T. V. ZAMECHNIK

GENERAL PATHOLOGY

TYPICAL PATHOLOGIC PROCESSES

Manual
for third year students
of medical colleges
of higher education

ФЕДЕРАЛЬНОЕ АГЕНТСТВО ПО ЗДРАВООХРАНЕНИЮ
И СОЦИАЛЬНОМУ РАЗВИТИЮ

ВОЛГОГРАДСКИЙ ГОСУДАРСТВЕННЫЙ МЕДИЦИНСКИЙ УНИВЕРСИТЕТ

T. V. Zamechnik

"GENERAL PATHOLOGY. TYPICAL PATHOLOGICAL PROCESSES"

Part 2.

(manual for third year students of medical colleges of higher education)

Рекомендуется Учебно-методическим объединением по медицинскому и фармацевтическому образованию вузов России в качестве учебного пособия для иностранных студентов медицинских вузов, обучающихся на английском языке

УМО-711
09.11.04

Volgograd 2005

УДК 616-091(07)
ББК 52.5+81.2 Англ

"General pathology. Typical pathologic processes." Part 2. (Manual for third year students of medical colleges of higher education.)

Typical disorders of Peripheral Circulation.
Disturbances of Fluid balance.
Pathogenesis of Shock.

The manual contains lectures, tests & situational tasks, covering the following problems: typical disorders of peripheral circulation, disturbances of water – salt metabolism, pathogenesis of shock. This manual caters for third year students of medical institutions both for their independent and classroom activities.

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Approved by the Association for Academic and Methodological Issues.

УДК 616-091(07)
ББК 52.5+81.2 Англ

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Замечник Т.В.
Общая патология. Часть 2. (на англ. языке). – Волгоград: Изд-во ВолГМУ, 2005. – 86 с.

REGIONAL BLOOD FLOW DISTURBANCES.

Numerous disorders of the regional (peripheral, local, organotissular) blood flow are subdivided into blood flow disturbances in the vessels of medium diameter and blood and lymph flow disturbances in the vessels of microcirculation.

Blood flow disturbances in the vessels of medium diameter.

Blood flow disturbances in the vessels of medium diameter can be classified as pathological, arterial hyperemia, venous hyperemia, ischemia and stasis.

Arterial (active) hyperemia.

Arterial hyperemia is increased accumulation of blood flow and increased volume of blood circulating through the vessels of organs and tissues due to the dilatation of the arteries and arterioles.

The causes of arterial hyperemias can be of various etiology and nature.

- According to the origin we can distinguish arterial hyperemias resulting from endogenous and exogenous agents.

1. Exogenous agents causing arterial hyperemia affect an organ or tissue from outside. They can be classified as infectious (microorganisms and/or their endo- and exotoxins) and noninfectious factors of various nature.
2. Endogenous factors, resulting in arterial hyperemia form in the organisms (e.g. salt and concrement deposits in the tissues of kidneys, liver, subcutaneous fat; the formation of biologically active substances causing the reduction of the tone of smooth muscle of arterioles (vasodilatation), adenosine, prostaglandin, kinines; accumulation of organic acids (lactic, pyruvic, ketoglutaric).

- According to the nature of the causative (etiological) agent we can distinguish arterial hyperemia of physical, chemical and biological genesis.

1. Physical agent (e.g. mechanical exposure, very high t^0, electric current).
2. Chemical agent (e.g. organic and inorganic acids, alkali, spirits (alcohol), aldehydes.

3. Biological agent(e.g. physiologically active substances forming in the body: adenosine, acetylcholine, nitric (nitrogen) oxide.

Mechanisms of development

Lumen dilation of the small arteries and arterioles results from the action of neurogenic, humoral, neuromyoparalitic, mechanisms or their combinations.

- Neurogenic mechanisms. One can distinguish neurogenic and neuroparalytic types of neurogenic mechanism of arterial hyperemia development.

1. Neurotonic mechanism. It is characterized by predominance of the parasympathetic nervous system effects (in comparison with the sympathetic one) on arterial vascular walls.
2. Neuroparalytic mechanism. It is characterized by reduction or absence (paralysis) of the sympathetic nervous system effects on the walls of the arteries and arterioles.

- Humoral mechanism. It is characterized by a locally increased content of vasodilators – biologically active substances having a vasodilating effect (adenosine, nitrogen oxide, prostaglandine E, prost. 1 g, kinines) and by increased sensitivity of receptors of arterial vascular walls to vasodilators.
- Neuroparalytic mechanism.

1. It is characterized by:

➢ the depletion of catecholamine deposits in synqptic vesicles of varicose terminal sympathetic nervous fibers in the wall of arterioles;

➢ the reduction of the smooth muscle tonus of arterial vessels;

2. Causes

➢ prolonged effect of various factors of physical and chemical nature on tissues and organs (e.g. heat when hot-water bottles, hot compresses, mustard plasters, therapeutic mud are administered (used); diathermic currents).

➢ When prolonged pressure on the walls of the arteries is withdrawn (e.g. ascetic fluid, tight bandage, tight clothes).

The prolonged effect of the above-stated factors considerably reduces or completely removes the myogenic and regulatory (mainly, adrenergic) tone of the walls of arterial vessels. In this connection they dilate and the quantity of arterial blood circulating in them increases.

Types of arterial hyperemias

One can distinguish physiological and pathological hyperemias. The criteria for distinguishing them are adequacy and adaptability.

- Adequacy is a feature when arterial hyperemia corresponds to the modified function and metabolism in organs and tissues;
- Adaptability is the presence (or absence) of adaptive biological meaning of arterial hyperemia in each particular case.

Physiological arterial hyperemia

Physiological arterial hyperemia has an adaptive meaning. It can be functional and protective.

- Functional hyperemia develops in organs and tissues due to their increased activity (e.g. hyperemia in a contracting muscle or in a highly active organ).
- Protective hyperemia develops when protective reactions and processes are in progress (e.g. in the inflammation focus, or around a foreign graft (transplantant), necrotic zone, or bleeding zone). In this case arterial hyperemia induces the transport of oxygen, metabolic substrates, Igs, phagocytes, lymphocytes to tissues and other cells and agents essential for local protective and restorative reactions.

Pathological arterial hyperemia

Pathological arterial hyperemia doesn't involve any changes of organ and tissue functions but impairs adaptability and causes damage.

Pathological arterial hyperemia is associated with impaired blood supply, microhemocirculation, transcapillary metabolism, sometimes by hemorrhages.

Examples:

- Pathological arterial hyperemia of the brain in hypertensive crisis.

- Pathological arterial hyperemia of different organs and tissues developing according to the neuromyoparalytic mechanism (e.g. in the organs of the abdominal cavity after ascites, in the skin and muscles after a tight tourniquet is removed; at the site of chronic inflammation; at the site which was exposed to heat for some hours (sun heat, hot-water bottle; mustard plaster application) in the area of sympathetic denervation).

Arterial hyperemia manifestations

- Increased number and diameter of arterial vessels at the site of arterial hyperemia.
- Reddening of an organ, tissue or their site due to increased flow of arterial blood, dilatation of the lumen of arterioles and precapillaries, increased number of functioning capillaries, arterialization[vascularization] of venous blood (i.e. increase of HbO_2 level in venous blood).

The temperature

- The t^0 increase of tissues and organs at the site of hyperemia results from warmer arterial blood flow and higher metabolic intensity.
- Increased lymphopoiesis and lymph outflow due to increased perfusion pressure in the vessels of the microcirculatory bloodstream.
- Increased volume and turgor of an organ or tissue as a result of their higher blood and lymph volume.
- Changes in the vessels of microcirculatory bloodstream.

1. An increase of the diameter of arterioles and precapillaries
2. Increased number of functioning capillaries (i.e. capillaries through which plasma and blood corpuscles flow).
3. Accelerated blood flow through microvessels.
4. Reduced diameter of the axon (blood cell flow along the central axis of an arteriole) and increased width of plasma flow containing small amounts of blood corpuscles around this axon. It is caused by increased centripetal forces bouncing

blood cells to the center of the lumen of vessels as blood flows faster as in case of arterial hypertension.

The effects of arterial hyperemia

Activation of the specific function (functions) of an organ or tissue and potentiation of their non-specific functions and processes are observed in various physiological types of arterial hyperemia.

Example: activation of local immunity (due to increased flow of Ig, lymphocytes, phagocytizing cells and other agents with arterial blood), acceleration of plastic processes, increase of lymphopoiesis and lymph outflow from tissues.

1. Metabolic and oxygen supply disorders may cause hypertrophy and hyperplasia.

   It is the effects of arterial hypertensions which a number of treatments are targeted at (e.g. the administration of compresses, mustard plasters, physiotherapeutic treatments; injections of vasodilators; in surgeries for transecting sympathetic nerve trunks and excising sympathetic ganglia in certain types of angina pectoris, etc.) All these treatments are aimed at inducing hyperemia.

   These treatments are administered in case of organ and tissue damage, their ischemia, impaired trophism and plastic processes in them, decreased local immunity.

   Overextension and microrupture of vascular walls of microcirculatory bloodstream, micro- and macro- hematomas, internal and external hemorrhages in tissues are observed in pathological types of arterial hyperemia. The aim of arterial hyperemia therapy is to eliminate and prevent these negative effects.

Venous hyperemia

Venous hyperemia is increased blood volume coupled with reduced blood flow circulating through tissue and organ vessels. Venous hyperemia unlike arterial hyperemia results from a slower rate or an arrest of venous blood outflow through vessels.

Causes

The major cause of venous hyperemia is a mechanical obstruction hindering venous blood outflow from tissues or organs. It may be caused by a narrowed lumen of a venule or a vein when it is compressed (by a tumor, edematic tissue, a scar, a tourniquet, a tight bandage) and obturation (by a thrombus, embolus or tumor); cardiac insufficiency, low elasticity of venous walls associated with the formation of dilatated or constricted sites in them.

Manifestations

- Increased diameter of the lumen of venous vessels and their number at the site of hyperemia.
- Tissue and organ cyanosis due to increased venous blood volume in them and reduced HbO_2 level in the venous blood. The latter is the result of the utilization of oxygen taken by tissues from the blood due to its slow flow through capillaries.
- Reduced temperature of tissues and organs at the site of venous (passive) congestion resulting from increased volume of colder (in comparison with arterial blood) venous blood and lower intensity of tissular metabolism (resulting from reduced arterial flow to tissues at the site of venous hyperemia).
- Tissue and organ edema occurs due to increased intravascular pressure in capillaries and venules. In case of prolonged venous hyperemia edema is potentiated by its osmotic, oncotic and membranogenic pathogenetic factors

Water metabolism disturbances

- Tissue hematomas and hemorrhages (internal and external) resulting from overdistention and microruptures of venous vessel walls (postcapillaries and venules).
- Changes in the vessels of microcirculatory bloodstream.

1. Increased diameter of capillaries, postcapillaries and venules resulting from the distension of microvessel walls due to venous blood excess.
2. Increased number of functioning capillaries at the initial stage of venous hyperemia (resulting from venous blood outflow through earlier non-functioning capillary network) and their reduced number at further stages (due to blood flow arrest as a result of formation of microthrombus and blood cell aggregates in postcapillaries and venules).
3. Slow rate or even arrest of venous blood outflow.
4. Significant dilation of the axon diameter and disappearance of plasma flow in venules and veins.
5. Pendular movement of blood in venules and veins.

"Forward" - from capillaries to venules and veins. Caused by propagation of a systolic wave of cardiac output.

"Backward" - from veins to venules and capillaries. Caused by the fact that venous blood flow rebounds from the mechanical barrier (thrombus, embolus, constricted (narrowed) site of the venule).

Pathogenetic effects of venous hyperemia

Venous hyperemia damages tissues and organs which is caused by a number of pathogenic factors.

- The major pathogenic factors are: hypoxia (of circulatory type at the initial stage of the process and of mixed type when the process is long-term), tissue edema (resulting from increased hemodynamic pressure on the wall of venules and veins).
- Tissue hematomas (resulting from overdistension and rupture of postcapillary and venular walls) and hemorhages (external and internal).
- Consequences: reduction of specific and non-specific functions of organs and tissues, hypotrophy and hypoplasia of structural elements in tissues and organs, necrosis of parenchymatous cells and connective tissue development (sclerosis, cirrhosis) in organs.
- **Ischemia**

Ischemia – is an imbalance between the supply of tissues with arterial blood flow and their need in it. The need in blood supply always exceeds actual amount of blood flowing through arteries.

Causes

Causes of ischemia may be of various origin and nature.

- According to its nature ischemias can be divided into physical, chemical and biological ones.

1. Physical factors are compression of arterial vessels (e.g. by tumors, scar tissue, foreign bodies, tourniquets), narrowing or blocking of a lumen from inside (e.g. by a thrombus, embolus, atherosclerotic plaque), exposure to extremely cold temperatures.
2. Chemical factors. Many chemical compounds can stimulate contractions of smooth muscle of arterial vessels and cause constriction of their lumen. Examples: nicotine, a number of medicines (mezatone, ephedrine, adrenaline derivatives, alcohol dehydrogenase, angiotensin).
3. Biological factors: biologically active substances having vasoconstrictive effects (e.g. catecholamines, angiotensin II, alcohol dehydrogenase, endothelin), biologically active substances of microbic origin, their exo- and endotoxins, metabolites having a vasoconstrictive effect.

- According to its origin the cause of ischemia may be of endogenous or exogenous origin (infectious and noninfectious).

Mechanisms of ischemia development.

Mechanisms causing a reduction of arterial blood flow to tissues and organs may be neurogenic, humoral and mechnical.

- Neurogenic mechanism (neurotonic and neuroparalytic).

1. Neurotonic mechanism is characterized by the prevalence of the sympathetic nervous system effects on the walls of arterioles in comparison with those of the parasympathetic one. It also involves increased output of noradrenaline from adrenogenic terminals. Causes: activation of the sympathetic effects on tissues and organs (e.g. in various types of stress, exposure of tissues to low temperatures, mechanical trauma, chemical substances) and enhanced adenoreactive properties of arteriole walls (e.g. during their sensibilization to vasoconstrictive agents - in conditions of increased Ca^{2+} level or cyclic adenosine monophosphate in myocytes).

2. Neuroparalytic mechanism is characterized by elimination or reduction ("paralysis") of parasympathetic effects on the walls of arterioles. Cause: inhibition or blockade of nervous impulse propagation through parasympathetic fibers to arterioles (so that acetylcholine release from nerve fibers in the walls of the arteries, arterioles and precapillaries occurs). This can be observed in case of neuritis, mechanical traumas, tumor development, ganglionectomy or transection of parasympathetic nerves.
3. Humoral mechanism is characterized by increased level of substances having a vasoconstrictive effect in tissues (e.g. angiotensin II, alcohol dehydrogenase, thromboxane A, adrenaline, prostaglandin) and sensitivity of receptors of arteriole walls to the agents having a vasoconstrictive effect (e.g. when $[Ca^{2+}]$ or $[Na^{+}]$ increases in tissues).
4. Etiological factor of mechanical character. It is characterized by the presence of a mechanical obstruction to the blood flow through arterial vessels. Causes: compression of an arterial vessel by a tumor, a scar, edematic tissue, a tourniquet or narrowing (or even complete obturation) of an arteriole lumen (e.g. by a thrombus, aggregates of blood cells, an embolus).
5. Embolus and embolism.

Embolus is a mass, circulating in cardiac cavities, in blood and lymph vessels, which doesn't occur in the normal state:

- Emboli may be endogenous and exogenous according to their origin, and arterial and venous according to their localization in vessels.
- Exogenous emboli: they are mostly air bubbles (getting into large veins when damaged/wounded) or foreign bodies (e.g. bullet splinters or oil-base drugs when they infused in a cold state).
- Endogenous emboli are as follows:

❖ fragments of thrombi (thromboemboli);

❖ portions of fatty tissue or bone forming during organ growth or tubular bone fractures;

❖ small fragments of disintegrating tumour tissue or destroyed normal tissue.

- ❖ Conglomerates of microbial cells, multicellular or unicellular (single-cell) parasites.
- ❖ Gas bubbles, normally soluble in the blood plasma, but forming as a result of a rapid drop of pressure - during plane or spaceship depressurization as well as when rising from a depth.

1. Arterial emboli obstruct arterial vessels of the systemic circulation (penetrate from pulmonary veins or left heart chambers or veins of systemic circulation).
2. Venous emboli are often found in small venous vessels of the portal vein.
3. Embolism is circulation of a plug in the bloodslream and lymphatic flow, it doesn't occur in the normal state, and obstruction or constriction of a blood or lymph vessel by a plug.

Mechanisms of ischemia development are characterized by a significant increase of oxygen intake and metabolic substrate intake by tissues. In addition, the need in oxygen and substrates of metabolism exceeds the amount which is actually delivered to tissues.

- The main common cause is markedly intensified functioning of organs or tissues resulting in intensification of metabolic processes in them.

Examples.

1. Ischemia of muscles (including myocardium) due to intensive and prolonged physical exertion.
2. Myocardial ischemia when there is an acute significant increase of arterial blood pressure (e.g. in the conditions of hypertensive crisis) and emotional stress. In the latter case the activity of the heart significantly increases affected by catecholamine excess causing positive chrono- and inotropic effects. Under such circumstances blood flow to myocardium through coronary arteries increases. However, the work of myocardium (and consequently, its need in blood supply) increases to a considerable extent. Myocardial ischemia manifests itself as an attack of angina pectoris, and quite often ischemic necrosis (myocardial infarction).

Simultaneously, signs of narrowing of cardiac arterial vessels are observed which results from arteriosclerotic changes in them.

Consequences of ischemia.

The major consequences of ischemia resulting from hypoxia and numerous biologically active substances

The character, evidence and the scope of consequences of ischemia depend on many factors. The most significant of them are:

1. The rate of ischemia development (the higher it is, the more significant is the extent of tissue damage)
2. The diameter of the affected artery and arteriole (the larger it is the more severe is the lesion).
3. "Sensitivity" of a tissue or an organ to ischemia (it is very high in the tissues of brain, heart, kidneys)

- Ischemia or venous hyperemia may result in stasis due to significantly slackened blood flow (during ischemia as a result of decreased blood flow, during venous hyperemia as a result of slackening of its flow) or due to formation or activation of substances causing agglutination of corpuscular elements of blood, formation of aggregates and thrombi from them.
- Proaggregants are factors causing aggregation and agglutination of the corpuscular elements of blood.

Pathogenesis

The final stage of stasis involves the process of aggregation and agglutination of the corpuscular elements of blood which results in blood thickening and its fluidity reduction. This process is activated by proaggregants, cations and high molecular weight proteins.

- Proaggregants (thromboxane A, adenosine phosphate, prostaglandin, prostaglandin E, catecholamines, AT to corpuscular elements of blood) cause adhesion, aggregation, agglutination of the corpuscular elements of blood followed by their lysis when biologically active substances are released from them (including proaggregants, stimulating aggregation and agglutination).

- Cations: K^+, Ca^{2+}, Na^+, Mg^{2+} are released from blood cells, the affected walls of vessels and tissues. The excess of cations, absorbing on the cytolemma of the corpuscular elements of blood, neutralizes their negative superficial charge or even changes it for the opposite. While unaffected cells (due to the negative charge) rebound from one another, affected cells ("neutralized") form aggregates. "Recharged" blood cells aggregate more actively. Having a positive superficial charge they approach neutralized cells, mainly, affected ones (with a negative charge), forming aggregates adhering to the intima of vessels (the inner coat of vessels).
- High molecular weight proteins (e.g. y-globulins, fibrogen) change the superficial charge of unaffected cells (getting into contact with the negatively charged cell surface with the help of positively charged amino group) and stimulate aggregation of formed blood elements and adhesion of their conglomerates to the vascular wall (this is achieved by fixation of a great number of protein mycells having adhesive properties on the surface of the formed blood elements).

Types of stasis.

All types of stasis are divided into primary and secondary ones.

- Primary actual stasis. Primary stasis formation starts from the activation of corpuscular blood elements releasing a large quantity of proaggregants and/or procoagulants. At the next stage the corpuscular elements of blood aggregate, agglutinate and attach to the walls of a microvessel. This causes inhibition or arrest of blood flow through vessels.
- Secondary stasis (ischemic and congestive)

1. Ischemic stasis develops as an outcome of severe forms of ischemia due to decreased arterial blood flow reduction, slower rate of its flow, or its turbulent character. This leads to aggregation and adhesion of blood cells.
2. Congestive (venous congestive) variant of stasis results from slower rate of venous blood outflow, pachyemia, changes of physical and chemical properties, damage of the blood corpuscles (particularly, due to hypoxia). Subsequently, blood cells adhere to one another and to the walls of microvessels.

Manifestations of stasis.

Typical changes in the vessels of microcirculatory bloodstream occur during stasis. They can be as follows:

- reduction of the inner diameter in ischemic stasis, increase of the lumen of vessels of microcirculation in congestive stasis,
- increased number of aggregates of blood corpuscles in the lumen of vessels and on their walls,
- microhemorrhages (more often in congestive stasis).

The consequences of stasis.

When agents causing stasis are quickly withdrawn blood flow in the vessels of microcirculation is restored without entailing any noticeable changes in tissues.

Prolonged stasis results in dystrophyc changes in tissues (quite often to death of a tissue site or an organ).

Blood circulation disturbances and lymphokinesis in the vessels of microcirculation.

Microcirculation is a regular flow of blood and lymph through microvessels, transport of transcappilary plasma and blood corpuscles, fluid transfer outward vessels.

Microcirculatory bed. A number of arterioles, capillaries and venules form a structural and functional unit of the cardiovascular system, namely, a microcirculatory(terminal) bed. A terminal bed is structured as follows. A metarteriole branching into anastomizing actual capillaries forming a network branches from the terminal arteriole. The venous part of capillaries continues to precapillary venules.

At the site where a capillary branches from an arteriole there is a precapillary sphincter – accumulation of circularly oriented smooth muscle cells. Sphincters control local blood volume passing through actual capillaries. Blood volume passing through the terminal vascular bed is determined by arteriole tone of smooth muscle cells. Arteriolovenular anastomoses, connecting arterioles directly to small veins (juxtacapillary blood flow) are also in themicrocirculatory bed.

Walls of anastomosis vessels contain many smooth muscle cells. Arteriovenous anastomoses are present in large quantities in some areas of the skin where they play an

important role in temperature regulation(lobule of the ear, fingers). Small lymph vessels and intercellular spaces are also part of the microcirculatory bed.

Causes of microcirculation disturbances

Numerous causes including various microcirculation disturbances are classified into three groups.

- Central and regional circulatory disturbances. The major ones are cardiac insufficiency, pathological forms of arterial hyperemia, venous hyperemia, ischemia.
- Changes of viscosity and blood and lymph volume develop as a result of hemoconcentration and hemodilution.

1. Hemo (lympho) concentration. Causes: hypohydration of the body associated with developing polycythemic hypovolemia, polycythemia, hyperproteinemia (mainly hyperfibrinogenemia).
2. Hemo (lympho) dilution. Causes: hyperhydration of the organisms associated with developing oligothemic hypervolemia, pancytopenia (decreased quantity of all blood corpuscles), increased aggregation and agglutination of blood corpuscles (resulting in a significant increase of blood viscosity), DIC - syndrome (disseminated intravascular coagulation).

- Damage of vascular walls in the microcirculatory bed.

It is usually observed in atherosclerosis, inflammation, cirrhosis, tumours, etc.

Typical forms of microcirculation disturbances

Three groups of typical forms of microcirculation disturbances are classified as follows: intravascular, transmural and extravascular. Microcirculation disturbances cause capillary trophic insufficiency,

Intravascular disturbances of microcirculation

Typical forms of intravascular disturbances of microcirculation

Slow rate (up to stasis) of blood and lymphatic flow is the major cause. This may be causes by hemo- and lymphodynamics disturbances (e.g. in cardiac insufficiency, venous hyperemia ischemia).

Increased blood and lymph viscosity as a result of hemo- (lympho-) concentration due to prolonged vomiting, diarrhea; plasmorrhagia due to burns, polycytemia, hyperprotenemia, blood cell aggregation, intravascular coagulation, microthrombosis. Significant narrowing of a microvascular lumen (squeezed by a tumour, edematic tissue, caused by formation of thrombi or potentiation of an embolus, swelling or hyperplasia of endothelial cells, atherosclerotic plaque formation, etc).

Manifestations are similar to those which are observed in the vessels of microcirculation in venous hyperemia, ischemia and stasis.

- Blood flow acceleration.

The major causes.

- Hemodynamic disorders (e.g. in arterial hypertension, pathological arterial hyperemia or discharge of arterial blood into the venous stream through arteriovenular shunts.
- Blood viscosity reduction due to hemodilution (in water intoxication); hypoproteinemia, renal insufficiency (at an oliguric or anuric stage); pancytopenia.
- Disturbed blood and/or lymph flow turbulence.

The most common causes.

1. Changes of blood viscosity and state of aggregation (as a result of formation of blood cell aggregates when the increased number of blood corpuscles exceeds the norm or in hyperfibrinogenemia or in case of microthrombus formation).
2. The damage of the walls of microvessels affecting their smoothness in vasculitis, hyperplasia of endothelial cells, atheriosclerosis, fibrous changes in different layers of vascular walls, tumour development in them, etc.)

- Increased juxtacapillary blood flow. It occurs when arteriolovenular shunts are opened and blood is discharged from arterioles into venules avoiding capillary network of the microcirculatory bed.

1. The cause: spasm of smooth muscle arterioles and closure of precapillary sphincters as in case of an increase in catecholamine content in blood (e.g. in hypercatecholamine crisis in patients with pheochromocytoma), or in case of a

significant increase of the sympathetic nervous system tone (e.g. in stress situations), or in case of hypertensive crisis (e.g. patients with hypertension).

2. Manifestations: ischemia in the area where blood is discharged from arterioles into venules, opening and/or increase of the diameter of arteriovenular shunts. Turbulent character of blood flow at the sites where the shunting vessels branch from or enter venules which is conditioned by the fact that arteriovenular shunts branch from arterioles and enter venules, as a rule, at a considerable angle; it is accompained by the process in the course of which blood corpuscles strike one another and vascular walls, which results in proaggregate and procoagulant release and aggregate and thrombus formation).

Transmural disturbances of microcirculation

Either a fluid part of blood (in this case we deal with permeability) or cell elements (in this case we deal with emigration) may pass through walls of microvessels. According to the prevalence either of permeability or of emigration transmural disturbances are subdivided into two categories: permeability disturbances and emigration disturbances.

Permeability disturbances. In different pathological conditions volume of blood plasma and/or lymph passing through a vascular wall can increase or decrease.

- Increased permeability.
- The major cause of increased permeability of the walls of microvessels
- Consequences. Increased permeability of microvascular walls activates the mechanisms of fluid transfer: filtration (fluid transport according to hydrostatic pressure gradient); diffusion (fluid transport which does not involve any energy losses); osmosis directed fluid diffusion according to osmotic pressure gradient).

Decreased permeability

- Causes: thickening and/or induration of the vascular walls, or disturbances of energy supply of intracellular processes.
- Consequences. Decreased efficiency of fluid transfer mechanisms: filtration, diffusion, transcytosis, osmosis.

Emigration disturbances. In different pathological conditions the number of blood corpuscles passing through vascular walls may increase or decrease.

Leucocyte emigration through microvascular walls also occurs in the normal state. Excessive leucocyte emigration, thrombocyte and erythrocyte release from blood followed by microhemorrhages are considered pathological.

Extravascular disturbances of microcirculation

Extravascular disturbances of microcirculation are accompanied by increased or decreased volume of intracellular fluid which results in its slower flow into microcirculatory vessels.

- Increased volume of intracellular fluid coupled with its slower flow from the interstitial space.

The cause: local pathological processes (inflammation, allergic reactions, newgrowth, sclerotic processes, venous hyperemia and/or stasis).

Consequences.

- Increased content of the products of normal and disturbed metabolism in the interstitial fluid. They can have a cytotoxic and cytolytic effect.
- Ion imbalance (causing tissue edema, disturbing membrane rest potential and action potential formation).
- The formation of excessive biologically active substances or their activation (e.g. tumor necrosis factor, procoagualants) which can cause a more severe damage of cells, initiate blood and lymph circulation disturbances, plastic process.

- Disorders of O_2, CO_2 metabolism, metabolism of substrates and metabolites. Cell compression by excessive interstitial fluid.
- Increased volume of intracellular fluid followed by disturbances of its outflow from interstitial space.

Causes:

- Hypohydration of the organism, tissues and organs (e.g. as a result of prolonoged diarrhea, plasmorrhagia, profuse sweating).
- Reduced lymph formation (e.g. in tissue ischemia or hypovolemia).
- Decreased efficiency of fluid filtration in arterioles and precapillaries and/or its increased reabsorbtion in postcapillaries and venules (e.g. in dystrophic and sclerotic processes in tissues).
- Consequences are similar to those which are observed when the volume of the intestinal fluid increases and its outflow becomes slower (see the above-stated information).

Capillarotrophic insufficiency.

Capillarotrophic insufficiency is a state characterized by blood and lymph circulation disturbances in the vessels of microcirculation, disorders of fluid and blood corpuscles transport through the microcircular walls, slower outflow of the intracellular fluid and metabolic disorders in tissues and organs

As a result of the above-stated changes different types of dystrophy develop, plastic (flexible) processes in tissues are impaired, vitality of organs and the body in general decreases.

Sludge

Sludge is a phenomenon characterized by adhesion, aggregation and agglutination of blood corpuscles which causes blood to disintegrate into conglomerates of erythrocytes, leukocytes, thrombocytes and plasma and induces microcirculation disturbances.

Peripheral circulation and microcirculation disturbances: hyperemia, ischemia.

First level tests.

1. Which blood vessels are involved in peripheral circulation?
    1. Muscular-elastic arteries.
    2. Small arteries.
    3. Small veins.
    4. Microcirculatory vessels.
    5. Arterial veins.

2. Pick out microcirculatory vessels:
    1. Large arteries.
    2. Small arteries.
    3. Arterioles.
    4. Capillaries.
    5. Veinlets.
    6. Arteriovenular anastomoses (shunts).
    7. Veins.

3. Which are the regulating mechanisms of microcirculatory vessels:
    1. Reflex.
    2. Humoral.
    3. Hemitic.
    4. Genetic.

4. Which factors cause vasoconstrictive effects:
    1. Catecholamines.
    2. Acetylcholine.
    3. Somatostatin.
    4. Angiotensin-II.
    5. Vasopressin.
    6. Oxytocin.
    7. Serotonin.
    8. Thyrotropin.
    9. Potassium.
    10. Calcium.
    11. Somatomedins.
    12. Thromboxane – A-2.

5. Which factors cause vasodilatation:
    1. Catecholamines.

2. Acetylcholine.
3. Histamine.
4. Somatostatine.
5. Angiotensin-II.
6. Vasopressin.
7. Oxytocin.
8. Bradykinin.
9. Calcium.
10. Potassium.
11. Adenosine.
12. Acidic metabolites.
13. Prostacyclin.

6. Pick out typical peripheral circulation disturbances.
   1. Coarctation of aorta.
   2. Arterial hyperemia.
   3. Venous hyperemia.
   4. Pathologic blood pool.
   5. Ischemia.
   6. Ischemic cardiac disease.
   7. Hypertension.
   8. Thrombosis.
   9. Hemorheologic disorders.
   10. Embolism.
   11. Angiopathy.

7. Which are the manifestations of microcirculation disturbances:
   1. Change in the linear and volumetric blood flow rate.
   2. Angiopathy.
   3. Centralization of blood circulation (blood flow shunting).
   4. Aggregation of formed elements of blood.
   5. Thrombocytopathy.
   6. Sludge.
   7. Change in the number of the functioning capillaries.
   8. Coagulopathy.
   9. Telangiectasia.
   10. Manifestation of plasmatic capillaries.
   11. Vessel diameter change.
   12. Thrombohemorrhagic syndrome.
   13. Disturbances of blood rheological properties.
   14. Stasis.

8. What does the term "centralization of circulation" mean?

1. Blood circulation in arterial vessels.
2. Blood circulation in arteriovenular anastomoses (shuntings) avoiding capillaries.
3. Concentration of most part of blood volume in vital organs (brain, heart, lives, kidneys).
4. Increased venous return to the heart and increased minute cardiac output.

9. Which part of the vascular system does corpuscle aggregation start in?
   1. Arterial vessels.
   2. Arteriole.
   3. Capillary stream.
   4. Venular part of the microcirculatory bloodstream.

10. What are the mechanisms of aggregate formation?
   1. Vascular wall damage.
   2. Blood flow impairment.
   3. Changes in protein composition of blood.
   4. Quantitative and qualitative corpuscles.
   5. All the above-mentioned factors.

11. What does the term "sludge" mean?
   1. Penetration of foreign bodies into the blood and their accumulation in it.
   2. Formation of a large quantity of immunocomplexes in blood.
   3. An extreme degree of corpuscle aggregation.
   4. Septicemia.

12. Pick out pathogenic factors affecting reological properties of blood.
   1. Vascular wall state.
   2. Intercellular fluid composition.
   3. Number of corpuscles.
   4. Qualitative properties of corpuscles.
   5. Glucose level in blood.
   6. Interaction of corpuscles with the vascular wall and with one another.
   7. Leukocytic formula shifts.
   8. Presence of corpuscular aggregates.
   9. Quantative content and qualitative characteristics of blood proteins.
   10. State of water-salt metabolism.
   11. All the above-mentioned factors.

13. Pick out various types of arterial hyperemia according to the mechanisms of its development:
   1. Dyshormonal.
   2. Active.

3. Neurotonic.
4. Miotonic.
5. Neuroparalytic.
6. Mioparalytic.
7. Neurohumoral.
8. Obturational.
9. Caused by accumulation of the biologically active substances.

14. Active hyperemia occurs as a result of:
    1. Muscular work.
    2. Increased strain of a definite organ and its hyperfunction.
    3. Both.

15. Neurotonic hyperemia occurs as a result of:
    1. Increased tone of vasodilators.
    2. Decreased tone of vasoconstrictors.
    3. Increased tone of the upper sections of the CNS.
    4. Increased contractility of myocardium.

16. Neuroparalytic hyperemia occurs as a result of:
    1. Decreased tone of the parasympathetic nerve.
    2. Decreased tone of the sympathetic nerve.
    3. Myoparalysis of the vascular wall.
    4. Paralysis of the extremities caused by traumas and diseases of the spinal cord.

17. Myoparalytic hyperemia may occur:
    1. Under the effect of chemical irritants (benzol, turpentine, mustard, etc).
    2. In a postcompession state (reactive hyperemia).
    3. Due to the loss of muscle tone resulting from exposure to cold.
    4. According to vacant hyperemia type (cupping glasses).
    5. Under the effect of all the above-mentioned factors.

18. Arterial hyperemia may occur under the effect of the following biologically active substances:
    1. Acetilcholine.
    2. Catecholamines.
    3. Kinins.
    4. Histamine.
    5. Serotonin.
    6. Adenosine.
    7. Thromboplastin.
    8. Prostaglandin A and E.
    9. Kailons.

10. Histones.
11. Acid metabolites.

19. What are the changes of microcirculation and hydrostatic pressure in case of arterial hyperemia:

1. Arterial dilatation.
2. Development of additional arterioles.
3. Increased number of functioning capillaries.
4. Development of plasmatic capillaries.
5. Increased linear and volumentric blood flow rate.
6. Decreased linear and volumentric blood flow rate.
7. Increased hydrostatic pressure in vessels.
8. Increased intravascular oncotic pressure.
9. Decreased hydrostatic pressure in vessels.

20. Name the causes of venous hyperemia:

1. Arteriolovenular anastomosis.
2. Vascular embarrassment.
3. Atherosclerosis.
4. Thrombosis.
5. Spasm of venous vessels (veins).
6. Cardiac insufficiency (heart failure).
7. Circulatory collapse (vein atony).

21. Pick out the changes of microcirculation and hydrostatic pressure in case of venous hyperemia:

1. Venular dilatation.
2. Capillary dilatation.
3. Arteriolar dilatation.
4. Decreased linear and volumentric blood flow rate.
5. Increased linear and volumentric blood flow rate.
6. Push-like and pendulum-like blood flow.
7. Stasis.
8. Embolism.
9. Thrombosis.
10. Increased hydrostatic pressure in vessels.
11. Decreased hydrostatic pressure in vessels.

22. Pick out the major macroscopic (clinical) signs of arterial (A) and venous (V) hyperemia:

1. Reddening.
2. Cyanosis.
3. A temperature increase at the site of hyperemia.

4. A temperature decrease at the site of hyperemia.
5. Enlargement of an organ or volume of tissue.
6. Increased blood flow rate.
7. Decreased blood flow rate.

23. Which are the types of ischemia according to the pathogenetic classification:
1. Angiospastic ischemia.
2. Congestive ischemia.
3. Obturation ischemia.
4. Hypokinetic ischemia.
5. Obstructive ischemia.
6. Compression ischemia.

24. Which humoral factors can cause an angiospasm?
1. Catecholamines.
2. Acetylcholine.
3. Angiotensin-I.
4. Angiotensin-II.
5. Kinins.
6. Vasopressin.
7. Serotonin.
8. Prostacyclin.
9. Thromboxane-A_2.
10. Oxytocin.

25. Which electrolytes induce the development of an angiospasm?
1. Potassium.
2. Calcium.
3. Sodium.
4. Magnesium.

26 What are the major causes of obturation ischemia:
1. Occlusion of an artery with a thrombus.
2. Occlusion of an artery with an embolus.
3. Vascular wall changes resulting in stenosis of an artery.
4. Mechanical compression of arterial vessels from outside.

27. Pick out the changes of microcirculation and hydrostatic pressure typical of ischemia:
1. Decreased linear and volumentric blood flow rate.
2. Increased linear and volumentric blood flow rate.
3. Decreased number of functioning capillaries.
4. Increased number of functioning capillaries.

5. Decreased hydrostatic pressure in vessels.
6. Increased hydrostatic pressure in vessels.
7. Decreased diameter of arterial vessels.

28. What are the principal clinical manifestations of ischemia?
1. Cyanosis of an ischemic site.
2. Pallor of an ischemic site.
3. Decreased temperature at the site of ischemia.
4. Lack of noticeable changes of temperature of inner organs in case of ischemia.
5. Decreased volume of an organ or an ischemic site.
6. Increased volume of an ischemic site.

29. What are the outcomes of ischemia?
1. Complete restoration of the structure and functions of an organ.
2. Development of dystrophy and necrosis at the ischemic site involving replacement with connective tissue. Partial restoration of functions of an organ.
3. Irreversible structural and functional changes of vital organs with a fatal outcome.
4. All variants.

Second level tests.

31. Give the definition for the notion "hyperemia". What does the term "arterial hyperemia" mean?

32. What does the term "venous hyperemia" mean?

33. Name the changes of microcirculation and hydrostatic pressure of the vessels in arterial hyperemia:
1.
2.
3.
4.

34. Name the major macroscopic (clinical) manifestation of arterial hyperemia:
1.
2.
3.

35. What are the mechanisms of redness development as a result of arterial hyperemia:

1.
2.
3.

36. What are the mechanisms causing a temperature increase at the site of arterial hyperemia:
1.
2.

37. What are the mechanisms causing an increase in the area of the site of arterial hyperemia:
1.
2.

38. Whar are the consequences of arterial hyperemia:
1. Positive:
2. Negative:

39. What are the causes of venous hyperemia:
1. Local: a)
b)
2. Systemic: a)
b)

40. Name the disturbances of microcirculation and hydrostatic pressure in venous hyperemia:
1.
2.
3.
4.
5.
6.
7.
8.

41. Explain the mechanisms of push-like and pendulum-like blood flow formation.

42. Name the mechanisms of stasis formation:
1.
2.

43. Enumerate the major macroscopic (clinical) manifestations of venous hyperemia:
1.
2.

44. What are the mechanisms of cyanosis development:

1.
2.

45. What are the mechanisms causing a temperature decrease at the site of venous hyperemia:

1.
2.

46. What are the mechanisms causing a considerable increase of tissue mass in venous hyperemia:

1.
2.

47. Complete the scheme of a vicious circle formation in case of developing venous hyperemia :

blood outflow obstruction → hydrostatic pressure increase in venous vessels → plasma transsudation enchancement in intercellular space → edema.

48. Complete the scheme of venous hyperemia consequences (fill in the gaps):

venous hyperemia → _____ blood flow rate → hypoxia → _____ glycolysis → deficiency _____, accumulation _____ → cell damage, excrescence/growth _____ tissue.

49. What factors does venous hyperemia outcomes depend upon?

1.
2.
3.

50. Give the definition for the notion "ischemia".

51. Give the pathogenic classification of ischemia:

1.
2.
3.

52. Name the disturbances of microcirculation and hydrostatic pressure in ischemia:

1.
2.
3.
4.
5.

53. Name the major general clinical manifestations of ischemia:

1.
2.
3.
4.

54. What is the mechanism causing reddening of an ischemic site of a tissue?

55. What is the mechanism causing a temperature decrease at the site of ischemia?

1.
2.

56. What is the mechanism causing a decrease of the mass of an ischemic site?

57. What is the mechanism of pain development in ischemia?

58. Which facts influence ischemia outcomes:

1.
2.
3.
4.
5.
6.
7.

59. Give the scheme of cause-and-effect interrelation characterizing the major steps of ischemia pathogenesis.

Task 1

Patient K. Was admitted to the surgical department in an ambulance as he had a knife wound in the left shoulder. His humeral artery was damaged. Heavy bleeding which started after he had been wounded, was quickly stopped by application of a rubber toumiguet on the upper third of the shoulder. The skin on the left arm is pale, cold to the touch, its sensitivity is low. Arterial pressure is within the normal range.

What is the mechanism of development of the described symptoms?
What is ischemia and what are its causes?
What are the consequences of ischemia?
What is the mechanism of development of collaterals?

Task 2

A group of students were examined by the doctor right after jogging for a long time. The examination revealed marked hyperaemia of the facial skin of the students under study. The skin was bright red, wet with perspiration and hot to the touch. The pulse rate varied from 110 beats per minute to 150 beats per minute, the respiration rate was from 40 to 60 per minute.

What type of hyperaemia developed in the students?
What are the types of arterial hyperaemia?
What is the biological role of arterial hyperaemia?

Task 3

Patient M. was delivered to a surgical clinic as he had a penetrating wound in the right part of the chest. To prevent a pleuropulmonary shock in the patient the A. V. Vishnevsky's right-hand vagosympathetic blockade was done. The patient was given local anesthesia and the wound was treated. The wound was stitched in layers and an aseptic bandage was applied. The vagosympathetic blockade caused reddening of the right side of the patient's neck and face.

What type of arterial hyperaemia developed in the patient?
What are the mechanisms of vasodilation?
What is the pathogenesis of the symptoms in arterial hyperaemia?

Questions for discussion

1. The concept of peripheral circulation, its significance for homeostasis.
2. Typical disturbances of microcirculation. Hyperemia, its types.
3. Causes and pathogenesis of arterial hyperemia, its signs.
4. Etiology and pathogenesis of neuroparalytic arterial hyperemia.
5. Etiology and pathogenesis of neurotonic arterial hyperemia.
6. Etiology and pathogenesis of myoparalytic arterial hyperemia.
7. Etiology and pathogenesis of venous hyperemia and its clinical manifestations.
8. The concept of ischemia. Etiology and pathogenesis of its development. Outcomes of ischemia.
9. Stasis and its types.
10. Types of sludge. Pathogenesis of sludge types.

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FLUID BALANCE DISTURBANCES.

WATER METABOLISM REGULATION IN THE ORGANISM

The water metabolism regulation system is of sophisticated structure. The adaptive objective of this system is to maintain the optimal fluid volume in the organism. Being affected by pathogenic factors and/or with the modified concentration of fluid and salts in the organism this system either eliminates the abnormalities or reduces their influence. Water metabolism regulation system is closely connected with the systems of salt metabolism and osmotic pressure control. Water metabolism regulation system includes the central, afferent and efferent parts.

- **The central part of the water metabolism control system** is thirst centre (regulating water level). Its neurons are mainly in the front section of hypothalamus. This centre is connected with the areas of great brain cortex which make possible to experience the feelings of thirst and water comfort.
- **The afferent part of the system** includes sensory nerve endings and nerve fibres from different organs and tissues of the organism (oral mucosa, vascular channel, stomach, intestine and tissues), distant receptors (mainly optic and acoustic ones).

The afferent impulses from the receptors of various types (chemoceptors, osmoceptors, baroceptors, thermoreceptors and possibly some others) reach hypothalamic neurons. Regulatory stimuli from the thirst centre neurions (nerve and humoral) are transmitted to affector structures.

- **The efferent part** of the water metabolism regulation system includes kidneys, sweat glands, intestines and lungs. These organs (kidneys to a greater extent and lungs to a smaller extent) are responsible for eliminating disturbances of water and salt balance in the organism. Being affected by pathogenic factors and/or with the modified concentration of fluid and salts in the organism the system of water metabolism regulation either eliminates these abnormalities or reduces their influence. Insufficient efficiency of this system gives rise to a number of water metabolism disturbances.

TYPICAL WATER BALANCE DISTURBANCES

All kinds of water exchange disturbances (**dyshydria**) are classified into **hypohydration** (water loss) and **hyperhydration** (hyperhydria), including the clinically important form of hyperhydration, i. e. **edema.** Each typical form of dyshydria can be characterized by means of two basic criteria, the first being the osmolality of extracellular fluid. On the basis of this criterion three forms of dyshydria are singled out:

1.hypoosmolalic (with plasma osmolality under 280 mosm/kg H_2O);

2.hyperosmolalic (with plasma osmolality above 300 mosm/kg H_2O);

3.isoosmolalic.

The second criterion is the sector of the organism in which dyshydria predominantly develops. On the basis of this criteria
-cellular,
-extracellular
-mixed (associated) forms of hypo- and hyperhydration are singled out.

Hypohydration.

The characteristic feature of all kinds of hypohydration is the negative fluid balance: the predominance of water loss over its intake by the organism.

Hypohydration causes. The causes of hypohydration may be either insufficient water supply of the organism or its increased loss. Insufficient water supply of the organism may occur in time of the so-called water "water starvation", i. e. the deficient intake of liquid with food and drink by the organism (e. g. in time of forced starvation, or when there is no opportunity to secure the regular drinking regime in time of acts of God or hostilities). The other possible causes may be mental disorders or traumas, reducing or eliminating the feeling of thirst (for example, in concussion of the brain; when the neurons of the thirst centre have been damaged due to hemorrhage, ischemia, tumor growth as well as in hysteria and neurosis), somatic diseases, hampering food and liquid intake (for example, in impaired swallowing, esophageal occlusion, in the trauma of the facial part of the skull).

Increased water loss by the organism may occur in continuous polyuria (for example, in patients with renal failure, diabetes mellitus or when diuretics are not properly administered),gastrointestinal disorders (for example, in continuous profuse salivary discharge, recurrent vomiting, chronic constipation), heavy blood loss (for example, caused by blood vessel and/or heart injury), pathological processes, causing the heavy loss of lymph (for example, in case of extensive burns, lymphatic trunks damaged or injured by a tumour), prolonged or profuse sweating (for example, in the conditions of hot dry climate or industrial processes involving increased air temperature and decreased humidity in the workshop), hyperthermal states of the organism including fever. 1° C body temperature increase results in the discharge of 400-500 ml of liquid daily as a result of sweating.

According to the osmolality of extracellular fluid three types of hypohydration are singled out: hypoosmolalic, hyperosmolalic and isoosmolalic.

HYPOOSMOLALIC HYPOHYDRATION

In hypoosmolalic hypohydration the organism's salt losses are predominant as compared to water losses and the decrease in extracellular fluid osmolality.

Causes:

-hypoaldesteronism. It is associated with decreased reabsorption of Na^+ ions in the kidneys, decreased osmolality of blood plasma and water reabsorption which results in the organism's hypohydration.

-continuous profuse sweating involving the discharge of a great amount of salts.

-recurrent or uncontrollable vomiting (for example, in case of poisoning or pregnancy) causing Na^+ and K^+ losses.

-diabetes mellitus or diabetes insipidus (for example, when ADH is deficient) combined with the excretion of K^+ salts, Na^+ glucose, albumins.

-profuse diarrhea (for example, in cholera or malabsorption syndrome) associated with the loss of intestinal juice containing K^+, Na^+, Ca^{2+} and other cations.

-improper or unjustified implementation of dialysis procedures (hemodialysis or peritoneal dialysis with low osmolality of dialyzing solution. This results in the diffusion of ions from blood plasma and the fluid for dialysis.

-the correction of isoosmolalic hypohydration with the help of solutions with decreased salt concentration.

The extracellular form of hypoosmolalic hypohydration is conditioned mainly by the organism's predominant fluid loss. However, its severe and/or continuous varieties are associated with fluid transport into the cell (according to osmolality Gradient). Alongside with that intracellular hyperhydration (cell swelling) determining the extent of extracellular hypohydration may be registered.

Consequences and manifestations.

Mucous and cutaneous dryness, decreased salivary secretion (hyposalivation), decreased elasticity and tension (turgor) of skin, muscles, recession and softening of eyeballs, reduced amount of daily excreted urine. All these manifestations result from the organism's hypohydration, the reduced volume of intercellular fluid and the volume of circulating blood, decreased perfusion and hemodymanic pressure in arterioles and precapillaries. It should be noted that patients with hypoosmolalic hypohydration do not feel thirst due to low blood plasma osmolality and cell hyperhydration.

HYPEROSMOLALIC HYPOHYDRATION

In hyperosmolalic hypohydration the organism's water losses are predominant as compared to salt losses. Increased osmolality of intercellular fluid leads to water

transport from the cells into extracellular space. Under such conditions general (cellular and intracellular) hypohydration may develop.

Causes:

- Insufficient water intake (for example, in the so called "dry starvation" when a person refuses to drink water; when there is lack of drinking water supply in time of hostilities, acts of God, emergency situations).
- Hyperthermal states (including fever), associated with heavy prolonged sweating.
- Polyuria (for example, in diabetes insipidus (nephritic) involving the loss of a great amount of liquid with low concentration of osmotically active substances: ions, glucose, nitrous compounds by the organism; in diabetes mellitus due to osmotic polyuria in combination with high hyperglycemia). Prolonged artificial lung ventilation (ALV) with insufficiently moistened gaseous mixture.
- Drinking sea water in the conditions of the organism's hypohydration.
- Parenteral infusion of solutions of increased osmolality (for example, in treating disturbances of acid base equilibrium; in artificial feeding of patients with dystrophy).

Consequences and manifestations:

- Decreased volume of circulating blood;
- Increased Ht resulting in blood viscosity;
- Systemic disturbances of blood circulation (central, organ-tissular, microcirculatory);
- Disturbed acid base equilibrium (mainly acidosis) resulting from impaired hemodynamics, respiration and metabolism;
- Hypoxia.

As is seen the manifestations of hyperosmolalic hypohydration are quite similar (but not identical) to those of hypoosmolalic hypohydration. However, considerable cell hypohydration as well as the death of some of the cells in

hyperosmolalic hypohydration results in a more aggravated course of this pathology. This accounts for the fact that some other signs may occur in hyperosmolalic hyphydration.

- Fever due to the release of pyrogen from injured cells.
- Mental disorders (psychomotoric agitation, anxiety, fear of death, and mental confusion and loss of consciousness).
- excruciating unquenchable thirst due to extra- and intracellular hypohydration. It makes the patient drink any liquid (sea water and other water unfit for drinking, sewage, etc.), which is aggravating his condition even more. In children hyperosmolalic hypohydration develops at a higher rate and its course is more aggravated. This is conditioned by higher intensity of fluid excretion from the organism by kidneys, lungs, through the skin as compared to that of adults (when calculated per unit of body surface).

ISOOSMOLALIC HYPOHYDRATION

Isoosmolalic hypohydration involves an approximately equivalent reduction of water and salt concentration in the organism.

Causes:

Acute heavy blood loss at its initial stage (i.e. before the emergency compensatory mechanisms are brought into action).

Profuse recurrent vomiting. Profuse diarrhea. Extensive burns. Polyuria caused by bigger doses of diuretics.

Consequences and manifestations.

Consequences and manifestations of isoosmolalic hypohydration are conditioned by the reduced volume of extracellular fluid resulting in blood circulation disturbances:

- Reduced volume of circulating blood;
- Increased blood viscosity;
- Disturbances of central, organ-tissular and microhemocirculation;

- Disturbances of acid base equilibrium (for example, apidisis in profuse diarrhea and heavy blood loss, alkalosis in recurrent vomiting);
- Hypoxia (especially after heavy blood loss). The prompt action of compensatory mechanisms, as a rule, eliminates or considerably decreases the extent of hypohydration and severity of its manifestations.

MECHANISMS OF HYPOHYDRATION COMPENSATION

The general mechanisms of dehydration compensation include the activation of the neurons of the hypothalamic thirst centre and the activation of the system "renin - angiotensin – aldosteron". In the first case the increased amount of antidiuretic hormone (ADH or vasopressin) is secreted into the blood and diuresis decreases. In the second case the mineraloicorticoid hormone aldosteron increases the renal reabsorption of Na^+, which results in water staying in the organism.

Thirst

The feeling of thirst emerges when there is 1-2% deficit of water. It considerably increases in the conditions of excess sodium in the blood plasma – hypernatremia (hyperosmolality). 2,5-4 l water deficit causes a painful, excruciating feeling of thirst. This feeling sometimes makes people take a liquid which is unfit for drinking (for example, sea or dirty water), which aggravates the condition of the organism even more.

Causes of thirst:

Increased osmolality of extracellular fluid (mainly that of blood plasma being more than 285 mosm/kg H_2O).

Decreased amount of water in the cells.

Decreased level of angiotensin II in blood plasma, which immediately stimulates the thirst centre neurons.

Antidiuretic hormone

The activation of ADH (vasopressin) synthesis in the neurons of supraoptic and paraventricular hypothalamic nuclei and its secretion into blood from the posterior lobe of hypophysis result in decreased diuresis and vasoconstrictive effects.

Compensatory reactions are efficient in the organism's hypohydration of a mild degree, when water deficit does not exceed 5 % as compared to the norm. In hypohydration of more severe degrees special medical aid is necessary.

THE PRINCIPLES OF HYPOHYDRATION ELIMINATION

- Etiotropic principle involves eliminating or decreasing the severity and the length of the causal factor action . This therapy is individual for each patient.

- Pathogenetic principle implies:

1. Eliminating water deficit in the organism which is achieved by infusing the lacking amount of liquid.
2. Decreasing the degree of ion disbalance. This must be preceded by the analysis of their concentration in blood plasma as well as osmolality. Having taken into consideration these factors the liquid containing the required number of ions is prepared or chosen.
3. Eliminating acid base equilibrium disturbances.
4. Normalizing central, organ-tissular and microhemocirculation. The particular measures are determined to a great extent by the degree of blood circulation disturbances, the major pathology , the degree of hypoxia and its consequences.

A symptomatic principle is aimed at eliminating or decreasing the severity of the symptoms, aggravating the condition of hypohydration. Pain-relieving and sedative drugs as well as drugs for relieving a headache and cardiotropic drugs are administered. The particular therapeutic measures must be strictly individual.

Hyperhydration

Hyperhydration is characterized by the positive fluid balance: predominant water intake by the organism as compared to water excretion and losses. According to the osmolality of extracellular fluid hypoosmolalic, hyperosmolalic and isoosmolalic hyperhydration are singled out.

HYPOOSMOLALIC HYPERHYDRATION

Hypoosmolalic hyperhydration is characterized by excess extracellular fluid of low osmolality in the organism. Hypoosmolalic hyperhydration involves a fluid volume increase both in the extra- and intracellular sector, as excess extracellular fluid according to the gradient of osmotic and oncotic pressure enters the cells.

Causes:

- Excessive infusion of fluids with low concentration of salts or lacking salts into the organism. Most frequently this occurs in the course of repeated enteric infusion of water into the organism. This state is designated as "water poisoning". Such a situation may arise when patients with mental disorders repeatedly consume a great amount of water or drinks, when water is infused into the gastrointestinal tract through a catheter or a fistula (for example, for gastric or intestinal lavage). The development of "water poisoning" is alleviated with the excretory hypofunction of the kidneys.
- Increased concentration of ADH in blood as a result of its hyperproduction in the hypothalamus (for example, in Parhon's syndrome).
- Renal failure (with considerable excretory hypofunction of the kidneys).
- Marked circulatory insufficiency involving edema development.

Consequences and manifestations:

- Increased volume of circulating blood (hypervolemia) and hemodilution.

Hypervolemia and hemodilution are conditioned by water transport into the vascular channel due to higher osmotic and oncotic blood pressure as compared to that of intercellular fluid.

- Polyuria is increased urination due to higher filtration pressure in renal corpuscles. Polyuria may not occur at the hypo- or anuria stage of renal failure.
- Erythrocyte hemolysis.
- The emergence of intracellular components in blood plasma (for example, enzymes and other macromolecules) due to the injure or death of cells of different tissues and organs.
- Vomiting and diarrhea due to the organism's intoxication (as a result of the release of excess ions, metabolism products, enzymes and other substances from injured or dead cells.

- Psychoneurological disorders: flabbiness, apathy, disturbed consciousness, frequent convulsions. The enlisted disorders result from brain cell injury as a result of their swelling.
- Hypoosmolalic syndrome. It develops when blood plasma osmolality decreases up to 280 mosm/kg H_2O or even lower, as a rule, as a result of hyponatremia (this syndrome may occur both in hypo- and hyperhydration of the organism).

Blood plasma osmolality decrease under 250 mosm/kg H_2O may result in irreversible changes in the organism and its death.

HYPEROSMOLALIC HYPERHYDRATION

Hyperosmolalic hyperhydration is characterized by increased osmolality of extracellular fluid, which is higher than that in the cells.

Causes:

- Forced intake of sea water. It happens when there has not been fresh water for a long time (for example, during sea and ocean catastrophes, when flying vehicles fall down into seas or oceans).
- Infusion of the solutions with increased concentration of salts into the organism without controlling their concentration in blood plasma (for example, in running remedial measures in patients with iso- or hypoosmolalic hypohydration, acid base equilibrium disturbances).
- Hyperaldosteronism, causing the excessive reabsorption of Na^+ in the kidneys.
- Renal failure associated with salt excretion decrease (for example, in "renal tubulo- and/or enzymopathy". The above-mentioned causes (as well as some others) account for the increase in the volume and the osmolality of extracellular fluid. The latter leads to cell hypohydration (as a result of fluid escape from the cell into extracellular space according to the osmotic pressure gradient). Thus, mixed (associated) dyshydria develops: extracellular hyperhydration and intracellular hypohydration.

Consequences and manifestations:

- Hypervolemia.
- Increased volume of circulating blood.
- Increased cardiac output, followed by its decrease in case of cardiac insufficiency development.
- Increased arterial blood pressure. Increased central venous blood pressure. All the above-mentioned signs of hyperosmolalic hypohydration result from the blood plasma volume increase.
- Brain edema.
- Pulmonary edema. The last two manifestations develop as a result of intracellular hyperhydration as well as the increased volume of intercellular fluid (edema) due to cardiac insufficiency.
- Hypoxia caused by cardiac insufficiency development, blood circulation disturbances and respiratory disorders.
- Mental disorders, caused by brain injury due to its edema, increasing hypoxia and intoxication of the organism.
- Powerful thirst developing as a result of blood plasma hyperosmolality and cell hypohydration. The additional supply of the organism with water under these conditions aggravates the patient's state.
- Hyperosmolalic syndrome. It occurs when blood plasma osmolality increases (most often due to excess Na^+ and/or glucose) above 300 mosm/kg H_2O (both in hyper- and hypohydration of the organism). This reveals the signs of cell hypohydration.

ISOOSMOLALIC HYPERHYDRATION

Isoosmolalic hyperhydration is characterized by the increased volume of extracellular fluid of normal osmolality.

Causes:

- Infusion of a great amount of isotonic solutions (for example, sodium chloride, potassium chloride, sodium hydrocarbonate).

- Insufficient blood circulation, resulting in the increased volume of extracellular fluid due to increased hemodymanic and filtration pressure in arterioles and precapillaries; decreased efficiency of liquid reabsorption in postcapillaries and venules.

- Increased permeability of microvessel walls which facilitates fluid filtration in precapillary arterioles (for example, in intoxication, some infections, toxemia of pregnancy).

- Hyperproteinemia, in which fluid is transported from the vascular channel into intercellular space according to the oncotic pressure gradient (for example, in general or protein starvation, hepatic insufficiency, nephritic syndrome).

- Chronic lymphostasis, in which the drainage of intercellular fluid into lymph vessels is slowed down. The enlisted factors alongside with some others cause the increase of circulating blood volume and intercellular fluid. The developing hyperhydration may be easily eliminated if the system of water metabolism regulation is in optimal condition.

Consequences and manifestations:

- Increased blood volume; its general and circulating fractions (oligocytemic hypervolemia).

- Increased arterial blood pressure, caused by hypervolemia, increased cardiac output and peripheral vascular resistance.

- Cardiac insufficiency development especially in prolonged hypervolemia. The latter causes cardiac overload (both with blood volume and increased vascular resistance).

- Edema development. It is based on ICMO- and lymphodynamic membranogenic and oncotic factors. Edema development may considerably aggravate the patient's state if edema develops in the lungs or in the brain.

THE MECHANISMS OF HYPERHYDRATION COMPENSATION

The general mechanism of hyperhydration compensation first of all appears to be diuresis stimulation, which is achieved in various ways including decreasing

vasopressin (ADH) synthesis and secretion. Compensatory reactions activated in hyperhydration are efficient in mild and moderate hyperhydration conditions. In its more severe forms drastic remedial measures are required.

HYPERHYDRATION ELIMINATION PRINCIPLES

- Etiotropic principle, most commonly applied in hyperhydration treatment, consists in eliminating or decreasing the severity and the length of the causal factor action (for example, the excessive infusion of fluid into the organism, renal failure, endocrine disorders, blood circulation insufficiency) and in many cases liquidates the signs of the organism's hyperhydration .

- Pathogenetic principle implies the disruption of the main links of hyperhydration pathogenesis.

To achieve this:

Excess fluid is excreted from the organism. For this diuretics of different action are commonly administered.

Either the disturbed ion balance is eliminated or its degree is decreased. This is based on the analysis of ion concentration in the patient's blood plasma as well as its osmolality. Having taken into consideration these factors, liquids containing the required concentration of particular ions are infused.

Blood circulation is normalized by optimizing cardiac activity , vascular tone, blood volume and its rheological properties. For this cardiotropic and vasoactive drugs, blood plasma and plasma substitutes are administered.

Symptomatic therapy involves eliminating the organism's changes which cause more severe hyperhydration (for example, pulmonary edema, brain edema, cardiac arrhythmia, attacks of angina, hypertensive reactions).

Edema

Edema is one of the most common forms of hyperhydration.

Edema is a typical form of disturbed fluid balance of the organism, which is characterized by the accumulation of excess fluid in intercellular space.

Kinds of dematous fluid:

Edematous fluid may be of various composition and consistency. It may be in the form of:

- Transudate, i. e. lacking protein (less than 2%) fluid.
- Exudate, i. e. rich in protein (more than 3 % sometimes as much as 7-8%) fluid, which frequently contains formed elements of blood.
- Mucus, which is the mixture of water and colloids of interstitial tissue, containing hyaluronic and chondroitinsulphuric acids. This kind of edema is called mucous edema or myxedema. Myxedema develops as a result of the deficit of thyroid gland hormones containing iodine.

EDEMA CLASSIFICATION

Edemas are classified according to their localization, the extent of their spread, the rate of their development and the basic pathogenetic factor of edema development.

- According to edema localization general edema (anasarca) and dropsy are singled out. Anasarca is the edema of subcutaneous cellular tissue. Dropsy is the edema of a body cavity (accumulation of transudate in it). Ascites is the accumulation of excess transudate in the abdominal cavity.

Hydrothorax is the accumulation of transudate in the chest. Hydropericardium is excess fluid in the pericardum cavity. Hydrocele is the accumulation of transudate between the folia of the testicular serous membrane. Hydrocephaly is excess fluid in the brain ventricles (inner dropsy of the brain) and/or between the brain and the skull - in subrachnoid or subdural space (outer dropsy of the brain).

- According to the extent of their spread local and general edemas are singled out.

Local edema (for example, in the tissue or organ at the point of inflammation or allergic reaction development). General edema is the accumulation of excess fluid in all organs or tissues (for example, hypoproteinemic edemas in hepatic insufficiency or nephritic syndrome).

- According to the rate of edema development instantaneous and acute development or chronic development are singled out. Instantaneous edema develops

within a few seconds after being affected (for example, after being bitten by insects or snakes). Acute edema normally develops within an hour after the causal factor action (for example, pulmonary edema in acute myocardial infarction). Chronic edema develops within several days or weeks (for example, nephrotic edema in time of starvation).

- According to the basic pathogenic factor hydrodynamic, lymphogenic, oncotic, osmotic and membranogenic edemas are singled out.

PATHOGENIC FACTORS OF EDEMA DEVELOPMENT

Hydrodynamic factor.

Hydrodynamic (hemodynamic, hydrostatic, mechanical) factor is characterized by increased efficient hydrostatic pressure.

1. Increased venous blood pressure.

2. General venous blood pressure increases in cardiac insufficiency due to its decreased contractile and pumping functions.

3. Local venous blood pressure increases when there is obturation of venous vessels (for example, with a thrombus or embolus) or when veins or venules are squeezed (for example, by a tumour, a scar, edematous tissue). 4.Increased volume of circulating blood (for example, in hypervolemia, polycythemia, water poisoning).

5.Tissue turgor decreases. Turgor decrease is an important factor, potentiating the mechanism of fluid filtration from the vessel into the tissue.

Mechanisms of action of lymphogenous (lymphatic) pathogenetic factor of edematization are different in dynamic and mechanical lymph insufficiency.

<u>*Dynamic lymph insufficiency.*</u> This mechanism of lymphatic edematization is caused by a considerable increase of lymphization. In this case lymph vessels seem to be unable to trasport considerably increased volume of lymph into general blood supply. The same features can be observed in hyperproteinemia in patients with nephrosis or hepatic insufficiency.

Mechanical lymph insufficiency. It is the so-called mechanical protection against the drainage of lymph through the vessels caused by their squeeze or obturation. In such cases one can observe considerable tissue edematization accompanied by an increase in size and mass. Edematization in the lower extremities is usually referred to as elephantiasis. In elephantiasis a leg can increase in size and mass considerably (up to 40-50 kg). The same process can occur in the upper extremities, genital organs and some other, quite often large parts of the human body. It is necessary to note that lymphogenous (lymphatic) edemas can cause accumulation of fluid rich in proteins (up to 3-4 g). One can also observe excessive formation of collagenous fibers and other elements of connective tissue that can cause deformation of organs and tissues.

Oncotic factor. The main peculiarities of the oncotic factor (hyperalbuminemic, hyperprogeinemic) are a reduction of oncotic blood pressure or/and an increase of oncotic pressure in the intercellular fluid.

Hyperproteinemia (mainly due to hyperalbuminosis as albumins are 2.5 times more hydrophilic than globulins) is often caused by:

1) Insufficient intake of proteins during starvation or protein deprivation;
2) Disorders related to cavity or/and membrane digestion (e.g. in cases of resection of intestinal fragments, dysbacteriosis, malabsorption);
3) Reduced synthesis of albumins in the liver (e.g. under the influence of hepatotropic poison, advanced cirrhosis);
4) Excessive loss of proteins in the body (e.g. in case of nephrosis excreted with urine, in extensive burns with plasma, in intestinal and stomach disorders with feces);

The factors which can cause increased *oncotic interstitial fluid pressure* are regional and they usually produce or potentiate local edematization. Hyperoncia of interstitial fluid can be caused by:

1. Excessive transport of blood proteins into intercellular space. It can be associated with increased permeability of the walls of small vessels
2. Escape of proteins of the cells into intercellular fluid in case of cell damage or destruction (e.g. in the focus of inflammation, ischemia, allergic reactions);
3. Increased hydrophility of protein micella in interstitial fluid.

- accumulation of excessive amounts of some ions in interstice (e.g. H+, K+, Na+);

- insufficient amounts of the ions of Ca2+;
- excessive amounts of such as histamine, serotonin;
- deficient amounts of thyroid hormones containing iodine.

Mechanism of action of the oncotic factor consists in reducing efficient oncotic absorptive force (as a consequence of hyperproteinemia or/and hyperoncia of the tissues). As a result, the volume of filtrated water from small vessels into interstitial fluid according to the gradient of oncotic pressure increases, whereas resorption of fluid from intercellular space into postcapillaries and venules decreases.

The osmotic factor of edematization consists either in increasing osmolality of interstitial fluid or in decreasing osmolality of the plasma, or in combining both processes.

Mechanism of action of the osmotic factor consists in excessive trasportation of water from the cells and vessels of the microcirculatory channel into intercellular fluid according to the gradient of osmotic pressure (higher in interstice). This mechanism is considered a component of pathogenesis in cardiac, nephritic, hepatic and other edemas. In the above-mentioned edemas the volume of extracellular fluid increases.

The membranogenic factor is characterized by a considerbale increase in the permeability of the vessel walls in the microcirculatory channel for water, fine-molecular and macromolecular substances (proteins are most significant)..

Mechanisms of action of the membranogenic factor of edematization.

1) Facilitation of water filtration. In this relation the drainage of fluid from the blood and lymph into interstitial space increases. On the other hand, this mechanism is balanced with increased water reabsorption in the venous part of capillaries related to thinning of their walls.
2) Increased amounts of protein molecules from small capillaries into interstitial fluid. On the one hand, it can lead to decreased oncotic pressure of the plasma and lymph but, on the other hand, it leads to the development of hyperoncia of intercellular fluid. Due to the increased permeability of the walls of small capillaries the fluid passes into intercellular space according to the gradient of oncotic pressure. It is this process that underlies edematization of the tissues in

case of inflammation, local allergies, stings, poisonings, effect of pure oxygen, and especially when atmospheric pressure is high.

In practice, edematization which developed under the influence of one of the mentioned pathogenetic factors is not very common. In other words, there are no monopathogenetic edemas. Thus, in each case of edematization one can distinguish:

- initial (primary) pathogenetic factor in the patient;
- secondary pathogenetic factors.

EDEMAS DUE TO CARDIAC INSUFFICIENCY

Risk factors associated with edematizaton are as follows:

- cardiac insufficiency (i.e. state in which a person´s heart does not supply organs and tissues with the amount of blood necessary for their functioning and maintaining plastic processes). Cardiac insufficiency is characterized by lower (compared with normal) of cardiac output and primary circulatory hypoxia.

Initial pathogenetic factor is a hydrodynamic factor.

Sequence and significance of pathogenetic factors of edematization are different depending on the dynamics of blood circulation disorders and their complications. Pathogenesis of a cardiac edema includes all of the mentioned factors:

- Decreased cardiac output. Reduced volume of circulating blood
- *Activation of baroreceptors in the walls of blood vessels.*
- Narrowing of the arterioles of the cortical substance of kidneys.
- Increased blood supply in the medullary substance of kidneys.
- Increased reabsorption of Na^+ in venal tubules of kidneys which can lead to hyperosmia of the blood.
- *Activation of osmoreceptors.*
- Increased synthesis and release of antidiuretic hormone in the blood.
- Increased water reabsorption in kidneys.
- Increased efficient hydrodynamic pressure.
- Activation of water filtration in the arterial part of the capillaries accompanied by inhibition of water reabsorption in the venous part of small capillaries. Reduced

flow of blood in the vessels of kidneys. The main cause is decreased cardiac output.

- Activation of the system renin-angiotensin-aldosteron.
- Increased reabsorption of Na+ in the venal tubules of kidneys.
- Systemic increase of the venous blood pressure both in great and peripheral venous blood vessels.
- Slackened drainage of lymph from tissues which results in developing mechanical lymph insufficiency.
- Increased volume of interstitial fluid, i.e. rate of edematization.
- Disorders related to the drainage of osmotically active substances (e.g. ions, inorganic and organic compounds) caused by venous hemostasia (i.e. venous hyperemia) and lymph insufficiency.
- Increased amounts of metabolites (e.g. lactic acid, pyroracemic acid, peptides, amino acids) caused by metabolism disorders in case of hypoxia.
- Activation of non-enzymic hydrolysis of the components of basement membrane in the walls of the vessels. It can also lead to an increase of their permeability.
- Increased formation and activation of which provide the increase of permeability in the walls of small vessels (e.g. histamine, serotonin, kinin, separate factors of the complement).
- Increased escape of proteins from the blood into interstitial space.
- Disorders related to beloxynthetic function of the liver which can lead to hyperalbuminosis.
- Reduced efficient oncotic absorptive force.
- Increased outflow of water from small capillaries into intercellular space according to the increased gradient of oncotic pressure.

Hence, edematizaton occuring in case of cardiac insufficiency is the result of a combination of all pathogenetic factors such as hydrodynamic, osmotic, oncotic, membranogenic and lymphatic ones.

PULMONARY EDEMAS

Risk factors of pulmonary edematization are as follows:

1) Cardiac insufficiency (both left ventricular or general

Mechanisms of action

- Initial and basic pathogenetic factors are hemodynamic factors. They are characterized by:
- Reduced contractility of the myocardium of the left ventricle.
- Increased systolic residual volume of the blood in the left ventricle.
- Increased end-diastolic volume and pressure in the left ventricle of the heart.
- Increased blood pressure in the vessels of the pulmonary circulation (higher than 25-30 mm Hg).
- Increased efficient hydrodynamic pressure. If it exceeds efficient oncotic absorptive force, transudate passes into intercellular space of the lungs (interstitial edematization may develop).

2) Pulmonary edemas developing under the influence of toxic substances.

Membranogenic factors which can be associated with increased permeability of the walls of small vessels are regarded as the initial and basic pathogenic factors.

The causes can be related to:

a) Toxic substances (e.g. poisonous substances like phosgene);

b) High concentration of compressed oxygen. The experiment has shown that if the pressure is higher than 350 mm Hg one can develop pulmonary edemas and bronchial hemorrhage. The use of 100 % oxygen in the experiment can bring about advanced interstitial and alveolar edematization accompanied by the symptoms of destruction of endothelium and alveolocytes. Thus, to treat hypoxia one should use gaseous mixtures containing 30-50% oxygen. It is sufficient for maintaining required exchange of gases in the healthy lungs.

Factors which can lead to the increase of permeability of the walls of the vessels under the unfluence of toxic substances are as follows:

1) Acidosis which can cause non-enzymic hydrolysis of the ground substance in the basement membrane of small vessels;

2) Increased activity of hydrolytic enzymes.

3) Formation of ducts between rounded impaired cells of endothelium.

KIDNEY EDEMAS

Various forms of kidney pathology are usually accompanied by more or less marked edematization. Initial pathogenetic factors are different in patients with nephritis and nephrosis.

Edemas developing in nephrosis.

Nephrosis is a pathology of kidneys of primarily non-inflammatory genesis. Nephrosis is characterized by diffuse destruction of the parenchyma of kidneys. The causes of nephrosis can be related to: 1) primary impairment of kidneys (e.g. focal glomerulosclerosis); 2) secondary modification of nephritic tissue (e.g. in diabetes mellitus, immunopathologic states, amiloidosis, intoxication caused by).

The initial pathogenetic factor of edematization is oncotic factor.

Risk factors of kidney edematization are as follows:

1) Increased permeability of the membranes of nephritic glomerules for the proteins. In this case, the blood loses not only albumins but also globulins, transferrin, haptoglobin, peruloplasmin and some other proteins.

2) Disorders related to reabsorption of proteins in venal tubules of kidneys.

All of the above mentioned blood disorders lead to considerable changes in the content of proteins in the body.

Main links of pathogenesis

Protein losses with urine (i.e. proteinuria).⇒ Daily protein losses in patients with nephrosis can reach 35-55 g/l (normally, utilization is no more than 50 mg). ⇒ Reduced concentration of proteins in the plasma (i.e. hypoproteinemia). Protein levels can drop up to 20-25 g/l (normally it should be 65-55 g/l).⇒ Decrease of efficient oncotic absorptive force. ⇒ Increase of water filtration in small vessels and accumulation of excessive water in intercellular space and body cavities (i.e. edema). ⇒ Squeeze of lymph vessels by edematous tissues caused by the development of mechanical lymph insufficiency and increase of edematization. ⇒

Reduced volume of circulating blood (i.e. hypovolemia). ⇒ Activation of vascular baroreceptors which provide increased Na+ reabsorption in venal tubules of kidneys.

⇒ Reduced flow of blood in kidneys caused by hypovolemia which activates the system "renin-angiotensin-aldosteron". It potentiates reabsorption of Na+ in kidneys. ⇒ Increase of Na+ in the plasma (i.e. hypernatriemia). It activates osmoreceptors. ⇒ Stimulation of synthesis in neurons of hypothalamus and excretion of antidiuretic hormone into the blood. ⇒ Activation of water reabsorption in renal tubules. ⇒ Increase of efficient hydrostatic pressure in small vessels of tissues which potentiates accumulation of trasudate in interstitial space. Besides, transportation of water from the vessels of the microcirculatory system into interstice provides intensive hypovolemia and lymph insufficiency.

Thus, during nephrotic edematization pathogenetic factors potentiating edematization are combined. In nephrotic edematization oncotic, hydrostatic and lymphatic pathogenetic factors usually participate.

Edemas developing in patients with nephritis.

Nephritis is a disease which is characterized by diffuse impairment of kidneys of primarily inflammatory or/and immunoinflammatory genesis.

Nephritis can be caused by: disorders of blood circulation in kidneys (more often ischemia) in patients with inflammatory or immunoinflammatory diseases such as chronic diffuse glomerulonephritis. In this case, nephritic tissues (including vessels of kidneys) can be squeezed by inflammatory exudate. The rigid capsule of the kidney is . Therefore, even small amounts of exudate can cause the squeeze of its parenchyma. It can result in the disorders of blood supply of kidneys including the cells of juxtaglomerular apparatus.

The initial pathogenetic factor is a hydrostatic factor (due to reduced blood supply of the cells of juxtaglomerular apparatus).

Links of pathogenesis

Stimulation of synthesis and excretion of renin into the blood by the cells of juxtaglomerular apparatus.⇒ Production of angiotensin in the blood under the influence of renin which is converted into angiotensin II with the help of angiotensin-

converting enzymes. This process usually takes place in the lungs and walls of the vessels. A small portion of angiotensin II converts into angiotensin III.

Stimulation of angiotensin II and, to some extent, angiotensin III provides excretion of aldosteron by the cells of glomerular zone of the adrenal cortex. ⇒

Increased reabsorption of Na+ in venal tubules of kidneys is associated with the development of hypernatremia.⇒ Activation of osmoreceptors is usually accompanied by excretion of antidiuretic hormone into the blood. Increased water reabsorption in renal tubules is associated with the development of hypervolemia. ⇒ Increased efficient hydrostatic pressure which can cause increased fluid filtration in the arterial part of capillaries and inhibition of water reabsorption in the venous part of capillaries.

Edema is an accumulation of excessive interstitial fluid. Reduced volume of glomerular filtration accompanied by potentiating hypervolemia can result in a decrease in the number of functioning nephrons damaged during glomerulonephritis. The most common increased permeability of the walls of vessels is usually referred to as generalized capillaritis. It makes the process of transportation of proteins and water into interstice as well as reabsorption of fluid in kidneys much easier. Generalized capillaritis can be caused by: formation of the basement membrane of nephritic glomerules. They destroy not only basement membranes of glomerules but also basement membranes of small vessels having similar antigens.

Increased permeability of glomerular filter for proteins (i.e. proteinuria). Development of hyperproteinemia. Reduced efficient oncotic absorptive force which can provide the enlargement of edema. Thus, in nephritic edematization one should take into consideration the following factors: hydrodynamic, oncotic, membranogenic ones.

PATHOGENIC AND ADAPTIVE ROLE OF EDEMAS

Pathogenic role of edemas includes a mechanical squeeze of the tissues.

Complications of the squeeze can be as follows:

1) Disorders of blood formation and lymphization caused by the squeeze of the vessels. The flow of blood and lymph is impaired mainly in the vessels of microcirculatory channel (it is usually accompanied by the development of ischemia, venous hyperemia, blood stasis, lymphostasis), though in case of accumulation of

edematous fluid in some cavities of the body (e.g. in ascites, hydrothorax, in pericardial cavity) great vessels and even the heart can be squeezed.
2) Emergence of painful sensations due to extension or/and displacement of the tissues and nerve endings.

Metabolism disorders in blood and cells accompanied by the development of dystrophy.

The causes are as follows: 1) Increase of the distance between the capillary and the cells caused by excessive water in intercellular space; 2) Thickening of the walls of vessels (in case of edematization).

Excessive growth of cellular and noncellular elements of the connective tissue in the area of edematization (sclerosis).

The causes are as follows: 1) Influence of growth factors excreted by the damaged and nondamaged cells of the tissues in the area of edematization; 2) Influence of metabolites which are released from alternating cells of the edematous tissue.

Mechanisms of development

a) Proliferation of fibroblasts of the connective tissue in the area of edematization.

b) Increased synthesis of collagen by the cells. Extracellular fibrillogenesis.

Frequent infections in the area of edematization.

Frequent infections can be caused by: 1) Ischemia of the tissue in the area of edematization caused by the squeeze of arterioles; 2) Venous hyperemia in the edematous tissue caused by the compression of veins and venules.

Ischemia and venous hyperemia can often lead to hyperoxia, disorders of energy supply of the functioning and plastic processes occuring in the edematous tissues.

Mechanisms of realization

Inhibition of immune mechanisms and nonspecific protective factors of in edematous tissues.

Hypohydration of cells.

Psychoneurological disorders (e.g. in case of brain edema). Fever. Acid-base equilibrium disorders.

Causes of disorders

1) Metabolic disorders of salts and ions of Na+, K+, Cl, HCO3 in the cells and intercellular fluid. For example, the development of secondary aldosteronism in cardiac and renal edematization can lead to accumulation of excessive Na+ in the cells. Such cells usually develop alkalosis.

Functioning disorders of separate vital organs.

1) Disorders which can be fatal. For example, brain edemas, pulmonary edemas, renal edemas, hydropericardium and hydrothorax have a deleterious effect on the functioning of the respective organs, and they can be fatal for the patients.

Adaptive role of edemas. The adaptive role or adaptive significance of some reactions or processes developing in edematization consists in:

1) Reduced content of pathogenic substances in the blood as they are transported into edematous fluid (e.g. excessive ions, normal metabolic-waste products and abnormal metabolic-waste products, toxins in case of kidney, hepatic and cardiac edemas).

2) Low concentration of toxic substances which can damage the cells in edematous fluid (e.g. in allergic, inflammatory and toxic edemas). Edematous fluid dissloves toxic substances.

3) Prevention from the spread of toxic substances from the area of pathologic process or reaction throughout the body. Good examples are edemas developing in the focus of inflammation, local allergies, toxic substances. In this case edematous fluid causes the squeeze of lymph vessels and venous blood vessels. Thus, it prevents from the spread of pathogenic agents, toxins, metabolic-waste products and microorganisms throughout the tissues, organs and in the human body.

TREATMENT OF EDEMAS

The main methods of treating edemas include eryotropic, pathogenetic and symptomatic principles of managing edemas.

The pathogenetic method of managing edemas consists in blocking initial and some other factors of edematization. Efficient hydrostatic pressure can be normalized

by reducing increased venous blood pressure (e.g. diuretics, cardiotropic drugs, venous blood dilators) as well as by reducing the volume of circulating blood (e.g. diuretics, bloodletting).

One can treat blood hyperosmia and hypervolemia with some drugs blocking the system "renin-angiotensin-aldosteron". For this purpose one should use ß-adrenoblockers which provide a decrease of secretion of renin by kidneys; spinolactones which inhibit the effect of mineralocorticoids; blockers preventing excess aldosteron.

Lymph insufficiency can be treated by: 1) normalization of lymph levels (e.g. reduced volume of circulating blood). It can lead to reduced mechanical lymph insufficiency.

Preventing the drainage of lymph (e.g. thrombuses, cicatrices, tumors, stenosed lymph vessels). It can also lead to eliminating mechanical lymph insufficiency.

Efficient oncotic absorptive force is normalised by: 1) managing hyperproteinaemia (e.g. parenteral administration of solutions containing proteins, management of hepatic insufficiency or malabsorption).

Excessive oncotic pressure of interstitial fluid can be decreased by: 1) decreasing permeability of the walls of vessels for proteins with the help of steroid hormones; 2) elimination of inflammatory, allergic and other unfavourable reactons accompanied by the escape of proteins from damaged cells and/or an increase in their hydrophylity.

Efficient osmotic factor of edematization can be eliminated or alleviated by: 1) Managing tissue hyperosmia (e.g. normalization of the drainage of intercellular fluid through small vessels; management of pathological processes accompanied by the escape of osmotically active substances from damaged or destroyed cells; elimination of hypoxia and acidosis).

Normalization (increase) of osmolality of the plasma is usually treated by: 1) administration of physiological saline solutions of sodium (Na), potassium (K) and some other ions; 2) administration of the plasma and plasma substitutes.

Permeability of the walls of small vessels mainly for proteins and fluid, can be normalised by: 1) Eliminating or reducing hypoxia (e.g. management of cardiac, hepatic or pulmonary insufficiency, anemias).

Management of anemias. Anemia is usually treated either with buffered solutions or by managing hepatic or renal insufficiency. It can also be achieved by blocking the

factors which damage the cells of endothelium and/or extending the walls of small vessels (e.g. reducing venous blood hyperemia, lymphostasis, vasculitis).

The symptomatic factor is aimed at managing pathological processes, symptoms and reactions which make the patient feel even worse. It can be achieved by: 1) reducing hypoxia in pulmonary edematization; 2) liquidation of ascitis in cardiac insufficiency or portal hypertension; 3) elimination of excessive edematous fluid from pleural or articular cavities.

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Shock

Definition of shock and its criteria

Shock proper can be considered neither a symptom, nor a disease, nor a syndrome, it can't be considered separately from nosological notions, known in clinical practice and associated with certain lesions. Shock is a continuos pathologic systemic manifestation, which arises at the moment, when the power and the time of

action of primary lesions exceed the 'shock threshold' when a haemorrhage becomes a hemorrhagic shock, sepsis becomes a septic shock, a muscularskeletal trauma becomes a traumatic shock and so on. A generalized reaction appears.

At present, more than a hundred pathologic circumstances, which may bring about shock, are known. But in all types of shock the result is 'incongruous perfusion of tissues' which immediately affects 'incongruous cell metabolism', no matter what primary mechanism induced shock.

The attempts to define shock resulted in singling out a number of repeated elements, the so-called *shock criteria*:

1. A time interval necessary for a bodily general reaction and, for general mobilization of energetic and genetic mechanisms of the organism to start.
2. Anatomic and functional integrity (at least at the beginning) of the central neuroendocrine system, i.e. as a 'manager' able to transmit a reaction conveying the power of shock throughout the whole organism. As a rule, skull injuries and primary comatose states are not accompanied by shock; previous exhaustion of the neuroendocrine systems (in case of a skull injury) and enzymatic chains of cells (in case of acute poisoning) arises only after a weak general reaction starts, and a lethal outcome sets in before a real condition of shock takes place.
3. Decreased efficient volume of the circulating blood.
4. Onset of cell metabolism disturbance.
5. Potentially lethal character of lesions and their tendency to be self-supportive and irreversible.
6. Therefore, shock proper is not a cause of death; in fact, the same cause which induced a shock condition is the final cause of death, i.e. shock is one of the evolutionary possibilities of the organism directed towards death. In other words, shock is one of the most heroic ways in the struggle of the human organism against death.

Shock is a special conflicting condition of the organism homeostasis involving the loss of hemorheological and metabolic balance with a natural tendency to self-deterioration.

Shock is a generalized reaction of the organism. The ways of this generalization under the influence of a shockogenic factor are as follows:

1. The CNS (central nervous system) – connecting the organism with the environment.
2. The vegetative nervous system – spreading a shock reaction by means of mediators – acetylcholine, catecholamines.
3. The endocrine system.
4. Cell enzymatic system.
5. The cell genome.

There is a structural, functional and pharmacological interaction between these systems. Their integration is provided by a genetic code of each cell. Shocks of any aetiology have a number of pathogenic characteristics in common. They are:

1. Decreased volume of circulating blood volume (VCB) in combination with increased vessel resistance owing to catecholamines.
2. Hypoxia, lacticemia.
3. Rheodynamic disturbances.
4. Cell hypoxia, deficient energy genesis which is followed by accumulation of waste materials and acidosis.
5. Emergence of necrosis loci.
6. Damage of a cell nucleus, impairment of DNA-chains and irreversible disorganization of cells.

Classification.

1. An erectile phase.
2. A torpent phase.
3. Death – an agony phase.

Or: 1. A reversible shock – early, late and stability shock

2. An irreversible shock.

General pathogenesis of shock. Principles of diagnostics

According to its power, length and affected topographic area, shock passes two almost simultaneous stages – an intracellular stage and an extracellular one.

An *extracellular stage* involves all changes of the neuroendocrine regulation as well as those of circulation of systemic fluids (microcirculation, lymphatic circulation and interstitial circulation).

An *intracellular stage* quickly joins the previous stage owing to the information delivered by nervous impulses, which pass through cell membrane and reach the terminal points inside the polinucleotide chain of the genetic code. This stage involves all changes of intracellular regulation of enzymatic processes.

Shock is triggered by *excessive afferent impulses*. Moreover, it can be either painful (trauma) or painless (due to the stimulation of organ and tissue receptors as a result of blood circulation impaired by hypoxia, metabolism disturbances).

Excessive information, especially painful one, passes through different afferent tracts and reaches different parts of the brain (the reticular formation, hypothalamus, cortex). It stimulates their defense reactions, whose power becomes excessive. This entails emergency mobilization of skeletal muscles, a manifold increase in the activity of non-specific adaptation systems such as sympathoadrenal and hypophysial-corticoadrenal systems involving the relevant peripheral effects. It also involves secretion of neurohypophysial hormones and enzymatic substances (glucose and fatty acids) in the blood.

On the other hand, the bodily functions, which don't contribute to the survival of the organism are urgently inhibited in these conditions (alimentary, reproductive, proliferative, excretive systems, etc.).

The listed phenomena result from the vasoconstriction of peripheral vessels. A spasm arises due to the activation of α-adrenal vascular receptors including those in precapillary sphincters. A part of the organism is deprived of the blood. The skin and kidneys, splanchnic circulation and later skeletal muscles, in which β-adrenal receptors prevail, become 'sacrificed'. The spasm of vessels doesn' t affect the

circulation of the coronary, cerebral, hypophysial, thyroid areas as well as the adrenal cortex and diaphragm. The first consequence of spasm is mobilization of blood in the central vessels and shunting of some organs and tissues. Both resistive (arterial) and capacitive (venous) vessels, in which normally about 80% of blood is concentrated, undergo spasms. Spasms start in lymphatic nodes and blood vessels simultaneously. This results in VCB being filled with lymph whose volume reaches 2 – 4 litres. The vasoconstrictive reaction at the level of microcirculatory channel is a real 'autotransfusion' and it is the cause of blood circulation centralization, when blood from arterioles passes to the venous section through arteriolovenular anastomoses, avoiding the capillaries of 'sacrificed' organs. The heart, the brain and the liver are better supplied with blood because of the circulation centralization.

In case of a *cardiogenic shock* the primary problem is decreased myocardium contractility and cardiac output which may be caused by myocardial infarction, arrhythmia, defects of valves and tamponade. In this case a decrease in blood pressure is accompanied by a decrease in the stroke volume, which is registered by the baroreceptors of the aorta, while the activity of sympathetic nervous system increases. This leads to a higher heart rate and the vasoconstriction of the peripheral organs with a simultaneous increase of tone of the venous system and arterioles, which is accompanied by a rise in the blood pressure.

In case of a *hypovolemic shock* the primary insufficiency of the volume of circulating blood leads to the decreased cardiac output. The next reaction develops similarly to that of a cardiogenic shock. The differences between these kinds of shock are conditioned by the pressure of the filled left ventricle in the diastole: in case of a cardiogenic shock it increases, and in case of a hypovolemic shock it decreases.

In case of the *shock caused by vasodilation* a fall of arterial pressure is conditioned by a primary decrease in the peripheral resistance.

In case of a *septic shock* arteriovenous shunts, through which blood passes from the arterial to the venous channel (avoiding capillaries) open at once under the influence of endotoxins. The organism reacts by increasing the cardiac output which

involves higher heart rate and stroke volume. It is a *hyperdynamic reaction.* It can be interpreted in the following way: the organism tries to send to the periphery as much blood as it can to compensate the damage. At later stages the arterial pressure falls because of the volume deficiency and cardiac insufficiency.

In case of an *anaphylactic shock* the vessels lose their tone under the influence of histamine; peripheral resistance decreases sharply and the arterial pressure decreases. Both peripheral or volume vessels lose their tone. The accumulation of blood in capillaries and veins leads to a relative deficiency of circulating blood volume and decreased stroke volume. A sympatho-adrenal reaction doesn't develop here, as it is impaired in response to sympathetic irritation, thus, causing the dramatic development of an anaphylactic shock.

The main changes of hemodynamic indices in hypotonia developing according to cardiogenic, hypovolemic and vasodilator types are presented in Table 1.

Type of hypotonia	Hemodynamic changes		
	Peripheral	Cardiac output	CPPA
Cardiogenic	High	Low	High
Hypovolemic	High	Low/normal	Low
Vasodilator	Low	Low/normal	Low

Higher heart rate due to the stimulation of β-adrenal receptors resulting in increased stroke volume and minute circulatory volume are observed in this period. Therefore, the arterial pressure increases due to increased general peripheral resistance and minute circulatory volume. The speech and motor activity of a patient reflect the activation of the cortex in this period. This period of shock is called an *erectile phase* or an *early reversible shock.*

Therefore, neuroendocrine mechanisms may act as triggers in the pathogenesis of shock.

Carbohydrates, proteins and lipids from food or preserved in the body are used as energy substrates both in case of normal metabolism and in case of shock. Glycogen makes up only 1% of all energy reserves in the organism, but is of crucial

importance for brain nourishment and short intensive work of muscles in critical situations. The brain adapted to the use of glucose and keton bodies as substrates.

In case of shock the concentration of glucose in blood increases due to gluconeogenesis from substrates of anaerobic metabolism (lactate) and proteolysis (alanine and other amino acids). Gluconeogenesis is stimulated by increased amount of stress hormones – catecholamines, hydrocortisone, somatotropine, glucagon in blood. In a critical situation the liver plays an important role in maintaining glucose homeostasis (see Fig.1). In the liver glucose forms from glycogen as well as from glycerine (coming from adipose tissue) and lactate and amino acids (coming from muscles). Muscular glycogen can't be directly transformed into glucose because of the lack of gluconeogenesis enzymes in muscles. The liver and kidneys, to some extent, supply glucose-dependent tissues such as the CNS and peripheral nervous system, leucocytes, erythrocytes, spinal cord, medullar layer of the kidneys and intestine with glucose.

Protein metabolism is balanced by proteolysis and synthesis of new proteins. Protein metabolism changes significantly in case of shock: proteolysis in muscles increases abruptly, amino acids get from muscles to the liver and intestines. They act as substrates of gluconeogenesis and synthesis of acute phase proteins. Cytokines play an important role in changing protein metabolism (see Fig. 2). The synthesis of the acute phase proteins is stimulated in the liver, its main activators are interleukin 1, interleukine 6, tumour necrosis factor, hydrocortisone and glucagons (see Table 2).

The condition of reactivity determines the shock threshold and its course.

There may be specific and group reactivity. The role of the specific reactivity may be examplified with an anaphylactic shock. Only higher animals may have it, while lower animals may not. The following factors underlie specific reactivity: sex, age, constitution, condition of the body systems (immune, endocrine, nervous systems). No doubt, special reactivity depends on the sex. Thus, men are more tolerant to pain; the female organism is more tolerant to hypoxia and blood loss that

leads to the development of shock at different levels of damage. It is necessary to mention that the female reactivity changes depend on menstrual cycle, pregnancy.

The role of age in shock development is undoubted. An early child age is characterized by low reactivity due to incomplete development of the nervous, endocrine and immune systems, imperfect external and internal barriers. The highest reactivity is registered at a middle age, gradually decreasing by an old age. The research of V.V. Arshavskaya proved the fact, that the severity course and outcome of a shock depend on age in the experimental way.

For example, the exposure of the extremity of adult rabbits to the electric current causes the condition of violent shock, which in most cases is lethal.

The stimulation of the hind extremity of a newborn rabbit by the electric current of high power, i.e. of the same voltage as in the 1st experiment, causes a 1- 2-minute summarized motor reaction, which stops later and when the stimulation is longer (for 2 – 3 hours) the little rabbit moves normally. But, on the other hand, the experiment on dogs involving blood loss showed that the defence mechanisms of adult dogs are quickly activated and blood circulation becomes centralized, while defence mechanisms in puppies are not yet developed and the loss of relatively small amounts of blood may be lethal.

Besides, an anaphylactic shock starts developing at the moment when chemoreceptors of the sinocarotid zone are involved.

The role of constitution in shock development can be proved statistically. For example, cardiogenic and repale shocks often occur in hypersthenic people. Hyposthenic people are very sensitive to blood loss, that's why they are more subject to shock in case of blood loss unlike hyperstenic people.

The role of the nervous system can be proved by the fact, that the differences in its functioning determine the character of shock phases. For example, a choleric person has a more noticeably marked erectile phase of shock, while in a melancholiac person an erectile phase is more smooth and less marked.

Stress may play a different role in shock development. Depending on the phase of stress, when a stimulus acts, (an alarm phase or an emaciation phase), the severity, course and the terms of shock development may change. Previous diseases (radiation sickness, anemia, starvation) decrease the organism's tolerance to shock.

The factors determining the low tolerance of a child's organism to blood and other losses are as follows: high level of liquid – up to 70% of all volume per 24 h, higher heart rate, less efficient regulation of vessel tone due to the prevalence of sympathetic influences, the lability of thermoregulation. In case of shock reactivity changes being depressed in relation to infections and other morbific influences. Phagocytosis is depressed, sensitivity to drugs changes.

In conclusion, we shall give a short description of differential diagnostics of several shock conditions:

1. Syncope which is a temporary loss of consciousness as a result of insufficient blood flow to the brain (cardiac rate disturbance, stimulation of the carotid sinus, pulmonary embolism). The action of the vagus nerve prevails (in case of shock sympathetic innervation prevails).
2. Fainting is considered as a symptom and consists in incomplete transient loss of consciousness accompanied by decreased tone of muscular vessels of low extremities and bradycardia. In case of shock a person may have tachycardia, cool sweat, loss of consciousness or may go pale.
3. Coma is a partial or complete loss of consciousness when vegetative functions are normal and the correlating functions are depressed in case of primary brain lesions such as hypoxia, acidosis; it can occur at the final stage of shock.
4. Collapse occurs either in case of a sudden decrease of the content of vessels (haematogenic collapse) or in case of sudden dilation of vessels (vasomotoric collapse). Collapse is a sign of a haemodynamic disturbance between the lumen of vessels and the volume of blood in them. In case of shock

circulation becomes centralized, it can be treated with vasodilators while collapse is treated with vasoconstrictors.

The acute phase proteins are fibrinogen (which is necessary for haemostasis), α_2-macroglobulin, α_1-antitrypsin (the inhibitors of the systemic proteases), hepatocuprein (it removes the free radicals), C-reactive protein (it participates in opsonisation of bacteria, activation of the complement system and phagocytosis). Interleukin-1 and tumour necrosis factor suppress albumin synthesis in the liver. It is important because albumin synthesis requires most of amino acids as energy substrates to form acute phase proteins in the state of shock.

Table 2. The metabolic effects of cytokines in the state of shock

Tumour necrosis factor, interleukins-1, 6	- activation of lipolysis and increase of triglycerides in the plasma; - decrease of albumin synthesis in the liver; - increase of oxygen consumption; - activation of the metabolic processes; - increase of sequestration of amino acids by the liver; - increase of proteolysis in skeletal muscles; - activation of synthesis of the acute phase proteins in the liver; - decrease of albumin synthesis in the liver; - stimulation of insulin and glucagon secretion from the pancreas.

In critical conditions lipolysis in adipose tissue intensifies, being stimulated by hydrocortisone, catecholamins and glucagon. Besides, fatty acids and glycerin are formed from triglycerides. Fatty acids turn into ketone bodies through acetyl-CoA. However, ketosis is clearly marked as in this state the insulin level is often increased, besides, ketones are actively consumed by the heart and other organs as energy substrates of the CNS. Sometimes fatty hepatosis occuring in critical conditions can

be conditioned by high concentration of fatty acids in the cytosol of hepatocytes when their oxidation in the mitochondria is inhibited.

In case of oxygen deficit tissue metabolism changes from aerobic to anaerobic one. Moreover, pyruvate transforms into lactate and doesn't oxidize into carbon dioxide and water in the tricarbonic acid cycle. Increased lactate in blood is an indirect sign of inadequate oxygen supply of tissues. Blood tests showing the content of lactate, pyruvate, their proportion and lactate dehydrogenase activity are especially informative in the first 10 – 12 hours of a patient's stay in an intensive care unit. In the group of patients in the state of shock an increase of lactate above 5.7 mmole/litre resulted in 100% lethality (Shoemaker et al., 1993). In case of continuous hypoxia tests for lactate becomes of little significance due to the damage of cells and severe disturbances of cellular metabolism.

The evaluation of clinical significance of the physiological parameters of patients in a critical condition revealed that the most important parameters for predicting the survival rate are circulating blood volume (CBV) and cardiac index (CI), the second important parameters are oxygen transport to tissues (TO_2) and oxygen consumption by tissues (CO_2). At the same time such popular indices of oxygen metabolism as oxygen tension (PO_2) and saturation of haemoglobin with oxygen (SO_2) are of relatively small clinical significance for predicting the clinical outcome for patients in a critical condition (Tab. 3).

Table 3. The clinical significance of the physiological parameters for patients in a critical condition

in the order of their predictive value for the survival rate

Vital parameters	Level
Blood volume: for men	> 2,7 L/m^3
for women	> 3,0 L/m^3
Cardiac index	> 4,5 L/m^3
Oxygen transport to tissues (TO_2)	> 550 mls/min/m^3

Oxygen consumption by tissues (CO_2)	> 167 mls/min/m^3
Normal arterial pressure	< 20 mm Hg
Pressure of the pulmonary artery locking	< 250 dyne*s*cm^{-5}
(PPAL)	> 9,3 kPa (70 mm Hg)
Resistance in the pulmonary vessels	> 90%
C_aO_2	> 7,3 and < 7,5
S_aO_2	> 4,0 kPa (30 mm Hg)
pH	
P_aO_2	

The perspective research showed that in the group of patients whose vital parameters in critical conditions were maintained at the level indicated in Table 3, lethality was 13% in the post-resuscitation period, in the group of patients with uncontrolled laboratory-functional parameters it was 48% (Gosling et al., 1994).

Consequences of shock

If the organism goes safely through the phase of early reversible shock, it may survive. However, if it fails, the power of lifesupport systems, first of all, blood circulation and respiratory system, begins to decrease.

The continuous afferent impulsation from the point of a trauma is coupled with the stimulation of the receptors of internal organs, which results ~~from~~ developing hypoxia and the formation of products of disturbed metabolism, the so-called stimulators of the 2nd order. The accumulation of the biologically active substances (BAS) in blood – histamine, kinins, prostaglandins, acetylcholine, etc. – directly induces a decrease of excitability of different cerebral structures. The inhibition processes develop. The biological implication of this inhibition consists in maintaining energy homeostasis of the CNS as an organ by blocking its outward activity partially or fully, which, in its turn, substantially reduces the range of adaptive resources of an organism, but, to a large extent, saves energy, preserves vitality, prolongs vital activity of the brain.

Depressed regulating function of the CNS is one of the causes of a decrease in systemic arterial pressure. For example, at this stage early weakened or perverse sinocarotid pressor reflexes or even their disapperance are registered.

The BAS are of special importance in disturbing systemic hemodynamics and microcirculation. Damaged cells secrete prostaglandins, thromboxans and leukotrienes. The destruction of cells can activate the complement; lysosomal proteolytic enzymes as well as thromboplastin are released from the cells. All this leads to the activation of the proteolytic systems – kallikrein-kinin system, complement system, blood coagulation system, fibrinolysis. The activation of the complement cascade is accompanied by the formation of anaphylatoxins (C3a, C4a, C5a), which activate leucocytes and result in the formation of aggregates and microemboli; they adhere to the capillary endothelium causing its damage. The impaired integrity of endothelium, in its turn, causes the activation of leucocytes and a release of chemotoxins from them (thrombocyte-activating factor, leukotrienes). These and other inflammatory mediators condition shock local reactions; they can cause serious disturbances of the functions of organs and tissues, development of polyorgan insufficiency and death of an organism. It is very difficult to reveal the sequence and a range of these reactions; it is very difficult to reveal the dominant mechanism of damage. At present there are some data proving that shock development involves endomorphines, at least 9 myocardium-depressing factors and lysosomal cathepsines. The effects of tumour necrosis factor and interleukin-1 releasing from monocytes are primary in a septic shock.

In tissue ischemia the phenomenon of aggregation of leucocytes (neutrophils) was described not long ago. This phenomenon is especially significant for the pulmonary damage caused by shock and for developing a hemorrhagic shock. In a hemorrhagic shock treatment with antibodies against the leukocytic adhesive proteins CD18 is offered.

The BAS cause an increase of vascular permeability and therefore, a decrease of CBV. In serious shock the increase of bound water, i.e. located outside a vessel, amounts to 127% of the initial level.

Acidosis develops due to hypoxia and results in the relaxation of the precapillary sphincters. Therefore, the gole, remaining closed by the venules, opens. The quantity of the fluid accumulating in it is 3 – 4 times as much as compared to the norm. This phenomenon is called "pooling" or "sequestration" of blood. The similar changes in the extracellular space correspond to the stage of *late irreversible shock*.

Stagnation and acidosis pave the way for a start of intravascular coagulation (IC). The aggregation of the formed elements, a sludge-syndrome, formation of thrombi and emboli are observed, which impairs microcirculation and aggravates hypoxia.

The changes in microcirculation can be complicated by the disseminated intravascular coagulation (DIC), at which blood coagulability decreases and secondary bleedings are probable.

Besides, in shock the myocardium contractility decreases as a result of hypoxia, acidosis and the acting specific myocardium-suppressing factor – MSF, which is secreted by the ischemic pancreas.

A decrease of the vascular tone, massive outflow of the fluid from the vessels into the interstitial tissue, more serious rheological disorders of blood result in decreased reverse backward venous bloodflow.

Cellular stage of shock development

Hypoxia solely cannot account for a change in a shock cell as hypoxia can be avoided for a while owing to enzymatic rearrangement of a cell.

The following changes occur in shock states:

1) Deficiency of ATP develops, therefore, the mechanism of the hormonal action on a cell through AMP is impaired (combination of a hormone with a specific receptor activates adenylatecyclase; AMP, which effects the biological action of a hormone on a cell is synthesized).

2) Hyperactivity of the oxidative processes results in the accumulation of metabolites in a cell. In one hour of shock activation of glycolysis and glycogenolysis, inhibition of the tricarbonic acid cycle are marked; in two hours –

there is emaciation glycolysis and glycogenolysis, ATP is used completely, metabolites are stored.

3) Acidosis. If endocellular pH amounts to 5.5, corrosion of the lysosomal sacs begins. This results in the opening of the lysosomal cisterns, and the catalases are released into the blood.

4) During shock the cellular membrane potential decreases that is conducive to transmineralization, K^+ escape and Na^+ entry, the arrest of H^+ transfer through the membrane. These phenomena cause edema.

Till recently a cell was thought to be affected only at the late stages of shock, and the therapeutic efforts were targeted only hemodynamics. However, the experimental and clinical research has established that even before such signs of the disturbed perfusion as hypotonia or decreased urination arise, lactate acidosis, which is the evidence of early disturbances of cellular metabolism occurs. The membrane potential decreases and, therefore, the elective pumpes stop immediately (!) after the shock-causing factor collides with a macrosystem. In 6 (!) minutes after shock begins, the antibodies of anti-DNA were generated and their concentration correlates with the gravity of shock. Their presence is the evidence of a rapid autoimmune attack on the genetic matrix of protein synthesis and on the system of cellular coordination by means of perversion of nucleic acids.

The vitality of cells is impaired and they die forming necrotic zones. In the post-shock period these phenomena determine insufficiency of organs that is their disability to perform their specific functions.

The patient's condition gets worse again as kidneys, lungs, liver and other organs become affected after the serious, especially continuous, stages of shock and subsequent stabilization of the respiration and circulation; pathological dependences arise.

The disturbed perfusion of the heart disturbes its functioning which is accompanied by decreased cardiac output. That, in its turn, decreases the perfusion of all organs, including the blood supply of the heart. Haemorrhages in the

subendocardium arise in the heart after serious shock (the mechanism is not clear). The so-called "zonal lesions" are registered at hemorrhagic shock. The sarcomeres are excessively contracted, there are loci of microthromboses and micronecroses in these zones. As a rule, such changes arise after the periods of heart overstrain with increased heart rate and force. They are caused by high concentrations of catecholamins known as "adrenal myocarditis".

Disturbance of the pancreas perfusion results in the formation of peptides, which suppress the heart function. The example of suppression of the contractility of the cardiac muscle by the circulating myocardium-suppressing factor (MSF) is shown in Figure 6.

The hypoperfusion of the liver stimulates anaerobic metabolism and considerable lactification which is conducive to the development of metabolic acidosis, which, in its turn, disturbs the function of the cardiovascular system. In these conditions the liver becomes unable to inactivate active mediators and toxins circulating in the bloodstream. Shock whose duration is less than 10 hours is seldom accompanied by the necrosis of hepatocytes, but in 24 hours of shock necroses of the liver are probable. The serious complications that may set in are coagulopathy, DIC-syndrome and massive bleedings. They are conditioned by decreased synthesis of the coagulative factors in the liver, consumption of the plasma factors and thrombocytes. The level of factors II, V, VII, IX and X is often 50% lower. It has been shown recently that changes of factor V are not of prognostic significance. On the one hand, patients with fulminant hepatic insufficiency have a small chance to survive without liver transplantation with the ratio of factor V/factor VIII > 30; on the other hand, the upward tendency of the factor V for patients with coagulopathy can be considered as an early sign of rehabilitation.

The decreased perfusion of the intestine results in the disturbance of the mucosal barrier (the intestine is very sensitive to ischemia), bacteria can pass into the bloodstream and cause septic shock in addition. Besides, the disturbance of the mucous membranes causes additional fluid loss from an organism.

The poor perfusion of the kidneys disturbs their function and the excretion of acidic metabolites stops. That induces systemic acidosis. Decreased perfusion can result in tubular necrosis and accumulation of toxic metabolites.

If an acute lesion of the lung of any genesis progresses, the clinical presentation is described by the term "respiratory distress-syndrome" (RDS). The development of RDS results in more than 50% lethality. It can be characterized as respiratory insufficiency due to the interstitial edema of the lungs arising because of increased permeability of the pulmonary capillaries. Besides, both the alveoli and their capillary network are damaged. Clinically, acute respiratory insufficiency develops in patients; the pulse rate is increasing. The treatment with oxygen is non-effective; X-ray picture demonstrates diffuse infiltration.

The lesion of the brain may be generalized, resulting in a coma, but it may also be local. The main problem is hypoxia and ischemia of the brain, which result in the swelling of cells (i.e. to intracellular edema), as a result, intracranial pressure increases, which additionally decreases the blood supply of the brain and thus, the pathological circle closes.

As a rule, the intestine, filled with gram-negative bacteria, is considered as the initiator of nosocomial pneumonias in the post-resuscitation period as well as of septic state and polyorgan insufficiency. The functions of other organs – the heart, kidneys, lungs, liver, system of the mononuclear phagocytes, immune system – can be paralysed, and, finally, the brain function can be disturbed, a coma may occur. Polyorgan insufficiency is a dangerous complication, which may often cause death. There are few patients who can survive if they have insufficiency of three organs. Insufficiency of any system often makes traditional methods of treatment inefficient; in this case there is no standard way of treatment.

General principles of treatment

- Elimination of a shock-causing factor. Primary management of the wound using anaesthetics.

- Tranquillizers – to decrease the involvement of the vasomotor and cardiac centres in the shock reaction.
- The restoration of CBV (the plasma, blood substitutes) makes it possible to increase the venous return that increases stroke volume (SV) and minute blood volume (MBV).
- The restoration of systemic arterial pressure (SAP).
- To improve microcirculation: the administration of α-blockers, β-mimetics that results in the spasmolysis of the pre- and postcapillary sphincters, elimination of sequestration and helps to eliminate thrombosis and aggregation of thrombocytes.
- Levelling of endocrine metabolic disturbances. Glucocorticoids stabilise the membranes; glucagon increases MBV, AP; the inhibitors of the proteolytic enzymes decrease the quantity of vasoactive substances.
- Alkaline balance is normalised by the introduction of sodium bicarbonate and antihypoxants.
- Normalization of the coagulative balance – α-blockers, heparin.
- Antibacterial treatment and prevention of sepsis.

Shock

First Level Tests

1. Pick out the main etiologic factors of shock.
   1.Mechanical injury.
   2.Burning injury.
   3.Acute hemorrhage.
   4.Paroxymal tachycardia attack.
   5.Low temperature.
   6.Myocardial infarction.
   7.Lower extremity frostbite.
   8.Immunologic conflict.
   9.Endotoxin action.
   10.Acute poisoning.
   11.All factors.

2. Pick out the adequate experimental models of shock.
   1.Traumatic shock by Kennon.
   2.Hemorrhagic shock.
   3.Endotoxic shock.
   4.Anaphylactic shock.
   5.Crush syndrome.
   6.Posttransfusion shock.
   7.Histamine shock.
   8.Burn shock.
   9.All the above mentioned.

3. Pick out the clinical stages of shock and arrange them in the correct order.
   1.Neuroendocrinal.
   2.Erectile.
   3.Hypovolemic.
   4.Torpid.
   5.Terminal.
   6.Metabolic.

4. Pick out the stages of a pathogenic shock and arrange them in the correct order.
   1.Neuroendocrinal.
   2.Erectile.
   3.Torpid.
   4.Cadiovascular (hypovolemic).
   5.Metabolic.
   6.Terminal.

5. Which of the following phenomena occur in the initial period of a traumatic shock:
   1.Afferent increase from the site of trauma, from extero-and interoreceptors.
   2.Afferent decrease from extero-and interoreceptors.
   3.Central nervous system depression.
   4.Central nervous structure exitation.
   5.Activation of motor and vocalic reaction of victims.
   6.Cardiovascular and respiratory system depression.
   7.Cardiovascular and respiratory system exitation.
   8.Endocrine gland activation.
   9.Endocrine function depression.

6. Which of the following factors are the major ones in pathogenesis of nervous disorders at the initial stages of the development of shock:

1.Excessive afferentation from the site of trauma.
2.Circulatory hypoxia.
3.Intercentral interrelation disorder.
4.Energy metabolism disorder in the brain.
5.Endorphine and enkephalin formation increase.
6.All above mentioned factors.

7. Which of the following reactions are ensured by the activation of sympathoadrenal system at the initial period of shock:

1.Spasm of vessels having alpha adrenergic innervation.
2.Dilatation of vessels having beta adrenergic innervation.
3.Cardiac and cerebral vasospasm.
4.Cardiac and cerebral vasodilatation.
5.Centralization of circulation.
6.Pathologic blood pooling.
7.Organ contraction in blood pooling.
8.Tachycardia and increased minute circulation volume.
9.Bradycardia and decreased minute circulation volume.
10. Increased systemic arterial pressure.
11. Systemic arterial pressure diminution.
12. Lipolysis and glycogenolysis increase.
13. Lipolysis and glycogenolysis inhibition.
14. Increased gluconeogenesis.

8. Through what do glucocorticoids realize their role in compensatory reactions in a condition of shock:

1. Increased gluconeogenesis.
2. Lipolysis activation.
3. Lipogenesis activation.
4. Increased biologic membrane permeability.
5. Decreased biologic membrane permeability.
6.Energetic substrate quantity increase
7. Oxidation substrate quantity decrease
8. Sympathoadrenal system effect increase
9. Sympathoadrenal system effect inhibition
10. Increased organism's resistance.

9. Which of the following types of cortisteroidic insufficiency proceed in shock dynamics:

1.Absolute
2.Relative

3.Extrasuprarenal
4.All

10. Which of the following factors participate in shock hypotension:
1. Inadequate activation of sympathoadrenal system
2. Hypoxia and metabolic acidosis
3. Increased minute circulation volume
4. Pathologic blood pooling
5. Decreased circulation blood volume
6. Decreased minute circulation volume
7. Increased general peripheral resistance of vessels
8. Decreased general peripheral resistance of vessels
9. Bradycardia
10.Tachycardia
11.Disorders of central regulation of systemic arterial pressure

11. Which types of hypoxia are metabolic disorders associated with a condition of shock?
1. Respiratory
2. Blood hypoxia
3. Circulatory
4. Tissue hypoxia

12. Which type of hypoxia plays an initial role in the pathogenesis of metabolic disorders in a condition of shock?
1. Respiratory
2. Blood hypoxia
3. Circulatory
4. Tissue hypoxia

13. Which substance accumulates in tissues and blood as a resúlt of metabolic disorders in a condition of shock?
1. Lactate
2. Pyruvate
3. Histamine
4. Serotonin
5. Kinins
6. Prostaglandins
7. Ketone bodies
8. Peroxidic compounds
9. Potassium ions
10. All mentioned substances

14. Which of the following pathologic types of respiration can be registered at the terminal stage of shock:

1. Cheyne-stokes respiration
2. Biot's respiration
3. Kussmaul's respiration
4. Gasping respiration
5. All mentioned types of respiration

15. Which of the following does pathologic therapy of shock include:

1. Effective anesthesia
2. Elimination of injury, hemostasis
3. Blood and bloodsubstituting solution transfusion
4. Hyperbaric oxygenation
5. Antioxidant introduction
6. Acid-base balance correction
7. Glucocorticoid utilization
8. Detoxicational therapy
9. Hemostasis correction
10. All the above mentioned

Second level tests.

16. Give the definition for the notion "shock"

17. Enumerate the major types of shock

1.
2.
3.
4.
5.
6.
7.

18. Enumerate the main causes of shock

1.
2.
3.
4.
5.
6.
7.

19. Give the clinical classification of shock stages
    1.
    2.
    3.

20. Give the pathogenic classification of shock stages
    1.
    2.
    3.

21. Give the shock classification depending on systemic arterial pressure changes
    1.
    2.
    3.
    4.

22. Name the types of shock when an erectile stage is well pronounced:
    1.
    2.
    3.

23. Name the types of shock during which an erectile stage is less marked or almost absent:
    1.
    2.
    3.

24. Give the scheme of pathogenesis of systemic arterial pressure increase at an erectile stage of shock:

25. Give the scheme of pathogenesis of blood circulation being centralized and its most important consequences in a condition of shock:

26. Enumerate the clinical signs of an erectile stage of shock
    1.
    2.
    3.
    4.

27. What functional disorders of pituitary-adrenocortical system are registered in shock dynamics?

1.Erectile phase
2.Torpent phase

28. Name and characterize the types of corticosteroid insufficiency in a condition of shock:

1.
2.
3.

29. Show the direction of changes at an erectile stage of shock:

1.Systemic arterial pressure N, ↑, ↓
2.Cardiac contraction rate N, ↑, ↓
3.Catecholamine level in the blood N, ↑, ↓
4.Glucose level in the blood N, ↑, ↓
5.Pallor of cutaneous (skin cover) tegument N, ↑, ↓

30. Show the direction of changes at a torpent stage of shock:

1.Systemic arterial pressure N, ↑, ↓
2.Cardiac contraction rate N, ↑, ↓
3.Pallor of cutaneous tegument - yes/no

31. Enumerate the important phenomena of microcirculation disturbances in a condition of shock:

1.
2.
3.
4.
5.

32. Name the major pathogenic mechanism of shock hypotension:

1.
2.
3.
4.
5.

33. What does pathogenic blood pooling mean and what are its consequences?

34. Which mechanism in addition to pathologic blood pooling plays an important role in the development of hypovolemia in a condition of shock?

35. Name the major metabolic disorder which occur in a condition of shock:

1.
2.
3.
4.

36. What are the main mechanisms of intoxication in a condition of shock?

1.
2.
3.
4.

37. What types of hemostasis disorder can develop in a condition of shock?

38.Give the scheme of the pathogenesis of acidosis in a condition of shock:

39. Name the major consequences of the "shocked" lung for the organism

40. Name the major consequences of the "shocked" kidney (acute kidney insufficiency) for the organism

41. Enumerate the main principles of pathogenic shock therapy

1.
2.
3.
4.
5.
6.

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Подписано в печать 07.12.2005. Формат 60×84 1/16.
Гарнитура "Таймс". Бумага офсетная.
Усл.-печ. л. 5,25. Тираж 150 экз. Заказ 126

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