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Учреждение образования
«Гомельский государственный медицинский университет»

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

Тема: **Нарушения периферического кровообращения**

Theme: **Peripheral circulatory disorders**

Время 3 ак. часа

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. Venous hyperemia arises attached to mechanical hindrances to blood flow in veins (thrombosis, embolism, compression of vessels), decreasing of their tone, diminution of blood outflow due to weakening of heart work, protracted standing weakening, of muscles activity. Protracted venous stagnation is accompanied by atrophic and dystrophic changes and growth up of connective tissues. Ischemia leads to development of many diseases, for example, ischemic heart disease, infarct, 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 main forms of local circulatory disorders.
2. To know changes in microcirculatory with local circulatory disorders.
3. To know conditions of origin, etiology, types, pathogenesis, outcomes and consequences of thrombosis and embolism.
4. To know methods of diagnosing 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).
3. Scheme of vascular-platelet and macrocirculatory hemostasis, factors of the coagulation and anticoagulation systems, fibrinolysis system (physiology discipline).

Control questions of the lesson:

1. Arterial hyperemia: types, causes, mechanisms of development and manifestations.
2. Venous hyperemia: types, causes, mechanisms of development and manifestations.
3. Ischemia: types, causes, mechanisms of development and manifestations.
4. General changes in a body with local circulatory disorders.
5. Compensatory processes in disorders of peripheral blood flow.
6. Thrombosis: types of blood clots, causes, stages, mechanisms of thrombosis.
7. Embolism: types, causes and mechanisms of formation.
8. Significance, outcomes and consequences of thrombosis and embolism.

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 **lymphocirculation** (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.

Arterial hyperemia

Arterial hyperemia is characterized by a local deposition of the blood and an increase in blood flow rate through the organ or tissue resulting from a dilation of arterial vessels.

Depended from etiologic factors and mechanisms of development there are types of arterial hyperemia:

I. There are three types of **physiological arterial hyperemia:**

- 1) **working** – organ hyperfunction (muscle, intestine, etc)
- 2) **emotional** (psychogenic) – its conditional reflex (shame, excitement, confusion)
- 3) **reactive** (substitute) – hyperemia after short-term (transitory) ischemia.

II. There are types of **pathological arterial hyperemia:**

1. **Neurotonic arterial hyperemia**
2. **Neuroparalytic arterial hyperemia (angioneurotic)**
3. **Postischemic** – an increase in blood flow to an organ or tissue after temporary cessation of circulation.
4. **Inflammatory** – it is a compensatory-adaptive process under the influence of vasoactive substances, inflammatory mediators
5. **Collateral** – e. myocardial infarction - a vascular necrosis (ischemic, in fact) with a hemorrhagic halo as determined by the development of collaterals. This arterial hyperemia bypassing in the small circle is due to the presence of an interatrial or interventricular defects with discharge of blood from left to right. Lung arteries elastic and muscular-elastic types are dilate and muscle type is constrict in law-Bayliss Ostroumova. This is development of the precapillary pulmonary hypertension.
6. **In arterio-venous shunts** – marked in vascular damage, with the sucks action by veins, etc.
7. **Vacuum** – in the area with low pressure.

Mechanisms of arterial hyperemia:

I. Neurogenic mechanism has 2 types:

1. Neurotonic mechanism (predominance effects of parasympathetic nervous over sympathetic on arterial vessel walls due to:

- activation of parasympathetic effector and an increase in level of acetylcholine in the neuromuscular synapses of vascular walls (observed at irritation of parasympathetic ganglia, for example, in inflammation, tumor compression, scars, trauma);

- increase the sensitivity of cholinergic receptors of vessels walls to the action of acetylcholine (with an increase in the extracellular level of potassium, hydrogen).

2. Neuroparalytic mechanism is characterized by a reduction or absence ("paralysis") of sympathetic nerve effects on the walls of arteries and arterioles when:

- inhibiting or stopping the conduction of nerve impulses along sympathetic fibers (in damage to the sympathetic ganglia or nerve endings as a result of trauma, inflammation, during surgery);
- reduction in adrenergic properties of arteries (arterioles) walls (in the focus of inflammation due to physico-chemical changes in it - acidosis, a decrease in the level of potassium ions, etc.).

II. The neuromyoparalytic mechanism is characterized by:

1. The depletion of catecholamine depot in the vesicles of sympathetic nerve endings in the walls of arterioles and precapillaries.
2. Decreased tone of muscle fibers of arterial vessels and precapillaries.

Causes: prolonged action on tissues or organs of various factors (heat, mustard plasters, therapeutic mud, etc.), the termination of prolonged pressure on the walls of arteries (for example, ascitic fluid, tight bandage, pressing clothing).

The effect of these factors over a long time significantly reduces or completely removes the myogenic and regulatory (mainly adrenergic) tonus of arterial vessel walls.

III. The humoral mechanism:

1. Increase in the level of BAS with vasodilating action (adenosine, NO, PgE, PgI2, kinin).
2. Increased sensitivity of receptors of arterial (precapillaries) walls to vasodilators.

Manifestations and their mechanisms:

1. Redness – reduction of deoxygenated hemoglobin in the capillary bed.
2. Increased temperature – increased inflow of warm arterial blood.
3. Vessel pulsation.
4. Slight swelling – mild accumulation of fluid in the interstitial space resulted from an increase in filtration rate.
5. Increased number of functioning capillaries – an increase in capillary hydrostatic pressure.
6. Increased arteriole diameter and blood flow rate – metabolic mechanism.
7. Increased lymphatic outflow – mild elevation of interstitial hydrostatic pressure.

Humoral mechanism is responsible for a *reactive hyperemia*, which is the most common form of arterial hyperemia. When the blood supply to tissue is blocked for a few seconds to several hours and then is unblocked, the flow through the tissue can increase to about five times normal. The duration of reactive hyperemia depends on the duration of the ischemic period. Reactive hyperemia may have very harmful effects on the myocardium and brain. It can be accompanied by increased production of free oxygen radicals and an impairment of intracellular calcium exchange.

Venous hyperemia.

Venous hyperemia is characterized by a local deposition of blood and a decrease of blood flow rate through the organ or tissue resulting from a delay or cessation of blood outflow via the venous vessels.

Mechanisms of venous hyperemia:

- A) Heart disorders;
- B) reducing the suction effect of the chest;
- C) blockade (compression - tumor, swelling tissue, scar or tourniquet; obstruction by thrombus or embolus
- D) A decrease in venous wall elasticity combined with vein extension, venous valves failure, development of collateral blood circulation.

Types of venous hyperemia:

1. **general venous hyperemia** -in heart pathology, reflecting acute or chronic cardiovascular insufficiency.

2. **acute general venous hyperemia**. Due to lack of oxygen in venous blood, hypoxia and acidosis developed in the tissues, vascular permeability is increased (primarily in the microcirculatory bed), it leads to plasma saturation and edema, dystrophy. The organs that deposit blood - lungs, liver, skin with the subcutaneous fat, kidneys, spleen - are affected.

3. **chronic general venous hyperemia** is characterized by the same processes as acute, as well as atrophy of the parenchyma and sclerosis of the stroma due to the activation of fibroblasts and the proliferation of connective tissue, leading to compaction (induration) of the affected organs.

4. **local venous hyperemia**: obturation of vein by thrombus, embolus, inflammatory process; compression of vein by tourniquet, tumor, scar tissue; collateral, formed with difficulty of outflow of blood along the main venous vessel.

Manifestations and their mechanisms:

1. **Cyanosis**: accumulation of deoxygenated hemoglobin in the capillary bed.
2. **Edema**: an elevation of hydrostatic pressure in veins and capillaries.
3. **Decreased local temperature** – a decrease in the rate of metabolic process and reduced inflow of warm arterial blood.
4. **Increased diameter of venous vessels** and decreased blood flow.
5. **Decreased lymphatic outflow** – compression of lymphatic capillaries caused by high interstitial hydrostatic pressure.
6. **Decreased capillary blood flow and stasis.**

Morphology of congestion

Because of the increase in venous blood, organs become swollen and purplish. With long continued over-distension, the wall of the venules shows reactive thickening and there is mild intestinal fibrosis of the organs, giving them a very firm consistency. These changes are seen typically in the kidney and spleen. Important additional changes are found in the lungs and liver.

Lungs. The lungs are bulky, congested and brownish in color. Pulmonary venous engorgement leads to alveolar hemorrhage. Hemoglobin from intra-alveolar blood is transformed into hemosiderin, which is then phagocytized by macrophages. These macrophages are known as heart failure cells. Phagocytes full of brown pigment migrate into intestinal tissue and to the lymph node. The sectioned surface is dark brown. Its process in lungs is named as “*brown induration*” of the lungs.

Spleen. Chronic venous congestion of the spleen occurs in right heart failure and in portal hypertension from cirrhosis of liver. The spleen in early stage is moderately enlarged while in long-standing cases there is progressive enlargement and may weigh up to 500 g to 1000 g. The organ is deeply congested, tense and cyanotic (“*cyanotic induration of the spleen*”). Sectioned surface is gray tan. The red pulp shows congestion and marked sinusoidal dilatation with areas of recent and old hemorrhages. These hemorrhages may get organized. This advanced stage seen more commonly in hepatic cirrhosis is called *congestive splenomegaly* and is the commonest cause of hypersplenism.

Liver. Chronic venous congestion of the liver occurs in right heart failure and sometimes due to occlusion of inferior vena cava and hepatic vein. The liver is enlarged and tender and the capsule is tense. Cut surface shows characteristic “*nutmeg liver*” due to red and yellow mottled appearance. The changes of congestion are more marked in the centrilobular zone due to severe hypoxia than in the peripheral zone. The centrilobular hepatocytes undergo degenerative changes, and eventually *centrilobular hemorrhagic necrosis* may be seen. The peripheral zone of the lobule is less severely affected by chronic hypoxia and shows some *fatty change* in the hepatocytes. If the patient has periods of remission, the remaining liver cells may undergo compensatory hyperplasia. This results in small, irregular, pale nodules alternating with areas of fibrosis – so-called cardiac cirrhosis. It's not true cirrhosis and does not cause hepatic failure.

Consequences of venous hyperemia: hypoxia, hypotrophy atrophy, hypoplasia, sclerosis, necrosis, induration of organs, edema, stasis, hemorrhage, thrombosis.

Ischemia

Ischemia is an imbalance between the supply and demand of the organ or tissue for blood. It implies insufficient oxygen and nutrients delivery and inadequate removal of metabolites.

Types of ischemia

- Angiospastic (reflex).
- Obstructive.
- Compressive.
- Because of redistribution of blood.

Mechanisms of ischemia:

- Neurogenic mechanisms** (neurotonic and neuromyolytic) of ischemia development.

- **neurotonic mechanism** is predominance of the effects of the sympathetic nervous system on the walls of arterioles in comparison with the parasympathetic (increases releasing of catecholamines and / or increases the sensitivity of adrenoceptors of arterioles walls (f.e. stress, the effect on tissues of low temperature, mechanical trauma, chemicals).

- **neuromyolytic mechanism** It is characterized by the elimination or reduction ("paralysis") of parasympathetic influences on the walls of arterioles.

- Humoral mechanism**

- increasing the content of substances with **vasoconstrictive action** (eg, **angiotensin II**, **thromboxane A2**, **adrenaline**, **PgF**) in the tissues

- increasing the sensitivity of arteriolar wall receptors to agents with a **vasoconstrictive effect** (for example, with an increase in tissues $[Ca^{2+}]$ or $[Na^{+}]$). This leads to a contraction of SMC walls of arterioles, narrowing them and to the development of ischemia.

- Mechanical:**

- **compression** (compression) of the arterial vessel with a tumor, scar, edematous tissue, tourniquet;

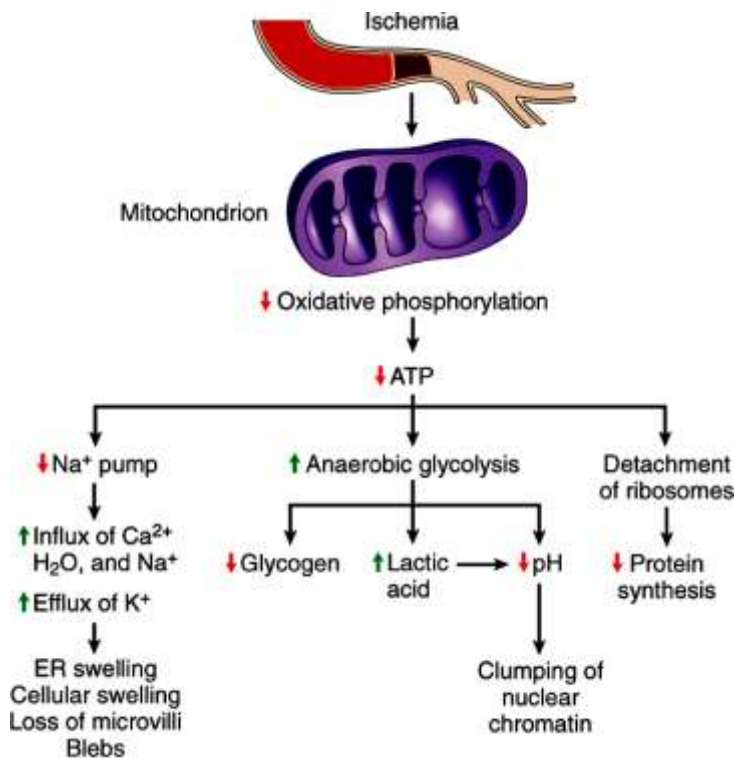
- **obstruction** (until complete closure: obturation), decrease of the arterioles lumen (for example, thrombus, aggregate of formed blood elements, embolus).

- **an increase in blood viscosity**: polycythemia, massive hemoglobinemia or myoglobinemia.

- Increase in metabolic demand** outpacing the blood supply.

- Rapid lowering of the systemic blood pressure** as in shock or collapse.

- Combination** of the listed above.



Manifestations and their mechanisms:

- A decrease in diameter and number of visible vessels.

- Pallor: reduction in the amount of hemoglobin.

- A decrease or disappearance of pulsation.

- A reduction of lymph output due to a decrease in interstitial pressure caused by reduction of water filtration from capillaries into interstitium.

- A decrease in local temperature due to a reduced blood inflow and decreased rate of oxygen-dependent metabolism.

- A reduction in diameter of arterioles and precapillaries, a decreased capillary bed and low blood flow velocity.

The consequences of ischemia: coagulation necrosis or infarct, apoptosis. Moderate ischemia can result in hypotrophy, atrophy and sclerosis.

Figure 2 Mechanism of cell damage in ischemia

Morphologic features

The primary response of acute ischemia is cellular swelling or edema with dilation of the endoplasmic reticulum, dissociation of polysomes into monosomes, swelling of mitochondria, and also increased concentration of water, sodium, and chloride and decreased concentration of potassium into the cytoplasm. If the duration of ischemia is short, the structure and the function of tissue may be restored.

If ischemia persists, irreversible injury ensues with severe vacuolization of the mitochondria including their cristae, extensive damage to cytoplasm membranes, and swelling of lysosomes. When the lesion is continuous, infarction, atrophy or sclerosis may develop.

Infarction

Infarction is an area of ischemic necrosis within a tissue or an organ, produced by occlusion of either its arterial supply or its venous drainage.

Types of infarctions:

Ischemic (white) infarction is encountered with arterial occlusion and in solid tissues (spleen).

Red (hemorrhagic) infarction is encountered with venous occlusion, in tissue as with double circulation, and in tissue previously congested (lung, intestine).

White infarction with hemorrhagic halo (kidneys, heart).

Pathogenesis

The process of infarction takes place as follows: localised hyperemia due to local anoxemia. Within a few hours, the affected part becomes swollen due to edema and hemorrhage. Cellular changes such as cloudy swelling and degeneration appear early. There is progressive autolysis of the necrotic tissue and hemolysis of the red cells. An acute inflammatory reaction and hyperemia appear at the same time in the surrounding tissues. Blood pigments, hematin and hemosiderin, liberated by hemolysis is deposited in the infarct. Following this, there is progressive ingrowth of granulation tissue from the margin of the infarct.

Postischemic reperfusion phenomenon

There are two modern hypotheses of reperfusion mechanisms:

1. **«Calcium» hypothesis** — an overload of cardiomyocytes with calcium ions results in reperfusion contracture, a decrease in diastolic volume and cardiac output.
2. **«Free radical» hypothesis** — the toxic effect of oxygen on the myocardium in reoxygenation after ischemia.

Ischemic syndromes also include:

Ischemic preconditioning «intermittent ischemia» [Gurin, 1997], phenomenon of metabolic adaptation that occurs after one or several short intermediate 5 minute ischemia reperfusion and to increase the stability of myocardium to the damaging effect of a long period of ischemia and reperfusion.

The mechanism of the phenomenon is associated with activation of ATP-dependent potassium channel => formed a tendency to normalization of intra- and extracellular ion balance.

Thrombosis

Thrombosis is a pathologic process, which denotes the formation of a clotted mass of blood within the noninterrupted vascular system.

Influences predisposing to thrombosis:

1. Injury to endothelium;
2. Alterations in the normal blood flow;
3. Alterations in the blood coagulation system (hypercoagulability).

Blood vessels and platelets the first react to injury (primary hemostasis), followed by blood coagulation occurs with the participation of plasma factors (secondary), although both of these mechanisms are mutually potentiate each other and function conjugately.

Mechanisms of formation

The mechanism of vascular-platelet hemostasis

Activation of vascular-platelet (primary) hemostasis makes a complete stop of bleeding from capillaries and venules and temporary stop of bleeding from veins, arterioles and arteries by forming the primary hemostatic plug from which upon activation of the secondary (coagulation) hemostasis formed thrombus.

Key mechanisms of thrombosis are: damage of vascular endothelium; local vasoconstriction; adhesion of platelets to the site of naked subendothelium; platelet aggregation; activation of blood clotting while reducing its lytic properties.

1. Damage of endothelium and the primary vasospasm

Microvessels respond to damage by short-term spasm, causing them bleeding does not occur in the first 20-30 seconds. Reflex spasm of blood vessels by contraction of smooth muscle cells of the vascular wall and supported by vasospastic agents secreted by the endothelium and platelets (serotonin, TxA₂, norepinephrine, and others).

Endothelial damage is accompanied by a decrease in of the vascular wall and thromboresistance naked subendothelium that contains collagen and expresses the adhesion proteins - von Willebrand factor, fibronectin, thrombospondin.

2. The adhesion of platelets to the site of naked subendothelium

Carried out in the first few seconds after endothelial damage due to:

- reducing amount of surface negative charge of the vascular wall in violation of its integrity;
- platelets receptor to collagen.

The stabilization of the resulting compound is carried adhesion proteins - von Willebrand factor, fibronectin and thrombospondin, forming "bridges" between their complementary platelet glycoprotein and collagen.

3. Activation of platelets and secondary vasospasm

The activation of platelets is caused by thrombin that formed from prothrombin under the influence of tissue thromboplastin, PAF, ADP (released together with thromboplastin at the vascular wall damage), Ca²⁺, adrenaline.

The process of platelets activation is associated with the chemical modification of membranes and induction of enzyme glycosyltransferase, phospholipase A₂ in them. Glycosyltransferase interacts with specific receptor on the molecule of collagen and thereby provides "landing" of platelets on the subendothelium.

Phospholipase A₂ starts the hydrolysis of phosphatidylethanolamine, that lead to the release of arachidonic acid. From arachidonic acid by the action of COG formed prostaglandins PgG₂, PgH₂, that transforming to the TxA₂ (a potent inducer of platelet aggregation and vasoconstrictor) under the influence of an enzyme thromboxane synthetase. Prostaglandins contribute to the accumulation of cAMP in platelets, regulate protein phosphorylation and activation of calmodulin, that transporting Ca²⁺ from the dense tubular system of platelets into the cytoplasm. As a result, there is an activation of contractile protein of actomyosin complex, which is accompanied by a contraction of microfilaments of platelets with the pseudopodia formation. This further enhances platelet adhesion to the damaged endothelium.

At the same time, by the Ca²⁺-induced contraction of microtubules occurs emptying of granules at two phases: the first phase – release the contents from dense granules, the second – α-granules. TxA₂ and dismissed from the dense granules of platelets vasoactive substances cause secondary vasospasm.

4. Platelets aggregation

During degranulation of platelets are released TxA₂, ADP, serotonin, β-thromboglobulin, platelet factor 4, fibrinogen and others components of dense granules and α-granules. They cause sticking of platelets together and with collagen. In addition, the appearance of the paf in the bloodstream (at endothelial destruction) and components of platelet granules leads to the activation of intact platelet, their aggregation with platelets that adherent on the endothelium.

Platelets aggregation does not develop in the absence of extracellular Ca²⁺, fibrinogen.

5. The formation of hemostatic plug

As a result of platelet aggregation formed primary (temporary) hemostatic plug that obturate vascular defects (does not contain fibrin). Subsequently, on the surface of platelets aggregate adsorbed plasma coagulation factors and starts the "internal cascade" of coagulation that ends by the precipitation of stabilized fibrin fibers and the formation of platelet plug on the basis of a blood clot (thrombus).

At contraction of platelets thrombosthenin the thrombus compacted (clot retraction).

"External cascade" of blood clotting involves the release of tissue thromboplastin. Additionally, platelets can independently (in the absence of contact factors) start of blood clotting by the interaction of the factor Va (exposed on their surface) with factor Xa of plasma, catalyzes the conversion of prothrombin to thrombin.

The mechanism of coagulation hemostasis

There are three stages of the blood clotting process. The first stage ends with the formation of active prothrombinase complex on membrane phospholipids, which includes factors X, V, and Ca²⁺ + by internal and external mechanisms. The second stage is characterized by the formation of thrombin (the

active form of factor II). In the third stage (final phase of blood clotting) there is a formation and stabilization of fibrin clot.

Normal hemostasis is attained by cooperation and interaction of primary (vascular platelet) and secondary (coagulation) mechanisms of hemostasis impairments.

Types of thrombi

According to the degree of the lumen obstruction, thrombi may be:

- Occlusive thrombi most commonly develop in small arteries and veins.
- Wall-attached or parietal thrombi develop in large arteries and heart cavities.
- Axial.
- Globe-shaped (in the heart).

According to the morphology

Thrombi may be of various shapes, size and composition depending upon the site of origin and it is attached to the vascular wall; it is dense, with corrugated surface. It is composed of branching bars of stuck thrombocytes and bands of fibrin with erythrocytes and leukocytes located between them.

Morphological types of thrombi

- **White thrombus** – consists mainly of platelets, fibrin and leukocytes; forms slowly in rapid circulation of the blood (usually in the arteries);
- **Red thrombus** – consists of platelets, fibrin and excessive amount of erythrocytes; forms rapidly at slow blood circulation (usually in veins). Venous thrombi are dark-red colored dry masses with dim surface.
- **Mixed or laminated thrombus** – has laminated structure, contains white and red elements of thrombus (usually forms in veins, aneurysms of aorta and heart). Mixed thrombus consists of core or head (white thrombus), body (white and red) and tail (has construction of red thrombus). Core is connected with endothelium. Mixed thrombus is of gray-red color with rough dim surface, fixed to the intima of the vessel. Body and tail are located freely in the vessel's lumen.
- **Hyaline thrombus** consists of precipitating plasma proteins, destructed erythrocytes, leukocytes and thrombocytes. They do not contain fibrin. They resemble hyaline and are located in the microcirculatory bed.
- **Agonal thrombus** – consists of the yellowish fibrin and localizes in the apex of the right ventricle of the heart and may extend into pulmonary artery. It is formed in the last minutes of the life when the death occurs slowly. Red clot forms in case of the rapid death.

The distinguishing features between thrombi formed in rapidly-flowing arterial circulation and slow-moving venous blood are given in Table 1.

TABLE 1. Distinguishing Features of Arterial and Venous Thrombi.

Feature	Arterial thrombi	Venous thrombi
Blood flow	Formed in rapidly-flowing blood of arteries and heart	Formed in slow-moving blood in -veins
Sites	Common in coronary, cerebral, iliac and femoral arteries	Common in superficial varicose veins, deep leg veins, popliteal, femoral and iliac veins
Thrombogenesis	Formed following endothelial cell injury, e.g. in atherosclerosis	Formed following venous stasis, e.g. in abdominal operations, child-birth
Development	Usually mural, not occluding the lumen completely, may propagate.	Usually occlusive, take the cast of the vessel in which formed, may propagate in both directions.
Macroscopy	Grey-white, friable with lines of Zahn on surface.	Red-blue with fibrin strands and lines of Zahn.
Microscopy	Distinct lines of Zahn composed of platelets, fibrin with entangled red and white blood cells.	Lines of Zahn with more abundant red cells.
Effects	Ischemia leading to infarcts, e.g. of heart, brain etc.	Thromboembolism, edema, skin ulcers, poor wound healing.

Outcomes of the thrombosis

1. Favourable outcomes:

- **Aseptic autolysis** (dissolution) by fibrinolytic system, proteinolytic enzymes of macrophages and leukocytes.
- **Organization** by the replacement of connective tissue.
- **Recanalization** is the re-establishment of the vascular lumen through occluding thrombus.
- **Incorporation or vascularization** means restoration of the circulation in the vessel because of the formation of the new vessels through the thrombotic mass.
- **Petrification or dystrophy calcification** – accumulation of the calcium salts in the thrombotic masses.

2. Unfavourable outcomes:

- **Thromboembolism.**
- **Septic autolysis.**
- **Propagation** with following obstruction of some critical vessel.

Embolism

Embolism is the passage through the venous or arterial circulations of any material capable of lodging in a blood vessel and they're by obstructing the lumen. The transported intravascular mass detached from its site of origin is called an embolus.

Types of embolism

According to localization:

- Small blood circulation.
- Large blood circulation.
- System of vena portae.

According to the direction of the movement of embolus:

- **Orthograde** (by blood flow)
- **Retrograde** (against blood flow). Metastasis of the carcinoma prostate in the spine takes place.
- **Paradoxical** (emboli arising in the venous circulation may by pass the lungs by travelling through an incompletely closed foramen ovale, subsequently blocking flow in systemic arteries).

According to the nature of the embolus:

I. Exogenous embolism:

- **Air** – from large vein with a damage of neck and chest, and that is very important for iatrogenic disease.
- **Gas** – is the result of bubbling in the blood soluble gas with rapid transition from high pressure to normal or from normal to a low.
- **Microbial** – marked at septicopyemia, as a factor in the development of metastatic abscesses.
- **Parasite** – occurs when helminthiasis. For example, in ascariasis possible pulmonary embolism. In tropical countries, common embolism lymph vessels of the extremities, leading to disruption of lymph drainage from the extremities to the formation of elephantiasis.

II. Endogenous embolism:

- **Thromboembolism:** Venous – v.femoralis, pelvic vessels; - Arterial – left heart thrombus, dissection. Is the most dangerous type of pulmonary embolism (PE) with the development pulmocoronary reflex, leading to the death of patients.
- **Fat:** in trauma with fractures of long bones or crush fat, when the fat entry in the bloodstream. Often a complication of crush syndrome (declamping shock, crush syndrome).
- **Amniotic fluid embolism:** marked pathological birth or wrong maternity aid. Is the major factor initiating DIC (disseminated intravascular coagulation).
- **Tissue** - the fragmentation of tissue - chorionic villi, the tumor site - one of the ways of metastasis, etc.
- **Cell** (highlighted by some authors – resembling with tissue type).

Thromboembolism

A detached thrombus or part of thrombus constitutes the most common type of embolism. These may arise in the arterial or venous circulation:

The effects of *arterial emboli* depend upon their size, site of lodgement, and adequacy of collateral circulation:

- Infarction.
- Gangrene.
- Arteritis and mycotic aneurysm.
- Myocardial infarction.
- Sudden death.

The most significant effect of *venous embolism* is obstruction of pulmonary arterial circulation leading to pulmonary embolism.

Pulmonary thromboembolism

Pulmonary embolism is the most common and fatal form of venous thromboembolism in which there is occlusion of pulmonary arterial tree by thromboemboli. Pulmonary emboli are more common in hospitalised or bedridden patients. The majority of emboli arise from the deep veins of the low extremities; most of the fatal ones arise from the iliofemoral veins.

Condition that favor the development of pulmonary thromboembolism are:

- Stasis (heart failure, chronic venous insufficiency).
- Injury (trauma, surgery, parturition).
- Hormonal imbalance (oral contraceptive use).
- Advanced age.
- Immobilization (orthopedic, paralysis, bed rest).
- Sickle cell disease.

Pathogenesis

Detachment of thrombi from any of the above-mentioned sites produces a thromboembolus that flows through venous drainage into the large veins draining into right side of the heart.

If the thrombus is large, it is impacted at the bifurcation of the main pulmonary artery (saddle embolus), or may be found in the right ventricle or its outflow tract.

More commonly, there are multiple emboli, or a large embolus may be fragmented into many smaller emboli.

Paradoxical embolism may occur by passage of an embolus from right heart into the left heart through atrial or ventricular septal defect.

Consequences of thromboembolism

1. Consequences of pulmonary embolism. These include:

Pulmonary Syndrome (Infarction). The pulmonary syndrome clinically resembles pneumonia. Pleural effusion is common and often bloody. Pathologically, pyramidal segments of hemorrhagic infarction are seen at the periphery of the lung. Obstruction of terminal branches (endarteries) leads to central *pulmonary hemorrhage*.

Circulatory Syndrome (Without Infarction). Embolism produces pulmonary hypertension by mechanical blockage of the arterial bed. Reflex vasoconstriction and bronchial constriction due to release of vasoactive substances may contribute to a reduction in the size of the functional pulmonary vascular bed. Whether a patient develops the pulmonary or the circulatory syndrome depends on the thromboembolic load and the availability of circulatory reserve of the bronchial arteries. *Pulmonary hypertension may lead to chronic cor pulmonale and pulmonary arteriosclerosis.* Numerous small emboli may obstruct most of the pulmonary circulation resulting in acute right heart failure (*Acute cor pulmonale*).

Massive Pulmonary Embolism. Massive pulmonary emboli typically cause sudden obstruction of blood flow through one or both of the major pulmonary arteries. The patient often goes into shock immediately - resumably because of certain: neurologic reflexes - and may die within minutes. This catastrophe is characteristically precipitated when a patient who has been recuperating from surgery gets out of bed for the first time.

2. Consequences of emboli in peripheral arteries. The heart is the most common source of systemic emboli, which usually arise from mural thrombi (in atrial fibrillation, mitral valve disease,

myocardial infarction, left ventricular aneurysm, heart failure of any etiology, cardiomyopathy) or diseased valves (bacterial endocarditis, marantic endocarditis).

Clinical and morphological features: arterial emboli to the brain cause strokes; in the mesenteric circulation they cause infarction of the bowel; embolism of an artery of the legs leads to sudden pain, absence of pulse, and a cold limb; renal artery embolism may infarct the entire kidney but more commonly results in small peripheral infarcts; coronary artery embolism results in myocardial infarctions.

Thus, the effects and sites of arterial emboli are in striking contrast to venous emboli, which are often lodged in the lungs.

Questions for self-control of knowledge:

1. What are etiology, pathogenesis, clinical manifestations and types of arterial hyperemia?
2. Specify mechanisms and clinical manifestations of venous hyperemia (Muscat liver, brown induration of lungs, etc.).
3. What are causes, mechanisms, forms and manifestations of ischemia in various organs.
4. Explain mechanism of postischemic reperfusion phenomenon in organ.
5. What is biological significance of stasis for typical pathological processes?
6. What are differences thrombus from emboli, significance, outcomes and consequences of thrombosis.
7. Give a definition of "embolism." What are etiology and pathogenesis of embolism? Describe a concept of pulmonary thromboembolism (PTE). Name types, manifestations and outcomes. What is basis of pathophysiological pharmacological correction of PTE?
8. How manifest a disorder of microcirculation in arterial and venous hyperemia, ischemia? Explain relation of violations of macro-and microcirculation during local circulatory disorders.

Tasks for self-managed student work:

1. Mechanisms of reperfusion tissue damage.
2. Modern ideas about mechanisms of blood clotting and thrombosis.
3. Pulmonary embolism.

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