

Министерство здравоохранения республики Беларусь
Учреждение образования
«Гомельский государственный медицинский университет»

Кафедра патологической физиологии
Обсуждено на заседании кафедры
Протокол №7 от 30.08.2017

МЕТОДИЧЕСКАЯ РАЗРАБОТКА
Для проведения занятия со студентами
3 курса ФПСЗС, обучающихся на английском языке
по патологической физиологии

Тема: Типовые формы нарушения микроциркуляции

Theme: Typical forms of microcirculatory disorders

Время 3 ак. часа

1.Actuality of the theme. Arterial hyperemia as a typical pathological process is observed in inflammation, many infectious diseases (measles, spotted fever, scarlet fever), damages of nervous plexus, neuralgias etc. Knowledge of causes, mechanisms and symptoms of arterial hyperemia matters practically. Doctors use the surgical, pharmacological, physiotherapeutic influences, which cause artificial arterial hyperemia. The aim of these influences is improve metabolism, blood and lymphatic circulation in damaged area. Ischemia leads to development of many diseases, for example, ischemic heart disease, insult, obliterative endarteritis. The ischemia consequences depend on whole row of factors – development speed, duration and localizations of ischemia, character of collateral circulation blood, functional condition of the organ.

Learning goals of the lesson: to study typical forms of microcirculation disorders, their etiology, pathogenesis, manifestations; main forms of local circulatory disorders.

Educational goals of the lesson: formation of scientific outlook and theoretical basis of future specialists on the basis of fundamental knowledge and the latest achievements of pathological physiology.

Objectives of the lesson:

1. To know causes, mechanisms, manifestations of intravascular, transmural, extravascular disorders of microcirculation.
2. To know typical disorders of lymphodynamics, mechanisms and manifestations.
3. To know methods of diagnosis of microcirculation disorders and regional vascular pathology.

To repeat the following questions from related disciplines to ensure absolute mastery of the material:

1. Structure of histion (histology, cytology, embryology disciplines).
2. Structure and function of blood vessels (human anatomy discipline).

Control questions of the lesson:

1. Typical microcirculatory disorders: classification, causes and mechanisms of development.
2. "Sludge" -phenomenon: definition, types, causes, mechanisms of development and manifestation.
3. Stasis: definition, types, causes, mechanisms of development and manifestations.
4. Capillary-trophic insufficiency.
5. Typical disorders of lymphodynamics: types, causes, mechanisms of development and manifestations.
6. Principles of therapy of disorders of regional circulation and microcirculation.

Calculation of study time

Total study time 3 ac.hours

№ п/п	Contents	Calculation of study time
1.	Introduction. Motivational characteristic of the theme	3 minutes
2.	Written control of students on the topic of the lesson	15 minutes
3.	Interviews with students about the topic of the lesson	60 minutes
4.	Self-managed student work	15 minutes
5.	Summing up the results of the lesson	5 minutes
6.	Decision of situational tasks	20 minutes
7.	Task for the next lesson	2 minutes

Additional materials:

Typical disorders of peripheral blood flow

There are two groups of disorders of peripheral blood flow.

- 1) **systemic** disorders, which connecting with insufficiency of cardio-vascular system. (disorders of general hemodynamic)
- 2) disorders of **local** peripheral flow – it is disorders circulation of the blood in organs and tissues.

These disorders distinguish on two groups in dependence of sizes of vessels:

- 1 – disorders of microcirculation – the diameter of vessels is less 100 micrometer,
- 2 – disorders of macrocirculation – the diameter of vessels is more 100 micrometer.

Disorders of microcirculation.

There are two groups: disorders of **hemomicrocirculation** (in blood vessels) and **lymphcirculation** (in lymphatic vessels).

Disorders of hemomicrocirculation – it is a typical pathological process, what characterized by disorders of blood circulation in microcirculatory bloodstream.

Microcirculatory bloodstream consists of arterioles, precapillaries, precapillary sphincters, capillaries, postcapillaries, venules, small veins, arteriovenular anastomoses, and lymphatic vessels.

Distinguish three groups of **reasons (causes) of disorders of hemomicrocirculation:**

- 1) intravascular disturbances
- 2) disturbances of structure and function of vascular wall,
- 3) extravascular disturbances.

Causes of intravascular disturbances

1. Slowing or excessive acceleration of blood flow and / or lymph
2. Violation of turbulence in blood flow and / or lymph.
3. Excessive increase in juxtacapillary blood flow

Reasons for the slowing of blood flow and / or lymph:

- disorders of hemo and lymphodynamics (eg, heart failure, venous congestion, ischemia, lymphorrhea);
- an increase in blood viscosity (eg, as a result of hemoconcentration during prolonged vomiting, diarrhea, plasmorrhages burns, polycythemia, hyperproteinemia disseminated intravascular coagulation);
- narrowing of microvessels (due to compression them by tumor, edematous tissue, formation of blood clots in them, embolism, swelling or hyperplasia of endothelial cells, formation of atherosclerotic plaques and etc.).

Reasons for the excessive acceleration of blood flow and / or lymph:

- Violations of hemodialysis and / or lymphodynamics (for example, pathological arterial hyperemia or shunt the arterial blood in the venous bed through arteriolo-venular shunts);
- Decrease in blood viscosity (at hemodilution, hypoproteinemia, renal failure, pancytopenia).

Violation of turbulence in blood flow and / or lymph.

- damage of microvessels walls and / or violation them smoothness (vasculitis, hyperplasia of endothelial cells, arteriosclerosis, fibrotic changes in the vascular wall and the like).
- changes in blood aggregation (for example, the formation of parietal microthrombi violating laminar blood flow).

Excessive increase in juxtacapillary blood flow

Develops at the opening of the arterio-venous and arteriolo-venular shunts and manifested an excess discharge of blood from the arteries and arterioles in the veins and venules, bypassing the capillary network of the microcirculatory bed. Reasons:

- spasm of arterioles and precapillary sphincters closing with a significant increase in the level of catecholamines in the blood (with hyper catecholamine crisis in patients with a tumor of the adrenal medulla - pheochromocytoma);
- at excessive increase in tone of the sympathetic nervous system (under stress).

Transmural disturbances of microcirculation

They may be classified into two major groups:

1. Increased permeability of blood vessels
2. Decreased permeability of blood vessels

Mechanisms of an increase in vascular permeability include: formation of endothelial gaps, cytoskeletal reorganization, increased transcytosis, direct endothelial injury, development of acidosis (non-enzymatic hydrolysis of the basic substance vascular basement membrane), activation of hydrolases (enzymatic hydrolysis of the basic substance vascular basement membrane), hyperextension of the microvessels walls.

Mechanisms of a decrease in vascular permeability include: thickening of the microvessels walls (chronic vasculitis), sealing of the microvessels walls due to their calcification.

In accordance with the classical theory of Starling (1909), the passage of liquid and dissolved substances from the blood into tissues is carried out through a semipermeable membrane of capillary vessels under the influence of filtration pressure (FP):

$FP = (HBP + OTP) - (HTP + OBP)$, where:

FP is the filtration pressure;

HBP - hydrodynamic blood pressure on the vessel wall (in the arterial end of the capillary) - 32.5 mm Hg

OTP - oncotic tissue pressure - 4.5 mm Hg

HTP - hydrodynamic tissue pressure - 3 mm Hg

OBP - oncotic blood pressure - 25 mm Hg

Therefore, in the arterial capillary vessel, the effective filtration pressure is 9 mm Hg, which transfers the liquid from the blood to the tissues.

In venous segment of capillaries and in venules, the hydrodynamic blood pressure is significantly reduced (to 17.5 mm Hg) as a result of the partial transition of the fluid to the interstitium. As a result, $FP = (17.5 + 4.5) - (3 + 25) = -6$ mmHg, which cause a partial resorption of the liquid.

Extravascular disturbances

Extravascular disturbances include **increased or decreased flow of interstitial fluid**. Interstitial fluid flow depends on diffusion, filtration and lymph production. The low rate of filtration results from a decrease in hydrostatic capillary pressure, the density of capillary bed and the permeability of capillary wall. The lowering of lymph flow may result from low interstitial hydrostatic pressure, high hydrostatic pressure in lymphatic vessels and impairment contraction of endothelial cells forming lymphatic capillaries.

The reaction of the tissue basophils in connective tissue surrounding vessels to damaging agents. In some pathological processes (inflammation, allergic tissue damage) from tissue basophils at their degranulation released bioactive substances and enzymes in the interstitial space surrounding microvasculature. Under the action of damaging agents on the tissue from lysosomes is released and activated proteolytic enzymes they digest complex protein-polysaccharide complexes of the main interstitial substance. A consequence are destructive changes in basement membrane of microvessels and in fibrous structures forming a skeleton, which encloses microvessels. These defects lead to changes in vascular permeability, their lumen and slowing blood flow.

Stasis

Stasis (stasis - stop) **is arrest of blood flow in the vessels of microcirculatory system (capillaries).**

The capillaries and veins are dilated paralytically and filled with blood. In the lumen of some capillaries the homogenous eosinophilic masses can be seen. They are columns of erythrocytes stucked together,

which is called prestasis. Sludge syndrome (phenomenon) is regarded as a type of stasis. It is characterized by sticking of erythrocytes, leukocytes and thrombocytes to each other, which is accompanied by blood viscosity increase.

Stasis may be discirculatory as a result of venous hyperemia or ischemia. **Causes of stasis:**

- Physical factors (temperature elevation, cold).
- Chemical factors.
- Infection.
- Infectious-allergic factors.
- Autoimmune factors.

Types of stasis:

1. true stasis,
2. ischemic stasis
3. venous-congestive stasis.

True stasis begins with cell aggregation and cell adhesion to the vessel wall and is followed by hemodynamic changes.

Reasons of the true stasis:

- damage to the capillary walls;
- chemical agents acting on the red blood cells;
- decrease in the rate of blood flow in the capillaries

Pathogenesis

The mechanism of a true stasis development is based on the intravascular aggregation of erythrocytes (adherence) and formation of conglomerates, which make the flow difficult. It also causes increasing of the peripheral resistance.

Aggregation of erythrocytes occurs as a result of changing of the physical properties of erythrocyte plasmalemma under direct effect of the factors, entering the capillary. The surface of erythrocytes, which is smooth under normal conditions, becomes "fuzzy". Aggregation of erythrocytes occurs as a result.

A significant role in pathogenesis of a true stasis belongs to a hemoconcentration and increased permeability of capillary walls. Etiological factor itself and metabolites, produced in tissues, promote it. A special significance in genesis of stasis belongs to the biological active substances (serotonin, bradykinin, histamine), local acidosis and a change in the blood colloid state. It results in increasing of vessel permeability and dilatation of vessels leading to hemocoagulation, slowing of the blood flow, aggregation of erythrocytes and, consequently, to stasis. It is important to emphasize that stasis alone does not induce thrombosis. Stasis of poorly oxygenated blood causes chronic tissue hypoxia.

Sludge-phenomenon

Sludge-phenomenon is defined as aggregation, adhesion and agglutination of blood cells, mainly erythrocytes, with further separation of blood into small and large cell aggregates and plasma. Mechanisms of the sludge-phenomenon are presented on the scheme above

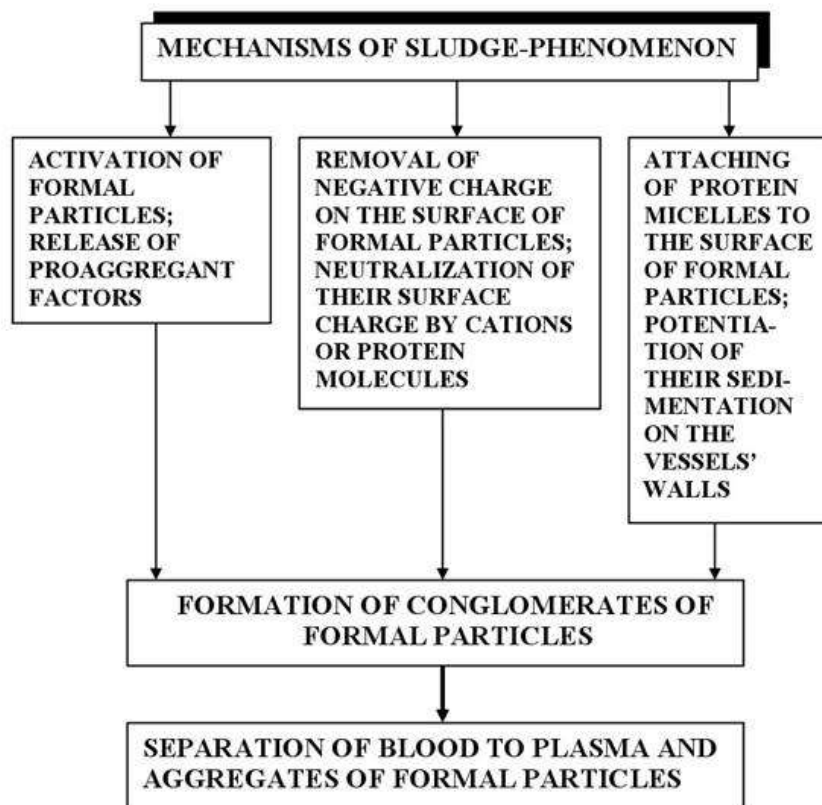


Figure 1 Mechanisms of the sludge-phenomenon

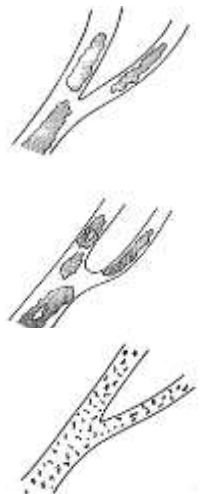
Types of sludge:

I. Depending on the nature of the impact:

- **reversible** (when only rouleaux (erythrocytes aggregates))
- **irreversible** (with the agglutination of red blood cells and the development of viscous metamorphosis).

II. Depending on the size of aggregates, the nature of their, contours and the packing density of erythrocytes:

- **classic** - the large size of the aggregates, the rough outline of the contours and the dense packing of erythrocytes. This type of sludge occurs when an obstruction (such as ligatures) prevents the free flow of blood through the vessel, and in many pathological processes;
- **dextran** - aggregates of various sizes, round shape, the dense packing of erythrocytes, the free space in the aggregates in the form of cavities;
- **amorphous** - a huge number of small aggregates in the form of granules consisting of several erythrocytes. This kind of sludge occurs the introduction into the bloodstream of ethanol, ATP, ADP, prothrombin, serotonin, noradrenaline



Consequences of sludge:

1. Violation of blood flow intravascularly (slowing down to stasis, turbulent blood flow, including arteriolo-venular shunts), disorders of processes of transcapillary current of blood cells
2. Violation of metabolism in tissues and organs with the development of dystrophy and disorder of plastic processes in them.
3. The development of hypoxia and acidosis in tissues and organs.

Thus, sludge, appearing first as a local response to tissue damage, eventually leading to the initiation and severity of capillary-trophic failure.

Capillary trophic failure

Capillary trophic failure (CTF) -a condition characterized by a violation of blood and lymph circulation in the vessels of microcirculatory, disorders of transport fluid and blood cells through the walls of microvessels, slowdown flow/outflow of interstitial fluid and metabolic disorders in the tissues and organs.

The etiology of CTF

- Hereditary factors (hereditary defect in the mechanisms of regulation (kinin system) (congenital angioedema).
- Acquired (disorder of neuro-endocrine-humoral mechanisms of regulation of pathogenic factors directly on capillary-connective tissue structures)

Types of CTF:

By origin

- **Primary** (first damaged capillary-connective tissue structures, then the organs and tissues)
- **Secondary** (primary disorders localized in the tissues themselves, their parenchyma and capillary-coupling structures are damaged by a second).

By the nature of defeat:

- **Functional** (transcapillary exchange violations result from disorders of regulation mechanisms)
- **Organic** (violations occur as a result of morphological changes themselves capillary connecting structures).

By the prevalence: systemic and regional.

By phases of violation transcapillary exchange: compensated and decompensated.

Consequences: dystrophy, a violation of plastic processes in the tissues, organs and disorder vital activity of the whole organism.

Lymphatic insufficiency

The forms of lymphatic insufficiency:

I. By etiology:

1. **Mechanical failure:** due to the presence of **organic** (**compression** of the tumor, scar, extirpation of the lymph nodes and blood vessels) or **functional reasons** (increased pressure in the main blood vessels, lymph vessels spasm).
2. **Dynamic failure:** the volume of **interstitial fluid extravasation exceeds the capacity of the lymphatic system** to ensure effective drainage fabric.
3. **Resorption** Failure due to structural **changes in the interstitial tissue, the accumulation of proteins** and deposition of abnormal forms in the interstitium.

II. By volume of defeat: general and local.

III. By speed of the emergence and development: acute and chronic.

The main clinical and pathophysiological manifestations of lymphatic insufficiency is the accumulation of proteins and their degradation products in the interstitial tissue and fibrosis.

Questions for self-control of knowledge:

1. Give a definition of "microcirculation". What are functions of microvasculature, methods for studying microcirculation?
2. What are links of microcirculatory system, give characteristic of its components.
3. Describe general causes of microcirculatory disorders.
4. What are etiology and pathogenesis of typical forms of microcirculatory disorders (intravascular, transmural, extravascular)?
5. What is "sludge"-phenomenon? What is significance of sludge?
6. What are causes of true stasis and detect principal mechanisms of its development.

7. What are causes, mechanisms of development, manifestations of capillary-trophic insufficiency syndrome?
8. Describe various forms of lymphatic insufficiency. What are main clinical and anatomic manifestations of acute and chronic forms?
9. What general changes in body in local blood circulation disorders.

Tasks for self-managed student work:

1. "Sludge" phenomenon.
2. Capillary-trophic insufficiency.
3. Insufficiency of lymphatic system.

Literature

Basis literature:

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