

MEDICAL UNIVERSITY - PLOVDIV
FACULTY OF MEDICINE

SYLLABUS
IN
CLINICAL IMMUNOLOGY

Adopted by the Department Council - Protocol №6/13.06.2022

Approved by the Faculty Council - Protocol №6/15.06.2022

CLINICAL IMMUNOLOGY

Curriculum

Discipline	Exam in semester	Classroom employment				Extracurricular credits	Total credits	Hours by year and semester	
		Total	Lectures	Practical exercises	Credits			IV year	
								VII	VIII
Immunology	VII/VIII	36	18	18	1.2	0.6	1.8	18/18	18/18

DISCIPLINE DESCRIPTION: Clinical immunology

TYPE OF COURSE ACCORDING TO USR: Compulsory

EDUCATIONAL DEGREE: Master / M /

FORMS OF EDUCATION: Regular

COURSE OF TRAINING: IV year: VII semester – Bulgarian-speaking students;

VIII semester – English-speaking students

DURATION OF DISCIPLINE: 1 semester

HOURS: 18 hours of lectures, 18 hours of practical exercises

TEACHING AIDS:

- multimedia
- demonstration materials
- lectures
- textbook
- electronic platforms (MS Office 365, Zoom, etc.)

FORMS OF ASSESSMENT: Exam

FORMATION OF THE FINAL EXAM GRADE:

The final grade is multicomponent and includes the grades from the written final exam and the following components:

- the average grade from current control (colloquium, MCQ tests)
- grade from the oral final exam

If one of the components of the final grade is Weak 2, then the final grade is necessarily Weak 2.

ASPECTS OF THE FINAL GRADE FORMATION:

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

Q final grade = K1 **Q** grade from current control + K2 **Q** grade from written exam + K3 **Q** grade from oral exam

K1 = 0.20; K2 = 0.50; K3 = 0.30

Semester exam: Yes

State exam: No

Main lecturer:

Habilitated lecturer

Prof. Dr. Mariana Murdzheva, MD, PhD

Department: Medical Microbiology and Immunology "Prof. Dr. Elisei Yanev"

ANNOTATION

The main goal of the training in the discipline of clinical immunology is in-depth acquaintance of medical students with the characteristics of innate and adaptive immunity, immunopathology (infectious immunopathology, immunodeficiency, allergies, autoimmunity, autoaggression and autoimmune diseases, tumor immunology), transplant immunology, reproductive immunology, immunological diagnostics and immunomodulation.

The goal is coordinated with:

- the volume and the credit rating of the course (according to the ECTS system), visible from the curriculum available on the website of MU - Plovdiv;
- the qualification characteristics of the specialty;
- educational degree (master's degree).

The aim is consistent with the place of the discipline of clinical immunology in the specialty Medicine in its importance and in chronology in the curriculum. As a fundamental discipline, clinical immunology serves the next stages of the medical students education.

MAIN TASKS OF THE CURRICULUM

The main tasks of the curriculum in "Clinical Immunology" are:

1. Providing information on immunomediated diseases such as immune deficiencies, allergies, autoimmune diseases, tumor processes, transplant rejection processes, reproductive failures with immune genesis.
2. Providing knowledge to students to study the immune system of a person in health and pathology, by applying specific immunological methods and their interpretation.
3. Determining the indicators for monitoring the activity of the disease process affecting the immune system, as well as the indications for immunomodulatory therapy and drug monitoring.
4. Gaining experience in experimental immunology.

EXPECTED RESULTS

After completing the course in clinical immunology, medical students should be familiar with the factors and mechanisms of natural resistance and adaptive immunity in health and pathology, the causes of immunopathogenesis, clinical manifestation, immunological diagnosis and immunotherapy of immunopathological conditions. They must have mastered modern methods for immunodiagnosics and immunotherapy of infectious immunopathology, immunodeficiency diseases, allergies, autoimmune diseases, malignancies, pre- and post-transplant monitoring, to know well the immune mechanisms in transplantation and transplant reactions. The ability to properly handle the methods and means of immunoprophylaxis and immunotherapy.

LECTURE PROGRAMME

IV year, VII term (Bulgarian students),

VIII term (English-speaking students) (2 study hours)

Nº	TOPIC	HOURS	DATE
1.	Clinical immunology. Innate resistance and acquired immunity. Immune system. Development of the immune response.	2	
2.	Immunopathology. Immunodeficiency conditions and diseases.	2	
3.	Immunopathology. Allergies.	2	
4.	Autoimmunity. Autoimmune reactions and diseases.	2	
5.	Autoantibodies in the diagnostics of autoimmune diseases.	2	
6.	Tumor immunology.	2	
7.	Transplantation immunology. Reproductive immunology.	2	
8.	Infectious immunity. Role in bacterial, mycotic and viral infections.	2	
9.	Immunoprophylaxis and immunotherapy.	2	

HOURS: 18

PROGRAMME FOR PRACTICAL CLASSES

IV year, VII term (Bulgarian students),
VIII term (English-speaking students) (2 study hours)

№	TOPIC	HOURS	DATE
1.	Laboratory methods for the study of humoral immune response.	2	
2.	Laboratory methods for the study of cell-mediated immune response.	2	
3.	Immune status and monitoring. Molecular biological methods in clinical immunology.	2	
4.	Test on practicals 1-3. Immunological methods for the study of allergic diseases.	2	
5.	Immunological methods for the diagnosis of organ-non-specific autoimmune diseases.	2	
6.	Immunological methods for the diagnosis of organ-specific autoimmune diseases.	2	
7.	Immunological diagnosis of tumor diseases.	2	
8.	Test on practicals 4-7. Tissue compatibility study. Transplantation immunology.	2	
9.	Seminar and test on practicals 1-8.	2	

HOURS: 18

LECTURES - THESES

LECTURE №1 – 2 hours

Clinical immunology. Innate resistance and acquired immunity. Immune system. Development of the immune response.

Clinical immunology. Subject and sections - general characteristics. Basic humoral and cellular immunological effector mechanisms for the development of protective and immunopathological reactions. Innate resistance. Essence and comparison with acquired immunity. Factors of innate resistance - mechanical barriers, cellular and humoral. Clinical importance of the mechanisms of innate resistance. Inflammation as a protective and pathological manifestation. Acquired immunity and immune response. The immune system - the basis of the immune response. Anatomy and structure: immune organs (central and peripheral); cells (populations, markers and functions); molecules (intracellular interaction and antibodies); HLA genes and products. Development of the immune response. Stages of the immune response. Types and forms of immune response depending on the antigen (development of immune response against extracellular and intracellular antigens). Dynamics of the immune response - primary and secondary. Immune memory. Regulation of the immune response.

LECTURE №2 – 2 hours

Immunopathology. Immunodeficiency conditions and diseases.

Immunodeficiency conditions. Definition, origin. Immunological characteristics of congenital and acquired immunodeficiencies. Syndromes and diseases. Monoclonal gammopathies - nature and examples.

LECTURE №3 – 2 hours

Immunopathology. Allergies

Allergies. Definition, types of allergens. Types of allergic reactions - characteristics, mechanisms of damage, diseases and syndromes. Examples.

LECTURE №4 – 2 hours

Autoimmunity. Autoimmune reactions and diseases.

Autoimmune reactions and diseases. Definition. Immunological tolerance - definition, immune processes for its implementation and maintenance. Causes of development and mechanisms of damage in autoimmune reactions and diseases. Types of autoimmune diseases - organ-specific and non-specific. Immunological characteristics.

LECTURE №5 – 2 hours

Autoantibodies in the diagnostics of autoimmune diseases.

Immunological indicators and tests for organ-specific autoimmune diseases (autoimmune thyroiditis, thyrotoxicosis, autoimmune hepatitis, PBC, MS, myasthenia gravis, type 2 diabetes, autoimmune hemolytic anemia). Anti-thyroid antibodies - against thyroglobulin, thyroid peroxidase, TSH receptor. AMA, ASMA, anti-GBM, anti-insulin, etc. The most common autoantibodies in systemic autoimmune diseases (ANA, anti-dsDNA, anti-ssDNA, anti-ENA - Sm, RNP, Ro, La, Scl-70, anti-Jo1, RF). IIFA of rat liver and McCoy-Plovdiv. Types of fluorescence at ANA detection. ELISA and immunoblot for autoantibodies in systemic autoimmune diseases

LECTURE №6 – 2 hours

Tumor immunology.

Tumor immunology. Types of tumor antigens. Immunological mechanisms against tumors. Reasons for "escape" of the tumor from immunological control. Immunological diagnosis of tumor diseases. Tumor immunoprophylaxis and immunotherapy - basic approaches.

LECTURE №7 – 2 hours

Transplantation immunology. Reproductive immunology.

Transplantation immunology. Importance of MHC for accepting or rejecting the transplant. Immune response after transplantation - reactions and mechanisms of transplant rejection; graft versus host reaction. Pre- and post-transplant immunological monitoring. Chemotransfusion reactions - immunological bases, types, causes, examples. Reproductive immunology. The immunological paradox of pregnancy. The feto-placental unit as an immune organ - structure and antigens. Immunological conflicts during pregnancy. Immunological causes of infertility and abortion.

LECTURE №8 – 2 hours

Infectious immunity.

Role in bacterial, mycotic and viral infections. Infectious immunology. Immune reactions in bacterial, mycotic and viral infections.

LECTURE №9 – 2 hours

Immunoprophylaxis and immunotherapy.

Immunomodulation - definition and directions. Immunostimulation - specific and nonspecific immunological prophylaxis and therapy. Examples and application.

PRACTICAL CLASSES - THESES

PRACTICAL CLASS №1 – 2 hours

Laboratory methods for the study of humoral immune response

QUESTIONS FOR THEORETICAL PREPARATION: Innate resistance, acquired immunity, non-specific humoral factors. Methods of examination in health and disease. Humoral (antibody-dependent) immune response. Immunoglobulins - biological properties, paraproteinemias, specific antibodies. Laboratory methods for the study of humoral immunity: immunoprecipitation, immunodiffusion, immunoelectrophoresis, immuno-nephelometry, immunoturbidimetry, agglutination reaction, neutralization reaction, labeled immune reactions.

DEMONSTRATION OF: Various agglutination reactions - Gruber type, latex agglutination, Widal type, RHA, RPHA, RDHA. Precipitation reactions - Mancini, Ouchterlony. Electrophoresis and immunoelectrophoresis. Immunoglobulin and complement nephelometry. AST, CFT. ELISA reader machine. IFA in autoantibodies. Images of rocket and counter electrophoresis.

PRACTICAL TASKS: Reporting of Widal reaction, RPHA, AST, RDHA, CFT, latex agglutination and IFA. Reporting and interpretation of results from quantitative study of immunoglobulin classes by nephelometry.

PRACTICAL CLASS №2 – 2 hours

Laboratory methods for the study of cell-mediated immune response

QUESTIONS FOR THEORETICAL PREPARATION: Innate immune cells - neutrophils, monocytes, macrophages, NK cells. Examination of the phagocytic system - NBT, flow cytometry. Acquired immune cells - T and B lymphocytes and their subpopulations. Clinical significance of the study of cells of the innate and acquired immune response.

DEMONSTRATION OF: Determination by flow cytometry of antigenic (CD) markers of T, B lymphocytes and NK cells. Cytokines - determination by ELISA. Blood smear with erythrocytes, lymphocytes and leukocytes. NBT test. FACS - scheme and principle of operation.

PRACTICAL TASKS: Determination of NBT test. Histogram reading from a flow cytometry of immune cells.

PRACTICAL CLASS №3 – 2 hours

Immune status and monitoring. Molecular biological methods in clinical immunology

QUESTIONS FOR THEORETICAL PREPARATION: Methods for the study of humoral and cellular immune response (**practical classes 1 and 2**). Clinical significance of the studied parameters. Immunodeficiency diseases. Terminology: immune status, immunological monitoring, diagnostic sensitivity and specificity. Indications for immunological monitoring. Basic indicators for the study of immune reactivity. Minimum panel for determination of lymphocyte populations by flow cytometry. Clinical application of flow cytometry.

DEMONSTRATION OF: Determination of NBT test. Flow cytometric analysis of FACSCanto.

PRACTICAL TASKS: Clinical cases on documents.

PRACTICAL CLASS №4 – 2 hours

Test on practicals 1-3. Immunological methods for the study of allergic diseases.

QUESTIONS FOR THEORETICAL PREPARATION: Types of allergic reactions - mechanisms and diseases. Immunological methods for the study of allergic diseases: in vivo and in vitro tests.

DEMONSTRATION OF: Discussion of types of allergens and types of allergic reactions and immunological tests for allergy testing – skin allergy tests. Algorithm for testing type I allergies. Modern methods for the study of IgE. ELISA plate with total IgE and patient allergy test card. Immunoblot strips.

PRACTICAL TASKS: Reporting of ELISA-IgE. Examples of allergy panels. Work on clinical cases.

PRACTICAL CLASS №5 – 2 hours

Immunological methods for the diagnosis of organ-non-specific autoimmune diseases

QUESTIONS FOR THEORETICAL PREPARATION: Autoimmunity and autoimmune diseases. Characteristics of the autoimmune response. Autoimmune diseases. Mechanisms of occurrence. Genetic predisposition. Classification of autoimmune diseases. Immunological diagnosis. Immunological features in more common systemic autoimmune diseases.

DEMONSTRATION OF: The most common autoantibodies in systemic autoimmune diseases (ANA, anti-dsDNA, anti-ssDNA, anti-ENA - Sm, RNP, Ro, La, Scl-70, anti-Jo1, RF). IIFA of rat liver and McCoy-Plovdiv. Type of fluorescence at ANA detection. ELISA for autoantibodies in systemic autoimmune diseases.

PRACTICAL TASKS: Fluorescence type with IIFA. ELISA reporting and interpretation for ANA. Discussion of clinical cases.

PRACTICAL CLASS №6 – 2 hours

Immunological methods for the diagnosis of organ-specific autoimmune diseases

QUESTIONS FOR THEORETICAL PREPARATION: Immunological indicators and tests for organ-specific autoimmune diseases (autoimmune thyroiditis, thyrotoxicosis, autoimmune hepatitis, PBC, MS, myasthenia gravis, type 2 diabetes, autoimmune hemolytic anemia). Anti-thyroid antibodies - against thyroglobulin, thyroid peroxidase, TSH receptor. AMA, ASMA, anti-GBM, anti-insulin, etc.

DEMONSTRATION OF: The most common autoantibodies in organ-specific autoimmune diseases (ANCA, AGBM, anti-TG, anti-TPO, AMA, ASMA). IIFA of rat stomach and kidney for AMA, ASMA. ELISA for autoantibodies in organ-specific autoimmune diseases (anti-GBM, anti-LKM).

PRACTICAL TASKS: Reporting of AMA and ASMA with IIFA. Reporting of anti-TG, anti-TPO by ELISA. Anti-LKM by ELISA. Interpretation of the results. Discussion of clinical cases.

PRACTICAL CLASS №7 – 2 hours

Immunological diagnosis of tumor diseases

QUESTIONS FOR THEORETICAL PREPARATION: Subject and tasks of tumor immunology. Carcinogens. Cellular oncogenes. Tumor antigens. Antitumor protection. Mechanisms of immunological "escape" of tumor cells from immune control. Immunological diagnosis of tumors. Serological determination of tumor markers. In vitro anti-tumor immunity tests. Immunotherapy of tumors.

DEMONSTRATION OF: Flow cytometric examination in lymphoblastic leukemias. Immunocytogenetic analysis of chromosomal translocations and deletions. Serological examination of various tumor markers by ELISA, RIA, etc. Monitoring of serum concentrations of CEA in rectal cancer. Methods for testing various hormones. Methods for proving genes encoding tumor antigens. Methods for detecting monoclonal immunoglobulins. Analysis of CMI and HI of the body against tumors.

PRACTICAL TASKS: Procedures and methodology for determining the immune status in the immunological laboratory for cancer patients.

PRACTICAL CLASS №8 - 2 hours

Test on practicals 4-7. Examination of tissue compatibility. Transplantation immunology.

QUESTIONS FOR THEORETICAL PREPARATION: Tissue compatibility antigens. Transplantation. Immune response after transplantation. Rejection reactions. Graft versus host disease (GvHD). Immunological monitoring. Prevention and treatment of rejection reactions.

DEMONSTRATION OF: Molecular tests - PCR, RFLP, HLA typing by NGS.

PRACTICAL TASKS: Discussion of clinical cases.

PRACTICAL CLASS №9 - 2 hours

Seminar and test on practicals 1-8.

LITERATURE

Obligatory:

1. Lecture theses in clinical immunology
<https://muplovdivbg.sharepoint.com/teams/FacultyofPharmacy>;
2. Clinical Immunology: Principles and Practice, 4e. Robert Rich, Thomas A Fleisher, William T. Shearer, Harry Schroeder, Anthony J. Frew, Cornella Weyand.Elsevier Saunders, 2013, ISBN-13: 978-0723436911, 1235 pp.

Recommended:

1. Immunology for medical students – 2nd ed. Roderick Nairn,Matthew Helbert, 2006, eBook ISBN: 9780702058479, 320pp;
2. Essentials of Clinical Immunology, Helen Chapel, Mansel Haeney, Siraj Misbah, Neil Snowden, 6th Edition, Wiley-Blackwell, 2014, ISBN: 978-1-118-47295-8, 376pp;
3. Essential Clinical Immunology, John Zabriskie, Cambridge University Press, 1 e, 2009, ISBN-10: 0521704898, 372pp;
4. Basic immunology: functions and disorders of the immune system 5th ed. Abbas,Abul K. et al.,2015, ISBN: 9780323390828, 352pp;
5. Cellular and molecular immunology – 9th ed. Abbas, Abul K. et al., 2017, ISBN: 9780323479783, 608pp.

SYLLABUS

FOR CLINICAL IMMUNOLOGY EXAM

Topic 1. Clinical Immunology. Subject and parts – general characteristics. Basic humoral and cellular mechanisms for the development of defense and immunopathological reactions.

Topic 2. Innate immunity. Comparison with adaptive immunity. Factors of innate immunity – mechanical barriers, cellular and humoral factors. Clinical significance of innate immunity mechanisms. The inflammation as a defense and pathological process.

Topic 3. Adaptive immunity and immune response. Immune system – the basis of the immune response. Anatomy and structure of the immune system – immune organs (primary and secondary), immune cells (populations, markers, and function), molecules (cytokines and antibodies), HLA genes, and their products.

Topic 4. Development of immune response. Stages of the immune response. Types and forms of the immune response according to the antigen (immune response against intracellular and extracellular antigens). Dynamics of the immune response – primary and secondary immune response. Immune memory. Regulation of immune response.

Topic 5. Infectious Immunology. Immune response in bacterial, mycotic and viral infections.

Topic 6. Immune deficiencies. Definition and origin. Immunological characteristics of primary and secondary immune deficiencies. Syndromes and diseases. Monoclonal gammopathy - nature and examples.

Topic 7. Allergy. Terms. Types of allergens. Types of allergic reactions – characteristics, mechanism of tissue damage, diseases and syndromes – examples.

Topic 8. Autoimmune reactions and diseases. Terms. Immune tolerance – definition, underlying mechanisms, and immune processes for its maintenance. Reasons and mechanisms for the development of autoimmunity. Types of autoimmune diseases – organ-specific and non-organ-specific. Immunological characteristics.

Topic 9. Tumor immunology. Tumor antigens. Immunological mechanisms against tumors. Immunological diagnosis of the tumor diseases. Mechanisms by which the tumor escapes the immune control. Anti-tumor immune prophylaxis and immune therapy – basic approaches.

Topic 10. Transplantation immunity. The role of MHC molecules in transplantation. Post-transplantation immune response – types of reactions and mechanisms; graft versus host disease. Pre- and post-transplantation immune monitoring. Haemotransfusion reactions – immunological mechanism, types, reasons, examples.

Topic 11. Reproductive immunology. The immunological paradox of pregnancy. The fetoplacental unit as an immune organ - structure and antigens. Immunological conflicts during pregnancy. Immunological causes of infertility and abortion.

Topic 12. Immunological methods for testing innate and adaptive humoral factors – tests for complement and other serum proteins (agglutination, precipitation, complement-fixation, and labeled immune reactions) – principles, clinical application, and interpretation.

Topic 13. Immunological methods for testing innate and adaptive cellular factors – tests for phagocytosis, immunophenotyping, lymphocyte functional assays – principles, clinical application, and interpretation. Immune status and monitoring – examples in various immune disorders.

Topic 14. Immune modulation – terms and parts. Immune stimulation – specific and non-specific immune prophylaxis and therapy. Examples and application.