MINISTRY OF HEALTH OF UKRAINE

BOGOMOLETS NATIONAL MEDICAL UNIVERSITY

DEPARTMENT OF CLINICAL IMMUNOLOGY AND ALLERGY WITH SECTION OF MEDICAL GENETICS

INFORMATION FOR STUDENTS OF MEDICAL FACULTIES

Kyiv 2017

AUDIENCES FOR PRACTICAL CLASSES

Discipline	# of room	Address, building, floor, block, etc.
Clinical Immunology /Allergy	# 514, unit 1 Associate-Professor Galyna Fedoruk	Center for Primary Care #1» Podolsk district of the Kyiv city, 47 Voloska Street, 5th floor
Clinical Immunology /Allergy	# 514, unit 2 Assistant-Professor Olena Svidro	Center for Primary Care #1» Podolsk district of the Kyiv city, 47 Voloska Street, 5th floor
Clinical Immunology /Allergy	# 514, unit 2 Assistant-Professor Olga Akhtemiichuk	Center for Primary Care #1» Podolsk district of the Kyiv city, 47 Voloska Street, 5th floor
Clinical Immunology /Allergy	Conference room Associate-Professor Yuriy Bisyuk	Center for Primary Care #1» Podolsk district of the Kyiv city, 47 Voloska Street, 4th floor
Clinical Immunology /Allergy	# 328 Assistant-Professor Daria Plakhotna	Children's Polyclinic #3 Podolsk district of the Kyiv city, 26 Turivska Street, 3rd floor
Clinical Immunology /Allergy	# 329 Assistant-Professor Nataliya Gumenyuk	Children's Polyclinic #3 Podolsk district of the Kyiv city, 26 Turivska Street, 3rd floor
Clinical Immunology /Allergy	# 331 Assistant-Professor Nataliya Udovenko	Children's Polyclinic #3 Podolsk district of the Kyiv city, 26 Turivska Street, 3rd floor
Clinical Immunology /Allergy	# 332 Assistant-Professor Vladislav Tsarik	Children's Polyclinic #3 Podolsk district of the Kyiv city, 26 Turivska Street, 3rd floor
Clinical Immunology /Allergy	# 332 Assistant-Professor Maya Ischenko	Children's Polyclinic #3 Podolsk district of the Kyiv city, 26 Turivska Street, 3rd floor

LECTURE ROOM

Discipline	# of room	Number of seats	Address, building, floor, block, etc.
	Conference room	160	Center for Primary Care #1» Podolsk district of the Kyiv city, 47 Voloska Street, 4th floor

Head of Department,

Professor **Andriy Kurchenko**

THE CALENDAR - THEMATIC PLAN OF LECTURES

OF CLINICAL IMMUNOLOGY AND ALLERGOLOGY

FOR 5TH YEAR STUDENTS OF MEDICAL FACULTIES

10 SEMESTER 2016/2017 ACADEMIC YEAR

LECTURE #1. Main tasks and problems of clinical immunology and allergy. The principles of the immune system, clinical and laboratory evaluation of its disorders.

Questions to the lecture:

1. The main objectives of clinical immunology and allergy at the present stage of development of medicine.

2. Place the immune system in maintaining homeostasis of the organism.

3. Leading factors of immune regulation.

4. The role of modern knowledge about the principles of the various parts of the immune system to maintain health and correct inspection of patients.

5. New features of modern immunodiagnosis in clinical and scientific practice. Evaluation of the immune status of the patient. Construction of diagnostic algorithms and selection of treatment regimens.

LECTURE # 2. Disorders of the immune system. Current views on atopic diseases as the systemic disease. Allergic diseases. Classification, clinical examples.

Questions to the lecture:

1. The place of diseases of the immune system in general morbidity Ukraine and in the World.

2. The role of heredity and environmental factors in the development of immunopathology.

3. The need for primary diagnosis immunopathology GPs.

4. immunotherapy and immunoprophylaxis for example HIV / AIDS.

5. Reasons for the growing number of allergic diseases in the world and forecast prevalence of the future.

6. The atopy, the importance of early diagnosis algorithm and assist in emergency conditions.

7. Clinical examples of allergic diseases, the importance of proper diagnostic algorithm to provide proper patient care.

8. Modern allergy diagnostics.

9. Current approaches to the treatment of allergic diseases.

Head of Department,

Professor **Andriy Kurchenko**

THE THEMATIC PLAN OF PRACTICAL CLASSES
OF CLINICAL IMMUNOLOGY AND ALLERGOLOGY
5TH YEAR STUDENTS OF MEDICAL FACULTIES
9 - 10 SEMESTERS OF THE ACADEMIC YEAR 2016/2017

#	*Topics*	*Number of hours*
Day 1	The structure and principles of functioning of the immune system. The concept of immunogram. Immune inflammation and infectious disease. HIV infection: immunopathogenesis, immune-diagnostics, immunotherapy.	6
Day 2	Congenital and acquired immunodeficiency disease. Basic principles immunotropic therapy. Immunorehabilitation, immunization.	6
Day 3	Atopic diseases. Other allergic (non-atopic) disease. Differential diagnosis of allergy and peseudoallergy.	6
Day 4	Immune aspects of transplantation, autoimmune diseases and cancers	4
	Final Module Test	2
Total		**26**

Head of Department,

Professor **Andriy Kurchenko**

CALCULATION OF THE SCORES:

NUMBER OF PRACTICAL CLASSES - 4

TOTAL POINTS FOR PRACTICAL CLASSES - 110 POINTS

(15 TO 27.5 POINTS PER PRACTICAL CLASS)

The maximum score per 1 practical lesson is 27.5 points. Maximum 2.5 points per workbook on the topic, 5 points for tests and 20 points during classes.

To control the initial or final level of knowledge offered 10 questions from a bank of tests. The maximum a student can receive is 5 points. The value of the question with the correct answer is 0.2 points. If the student scored less than 70% correct answers on tests will gets 0 points.

Scores for the writing and defense case history is maximum 5 points (score 5 - 5 points; score 4 - 4 points; score 3 - 3 points; score 2 - 0 points).

The program was applied such a system to convert the traditional system of points:

Traditional Score	***Converting points***
«5»	27.5 points
«4»	20 points
«3»	15 points
«2»	<15 points

The maximum number of points that can be collected by student during a module is 110 points. It is calculated by multiplying the number of points that corresponds with "5", the number of topics in the module with addition of marks for individual independent work.

The minimum number of points that can be collected by student during a module is calculated by multiplying the number of points corresponds with "3", the number of topics in the module.

Evaluation of individual students' independent work (individual tasks):

Points for individual tasks charged to the student only at successful their implementation and protection. The number of points accrued by different types of individual tasks, depending on their volume and value, but not more than 10 points. They are added to the amount of points gained by a student for current educational activity.

The program follows the next scoring system for individual tasks:

10 - winners were awarded diplomas and third place in the National Olympiad in clinical immunology and allergy or student scientific conference (provided training Science of Clinical Immunology and Allergy);

9 - participants of the Ukrainian Student National Olympiad of Clinical Immunology and Allergology;

8 - members of student scientific conference (provided training Science of Clinical Immunology and Allergy);

7 - 3 - preparation of the abstract (number of points depends on the quality of training and the ability to respond to additional questions) - you can prepare for cycle 1 essay topics independent (extracurricular) work in coordination with the teacher.

The final module control is carried out on completion of all topics module on the last control lesson from the module.

The final module control students who attended all the prescribed curriculum with courses for classroom training sessions and the study module scored the number of points not less than the

minimum. Students, who had to have passes training sessions, adjustments are made to the individual curriculum and academic debt permitted to work up to a certain fixed period.

The maximum number of points that a student can collect at the final module test is 80 points. The final module credit is considered passed if the student scored at least 60% of the maximum number of points which is 50 points.

Head of Department,

Professor **Andriy Kurchenko**

REQUIRED KNOWLEDGE AND SKILLS 5 TH YEAR STUDENT OF MEDICAL FACULTY

1. GENERAL CLINICAL INVESTIGATIONS

- Collect complaints, history of disease, history of life (including professional history);

- To conduct palpation of lymph nodes;

- examine the state of breathing (the review chest and upper respiratory tract, chest palpation, percussion and auscultation of the lungs);

- examine the condition of the skin.

2. THE ABILITY TO PUT A PRIMARY DIAGNOSIS AND LABORATORY AND / OR INSTRUMENTAL EXAMINATION OF PATIENTS IN INTERNAL ORGANS DISEASES:

1. Allergic rhinitis
2. Urticaria
3. Atopic dermatitis
4. Allergic contact dermatitis
5. Serum Sickness
6. Exogenous allergic alveolitis
7. HIV / AIDS
8. Primary immunodeficiencies
9. The secondary immunodeficiencies
10. Systemic lupus erythematosus.
11. Rheumatoid arthritis.
12. Sepsis

DISEASES OF THE IMMUNE SYSTEM DURING A COMBAT SURGICAL TRAUMA AND DISASTER

1. Radiation damage to the immune system.
2. Burn disease.
3. Sepsis

INTERPRETATION OF LABORATORY AND INSTRUMENTAL METHODS

1. Quantitative and functional immunological tests. Immunogram and main parameters.
2. Methods of determining quantitative and functional characteristics of T lymphocytes.
3. Methods of determining quantitative and functional characteristics of B lymphocytes.
4. Methods for determining the phagocytic activity.
5. Methods of determining the concentration of serum immunoglobulins of main classes.
6. Identify irritation of the immune system by using of complete blood count.
7. To interpret the skin prick test.
8. Master the skills to perform spirometry and peakflowmetry.

9. To interpret the test data on the selection of donor and recipient for transplantation.

SKILLS, BASED ON EXAMINATION OF THE PATIENT, TO FORMULATE CLINICAL DIAGNOSIS AND PRESCRIBE IMMUNOTHERAPY FOR IMMUNODEPENDENT DISEASES

1. Bruton's disease.
2. Common variable immunodeficiency.
3. Di - George Syndrome
4. Systemic lupus erythematosus.
5. Rheumatoid arthritis.
6. Asthma.
7. Hay fever.

IMMUNODEPENDENT DISEASE DURING A COMBAT SURGICAL TRAUMA AND DISASTER

1. Immunological changes in radiation injuries and their correction.
2. Immunocorrection of burn disease.
3. Sepsis.

CLINICAL PHARMACOLOGY MAIN GROUPS OF DRUGS

1. Immunoglobulins.
2. Antihistamines.
3. Glucocorticoids
4. Immunosuppressants.
4. NSAIDs.
5. Monoclonal antibodies.

THE ABILITY TO DIAGNOSE AND TO ASSIST IN EMERGENCY CONDITIONS

1. Anaphylactic shock.
2. Congenital angioedema.
3. Acquired angioedema

CONDUCTING MEDICAL MANIPULATIONS

1. Spirometry.
2. Peakflowmetry.

THE ABILITY TO ISSUE MEDICAL RECORDS

1. Outpatient medical card.

2. Recipes for all sections of the course.

THE LIST OF DRUGS THAT NEED TO KNOW THE STUDENT 5TH YEAR:

1. Prednisolone (Table.).
2. Epinephrine solution.
3. Cetirizine.
4. Desloratadine.
5. Salbutamol.
6. Beclomethasone propionate.
7. Dexamethasone solution.
8. The normal human immunoglobulin.
9. Infliximab.
10. Omalizumab.

Head of Department,

Professor **Andriy Kurchenko**

Recommended Books for

Clinical Immunology and Allergology

For 5 year students (2016-2017 Academic Year)

MAIN:

1. Clinical Immunology: Principles and Practice / Robert R. Rich, Thomas A. Fleisher, William T. Shearer, Harry W. Schroeder Jr., Anthony J. Frew, and Cornelia M. – 2013 – 1295 p.

2. Abbas, Abul K., author. Cellular and molecular immunology / Abul K. Abbas, Andrew H. Lichtman, Shiv Pillai; illustrations by David L. Baker, Alexandra Baker. – Eighth edition. – 2015 – 535 p.

3. Allergy. – 4th ed. / Stephen T. Holgate, Martin K. Church, David H. Broide, and Fernando D. Martinez. – 4th ed. – 2012. – 399 p.

ADDITIONAL:

1. Roitt’s essential immunology / Peter J. Delves [et al.]. – 12th ed. – 2011 – 546 p.

2. Case studies in immunology: a clinical companion / I Raif Geha, Luigi Notarangelo. – 6th ed. – 2011. – 363 p.

3. How the immune system works / Lauren Sompayrac. – 4th ed. – 2012. – 141 p.

4. Global Strategy For Asthma Management and Prevention (GINA) – Updated 2016. – 109 p.

5. Janeway's immunobiology / I Kenneth Murphy with acknowledgment to Paul Travers, Mark Walport; with contributions by Allan Mowat, Casey T. Weaver. – 9th ed. – 2017 – 904 p.

ADDITIONAL MATERIALS
FOR PRACTICAL CLASSES PREPEARING
"CLINICAL IMMUNOLOGY AND ALLERGOLOGY"
FOR STUDENT 5TH YEAR MEDICAL FACULTIES IN 2016/17 SCHOOL YEAR

THE STRUCTURE AND PRINCIPLES OF THE IMMUNE SYSTEM. DEVELOPMENTAL IMMUNOLOGY. IMMUNOLOGICAL RESEARCH METHODS. THE CONCEPT OF IMMUNOGRAM.

Issues to be considered during the class

Definition of immunity and its types. Primary and secondary organs of immune system. Factors of innate immunity: cells-mediated (monocyte-macrophage system, killers, granulocytes), humoral (complement system, cytokines ect.). Antigens and their characteristic. Adaptive immunity, its properties, stages of formation and cooperation of immune cells participating in immune response.

Populations (T- and B-lymphocytes) and subpopulations (T-helpers 1 and 2, T-regulatory, CTL) of lymphocytes, stages of maturation and differentiation, their function. Immunoglobulins, structure, function. Thymus-dependent and non-thymus-dependent mechanism of antibodies synthesis. Structure and properties of circulating immune complexes. Major histocompatibility complex (MHC): structure, properties, function. Regulation of immunity.

Characteristic of immunologic anamnesis. Clinical methods of immune system evaluation. Instrumental methods of immune system evaluation. Innate humoral factors of defense. Cell-mediated immunity evaluation. Complex evaluation of local immunity.

Complex approach to human immunity investigation. Major complains of patient with immune disorders. Characteristic of immunological diagnosis. Determination of main symptoms and syndromes of immune disorders. Physical symptoms of immune pathology. Instrumental studies of patient with immune pathology (USG, X-ray, immunohistochemistry ect.).

Immunogram, results interpretation. Abilities and limitations of immunological methods. Characteristic of immunological diagnosis making.

Age characteristic of bone marrow, thymus and peripheral lymphoid organs. Age characteristic of immune cells functioning. Age characteristic of inflammatory reactions. Role of mother's organism in formation of immune system of fetus. Immune system of fetus, newborn and child in different age.

Thymus and aging. Immunoregulatory processes in middle age. Immune theory of aging. Immunopathology in senior persons.

Different approaches of immune therapy administration in different age.

Aim of study

Immunology is a broad branch of biomedical science that covers the study of all aspects of the immune system in all organisms. It deals with, among other things, the physiological functioning of the immune system in states of both health and disease; malfunctions of the immune system in immunological disorders (autoimmune diseases, hypersensitivities, immune deficiency, transplant rejection); the physical, chemical and physiological characteristics of the components of the immune system in vitro, in situ, and in vivo. Immunology has applications in several disciplines of science, and as such is further divided.

Clinical immunology is the study of diseases caused by disorders of the immune system (failure, aberrant action, and malignant growth of the cellular elements of the system). It also involves diseases of other systems, where immune reactions play a part in the pathology and clinical features.

The diseases caused by disorders of the immune system fall into two broad categories: immunodeficiency, in which parts of the immune system fail to provide an adequate response (examples include chronic granulomatous disease), and autoimmunity, in which the immune system attacks its own host's body (examples include systemic lupus erythematosus, rheumatoid arthritis, Hashimoto's disease and myasthenia gravis). Other immune system disorders include different hypersensitivities, in which the system responds inappropriately to harmless compounds (asthma and other allergies) or responds too intensely.

Purposes of discipline

1. Familiarize students with principles of immune system functioning.

2. Determine main difference between innate and adaptive immunity.

3. Investigate basic mechanisms of T- and B-lymphocytes cooperation.

4. Learn main parameters of human immunogram in normal and pathology.

5. Learn methods of immunological tests of I and II level and their estimation in pathological conditions.

Student has to know:

1. Define “immunity”, factors of innate and adaptive immunity.

2. Main data about immune system structure and function.

4. Characteristic of phagocytosis, complement system, T- and B-lymphocyte systems, scheme of main stages of immune response.

5. Methods of immune status estimation.

6. Methods of quantitative and functional characteristic of T- and B-lymphocyte estimation.

7. Methods of phagocytic activity estimation.

Student has to be able to do:

1. Characterize antiviral immunity development.

2. Characterize antibacterial immunity development.

3. Characterize immunity development in case of autoimmune disorders.

4. Characterize antifungal immunity development.

5. Point indications for immunological ivestivation.

6. Characterize immune state of patient.

7. Estimate results immunological tests of I and II level in different conditions.

Interdisciplinary integration

Subject	Know	Can
Anatomy	Haemopoietic organs of immune system	Name primary and secondary lymphoid organs, lymphatic ducts
Biology, histology, embryology.	Immunity as mechanism of functional and structure homeostasis. Essentials of immuno-embryogenesis.	Distinguish basic phylogenetic levels of immunity evolution, primitive cell-mediated immunity and integral cell-mediated and humoral immunity
Biochemistry	Chemical structure and biological action of mediators of cell-mediated immunity	Immunophoretic determination of immunoglobulins.
Pathophysiology	Phagocytosis in the focus of inflammation, immunological tolerance, reactivity, allergy.	Name immunocompetent cells, participating in defense reactions of cell-mediated and humoral immunity
Normal physiology	Interaction of nervous, endocrine and immune system for functional and structure homeostasis maintaining	On practical classes determine interaction of nervous, endocrine and immune system.
Pathological anatomy	Role of immune disorders in mesenchymal and protein dystrophies, mucous and fibrinoid degeneration if connective tissue	Determine mesenchymal and protein dystrophies, mucous and fibrinoid degeneration if connective tissue. Types of tissue reactions in collagenoses.
Microbiology, virusology	Specific and non-specific mechanisms of defense. Types of antigenes, immunity, allergies.	Perform agglutination test, Coombs' test, precipitation. Titration of complement, bacteriolysis and haemolysis tests, immunofluorescence test
Propedeutics of internal diseases	Role of immune system in pathogenesis of different diseases.	Interpretation of rosette test, Manchini immunoglobulins, phagocytic activity of blood.

Independent student's work

Main theoretical aspects of theme.

Immune, neurological and endocrine regulation of functions.

Apoptosis as regulator of immune response.

Immunology of mucosae.

Tasks for final module test

1. Subject and aims of clinical immunology and allergology. History of immunology development. Main branches of further research.

2. Contemporary views on immune system structure, function and ontogenesis. Primar and secondary organs of immune system.

3. Principles of functioning of immune system in children and senior**.**

4. Innate cells factors of defense, their interaction in immune response.

5. Monocyte-macrophage system: functional characteristic, role in immune response realization. Contemporary views on phagocytosis.

6. Killing effect as part of immunobiological supervision. Types of killer cells. Their function, properties. Role of granulocytes in immune response.

7. Humoral factors of innate immunity.

8. Complement system. Biological consequences of its activation.

9. Antigenes, their structure, functions. Haptens.

10. Stages of T- abd B-lymphocytes maturation and differentiation.

11. T-lymphocytes. Structure of T-cell receptor. T-cell populations. Main markers and clusters of differentiation.

12. Th 1 and Th2. Importance of balance (Th1\Th2).

13. T-regulatory cells, main function.

14. Apoptosis as special form of cell death. Its role it physiological and pathological processes.

15. B-lymphocytes, markers and functions. Structure of receptor.

16. T-dependent and T-independent immune responses.

17. Immunoglobulins: structure, functions, classes. Role pf immune complexes in pathology.

18. Cytokines – mediators of immune system, Interleukins, classification, function and role in immune processes.

19. Growth factors. Tumor necrotic factors, interferons and adhesive molecules. Characteristic and role in immune response.

20. Immune system of mucosae. Gut-associated lymphoid tissue (GALT).

21. Contemporary views on structure and function of MHC

22. Structure of HLA antigens. Predisposition to diseases according to HLA phenotype.

23. Quantitative and functional immunological tests. Immunogram, main parameters.

24. Method of quantitative and functional T-lymphocyte characteristic determination: rosette test, tests with monoclonal antibodies, blast-transformation reaction with mitogenes.

25. Method of quantitative and functional B-lymphocyte characteristic determination: rosette test, tests with monoclonal antibodies, blast-transformation reaction with mitogenes, circulating immune complexes level.

26. Method of phagocyte activity estimation.

27. Quantitative method of main classes' serum immunoglobulins determination.

List of practical skills for final module test.

1. Perform physical examination and history taking of patients with immunodeficiency. (take immunological anamnesis, estimate hereditary risks).

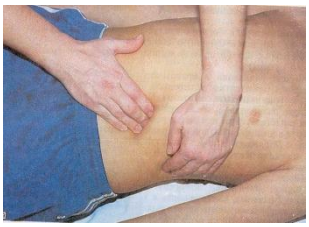
2. Be able to fill immunological question list of patient, and according to received data postulate "risk group"

3. Be able to choose proper tests to perform for patient with immunopathology.

4. Reveal presence of clinical signs and symptoms, relating to immune pathology.

Appendix 1

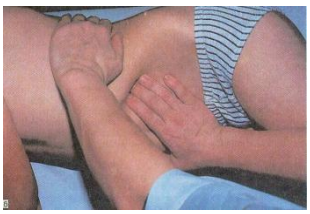
METHODS OF INVESTIGATION OF IMMUNE SYSTEM ORGANS



Methods of investigation of the spleen

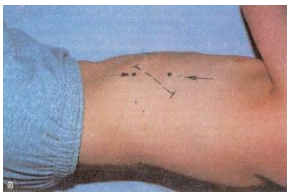
Examination: Prominence in the left part of the abdomen may be observed in considerable enlargement of the spleen (e.g., in chronic myeloleukosis).

Palpation: Palpation of the spleen is made when a patient lies on the back or on the right side. In the first case, a patient lies on the coach on the low pillow with the arms along the trunk and the legs completely relaxed. In the second case, a patient lies on the right side with the head a bit bent to the chest; the left arm



bent in the elbow joint rests on the front surface of the chest; the right leg is stretched out and the left one is bent in the knee and hip joints. In this position relaxation of abdomen is maximum, and the spleen shifts forward. The doctor sits to the right from the patient with the face to the patient. The left hand of the doctor is on the chest of the patient between VII and X ribs along the axillary lines and presses it a little to limit its movement in respiration. The right hand of the doctor with the fingers a little bent is on the anterior-lateral surface of the peritoneal wall of the patient at the edge of the costal arch, where the end of X rib is connected with it. If on base of the data of the examination or prior percussion, the enlargement of the spleen may be suspected, the position of the right

hand is at the supposed anterior-lower margin. Then, when the patient breathes in, the right hand of the doctor presses the peritoneal wall in a little, forming a pocket, and the doctor asks the patient to take a deep breath. At the moment of inspiration, if the spleen is palpable, it moves down by the descending diaphragm and approaches the fingers of the right hand of the doctor, rests against them and slips under them. This procedure is repeated several times.



ATTENTION IS PAID TO THE DIMENSIONS, MOBILITY, CONSISTENCE, TENDERNESS, SHAPE, INCISIONS ON THE FRONT BORDER. ONE OR SEVERAL INCISIONS ON THE FRONT BORDER ARE DETERMINED IN ITS CONSIDERABLE ENLARGMENT AND ALLOWS DIFFERENTIATING IT FROM OTHER ENLARGED ABDOMINAL ORGANS

Normally, the spleen is not palpable. It becomes approachable in its prolapse and more often in its enlargement.

Percussion is used only to determine an approximate size of the spleen. It is performed with a patient standing or lying on the right side. One should percuss very gently, from the clear sound to dullness. To determine the diameter of spleen dullness, the percussion is performed along the line, which is 4 cm lateral from linea costoarticularis sinistra (connecting the sternoclavicular joint with a free end of the eleventh rib). Normally, spleen dullness is between the ninth and eleventh ribs, its size being 4-6 cm. The spleen log is percussed along the tenth rib. Normally, its size is 6-8 cm.

Auscultation. In perisplenitis one can hear friction of peritoneal layers above the place of its location.

Laboratory investigations and instrumental methods of investigation:

Puncture allows determining the character of changes in cell composition. It is performed without anesthesia with a simple injection needle put on a 10 ml syringe with a patient holding the breath at the height of inspiration. Smears are prepared from the liquid received.

x-ray investigation is performed after introduction of oxygen into the abdomen. Splenoportography is made to investigate splenic vessels.

Radioisotope investigation. Scanning is made with the help of the patient's own erythrocytes labeled by radioactive chrome or with the help of gold colloidal solution caught by reticuloendothelial cells. This method allows determining the size and revealing the nodal involvement.

Methods of investigation of thymus

Chest radiograph is made in lateral projection. If there is no shadow of the thymus in a child not having undergone stresses one may suppose hypothyroidism.

To diagnose thymomegalia, cardiothymic-thoracic ratio is counted on a chest roentgenogram. The ratio is a correlation between the width of a vascular band at tracheal bifurcation and the width of the chest at the level of the diaphragmatic dome. In normal, the ratio is less than 0.33.

Methods of investigation of lymph nodes

Groups of lymph nodes:

1. Occipital lymph nodes are located on the lumps (bumps) of the occipital bone and collect lymph from the scalp and posterior neck.

2. Retroauricular (mastoid) lymph nodes are located behind the ears in the region of the mastoid process.

3. Submandibular lymph nodes are situated under the branches of the mandible, collect lymph from the face and mucosa of the gums.

4. Genial lymph nodes receive lymph from the lower lip and the mucosa of the gums.

5. Anterior cervical and tonsillar lymph nodes are located to the front from the sternocleidomastoid muscle mainly superior triangle of the neck and receive lymph from the face skin, parotids, mucosa of the nose, throat and mouth.

6. Posterior cervical lymph nodes are located to the back from the sternocleidomastoid muscle and receive lymph from the skin of the neck and partly from the larynx.

7. Supraclavicular lymph nodes are situated in the region of supraclavicular fossae and collect lymph from the upper part of the chest, pleura and apices of the lungs.

8. Subclavian lymph nodes receive lymph from the skin of the chest and pleura.

9. Axillary lymph nodes collect lymph from the skin of the upper extremities.

10. Thoracic lymph nodes are located to the inside from the anterior axillary line under the lower edge of the longissimus thoracic muscle and receive lymph from the skin of the chest, parietal pleura, lungs and mammary glands.

11. Inguinal lymph nodes are located along the inguinal ligament and collect lymph from the lower extremities, the lower part of the abdomen, buttocks, perineum, genitals and the back passage.

12. Popliteal lymph nodes receive lymph from the skin of the foot.

On examination one can reveal enlargement of superficial lymph nodes only.

On palpation the following parameters are determined:

1. the size: in normal diameter is 0.3-0.5 cm.

2. the number: less than 3 palpable nodes are considered single; more than that are multiple.

3. consistence: soft/elastic/dense. Normal nodes are soft and elastic.

4. mobility. Normal nodes are movable.

5. connection with the skin, subcutaneous cellular tissue and with each other. Normal nodes are not knit together.

6. sensitiveness and tenderness: in normal, nodes are neither sensitive nor painful.

To palpate occipital lymph nodes the hands are placed flat on the back of the head. Moving the fingers circularly and pressing them to the skin of a child, the whole surface of the bone is felt. In healthy children, the occipital lymph nodes are not always palpable.

To reveal parotid lymph nodes the region of the mastoid, as well as a place to the front from the lobe of the ear and external acoustic meatus are thoroughly felt.

Genial lymph nodes are palpated with the fingers moving from behind forward near the middle line of the genial region.

To palpate submandibular lymph nodes the head is bent down a little. Four finger of a half-bent hand with the palm up are placed under the branches of the mandible and moved forward slowly.

Usually these lymph nodes are easily palpable (of a size of) and easily grasped with the fingers.

Anterior cervical lymph nodes can be palpated moving the fingers over the anterior surface of the sternocleidomastoid muscle from above (at the level of the angle of the mandible) down, mainly in the superior triangle of the neck.

Posterior cervical lymph nodes are felt over the posterior surface of the sternocleidomastoid muscle moving fingers from top down along the muscular fibers, mainly in the inferior triangle of the neck.

To feel supraclavicular lymph nodes a patient should lower the shoulders and bend a head down a little for the muscles to be relaxed absolutely. Fingers are placed in the supraclavicular region laterally from the sternocleidomastoid muscle. In normal these nodes are not palpable.

To reveal subclavian lymph nodes palpation is performed in the subclavian region along upper ribs. In normal, they are not palpable.

On palpation of axillary lymph nodes the patient is asked to put arms aside. The investigator places fingers as deep and high as possible into the axillae, and the patient lowers the arms. Fingers slide from top down pressing soft tissues to the chest a little. This group of lymph nodes is usually well palpable.

Thoracic lymph nodes are felt on the anterior surface of the chest under the lower edge of the longissimus thoracic muscle. In normal, they are not palpable.

To examine ulnar lymph nodes the arm of the child is bent in the ulnar joint at the right angle, holding it by the palm with one hand and feeling the bicipital groove in the ulnar region and a little higher. In healthy children these nodes are not always palpable.

Inguinal lymph nodes are palpated along the inguinal ligament in both healthy and ill people.

To palpate popliteal lymph nodes the leg of the child is bent in the popliteal joint and soft tissues are felt in the region of the popliteal fossa. In normal they are not revealed.

Lymph nodes may be called normal if they are of a size of a little pea, single, of soft elastic consistence, movable, not knit with the skin and each other, painless.

Lymphadenopathy is enlargement of lymph nodes, sometimes accompanied by changes in their consistence.

Polyadenemia is increase in the number of lymph nodes.

To diagnose lymph node involvement more exactly, puncture, biopsy and lymphography are used in addition to physical examination.

Example of the conclusion:

Submandibular, anterior cervical, axillary and inguinal lymph nodes are palpated; they are single, up to 0.3 cm, soft and elastic, not connected with each other and the skin, movable, painless. – Norm.

SYMPTOMATOLOGY OF LYMPH NODE INVOLVEMENT

In patients there may be local and general changes in lymph nodes. At this, reactive hyperplasia is possible as a result of immune response to infection. Direct participation of lymph nodes in inflammatory and tumoral processes may also take place.

Local (regional) enlargement of lymph nodes occurs in purulent cutaneous processes: folliculitis, pyoderma, furunculosis, multiple miliary abscesses, infected wound, hidradenitis, etc.

In diphtheria, scarlet fever, simple quinsy there is reaction of cervical groups of lymph nodes.

In massive infection or in weakening of the organism, usual lymphadenitis may develop. Lymph nodes become dense, painful, the skin above them may become red, there is swelling of the adjacent tissues (periadenitis). Fluctuation develops in consequent purulent fusion. The result of a node fusion may be involvement of cellular tissue (adenophlegmon).

Tuberculosis of peripheral lymph nodes is limited by a certain region, most often by cervical groups. Lymph nodes are a voluminal, dense, painless sac, tending to caseous decomposition and fistula formation, after which there are uneven “star-shaped” scars. The nodes are knit with each other, skin and subcutaneous cellular tissue.

Appendix 2

METHODS USED TO ESTIMATE IMMUNE STATUS

Methods of immunodiagnosis are divided into screening (I level preliminary tests) and specific (II level tests).

Screening tests

1. Determination of absolute number of lymphocytes:

Calculation is made by the formula:

$$\frac{\text{leukocytes} \times \%\ \text{lymphocytes}}{100}$$

Normal:

children	6.8-10x109/L
adults	4.6-7.1x109/L

An increase in the absolute number of lymphocytes (lymphocytosis) is observed during convalescence after acute infectious diseases, in infectious mononucleosis, rubella, brucellosis, thyrotoxicosis, and lympholeukosis.

2. Determination of percentage and absolute number of mature T-lymphocytes CD3+ and two main subpopulations of CD4+ helpers and CD8+ effectors

These methods are based on the fact that on the T-lymphocyte surface there is a number of receptors and superficial molecules, i.e. differential antigens. To reveal them, monoclonal antibodies to differential antigens of T lymphocytes are necessary. With the help of superficial antigen markers one can define a population, subpopulation of the cells, the stage of their differentiation and activation. A test of indirect immunofluorescence is based on the ability of mono-antibodies to fix on the cellular surface and allows revealing specific antigen determinants to CD3, CD4, CD8 after additional processing of lymphocytes with anti-immunoglobulins labeled with FITC.

The method of flow cytometry is more exact.

Normal:

CD3	children	62-69%	1.8-3.0x109/L
	adults	67-76%	1.1-1.7x109/L
CD4	children	30-40%	1.0-1.8x109/L
	adults	38-46%	0.7-1.1x109/L
CD8	children	25-32%	0.8-1.5x109/L
	adults	31-40%	0.5-0.9x109/L

3. Determination of percentage and absolute number of mature B lymphocytes

The methods are based on the fact that on the surface there are receptors for Fc fragment of immunoglobulins, for the third component of 9C3 complement, for murine, sheep and rabbit erythrocytes, and immunoglobulin determinants. The most significant superficial makers of B lymphocytes are receptors to CD12, CD20, CD22, defined with the help of MAB method of flow cytometry.

Normal:

CD22	children	21-28%	0.7-1.3x109/L
	adults	11-16%	0.2-0.5x109/L

4. Determination of number of null lymphocytes

These are the cells that lack signs both T- and B-lymphocytes, as they have no antigen receptors or their receptors are blocked. These might be immature lymphocytes, or old cells having lost the receptors, or the cells damaged by toxins or immunosuppressants. In a number of diseases, their quantity grows either in case of cell damage or due to release of immature or defective cells. To determine their number, T- and B-lymphocytes are subtracted from the total quantity of lymphocytes.

5. Quantitative determination of immunoglobulins

The most widely used method is that by Manchini (1970), based on radial immunodiffusion (RID) in a gel, which contains monospecific serum against immunoglobulins. Then a standard antigen is introduced into the wells, a precipitation ring is measured, and Ig concentration is determined by calibration graph.

A highly sensitive method for determination of immunoglobulins in serum is enzyme-linked immunosorbent assay (ELISA).

IgG	7.5-15.45 g/L
IgA	1.25-2.5 g/L
IgM	0.65-1.65 g/L
IgE	up to “% IU/L

1. Determination of circulating immune complexes (CIC) in serum

CICs are the result of a compensatory reaction of antibody formation, directed at eliminating antigens. Formation of soluble Ag-Ab complexes provoke a number of pathologic conditions: SLE (systemic lupus erythematosus), rheumatoid arthritis and others. Determination of complexes is performed by spectrophotometry of blood serum, processed with polyethylene glycol. The method is simple and available. Normal of CICs is 0.006-0.110 extension units.

2. Phagocytic index.

To study consumption it is used yeast, latex particles, Staphylococcus aureus. The number of the particles engulfed by neutrophils in colored preparations is counted with the help of luminescent microscope and flow cytometer. It is counted those neutrophils, which have engulfed three and more particles.

Normal is 40-80%.

3. Phagocytic numberмis an average ability of every phagocyte for engulfing. It is equal to arithmetic average of the total number of inclusions in 5 phagocytes.

Normal is 4-6 standard units.

SPECIFIC TESTS: II LEVEL TESTS

1. Reaction of lymphocyte blast transformation (RLBT)

allows determining of a lymphocyte ability to transform into blasts in presence of mitogens. Blast transformation is evidence of the ability of a cell for further proliferation and differentiation.

They investigate proliferative response of T-lymphocytes upon phytohemagglutinin (PHA), con A (concanavalin A), and response of B-lymphocytes to pokeweed mitogen (PWM).

2. Determination of “activation markers” CD25 and HLA on T-lymphocytes.

3. Investigation of cytokine and γ-interferon products, IL-2, IL-4, TNF, IL-6.

4. Study of proliferative response to a specific antigen in RLBT.

5. Investigation of T-lymphocyte apoptosis through CD95 determination.

6. Determination of specific immunoglobulins.

7. Determination of sector IgA.

8. Bactericidal capacity of phagocytes by NBT test.

Nitroblue tetrazolium test is based on the capacity to reduce soluble NBT dye engulfed by a phagocyte into insoluble diformazan under the influence of superoxide anion (O3→O2) formed during NADP+ oxidase reaction. NBT test data are considerably increased at the early stage of the disease in many acute infections. They are often decreased in subacute and chronic forms.

9. Phagocytic chemotaxis intensity.

10. Investigation of neutrophil adhesion capacity to plastic and estimation of the number of cells with adhesive molecules CD11/CD18 on the membrane.

Appendix 3

THE MAIN RULES OF IMMUNOGRAM INTERPRETATION

RULE 1

Complex analysis of an immunogram is more informative than estimation of every index taken separately. No doubt, all the constituents of an immunogram may be considered separately with respect to symptoms. It is especially so when the matter concerns the main groups of the indices, such as neutrophil formula, or formula of lymphocyte subpopulations. Nevertheless, the base for diagnosis and prognosis should always be the total of changes of all the immunogram indices as more informative in principle.

RULE 2

Valid analysis of an immunogram may be done only in combination with estimation of clinical picture in the given patient.

In most cases, analysis of an immunogram without taking into account clinical picture is of no use (except for severe impairments of immune system).

In severe impairments, an immunogram itself is of diagnostic value. Thus, abrupt leucocytosis, defined by an increase in lymphocyte number at the expense of B-cells, enables to suppose in a patient chronic B-leukosis.

In overwhelming majority of diseases, one must not make any diagnostic suppositions on base of an immunogram only without careful analysis of clinical picture, as it may lead to a wrong clinical diagnosis. The same shifts in immunogram indices may occur in principally different pathologies and at the different stages of the same process; depending on this their interpretation will vary. The same shift of any index may be considered as a favorable or unfavorable symptom depending on the stage of the process, its type and peculiarities.

RULE 3

Immunogram analysis in dynamics is always more informative in both diagnosis and prognosis in comparison with a single immunogram.

Immunogram analysis during a disease makes prognosis and control over the process significantly more informative. Knowing the main laws of dynamics of changes in immunological indices in an

inflammatory process, it is possible to follow effectively the development of the process on base of an immunogram in dynamics only, of course, in comparison with clinical picture.

RULE 4

In overwhelming majority of cases, immunogram analysis enables to do approximate, not final conclusions as to diagnosis and prognosis.

RULE 5

In an immunogram, both correlation of different populations and subpopulations of immunologically competent cells (ICC) and their absolute values are of great practical importance.

In blood of healthy people, absolute numbers of the total of leukocytes, as well as of cells of separate populations vary much more than different ratios of these cells, including relative number of cells of different populations (blood cell formula). Absolute values of all the ICCs undergo very big physiological fluctuations (up to 2-4 times) depending on biological rhythm, time of meals, physical exertion. At the same time, relative number (percentage) of these cells is more or less stable and may change significantly only during immune reactions. That is why it is the relative content of blood cells of different populations and subpopulations that is the most informative for diagnosis and prognosis. Long-term practice of blood tests confirmed this thesis.

RULE 6

If shifts in the immunogram indices do not correspond with clinical picture of the diseases, it is evidence of a severe, unfavorable development of the process. The more pathogenic foreign intervention and the wider an area of its spread, the more severe an inflammatory process and the more a number and expressiveness of immunogram shifts. If immunogram shifts correspond with severity of an inflammatory process, we deal with an adequate reaction of immune system to a foreign agent.

However, in development of the pathological process, immunogram shifts may be more or less expressed, than they should be according to clinical picture. It is evidence of the fact that reaction of immune system to a foreign agent is weaker or stronger than it is enough for its neutralization.

Suppression of immune reaction (anergy, in fact) inadequate for the developing inflammatory process may result from antigenic mimicry, exhaustion, toxic suppression or breakdown towards blockade of regulating mechanisms of immune system.

Inadequate intensification of immune reactions (allergy) is determined by discontinuance of regulation of specific immune clone of cells and its uncontrolled intensification. That is why misfit between immunogram changes and clinical signs of the process is a bad symptom, indicating that immune system does not work properly, which causes aggravation of the pathological process.

Identification of the first signs of such a misfit in time is one of the main tasks of immunogram interpretation. It is evidence of the necessity to administer proper treatment to the patient.

Appendix 4

Complete blood count

Hemoglobin	135 g/L
Erythrocytes	3.9x1012/L
Leukocytes	3.8x109/L

Eosinophils	1%
Rod nuclear cells	6%
Segmented cells	72%
Lymphocytes	16%
Monocytes	5%
ESR	12 mm/h
Complete blood count	
Hemoglobin	167 g/L
Erythrocytes	4.9x1012/L
Leukocytes	5.2x109/L
Eosinophils	2%
Rod nuclear cells	4%
Segmented cells	61%
Lymphocytes	27%
Monocytes	6%
ESR	2 mm/h
Complete blood count	
Hemoglobin	147 g/L
Erythrocytes	4.4x1012/L
Leukocytes	4.6x109/L
Eosinophils	5%
Rod nuclear cells	3%
Segmented cells	59%
Lymphocytes	26%
Monocytes	7%
ESR	5 mm/h
Complete blood count	
Hemoglobin	125 g/L
Erythrocytes	3.7x1012/L
Leukocytes	4.1x109/L
Eosinophils	2%

Rod nuclear cells	7%
Segmented cells	66%
Lymphocytes	21%
Monocytes	4%
ESR	11 mm/h
Complete blood count	
Hemoglobin	135 g/L
Erythrocytes	3.9x1012/L
Leukocytes	3.8x109/L
Eosinophils	1%
Rod nuclear cells	6%
Segmented cells	72%
Lymphocytes	16%
Monocytes	5%
ESR	12 mm/h

Record of immunological investigation No. 4

Surname: Ignatjeva Age:_____ Date: June 5

Leukogram: EOSINO 0%; Young __%; Rod nuclear 7%; Segmented 70; LYMPH 17%; MONO 4%; Others ____%; ESR 20 mm/h

Immunological indices	In a patient		Normal in children/adults	
	-%	x10 L	-%	x10 L
Leukocytes		8	C A	6.8-10 4.6-7.1
Lymphocytes	17	1.36	C 38-53 A 28-39	2.9-5.1 1.6-2.4
T-lymphocytes (CD3)	46		C 62-69 A 67-76	1.8-3.0 1.1-1.7
T-lymphocytes (CD4)	40		C 30-40 A 38-46	1.0-1.8 0.7-1.1

T-lymphocytes (CD8)	6		C 25-32 A 31-40	0.8-1.5 0.5-0.9
IRI CD4/CD8	6.6		C 1.2-1.8 A 1.0-1.5	
Activated T and B lymphocytes and monocytes (CD25)			C up to 25 A up to 40	0.2-0.9 0.2-0.9
B-lymphocytes (CD22)	11		C 21-28 A 11-16	0.7-1.3 0.2-0.5
O-lymphocytes	43		up to 40	0.1-0.8
NK (CD16)	22		C 8-15 A 10-19	0.2-0.6 0.2-0.4
CIC E 280 (ηm)	0.105		ОП 0.066-0.110	extension units
Immunoglobulins:				
EIA IgG	19		7.5-15.45	
IgA	2		1.25-2.5	
IgM	1.9		0.65-1.65	
IgE	2		Up to 25 IU/L	
Phagocytic index	35		40-80%	
Phagocytic number	3		4-6 standard units	
CPI	19		N>20%	

Conclusion:_____

Made by:_____

Record of immunological investigation No. 4

Surname: Ignatjeva Age:_____ Date: June 5

Leukogram: EOSINO 0%; Young __%; Rod nuclear 7%; Segmented 70; LYMPH 17%; MONO 4%; Others ____%; ESR 20 mm/h

Immunological indices	In a patient		Normal in children/adults	
	-%	x10 L	-%	x10 L

Leukocytes		7	C A	6.8-10 4.6-7.1
Lymphocytes	30	2.1	C 38-53 A 28-39	2.9-5.1 1.6-2.4
T-lymphocytes (CD3)	61		C 62-69 A 67-76	1.8-3.0 1.1-1.7
T-lymphocytes (CD4)	38		C 30-40 A 38-46	1.0-1.8 0.7-1.1
T-lymphocytes (CD8)	22		C 25-32 A 31-40	0.8-1.5 0.5-0.9
IRI CD4/CD8	1.7		C 1.2-1.8 A 1.0-1.5	
Activated T and B lymphocytes and monocytes (CD25)			C up to 25 A up to 40	0.2-0.9 0.2-0.9
B-lymphocytes (CD22)	29		C 21-28 A 11-16	0.7-1.3 0.2-0.5
O-lymphocytes	22		up to 40	0.1-0.8
NK (CD16)	25		C 8-15 A 10-19	0.2-0.6 0.2-0.4
CIC E 280 (ηm)	0.100		OD 0.066-0.110	extension units
Immunoglobulins:				
EIA IgG	19		7.5-15.45	
IgA	2		1.25-2.5	
IgM	2		0.65-1.65	
IgE	2.1		Up to 25 IU/L	
Phagocytic index	35		40-80%	
Phagocytic number	3		4-6 standard units	
CPI	19		N>20%	

Conclusion:_____

Made by:_____

Appendix 5.1

INTERPRETATION OF IMMUNOGRAM READINGS

CBC	Increase	Decrease
Erythrocyte sedimentation rate	Infection Inflammation + systemic diseases Tumoral growth Anemia	Mastocytoma
Number of thrombocytes	Impairment in coagulation system	Chronic stress Presence of blood AID Toxic action of drug therapy
Number of erythrocytes	In hemoblastosis + Hb	Due to anemia in: Hematologic diseases Acute and chronic hemorrhages Gastritis and ulcer Fibromyoma of womb Sepsis or chronic infection Tumor Malnutrition Worm invasion Accompanies prolonged rheumatoid arthritis Secondary immunodeficiency
Number of leukocytes	Acute infectious process Inflammation Leukosis	IDS after acute infection, antibiotic and interferon therapy
Number of lymphocytes	Persistent lymphocytosis: chronic infectious process, caused by bacteria or protozoa, AID and allergic, lymphoproliferative diseases	Persistent lymphopenia in chronic infectious-viral diseases + HIV-infection Conditions after chemotherapy or roentgen radiation, prolonged antibiotic treatment

		Aplasia of bone marrow Chronic stress Drug addiction and/or alcoholism
Number of neutrophils	Systemic inflammation Post-operative complications Osteomyelitis Septic conditions Exacerbation of bronchial asthma	Connected with lymphocytosis Primary IDS due to damage to the neutrophil link
Number of eosinophils	Allergic diseases Worm invasions Eosinophilic leukosis Over-use of NSAID - inhibitors of prostaglandins	
Number of basophiles	Exacerbation of bronchial asthma	

T-cell link		
Index	Increase	Decrease
Relative number of T-cells (CD3+%) mm3	In highly polarized Th1 type immune response to a viral antigen	In IDS In sudden increase of B-lymphocyte part in Th2 type response
Absolute number of T-cells (CD3+%) mm3	-Lymphocytosis -increase in relative number of T-lymphocytes. In highly polarized Th1 response	- Lymphopenia - T-cell immunodeficiency
Relative number of T-helpers (CD4+%)	- In Th2 type immune response. In this case increase in correlation CD4/CD8 is connected with Th increase only, relative number of CD8 lymphocytes being the same - In exacerbation of allergic diseases - In autoimmune variant of response, accompanied by predominant	One of the features of T-cell IDS + HIV-infection

	autoantibodies formation	
Absolute number of T-helpers CD4+/mm3	- with lymphocytosis and great number of cells in T-population of lymphocytes due to this - increase in relative number of T-helpers in Th2 type immune response - in allergic or autoimmune diseases	- In T-cell IDS (primary and secondary) - HIV-infection
Relative number of T-killers/suppressors (CD8+%) mm3	- lymphocytosis - increase in absolute number of T-cells - with increase in absolute number of antigen-specific cytotoxic cells - during immune response to infectious, vaccinal, tumoral, allogeneic transplantation antigens (+abortion)	- in autoimmune and allergic diseases. At this CD4/CD8 correlation coefficient is above normal - infectious and allergic pathology (CD8-lymphocytes migrate to the pathology focus)
Number of T-cells "double negative" CD3+ CD4- CD8- (3-5%)	Appearance of T-cells with phenotype CD3+ CD4- CD8- - reflects impairment of maturation of T-cells in AID - ionizing radiation, even in small doses	
CD4/CD8 correlation due to:	- increase in T-helpers (number of T-killers being normal) - Th2 immune response to allo- and autoantigen - decrease in CD8 lymphocytes - migration of T-killers to the pathology focus in infectious pathology, autoimmune and allergic diseases - increase in CD4 and decrease in CD8 lymphocytes - in mixed Th1/Th2 response to allo- and autoantigen	- increase in T-killers (number of T-helpers being normal) - In viral or bacterial infection during growing of number of antigen-specific cytotoxic T-cells - decrease in CD4 lymphocytes - intense apoptosis of T-helpers (HIV-infection) - increase in CD8 and decrease in CD4 lymphocytes - correlates with HIV-infection progress, reaching 0.1 at the terminal stage
Number of T-cells with CD25 receptor (low affinity receptor for IL-2)	Activation of immune system during response to Ag (proliferation of T-cells under the influence of T-cell growth factor IL-2)	Absence causes primary T-cell immune disease - In HIV-infection falls suddenly

B-cell link		
Index	Increase	Decrease
Relative number of B-lymphocytes (CD20%)	In Th2 immune response – for infections caused by bacteria, protozoa, fungi - AID and allergic diseases developing by Th2 type - necessary to be correlated with presence or absence of plasmatic cells in clinical blood test and Ig level (A, M, D, E) Increase in B-lymphocytes, considerable number of null cells in studying subpopulations with a standard set of monoclonal Ab requires excluding a hematologic lymphoproliferative disease	- active Ab formation - primary B-cell immune disease (Bruton's disease) - accumulation of B-cells in a target organ
Absolute number of B-lymphocytes (CD20/mm2)	- consequence of absolute lymphocytosis - reflection of Th2 response to allo- and autoantigens	- in lymphopenia - in active Ab formation - in primary B-cell immune disease (Bruton's disease) - accumulation of B-cells in a target organ
Relative number of NK cells (CD 16%)	- in viral and bacterial infections - in tumoral process - allergic and autoimmune diseases	- in prolonged infection - malignant growth - migration of the cells to the pathology focus - in allergic and autoimmune diseases
Absolute number of NK cells (CD 16/mm2)	- absolute lymphocytosis	- lymphopenia - prolonged infection - malignant growth - migration of the cells to the pathology focus - in allergic and autoimmune diseases
Number of cells with HLA II marker (is situated on B-cells, activated T-cells and	- reflects active immune response to a foreign Ag	- in AID - malignant growth

monocytes. One of the "activation" markers, like CD95 and CD25)		
Number of cells with CD95 marker CD95 receptor is on T-helpers CD95L is on T-killers	- activation of immune system - a marker of preparedness to apoptosis, which occurs in interaction CD95/CD95L - in acute viral infection, some stages of HIV-infection, virus hepatitis	- characteristic of AID, malignant diseases This decrease is one of the reasons of preservation and accumulation of autoreactive and transformed tumoral cells in the patient's organism

CYTOKINES

Index	Increase	Decrease
Interleukin 1β (IL-1β)	- in autoimmune pathology - in acute course of autoimmune thyroiditis - in thyrotoxicosis - I type insulin-dependent diabetes - rheumatoid arthritis - Crohn's disease - exacerbation of bronchial asthma - acuteness of the process correlates with IL-1β production level "Non-immunologic" processes, such as ischemic heart disease, hypertension, are also accompanied by a slight increase in IL-1β spontaneous production, a decrease in induced one, and in some cases by an increase of the level in blood serum	- chronic processes of autoimmune, allergic and infectious genesis
Receptor antagonist to IL-1 (IL-1RA)	- characteristic of inflammation - estimates functional state of the cells, taking part in immune response and inflammation	
Interleukin-2 (IL-2)	- in lymphoproliferative diseases, when IL-2 is an auto- or paracrine growth factor for transformed cells. - AID	- T-cell immunodeficiency
Interleukin-4 (IL-4)	- in presence of Th2 pre-activation by antigens: allergic - in response to Ag, to which there are already	- in chronic immunopatho-logical Th2 process - in prolonged allergic disease

	antigen-specific Th2 (primary Th2) - accompanies systemic Th2 response in systemic allergic reaction	(sometimes these changes combine with absence of general IgE in blood serum)
Interferon-gamma (INF-γ)	Estimation of this cytokine level in blood serum simultaneously with IL-4 is important to determine an immune response type: Th1 or, more often, Th2. Th1 immune response is characterized by predominant production of INF-γ by immune system cells and induction of cell response. Besides, INF-γ is an anti-inflammatory cytokine and its increase defines the inflammation level. Reflects functional state of immunocytes.	
Interleukin-6 (IL-6)	- increase in spontaneous and induced production is connected with pre-existing cell activation in vivo in active antibody formation in response to Ag - in highly polarized Th2 response, as IL-6 completes transition of B-lymphocytes into plasmatic antibody-producing cells	- decrease in stimulated IL-6 production is connected with persistence of Ag, which induces Th2 response
Interleukin-8 (IL-8)	- increase in spontaneous production of IL and/or its level in blood serum, which is a chemo-attractant for neutrophils and other cells, participating in immune response, may reflect activation of neutrophil function in response to penetration of bacterial antigens into the organism. Usually it is accompanied by increased migration of neutrophils in response to IL addition into neutrophil culture. - paradoxical is an increase during bronchial asthma, accompanied by decreased migration of neutrophils - reflects activation of producing cells in response to bacterial Ag.	- decrease in IL induced production is connected with infectious process becoming chronic and partial resistance of producing cells to effect of an inductor
Interleukin-10 (IL-10)	- increase in spontaneous production of anti-inflammatory cytokine IL10 and/or its level in blood serum may combine with increased production of anti-inflammatory cytokines, taking into account their antagonism - as a favorable sign in case of AID and allergic diseases may accompany remission of the disease - in case of response to alloantigen (in infectious pathology) increase may contribute to the disease becoming chronic and show ineffectiveness of the	- reflect duration of the process

	pathogen elimination	
Tumor necrosis factor-α (TNF-α)	- characteristic of inflammatory processes - cell elimination by direct cytotoxicity or apoptosis using pathway TNF-α – receptor o TNF-α - Induced production allows estimating the immune system cell condition, their ability to respond adequately to antigen stimulation - Reflects the severity of the pathologic process in disseminated sclerosis, psoriasis, autoimmune thyroiditis, diabetes	
Interferon-α (INF-α)	Impairment of its production causes recurring virus infections, especially herpetic infection - Decrease in induced production in response to antigen is accompanied by clinical manifestations of chronic virus infection	
Immunoglobulins of blood serum	Main effector properties of IgE: - induction of release of biogenic amines - induction of cytological activity of eosinophils, monocytes and macrophages Hyper IgE – for atopy: - helminthiasis - isolated IgA deficiency - thymus hypoplasia (DiGeorge syndrome, Wiskott-Aldrich syndrome) - chronic granulomatosis in children - Job syndrome - increased total IgE in Th2 immune response is not always evidence of an allergic disease	

Appendix 5.2

TASK No. 1

Estimate the indices of the immunograms in the two male patients with pneumonia, at the early stage of the process, on the second day after the onset of the disease. According to clinical and roentgenological data, both patients are established to have foci of inflammation in lower lobes of the right lung.

Index	WBC	BASO	EOSINO %	Rod nuclear	Segmented	LYMP	MONO %	ESR	T-lymp	B-lymp	% phagoc.

	x109	%		cells, %	cells %	H %		mm/h	h, %	h, %	neutro
Patient K, 39 years	9.2	0	1	9	70	12	8	20	45	15	90
Patient D., 62 years	4.2	0	2	2	61	27	8	10	43	10	60

TASK No. 2

Which initial diagnosis may be made on base of the data of the immunogram?

Index	WBC x109	BASO %	EOSINO %	Rod nuclear cells, %	Segmented cells %	LYMPH %	MONO %	T-lymph %	B-lymph %
Patient (F, 28)	82.5	0	1	0	12	86	1	10	78

TASK No. 3

Which initial diagnosis may be made on base of the data of the immunogram?

Index	WBC x109	BASO %	EOSINO %	Rod nuclear cells, %	Segmented cells %	LYMPH %	MONO %	T-lymph %	B-lymph %	T-helpers, %	T-suppressors %
Patient G., (M, 35)	3.0	1	6	17	50	15	11	30	29	2	28

TASK No. 4

Compare the indices of the immunogram in a 36-year-old man during the clinical health and during the grippe. Estimate the changed parameters of the immunogram.

Index	WBC x109	BASO %	EOSINO %	Rod nuclear cells, %	Segmented cells %	LYMPH %	MONO %	T-lymph %	B-lymph %	T-helpers, %	T-suppressors %

Health	3.1	0	1	2	62	32	3	79	8	60	19
Grippe	4.9	0	3	1	60	29	7	58	5	44	6

TASK No. 5

A male patient was admitted to the in-patient department complaining of the pains in the chest, cough with a little sputum, elevated temperature up to 39ºC, chills, bad malaise. Roentgenological readings: in the upper lobe of the right lung there is a big shadow with fuzzy outline. Then there appeared profuse purulent sputum during cough, the temperature decreased. Estimate the parameters of immune status, received in investigating the patient.

Index	WBC x10 9	BASO %	EOSINO %	Rod nuclear cells, %	Segmented cells %	LYMPH %	MONO %	T-lymph %	B-lymph %	T-helpers, %	T-suppressors %	ESR mm/h	% phagoc. neutro
Patient M., 31 years	0	0	2	62	32	4	50	10	44	12	12	7	45

IMMUNE INFLAMMATION AND INFECTIOUS DISEASES. HIV-INFECTION: IMMUNOPATHOGENESIS, IMMUNODIAGNOSTIC, IMMUNOCORRECTION. PRINCIPLES OF IMMUNOTHERAPY ADMINISTRATION. IMMUNOREHABILITATION, IMMUNOPROPHYLACTIC.

Issues to be considered during the class

Mechanisms of immune defense in case of bacterial and viral infection. Role of immune system in antifungal and antihelminth immunity. Role of immune system in opportunistic infections and protozoan diseases. Immunological methods in diagnostic of infectious diseases.

Immune response in acute inflammation. Parameters of immunogram, leucogram proteinpgram in acute, recurrent and chronic inflammation.

Types and characteristic of infectious diseases specific immuneprophylactic. Immune-mediated reactions and complications in vaccination.

Etiology, immunopathogenesis, diagnostic and immunotherapy of AIDS. Immunological methods in AIDS diagnostic. Immunogram dynamic in HIV-infected and patients with AIDS. Immunoprophylactic of HIV-infection.

Classification of drug affecting immune system. Their mechanism of action. Principles of usage, indications and contraindications, adjustment of drug dosage, immunological control of efficacy. Immunosuppressive drugs, immunomodulating, drugs, blocking mediators of immune reactions. Anti-inflammatory drugs, substitution therapy, cytokine therapy, antireceptor drugs ect.

Major principles of immunoprophylactic of bacterial and viral infections.

Types of immunorehabilitation, strategy, tactics, and major principles.

Aim of Study

The use of immune system components to treat a disease or disorder is known as immunotherapy. Immunotherapy is most commonly used in the context of the treatment of cancers together with chemotherapy (drugs) and radiotherapy (radiation). However, immunotherapy is also often used in the immunosuppressed (such as HIV patients) and people suffering from other immune deficiencies or autoimmune diseases.

The specificity of the bond between antibody and antigen has made it an excellent tool in the detection of substances in a variety of diagnostic techniques. Antibodies specific for a desired antigen can be conjugated with a radiolabel, fluorescent label, or color-forming enzyme and are used as a "probe" to detect it. However, the similarity between some antigens can lead to false positives and other errors in such tests by antibodies cross-reacting with antigens that aren't exact matches

Purposes of discipline

Student has to know:

1. Mechanisms of immune defense in case of bacterial and viral infection.
2. Etiology, immunopathogenesis, diagnostic and immunotherapy of AIDS.
3. Classification of drug affecting immune system. Their mechanism of action
4. Types of immunorehabilitation.

Student has to be able to do:

1. On the ground of clinical data prescribe drugs, affecting immune system, be familiar with indications and contraindications, dosage counting, immunological control of effectivity.
2. Estimate indications and contraindications to immunoprophylactic of bacterial and viral infections.
3. Characterize the dynamic of leucogram, immunogram and proteinogram parameters in acute, recurrent and chronic inflammation

Interdiscipline integration

Subject	Know	Can
Anatomy	Haemopoietic organs of immune system	Name primary and secondary lymphoid organs, lymphatic ducts
Biology, histology, embryology.	Immunity as mechanism of functional and structure homeostasis. Essentials of immuno-embryogenesis.	Distinguish basic phylogenetic levels of immunity evolution, primitive cell-mediated immunity and integral cell-mediated and humoral immunity

Biochemistry	Chemical structure and biological action of mediators of cell-mediated immunity	Immunophoretic determination of immunoglobulins.
Pathophysiology	Phagocytosis in the focus of inflammation, immunological tolerance, reactivity, allergy.	Name immunocompetent cells, participating in defense reactions of cell-mediated and humoral immunity
Normal physiology	Interaction of nervous, endocrine and immune system for functional and structure homeostasis maintaining	On practical classes determine interaction of nervous, endocrine and immune system.
Pathological anatomy	Role of immune disorders in mesenchymal and protein dystrophies, mucous and fibrinoid degeneration if connective tissue	Determine mesenchymal and protein dystrophies, mucous and fibrinoid degeneration if connective tissue. Types of tissue reactions in collagenoses.
Microbiology, virusology	Specific and non-specific mechanisms of defense. Types of antigenes, immunity, allergies.	Perform agglutination test, Coombs' test, precipitation. Titration of complement, bacteriolysis and haemolysis tests, immunofluorescence test
Propedeutics of internal diseases	Role of immune system in pathogenesis of different diseases.	Interpretation of rosette test, Manchini immunoglobulins, phagocytic activity of blood.

Independent student's work

Main theoretical aspects of theme.

Immune, neurological and endocrine regulation of functions.

Apoptosis as regulator of immune response.

Immunology of mucosae.

Task for final module test

1. Immunopathogenesis, stages, classification of HIV-infection and AIDS.
2. Clinical and laboratory diagnostic, principles of treatment.
3. Major principles of HIV prophylactic in Ukraine. Medical staff as "risk group" for HIV infection.

List of practical skills for final module test.

1. Train skills of leucogram and immunogram data understanding
2. Find signs of immune system disorders in leucogram.
3. Prescribe immunostimulating treatment, estimate forecast, perform primary and secondary immunoprophylactic of immunodependent diseases.
4. Know classification of drug affecting immune system. Their mechanism of action. Principles of usage, indications and contraindications, adjustment of drug dosage, immunological control of efficacy.
5. Be able to perform vaccination
6. Estimate efficacy of immune therapy in dynamic.
7. Perform replacement therapy with immunoglobulins.
8. Perform antiviral interferon therapy.

PRIMARY AND ACQUIRED IMMUNODEFICIENCY DISEASES

Issues to be considered during the class

Primary immunodeficiencies: definition, classification, mechanism of development. Clinical sings, immunodiagnostic, doctor's tactics, principles of treatment: combined, T- and B-dependent immunodeficiencies, immunodeficiencies associated with phagocytosis impairment and deficiency of complement proteins.

Acquired immunodeficiencies: definition, etiology, mechanism of development, classification, diagnostic. Role of acquired immunodeficiencies in pathogenesis of different diseases. Early determination of acquired immune deficiency in the organism. Major principles of treatment.

Rapid fatigue syndrome, chronic fatigue syndrome.

Aim of study

Immunodeficiency (or immune deficiency) is a state in which the immune system's ability to fight infectious disease is compromised or entirely absent. Most cases of immunodeficiency are acquired ("secondary") but some people are born with defects in the immune system, or primary immunodeficiency. Transplant patients take medications to suppress their immune system as an anti-rejection measure, as do some patients suffering from an over-active immune system. A person who has an immunodeficiency of any kind is said to be immunocompromised. An immunocompromised person may be particularly vulnerable to opportunistic infections, in addition to normal infections that could affect everyone.

Primary immunodeficiency

A number of rare diseases feature a heightened susceptibility to infections from childhood onward. Many of these disorders are hereditary and are autosomal recessive or X-linked. There are over 80 recognised primary immunodeficiency syndromes; they are generally grouped by the part of the immune system that is malfunctioning, such as lymphocytes or granulocytes.

The treatment of primary immunodeficiencies depends on the nature of the defect, and may involve antibody infusions, long-term antibiotics and (in certain cases) stem cell transplantation.

Acquired immunodeficiency

Immune deficiency may also be the result of particular external processes or diseases; the resultant state is called "secondary" or "acquired" immunodeficiency. Common causes for secondary immunodeficiency are malnutrition, aging and particular medications (e.g. chemotherapy, disease-modifying antirheumatic drugs, immunosuppressive drugs after organ transplants, glucocorticoids).

Many specific diseases directly or indirectly impair the immune system. This includes many types of cancer, particularly those of the bone marrow and blood cells (leukemia, lymphoma, multiple myeloma), and certain chronic infections. Immunodeficiency is also the hallmark of acquired immunodeficiency syndrome (AIDS), caused by the human immunodeficiency virus (HIV). HIV directly impairs the immune system by attacking T helper cells.

Purposes of discipline

1. Acquaint students with immunodeficiency states, ways of correction.

2. Learn up-to-date principles of immunocorrective therapy, present classification of immune modulation, types, drugs and their prescription.

Student has to know:

1. Definition of immunodeficiencies, epidemiology of IDs.
2. Pathogenesis and classification of IDs.
3. Clinical symptoms and syndromes of PIDs and SIDs.
4. Treatment of patients with immune deficiencies.
5. Present-day abilities to influence immune system.

Student has to be able to do:

1. Take immunological anamnesis.
2. Distinguish primary and secondary immunodeficiencies states.
3. Estimate data of leucogram and immunogram for patients with IDs.
4. Name indications and contraindications for immune therapy administration. Prescribe proper immune therapy for patient with IDs.

Interdiscipline integration

Subject	Know	Can
Anatomy	Haemopoietic organs of immune system	Name primary and secondary lymphoid organs, lymphatic ducts
histology, embryology	Lymphocytes development from stem cell to effector cells of humoral and cell-mediated immunity. Morphology of induction stage and proliferation stage. Essentials of immunoembryogenesis. Role of granulocytes and connective tissue cells in organism defense.	Distinguish immunological reactions of human embryogenesis. Analyse leucogram, its normal range.
Biology	Role of immunity in regeneration. Immunological tolerance.	Point immunocompetent cells.
Normal physiology	Circulation of stem cell and lymphocytes in organism.	Understand connection between nervous, endocrine and immune regulation of homeostasis. Понимание взаимосвязи нервной, эндокринной и иммунной систем в поддержании гомеостаза. Analyse leucogram, its normal range.
Microbiology, virusology	Compare reaction antigen-antibody, give estimation. Role in defense reactions and pathology	Analyse reaction of immobilization.
Pathophysiology	Role of immunity in immune deficiesncy development	Establish function of phgocytosis and interpret leucogram
Pathomorphology	Pathomorphological characteristic of primary and secondary iimune deficiencies. Pathomorphology of phagocyte-dependent IDs	Immunomorphology methods
Radiology	Biological action of different kinds of radiation on living organisms. IDs in region of nuclear damage.	X-ray examination and USG of immune organs.
Internal medicine	Principles of immune therapy in internal medicine.	Make prescription taking immune therapy into consideration.
Pharmacology	Influence of different drugs on immune system. Vitamins and immunity, Immunostimulating and immunosuppressive effect of corticosteroids. Allergic states.	Reaction of active leucocytolysis

Independent student's work

Oral presentation of themes, given for independent work.

Immunopathogenesis and immune therapy of sepsis.

Tasks for final module test

1. Classification of immune deficiencies. T-, B- and combine primary immunodeficiencies: mechanisms of development, course of disease, immune diagnostic and treatment.
2. Primary immunodeficiencies of phagocytosis and complement system, mechanisms of development, course of disease, immune diagnostic and treatment.
3. Acquired immune deficiencies. Etiology, clinical signs, immune diagnostic and treatment
4. Syndrome of lasting fever: etiology, clinical manifestation, instrumental and laboratory diagnostic criteria, differential diagnosis, immune therapy and prophylactic.
5. Lymphadenopathy syndrome. Etiology, pathogenesis, classification, investigations, diagnostic criteria, immune therapy and prophylactic.

List of practical skills for final module test.

1. Reveal presents of symptoms, indicating immune system disorders.
2. Perform differential diagnosis in patients with primary and secondary immunodeficiency states.
3. Make interpretation of leucograms and immunograms, taking period of disease, clinical manifestation into consideration.
4. Describe influence of environmental factors on immune system
5. Reveal clinical signs of local immunity decompensation.

Appendix 1, 2

SCREENING CLINICAL AND ANAMNESTIC CRITERIA
TO REVEAL DYSFUNCTION OF THE IMMUNE SYSTEM

I. Clinical symptoms:

1. Marked stigmatization;

2. Lymphadenopathy with early decompensation (tonsillectomy, appendectomy)

3. Thymus hyperplasia;

4. Hypoplasia and aplasia of lymphoid tissue, especially in inflammatory processes

5. Chronic and recurrent staphylo- and streptoderma;

6. Hepatosplenomegaly

II. Family history (family tree)

1. Unclear cases of newborn and infant death, as well as fatal outcomes due to infection, mucoviscidosis, etc.
2. Chronic and recurrent diseases in the relatives;

3. Hemopathy;
4. Development anomaly, stigmas of dysembryogenesis;
5. Endocrinopathy;
6. Allergic diseases;
7. Autoimmune diseases (systemic lupus erythematosus, Hashimoto thyroiditis, diabetes mellitus)
8. Malignant growth;
9. Blood relationship of the parents.

III. Antenatal anamnesis

1. Viral and bacterial diseases in the mother with the first trimester of the pregnancy;
2. Taking drugs, especially antibacterial, sulfanilamide and anti-inflammatory ones;
3. Influence of different etiologic factors;
4. Insalubrity at work and at home;
5. Toxicosis of the first half of pregnancy;
6. Threat of miscarriage at the early term (prolonged taking of hormonal drugs);
7. Abnormal nutrition of the pregnant and nursing mother;
8. Exacerbation of chronic diseases of mother during pregnancy;
9. Great stresses;
10. Pathology during delivery

IV. Anamnesis vitae and morbi

1. Development of the disease at the early age;
2. Early development of the recurrent infections: thrush, bronchopulmonary diseases, purulent otitis, sinusitis and pansinusitis, diarrhea, eczema, furunculosis, abscesses, herpetic eruption, osteomyelitis, pyuria of unclear etiology, sepsis;
3. Severity and acuteness of the disease;
4. Subfebrile temperature for a long time;
5. Generalized processes and reactions;
6. Ineffectiveness of the administered treatment;
7. Development of autoimmune and neoplastic diseases;
8. Reactions of vaccination;
9. Allergic reactions on drugs;
10. Frequent and prolonged taking of glucocorticoid, cytostatic, sulfanilamide, antihistamine preparations, etc., especially at the early age.

V. On examination of a child

1. Lymphopenia less than 1.0x109/L, alymphocytosis, pancytopenia;
2. Slowed ESR on the background of bacterial diseases;
3. Hypoglobulinemia, especially of y-fractions;
4. Severe hemolytic or aplastic anemia.

Explanation to clinical and anamnestic tests

1. If there is one or more criteria from group II (family history) and one or more criteria from group IV (anamnesis morbi) and group I (clinical symptoms), primary immunodeficiency should be supposed.
2. If there are no criteria from group II (absence of above-mentioned diseases in family history), but there are one or more criteria from groups II (antenatal anamnesis), IV (anamnesis morbi) and I (clinical symptoms), primary congenital immunodeficiency should be supposed.
3. If there are no data of groups II (family history) and III (antenatal anamnesis), but there are one or more criteria from groups IV (anamnesis morbi) and I (clinical symptoms), secondary immune insufficiency or acquired immunodeficiency should be supposed.

<u>Screening immunological tests are:</u>

1. Contents of immunoglobulins G, A, M in blood serum;
2. Contents of T-lymphocytes in blood;
3. Contents of B-lymphocytes;
4. Estimation of phagocytosis

According to WHO, there are more than 70 kinds of primary immunodeficiency. In Russia, the diagnosis of primary immunodeficiency is proved in some hundreds of people, that is in our country the correct diagnosis is made in 1-2 persons out of 1000 only. If a child has more than one of the listed signs, the possibility of immunodeficiency is high.

Primary immunodeficiency: 10 signs requiring more attention

1. Frequent otitis: not less than 6-8 times a year.
2. Several proved severe sinusitis: not less than 4-6 times a year.
3. More than 2 proved pneumonias.
4. Recurrent deep abscesses of skin or inner organs.
5. Necessity to apply prolonged antibiotic therapy to control infection – up to 2 months and more
6. Necessity to introduce antibiotics intravenously to control infection.
7. Not less than 2 deep infections, such as meningitis, osteomyelitis, sepsis.
8. Retardation of an infant in growth and mass.
9. Persistent thrush or fungal skin lesion at the age of more than 1 year.
10. In the family: primary immunodeficiency or facts of early death from severe infections.

Appendix 3

Recommendations as to the use of primary diagnosis of immunodeficiency are given below:

Panel of the screening tests:

1. Number of leukocytes and calculation of smear:

    - absolute number of neutrophils;

    - absolute number of lymphocytes;

    - absolute number of thrombocytes.

2. The level of g-globulins (proteinogram of blood serum).

3. Serum immunoglobulins:

    - IgG

    -IgM

    - IgM

4. The level of specific antibodies.

5. Skin tests of delayed hypersensitivity.

Primary immunodeficiency revealed by the tests of this panel

1. x-linked agammaglobulinemia
2. General variable immunological insufficiency
3. Hyper-IgM-syndrome.
4. Selective IgA deficiency.
5. Severe combined immunodeficiency.
6. Wiskott-Aldrich syndrome.
7. Neutropenia.

* Use of this screening panel allows differentiating the most spread PID

The further diagnosis allows revealing another series of the diseases or specifying initial diagnosis.

If clinically one can observe immunodeficiency, but it lab tests fail to prove it, it is advisable to carry out the investigations in the center specializing in congenital immunity defects and included into the international network. At this, clinical diagnosis "undifferentiated PID" may be made if on its basis the doctor determines prognosis and administers treatment correctly.

Appendix 4

Record of immunological investigation No. 15

Surname: *Krulosova* Age:_15___ Date: _____

Leukogram: EOSINO 4%; Young __%; Rod nuclear 3%; Segmented 53; LYMPH 32%; MONO 8%; Others ____%

Immunological indices	In a patient		Normal in children/adults	
	-%	x10 L	-%	x10 L
Leukocytes		5.2	C A	6.8-10 4.6-7.1
Lymphocytes	32%	1.66	C 38-53 A 28-39	2.9-5.1 1.6-2.4
T-lymphocytes (CD3)	68	1.1	C 62-69 A 67-76	1.8-3.0 1.1-1.7
T-lymphocytes (CD4)	28	0.4	C 30-40 A 38-46	1.0-1.8 0.7-1.1
T-lymphocytes (CD8)	40	0.6	C 25-32 A 31-40	0.8-1.5 0.5-0.9
Immune regulation index CD4/CD8		0.7	C 1.2-1.8 A 1.0-1.5	

Activated T and B lymphocytes and monocytes (CD25)	20%	0.3	C up to 25 A up to 40	0.2-0.9 0.2-0.9
B-lymphocytes (CD22)	12%	0.2	C 21-28 A 11-16	0.7-1.3 0.2-0.5
O-lymphocytes	near 19	0.3	up to 40	0.1-0.8
NK (CD16)			C 8-15 A 10-19	0.2-0.6 0.2-0.4
CIC E 280 (ηm)			OD 0.066-0.110	extension units
Immunoglobulins:				
EIA IgG	3.2		7.5-15.45	
IgA	0.15		1.25-2.5	
IgM	0.65		0.65-1.65	
IgE			Up to 25 IU/L	
Phagocytic index	57%		40-80%	
Phagocytic number	4 s.u.		4-6 standard units	
CPI	20%		N>20%	

Conclusion:_____

Made by:_____

Record of immunological investigation No. 16

Surname: *Kisin* Age:_12___ Date: _____

Leukogram: EOSINO 2%; Young __%; Rod nuclear 5%; Segmented 62; LYMPH 23%; MONO 8%; Others ____%

Immunological indices	In a patient		Normal in children/adults	
	-%	x10 L	-%	x10 L
Leukocytes		5.4	C A	6.8-10 4.6-7.1

Lymphocytes	23%	1.2	C 38-53 A 28-39	2.9-5.1 1.6-2.4
T-lymphocytes (CD3)	31	0.3	C 62-69 A 67-76	1.8-3.0 1.1-1.7
T-lymphocytes (CD4)	17	0.2	C 30-40 A 38-46	1.0-1.8 0.7-1.1
T-lymphocytes (CD8)	14	0.1	C 25-32 A 31-40	0.8-1.5 0.5-0.9
Immune regulation index CD4/CD8		1.2	C 1.2-1.8 A 1.0-1.5	
Activated T and B lymphocytes and monocytes (CD25)	13	0.1	C up to 25 A up to 40	0.2-0.9 0.2-0.9
B-lymphocytes (CD22)	25%	1.3	C 21-28 A 11-16	0.7-1.3 0.2-0.5
O-lymphocytes	near 30	0.3	up to 40	0.1-0.8
NK (CD16)	8%	0.09	C 8-15 A 10-19	0.2-0.6 0.2-0.4
CIC E 280 (ηm)	0.072		OD 0.066-0.110	extension units
Immunoglobulins:				
EIA IgG	12.1		7.5-15.45	
IgA	1.7		1.25-2.5	
IgM	0.92		0.65-1.65	
IgE			Up to 25 IU/L	
Phagocytic index	70		40-80%	
Phagocytic number	4		4-6 standard units	
CPI	20		N>20%	

Conclusion:_____

Made by:_____

Appendix 5

TOPIC: PRIMARY IMMUNODEFICIENCY

TASK 1

An 18-month-old boy was admitted to the hospital with lobar pneumonia. According to the mother, the boy is often ill with otitis, bronchitis, conjunctivitis. CBC: Hb: 80g/L; erythrocytes: 3.5x10/L; leukocytes: 5.6x10/L. Immunogram: IgG 1.8 g/l; IgA, M are not determined.

Which primary deficiency does the child have?

1. Bruton disease.
2. DiGeorge syndrome.
3. Autosome-recessive agammaglobulinemia
4. General variable immunodeficiency
5. Chronic granulomatosis

TASK 2

A 5-year-old girl was admitted to the in-patient department with purulent pansinusitis. In spite of the treatment, there is no improvement; pains, purulent discharge, subfebrile temperature are persisting. On examination vaginal candidosis, single telangiectasia on the skin of the face and auricles were revealed, the vessels of bulbar conjunctiva were dilated. She was born from the first normal pregnancy. The parents are liquidators of the Chernobyl catastrophe. According to the mother, she has had frequent acute respiratory diseases since 2 years of age, started walking late, is walking "sidelong".

Which primary immunodeficiency may be supposed in this child?

1. Reticular dysgenesis
2. Wiskott-Aldrich syndrome
3. Louis-Bar syndrome
4. DiGeorge syndrome
5. Nezelof syndrome

TASK 3

A 3-month-old boy was admitted to the children's department with an abscess in the right axilla, pustular rash on the skin of the face and inguinal area. On examination, enlargement of axilla and inguinal lymph nodes and enlargement of the liver and kidneys were revealed. After antibacterial treatment, pustular rash has reduced considerably. In the area of abscess, a fistula has formed, the discharge being purulent. The defect of which link of immunity does the child have:

1. humoral;
2. cellular;
3. combined;
4. phagocytosis;
5. complement

Which primary immunodeficiency may be supposed:

1. Chédiak-Higashi syndrome;
2. chronic granulomatosis;
3. Job syndrome;

4. Nezelof syndrome;
5. Wiskott-Aldrich syndrome

Which specifying tests (of the II level) will change in this pathology:

1. RLBT
2. Immune regulation index
3. NBT-test
4. CIC level
5. complement

TASK 4

A 2.5-year-old boy was admitted to the children's department complaining of rash on the skin of the face, neck, chest, bending areas of the arms, skin itching, elevated irritability, frequent weeping, frequent epistaxis. Mother was ill with the severe grippe during pregnancy. According to the mother, the child grew and developed normally till 6 months. Since 6 months, he has often been ill with acute bronchitis and had pneumonia twice.

On examination: hyperemia and edemas of the skin of the face, there are grouped vesicular eruptions, pronounced local edema. There are papulovesicular eruptions, crusts and traces of scratches on the skin of the neck and bending area of the arms. Which primary deficiency may be supposed?

1. Good syndrome;
2. Louis-Bar syndrome;
3. Wiskott-Aldrich syndrome;
4. DiGeorge syndrome;
5. Job syndrome.

Which changes are characteristic of an immunogram , if

A. 1 and 5 are correct;

B. 2, 3 and 4 are correct;

C. 2, 4 and 5 are correct.

1. Decrease in IgM, increase in IgE and IgA;
2. Normal level of Ig A, M, G, and increased IgE
3. T-lymphocytes are within normal;
4. Increased number of B-lymphocytes;
5. Decrease in RLBT on PHA

FUNDAMENTALS OF TRANSPLANTATION IMMUNITY. IMMUNOLOGY OF TUMORS.

Issues to be considered during the class

Main terms, definition (auto-, allo-, xenotransplantation).

Pretransplantation monitoring. Mechanism of allotransplant rejection: hyper acute, acute, chronic. Post-transplantation infectious complications, criteria of diagnostic. Immunosuppressive therapy: mechanism of action, principles of administration, complications. New immunological methods and therapy in transplantology.

Problastom and conrablastom mechanisms of interaction between host's organism and tumor. Factors of immune resistense of tumors. Characteristic of tumor-associated genes. Immune changes in patients with oncopathology. Immunodiagnostic, including CD-phenotyping of tumors. Contemporary principles of immunotherapy of patients with oncopathology.

Aim of study

Transplantation medicine is one of the most challenging and complex areas of modern medicine. Some of the key areas for medical management are the problems of organ rejection - where the body has an immune response to an organ which causes failure of the transplant and of ensuring that the organ can be kept in a functioning state while it is transplanted from one body to another. This is a very time sensitive process.

Purposes of discipline

1. Problastom and conrablastom mechanisms of interaction between host's organism and tumor
2. Mechanism of immune tolerance disorders, role of genetic factors.
3. Pretransplantation monitoring. Mechanism of allotransplant rejection: hyper acute, acute, chronic.

Student has to know:

1. Immunosuppresive action of tumors and other immune changes.
2. Differential immunodiagnostic of tumors according to CD-phenotype classification.
3. New immunological methods and therapy in transplantology.

Student has to be able to do:

1. Diagnose hyperacute, acute and chronic crisis of graft rejection.
2. Immunodiagnostic of tumors.

Interdiscipline integration

Subject	Know	Can

Anatomy	Haemopoietic organs of immune system	Name primary and secondary lymphoid organs, lymphatic ducts
Biology, histology, embryology.	Immunity as mechanism of functional and structure homeostasis. Essentials of immuno-embryogenesis.	Distinguish basic phylogenetic levels of immunity evolution, primitive cell-mediated immunity and integral cell-mediated and humoral immunity
Biochemistry	Chemical structure and biological action of mediators of cell-mediated immunity	Immunophoretic determination of immunoglobulins.
Pathophysiology	Phagocytosis in the focus of inflammation, immunological tolerance, reactivity, allergy.	Name immunocompetent cells, participating in defense reactions of cell-mediated and humoral immunity
Normal physiology	Interaction of nervous, endocrine and immune system for functional and structure homeostasis maintaining	On practical classes determine interaction of nervous, endocrine and immune system.
Pathological anatomy	Role of immune disorders in mesenchymal and protein dystrophies, mucous and fibrinoid degeneration if connective tissue	Determine mesenchymal and protein dystrophies, mucous and fibrinoid degeneration if connective tissue. Types of tissue reactions in collagenoses.
Microbiology, virusology	Specific and non-specific mechanisms of defense. Types of antigenes, immunity, allergies.	Perform agglutination test, Coombs' test, precipitation. Titration of complement, bacteriolysis and haemolysis tests, immunofluorescence test
Propedeutics of internal diseases	Role of immune system in pathogenesis of different diseases.	Interpretation of rosette test, Manchini immunoglobulins, phagocytic activity of blood.

Independent student's work

Oral presentation of themes, given for independent work.

Immunopathogenesis and immune therapy of sepsis.

Tasks for final module test

1. Transplantation immunology. Indications and contraindication for grafting. Donor-recipient selection. Preexisting antilymphocytotoxic antibodies, their value.
2. Pre- and post-grafting monitoring. Types of rejection crises, characteristic and prognosis.
3. Antitumor factors, tumor's factors of immune resistance. Problastom factors, suppressing immunity and problastom factors stimulating tumor's growth. Tumor-associated antigens.
4. Immune changes in patients with tumor. Immune diagnostic in oncology. Up-to-date immune therapy of tumors.

List of practical skills for final module test.

1. Diagnose hyperacute, acute and chronic crisis of graft rejection.
2. Distinguish crisis of graft rejection and infectious complications after transplantation.
3. Prescribe immunosuppressive therapy after grafting and estimate its efficacy.
4. Interpret immunogram data in patients with tumor. Estimate antiblastom defense factors.
5. Characterize tumor-associated antigens in early tumor diagnosis and recurrence revealing.
6. Know immunotherapy and immunoprophylactic of tumors.

ATOPIC DISEASES.

Issues to be considered during the class

Role of genetic factors and environment in immunopathogenesis of allergy. Contemporary views on allergy and atopic diseases. Atopic diseases as system diseases.

Types and stages of immunologic reaction. Contemporary aspects of allergy diagnosis. Screening method in allergy. Elimination and challenge in allergology. Types of skin tests.

Treatment of allergy. Specific immunotherapy, indications and contraindications.

Characteristic of hives immunopathogenesis ect. Drug allergy: causes, immunopathogenesis, clinical manifestation, allergodiagnostic and prophylactic.

Aim of study

Hypersensitivity (also called hypersensitivity reaction) refers to undesirable (damaging, discomfort-producing and sometimes fatal) reactions produced by the normal immune system. Hypersensitivity reactions require a pre-sensitized (immune) state of the host. The four-group classification was expounded by P. H. G. Gell and Robin Coombs in 1963.

Mild allergies like hay fever are highly prevalent in the human population and cause symptoms such as allergic conjunctivitis, itchiness, and runny nose. Allergies can play a major role in conditions such as asthma. In some people, severe allergies to environmental or dietary allergens or to medication may result in life-threatening anaphylactic reactions and potentially death.

A variety of tests now exist to diagnose allergic conditions; these include testing the skin for responses to known allergens or analyzing the blood for the presence and levels of allergen-specific IgE. Treatments for allergies include allergen avoidance, use of anti-histamines, steroids or other oral medications, immunotherapy to desensitize the response to allergen, and targeted therapy.

Purposes of discipline

Learn major principles of specific and non-specific methods of allergy diagnosis.

Train to take history and anamnesis of allergic patient.

Student has to know:

1. Classification of allergic reactions.
2. Role of organism's reactivity in allergy development.
3. Principles of allergy diagnosing
4. Major principles of specific and non-specific methods of allergy treatment and diagnosing.
5. Clinical and laboratory criteria of allergy and pseudoallergy.

Student has to be able to do:

1. Take history and anamnesis of allergic patient.
2. Take part in skin test with allergens.
3. Estimate skin test results
4. Take part in specific hyposensibilization
5. Diagnose pseudoallergy in children and adult
6. How to give emergency help for patients with allergy and psuedoallergy.

Interdiscipline integration

Subject	Know	Can

Anatomy	Haemopoietic organs of immune system	Name primary and secondary lymphoid organs, lymphatic ducts
Histology, embryology	Morphology of induction stage and proliferation stage of immune response	Characterize macro- and microphages of peripheral blood
Biochemistry	Molecular basis of antibody-antigen interaction.	Make interpretation of Manchini precipitation test in gel
Microbiology, virusology	Immunological mechanisms of sensibilization, anaphylactic shock, de sensibilization and passive anaphylaxis Skin tests	Distinguish immediate and delayed type reactions during skin test
Pathophysiology	Phases of allergy, sensibilization.	Reaction of active leucocytolysis interpretation
Pathomorphology	Morphology of allergic necrosis.	Find allergic necrosis in tissues
Pharmacology	Pharmacology of allergic states	Reaction of active leucocytolysis interpretation
Dermatology and venerology	Skin changes in vasculitis, dermatitis	Explain changes in leukogram and immunogram
Otolaryngology	Immune mechanisms in pathology	Distinguish allergic and non-allergic rhinitis
Ophthalmology	Allergic diseases of cornea, retina.	Reveal allergic reactions of eyes.

Independent student's work

Main theoretical aspects of theme.

- Specific immunotherapy: Principles destination. Indications and contraindications, complications development
- Drug allergy.

Tasks for final module test

1. Causes of allergy development. Stages of allergic reaction.

2. Allergy and atopy. Classification of allergens.

3. Allergy diagnosis, laboratory tests, skin and provocative tests.

4. Principles of antiallergic therapy. Immune methods of treatment.

5. Specific immunotherapy. Mechanism of action, indications and contraindications, prognosis of efficacy.

6. Pollinosis, allergic rhinitis, allergic conjunctivitis. Etiology, immunopathogenesis, clinical manifestation, diagnosis, therapy.

7. Drug allergy, immunopathogenesis, clinical manifestation, diagnosis, therapy and prophylactic.

8. Characteristic of pseudoallergy, Differential diagnostic. Mechanisms of histamine liberation in pseudoallergy development, treatment.

9. Pseudoallergy in complement activation impairment. Arachidonic acid metabolism disorders. Principles of treatment.

List of practical skills for final module test.

1. Perform clinical and allergological examination.
2. Perform history taking and physical examination of patient with allergy.
3. Compose plan of investigations necessary for patient with allergy
4. Perform skin prick-tests.
5. Perform allegic test data estimation.
6. Determine allergens with similar antigen epitopes to make recommendations about allergic prophylactic.
7. Make differential diagnosis based on laboratory data and instrumental studies.
8. Prescribe medications; make a forecast, Perform primary and secondary prophylactic.
9. Perform emergency help in acute allergic and pseudoallergic reactions
10. Use standards of diagnosis and treatment.
11. Prescribe antiallergic drugs

Appendix 1

ALLERGIC HISTORY

1. Allergic diseases in the family in the past and at present:
   In father and his relatives

   In mother and her relatives

   In the patient's children

2. Allergic diseases the patient has had earlier
3. Reaction to introduction of vaccines (when, which)
4. Reaction to introduction of drugs (which and when)
5. Seasonality of exacerbations
6. Influence of the weather and physical factors (changes in the weather, rain, overheating, etc.)
7. Effect of physical exertions
8. Connection with acute infectious-respiratory diseases of airways and ENT (ear, nose, throat) diseases
9. Effect of negative emotions, stresses
10. Connection between the disease and pregnancy, delivery, breast-feeding, periods
11. When and where attacks of the disease or worsening in the condition develop most often (at home, at work, in the open air, in the forest, in the field, by day, at night)
12. Influence of contact with dust on the course of the disease
13. Influence of inhalation of tobacco smoke, cold air, strong smells on the course of the disease
14. Reaction to foodstuffs, alcohol
15. Pets
16. Living conditions (type of heating, carpets, sofas and armchairs, books, bedding)
17. Conditions of work, occupational insalubrity
18. Effectiveness of the drugs taken earlier
19. The findings of previous allergic investigations

Taking an allergic history of a child, it is necessary to find out:

1. Peculiarities of pregnancy in the mother
2. Mother's nutrition during pregnancy
3. Mother's diseases during pregnancy
4. Taking medicines and food supplements during pregnancy
5. Complications during delivery
6. Type of feeding

THE ROLE OF ALLERGIC HISTORY TO IDENTIFY A CAUSATIVE ALLERGEN

To reveal a specific allergen, it is necessary to take an allergic anamnesis in detail, which will allow finding out the causative relation between contact with an allergen and development of symptoms of the disease or absence of such a relation. Timely revealing of the guilty allergen will determine the level of elimination measures, as well as necessity to carry out specific immunotherapy with allergens. This will decrease need in pharmacotherapy considerably and in many cases prevent progressing of the disease.

TYPICAL SYMPTOMS CAUSED BY MAIN ALLERGENS

ALLERGENS	SYMPTOMS
Home dust	Perennial symptoms Exacerbations during tidying up Pronounced exacerbations while staying at old wooden houses, in contact with old furniture Effect of elimination on hospitalization
Pollen	Seasonal symptoms or seasonal worsening of the symptoms Pronounced improvement when changing a geographical zone during exacerbation Better condition in rainy weather (pollen is laid to the ground) Worsening of symptoms in sunny windy weather Worsening of symptoms in the morning, outdoors Worsening of symptoms when working in the garden, in the field, meadows and forests
Animal allergens	Perennial symptoms if there is a pet at home Episodic exacerbations when visiting flats and other places (circus, vivarium, stable) where animals are kept Pronounced improvement (after weeks) if the pet leaves the house In professional contact with animals worsening of symptoms at workdays, better condition at the weekend and on holiday
Mushroom spores	Seasonal symptoms or seasonal worsening of the symptoms

	Pronounced improvement when changing a geographical zone during exacerbation Better condition in rainy weather Worsening of symptoms in sunny windy weather Perennial symptoms in the regions with warm climate Seasonal symptoms in the countries with continental climate Better condition in the geographical zones with dry climate Better condition after snowfall Exacerbations connected with visiting cellars, grain-elevators, silo pits, breweries, storehouses, as well as in contact with old leaves, moldy hay

Appendix 2

Drop test

Indications: history findings, showing a high degree of sensitization to chemical and medical substances.

Contraindications:

1. acute phase of an allergic disease;
2. exacerbation of accompanying chronic diseases;
3. acute intercurrent infectious diseases;
4. tuberculosis and positive tuberculin test;
5. decompensation due to diseases of the heart, lungs and kidneys;
6. a period of treatment with histamine preparations, membrane stabilizers, hormones, sympathomimetic preparations (for most antihistamine drugs of the 1st generation the interval between cancellation of the preparation and the test should be 24-48 hours; for preparations of the 2nd generation – terphenadine, cetirizine, claritin, hydroxyzine – 4-5 days; for astemizole, due to a long period of partial ejection, not less than 4-5 weeks. For membrane stabilizers, steroids it should be 1 month, and for sympathomimetics 8 hours).
7. blood diseases, cancer, systemic and autoimmune diseases;
8. spasmodic syndrome, mental diseases;
9. pregnancy, breast-feeding, first 2-3 days of menstrual cycle;
10. age up to 3 years;
11. systemic allergic reactions (anaphylactic shock, Lyell's or Stevens-Johnson syndrome) in anamnesis.

The technique of carrying out:

1. to rub the skin of bending surface of the forearm with 70% alcohol;
2. to put a drop of allergen on the skin;
3. at the same time to put a drop of dissolvent on the skin as a control;
4. to estimate the results in 20 minutes.

Estimation of the drop test

The result of the reaction	***Local reaction of the skin***
Negative	***Corresponds with the control***
Doubtful	Slight hyperemia
Slightly positive	Hyperemia + itching
Moderately positive	Hyperemia + itching + blister
Distinctly positive	Hyperemia + itching + blister + vesicles

Appendix 3

Application test

Indications: history findings, showing the role of occupational allergy, for diagnosis of contact dermatitis

Contraindications:

1. acute phase of an allergic disease;
2. exacerbation of accompanying chronic diseases;
3. acute intercurrent infectious diseases;
4. tuberculosis and positive tuberculin test;
5. decompensation due to diseases of the heart, lungs and kidneys;
6. a period of treatment with histamine preparations, membrane stabilizers, hormones, sympathomimetic preparations (for most antihistamine drugs of the 1st generation the interval between cancellation of the preparation and the test should be 24-48 hours; for preparations of the 2nd generation – terphenadine, cetirizine, claritin, hydroxyzine – 4-5 days; for astemizole, due to a long period of partial ejection, not less than 4-5 weeks. For membrane stabilizers, steroids it should be 1 month, and for sympathomimetics 8 hours).
7. blood diseases, cancer, systemic and autoimmune diseases;
8. spasmodic syndrome, mental diseases;
9. pregnancy, breast-feeding, first 2-3 days of menstrual cycle;
10. age up to 3;
11. systemic allergic reactions (anaphylactic shock, Lyell's or Stevens-Johnson syndrome) in anamnesis.

The technique of carrying out:

1. to rub skin of bending surface of the forearm with 70% alcohol;
2. to wet four-layer gauze with an allergen solution;
3. to put it on the skin of the forearm;
4. at the same time, to put a piece of gauze moistened in the dissolvent;
5. to estimate the result in 30 minutes

Estimation of the skin application test

The result of the reaction	Local reaction of the skin
Negative	Corresponds with the control
Slightly positive	Hyperemia
Positive	Hyperemia + blister
Distinctly positive	Hyperemia + blister + vesicles

Appendix 4

Scarification test

Indications: revealing the causative allergen and the degree of sensitization to it

Contraindications:

1. acute phase of an allergic disease;
2. exacerbation of accompanying chronic diseases;
3. acute intercurrent infectious diseases;
4. tuberculosis and positive tuberculin test;
5. decompensation due to diseases of the heart, lungs and kidneys;
6. a period of treatment with histamine preparations, membrane stabilizers, hormones, sympathomimetic preparations (for most antihistamine drugs of the 1st generation the interval between cancellation of the preparation and the test should be 24-48 hours; for preparations of the 2nd generation – terphenadine, cetirizine, claritin, hydroxyzine – 4-5 days; for astemizole, due to a long period of partial ejection, not less than 4-5 weeks. For membrane stabilizers, steroids it should be 1 month, and for sympathomimetics 8 hours).
7. blood diseases, cancer, systemic and autoimmune diseases;
8. spasmodic syndrome, mental diseases;
9. pregnancy, breast-feeding, first 2-3 days of menstrual cycle;
10. age up to 3;
11. systemic allergic reactions (anaphylactic shock, Lyell's or Stevens-Johnson syndrome) in anamnesis.

The technique of carrying out:

1. to rub skin of bending surface of the forearm with 70% alcohol;
2. on the skin of the forearm to put a drop of 0.01% histamine solution, test-control liquid, allergens at the distance 4-5 cm from each other, but not more than 10-15 tests
3. with sterile scarifiers to draw 2 parallel scratches 4-5 mm in length at the distance of 2 mm from each other (for children under 5 one scratch is enough) through every drop, separately for every allergen. Scratches are drawn superficially, damaging epidermis only and not injuring blood vessels.
4. in 10 minutes to dry every drop with a separate cotton tampon;
5. in another 10 minutes to estimate the result of the test.

Estimation of the scarification test

The result of the reaction	Local reaction of the skin
Negative	Corresponds with the control
Doubtful	Hyperemia without blister
Slightly positive	Papule (blister) up to 2-3 mm + hyperemia
Positive	Papule (blister) up to 5 mm + hyperemia
Distinctly positive	Papule (blister) up to 5-10 mm + hyperemia + pseudopodia
Very distinctly positive	Papule (blister) more than 10 mm + hyperemia + pseudopodia

Appendix 5

Prick-test

The technique of carrying out:

1. to rub skin of bending surface of the forearm with 70% alcohol;
2. on the skin of the forearm to put a drop of 0.01% histamine solution, test-control liquid, allergens at the distance 4-5 cm from each other, but not more than 10-15 tests
1. with a prick-lancet, separately for every allergen, to make a prick into the skin 1-1.5 cm deep through every drop
2. to estimate the results of the test in 20 minutes

Estimation of the skin prick-test

The result of the reaction	Local reaction of the skin
Negative	Corresponds with the control
Slightly positive	Papule 3 mm
Positive	Papule (blister) 5 mm and more
Distinctly positive	Papule (blister) 10 and more + pseudopodia

Appendix 6

Intracutaneous test

Indications: diagnosis of infectious allergy (revealing sensitization to allergens of bacterial and fungous origin), discrepancy between history findings and results of application and scarification tests (skin tests are doubtful or negative, history findings being distinctly positive) with non-infectious allergens

Contraindications:

1. acute phase of an allergic disease;
2. exacerbation of accompanying chronic diseases;
3. acute intercurrent infectious diseases;
4. tuberculosis and positive tuberculin test;
5. decompensation due to diseases of the heart, lungs and kidneys;
6. a period of treatment with histamine preparations, membrane stabilizers, hormones, sympathomimetic preparations (for most antihistamine drugs of the 1st generation the interval between cancellation of the preparation and the test should be 24-48 hours; for preparations of the 2nd generation – terphenadine, cetirizine, claritin, hydroxyzine – 4-5 days; for astemizole, due to a long period of partial ejection, not less than 4-5 weeks. For membrane stabilizers, steroids it should be 1 month, and for sympathomimetics 8 hours).
7. blood diseases, cancer, systemic and autoimmune diseases;
8. spasmodic syndrome, mental diseases;
9. pregnancy, breast-feeding, first 2-3 days of menstrual cycle;
10. age up to 3;
11. systemic allergic reactions (anaphylactic shock, Lyell's or Stevens-Johnson syndrome) in anamnesis.

Preparing for the test:

1. Sanitation of foci of chronic infection in case of allergic investigation with infectious allergens;
2. in carrying out tests with fungous allergens 2 days before and in the day of investigation to exclude foodstuffs comprising microscopic fungi (moldy sorts of cheese, kefir, cottage cheese, beer, Champagne, kvass)
3. to cancel antibacterial drugs.

The technique of carrying out:

1. to rub skin of bending surface of the forearm with 70% alcohol;
2. to introduce test-control liquid intracutaneously with an insulin syringe;
3. on the skin of the forearm to put a drop of 0.01% histamine solution and make 2 parallel scratches through the drop with a sterile scarifier
4. to introduce 0.02 ml in concentration 1:10 intracutaneously with an insulin syringe. Allergens are introduced at the distance of 4-5 cm from each other. The number of the allergens should not exceed 4-5
5. the result of the test is estimated in 20 minutes and 24-48 hours.

Estimation of the intracutaneous test

The result of the reaction	Local reaction of the skin in 20 minutes	Local reaction of the skin in 24-48 hours
Negative	Corresponds with the control	Corresponds with the control
Doubtful	Delayed resolution of the blister	Slight hyperemia without infiltration
Slightly positive	Papule (blister) 4-8 cm + an area of hyperemia	Hyperemia, infiltration 5-10 mm in diameter
Positive	Papule (blister) 9-15 cm + an area of hyperemia	Hyperemia, infiltration 11-15 mm in diameter
Distinctly positive	Papule (blister) 16-20 cm + an area of hyperemia + pseudopodia	Hyperemia, infiltration 16-20 mm in diameter
Very distinctly positive	Papule (blister) more than 20 mm + pseudopodia + lymphangitis + vesicles	Hyperemia, infiltration more than 20 mm in diameter, possible vesicles

Interpretation of the results of the skin tests:

IF:	AND:	THEN:
Anamnesis indicates presence of sensitization	The results of skin tests are positive	Allergic nature of the disease is highly probable
Anamnesis does not indicate presence of sensitization	The results of skin tests are positive	Repeated examination of the patient under the conditions of natural contact with the allergen should be made
Anamnesis indicates presence of sensitization	The results of skin tests are negative	1. to exclude the possible causes of pseudo-negative results (taking antihistamine preparations, low-grade preparations, incorrect carrying out the test) 2. to estimate the condition of the patient during natural contact with the allergen 3. if necessary, to carry out provocative tests

Appendix 7

Provocative tests

Indications: used in case of discrepancy between the history findings and the results of skin tests

Contraindications: the same as in skin testing

Nasal test

Indications: revealing the causative allergen in patients with allergic rhinitis

The technique of carrying out:

1. to make testing is necessary during remission;
2. to exclude antihistamine preparations, vasoconstrictor drops and topic forms of cromolyn sodium (intal)
3. to perform rhinoscopy, to study smear-print from the mucous membrane
4. to introduce 2-3 drops of test-control liquid into the nasal passage
5. in absence of the reaction, 15-20 minutes later, to drop increasing concentrations of allergen (as a rule, beginning with dilution 1:100)
6. to estimate the result on basis of clinical manifestations: itching, sneezing, rhinorrhea, difficult nasal breathing, decrease in the indices of rhinospirometry and appearance of eosinophils in nasal secretion
7. if the result is positive, to wash the nasal cavity with physiological solution and to drop vasoconstrictor drops

Conjunctival test

Indications: diagnosis of allergic conjunctivitis, revealing the causative allergen in patients with allergic conjunctivitis

The technique of carrying out:

1. to make testing is necessary during remission, if there are no symptoms of conjunctivitis;

2. to exclude antihistamine preparations, vasoconstrictor drops and topic forms of cromolyn sodium (intal)
3. to drop 1-2 drops of test-control liquid into the lower conjunctival sac, moving the lower eyelid aside;
4. in absence of the reaction, 15-20 minutes later, to drop increasing concentrations of allergen solution (as a rule, beginning with dilution 1:1000)
5. to estimate the result on basis of clinical manifestations: itching of the eyelids, hyperemia, lachrymation and appearance of eosinophils in the nasal secretion;
6. if the result is positive, the conjunctival sac is washed with physiological solution and vasoconstrictor drops are dropped

Inhalation test:

Indications:

1. to reveal etiologically significant allergens in patients with bronchial asthma;
2. to estimate the efficacy of medical treatment;
3. to reveal non-specific factors causing bronchospasm;
4. to determine professional fitness of the patient (revealing latent bronchospasm)

Technique of carrying out

1. before the test, to take spirography. To calculate the value of FCV, FEV_1, Tiffno index
2. through the inhalator, to give the patient to inhale control solution;
3. to register the spirogram, to determine FCV, FEV_1, Tiffno index
4. through the inhalator, to give the patient to inhale allergen solution, beginning with the minimal concentration up to that, which will give a pronounced reaction;
5. every 10 minutes after the next inhalation, to register FEV1 three times;
6. after the last introduction of the allergen, FEV1 is measured every 10 minutes during one hour, and in 90 minutes, 120 minutes, and then every hour during 7 hours;
7. the test is considered positive, if FEV decreases by 20% from the initial value.

Sublingual test

Indications: diagnosis of food and drug allergy

The technique of carrying out:

The allergen is put on the mucous membrane of the sublingual area. In food allergy, natural products are used in dilution 1:10; in drug allergy 1/8- 1/4 of one-time dose of the solved substance is taken.

The test is considered positive if there appears hyperemia, edema, itching, skin eruption in the sublingual area.

Appendix 8

Immune-laboratory methods of diagnosis of allergic diseases

Indications:

- early childhood;
- patients with high degree of sensitization;
- a persistent recurrent course without periods of remission;
- impossibility to cancel antihistamine and other preparations;
- polyvalent allergy;
- distinctly changed reactivity of the skin;
- pseudo-positive or pseudo-negative result in skin testing;
- dermatographism

The methods to reveal sensitization of I type (IgE-mediated)

1. **the enzyme immunoassay (EIA) to detect specific IgE.** With the help of EIA, a count of allergen-specific IgE in the patient's blood is made. The principle of this method is the following. At the first stage of the investigation, the tested allergen is linked covalently with solid phase (paper disk, activated polymer). In adding the patient's serum, there occurs linking of the allergen fixed on the solid phase with the antibody, if in the serum there are antibodies corresponding with this allergen. After washing of non-linked IgE, antibodies against IgE labeled with fluorochrom (horse-radish peroxidase) are added. The complex of the allergen on the solid phase + specific IgE + antibodies anti-IgE is formed. The levels of specific IgE-binding is determined on basis of intensity of fluorescence compared with negative control.

2. **the radioallergosorbent test (RAST) to detect specific IgE.** With the help of RAST, a count of allergen-specific IgE in the patient's blood is made. The allergen binds covalently with paper disk, reacts with specific IgE in the patient's blood. After washing of non-linked IgE, radiolabeled (1-125) antibodies against IgE are added. The complex of specific IgE + labeled anti-IgE is formed. The levels of specific IgE are determined with gamma-counter.

3. **the indirect basophile test (Shelley test)** is based on the study of morphological changes in basophiles due to interaction between the patient's serum and specific allergen. Neutral red color dyes basophile granules brick-red selectively, which allows their differentiating from other cells. The reaction is watched under the microscope in the immersion system. Non-changed basophiles are of a round shape; dyed granules are inside the cells. In the positive reaction, there is a deformation of the cells, formation of pseudopodia, intensified moving of the granules and rarely granules' leaving the cell with its rupture. In every preparation, 40 basophiles are counted, and the percentage of morphologically changed cells is calculated in the experiment and in control. Conventionally, three degrees of reaction are distinguished: slight, when the percentage of the changed cells in the experiment is 10% more than that in control; moderate, if it is 15% more, and distinctly positive, if it is more than 20%.

4. **Direct basophile test (Shelley test)** is based on the study of morphological changes in basophiles in the peripheral blood of the patient with an allergic disease in interaction with a specific allergen. The estimation of the reaction is the same as in the indirect basophile test.

5. **Reaction of release of histamine from basophiles** of the peripheral blood is based on the calculation of the percentage of histamine release after processing of basophiles with specific allergens.

Methods to reveal II type sensitization (cytotoxic)

EIA, radioimmune test, Coombs' test in autoimmune hemolytic anemia

Methods to reveal III type sensitization (immune complex)

Determination of CIC, precipitating antibodies.

Methods to reveal IV type sensitization (delayed reactions)

1. **Reaction of lymphocyte blast transformation (RLBT)** is a test of estimation of functional activity of the pool T-lymphocytes. There are different methods: with mitogen to estimate preparedness of T-lymphocytes for stimulation; with antigen to determine the degree of sensitization to the given antigen.

Non-specific methods of investigation:

1. determination of histamine and histaminase concentration;
2. determination of histamine-pectic activity of the blood serum

Appendix 9

SITUATIONAL TASKS

TASK 1

A 22-year-old woman came to see a doctor complaining of the stuffy nose, attacks of sneezing, watery discharge from the nose, bothering her during last 3 years from August to September. The patient was made skin scarification tests with pollen allergens (ambrosia, wormwood, and goose-foot). The result of the tests is negative.

Which diagnostic measures are necessary to specify the causes of the diseases in this patient?

TASK 2

A 20-year-old man is complaining of attacks of heavy breathing, itching of the eyelids, lachrymation, tickling in the throat, which develop during tidying-up, shaking out carpets and bedding. History: in the childhood suffered from atopic dermatitis.

Which etiological factors are the most probable in this case?

Which methods of investigation may prove them?

Which elimination measures must be taken for the patient?

TASK 3

A 19-year-old woman is followed in the antenatal clinic because of pregnancy (10-12 weeks).
History: she is known to have been ill with pollinosis for 5 years; sensitization to ambrosia and goose-foot allergens was revealed.

Which preparations should be preferred in case of exacerbation of allergic rhinitis?

What recommendations may be given to prevent atopic diseases in the future child?

TASK 4

In a 52-year-old man, after the contact with synthetic detergents, multiple eruptions have developed on the skin of the arms and abdomen, accompanied with pronounced itching. History: the patient is known to have been ill with ischemic heart disease: post-infarction cardiosclerosis, blockade of the right leg of the His' band.

Which antihistamine preparations should be administered in such a situation?

BRONCHIAL ASTHMA.

Issues to be considered during the class

Immunopathology of respiratory system: allergic rhinitis, hay fever, bronchial asthma. Specific diagnostic and hyposensitizing. Bronchial asthma: etiology, immunopathogenesis, up-to-date classification, clinical manifestation, treatment. Atopic forms of BA: clinical manifestation, diagnostic, treatment.

Aim of study

Asthma is a predisposition to chronic inflammation of the lungs in which the airways (bronchi) are reversibly narrowed. Asthma affects 7% of the population, and 300 million worldwide. During asthma attacks (exacerbations of asthma), the smooth muscle cells in the bronchi constrict, and the airways become inflamed and swollen. Breathing becomes difficult, and asthma causes 4,000 deaths a year in the U.S. Attacks can be prevented by avoiding triggering factors and by drug treatment. Drugs are used for acute attacks, commonly inhaled beta-2 agonists. In more serious cases, drugs are used for long-term prevention, starting with inhaled corticosteroids, and then long-acting β2-agonists if necessary. Leukotriene antagonists are less effective than corticosteroids but have no side effects. Monoclonal antibodies such as mepolizumab and omalizumab are sometimes effective. Prognosis is good with treatm

Because of the spectrum of severity within asthma, some people with asthma only rarely experience symptoms, usually in response to triggers, where as other more severe cases may have marked airflow obstruction at all times.

Asthma exists in two states: the steady-state of chronic asthma, and the acute state of an acute asthma exacerbation. The symptoms are different depending on what state the patient is in.

Common symptoms of asthma in a steady-state include: nighttime coughing, shortness of breath with exertion but no dyspnea at rest, a chronic 'throat-clearing' type cough, and complaints of a tight feeling in the chest. Severity often correlates to an increase in symptoms. Symptoms can worsen gradually and rather insidiously, up to the point of an acute exacerbation of asthma. It is a common misconception that all people with asthma wheeze—some never wheeze, and their disease may be confused with another Chronic obstructive pulmonary disease such as emphysema or chronic bronchitis.

Purposes of discipline

Student has to know:

1. Definition of BA.
2. Classification of BA (GINA 2012)
3. Etiology and immunopathogenesis of different forms of BA. Prevalence of allergic reactions in different forms of BA
4. Course of BA depending on severity, complications
5. Diagnostic of BA

Student has to be able to do:

1. Reveal bronchi hyperreactivity and obstruction with peakflowmetry
2. Estimate results of provocative teest eith ACh and metacholine.
3. Estimate the level of asthma severity according to new classification.
4. Exacerbation of Asthma and its stages.

Interdiscipline integration

Subject	Know	Can
Anatomy	Haemopoietic organs of immune system	Name primary and secondary lymphoid organs, lymphatic ducts
Histology, embryology	Morphology of induction stage and proliferation stage of immune response	Characterize macro- and microphages of peripheral blood
Biochemistry	Molecular basis of antibody-antigen interaction.	Make interpretation of Manchini precipitation test in gel
Microbiology, virusology	Immunological mechanisms of sensibilization, anaphylactic shock, de sensibilization and passive anaphylaxis Skin tests	Distinguish immediate and delayed type reactions during skin test
Pathophysiology	Phases of allergy, sensibilization.	Reaction of active leucocytolysis interpretation
Pathomorphology	Morphology of allergic necrosis.	Find allergic necrosis in tissues
Pharmacology	Pharmacology of allergic states	Reaction of active leucocytolysis interpretation
Dermatology and venerology	Skin changes in vasculitis, dermatitis	Explain changes in leukogram and immunogram
Otolaryngology	Immune mechanisms in pathology	Distinguish allergic and non-allergic rhinitis
Ophthalmology	Allergic diseases of cornea, retina.	Reveal allergic reactions of eyes.

Independent student's work

Main theoretical aspects of theme.

- Specific immunotherapy: Principles destination. Indications and contraindications, complications development
- Drug allergy.

Tasks for final module test

1. Mechanism of IgE-mediated pathogenesis of BA. Differential diagnosis with COPD.

2. Contemporary anticytokines and anti-antibodies drugs in BA management.

List of practical skills for final module test.

1. Perform emergency help in acute asthma exacerbation.

2. Prescribe controller medication therapy for patients with BA.

3. Perform peakflowmetry and estimate its results.

Appendix 1

Peakflowmetry is a method of peak (maximal) expiratory flow (PEF) measurement, a convenient portable way of monitoring for 24 hrs with recording of the findings on a special form. With the help of this method one can determine:

a) provocative effect of professional and non-professional inductors of allergy;

b) trigger influence of different non-specific factors on the course of BA;

c) variability of changes in PEF during 24 hrs according to the formula:

$$PEF\,24hrs(\%) = \frac{PEF\ \max(L/\min) - PEF\ \min(L/\min)}{PEF\ \max(L/\min)} \times 100$$

d) volume (glucocorticoids in μg) of the administered drug therapy. That is, on the one hand, one can manage the disease, on the other hand, one can prevent developing of the obstruction at the stages when clinically, there is no evident worsening of the patient's condition.

PEF monitoring allows a patient seeing a doctor in time to correct treatment or, having acquired the corresponding knowledge at the asthma-school, making a proper decision him/herself, not waiting for the subjective worsening of the condition.

Here is a scale of standard values of peak expiratory flow (Table 3)

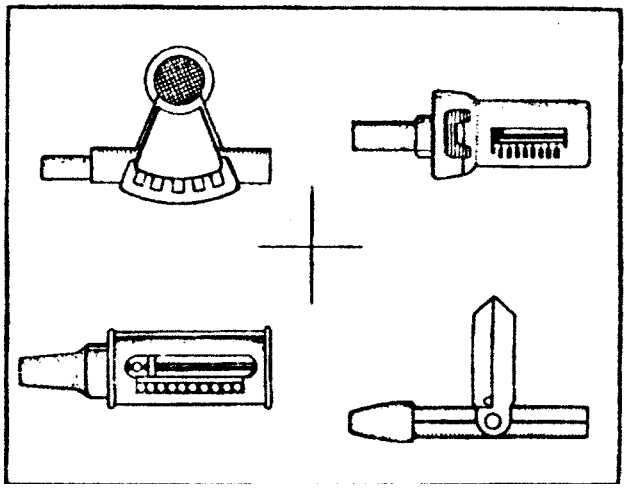
Table

Height	Age, years															
	15	20	25	30	35	40	45	50	55	60	65	70				
Men													Children (under 15)			
160	530	570	595	605	610	605	600	585	570	555	535	520	Height		Height	
168	545	580	605	620	625	620	615	600	585	565	550	530	100	120	145	345

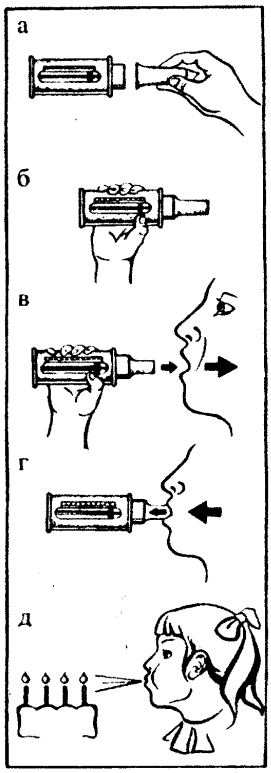
175	555	590	610	630	635	635	625	610	595	580	560	540	105	145	150	370
183	565	600	630	640	650	645	635	625	605	585	570	550	110	170	155	395
191	575	610	635	650	660	655	650	635	620	600	580	570	115	195	160	420
Women													120	220	165	445
152	445	475	470	475	475	470	460	445	435	425	410	395	125	245	170	470
160	455	480	485	490	485	480	470	455	445	430	420	405	130	270	175	495
168	465	485	495	500	500	490	480	465	455	440	425	415	135	295	180	520
175	475	495	505	510	505	500	490	475	465	450	435	425	140	320	185	545

After being taught according to a special program, which provides the patient with the adequate idea about the character of the disease, the patient can monitor the findings of PEF him/herself. It allows him/her understanding changes in his/her condition well and making a right decision.

The patient must be taught the principles of self-examination: keeping a diary and estimating his/her condition according to the special scale, using peakflowmetry correctly.



Types of peakflowmeters



How to use peakflowmeter

а – to put the nozzle on the peakflowmeter

б – to stand up and to hold the peakflowmeter horizontally; to make sure that the slider is immobile and at the beginning of the scale

в, г – to take a deep breath, to grasp the nozzle with the lips and to breathe out as soon as possible; to mark the result; to repeat stages б – г twice, to choose the highest result, and to compare the received data with the normal;

д – children should be explained that they should breathe out as if they were blowing out the candles on the birthday cake

According to the special program, the patient should be taught to use correctly the methods of self-control of obstruction, to apply peakflowmeter, spacer, nebulizer, to choose elementary dosage and to take aerosol drugs. Partially, these tasks are solved on basis of monitoring of the findings of peakflowmetry – PEF early in the morning in mild BA and in the morning, in the afternoon and in the evening in persisting moderate and severe course of the disease, recording all the data in the protocol-schedule. Monitoring of PEF allow predicting exacerbation of the disease, as on the eve of that, suppression of the parameters develop before the subjective signs of obstruction.

Height:	Date; Day	Sun.			Mon.			Tus.			Wed.			Thurs.			Fr.			Sat.		
	Time	Morning	Afternoon	Evening	Morning	Afternoon	Evening	Morning	Afternoon	Evening	Morning	Afternoon	Evening	Morning	Afternoon	Evening	Morning	Afternoon	Evening	Morning	Afternoon	Evening

Age: Date of birth:	L/min	700																				
		650																				
		600																				
		550																				
		500																				
Name, Surname:		450																				
		400																				
		350																				
		300																				
		250																				
		200																				
		150																				
		100																				
Other notes																						
Drugs and doses																						

Protocol-schedule for monitoring of the peakflowmetry findings

The received data of the experimental PEF are compared with the normal ones from Table, and the percentage of deviation from the normal is counted.

$$PEF(\%\,from normal) = \frac{PEF\,\mathrm{exp}\,erimental}{PEF normal} \times 100\%$$

At the same time, daily variability index is counted.

$$DVI(\%) = \frac{PEF\,\mathrm{max} - PEF\,\mathrm{min}}{PEF\,\mathrm{max}} \times 100$$

On monitoring PEF, the patient may predict worsening of his/her condition on basis of variable deviations of peakflowmetry values during 24 hrs and their increasing suppression, i.e. without calculation the parameters in percentage terms.

For the patient to be easier to estimate his/her condition on basis of the registered curve of peakflowmetry, it was elaborated the system of areas, which is adapted to the colors of the traffic lights: green, yellow, and red.

The green area reflects a relative well-being of the patient: it corresponds to PEF>80%, and daily variability <15%. Under such conditions, the symptoms of asthma may be absent or minimal.

The yellow area: PEF is 50-80%, daily variability 20-30%. If this situation develops gradually or suddenly, it is necessary to increase the volume of drugs, and the taught patient may make this decision him/herself.

The red area is a sign of alarm: if PEF is <50% and daily variability increases up to >30%, the patient must see the doctor, to determine the adequate therapy of BA together with him. The transition of the PEF values from the red area into the yellow one and decrease in the administered drugs is performed under the control of the doctor.

Appendix 2

Spirography

Functions of external respiration are studied with the help of spirographs, which give visual (on the monitor of the computer) or graphical representing of spirogram.

While analyzing spirograms, they estimate volume, rate, and parameters of pulmonary ventilation

1. Measuring volume

Tidal volume (V_T) is the volume of air that is inspired or expired in a single breath during regular respiration (normal 500-800 ml). The values of the tidal volume change depending on the level of ventilation. The part of the tidal volume, which participates in the gas exchange, is called alveolar ventilation (V_A) and equal to 2/3 of V_t. The rest of it (1/3) is physiologic dead space (V_D), which is the sum of anatomic (150-200 ml) and alveolar dead spaces. Normally, the full dead space is equal to the anatomical one.

Inspiratory reserve volume (IRV) is the maximal volume of air that can be inspired additionally after a normal inspiration (1000-2000 ml in normal).

Expiratory reserve volume (ERV) is the maximal volume of air that can be expired additionally after a normal expiration (1000-1500 ml – 25% of VC).

Inspiratory capacity (IC) is the sum of V_T and inspiratory reserve volume, which characterizes the ability of lung tissue for stretching.

VC (vital capacity (of the lungs)) is the sum of V_T, IRV and ERV, the maximal volume of air that can be expired after a maximum inspiration (3000-5000 ml in normal). This value depends on the age (increasing till 35 and then gradually decreasing), sex (less in women than in men), height and weight, as well as on the body position. In normal, VC is a very variable value. In healthy persons it may deviate by ±15-20%. That's why, in practice, attention should be paid to VC less than 80% of normal.

FVC (forced vital capacity) is the volume of air that can be exhaled with the forced expiration after the maximal inspiration (70-80% of VC in normal).

RV (residual volume) is the volume of air remaining in the lungs after a maximal expiratory effort. In normal, it is not more than 25-30% of TLC in the young and about 35% of TLC in the elderly people.

FRC (functional residual capacity) is the volume of the air remaining in the lungs at the end of the normal expiration, the sum of ERV and RV (in normal, 40-50% of TLC).

TLC (total lung capacity) is the sum of VC and RV, the maximal volume of air contained in the lungs at the end of a maximal inspiration.

2. Measuring ventilation

During regular breathing, tidal volume and RMV (respiratory minute volume, the total ventilation per 1 minute). In calm breathing, normal is 6-8 L per 1 min. This parameter is very changeable and depends on the respiratory frequency (f) and tidal volume.

MVV (maximum voluntary ventilation) is the maximal minute volume, the maximum breathing capacity, that is the maximal volume of the air, which may be ventilated per 1 min., which characterizes functional capacity of external respiration. In normal, it is equal to 50-180 L

$MVV=V_{T(max)} \times f_{(max)}$

This parameter depends on the sex, age, weight and height, the body position.

3. Rate

FEV (forced expiratory volume during the 1^{st} sec.) is the volume of the air that is expired during the first second of the maximal quick expiration and determined percentage wise of FVC. Healthy persons expire not less than 70% of FVC during the first sec.

Tifno test: FEV/VC, expressed in %. In normal, 70-75%.

FEF 25 is maximal forced expiratory flow at the level of 25% of FVC.

FEF 50 is maximal forced expiratory flow at the level of 50% of FVC.

FEF 75 is maximal forced expiratory flow at the level of 75% of FVC.

These parameters are most valuable in diagnosis of initial impairment of bronchial conductivity. The lower border of the flow parameters is considered 60% of normal.

MFEF 25-75 is the mean forced expiratory flow: 25-75% of FVC are measured for a certain period of time. It characterizes the state of small respiratory airways.

Types of ventilation insufficiency

Impairment to the functions of the external respiration is due to different pathological processes in the airway. Depending of the mechanisms, they distinguish obstructive, restrictive and mixed impairment of pulmonary ventilation.

Obstructive type of ventilation insufficiency develops because of narrowing of the airway and increase in air resistance. Obstacles for the movement of the air may be observed in both upper and lower airway.

Restrictive type of ventilation impairment is connected with less respiratory surface of the lungs or less ability of the lung tissue to stretch.

For central obstruction (in large bronchi) elevated RV/TLC, considerable decrease in FEV and diminished VC are characteristic.

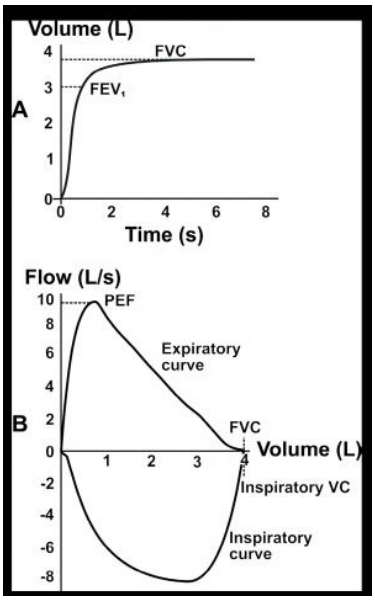
For peripheral obstruction (in small bronchi) considerable decrease in FEF75, FEF50, elevated TLC, at this VC being the same or deviated a little.

Mixed type of ventilation impairment is characterized by both obstructive and restrictive ventilation disorders, namely: decreased VC and TLC, elevated RV and diminished FEV_1, FEF75, FEF50.

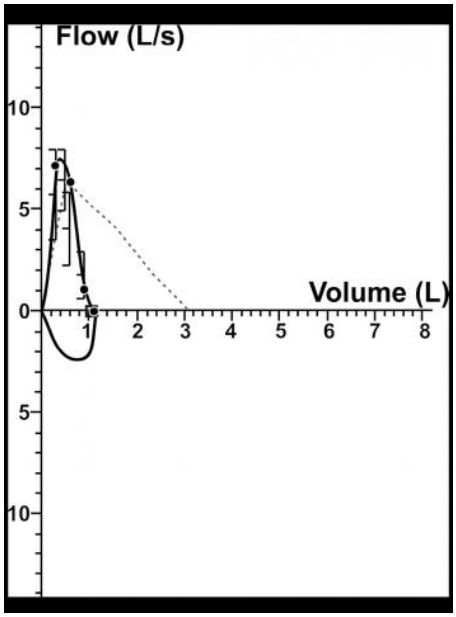
Table

Degrees of ventilation impairment

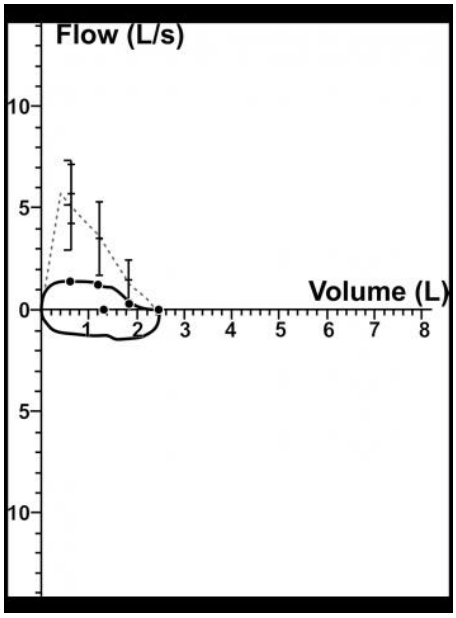
Parameter	Obstructive disorders				
	Absent	**Mild**	**Moderate**	**Severe**	**Very severe**
VC (%)	>80	>80	>80	decreased	very decreased
FEV/VC (%)	>75	60-75	40-60	<40	<40
FEV_1	>80	70-79	50-69	36-50	<36
MVV (%)	>80	65-80	45-65	30-45	<30
TLC (%)	80-120	120-150	150-175	>200	>200



A: volume-time, and B: flow-volume curves. In the flow-type spirometer, FEV1 is a derived value. It can only be read from the flow-volume graph if a 1-second timer is displayed.



Flow-volume curve exhibiting a typical restrictive pattern.



Example of fixed large airway obstruction.

Appendix 3

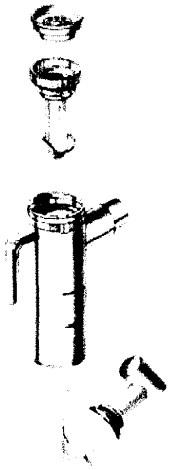
TECHNIQUE OF INHALATION THROUGH NEBULIZER

PREPARATION FOR THE INHALATION

Before the inhalation, it is necessary to wash the hands with soap, as there are always microorganisms on the skin.

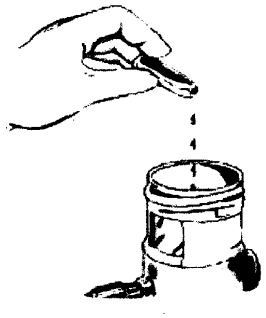
So, wash your hands thoroughly in warm water with soap.

Assemble the nebulizer and connect the nozzle or the mask.



Usually the inhalations are made through the nozzle. The inhalations through the nose are not so effective as in such a case, most of the preparation accumulates on the nasal mucous membrane. The inhalations through the mask are made to the little children who cannot breathe through the nozzle.

The solution for the inhalation is poured into the chamber of the nebulizer:



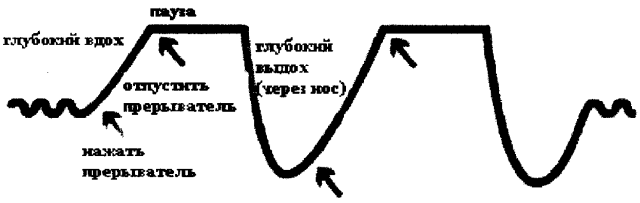
at first, not less than 2 ml of isotonic sodium chloride solution, then the dose of bronchodilator in drops according to the age. The chemist's pack should be kept in the fridge (if there are no other recommendations), in the tightly closed container. **The preparations should be used within 2 weeks after the chemist's pack was opened. <u>That is why the date of opening should be written down.</u>**

In some patients, the spray may cause cold reaction in the form of cough. In such a case, it is necessary to consult a doctor for him to administer the preliminary inhalation in the form of powder or spray.

CARRYING OUT THE INHALATION

To carry out the inhalation, the patient should sit straight, in a comfortable position, with all the muscles being relaxed. The nozzle should be tightly bitten and grasped with the lips. After every deep inspiration, it is necessary to hold the breath for a while, and then make a deep and complete expiration.

If the interrupter is used (in teenagers), it is pressed only during the inspiration and should be loosened during the expiration. In such a case, the preparation passes into the lungs only during the inspiration and the loss is less.



METERED-DOSE AEROSOL INHALER

For most of the drug to pass into the airway and have a medical effect, it is necessary to study the technique of the inhalations.

The rules of usage of metered-dose aerosol inhaler:

1. To turn over the container with the drug and to shake it thoroughly for 20 sec.
2. To take the protective cap away.
3. To breathe out.
4. To throw back the head a bit for the airway to become straight.
5. To grasp the nozzle of the container tightly with the lips, not closing the hole with the tongue. The bottom of the container looks down.
6. Breathing in as deep as possible, to press the bottom of the inhaler at the same time (to feel the preparation passing into the lungs).
7. To hold the breath for 8-10 sec.
8. To breathe out slowly through the nose.
9. The most typical errors in using of metered-dose inhalers (MDI) are:

1. the nozzle of the inhaler is not grasped tightly with the lips, at this some medicine being lost;
2. pressing the container and inspiration are not simultaneous;
3. the inspiration is not deep enough;
4. the inspiration is short, and not slow and smooth;
5. the patient does not hold his breath after the inhalation.

Many children and adults have difficulties to follow all the recommendations as for the use of the inhaler. Due to different mistakes, the drug does not reach the airway, and there is no expected improvement of breathing. This may intensify anxiety and scare of both parents and a child. That is why it is of great importance to master the technique of inhalation to be sure that everything is made, as it should. For the convenience of usage, different ways of introduction of drugs into the airway have been elaborated.

The technique of inhalation from the metered-dose inhaler with a spacer:

1. To turn over the container and to shake it thoroughly for 20 sec.
2. To take the protective cap away.
3. To connect the inhaler to the spacer.
4. To breathe out.
5. To grasp the nozzle tightly with the lips. If the spacer is with a mask, to press the mask to the face of the child.
6. To press the bottom of the container, that is to make an injection of the drug into the spacer.
7. The child makes several inspirations form the spacer.

Inhaling the drug through the spacer, there is no need to synchronize the inspiration with pressing on the container. However, the main stages of the inhalation are similar, and the injection is made when the child is ready to breathe from the spacer.

Dry powder metered-dose inhalers

Dry powder metered-dose inhalers (DMDI) provide with effective, environmentally friendly control of asthma. A wide range of DMDI is based on the natural coordination between the inspiration and formation of a respirable cloudlet. This is the most important success of DMDI.

The usage of powder inhalers is based on creation of turbulent streams when a strong air-blast breaks large particles of the drug, and due to this, they reach the lower parts of the airway.

Their advantage is easy usage (**no need to coordinate the inspiration and activation of the inhaler**), absence of **gas freon, relatively low price.**

In most devices, the metered mass of the preparation is 5-10 mg. **INTAL** was the first drug in the form of dry substance. They used the capsule with the preparation, which was inhaled through the special device: **Spinhaler.** Later on, **Dischalers** were created, in which 4-8 doses are in the blister. Then appear multidose devices of the drug introduction: **Turbuhaler, Multidisc (Discus)**.

In these inhalers, there is no propellant; that's why they do no harm to the environment, which corresponds with the Montreal Protocol, but there are still a number of problems.

A very important factor is humidity of the environment or moisture, appearing from the patient. Dry powder may aggregate into granules, which worsens aerosol properties and dosage. To prevent this, different methods are used. In particular, there are some additional appliances, for example, the propeller, which is activated during the inspiration and disperse the powder, and the small chamber, added to the Turbuhaler, like in metered-dose aerosol inhalers, which lessens the formation of moisture.

The inhalers containing the powder drug are divided according to the methods of usage:

- the drug is inside the inhaler;
- the additional drug is attached to the inhaler.

Manual introduction of the drug into the device		
Aerohaler	Ipratropium bromide	Activated by inspiration; capsules
Dischaler	Beclomethasone, Fluticasone, Salbutamol	Activated by inspiration; blisters
Rotahaler	Beclomethasone, Salbutamol	Activated by inspiration; capsules
Spinhaler	Sodium Chromoglycate	Activated by inspiration; capsules
The drug is inside the device		
Discus	***Fluticasone, Salmeterol***	Activated by inspiration; 60 doses

Isihaler	***Beclomethasone, Salbutamol***	Activated by inspiration; 200 doses
Turbuhaler	***Budesonide, Terbutaline***	Activated by inspiration; 200 doses

For effective dispersion of the drug in using the powder inhaler, the inspiration should be powerful, which is not always possible in the children.

Examples:

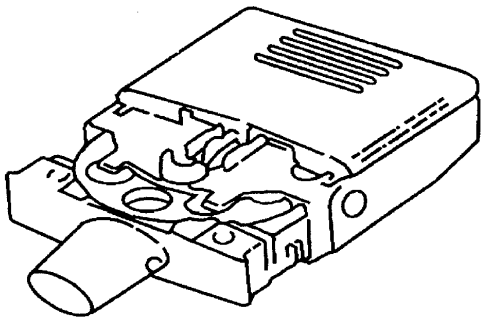
DISCHALER

Take away the cap from the nozzle. Then, take away the white cap and pull the white projection against stop.

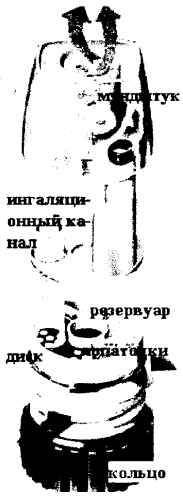
1. Put the foil disc into the wheel with the blisters inwards and return the projection into the original position.
2. The disc is turned when the projection returns to the original position. The blister appears in the special window. If the disc has 8 doses, turn it to the figure 8. Having placed the disc correctly, you always know how many doses are left.
3. Holding the Dischaler horizontally, raise the needle and pierce the blister. Remove the needle.
4. Holding the Dischaler horizontally, breathe out slowly and take the nozzle into the mouth. But **do not close the special hole for the air on the side of the nozzle!**
5. Breathe in through the mouth as deep and quick as possible.
6. Remove the Dischaler from the mouth and hold the breath for 10 sec.

YOU SHOULD ALWAYS DEMONSTRATE TO THE PATIENT

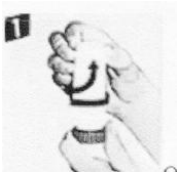
HOW TO USE THE DISCHALER CORRECTLY



Turbuhalers



How to use the Turbuhaler?

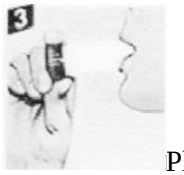


Unscrew the portective cap.

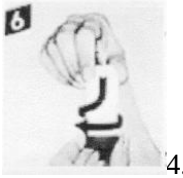
Hold the Turbuhaler vertically.

Turn the revolving part in one direction as far as you can, then in the opposite direction to the original position, to the click.

The note: you must not breathe out through the inhaler before the inhalation.



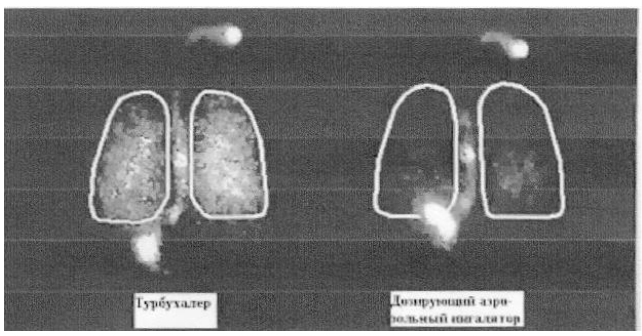
Place the nozzle between the teeth and grasp it with the lips



4. Breathe in deeply and strongly.

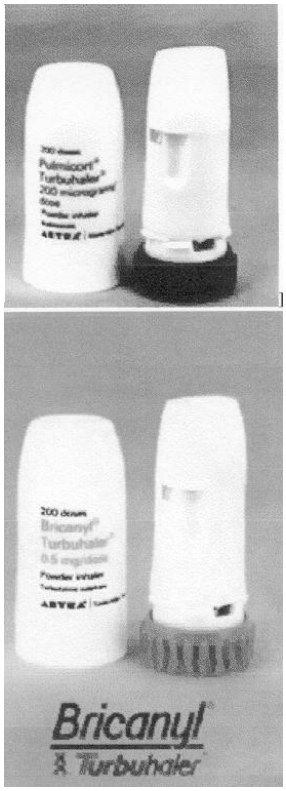
5. Remove the Turbuhaler from the mouth and breathe out.

6. Close the Turbuhaler with the protective cap.



The inhalations with the Turbuhaler improve the aerosol distribution in the lungs.

The preparations produced in Turbuhaler:



Pulmicort (Budesonide)

Bricanyl (β_2-agonist)

Oxys (Formoterol)

OTHER ALLERGIC (NON ATOPIC) DISEASE: TYPES, IMMUNOPATHOGENESIS, IMMUNE-DIAGNOSTICS, IMMUNOTHERAPY. DIFFERENTIAL DIAGNOSIS PSEUDOALLERGY AND ALLERGY.

Issues to be considered during the class

Non-atopic diseases: types, immunopathogenesis, immunodiagnostic, clinical manifestation and differential diagnosis.

Cell-mediated allergic diseases (serum disease, Arthus phenomenon, allergic alveolitis): immunopathogenesis, clinical manifestation, immunodiagnostic, immunotherapy.

Differential diagnostic of allergic and pseudoallergic reactions. Principles of anti-allergic therapy and immune methods of treatment in allergology.

Aim of study

The Arthus reaction was discovered by Nicolas Maurice Arthus in 1903. Arthus repeatedly injected horse serum subcutaneously into rabbits. After four injections, he found that there was edema and that the serum was absorbed slowly. Further injections eventually led to gangrene.

Serum sickness is a reaction to proteins in antiserum derived from an animal source. It is a type of hypersensitivity, specifically immune complex hypersensitivity (type III). The term serum sickness–like reaction (SSLR) is occasionally used to refer to similar illnesses that arise from the introduction of certain non-protein substances. It was first characterized by Clemens von Pirquet and Béla Schick in 1906.

Symptoms can take as long as fourteen days after exposure to appear, and may include signs and symptoms commonly associated with allergic reactions or infections, such as rashes, itching, joint pain (arthralgia), fever, and swollen lymph nodes (lymphadenopathy). Other signs include decreased blood pressure (hypotension) or even shock and an enlarged spleen, glomerulonephritis and proteinuria. While it may mimic an allergic reaction, it is different from true anaphylaxis, since the symptoms are not instantaneous.

Purposes of discipline

1. Learn types, immunopathogenesis, immunodiagnostic, clinical manifestation of non-atopic diseases:

2. Become familiar with cell-mediated allergic diseases (serum disease, Arthus phenomenon, allergic alveolitis): immunopathogenesis, clinical manifestation, immunodiagnostic, immunotherapy.

3. Discuss main difference between true allergy and pseudoallergy.

Student has to know:

1. mechanism of hypersensitivity class II, III, IV development.
2. Etiology, pathogenesis, clinical manifestation of non-atopic diseases.
3. immunodiagnostic of non-atopic diseases
4. Differential diagnostic of allergic and pseudoallergic reactions
5. Principles of anti-allergic therapy and immune methods of treatment in allergology

Student has to be able to do:

1. Take history and make physical examination of patients with allergic diseases.
2. Determine etiology (group of allergens) and pathogenetic factors of allergy.
3. Explain general methods of allergic investigation (laboratory tests, skin tests, provoking tests).
4. Make plan of patient's inspection, prove necessity of prescribed allergic tests, name indications and contraindications, possible complications.
5. Describe different courses and complications of allergic diseases.
6. Make forecast of disease, perform primary and secondary prophylactic of allergic diseases.
7. Differential diagnose of allergic and pseudoallergic reactions. Administer anti-allergic therapy, estimate efficacy.

Interdiscipline integration

Subject	Know	Can
Anatomy	Haemopoietic organs of immune system	Name primary and secondary lymphoid organs, lymphatic ducts
Biology, histology, embryology.	Immunity as mechanism of functional and structure homeostasis. Essentials	Distinguish basic phylogenetic levels of immunity evolution, primitive cell-mediated

	of immuno-embryogenesis.	immunity and integral cell-mediated and humoral immunity
Biochemistry	Chemical structure and biological action of mediators of cell-mediated immunity	Immunophoretic determination of immunoglobulins.
Pathophysiology	Phagocytosis in the focus of inflammation, immunological tolerance, reactivity, allergy.	Name immunocompetent cells, participating in defense reactions of cell-mediated and humoral immunity
Normal physiology	Interaction of nervous, endocrine and immune system for functional and structure homeostasis maintaining	On practical classes determine interaction of nervous, endocrine and immune system.
Pathological anatomy	Role of immune disorders in mesenchymal and protein dystrophies, mucous and fibrinoid degeneration if connective tissue	Determine mesenchymal and protein dystrophies, mucous and fibrinoid degeneration if connective tissue. Types of tissue reactions in collagenoses.
Microbiology, virusology	Specific and non-specific mechanisms of defense. Types of antigenes, immunity, allergies.	Perform agglutination test, Coombs' test, precipitation. Titration of complement, bacteriolysis and haemolysis tests, immunofluorescence test
Propedeutics of internal diseases	Role of immune system in pathogenesis of different diseases.	Interpretation of rosette test, Manchini immunoglobulins, phagocytic activity of blood.
Pharmacology	Mechanism of action, pharmacodynamic and pharmacokinetic of antihistamines, corticosteroids.	Prescribe receipt

Independent student's work

Main theoretical aspects of theme.

- Specific immunotherapy: Principles destination. Indications and contraindications, complications development
- Drug allergy.

Tasks for final module test

1. Characteristic of pseudoallergy, Differential diagnostic. Mechanisms of histamine liberation in pseudoallergy development, treatment.

2. Pseudoallergy in complement activation impairment. Arachidonic acid metabolism disorders. Principles of treatment.

List of practical skills for final module test.

1. Make differential diagnostic, basing on laboratory and instrumental studies.

2. Administer treatment, make forecast, perform primary and secondary prophylactic of allergic diseases.

3. Perform emergency help in acute allergic and pseudoallergic reactions

4. Use standard methods of diagnostic and treatment in allergology.

5. Learn principles of anti-allergic therapy prescription

IMMUNE ASPECTS OF AUTOIMMUNE DISEASES.

Issues to be considered during the class

Definition of autoimmune reactions, autoimmune diseases. Mechanism of immune tolerance disorders, role of genetic factors. Immunodiagnostic, immunopathogenesis. Role of immunological research methods in early verification of autoimmune disease. Autoimmunity in pathogenesis of different diseases. Contemporary principles of immune drugs usage, drugs of new generation in treatment patients with autoimmune pathology.

Aim of study

Autoimmune disease is a condition which is triggered by the immune system initiating an attack on self-molecules due to the deterioration of immunologic tolerance to auto-reactive immune cells. autoimmune disorders affect approximately 3% of the North American and European populations, >75% of those affected being women. The initiation of attacks against the body's self-molecules in autoimmune diseases, in most cases is unknown, but a number of studies suggest that they are strongly associated with factors such as genetics, infections and /or environment.

Purposes of discipline

1. Mechanism of immune tolerance disorders, role of genetic factors.

2. Contemporary principles of immune drugs usage. Drugs of new generation in treatment patients with autoimmune pathology.

Student has to know:

1. Immunodiagnostic, immunopathogenesis of pneumatic arthritis, SLE, autoimmune hepatitis.

Student has to be able to do:

1. Estimate laboratory data indicating autoimmune pathology.

Interdiscipline integration

Subject	Know	Can
Anatomy	Haemopoietic organs of immune system	Name primary and secondary lymphoid organs, lymphatic ducts
Biology, histology, embryology.	Immunity as mechanism of functional and structure homeostasis. Essentials of immuno-embryogenesis.	Distinguish basic phylogenetic levels of immunity evolution, primitive cell-mediated immunity and integral cell-mediated and humoral immunity
Biochemistry	Chemical structure and biological action of mediators of cell-mediated immunity	Immunophoretic determination of immunoglobulins.
Pathophysiology	Phagocytosis in the focus of inflammation, immunological tolerance, reactivity, allergy.	Name immunocompetent cells, participating in defense reactions of cell-mediated and humoral immunity
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Microbiology, virusology	Specific and non-specific mechanisms of defense. Types of antigenes, immunity, allergies.	Perform agglutination test, Coombs' test, precipitation. Titration of complement, bacteriolysis and haemolysis tests, immunofluorescence test
Propedeutics of internal diseases	Role of immune system in pathogenesis of different diseases.	Interpretation of rosette test, Manchini immunoglobulins, phagocytic activity of blood.

Independent student's work

Oral presentation of themes, given for independent work.

Immunopathogenesis and immune therapy of sepsis.

Epstein-Barr infection, Immunopathogenesis and immune therapy

Tasks for final module test

1. Definition of autoimmunity, autoimmune disease. Mechanism of immune tolerance disorders, role of genetic factors.
2. Classification, general principles of immune diagnostic of autoimmune diseases. Contemporary principles of immune drugs usage
3. Laboratory criteria of immunodiagnostic of autoimmune diseases.

List of practical skills for final module test.

1. Estimate laboratory criteria of immunodiagnostic of autoimmune diseases.
2. Use standard methods of immunodiagnostic and prescribe immunosuppressive therapy. Estimate its efficacy in autoimmune diseases.

Appendix 1

Immunological disorders in autoimmune diseases

Diseases	AMA	ANF	IgG	IgA	IgM
Viral hepatitis	-	↑	↑	↑↑↑	↑↑↑
Chronic active hepatitis	↑	↑↑	↑↑	↑↑	↑↑
Primary biliary cirrhosis	↑↑↑	↑	↑↑	↑↑	↑↑
Autoimmune cholangiopathy	_	↑↑↑	↑↑↑	↑	↑

Appendix 2

Scoring system of diagnosis of autoimmune hepatitis

Parameters	Score
1. Sex: female	+2
male	0
2. Correlation of activity of alkaline phosphatase and ALT:	
> 3	- 2
< 3	+2
3. Concentration of γ-globulins or IgG:	
more than twice higher than normal	+3
1.5-2 times higher than normal	+2
up to 1.5 times higher than normal	+1
lower than normal	0
4. The titer of antinuclear antibodies, antibodies to smooth muscles or antibodies to hepatorenal microsome antigen of the I type:	
> 1:80	+3
1:80	+2
1:40	+1
<1:40	0
5. Anti-mitochondrial antibodies:	
present	-2
absent	0
6. HBsAg, anti-HAV IgM	-3
7. RNA HCV or other hepatotropic viruses	-3
8. Anti-HCV, according to recombinant immunoblotting	-2
9. All the mentioned tests (6, 7, 8) are negative	0
10. Concomitant immune-mediated diseases	+1
11. Taking hepatotoxic preparations: yes	-2

	no		+1
12. Blood transfusions in anamnesis:	yes		-2
	no		+1
13. Alcohol consumption:	< 25 g a day		+2
	> 60 g a day		-2
14. Histological signs:	lobular hepatitis + bridging hepatic necrosis		+3
	graded necrosis only		+2
	rosettes		+1
	plasmatic cells		+1
	impairment of bile ducts		-1
	other etiological signs		-3
15. HLA B 8 – DR3 or DR 4 antigens			+1
16. Response to corticosteroid treatment:	complete		+2
	partial		0
	absent		-2
	exacerbation		-3
The score determining the diagnosis:	Before treatment:	definite	>15
		possible	10-15
	After treatment:	definite	>17
		possible	12-17

Appendix 3

The most numerous group of autoimmune diseases is associated with autoantibodies to intracellular autoantigens, the substrate of which includes cellular nuclei, cytoplasm enzymes, cytochrome P450 enzymes, mitochondria, and lysosomes.

Antinuclear antibodies (ANA) are antibodies to intracellular components of cellular nuclei. ANA react with different structures of the nucleus, which shows their specificity and allow their using as diagnostic markers (Table 1).

Antinuclear factor (ANF) is a specific immunological activity of immunoglobulins-autoantibodies to the whole somatic nucleus of the cell. Their fixation is determined by indirect immunofluorescent method with tissue section of rats and mice, a monolayer of Hep-2 cell culture and antiglobulin serum labeled with fluorescent dye used as a substrate.

ANF is a diagnostic marker of SLE, systemic scleroderma, mixed connective-tissue disease, etc. and used to distinguish subtypes of the disease.

Antinuclear antibodies and methods of their detection

Nosology	Immuno-fluorescent technique	EIA, contra-electrophoresis, immunoblotting
Systemic diseases of the connective tissue: systemic lupus erythematosus (SLE); rheumatoid arthritis; systemic scleroderma; dermatomyositis; mixed connective-tissue disease; Sjögren's disease; juvenile rheumatoid arthritis; cross syndromes.	Positive (high titers)	Antigens: ds: DNA, RNP, Sm, Ro; histon (H1, H2a-H2b, H3, H4), La, P, Scl-70, Jo-1 Dm/Scl, DNA polymerase, RNA polymerase, nucleosomes.
Diseases associated with ANF: drug-induced lupus, subacute cutaneous lupus erythematosus, hepatitis, cholangiopathy, Raynaud's syndrome, chronic active hepatitis, thyroiditis, urticaria, post-streptococcal arthritis, non-differentiated connective-tissue diseases.	Positive (high and low titers)	Antigens: histon, vimentin, actin, nuclear, centromere, topoisomerase 1.

Note: ANF – antinuclear factor; RNP – nuclear ribonucleoprotein.

Specificity of ANF may be partially characterized with the help of immunofluorescent method according to morphological signs of nuclear immunofluorescence.

MATERIALS
FOR FINAL MODULE TEST
"CLINICAL IMMUNOLOGY AND ALLERGOLOGY"
FOR STUDENT 5TH YEAR MEDICAL FACULTIES IN 2016/17 SCHOOL YEAR

The final module test is carried out on completion of study curriculum Module 1: "Clinical Immunology and Allergology" and is held on the last lesson of module.

The final module tests students who attended all provided the curriculum for classroom training sessions, and during a module number of points scored not less than the minimum. The minimum score for admission to the final module control is 66 points.

Student, who had to have blanks classes, adjustments are made to the individual curriculum and academic debt permitted to work up to a certain fixed period.

The maximum number of points that the student can get in the preparation of the final module control is 80 points. The final module loan is considered passed if the student scored at least 60% of the maximum number of points which is 50 points.

The final module test consists of two main parts:

1. The test questions control;
2. The solution of non-typical tasks.

The first part of the final module control.
(Control Test Questions)

The task is to control the test control knowledge and skills of students and preparation for taking an integrated licensing examination "Krok 2". Test control includes 30 tests, 15 of which are the clinical situation, and asked her 5 response options from which you must select the correct one. Questions test problems controlling knowledge of immunopathogenesis, clinical manifestations, indications and contraindications for the purpose immunotropic therapy, prevention of immunodeficiency diseases and immunodependent and reflect the training program "Clinical Immunology and Allergology" for students 5th year medical faculties.

Duration of test – 50 minutes.

Evaluation of the first part of the final module test.

The maximum score is 50 points this stage

The second part of the final module test.

(Non-typical tasks**)**

The student must justify correct patient diagnosis, interpret data of laboratory and instrumental studies appoint additional examination and advocate the use of immunotropic drugs, identify recommendations for secondary prevention.

Evaluation of the second part of the final module test.

The maximum score is 30 points this stage.

The total score for the preparation of the final-module control is defined as the sum of the scores of all the components of the final module control.

Head of Department,

Professor **Andriy Kurchenko**

Questions “Krok 2” and “USMLE”.

1. A researcher develops a specific antibody to the complement component C3b. Assume that intravenous administration of the antibody prevents the biological effects of C3b. Administration of the antibody would be expected to interfere with which of the following biological functions?
A. Decreased appetite
B. Fever
C. Increased collagen synthesis by fibroblasts
D. Opsonization to facilitate phagocytosis
E. Increased leukocyte adherence to endothelium

2. A 7-year-old girl is walking across a vacant lot and steps on a nail. The next day, her foot is sore and the wound appears inflamed. During these early stages of infection, which of the following compounds exert the most powerful chemotactic effect on neutrophils, causing them to migrate into the inflamed area?
A IL-1 and tumor necrosis factor
B. C5a and IL-8
C. LTC4 and LTD4
D. PGI2 and PGD2
E. Thromboxane and platelet activating factor

3. Which of the following enzymes does the neutrophil use to initiate the production of toxic oxygen compounds that kill bacteria?
A. Hydrogen peroxide
B. Myeloperoxidase
C. Superoxide
D. NADPH oxidase
E. Superoxide dismutase

4. C3 is cleaved to form C3a and C3b by C3 convertase. C3b is involved in all of the following EXCEPT
A. promoting phagocytosis.
B. altering vascular permeability.
C. forming alternative-pathway C3 convertase.
D. forming C5 convertase.

5. A 24 y.o. woman consulted a doctor about continued fever, night sweating. She lost 7 kg within the last 3 months. She had casual sexual contacts. Objectively: enlargement of all lymph nodes, hepatolienal syndrome. Blood count: leukocytes - 2,2*109/L. What disease can be suspected?
A. Infectionous mononucleosis
B. Chroniosepsis
C. HIV-infection
D. Lymphogranulomatosis
E. Tuberculosis

6. A 36 y.o. woman is in the 12-th week of her first pregnancy. She was treated for infertility in the past. She contacted a child who fell ill with rubella 2 days after their meeting. Woman doesn't know if she has ever been infected with rubella. What is the adequate tactics?
A Fetus wastage
B. Interferon prescription
C. Monitoring of the specific IgG IgM with the ELISA
D. Cyclovin prescription
E. Immunoglobulin injection

7. A traveler to a foreign country develops acute lymphatic filariasis four months after his return to the United States. His symptoms include scrotal inflammation, itching, and localized scrotal swelling and tenderness of the inguinal lymph nodes. Which of the following immune mechanisms does the body employ against the live filarial worms ?
A. Anti-receptor antibodies
B. Antibody-dependent cell-mediated cytotoxicity
C. Arthus reaction
D. Complement-mediated reactions
E. Deposition of circulating antigen-antibody complexes

8. A 22-year-old female comes to the sexually transmitted disease (STD) clinic for her first visit. She tells the nurse practitioner that she has had four different sexual partners in the last six months and only one of them used a condom. She also admits that she used IV drugs on several occasions two years ago. She notes fever, weight loss, lack of appetite, and periodic difficulty breathing over the past few months. She has an HIV test performed, which is positive. The physician decides to do a confirmatory test for HIV. Which one of the following tests would the physician order?
A. Western blot
B. FACS (Fluorescence activated cell sorting)
C. RAST (Radioallergosorbent Test)
D. RID (Radial immunodiffusion)
E. ELISA (Enzyme-linked immunosorbent assay)

9. A 7-month-old child is hospitalized for a yeast infection that does not respond to therapy. The patient has a history of multiple, acute pyogenic infections. Physical examination reveals that the spleen and lymph nodes are not palpable. A differential WBC count shows 95% neutrophils, 1% lymphocytes, and 4% monocytes. A bone marrow biopsy contains no plasma cells or lymphocytes. A chest x-ray reveals the absence of a thymic shadow. Tonsils are absent. These findings are most consistent with
A. severe combined immunodeficiency
B. chronic granulomatous disease
C. Bloom's syndrome
D. Waldenström's macroglobulinemia
E. Wiskott-Aldrich syndrome

10. An 8-month-old boy baby is evaluated because of repeated episodes of pneumococcal pneumonia. Serum studies demonstrate very low levels of IgM, IgG, and IgA. This patient's condition is thought to be related to a deficiency of which of the following proteins?
A. Adenosine deaminase
B. Class III MHC gene
C. Gamma chain of the IL-2 receptor
D. Tyrosine kinase
E. Purine nucleotide phosphorylase

11. A 4-year-old boy is seen by his pediatrician for epistaxis. The patient has a history of multiple bacterial and viral respiratory tract infections and eczema. An uncle had similar problems. Physical examination is remarkable for multiple petechial lesions on the skin and mucous membranes. Serum IgE is increased, and platelets are decreased. Which of the following is the most likely diagnosis?
A. Wiskott-Aldrich syndrome
B. Ataxia telangiectasia
C. DiGeorge syndrome
D. Selective IgA deficiency
E. Acquired hypogammaglobulinemia

12. A four-year-old boy is brought to the pediatrician because of several "boils" on his arm. His mother tells the physician that the boy has had similar lesions on several previous occasions that were treated successfully with antibiotics. She denies any history of eczema or typical childhood illnesses such as measles or chicken pox. The child has had all of his immunizations. Laboratory examination reveals a normal complete blood count, immunoglobulin levels, B cell and T cell counts, and complement levels. Serum calcium and parathyroid hormone levels are also normal. The nitroblue tetrazolium test is negative. Which of the following diagnoses is most consistent with these data?
A. Bruton's agammaglobulinemia
B. DiGeorge syndrome
C. Chronic granulomatous disease
D. SCID (severe combined immunodeficiency disease)
E. Wiskott-Aldrich syndrome

13. A 41 y.o. woman complains of weakness, fatigue, fever up to 380C, rash on the face skin, pain in the wrists and the elbows. On physical examination: erythematous rash on the cheeks with "butterfly" look, the wrists and elbow joints are involved symmetrically, swollen, sensitive, friction rub over the lungs, the heart sounds are weak, regular, HR- 88/min, BP- 160/95 mm Hg. CBC shows anemia, leucopenia, lymphopenia; on urine analysis: proteinuria, leukocyturia, casts. What is the main mechanism of disease development?
A. Production of myocytes antibodies
B. Production of myosin antibodies
C. Production of antibodies to endothelial cells
D. Production of antibodies to double-stranded DNA
E. Production of antimitochondrial antibodies

14. A baby boy was born in time, it was his mother's 1st pregnancy. The jaundice was revealed on the 2nd day of life, then it progressed. The adynamia, vomiting and hepatomegaly were presented. The indirect bilirubin level was 275 mcmol/L, the direct bilirubin level - 5 mcmol/L, Hb- 150 g/L. Mother's blood group - 0(I), Rh+, child's blood group - A(II), Rh+. Make a diagnosis.
A Physiological jaundice
B. Jaundice due to conjugation disorder
C. Hemolytic disease of newborn (ABO incompatibility), icteric type
D. Hemolytic disease of newborn (Rh - incompatibility)
E. Hepatitis

15. A 27 year old woman presents with muscle weakness,ptosis,has been receiving gentamicin injections for the last 7 days for a urinary infection.Thyroid function tests,serum creatine kinase, eletromyogram and musle biopsy are noraml.I/V administration of edrophoniumresults isn adramtic improvements in the pateints muscle strength.Which of the following is most likely diagnosis
A Toxic {drug induced}myopathy
B. Myasthenia gravis
C. Duchenne musclar dystrophy
D. Peripheral neuropathy
E. None of the above

16. A patient 55 years complains about pain, slight swelling in the joints of brushes, long constraint at mornings, limitation of mobility. 1 year is ill. Treated oneself with ibuprofen with a small effect. Objectively: swelling of metacarpal-phalange, proximal interphalange joints of the II-III fingers of both brushes with pain limitation of mobility. ESR 37 mm/hour. What researches are most informing for clarification of diagnosis of rheumatoid arthritis?
A. Determination of blood lipids level
B. Determination of uric acid in blood
C. Titers of antichlamidias antibodies

D. Presence of LE-cells
E. Rheumatoid factor, X-ray of brushes joints

17. A 6-year old asthmatic child is brought to the emergency room because of severe coughing and wheezing during the prior 24 h. The child had been taking theophylline without relief. Physical examination reveals a child who is anxious, has intercostal and suprasternal retractions, expiratory wheezing throughout all lung fields, and a respiratory rate of 60 breaths per minute. Initial treatment may include the administration of
A. N-acetyl cysteine and cromolyn by inhaler
B. Parenteral phenobarbital
C. Intravenous fluids in the first 2 h to correct a water deficiency.
D. Subcutaneous epinephrine
E. Parenteral gentamicyn

18. A 2 year old boy has been vomiting intermittently for 3 weeks and has been irritable, listless, and anorectic. His use of language has regressed to speaking single words. In your evaluation of this patient, the LEAST likely, diagnosis to consider is:
A Lead poisoning
B. Food allergy
C. Tuberculous meningitis
D. Brain tumor
E. Subdural hematoma

19. A college student sitting in the stands at a football game suddenly begins breathing hard and complains to his friends of tightness in his chest. Minutes later, he is sweating profusely and faints. It is discovered that he had been stung by a bee. Paramedics arrive, assess the situation, then successfully treat the young man. Which one of the following drugs was most likely initially administered in this case?
A. Epinephrine
B. Blocking antibody
C. Cromolyn sodium
D. Diphenhydramine
E. Theophylline

20. A 24-year-old man presents with complaints of itching on his arms and face. Physical examination reveals well-circumscribed wheals with raised, erythematous borders and blanched centers. Which form of hypersensitivity is this patient probably exhibiting?
A. Acute serum sickness (Type III)
B. Antibody-dependent cell-mediated cytotoxicity (Type II)
C. Immediate type hypersensitivity (Type I)
D. Delayed type hypersensitivity (Type IV)
E. Anti-receptor antibodies (Type II)

21. A 29-year-old Mexican American woman receives an intradermal tuberculin injection and later develops an indurated, erythematous papule 12 mm in diameter. This reaction is an example of which of the following?
A. Type IV hypersensitivity
B. Local anaphylaxis
C. T-cell mediated cytotoxicity
D. Type III hypersensitivity
E. Antibody-dependent cell-mediated cytotoxicity

22. A 45-year-old homeless man has a chronic cough, a cavitary lesion of the lung, and is sputum positive for acid-fast bacilli. Which of the following is the principal form of defense by which the patient's body fights this infection?
A. Antibody-mediated phagocytosis
B. Neutrophil ingestion of bacteria
C. IgA-mediated hypersensitivity
D. IgE-mediated hypersensitivity
E. Cell-mediated immunity

23. A Mexican immigrant presents with a 3-month history of weight loss, night sweats, a productive cough with blood-tinged sputum, anorexia, general malaise, and a low grade fever. A PPD skin test shows > 10 mm of induration. If the area of induration were biopsied, which of the following type of reactive cells would be found?
A. T lymphocyte
B. Eosinophil
C. Mast cell
D. Neutrophil
E. B lymphocyte

24. A 32-year-old medical technician had a history of acute eczematous dermatitis on her hands and wrist in the distribution of the latex gloves she wore. The skin of her hands was dry, crusted, and thickened. The eczematous reaction cleared after a 2-week vacation. After 72 hours back on the job, the eczematous dermatitis returned and continued to grow worse. Which of the following characterizes the technician's reaction to the latex gloves?
A. Irritant dermatitis
B. Type IV reaction
C. Type II reaction
D. Type III reaction
E. Type I reaction

25. A 36-year-old man with a history of mild asthma usually controlled with PRN use of an albuterol inhaler comes to your office as a new patient. He has recently moved from a different state and started a new job as a computer engineer. He and his wife bought an old house in the area where you practice. He said that since he moved his asthma symptoms have worsened. He now uses his albuterol inhaler more frequently and wakes up a few times during the night feeling short of breath. He does not have any pets at home and he does not smoke. Physical examination is normal. Spirometry performed in the office shows an FVC of 3.2 L (89% predicted) and an FEV1 of 2.7 L (84% predicted). Which of the following is the most appropriate next step in the management?
A. Start the patient on an inhaled corticosteroid
B. Order complete pulmonary function tests (PFTs) with diffusion capacity DLCO
C. Reassure the patient that these symptoms are not caused by his asthma
D. Order allergy skin testing
E. Start the patient on a leukotriene receptor antagonist

26. A 32-year-old man comes to see you complaining of nasal obstruction and clear nasal drainage. Further questioning indicates that he typically has problems all year long but that these two complaints are more pronounced during the spring and fall seasons. He denies episodes of thick nasal drainage or facial pain. He reports some itchy and watery eyes at these times but is not as concerned with these symptoms. Physical examination reveals pale, boggy nasal mucosa with swollen inferior turbinates. The nasal septum is midline. Which of the following is the best long-term management of his complaints?
A. Intranasal injected corticosteroid
B. Oral antibiotics
C. Nasal corticosteroid spray

D. Oral antihistamine
E. Oral corticosteroids

27. A 42-year-old man with a history of asthma has increasing shortness of breath and wheezing. He also is complaining of a cough for the past 2 weeks. Furthermore, he notes that he has had difficulty walking because his right foot seems to "drop." He is on low-dose steroids that were discontinued recently when he was started on inhaled steroids. He is also on a variety of inhalers, including albuterol, ipratropium, and salmeterol. He has no allergies. His temperature is 38.3 C (101.0 F) and other vital signs are stable. Pulmonary examination reveals mild crackles on the left and occasional wheezing. Chest x-ray shows patchy opacities. His leukocyte count is 13,000/mm3 with 15% eosinophils. Urinalysis is unremarkable. Which of the following is the most likely diagnosis?
A. Bacterial pneumonia
B. Goodpasture syndrome
C. Churg-Strauss syndrome
D. Sarcoidosis
E. Wegener granulomatosis

28. You are seeing a 32-year-old man with a runny nose. He describes a pattern of clear rhinorrhea and nasal obstruction that is worse in the spring and fall. Further questioning reveals that he experiences associated itchy, watery eyes during these seasons. Physical examination includes swollen, boggy nasal turbinates. In addition to your discussion about environmental control, he would like a prescription for a single medication that will provide relief of rhinorrhea and itchy, watery eyes. The best choice, in maximizing relief while minimizing side effects with long-term use, is which of the following agents?
A. Topical decongestant
B. Oral corticosteroids
C. Oral decongestant
D. Topical corticosteroid nasal spray
E. Oral antihistamines

29. You are requested by the emergency room to see a 42-year-old investment banker who came in complaining of chest pain. She noticed the chest pain when she was running across the street to catch a cab. She states that it lasted 5 minutes and was relieved with rest and with diaphoresis, dull in quality, and substernal in location. She characterized the pain as 6 on a 10-point pain scale. She denies any prior history of chest pain. She rarely exercises and lives a sedentary lifestyle. Her cardiac risk factors include hypertension and hypercholesterolemia, but no personal history of diabetes or tobacco use, or family history of cardiac disease. Her past medical history includes asthma in addition to hypertension and hypercholesterolemia. She is being treated with hydrochlorothiazide, an HMG CoA reductase inhibitor, albuterol by a metered dose inhaler, and salmeterol. Her vital signs are: blood pressure 164/89 mm Hg, heart rate 93/min, respiratory rate 16/min, temperature 37.1 C, and a room air saturation on ambient air of 98%. You diagnose the patient with acute coronary syndrome and administer an aspirin. Shortly thereafter, you notice that the patient is becoming increasingly short of breath and now has a respiratory rate of 31/min and oxygen saturation of 92% on ambient air. Her other vitals are unchanged. On physical examination, the patient has poor air movement and diffuse expiratory wheeze but no crackles on lung examination or jugular venous distention. Which of the following is a thorough physical examination likely to reveal?
A. Nasal polyps
B. Clubbing
C. Increased tactile fremitus
D. Bronchial breath sounds
E. Proximal pallor of the nail beds associated with a distal band of reddish brown

30. A 23-year-old man is admitted to the medical services with a severe asthma attack. He is also nauseous and has vomited twice today. The patient has a long history of severe asthma with multiple hospitalizations and one intubation 3 years ago. Two days prior to admission, he was exposed to dust while moving a file cabinet in his basement. Since that time, has had progressively worsening shortness of breath. He had tried home albuterol and ipratropium nebulizers, as well as his standard cromolyn therapy, but none of these interventions relieved his symptoms. In the hospital, the man's peak flow rates are decreased by nearly 50% from baseline. Which of the following agents should most likely be added to the patient's therapy to alleviate his current symptoms?

A. Beclomethasone
B. Hydrocortisone
C. Disodium cromoglycate
D. Prednisone
E. Theophylline

CARD 1

1. Killing effect as part of immunobiological supervision. The main types of killer cells.
2. Interferon drugs. The mechanism of action, side effects, indications and contraindications for the use of these drugs.
3. Situation Task

CARD 2

1. The cell of innate protective factors and their interaction in the implementation of the immune response.
2. Glucocorticosteroid drugs. The mechanism of action, side effects, indications and contraindications for use.

CARD 3

1. The main tasks and problems of modern clinical immunology. Groups diseases within the competence of clinical immunologist.
2. Preparations thymus and bone marrow. The mechanism of action, side effects, indications and contraindications for use.
3. Situation Task

CARD 4

1. Macrophages. Role in the development and implementation of an immune response. Immunological aspects of phagocytosis.
2. Thymus and bone marrow drugs. The mechanism of action, side effects, indications and contraindications for use.
3. Situation Task

CARD 5

1. Basic principles of classification of immunodeficiency. Congenital combined immunodeficiencies and immunodeficiencies of B- and T-cell links: mechanisms of development, clinical course, and treatment of immune.
2. Immunotropic drugs of microbial origin. The mechanism of action, side effects, indications and contraindications for use.
3. Situation Task

CARD 6

1. The antigens: their structure and function. Allergens and their classification. Diagnostic criteria of allergies.
2. Antihistamines 1st and 2nd generation. The mechanism of action, side effects, indications and contraindications for use.
3. Situation Task

CARD 7

1. Current understanding of the structure, function and ontogeny of the immune system. Non-specific and specific protective factors and their interaction in the implementation of the immune response.
2. Principles of anti-allergic and immunotropic therapy of allergy.
3. Situation Task

CARD 8

1. Transplantation immunology. Immunological indications and contraindications for transplantation of organs and tissues. Breeding pairs of donor-recipient.
2. Plant adaptogens and vitamins. The mechanism of action, side effects, indications and contraindications for use.
3. Situation Task

CARD 9

1. Humoral factors of innate immunity. Natural antibodies, interferons.

2. The blood products and immunoglobulins. The mechanism of action, side effects, indications and contraindications for use.

3. Situation Task

CARD 10

1. T - lymphocytes - helper 1 st, 2 nd and 3 rd type. The value of the functional balance between T helper Th1/Th2.

2. Principles and anti-allergic therapy treatments in immunotropic of allergy.

3. Situation Task

CARD 11

1. Immunological system mucous membranes. Lymphoid tissue associated with gastro - intestinal tract.

2. The concept of anti-tumor immunity. Current approaches to cancer immunodiagnosis. The concept of cancer antigens.

3. Situation Task

CARD 12

1. Mechanisms disruption tolerance, their role in the development of autoimmune diseases. Clinical examples of autoimmune diseases. Features immunopathogenesis of SLE.

2. Antihistamines of 3-th generation. The mechanism of action, side effects, indications and contraindications for use.

3. Situation Task

CARD 13

1. The concept immunodependent diseases. Classification, clinical features, and treatment of immune.

2. Fundamentals of modern molecular Allergic diagnosis and therapy.

3. Situation Task

CARD 14

1. Impact of harmful environmental factors on the immune system. Stress, frustration neuro-humoral and immune regulation. Rapid fatigue syndrome.

2. Laboratory criteria for diagnosis of autoimmune diseases.

3. Situation Task

CARD 15

1. Drug allergy. Immunopathogenesis, clinical, alerhodiahnostyka, treatment, allergy prevention.

2. Acquired immunodeficiency diseases, immune-diagnostics, clinic, therapy Immunotropic.

3. Situation Task

CARD 16

1. Rheumatoid arthritis: immunopathogenesis, immunodiagnosis, immunotherapy.

2. Allergy and atopy. Classification allergens. Causes and mechanisms of allergic conditions.

3. Situation Task

CARD 17

1. The mechanisms of the immune system interaction "host" and tumors.

2. Immunopathogenesis, stage of development, classification of HIV / AIDS.

3. Situation Task

CARD 18

1. The concept of allergy and pseudoallergy, differential diagnosis. Histaminliberatsiyni psevdoalerhichnyh mechanisms of reactions. Treatment.

2. Lymphadenopathy syndrome: etiology, pathogenesis, classification, research methods, immunological diagnostic criteria, differential diagnosis, basic principles of immunotherapy and immunoprophylaxis.

3. Situation Task

CARD 19

1. Features of pre and post transplantation immunological monitoring. Types of rejection crisis, their clinical and immunological characteristics and prognosis.

2. Current methods for evaluating immune status.

3. Situation Task

CARD 20

1. The concept of anti-tumor immunity. Targeted therapy in oncology. Clinical examples.

2. Congenital immunodeficiencies of phagocytic parts of the immune system and complement system: mechanisms of development, clinical course, and treatment of immune.

3. Situation Task

Questions for final module test (Clinical Immunology and Allergology)

1. Subject and aims of clinical immunology and allergology. History of immunology development. Main branches of further research.
2. Contemporary views on immune system structure, function and ontogenesis. Primary and secondary organs of immune system.
3. Principles of functioning of immune system in children and senior.
4. Innate cells factors of defense, their interaction in immune response.
5. Monocyte-macrophage system: functional characteristic, role in immune response realization. Contemporary views on phagocytosis.
6. Killing effect as part of immunobiological supervision. Types of killer cells. Their function, properties. Role of granulocytes in immune response.
7. Humoral factors of innate immunity.
8. Complement system. Biological consequences of its activation.
9. Antigenes, their structure, functions. Haptens.
10. Stages of T- abd B-lymphocytes maturation and differentiation.
11. T-lymphocytes. Structure of T-cell receptor. T-cell populations. Main markers and clusters of differentiation.
12. Th 1 and Th2. Importance of balance (Th1\Th2).
13. T-regulatory cells, main function.
14. Apoptosis as special form of cell death. Its role it physiological and pathological processes.
15. B-lymphocytes, markers and functions. Structure of receptor.
16. T-dependent and T-independent immune responses.
17. Immunoglobulins: structure, functions, classes. Role pf immune complexes in pathology.
18. Cytokines – mediators of immune system, Interleukins, classification, function and role in immune processes.
19. Growth factors. Tumor necrotic factors, interferons and adhesive molecules. Characteristic and role in immune response.
20. Immune system of mucosa. Gut-associated lymphoid tissue (GALT).
21. Contemporary views on structure and function of MHC
22. Structure of HLA antigens. Predisposition to diseases according to HLA phenotype.
23. Quantitative and functional immunological tests. Immunogram, main parameters.
24. Method of quantitative and functional T-lymphocyte characteristic determination: rosette test, tests with monoclonal antibodies, blast-transformation reaction with mitogenes.
25. Method of quantitative and functional B-lymphocyte characteristic determination: rosette test, tests with monoclonal antibodies, blast-transformation reaction with mitogenes, circulating immune complexes level.
26. Method of phagocyte activity estimation.
27. Quantitative method of main classes' serum immunoglobulins determination.
28. Immunopathogenesis, stages, classification of HIV-infection and AIDS.
29. Clinical and laboratory diagnostic, principles of treatment.
30. Major principles of HIV prophylactic in Ukraine. Medical staff as "risk group" for HIV infection.
31. Classification of immune deficiencies. T-, B- and combine primary immunodeficiencies: mechanisms of development, course of disease, immune diagnostic and treatment.
32. Primary immunodeficiencies of phagocytosis and complement system, mechanisms of development, course of disease, immune diagnostic and treatment.
33. Acquired immune deficiencies. Etiology, clinical signs, immune diagnostic and treatment syndrome of lasting fever: etiology, clinical manifestation, instrumental and laboratory diagnostic criteria, differential diagnosis, immune therapy and prophylactic.
34. Lymphadenopathy syndrome. Etiology, pathogenesis, classification, investigations, diagnostic criteria, immune therapy and prophylactic.
35. Transplantation immunology. Indications and contraindication for grafting. Donor-recipient selection. Preexisting antilymphocytotoxic antibodies, their value.

36. Pre- and post-grafting monitoring. Types of rejection crises, characteristic and prognosis.

37. Antitumor factors, tumor's factors of immune resistance. Problastom factors, suppressing immunity and problastom factors stimulating tumor's growth. Tumor-associated antigens.

38. Immune changes in patients with tumor. Immune diagnostic in oncology. Up-to-date immune therapy of tumors.

39. Definition of autoimmunity, autoimmune disease. Mechanism of immune tolerance disorders, role of genetic factors.

40. Classification, general principles of immune diagnostic of autoimmune diseases. Contemporary principles of immune drugs usage

41. Laboratory criteria of immunodiagnostic of autoimmune diseases.

42. Causes of allergy development. Stages of allergic reaction.

43. Allergy and atopy. Classification of allergens.

44. Allergy diagnosis, laboratory tests, skin and provocative tests.

45. Principles of antiallergic therapy. Immune methods of treatment.

46. Specific immunotherapy. Mechanism of action, indications and contraindications, prognosis of efficacy.

47. Pollinosis, allergic rhinitis, allergic conjunctivitis. Etiology, immunopathogenesis, clinical manifestation, diagnosis, therapy.

48. Drug allergy, immunopathogenesis, clinical manifestation, diagnosis, therapy and prophylactic.

49. Characteristic of pseudoallergy, Differential diagnostic. Mechanisms of histamine liberation in pseudoallergy development, treatment.

50. Pseudoallergy in complement activation impairment. Arachidonic acid metabolism disorders. Principles of treatment.

51. Non-atopic diseases: types, immunopathogenesis, immunodiagnostic, clinical manifestation and differential diagnosis.

52. Cell-mediated allergic diseases (serum disease, Arthus phenomenon, allergic alveolitis): immunopathogenesis, clinical manifestation, immunodiagnostic, immunotherapy

53 Bronchial asthma: etiology, immunopathogenesis, up-to-date classification, clinical manifestation, treatment.

54. Atopic forms of BA: clinical manifestation, diagnostic, treatment.