytes, and of atypical power cells (myeloblasts) the cytoplasm of which is rich in a large grain size.) monoblastny, erythromyelosis, megacaryoblastic and undifferentiated. Dedicated nosological forms also differ in their clinical symptoms and, most importantly, for the response to cytotoxic drug therapy. In adult patients with more common myeloid and lymphocytic, lymphoblastic children and (less frequently) non-differentiated variants of acute leukemia. In clinical practice, guided by the classification developed by the specialists of France, USA, UK, - FAB (FAB) -classification.

Acute myeloid leukemia. It is a tumor originating from the cells and progenitor myelopoiesis consisting mainly of granulocyte progenitor cell number - myeloblasts.

L = 70 x10^{9}/L

eosinophils	basophils	Neutrophils						lymphocyte	monocytes
		Myelo blasts	Promye locytes	Myelo cytes	Metamye locytes	band	segmented		
-	-	95	-	-	-	-	4	1	-

Acute undifferentiated leukemia. Morphological substrate of tumor cells presented II - III classes in modern scheme of hematopoiesis; morphologically they resemble lymphoblasts, but different cytochemical intact.

The definitive diagnosis of acute leukemia (especially in cases where the leukemic cells do not go into the peripheral blood) should be on the basis of study of bone marrow punctate. At the same time the main diagnostic feature is a monomorphic picture of the bone marrow with a predominance of the same type of power cell. Morphological criteria for the latter are very volatile; Like all tumor cells, leukemic blasts atypical differ progressing malignancy. As the disease progresses due to tumor progression, and under the influence of cytostatic therapy blast cells can drastically change their morphology, to lose the specificity of the enzyme.

L = 85 x10^{9}/L

		Neutrophils				
eosinophils	basophils	band	segmented	lymphocyte	monocytes	undifferentiated cells
-	-	-	-	-	-	100

Acute lymphoblastic leukemia. This is a tumor that arises from progenitor cells lymphopoiesis.

The introduction of immunological methods in leukemic possible to obtain unique information regarding the phenotypic diversity of leukemic lymphoblasts and create histogenetic reasonable classification of acute lymphoblastic leukemia.

In 1995 the European Group on immunological characterization of leukemia (European Group for the immunological characterisation of leukemia, EGIL) immunological classification of ALL was suggested. In accordance with this classification are 4 variants of T-ALL, which differ expression in the cytoplasm or membrane CLE-cell antigen, and 4 types of ALL B-line, based on an analysis of the expression of linearly and non-specific marker CD10 cyt JgM / mJgM.

In 50% of adult patients with acute myeloid leukemia and 80% of children with acute lymphoblastic leukemia blast cells are detected with an abnormal karyotype (aneuploidy, changes in chromosome structure).

L = 65 x109/L

Absent hiatu leukemicus (h.l.)

eosinophils	basophils	Neutrophils		Lymphocyte			monocytes
		band	segmented	Lympoblasts	Pro lymphocytes	lymphocyte	
-	-	-	7	65	20	8	-

L = 95 x109/L

Present hiatus leukemicus (h.l.)

eosinophils	basophils	Neutrophils		Lymphocyte			monocytes
		band	segmented	Lympoblasts	Pro lymphocytes	lymphocyte	
-	-	-	6	90	-	4	-

Chronic leukemias. Several simplified classification of chronic leukemia can be represented as follows: chronic myelogenous leukemia, chronic monocytic leukemia, erythremia, chronic lymphocytic leukemia, multiple myeloma, Waldenstrom's macroglobulinemia.

Chronic myelocytic leukemia. One of the most frequent diseases in the group of leukemia; tumor originating from progenitor cells myelopoiesis. Morphological substrate of chronic myeloid leukemia are mature and maturing cells of granulocytic hemopoietic stem. In a typical case (presence of Ph-chromosome in the blood-forming cells of the bone marrow) Open stage is characterized by neutrophilic leukocytosis with a marked nuclear shift to the left: the unit found myeloblasts, promyelocytes, myelocytes, metamyelocytes, sticks - and segmented granulocytes form. As a rule, develops hyperthrombocytosis. Children often observed juvenile (Ph-negative) form of chronic myeloid leukemia, characterized by high monocytosis and thrombocytopenia. Quite often a sign of chronic myeloid leukemia, especially in children, is an increase in the number of eosinophils and basophils (basophilic, eosinophilic Association). An important diagnostic feature of the disease is the enlargement of the spleen and liver, which is associated with the emergence of leukemic infiltration and foci of myeloid hematopoiesis in these organs.

Advanced stages of chronic myeloid leukemia naturally goes into terminal phase, characterized by a crisis of the so-called regional "(the appearance of bone marrow and peripheral blood significantly number power cells), progressive cytopenias (anemia, leukemia - and thrombocytopenia), the emergence of leukemic infiltrates in the skin, lymph nodes, myocardium and other organs. When polyclonal karyological examination revealed abnormal cells (aneuploidy), which is the main feature of the terminal phase - a new stage of tumor progression.

Early stage

L = 25 x10^9/L

eosinophils	basophils	Neutrophils						lymphocyte	monocytes
		Myelo blasts	Promye locytes	Myelo cytes	Metamye locytes	band	segmented		

10	7	-	-	6	12	13	48	3	1

height of the disease

9

		Neutrophils							
eosinophils	basophils	Myelo blasts	Promye locytes	Myelo cytes	Metamye locytes	band	segmented	lymphocyte	monocytes
8	7	1	5	9	11	12	44	3	-

Chronic lymphocytic leukemia. This immunocompetent tumor tissue consisting predominantly of mature lymphocytes, represented in most cases of B-cells.

Characteristic leukocytosis; Blood smears narrow cytoplasmatic mature lymphocytes predominate, the contents of which can reach 80% or more. An important feature is the appearance of shadows basket cells (crushed in the preparation of smears defective cells). The number of lymphocytes in the bone marrow is not less than 50% of all myelokaryocytes. Lymphoid tissue overgrowth occurs in the lymph nodes, spleen and liver, accompanied by an increase of the said bodies.

Functional inferiority forming lymphocytes leads to disruption of tumor immunological homeostasis in patients, which, in turn, causes autoimmune conflict (autoimmune hemolytic anemia and thrombocytopenia); infectious complications (due to violations of antibody), etc.

In contrast, chronic myeloid leukemia blast crisis are very rare, not well developed secondary resistance to cytostatic drugs.

L = 70 x10^{9}/L

eosinophils	basophils	Neutrophils		Lymphocyte			monocytes
		band	segmented	Lympoblasts	Pro lymphocytes	lymphocyte	
1	-	-	3	2	18	76	-

Erythremia (polycythemia vera, Vakeza disease). Disease tumor nature, characterized by a relatively benign course. The source of the growth of a tumor cell is myelopoiesis predecessor, the main substrate of the tumor - the red blood cells. The most characteristic changes in the peripheral blood: red blood cell count reaches (6-12h1012 / l), the level of hemoglobin - 160-200 g / l, hematocrit index increases up to 60-80%. Erythropoietin levels in the blood and urine in contrast to symptomatic erythrocytosis lowered. There leuco - and thrombocytosis, decreased erythrocyte sedimentation rate, blood viscosity increases. An important diagnostic feature is the increase in the mass of circulating red blood cells.

Multiple myeloma (plasmacytoma). Waldenstrom's Macroglobulinemia. Diseases from the group paraproteinemic Leukemia - cancer of immune cells (plasma and B-lymphocytes), synthesizing homogeneous (monoclonal) immunoglobulins.

General disorders in the body in leukemia

Manifested in the form of a number of syndromes: anemic, hemorrhagic, infectious, metastatic and intoxication.

1. Anemic syndrome.

Associated with inhibition of erythroid bone marrow.

2) Hemorrhagic Syndrome (bleeding from the gums, nose, intestines, may be bleeding in vital organs). Due to a decrease platelet production.

3) Infection Syndrome. The reason of it is functional inferiority leukemic white blood cells (decreased ability to phagocytosis, violation of enzyme homeostasis, inhibition of antibody synthesis in lymphocytes, etc.).

4) Metastatic syndrome. Manifested dysfunction of various organs and systems due to their appearance in leukemic infiltrates.

5) Intoxication syndrome. Flood-related organism nucleoproteins - toxic products formed during the decay (death) of the leukemic cells.

Used in the treatment of leukemia cytotoxic drugs can cause a range of side effects from normal organs and body systems, the combined term "cytostatic disease." Especially high sensitivity to the toxic effects of drugs antileukemic exhibit normal cell to quickly update system: bone marrow, lymphoid organs, the epithelium of the gastrointestinal tract, skin, hair follicles are actively proliferating tissue of the reproductive organs. In this connection, under the influence of

applied therapy clinical and morphological manifestations of a given species may vary considerably leukemia.

The causes of death in leukemia and anemia are sudden severe general intoxication, damage to vital organs (leukemic infiltration, extensive hemorrhage). The immediate cause of death of patients can become infectious complications (pneumonia, sepsis, peritonitis).

Principles for leukemia therapy.

- Inhibition of the primary foci of tumor progression in bone marrow, chemotherapy, cytostatics, X - ray, radiation therapy, stimulation of apoptosis.
- Effect of the secondary focus of tumor progression (metastases) - chemotherapy and radiotherapy.
- Transplantation of bone marrow.
- The use of immunomodulators and immunostimulants.
- Replacement therapy - blood transfusion, blood products.
- Symptomatic therapy.

Leukemoid reaction.

Leukemoid reactions are changes in the blood and organs of blood, resembling leukemia, but not always having reactive. Leukemoid reaction reflects very pronounced degree of activation of the immune system, whose cells via the production of cytokines induce potent stimulation of breeding and release into the blood of various forms of white blood cells. The main reasons leukemoid reactions correspond to the causal inflammation (reactive) leukocytosis. Depending on the predominance of leukocytes in the leukocyte formula leukemoid specific type of reaction is divided into two basic types:

3. Myeloid (increases the relative and absolute number and content of immature granulocyte number increases sharply in the blood);
4. Lymphocytic and monocytic, lymphocytic (relative and absolute number of immature forms of lymphocytic and monocytic number increases dramatically in the blood).

Moreover, as recovered leukemoid eosinophilic reaction type.

Leukemoid type of reaction depends on the nature of the pathological process: its etiology, pathogenetic features, localization, etc. For example, the flow of the blood from the affected intestinal endotoxin sepsis, cancer disintegration lead to severe stimulation granulocytopoiesis and the emergence leukemoid reaction myeloid type. Viral infections and bacterial infections caused by intracellular pathogens (tuberculosis, brucellosis, etc.), usually lead to leukemoid reaction of lymph or lymphatic-type monocytic.

Neutrophil form leukemoid reaction (reaction leukemoid myeloid type) is the most common. It is usually in the blood increases the concentration of white blood cells and there is a large number of immature neutrophil cell number (up to myelocytes and promyelocytes - a sharp shift to the left leukogram) that is similar to the blood picture of chronic leukemia. However, there are significant differences:

5. The absence of eosinophilic-basophilic Association (increasing the percentage of eosinophils and basophils), typical for myelogenous leukemia;
6. Generally normal platelet count (for myeloid leukemia usually characterized thrombocytosis, sometimes up to 600-1000 g / l);
7. Less pronounced shift to the left;
8. Toxogenic appearance of grain in neutrophils;
9. A significant increase in the activity of alkaline phosphatase (alkalinphosphotase) neutrophils, which disappears when myeloid leukemia.

Neutrophil leukemoid reaction characterized not only by an increase in the percentage of neutrophils in the hemogram, but also an increase in their absolute number.

e development of such a reaction is observed in the initial phase of acute generalized infectious inflammation (sepsis) and infectious nature. The latter is often arises in extensive tissue destruction resulting from:

- Severe poisoning (heavy metals, arsenic, certain medications, and others.);
- Extensive frostbite, thermal and chemical burns;
- Necrosis of tissue under the powerful action of ionizing radiation (in the initial phase of acute radiation sickness, later replaced by oppression leykopoeza);

- The collapse of the necrotic malignant neoplasms nodes.

The decisive criteria for the differential diagnosis of leukemoid reactions and leukemia are the data history, clinical examination and histological examination punctate red bone marrow, which allows to differentiate tumor (leukemic) and reactive proliferation of granulocytic germ.

L = 65 x10^{9}/L

		Neutrophils							
eosinophils	basophils	Myelo	Promye	Myelo	Metamye	band	segmented	lymphocyte	monocytes
		blasts	locytes	cytes	locytes				
-	-	-	1	6	13	15	50	14	1