

# **ACADEMIC STANDARD FOR THE DISCIPLINE “HEMATOLOGY”**

**1. Purpose of the training in the discipline "Hematology".** Hematology is a medical specialty, educational and scientific discipline that studies blood and blood-forming organs in normal conditions and pathology. Teaching, learning and practical training in the discipline are subordinated to the priority goal of MU-Plovdiv: The development of students' personal qualities, encouraging their initiative, creating habits of permanent self-education and the ability to learn on their own, acquiring "transferable" knowledge, key competencies and skills.

## **Type of the discipline “Hematology”**

-Compulsory

## **Degree of education:**

-Master ( M)

In order to achieve the educational degree "Master" in Medicine, the discipline " Hematology" has its specific goals:

- Knowledge of modern concepts of epidemiology, etiology, pathogenesis, diagnosis, prognosis and therapeutic approaches to congenital and acquired diseases of the blood and blood-forming organs.
- Knowledge of the informative value of specific laboratory-hematological, morphological, immunohematological, flow cytometric, cytogenetic, molecular-biological and imaging methods for examination of blood and hematopoietic organs in normal and pathology.
- Minimum practical skills and guidelines for early diagnosis of benign and malignant diseases of the blood and blood-forming organs, as well as hematological manifestations of congenital and acquired diseases of other organs and systems.
- Knowledge and interpretation of indicators for assessment of the coagulation system in norm and pathology, treatment of life-threatening hemorrhagic diathesis and therapeutic application of blood and blood bioproducts

## **Key components of the discipline "Hematology":**

- Clinical hematology
- Hematological diagnosis
- Thrombosis and hemostasis

- Transfusion hematology
- Stem cell transplantation

**Border areas of the discipline "Hematology".** Clinical hematology has a strong interdisciplinary nature - a separate subspecialty of internal medicine, diagnostic and therapeutic interactions with all other medical specialties and above all with the key to diagnose and monitor the effect of treatment of blood diseases: immunology, medical genetics and imaging.

**2. Learning content of the course.** The necessary theoretical and practical knowledge of the discipline are consistent and meet the priority goal in the training of students of MU and clinical hematology.

## **THESES AND THEMES OF THE LECTURE COURSE IN HEMATOLOGY**

### **Introduction to Clinical Hematology. Hematopoiesis. Anemia. Iron Metabolism. Iron Deficiency Anemia.**

Investigation of patients with blood diseases. Hematopoiesis. Stages in hematopoietic development. Cell Differentiation. Distribution of cell populations. Anemia. Classification. Degrees of anemic state. Iron Metabolism. Iron deficiency anemia. Definition. Classification. Pathogenesis. Clinical features - major syndromes. Laboratory tests. Diagnostic criteria. Differential Diagnosis. Treatment. Prognosis. Anemia in Chronic Diseases.

### **Metabolism of Vitamin B12 and Folates. Megaloblastic anemias. Hypo- and aplastic anemias. Aplastic anemia.**

Metabolism of vit B12. Metabolism of folic acid. Megaloblastic anemias. Classification. Pernicious anemia. Pathogenesis. Clinical features - major syndromes. Laboratory tests. Diagnostic criteria. Differential diagnosis. Treatment. Prognosis.

Hypo-and aplastic anemias. Pathogenesis. Classification. Aplastic anemia. Definition. Incidence. Pathogenesis. Diagnostic criteria. Differential Diagnosis Treatment. Prognosis.

### **Haemolytic anemias. Congenital haemolytic anemias.**

General data. Mechanism of hemolysis and hemolytic laboratory panel for intravascular and extravasal haemolysis. Congenital haemolytic anemias. Membranopathic haemolytic anemias.

Microspherocytosis. Clinical Features. Diagnostic criteria. Differential diagnosis. Treatment. Enzymopathic haemolytic anemias. Glucose - 6 phosphate dehydrogenase deficiency. Clinical features. Diagnostic criteria. Differential diagnosis. Treatment. Hemoglobinopathies. Structure of hemoglobin. Hemoglobinoses. Sickle Cell Anemia Clinical features. Diagnostic criteria. Differential diagnosis. Treatment. Thalassemia. Homozygous Beta – Thalassemia. Clinical Features. Diagnostic criteria. Laboratory monitoring of iron overload. Differential diagnosis. Treatment. Heterozygous beta-thalassemia.

**Acquired haemolytic anemias. Immune, autoimmune and drug-induced immune haemolytic anemias.** General data. Pathogenesis of the immune hemolytic process. Haemolytic disease of the newborn. Key mechanisms. Clinical manifestation. Diagnostic criteria. Differential diagnosis. Treatment. Prophylaxis. Post-transfusion haemolytic anemias. Autoimmune haemolytic anemias. Overall characteristic of cold and heat agglutinines. Autoimmune hemolytic anemia with warm antibodies. Clinical features. Diagnosis Treatment Autoimmune hemolytic anemia with cold antibodies. Cold Agglutinine disease. Clinical Features. Diagnosis. Treatment Indications for blood transfusion in autoimmune haemolytic anemias. Drug - induced immune haemolytic anemias

**Malignant Diseases of the Blood and Hematopoietic organs.** Major Pathogenetic Mechanisms of Neoplastic Growth. Classification of malignant diseases of the blood and hematopoietic organs. Acute leukemias. Mechanisms of neoplastic growth (oncogenesis). Classification of hematological malignancies. Acute myeloblastic leukemia. Classification. Risk Factors. Clinical manifestation. Diagnostic methods and diagnostic criteria. Differential diagnosis. Principles of treatment, treatment phases, therapeutic response. Prognosis. Acute lymphoblastic leukemia. Principal differences from myeloblastic leukemias. Classification. Clinical manifestation. Diagnostic methods and diagnostic criteria. Differential diagnosis. Prognostic factors. Principles of treatment, treatment phases, therapeutic response. Prognosis.

**Subacute myeloproliferative disorders - myelodysplastic syndromes** Definition. Pathogenesis. Classification. Clinical manifestation. Diagnostic methods and diagnostic criteria. Differential diagnosis. Prognostic factors. Principles of therapy, therapeutic response, prognosis.

**Myeloproliferative Neoplasms.** Chronic myeloid leukemia, Ph +. Polycythemia Vera. Essential thrombocythaemia. Primary myelofibrosis General characteristic. Classification. Chronic myeloid leukemia Ph +. Pathogenesis. Clinical features. Phases of the disease. Diagnostic methods and

diagnostic criteria. Differential diagnosis. Prognostic factors Contemporary treatment. Tyrosine kinase inhibitors Therapeutic Response and Monitoring. Polycythemia vera. Pathogenesis. Clinics. Phases of the disease. Diagnostic methods and diagnostic criteria. Differential diagnosis. Prognostic Factors. Treatment. Prognosis. Essential Thrombocythaemia. Pathogenesis. Clinics. Phases of the disease. Diagnostic methods and diagnostic criteria. Differential diagnosis. Prognostic Factors Treatment. Prognosis. Primary Myelofibrosis Pathogenesis. Clinics. Phases of the disease. Diagnostic methods and diagnostic criteria. Differential diagnosis. Prognostic Factors Treatment. Prognosis.

**Non-Hodgkin's Lymphomas.** Classification. Common data on lymphopoiesis and diagnostic methods of lymphoproliferative diseases. T-lymphocytes. B-lymphocytes. Natural killer cells. Chronic lymphocytic leukemia. Definition. Etiology. Pathogenesis. Clinic Staging Systems for CLL. Diagnostic criteria. Differential Diagnosis. Transformation. Treatment Monoclonal Antibodies Prognosis.

**Non-Hodgkin's lymphomas.** Classification. Definition. Pathogenesis. Cellular origin Histological variants. Immunohistochemical and flow cytometric panels. Ann Arbor Staging system. Clinic Prognostic Systems. Methods for Diagnosis and Staging. Differential diagnosis. Treatment. Prognosis. Follicular Lymphoma. Diffuse B-Large Cell Lymphoma. Lymphoplasmocytic lymphoma. Hairy Cell Leukemia. MALT - lymphomas. Mantle cell lymphoma.

**Hodgkin's Lymphoma.** Definition. Pathogenesis. Cellular origin Histological variants. Ann Arbor Staging system. Clinical manifestation. Prognostic Factors. Methods for Diagnosis and Staging. Differential diagnosis. Treatment. Prognosis.

**Plasma Cell Neoplasms. Multiple myeloma. AL-amyloidosis.** Definition Monoclonal immunoglobulins (paraproteins) Diagnostic methods. Multiple Myeloma. Definition Pathogenesis. Staging systems Durie & Salmon and International Staging System. Clinical manifestation - Major Syndromes. Prognostic Systems. Diagnostic Criteria. Differential diagnosis. Treatment. Prognosis. Light chain deposition disease. Definition. Pathogenesis Clinical manifestation. Diagnostic criteria Differential diagnosis. Treatment. AL-Amyloidosis. Definition. Pathogenesis. Clinical manifestation. Diagnostic criteria. Differential diagnosis. Treatment

**Principles of therapy of hematological malignancies:** surgical treatment, radiotherapy, chemotherapy. Cytostatics. Target therapy. Immunomodulators. Hematopoietic stem cell Transplantation. Surgical methods - Indications. Radiotherapy - Indications Cytostatics. Classification. Mechanism of action. Side effects. Target therapy. Mechanism of action. Classification. Definitions of Therapeutic response. Hematopoietic stem cell transplantation. Autologous – SCT. Methodology. Indications. Disadvantages of the method. Allogeneic - SCT Methodology. Indications. Disadvantages of the method .Side effects . Therapeutic response Post-transplantation monitoring.

**Hemostasis. Bleeding diatheses.** Mechanisms of hemostasis. Laboratory diagnostics, clotting assays. Congenital bleeding disorders (coagulopathies). Definition. Classification. Clinical Characteristics of haemorrhagic diathesis. Hemophilia A and Hemophilia B. Pathogenesis. Clinical manifestation. Classification. Diagnostic criteria Prenatal diagnosis. Treatment. Prophylactic strategy. Treatment of Haemophilia with Inhibitors. Von Villebrand's disease. Definition Pathogenesis Clinic Classification Diagnostic criteria Treatment

**Thrombocytopathies and thrombocytopenias.** Classification. Thrombocytopathies Definition. Classification. Hemostasis laboratory tests. Clinical manifestation. Treatment. Immune thrombocytopenia (ITP) . Pathogenesis. Clinical manifestation. Diagnostic Criteria. Treatment Splenectomy. Thrombopoietin receptor agonists. Hemostasis in Surgical Interventions. Management of ITP in Pregnancy

**Disseminated intravascular coagulation.** Definition. Etiopathogenesis. Phases. Clinical manifestation. Clinical forms. Diagnostic criteria. Differential diagnosis. Treatment Monitoring.  
Horarium of lecture course in hematology - 30 h/semester

### **Program for clinical practice in hematology.**

The content of the clinical practice is chronologically arranged and interrelated with the lecture material, so that in the practical training related to the respective lecture the already studied matter and concepts are used. There is no unnecessary overlap or "white spots" between "neighboring" disciplines. The clinical training is performed at the "patient's bed" with the nosology corresponding to the theme.

## **PROGRAM**

### I clinical practice (2+3 hours weekly)

- Methods for examination of hematologically ill. Medical history. Physical data, laboratory minimum.
- Specific methods: differential blood count , myelogram, trephine biopsy, immunohistochemistry, flow cytometry, hemostasis status, immunoelectrophoresis, imaging methods, isotope methods, classical cytogenetics, molecular genetic analysis

### II clinical practice (2+3 hours weekly)

- Erythrocyte lineage - cytogenesis, normal morphology and pathology.
- Iron deficiency anemia.

### III clinical practice (2+3 hours weekly)

- Megaloblastic anemias
- Congenital hemolytic anemias - M. Minkowski-Chauffard, enzymopathies

### IV clinical practice (2+3 hours weekly)

- Congenital hemolytic anemias - thalassemia and hemoglobinosis.
- Acquired hemolytic - isoimmune, autoimmune.

### V clinical practice (2+3 hours weekly)

- Bone marrow failure. Bone marrow transplantation.
- Colloquium - anemia. Treatment with blood and blood bioproducts

### VI clinical practice (2+3 hours weekly)

- Granulocyte series - cytogenesis, cytochemistry, normal morphology and pathology
- Acute myeloproliferative neoplasms - classification, clinic, diagnosis.

### VII clinical practice (2+3 hours weekly)

- Acute myeloproliferative neoplasms - treatment.
- Exacerbated myeloproliferative neoplasms.

### VIII clinical practice (2+3 hours weekly)

- Chronic myeloproliferative neoplasms - chronic myeloid leukemia
- Chronic myeloproliferative neoplasms - Polycythemia vera, essential thrombocytemia

### IX clinical practice (2+3 hours weekly)

- Colloquium MPNs. Cytostatics
- Lymphocyte lineage - cytogenesis, cytochemistry, normal morphology and pathology, functional characteristics

### X clinical practice (2+3 hours weekly)

- Acute lymphoproliferative diseases - classification, clinic, diagnosis and treatment.
- M. Hodgkin - clinic, staging, diagnosis.

XI clinical practice (2+3 hours weekly)

- M. Hodgkin - treatment.
- Non-Hodgkin's lymphoma

XII clinical practice (2+3 hours weekly)

- Non-Hodgkin's lymphoma -therapy
- Chronic lymphocytic leukemia

XIII clinical practice (2+3 hours weekly)

- Multiple myeloma
- Colloquium - lymphoproliferative neoplasms

XIV clinical practice (2+3 hours weekly)

- Coagulopathies. Hemophilia.
- Immune thrombocytopenia

XV clinical practice (2+3 hours weekly)

- Disseminated intravascular coagulation.
- Colloquium – bleeding disorders.

Horarium of clinical practice in hematology - 75 hours / semester

Forms of assessment: current, test, colloquia, papers, seminar discussions with controversies, extracurricular tasks for preparation and presentation

### **3. Prerequisites.**

The minimum required knowledge and practical skills that a student must have in order to start and successfully complete his / her training in hematology are:

- History and physical status in a patient with hematological disease
- Laboratory minimum for diagnostic clarification of hematological disease
- Working with an immersion microscope. Complete and differential blood count.

Quantitative and qualitative deviations in CBC / DBC

- Methodology for determining blood group affiliation, blood transfusion and blood products.
- Management of side effects and complications.

- Interpretation of coagulation disorders. Hemostasis parameters.
- Therapeutic response to emergencies in hematology: hemorrhagic shock, hemolytic shock, life-threatening hemorrhagic diathesis in congenital and acquired coagulopathies, hypercalcemia, tumor lysis syndrome
- Recognition and management in patients with postcytostatic complications of individual organ dysfunctions. Prevention of bacterial, viral and fungal superimposed infections.
- Early diagnosis of hematological malignancy. Symptoms, peripheral blood and biochemical abnormalities.
- Informative value and interpretation of data from: cytochemical studies, cellular and humoral immunity, phenotyping, immunohistochemistry, cytogenetic and molecular genetic data, imaging technics.

#### **4. Academic resources.**

The teaching team of clinical hematology should consist of specialists with professional experience and expertise, good communication skills, intelligent, intriguing, attractive and understandable conduct of a comprehensive cycle of training in the discipline of hematology. To train and motivate in joint developments the first steps in the methodology of the scientific process. To be able not only to present the modern possibilities of the discipline, to motivate its mastering, but also to orient the students for future realization in the field of clinical hematology.

#### **5. Material resources**

The material resources for the implementation of the training cycle in clinical hematology include: hematology hospital, day hospital and dispensary office, transplant sector, video monitor microscopy, own or specialized atlases hematology findings, ultrasound devices (demonstration - data - readings from video computing) CAT, MRI, PET, serum test for blood group antigens, immersion microscopes for self-reading of peripheral and bone marrow smear, software product or paper minimal diagnostic panel.

#### **6. Lectures.**

The lecture course is entirely in the form of presentations, which are provided to students live and electronically. During the lectures, specific clinical cases are demonstrated directly or with patients files Video monitoring microscopy of preparations of peripheral blood or bone marrow according to the respective nosology from atlases or own photographic material is



provided. Presentations are prepared, which are provided to students electronically so that they can prepare for each lesson.

### **7. Laboratory training.**

During the clinical training for methodology for determining the blood group affiliation, transfusion of blood and blood products, laboratory training are organized, methodical instructions, manuals and tests are provided.

### **8. Seminars**

For the seminars, which are held with a whole group, literature on the topic is recommended in advance, which will be discussed, including in the form of a debate. As a methodological form, preference is given to teamwork, team discussions and role-playing games. Students can be assigned tasks to prepare and defend their thesis (presentation) on a topic set by the teacher.

**9. Information resources. Basic literature. Sites.** The teacher must have developed practical training in the discipline, presenting the same in electronic form. The teacher should develop a list of recommended literature in the discipline, with priority given to available sources (to be separated as "basic literature"). The website is cited, from which suitable materials for the preparation of the student can be found. Information on the possibilities of the library and information center is provided.

**10. Control.** Students must work dynamically and intensively during the semester. It is based on the presumption that the way of acquiring knowledge and skills is an important factor for their depth, durability and applicability. According to the main sections of clinical hematology, the mastery of knowledge and skills is controlled 4 times per semester in the form of current control in its different variants. Students are provided with timely information and explanations of the results of this control, which will support their further preparation. The results of these tests are included as a component in the final assessment for the semester.

**11. Independent work and commitment of the student.** The independent work should be guided by the teacher (assistant), who should guide the student both in the literary sources and in the methods of their mastering. It is recommended to provide training tests, incl. on line, for independent work and practice of students.

**12. Cooperation between students and teaching staff** . This cooperation should be expressed in:

- Commitment of the teacher to the student and his preliminary preparation, current difficulties in mastering the material and opportunities with an individual learning program to achieve more.
- Use of reception hours for consultations.
- Scientific working groups
- Involvement of students in teams for research tasks, research, projects, etc.

### **13. Exams** .

The current grades provided for in the curriculum of the specialty are given for:

1. The results of the student in laboratory and / or seminar exercises, course and independent tasks, work of the student with the lecturer on scientific researches and projects, etc .
2. At least 2 (one in the middle and one at the end of the semester) tests or student work

**14. Evaluation standards:** Standards for assessing student achievement are defined so as to objectify student assessments, which should not be decisively dependent on the subject of the teacher. Example description of assessment standards:

- Excellent (6) - for good knowledge of information sources in clinical hematology, thoroughly mastered key and additional knowledge and skills, meaningful and correct understanding of the pathology of benign and malignant diseases of the blood and blood-forming organs, problem-solving skills, self-thinking and reasoning of decisions.
- Very good (5) - for very well mastered key and additional knowledge, meaningful and correct understanding of the subject, skills for applying what has been learned in complex case studies.
- Good (4) - for mastered key and additional knowledge for solving cases and tasks, but without being able to develop them to independent thinking;
- Intermediate (3) - for acquired key knowledge and solutions to simple problems.
- Weak (2) - does not meet any of the above requirements.

At the beginning of the hematology classes, students should be familiar with the assessment standards, the procedures for conducting current control and the possibilities for receiving feedback on their progress during the semester.

**15. Formation of the final assessment** The final grade determines the extent to which the given student has achieved the set goal of education. It is multi-component and includes a written final examination grade and at least one of the following components:

1. assessment (s) of current control and individual assignments;
2. assessment from an oral final exam;
3. assessment from a practical final exam;

Possible other components are:

- the assessment of laboratory and / or seminar exercises during the semester
- assessment of course assignments and individual papers during the semester
- the assessment of course projects in the discipline
- the assessment of ongoing inspections of control works
- the assessment of working with the lecturer in the discipline of research and projects
- evaluation of results from competitions and contests, etc.

For each component participating in the final assessment, a coefficient of significance is determined (from 0 to 1), and the total sum of the coefficients must always be 1. The final assessment is obtained as a sum of the six-point system scores from the various components multiplied by the respective coefficients of significance.

For example:

final grade =  $k_1$  grade from current control +  $k_2Q$  grade from written exam +  $k_3Q$  grade from oral exam  $k_1 = 0.20$ ;  $k_2 = 0.50$ ;  $k_3 = 0.30$  If one of the components of the final grade is weak (2), then the final grade is necessarily weak (2). The components involved in the formation of the assessment and the coefficients of significance for each discipline are determined by the Academic Council with the current academic standard of the discipline. In a semester exam, students' written work is assessed anonymously. The examination materials are stored and the students are given the opportunity to get acquainted with them and the grounds for assessment according to the order and procedure announced in advance. The period in which students have access to the examination materials and results is not longer than 5 working days after the date of the examination. Clinical hematology has a characteristic to which in this form the student is given access at the beginning of the study. This requirement is set in accordance with the Higher Education Act Art. 56. para. 1, "teachers are obliged to develop and publish in an appropriate manner and description of the lecture course conducted by them, including titles and sequence of topics from the curriculum, recommended reading, method of forming the assessment and form of testing knowledge and skills" .

The academic standard for academic discipline “Hematology” is approved by a decision of Faculty Council, Protocol 5 / 08.07.2020 and is published on the website of MU - Plovdiv, Section of Hematology, First Department of Internal Medicine

A handwritten signature in blue ink, consisting of several loops and a long horizontal stroke extending to the right.

Head of Hematology Section .....

/Assoc. Prof V. Goranova - Marinova MD, PhD/