

Ministry of health care of Ukraine  
Highest state scientific institution of the Ukraine  
«Ukrainian medical stomatological academy»

"Approved"

at a meeting of the Department of Experimental  
and Clinical Pharmacology with Clinical  
Immunology and Allergology

**Head of the department**

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**Methodical guidance for students' self-directed  
work when preparing for practical session**

Academic subject	Clinical Immunology and Allergology
Semantic module №1	Immunological status. Immunodeficiency diseases and immune-pathology
Topic 3	<b>Immune inflammation and infectious diseases. Understanding immunogramme</b>
Year of study	5
Faculty	medical

### 1. Relevance of theme:

The primary goal of clinical immunology at the present stage is a diagnostic immunopathology states in various diseases, early identification of patients with immune deficiencies and immunopathology, to establish the level of the immunological defect in the parameters of the immune status, development of means of correction of various forms of immunopathology. At the core of these tasks is based on modern methods of immunological studies.

Clinically, it is important to the future understanding of the age-old foundations of a doctor of immunology, as a factor that allows the individualization of the treatment process.

### 2. Learning objectives:

1. To master the subject and objectives of clinical immunology at the present stage
2. Establish the concept of modern achievements of Clinical Immunology and Allergology.
3. To learn the function of the immune system in a draft of human life, the age-old features of immune response and immune status in a draft of human life, and particularly a century of immunopathology (diseases of aging)
4. To master the modern methods of assessing the immune status of the person based on knowledge of normal immune status indicators, methods of determining the nature of the changes under different pathological conditions and principles of immunological staging diagnosis.
5. To be able to determine basic symptoms and syndromes of immune disorders. Understand the capabilities and limitations of immunologists their method of cells and in the in the district Ike.

### 3. Basic knowledge, skills necessary for studying the subject (interdisciplinary integration)

The name of the previous disciplines	These skills
Anatomy	Know the structure of the thymus, lymph nodes, plaques, spleen, bone marrow. Spend examination of patients.
Normal physiology	To know the functioning of the Central and Peripheral organs of the immune system. About know the basics of clinical and laboratory studies.
Biochemistry	Learn the basics of biochemical laboratory studies. Action and effect of cytokines of different groups of biologically active substances.
Microbiology and Virology	Know the immune response, diagnosis of bacteriuria rial and viral infections. About know the basics of special microbiological methods.
Therapy	Know the pathogenesis and clinical manifestations of allergic diseases and secondary immunodeficiencies. To be able to collect immunological and allergic history.
phthisiatry	To master the development of mechanisms of cell dependence immune response and the course of the clinical manifestations of tuberculosis.
Infectious diseases	Learn the pathogenesis, clinical manifestations of bacterial and viral infections. To be able to diagnose bacterial and viral infections.

### 4. Tasks for work during preparation for the classes.

4.1. The list of key terms, parameters, characteristics which the student is to assimilate while preparing for the class:

Term	Definition
Hybridoma	The hybrid cell line, which is formed after the merger of the tumor and 1 MFIs and the bottom of the first cell with a normal lymphocyte.
M and pathogenicity	The substance, which causes non-specific lymphocyte proliferation.
The reaction of precipitation	It occurs between the antibodies and soluble antigens mixed in certain proportions.

Munch metho	Test cially pleased immunazing in Gael.
Immune fluorescent	Antigen determination method using a fluorescent labeled antibody
Myeloma	The plasma-tumor cells capable of indefinite proliferation in culture.

#### 4.2. Theoretical questions for the class:

1. T-lymphocytes. The structure of the T-cell receptor. Subpopulations of T-lymphocytes. Basic differentiation markers and clusters
2. Quantitative and functional immunological tests. Immunogramms, the main indicators.
3. Methods for determination of quantitative and functional characteristics of T lymphocytes: test sockets form I tests with the use of monoclonal antibodies, RBTL of and pathogenicity.
4. Methods for determination of quantitative and functional characteristics of the B-lymphocytes: test sockets formation tests using monoclonal antibodies with RBTL and pathogenicity, C and K.
5. Methods for determining the phagocytic activity of lymphocytes.
6. Methods for determining the concentration of serum immunoglobulins of the main classes.

#### Content topics

The competence of the Clinical Immunology assigned several groups of diseases:

- 1) The basis for reduction system is emy or genetically caused or acquired (the so-called immune deficiencies, including AIDS).
- 2) Those that develop as a result of the fact that the specific antigens and/or sensitized lymphocytes directly or associated with different systems, lead to damage the host tissues (autoimmunity and allergy).
- 3) Those cases where the host tissue damage may be the result of the immune system in the host defense against microorganisms (Infection and Immunity), or the rejection of organs and tissues.
- 4) Diseases whose treatment involves the use of immunogenetics and immune therapy lyotropic minutes.

**T are independent of antibody production.** Independent of the T-lymphocyte helper cells (CD4<sup>+</sup> and so-kl s) stimulation of B-lymphocytes - a quick way to increase the number of natural and antigenspecific their antibodies represented by only one class of immunoglobulins - I GM.

Said stimulation of B-lymphocytes has the following features: 1) It is induced by the simultaneous binding of a large number of B-cells classroom antigenras knowledge feeling receptors repeatable same antigenic determinants of the pathogen; 2) does not require activation of B-cells antigen absorption such as processing.

**T-dependent antibody PRODUCTION.** In this case, the first B lymphocytes function as APC, and then differentiate into plasma and antit loprodutsir in presenting cells. For T-dependent immune response in their lymphocytes antigenal determine of receptors bind to the antigen, absorbing (internal and external) it. The phagosome B-lymphocyte antigen amenable to digestion. Peptides derived from such antigen on the back surface of B-lymphocytes in association with molecules of the major histocompatibility class AI. There are recognized by the T-cell receptor identification, which exists on the surface of CD4<sup>+</sup> Te-kl and to which in turn, leads to the transformation of B lymphocytes into plasma cells.

One of the key aspects of the clinical immunologist with patients is **immunological history**. It is stage of previous before labour second diagnosis of immunodeficiency states (and DC) and other forms of immunopathology based cells and co-anamnestich EQF their lack of signs of immune (I N). In a study of children's focus is on passport Dunn's, epidemiological and socio-environmental conditions, the first vaccination history, carried acute infections, family history and clinical signs, Dr. Thus the survey reveal adverse risk factors. In a study of adults do focus on the profession of the subject, the presence of occupational hazards, their nature and the ability to cause disease predefined professional, result in an adverse impact on IP. The basis of diagnosis to

constitute clinical signs. By CI and anamnesis study determined the presence of the patient's immune pathological syndrome. There are such and DS: infectious, allergic, auto immune, lymphoproliferative, primary immunodeficiency, secondary immunodeficiency.

### **Basic tests of laboratory diagnostics.**

#### **Laboratory tests Immunological share on tests I and II levels.**

##### **tests level I (approximate)**

They include:

- 1) counting the total number of lymphocytes (absolute and relative amount in peripheral blood);
- 2) determining the total number of T-lymphocytes but (absolute and relative amount);
- 3) assessment of the phagocytic activity of neutrophils;
- 4) identification of the main classes of serum immunoglobulins (I g G, I gM, I gA);
- 5) determining the titer of complement.

##### **tests level II (analytical) may include:**

- 1) definition of T and B lymphocytes and their subsets (CD4, CD8, formerly called T-helper cells, T suppressor);
- 2) determination of circulating immune complexes (K D);
- 3) staging of the reaction of blast transformation of lymphocytes (RBTL);
- 4) Braking reaction lymphocyte migration;
- 5) assessment of the intensity of cytokine production;
- 6) NBT-test;
- 7) determination of complement components;
- 8) definition of general and specific I g E;
- 9) posing skin tests of immediate and delayed hypersensitivity type.

##### **Methods of study of lymphocytes:**

- 1) study of surface markers;
- 2) functional tests;

##### **The methods are based on the study of surface markers:**

- 1) immunofluorescence methods ;
- 2) immune of fermentn th methods;
- 3) Rosettes formation.

##### **Methods of study of the functional state of lymphocytes:**

- 1) the reaction of blast transformation of lymphocytes with Con A and PHA;
- 2) assessment of the intensity of cytokine production;
- 3) lymphocyte migration inhibition reaction.

##### **Determination of the content of immunoglobulins**

- 1) method and radial immune odifuse;
- 2) method of linear and immune odfuse;
- 3) laser nephelometric method;
- 4) radioimmunoassay method;
- 5) immune of fermentny second method.

##### **Determination of phagocytic act and activity of neutrophils**

- 1) latex - test
- 2) NST - test

**Immunogramma** - A comprehensive study of peripheral blood cells with the main indicators of the primary immunological studies.

Two-stage system of immunological research is based on the use of cells and immune district ecological their laboratory and immunological tests, and includes:

1) previous diagnosis of immunodeficiency states (and DC) and other forms of immunopathology based on clinical signs of an immune defect, the formation of groups at risk for immune pathological their states with n cells and immune ecology and cally's test;

2) evaluation of the immune status of the results of laboratory tests to identify immunologic inadequacy of the immune response system of humoral and cellular immunity, the system we phagocytes (based on the level of test I); depth analisys of immune status by reading meters on the

basis of laboratory immunological tests Level II. In the case of deviations in the results of the immunological tests or clinical and immune pathological syndrome, confirmed by laboratory testing, carried out surveillance, and if necessary - specialized treatment.

**Reaction precipitation.** Most of these processes occur in the solution between the antibodies and soluble antigens mixed in certain proportions. By *Theory and deposition* precipitation - is the result of increasing the size of antigen-antibody aggregate (each molecule with multiple antigen molecules bound antibodies, and vice-versa). If the units reach a critical mass, they precipitate spontaneously, that is happening *precipitation*.

**Reactions of precipitation in Gael.**

a) *test and radial immune odifuse (RPM);*

b) *immunoelectrophoresis.*

**Immunological reactions on solid phase.**

a) *immune of fermentn second analysis (and FA) (enzyme - l immunosorbent assay - (EL AND SA));*

b) *radiology and immune response*

There are several variations of immunological reactions on solid phase.

a) *direct test;*

b) *undirect test;*

c) *uncurative test;*

g) *esternblot or immune oblot.*

**immunofluorescence** - a method for determining an antigen by fluorescence of labeled antibodies.

**Direct immunofluorescence.** Of fluorescently labeled antibody is incubated with the tissue slice, and then washed with excess of antibody. An antibody that is linked, is determined by microscopy.

**Indirect fluorescence.** *Reactions determination of complement.* Antibodies are contacted with the test antigen is detected using a fluorescently labeled secondary antibody (anti I g).

**Determination of lymphocyte surface antigen CD** widely used in surveys and n- and NF and IDC's IAOD us, in the diagnosis of hematological malignancies in about, immunodeficiency and other diseases caused by immune disorders, as well as to monitor the effectiveness and put transplant immunotherapy.

**Flow citoflourmeter** device that allows you to quickly evaluate the composition of the cell population by fluorescence and optical characteristics of the cells. With this device it is possible to determine the absolute and relative number of different cell populations and subpopulations. The main advantages of the technique include the speed of analysis and simultaneous evaluation of many cell parameters: size, optical density, surface antigens. Running citoflourmeter and I also used to analyze the cell cycle when DNA study.

**Polymerase chain reaction (LHP).** This reaction is used for the determination of small amounts of viral and microbial pathogens.

One of themselves threatening immunodeficiency states is **Acquired immunodeficiency syndrome (AIDS)** - severe infectious disease, which is the causative agent of human immunodeficiency virus (HIV), which manifests the deep impression system cell human immune system, the development of progressive infectious diseases and newly malignant.

**Pathogen:** HIV-1, HIV-2, HIV-3. HIV refers to viruses that contain double circuit **RNA**. **Receptors for HIV is a CD4 antigen, which is present on T lymphocytes and CD4 + cells** monocyte-macrophage series. With the CD4 molecule associated viral glycoprotein gp120.

The spectrum of immunological disorders involving activation through the direct action of HIV immune system cells, as well as the depletion of subpopulations and dysfunction of T cells and CD4 + oppression their response to antigens, pathogenicity, alloantigen and antibodies with anti-CLE parallel decreased production of IL-2 and other changes in cytokine production. As a result of these violations is lost the ability of cytotoxic T-cells to B and A-specific response and some antigenprezent their cellular functions. This increases the number of activated and unresponsiveness T cells CD8 + increased the contents of P2-m and kroglobul both on and neopterin occurs polyclonal B-cells full-time activation with the appearance of B-lymphocytes that unresponsiveness

to the action of T are independent activators increase the formation of autoantibodies and immune complexes.

***In the pathogenesis of HIV infection has 6 stages:***

"Zero" - the incubation period of a primary or latent - I seronegative (for 3-th month. and more)

- **1 stage** - severe viral reproduction and primary immune response - seropositive (up to 6-12 months.)

- **stage 2** - hyperreactivity humoral response (3-5 years)

- **stage 3** - Compensated immunodeficiency (T-cell counts less than 400 per 1 ml., T4 / T8 less than 0.6)

- **stage 4** - pronounced inhibition of cell of the immune system and the beginning of the CAC and decompensated and iteta humoral immune to fading from 3 of 4-but allergic skin reactions.

- **5 stage** - the total absence of delayed-type hypersensitivity reactions to development of local opportunist infections Eski x;

- **stage 6** - terminal - a profound violation of the cell and humoral immunity and generalizingopportunistic infections.

The first 4 stages of pathogenesis conventionally called "PRE-CH & D," the latest AIDS. The susceptibility of HIV to very large (100%). The dose, which infects - 1 viral particle, which is get caught in blood. The mechanism of transmission and factors.

***There are 3 modes of HIV transmission:***

1. When sexual intercourse;
2. From mother to fetus or child;
3. Transfusion of HIV infected blood and maintaining its products, through the sperm, with transplantation of tissues or organs.

With any method of HIV transmission occurs only as a result of contact of a healthy a person with infected body fluids - blood, semen, vaginal secretions, tissues or organs.

**Clinical stage of HIV infection**

**I. Asymptomatic.**

A. Persist generalizing of lymphadenopathy.

**II. Early signs of the disease (at least one)**

A. Weight loss less than 10%.

B. Minor changes in the skin and mucous membranes.

1. Seborrheic dermatitis minutes.

2. folliculitis

3. Pruritus and go.

4. Psoriasis

5. Fungal nail infections

6. Recurrent ulcers in the mouth

7. Necrotizing gingivitis

C. Shingles on a draft 5 years (in persons under 50 years)

D. Recurrent infection of the upper respiratory tract.

**III. Intermediate features (at least one)**

1. Progressive weight loss of more than 10%.

2. Diarrhea of unspecified origin (in the draft one month).

3. Oral candidiasis.

4. Leukoplakia.

5. Pulmonary tuberculosis.

6. Peripheral neuropathy.

7. Local form of Kaposi's sarcoma.

8. Dissemmination AOD shingles

9. Severe bacterial infections that recur (pneumonia, bacterial sinus etc).

**IV. Later signs of disease (at least one)**

1. Pneumonia is caused by Pneumocystis.

2. Toxoplasmosis.
  3. Cryptococcosis.
  4. Strong amount and doses.
  5. Cytomegalovirus infection.
  6. Common herpes.
  7. Candidiasis nutritionally yes.
  8. Atypical mycobacteriosis.
  9. Salmonellosis and septicemia.
  10. Behind lung tuberculosis.
  11. Lymphoma.
  12. Disseminating Kaposi's sarcoma.
  13. Cachexia.
  14. Caused by HIV encephalopathy (CNS disorders, dementia).
- D. Adelman. - Moscow, 2000. - 808 p.

#### **Diagnosis of HIV infection.**

Antibodies to HIV appear from the third week up to three months after infection with the virus and thereafter they can be found in the case when the virus inhibits the function of lymphocytes and antibody production. In order to diagnose HIV can be isolated in large amounts from cell lines, purified and used as antigen in serological tests. There are several types of tests for anti-HIV JSC. *Indirect method of the ELISA of SA* : Antigen-sample anti- I of enzyme.

**Competitive method of the ELISA of SA** : antigen-sample anti-HIV JSC

**"Sendv and Chev's second" method of the ELISA of SA or agglutination** : antigen test antigen (with the addition of the enzymes).

**The ELISA of SA - Enz and me - of L immunosorbent Assay or immune of fermentny second method.**

**Immunoblot and ng (Western blot).**

**Polymerase chain reaction.**

**Progress of infection (PRE-Clinical and Clinical AIDS)** detects, based on the complex clinical and laboratory criteria.

This period is characterized by the following laboratory abnormalities:

- a) strengthening of viremia. The level of RNA copies of HIV-infected blood is increased (1000 000-100 30 1 ml or more);
- b) changing the phenotype of the HIV virus, also This changes the tropism of the isolated strains (in the early period - preferably by macrophages, inability to infect T-cells).
- c) antibody titers to HIV proteins in the blood serum level of antibodies to p24 gradually reduced;
- g) the number of CD4<sup>+</sup> - T lymphocytes in the periphery of Cerebral blood th decreases (lower than 400-500 per 1 L). The main causative agents of infectious processes in patients with AIDS are given in the table.

#### **Pathogens With Pre and Clinical and Diagnostic infections**

The most simple, helminths	Viruses	Mushrooms	Bacteria
Pneumocystis (Pneumonia and carcinoma)	Herpes simplex virus(herpesvirus and infection, HSV)	Candida (Candidosis)	Mycobacteria (Mycobacter and intracellulare, the MA AND)
Toxoplasma (Toxoplasma gondii)	Cytomegalovirus (Cytomegalovirus, CMV)	Kryptokok (Cryptococcus neoformans)	Mycobacterium tuberculosis (Mycobacter and tuberculosis)
Cryptosporidium and I (Cryptospor)	Epstein-Barr virus (Virus Epstein-Barr, EBV)	D and stoplazma (H and stoplasma capulatum)	Salmonella (Salmonella typh)
Strongyloidiasis (C.		Asperg and la (Asperg)	I went and Nela (Leg)

Fuelleborn and)		and llus fum and gatus)	and onella pneumoph and la)
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### Preventing AIDS

Sanitary education for the WHO recommendations, should be aimed at behavioral change and hygiene practices. It is necessary to inform the public about the ways and factors of transmission of infection. An important place in ensure SRI do not spread AIDS should take screening tests to identify infected persons.

### Materials for students' self-directed work

#### A. Tests to verify the initial level of knowledge

##### 1. Antibodies are produced:

- a) T-helper cells;
- b) B-cells e t Cams and;
- c) epithelial cells;
- d) plasma cells;
- d) spleen cells.

##### 2. The most important role in the specific immune response by:

- a) lymphocytes +
- b) neutrophils;
- c) the platelets.
- g) macrophages

##### 3. What are the cells directly produce immunoglobulins Class A:

- a) cytotoxic lymphocytes;
- b) CD - 4 lymphocyte;
- c) plasma cells;
- g) macrophages;
- d) dendritic cells.

##### 4. I g G in serum of healthy adult blood by folds the total content of immunoglobulins :

- a) about 30%; c) about 70%;
- b) about 55%; d) about 90%.

##### 5. What is the immunoglobulin class of the G :

- a) antibodies;
- b) fraction range of serum proteins;
- c) nothing of the above;
- g) only proteins and antibodies.

##### 6. Which of the immune system cells recognize antigen only in complex with major histocompatibility molecule :

- a) T-cells;
- b) B-cells etki +
- c) neutrophils.
- g) monocytes

##### 7. The number of classes of immunoglobulins in humans:

- a) 3 ;                      6) 5 +                      c) 7.

##### 8. When serum electrophoresis electric field in the I gG migrate into the zone:

- a) albumin ;
- b) alpha-globulin;
- c) beta- globulin;
- d) gamma-globules and n on in. +

##### 9. How many nodes with in split I of gG?

- a) 3; b) 4; + C) 2.

##### 10. The T-helper cells are the following receptors on their surface:

- a) type 2 diabetes;                      ) CD4 +



- b) CLE; d) CD8.

### B. Tests to verify the initial level of knowledge

1. Patient 18 years old complains of pain in the knee and shin joints, fever up to 39,50C. During the week and a half before suffered a respiratory disease. In reviewing: body temperature 38,50C. There swelling of the knee joint and tibia. Pulse -. 106 / min, rhythmic. BP - 90/60 mm Hg Heart limits are not changed, the tone relaxed, soft systolic murmur at the apex. Which figure most associated with the possible etiology of the process?

- A Rheumatoid factor
- B 1-antitrypsin
- C Antistreptol and zine-0 +
- D Kreatink and Naz
- E Serumoko and etc.

2. The patient 62 years, contracted sharply in the summer (working air conditioning) : fever, shortness of breath, dry cough, pleural pain, myalgias, artalg and and. Objectively: Right crackles, noise, pleural friction. X-ray: long kept infiltration of the lower share. In the blood: Lake. -  $11 \times 10^9$  / l, p / I - 6, C - 70, L and Matt. - 8, ESR - 42 mm / yr. What is the most right character of pneumonia?

- A staphylococcus
- B Iomeneloz +
- C Streptococcus
- D Mycoplasma
- E Pnevmonococcus

3. The combination of weight loss, sweating, recurrent aphthous stomatitis, and herpes zoster, lymphadenopathy, allowed the doctor to suggest in patients with HIV infection. Further examination can be identified:

- A hypereosinophilic
- B Increased ratio T8 lymphocytes T4-
- C Neutrophilic shift to the left
- D Limfomonotsitoz
- E Reducing the ratio of T4- T8 + lymphocyte

4. The patient 46 years old complains of itching, sweating, especially at night, the temperature increase up to 38.6 C. Objectively: on the skin of the breast traces of scratching, supraclavicular lymph nodes the size of a pigeon's egg, not soldered to the skin. What Method of study is the most appropriate in the first place?

- A Immunogres
- B Complete blood count +
- C Panoramic radiography of the chest cavity
- D Puncture increased l imfouzla
- E Blood proteins on protein fractions

### Task №1.

Patient K., 44 years. 20 years working as a dental technician. In the last 2 months a marked itching hands, feeling the heat in the palms. These feelings are completely over the weekend. Two are given immune ogres we.

Index	A B E F S L M T In T Tx About Fa FZ Th / Ts
By the beginning of the work week.	4.3 0 3 3 69 22 3 70 9 21 63 21 32 62 3.0
After the end of the working week	4.6 0 9 1 62 25 3 84 10 6 54 16 26 82 3.3

**Question:**

1. What changes have you observed immunological parameters?
2. What in your view are related modifications detected immunogram, and what is the latest tactics of the patient?

**Answer.** The patient has the fastest - with a typical contact dermatitis syndrome "Weekend". The allergic nature of the disease confirmed and are immune organs we are : an increase level of eosinophils, helper-suppressive factor. The patient should be investigated to clarify the pathogenesis of the disease : dominated by pear and new the cytotoxic mechanism (general level I Ge and, if possible, - the specific I Ge or contact the sample with the opportunity for professional antigen.

**Task №2.**

Patient P., 18 years, was in substance abuse department for treatment of drug addiction. In a draft 1 year and 8 months makes the injection of drugs. During the review doctor found underweight (height 174 cm, weight 51 kg), increase in all groups of lymph nodes, liver and spleen increase. The symptoms of recurrent herpes infection. He has chronic diarrhea. In the last 6 months a draft three ill with pneumonia, is now worried about a bad cough. **Given the clinical immunogram** gG 24 g / l; I g A 10 g / l; Air 3,8h1012 / L, L3, 3h109 / l; B1%; E 3%; P / I 4%; C / I of 51%; Mon 8%; L and m 33%; T (CD52) 40%; Th (CD4) 9%; Tc (CD8) 14%;

**Q:** What disease is the patient? Tactics doctor.

**Answer:** 1. Already existing assays to calculate the absolute level of helper cells. Continue survey AIDS patients.

**Task №3.**

Patient B with clinic examination and forth Iyer's weed and ITCA aims to control survey method PLR after a 10-day course of antibiotic therapy. The result of the analysis is positive. The conclusion of the ineffectiveness of the treatment. The conclusion of the ineffectiveness of the therapy. Your point of view on the correctness of the clinical and laboratory examination of the patient.

**Answer.** Such a conclusion could be misleading due to the fact that Persist suppressive chlamydia give a positive result PLR-analysis as well. The final conclusion of the heal mostly can be made no earlier than a few weeks after a course of Antibes of antibiotic therapie. This period is required to change the epithelial layer of cells which are parasitic chlamydia.

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