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: “Tumours: leukemias, lymphomas, multiple myeloma. Anemias”

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 study the classification, morphology, and clinical features of haematological malignancies, including leukemias, lymphomas, and multiple myeloma, as well as the morphological basis of anemias. To analyze acute leukemias (acute lymphoblastic leukemia – ALL, acute myeloid leukemia – AML) and chronic leukemias (chronic lymphocytic leukemia – CLL, chronic myeloid leukemia – CML) with emphasis on peripheral blood and bone marrow findings, cytochemical stains, immunophenotyping, and genetic abnormalities (e.g., Philadelphia chromosome in CML). To examine the classification of lymphomas: Hodgkin lymphoma (nodular sclerosis, mixed cellularity, lymphocyte-rich, lymphocyte-depleted, nodular lymphocyte-predominant) and non-Hodgkin lymphomas (B-cell neoplasms: diffuse large B-cell lymphoma, follicular lymphoma, Burkitt lymphoma, mantle cell lymphoma, marginal zone lymphoma; T-cell and NK-cell neoplasms). To analyze the morphological features, immunophenotype, and genetic alterations characteristic of each lymphoma type. To study multiple myeloma (plasma cell myeloma) including its clinical features, diagnostic criteria (CRAB criteria: hyperCalcemia, Renal failure, Anemia, Bone lesions), and bone marrow histology. To examine anemias (iron deficiency anemia, megaloblastic anemia, hemolytic anemias, aplastic anemia) with emphasis on peripheral blood smear morphology and bone marrow findings.

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 classification of leukemias (acute and chronic, lymphoid and myeloid);
- The morphological features of leukemic cells in peripheral blood and bone marrow;
- The classification of lymphomas (Hodgkin and non-Hodgkin) and the characteristic histological features of common types;
- The diagnostic criteria, clinical features, and bone marrow findings in multiple myeloma;

- The classification, etiology, and morphological features of anemias (peripheral blood smear and bone marrow);
- The immunohistochemical and genetic markers used in haematological diagnosis.

Be able to:

- Identify leukaemic blasts and abnormal lymphocytes on peripheral blood and bone marrow smears;
- Recognize Reed–Sternberg cells in Hodgkin lymphoma;
- Distinguish between different types of anaemia based on red blood cell morphology;
- Diagnose pathological processes and diseases based on the description of macroscopic and microscopic changes in organs and tissues of the body (including lymph nodes, spleen, bone marrow).

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:

Haematological malignancies (leukemias, lymphomas, and multiple myeloma) account for a significant proportion of cancer diagnoses worldwide. Accurate diagnosis and classification of these diseases are essential for determining prognosis and selecting appropriate therapy, which ranges from chemotherapy and targeted agents to stem cell transplantation. Anemias are among the most common haematological disorders encountered in clinical practice, and morphological examination of the peripheral blood smear remains a critical diagnostic tool. Knowledge of the morphological features of these conditions is indispensable for physicians in internal medicine, paediatrics, oncology, haematology, and general practice. This topic provides the foundation for understanding blood disorders and their systemic manifestations.

QUESTIONS

1. Acute leukemias. Definition. Classification. Clinical and morphological manifestations. Complications and causes of death.
2. Chronic leukemias. Definition. Classification. Clinical and morphological manifestations. Complications and causes of death.
3. Multiple myeloma. Definition. Classification. Clinical and morphological manifestations. Complications and causes of death.
4. Lymphomas. Definition. Classification. Clinical and morphological manifestations of Hodgkin and non-Hodgkin’s lymphomas. Complications and causes of death.

5. Anemia: definition, classification, etiology. Morphology of anemia due to blood loss, impaired hematopoiesis (pernicious anemia), and hemolytic anemia. Morphology.

COURSE OF THE SESSION

Acute leukemia is a **rapidly progressing hematological malignancy** characterized by the uncontrolled proliferation of immature, abnormal white blood cells, leading to the suppression of normal blood cell production in the bone marrow.

Morphologically, leukemic cells are typically **poorly differentiated blasts** that accumulate in the bone marrow and often infiltrate other tissues.

Common localizations include the **bone marrow** and **extramedullary sites**.

Acute leukemia is classified into **two main types**: *acute lymphoblastic leukemia* (*ALL*), which affects lymphoid precursors, and *acute myeloid leukemia* (*AML*), which affects myeloid precursors.

Clinical manifestations of acute leukemia arise from bone marrow failure, leading to **anemia**, **thrombocytopenia**, and **neutropenia**. Patients may experience symptoms such as fatigue, weakness, easy bruising, bleeding, recurrent infections, and bone pain.

The disease can progress rapidly, requiring prompt diagnosis through bone marrow aspiration and biopsy, followed by aggressive treatment strategies such as chemotherapy, stem cell transplantation, or targeted therapies.

Chronic leukemias are **hematologic malignancies** characterized by the **slow**, **progressive accumulation** of **mature-appearing but abnormal** white blood cells.

Morphologically, the leukemic cells are often more differentiated than those in acute leukemias and **may resemble mature lymphocytes** or myeloid cells.

Common localizations include the **bone marrow**, **peripheral blood**, and **lymphoid organs**.

Chronic leukemias are classified into **two main types**: *chronic lymphocytic leukemia* (*CLL*), characterized by the proliferation of abnormal B lymphocytes, and *chronic myeloid leukemia* (*CML*), involving the overproduction of granulocytes.

Clinical manifestations of chronic leukemias are often insidious, and patients may remain **asymptomatic for extended periods**. Symptoms can include fatigue, unintentional weight loss, night sweats, and an enlarged spleen or lymph nodes.

Chronic leukemias tend to progress more slowly than acute leukemias, allowing for a more prolonged course of management, often involving watchful waiting, targeted therapies, or stem cell transplantation in select cases.

Lymphomas are a **diverse group of hematologic malignancies** that originate in the lymphatic system, primarily the **lymph nodes**.

Morphologically, lymphomas are characterized by the **proliferation of abnormal lymphocytes**, which can be classified into two main types: **Hodgkin lymphoma** (HL) and **non-Hodgkin lymphoma** (NHL).

HL is marked by the presence of **Reed-Sternberg cells**, large abnormal cells with characteristic bi-lobed or multi-lobed nuclei, surrounded by an inflammatory background.

In contrast, **NHL encompasses a wide variety of subtypes**, each displaying distinct morphological features.

Common localizations for lymphomas include **lymph nodes**, the **spleen**, **bone marrow**, and **extranodal sites such** as the gastrointestinal tract and skin.

Clinical manifestations of lymphomas can vary widely depending on the type, stage, and location of the disease.

Lymphadenopathy, or enlarged lymph nodes, is a common clinical sign in both Hodgkin and non-Hodgkin lymphomas. Other symptoms may include fever, night sweats, unintentional weight loss, fatigue, and itching.

In HL, **localized symptoms** known as B symptoms, such as **fever**, **night sweats**, and **weight loss**, are often associated with more advanced stages.

Extranodal involvement can lead to **specific symptoms based on the affected organ**, such as gastrointestinal symptoms in cases of gastrointestinal lymphomas or skin lesions in cutaneous lymphomas.

Diagnosis involves imaging studies, biopsy, and histopathological examination to classify the specific subtype.

Treatment strategies vary, including chemotherapy, radiation therapy, immunotherapy, and stem cell transplantation, tailored to the subtype and stage of the lymphoma.

Multiple myeloma is a **hematologic malignancy** characterized by the clonal **proliferation of plasma cells** within the bone marrow.

Morphologically, these plasma cells often produce **monoclonal immunoglobulins** (M proteins) and may form aggregates known as **Russell bodies**.

In addition to the direct infiltration of the bone marrow, myeloma cells can also cause **lytic bone lesions**, leading to characteristic **punched-out lesions on imaging studies**.

Common localizations for multiple myeloma include the **spine**, **pelvis**, **ribs**, and **long bones**.

Clinical manifestations of multiple myeloma can vary and are often related to bone marrow dysfunction, the presence of M proteins, and the effects of monoclonal gammopathy.

Patients may experience **bone pain**, especially in the back or ribs, due to **lytic bone lesions**. Fatigue, weakness, and anemia can result from bone marrow involvement and reduced red blood cell production.

Hypercalcemia, a common complication, can lead to symptoms such as excessive thirst, frequent urination, and confusion. **Renal impairment** may occur due to the deposition of monoclonal proteins in the kidneys.

Additionally, the overproduction of immunoglobulins can lead to **hyperviscosity syndrome**, characterized by symptoms such as headache, visual disturbances, and bleeding.

Diagnosis involves laboratory studies, imaging studies like skeletal surveys, and bone marrow biopsy. Treatment strategies include chemotherapy, immunomodulatory drugs, proteasome inhibitors, and stem cell transplantation. Regular monitoring is crucial to assess treatment response and manage complications associated with multiple myeloma.

Anemia is defined as a pathological condition characterized by a **decrease in the total number of red blood cells** (RBCs), the **hemoglobin concentration**, or the **hematocrit**, resulting in reduced oxygen-carrying capacity of the blood. Clinically, anemia manifests with symptoms such as **fatigue**, **pallor**, **dyspnea**, and **tachycardia**.

Anemia can be classified based on morphology (according to mean corpuscular volume) into **microcytic**, **normocytic**, and **macrocytic** types, or based on etiology into three main categories: **blood loss**, decreased RBC production (**impaired hematopoiesis**), and increased RBC destruction (**hemolytic anemia**).

1) Acute or chronic blood loss may result from *trauma*, *gastrointestinal bleeding*, or *heavy menstruation*.

2) Impaired hematopoiesis occurs in conditions such as *iron deficiency anemia*, *vitamin B12 or folate deficiency* (megaloblastic anemias), and *aplastic anemia*.

3) Hemolytic anemias result from increased RBC destruction due to intrinsic defects (e.g., *hereditary spherocytosis*, *sickle cell disease*) or extrinsic factors (e.g., *autoimmune hemolysis*, *mechanical trauma*).

Morphology of anemia due to blood loss

In acute blood loss, such as from trauma, the immediate morphological changes are minimal. Initially, the blood appears **normocytic and normochromic**.

Over several days, a regenerative response is evident, with **increased reticulocyte count** in the peripheral blood and hyperplasia of **erythroid precursors in the bone marrow**.

In chronic blood loss (e.g., from peptic ulcers or colon cancer), iron stores become depleted, leading to **iron deficiency anemia**, which is **microcytic** and **hypochromic**.

The bone marrow shows erythroid hyperplasia with small, pale red cells, while the peripheral smear reveals anisocytosis and poikilocytosis.

Morphology of pernicious anemia (impaired hematopoiesis)

Pernicious anemia is a type of **megaloblastic anemia** caused by vitamin B12 deficiency, often due to autoimmune gastritis with loss of intrinsic factor.

Bone marrow shows marked hypercellularity with ineffective erythropoiesis and megaloblastic changes—large erythroid precursors with open, immature nuclear chromatin and abundant cytoplasm.

Granulocyte and megakaryocyte precursors are also affected. The peripheral smear demonstrates **macrocytic anemia** with oval macrocytes, hypersegmented neutrophils, and sometimes pancytopenia.

In severe cases, nuclear-cytoplasmic asynchrony and erythroid dysplasia may be present.

Morphology of hemolytic anemia

Hemolytic anemias are characterized by premature destruction of RBCs, which can be intravascular or extravascular. The bone marrow shows compensatory

erythroid hyperplasia (normoblastic or slightly megaloblastic depending on folate stores).

In the peripheral blood, there is usually **normocytic normochromic anemia with increased reticulocytes**.

In hereditary spherocytosis, **spherical RBCs lacking central pallor** are seen. In sickle cell anemia, **sickle-shaped cells and target cells** are characteristic.

In autoimmune hemolytic anemia, **spherocytes** and **polychromasia** are seen. The spleen may show congestion and hemosiderin-laden macrophages due to increased RBC breakdown.

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.