Ministry of Health of the Republic of Belarus
Educational Institution
“Gomel State Medical University”

Department of Pathological Anatomy

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METHODICAL GUIDELINES

for conducting a practical class
in the academic discipline “Pathological Anatomy”
for students
of the 3rd year, Faculty of International Students (instruction in English),
enrolled in the specialty
7-07-0911-01 “General Medicine”

Topic: “Circulatory disorders: thrombosis, embolism, infarction, disseminated intravascular coagulation (DIC) syndrome”

Duration: 3 hours

Approved at the meeting of the Department of Pathological Anatomy
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EDUCATIONAL AND INSTRUCTIONAL GOALS, OBJECTIVES, AND MOTIVATION FOR MASTERING THE TOPIC

Educational Goal:

- To analyze the mechanisms of thrombus formation as a complex enzymatic process. To familiarize students with the coagulation and anticoagulation systems of the blood, the disruption of whose dynamic balance underlies thrombus formation. To indicate the general and local conditions that promote thrombogenesis. To draw attention to the frequency of thrombosis in patients with cardiovascular insufficiency, in various infectious and neoplastic diseases, and after surgical interventions. To emphasize the predisposition to thrombosis in patients with atherosclerosis and other diseases of the cardiovascular system. To study the types of thrombi, the conditions of their formation, and their fate. To trace the significance of thrombosis depending on the nature and caliber of the vessel. To note the protective-adaptive significance of the blood coagulation process.
- To define the phenomenon of embolism. To analyze the types of embolism according to the nature of the emboli (thrombus fragments, fat, air, gas, bacteria, tumor cells). To demonstrate the role of embolism in circulatory disorders and in the development of metastases (purulent processes, tumors). To note the frequency of pulmonary thromboembolism as a cause of death in patients.
- To analyze infarction as an example of indirect circulatory necrosis. When discussing the direct causes of infarcts (spasm, thrombosis, embolism), to indicate the importance of collaterals and general circulatory disturbances for their occurrence. To characterize the three types of infarcts, linking the conditions of their formation to the architectural features of organs.

Instructional Goal:

- Within the framework of the educational process for this academic discipline, the student must acquire not only theoretical knowledge, practical skills and abilities in the specialty but also develop their personal potential. They should cultivate qualities of responsibility and patriotism, be prepared to actively participate in the economic, socio-cultural, and public life of the country, recognize the social significance of their future professional activity, understand the norms of medical ethics and deontology, and learn to observe academic and labor discipline. In the course of studying the educational material, students should realize the importance of maintaining a healthy lifestyle and, as an example in the future, when performing professional duties, set an example for those around them and their patients.

Objectives: Upon completion of the practical session, the student must:

***Know*:**

- The causes, mechanisms, and morphological features of typical general pathological processes;
- The etiology, pathogenesis, and morphology of diseases at different stages of their development (morphogenesis), the structural basis of recovery,

complications, outcomes, and long-term consequences of diseases, as well as the causes and mechanisms of dying (thanatogenesis).

Be able to:

- Define thrombosis, name its causes and conditions;
- Provide a morphological characterization of a thrombus, distinguish it from a thromboembolus and a postmortem clot;
- Assess the significance of thrombosis and its outcomes for the organism;
- Define embolism and know its types;
- Assess the significance of embolism for the organism and the mechanism of death in pulmonary thromboembolism;
- Define infarction, know its causes and stages of development;
- Diagnose types of infarcts based on macroscopic and microscopic appearance;
- Assess the significance of infarction and its outcomes;
- Define Disseminated Intravascular Coagulation (DIC) syndrome, know its causes and mechanisms of development, changes in organs, outcomes, and significance for the organism.

Master:

- Basic techniques for working with a microscope;
- Skills in clinical-anatomical analysis;
- The fundamentals of synthetic generalization of morphological diagnostic signs of diseases and their correct interpretation in cause-and-effect relationships.

Motivation for Mastering the Topic:

Thrombosis, embolism, and infarction often become fatal complications of cardiovascular diseases, tumors, and surgical interventions, and their incidence is increasing every year. This knowledge is also essential for the future professional activity of a physician for assessing the quality and effectiveness of treatment, diagnosing and treating diseases, as well as for analyzing the sources of diagnostic errors in clinical practice.

QUESTIONS

1. Infarction. Definition. Classification. Etiology. Clinical examples. Outcomes.
2. Thrombosis. Definition. Pathophysiology. Thrombus morphology. Etiology. Clinical examples. Outcomes.
3. Embolism. Definition. Classification. Etiology. Clinical examples. Outcomes.
4. Disseminated intravascular coagulation (DIC). Definition. Pathophysiology. Etiology. Clinical examples. Outcomes. Blood stasis. Sludge phenomenon.

COURSE OF THE SESSION

Thrombosis refers to the formation of a blood clot inside a blood vessel or within the heart while the person is still alive.

1) **White Thrombus**: Composed mostly of platelets and fibrin, the white thrombus forms slowly where the blood flow is fast, such as in arteries.

2) **Red Thrombus**: This type of thrombus contains platelets, fibrin, and red blood cells. It forms quickly in areas where blood flow is slower, such as in veins.

3) **Mixed Thrombus**: The mixed thrombus has components of both white and red thrombi. It has three parts: the head, which resembles a white thrombus and attaches to the vessel wall; the body, which is a mix of white and red; and the tail, which is similar to a red thrombus. A key feature of a mixed thrombus is that its head is attached to the lining of the blood vessel, which differentiates it from clots that form after death, known as postmortem clots.

4) **Hyaline Thrombus**: Formed in small vessels of the microcirculation, the hyaline thrombus consists of plasma proteins, platelets, and fragments of red blood cells. It typically occurs in situations of widespread small vessel damage.

Virchow's triad

Rudolf Virchow's Triad is a foundational concept in medicine that describes the three critical factors leading to the formation of venous thrombosis. Venous thrombosis occurs when a blood clot (thrombus) forms within a vein, which can obstruct blood flow and cause serious complications, such as deep vein thrombosis (DVT) or pulmonary embolism (PE).

Virchow's Triad explains the interplay between the following three factors that create a conducive environment for clot formation:

1) **Endothelial Injury** (Damage to the blood vessel wall)

2) **Hypercoagulability** (Increased tendency for blood to clot)

3) **Circulatory Stasis** (Abnormal or slowed blood flow)

These factors are not mutually exclusive; they often act together, amplifying the risk of thrombosis. Understanding how these elements interact is key to predicting, diagnosing, and preventing venous thrombosis in a variety of clinical settings.

Virchow's triad

1) **Vascular Damage** (**Endothelial Injury**)

- *Mechanism*: The endothelium, the inner lining of blood vessels, acts as a protective barrier that prevents clot formation under normal conditions. When this barrier is disrupted, underlying collagen and tissue factors are exposed, leading to platelet adhesion, activation, and aggregation.
- *Causes*:
  - Trauma (surgical wounds, fractures)
  - Inflammation (vasculitis)
  - Atherosclerosis (plaque rupture)
  - Invasive procedures (catheters, IVs)
  - Radiation or chemotherapy

- *Clinical Example*: Vascular damage from surgery or a catheter insertion often predisposes patients to venous thrombosis.

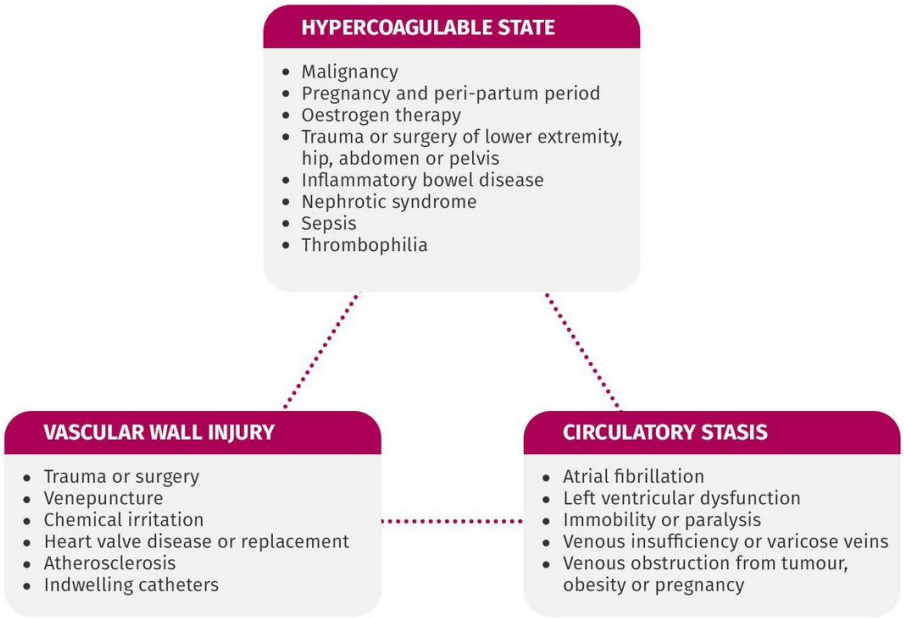
2) **Hypercoagulability**

- *Mechanism*: Hypercoagulability refers to an increased tendency for the blood to clot. This can result from an imbalance between pro-coagulant and anticoagulant factors. Genetic predispositions, such as Factor V Leiden mutation or deficiencies in natural anticoagulants like protein C and S, can enhance clot formation.
- *Causes*:
  - Genetic disorders (Factor V Leiden, Prothrombin G20210A mutation)
  - Acquired conditions (cancer, pregnancy, hormone replacement therapy)
  - Autoimmune diseases (antiphospholipid syndrome)
  - Dehydration, which increases blood viscosity
- *Clinical Example*: Patients with cancer are at higher risk of venous thromboembolism (VTE) due to tumor-related hypercoagulability.

3) **Abnormal Blood Flow** (**Circulatory Stasis**)

- *Mechanism*: Normally, blood flow prevents the accumulation of clotting factors by continuously washing them away. In stasis, blood flow slows or stops, allowing clotting factors and platelets to come into closer contact and initiate clot formation. Stasis is particularly important in veins.
- *Causes*:
  - Prolonged immobility (bed rest, long flights)
  - Venous insufficiency or varicose veins
  - Obstruction of blood flow (tumors, pregnancy)
  - Heart failure (reduces cardiac output and venous return)
- *Clinical Example*: Deep vein thrombosis (DVT) often occurs in individuals who are immobilized for long periods, such as those recovering from surgery or bedridden due to illness.

Virchow's triad



Outcomes of thrombosis

Favorable outcomes of thrombosis:

1) **Aseptic autolysis**: The thrombus gradually dissolves due to the action of proteolytic enzymes from blood and surrounding tissues, without causing infection.

2) **Organization**: Fibroblasts invade the thrombus, leading to its transformation into fibrous tissue, effectively stabilizing the clot and integrating it into the vessel wall.

3) **Vascularization**: New blood vessels grow into the organized thrombus, potentially restoring blood flow through the affected area.

4) **Petrification**: The thrombus calcifies and becomes a hard, stone-like structure, preventing further complications.

Unfavorable outcomes of thrombosis:

1) **Thromboembolism**: A part or the entire thrombus breaks off, travels through the bloodstream, and lodges in a distant vessel, potentially causing a life-threatening condition like pulmonary embolism or stroke.

2) **Septic fusion of a thrombus**: If the thrombus becomes infected, it can lead to septicemia, abscess formation, or further tissue destruction due to bacterial invasion.

Embolism

Embolism refers to the circulation of abnormal particles, such as clots, fat droplets, or air bubbles, in the blood or lymph, leading to the blockage of blood vessels.

Types of embolism based on the **movement direction** of the embolus:

1) **Ordinary (orthograde) embolism**: The embolus moves in the direction of normal blood flow, usually traveling from the veins towards the lungs (pulmonary embolism) or from the arteries to distant organs (systemic embolism).

2) **Retrograde embolism**: The embolus moves against the direction of blood flow due to the influence of gravity.

3) **Paradoxical embolism**: Occurs when an embolus from the venous system bypasses the lungs and enters the arterial system through a defect in the heart, such as an atrial or ventricular septal defect. This allows the embolus to travel to systemic circulation, potentially blocking arteries in vital organs.

1) **Thromboembolism** occurs when part of a blood clot breaks off and travels through the bloodstream, blocking vessels elsewhere. An example is **pulmonary embolism** (PE), where a clot from the deep veins of the legs (**deep** vein thrombosis, DVT) **travels to the lungs and blocks pulmonary arteries**. Symptoms include sudden shortness of breath and chest pain. Stroke can also result from thromboembolism when a clot forms in the heart (often due to atrial fibrillation) and blocks blood flow to the brain.

2) **Fat embolism** occurs when fat droplets enter the bloodstream, often following trauma. Fat embolism syndrome (FES) is commonly seen after **fractures** of long bones like the femur. Fat from bone marrow enters the bloodstream, lodging in the lungs, brain, or other organs. This causes respiratory distress, confusion, seizures, and a petechial rash. It can also occur after **liposuction** if fat is inadvertently introduced into the bloodstream.

3) **Air embolism** happens when air enters the circulation and disrupts blood flow. Venous air embolism can occur after **neck vein injuries**, where air is sucked into the vein. Symptoms include chest pain, cyanosis, and breathing difficulties. In surgery, accidental introduction of air during **intravenous administration** or neurosurgical procedures can lead to air embolism. In obstetrics, air embolism may occur during **delivery** or **abortion**.

4) **Gas embolism** involves the formation of gas bubbles in the bloodstream, often from rapid pressure changes. **Decompression sickness**, also known as "the bends," occurs when divers ascend too quickly, causing nitrogen bubbles to form in their blood and tissues. Symptoms include joint pain, dizziness, and paralysis. Hyperbaric oxygen therapy is a treatment that reduces gas bubble size by providing high levels of oxygen.

5) **Tissue embolism** occurs when fragments of tissue or cells enter the bloodstream. **Amniotic fluid** embolism can happen during or after childbirth when amniotic fluid enters the mother's bloodstream. This leads to cardiovascular collapse, respiratory failure, and disseminated intravascular coagulation (DIC). Tumor embolism is another example, where malignant tumor cells spread through blood vessels, blocking small vessels and contributing to **metastasis**.

6) **Microbial embolism** results from bacteria or other microorganisms traveling in the blood and blocking small vessels. In **infective endocarditis**, bacterial vegetations on heart valves can break off and cause embolism, leading to stroke or abscesses in the brain or lungs. Septicemia may lead to microemboli, causing tissue damage.

7) **Embolism by foreign bodies** occurs when non-biological materials enter the bloodstream. **Intravenous drug users** may experience embolism when fragments of needles or cotton enter the veins, leading to pulmonary embolism or sepsis. **Catheter embolism** can occur if a fragment breaks off during a medical procedure, causing vessel blockage and tissue damage.

Foreign body embolism

Extravascular embolized **crospovidone** and a few small fragments of microcrystalline cellulose with a foreign body giant cell reaction.

Crospovidone has a coral-like appearance and is an insoluble polymer of N-vinyl-2-pyrrolidone that is used as a disintegrant in pharmaceutical tablets.

It embolizes to the lungs when aqueous **suspensions** of pulverized tablets **are injected intravenously**.

Foreign body embolism

Hydrophilic polymers are widely used as surface coatings on **vascular medical devices**, including guidewires, introducer and delivery sheaths, and implantable stents and coils, as well as cardiac, central, and peripheral catheters.

These surface coatings have unique properties that enhance biocompatibility and maneuverability of **endovascular technologies**, while decreasing friction and reducing trauma to vessel walls.

Select polymers also enable targeted intravascular drug delivery while decreasing systemic toxicity and improving compliance.

Infarction

Infarction is the localized death of tissue due to the interruption of blood supply, leading to ischemia. This can result in necrosis, where the affected tissue becomes irreversibly damaged and can no longer function.

Classification of Infarction

1) By **Color**:

- **Red** (**Hemorrhagic**) Infarction: Occurs in tissues with dual blood supply (e.g., lungs, liver) or where blood flow is re-established after ischemia. The presence of blood in the necrotic area gives it a red color.
- **White** (**Anemic**) Infarction: Typically found in solid organs (e.g., heart, spleen, kidneys) with a single blood supply. It appears pale due to the absence of blood.

2) By **Timing**:

- **Acute** Infarction: Sudden onset due to an abrupt obstruction of blood flow (e.g., thrombosis, embolism).
- **Chronic** Infarction: Occurs over a longer period, often due to progressive ischemia (e.g., from atherosclerosis).

3) By **Tissue** Type:

- **Myocardial** Infarction: Infarction of heart muscle due to coronary artery blockage.
- **Cerebral** Infarction: Infarction of brain tissue, often referred to as a stroke, due to blockage of cerebral arteries.
- **Pulmonary** Infarction: Infarction of lung tissue, usually resulting from a pulmonary embolism.

Etiology of infarction

1) **Thrombosis**: Formation of a blood clot within a blood vessel, obstructing blood flow (e.g., coronary thrombosis).

2) **Embolism**: A clot or other debris travels through the bloodstream and lodges in a blood vessel, blocking circulation (e.g., pulmonary embolism).

3) **Atherosclerosis**: Plaque buildup in the arteries can lead to narrowing and eventual blockage, causing ischemia.

4) **Vasospasm**: Sudden constriction of a blood vessel can reduce or stop blood flow to an area (e.g., coronary vasospasm).

5) **Compression**: External pressure from tumors or swelling can obstruct blood vessels and cause ischemia.

Clinical examples of infarction

1) **Myocardial Infarction**: Often referred to as a heart attack, this occurs when a coronary artery is blocked, typically by a thrombus. Symptoms include chest pain, shortness of breath, and sweating. It can lead to heart failure or arrhythmias.

2) **Cerebral Infarction** (Stroke): Results from interrupted blood flow to the brain, leading to neurological deficits. It may present with sudden weakness, confusion, difficulty speaking, or loss of coordination.

3) **Pulmonary Infarction**: Occurs when a pulmonary embolism obstructs a blood vessel in the lungs, leading to symptoms such as sudden chest pain, difficulty breathing, and coughing up blood.

4) **Renal Infarction**: May occur due to renal artery thrombosis, presenting with flank pain, hematuria (blood in urine), and hypertension.

Outcomes of infarction

1) **Resolution**: In some cases, the infarcted tissue may be replaced by scar tissue, and function may be partially restored.

2) **Necrosis**: Irreversible cell death occurs, leading to loss of function in the affected organ or tissue.

3) **Organ Dysfunction**: Depending on the location of the infarction, there may be a significant loss of organ function (e.g., heart failure after myocardial infarction).

4) **Complications**: Infarction can lead to serious complications such as cardiac arrhythmias, heart failure, chronic kidney disease, or recurrent strokes.

5) **Death**: In severe cases, particularly with large areas of infarction or vital organs involved, infarction can lead to systemic complications and death.

DIC

Disseminated intravascular coagulation (DIC) syndrome is a complex and severe condition characterized by **widespread activation of the coagulation cascade**, leading to the formation of small blood clots throughout the microcirculation.

This process **disrupts the balance between clot formation and dissolution**, resulting in significant complications such as bleeding and organ dysfunction.

Early recognition and intervention in DIC are crucial to improving outcomes. Treatment typically involves addressing the underlying cause (e.g., infection control, volume resuscitation) and may require supportive measures such as blood product transfusions to manage coagulopathy and hemorrhage.

Key Features of DIC

1) **Widespread Clot Formation**: In DIC, small clots form in the microvasculature, leading to tissue ischemia and damage. This can result in complications such as acute kidney injury, liver failure, and respiratory distress.

2) **Bleeding Tendencies**: Despite the formation of clots, DIC leads to bleeding due to consumption of clotting factors and platelets, as well as the activation of the fibrinolytic system. This paradoxical effect can result in significant hemorrhages in the brain, gastrointestinal tract, or lungs.

3) The most common **causes** of DIC include:

- **Shock of Various Origins**: This includes cardiogenic (heart-related), hypovolemic (low blood volume), anaphylactic (severe allergic reaction), septic (infection), and neurogenic shock.
- **Severe Infections**: Sepsis is a frequent cause of DIC, where bacterial toxins lead to widespread inflammation and coagulation.
- **Obstetric Complications**: Conditions such as placental abruption, amniotic fluid embolism, or severe preeclampsia can lead to DIC.
- **Trauma and Surgery**: Major trauma or extensive surgical procedures.

Stages of DIC

1) **Hypercoagulation**: In the early phase, there is excessive clotting due to increased activation of the coagulation cascade. Patients may show signs of thrombosis in small blood vessels.

2) **Transitional Phase**: This stage represents a shift in the balance of coagulation and fibrinolysis. While clotting continues, the body starts to deplete clotting factors and platelets, increasing the risk of bleeding.

3) **Hypocoagulation**: The sustained activation of the coagulation cascade leads to a critical decrease in clotting factors and platelets, resulting in severe bleeding. This phase is marked by widespread hemorrhage and can lead to multi-organ failure.

4) **Recovery**: If the underlying cause is treated effectively, patients may enter a recovery phase where hemostasis is restored. However, the recovery process can be prolonged, and monitoring for complications remains essential.

DIC vs Local Thrombosis

The primary distinction between DIC and local thrombosis lies in the **systemic nature** of DIC. In DIC, both the coagulation and fibrinolytic systems are **activated simultaneously** throughout the body, leading to the potential for both thrombosis and hemorrhage.

In local thrombosis, the coagulation cascade is activated only in a **specific area**, and the systemic effects are minimal.

In some cases of DIC, thrombosis may dominate, resulting in tissue ischemia, while in other scenarios, excessive fibrinolysis may lead to significant bleeding. This complex interplay can culminate in acute multiple organ failure, significantly increasing the risk of mortality.

INFORMATIONAL AND METHODOLOGICAL PART

MAIN LITERATURE

1. Pathomorphology : textbook / ed. by I.V. Sorokina, V.D. Markovskyi, D.I. Halata. - 2nd ed. - Kyiv : AUS Medicine Publishing, 2020. - 327 p., [10] col. inserts : tab.

2. Klatt, E. C. Robbins and Cotran Atlas of Pathology : [with Student Consult Online Access] / Edward C. Klatt. - third edition. - Philadelphia : Elsevier, 2015. - 587 p. : il.

3. Robbins Basic pathology / [ed. by] Vinay Kumar, Abul K. Abbas, Jon C. Aster. - 9th ed. - [Philadelphia] : Elsevier ; Saunders. - 910 p. : ill., scheme, tab.

ADDITIONAL LITERATURE

1. Sobotta. Atlas of human anatomy. [V. 1]. General anatomy and musculoskeletal system / ed. by F. Paulsen, J. Waschke. - 15th ed. - München : Elsevier. Urban & Fischer, 2011. - 400 p. : ill., col. ill.

2. Sobotta. Atlas of human anatomy. [V. 2]. Internal organs / ed. by F. Paulsen, J. Waschke. - 15th ed. - München : Elsevier. Urban & Fischer, 2011. - 259 p. : ill., col. ill.

3. Sobotta. Atlas of human anatomy. [V. 3]. Head, neck, and neuroanatomy / ed. by F. Paulsen, J. Waschke. - 15th ed. - München : Elsevier. Urban & Fischer, 2011. - 370 p. : ill., col. ill.

4. Weir & Abrahams' imaging atlas of human anatomy / ed.: J. D. Spratt [and oth.] ; consultant eds.: J. Weir, P. H. Abrahams. – 5th ed. - [S.l.] : Elsevier, 2017. - xvi, 263 p. : ill.

NORMATIVE LEGAL ACTS AND DOCUMENTS

1. Order of the Ministry of Health of the Republic of Belarus No. 111 of 06/01/1993 "On further improvement of the pathological service of the Republic of Belarus"

Access mode: http://patan.by/menyu/administrativnyie-proczeduryi.html - The date fccess: 20.03.2022.

ELECTRONIC DATABASES

1. Physician's consultant. Electronic Medical Library = Consultant of the doctor. Electronic medical library [Electronic resource] / Publishing group "GEOTAR-Media", LLC "IPUZ". – Access mode: http://www.rosmedlib.ru/ . – Access date: 03/15/2022.

2. Springer Link [Electronic resource] / Springer International Publishing AG. – Access mode: https:link.springer.com. – Date of access: 03/15/2022.