MINISTRY OF HEALTH OF UKRAINE
Vinnytsia National Pirogov memorial Medical University

"Approved"
by Methodical Council
Department of Tuberculosis, Clinical Immunology
and Allergy
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Guidelines

for independent preparation for practical classes for 5th year medical students

Topic № 4

Academic discipline	**"Clinical immunology and allergology"**
Module №1	"Clinical immunology and allergology"
Content module № 1	Immune status, age features. Immunodeficiency and other immunodependent diseases principles of diagnosis, immunotherapy, immunoprophylaxis and immunorehabilitation.
Topic of the lesson	Congenital and acquired immunodeficiencies. Basic concepts of other immune-dependent diseases (transplant immunology, post-vaccination reactions and complications).
Course	5th
Faculty	"Medical business", "Pediatrics", "Medical and preventive business"
Number of hours	2

I . Relevance of the topic : Despite significant advances in basic medicine, including immunology, development of new technologies for diagnosis and treatment of immunopathology in recent decades, the prevalence of immunopathology (immunodeficiencies, allergic, autoimmune, lymphoproliferative (tumor) diseases).

Diagnosis of immunodeficiency has become a global medical and social problem. According to the European Association of Immunodeficiencies, the prevalence of genetic (primary) immunodeficiencies is 1: 250-500, severe immunodeficiencies - 1:10 000. Thus, the number of these patients in Europe should be 1 million 300 thousand patients, and in Ukraine - about *20 thousand,* on the dispensary register only about 1000, and patients of adult age about 110. Persons with the general variable immunodeficiency which is shown in adulthood, there should be about 2 thousand of them in Ukraine, and 12 cases are verified. According to Russian experts, the frequency of primary immunodeficiencies is 3: 1000 newborns, but the list of individual nosological forms and gene mutations reaches hundreds per 1000 population. Due to the growing incidence of tumors in Ukraine over the past 5 years by 25% oncoimmunology has taken a special place among the areas of fundamental immunology. There is a great need to study the mechanisms of immune surveillance in the tumor process and the creation of immunotherapeutic agents. The prevalence of autoimmune pathology, compared to other nosologies is insignificant (8-17%), it is not the cause of high mortality as oncopathology or cardiovascular disease, however, this pathology is the main factor in the disability of people of working age.

Today, knowledge about the immunological causes of infertility, immunological mechanisms of infertility, conflicts "mother-fetus" and "mother-father" of immune genesis, immunotherapy in obstetric and gynecological practice are especially important.

II. Learning objectives of the lesson .

Students must:

1. Conduct surveys and physical examinations of patients with congenital and acquired immunodeficiency.
2. To determine immunopathogenetic factors in the development of immune-dependent diseases.
3. To substantiate the use of basic immunodiagnostic methods used in clinical immunology, to determine the indications and contraindications for their implementation in patients with various immune-dependent diseases.
4. Interpret the donor-recipient pair phenotyping data (histocompatibility index determination) in preparation for organ and cell transplantation.
5. To substantiate the use of immunosuppressive therapy in the posttransplant period.
6. Identify clinical and laboratory signs of subacute, acute and chronic rejection crises.
7. Carry out a differential diagnosis between the crisis of rejection and infectious complications in patients after organ transplantation.
8. To determine laboratory signs of development of systemic and local immunosuppressive mechanisms in normal pregnancy.
9. To determine the mechanisms of development of immune-dependent forms of infertility.
10. Interpret the data of phenotyping of male-female pairs (determination of histocompatibility index) in the diagnosis of immunocompromised form of infertility.
11. Analyze the results of determining the indicators that characterize the factors of antiblastoma protection in a patient with suspected tumor.

12. Interpret the data of determination of tumor-associated antigens for early diagnosis of tumors, in assessing the effectiveness of treatment and to determine the presence or absence of metastases;
13. To substantiate the use of immunotropic therapy in patients with tumors;
14. Be able to use clinical and immunological criteria in the diagnosis of autoimmune pathology;
15. To determine the main immunological mechanisms in the development of autoimmune diseases;
16. To substantiate the use of immunosuppressive therapy in patients with autoimmune pathology;
17. Demonstrate mastery of moral and deontological principles of a medical specialist and the principles of professional subordination.

III. Individual development goals (educational goals)

To form students' sense of responsibility for the timeliness and correctness of professional actions in the diagnosis of immunodeficiency diseases and other immunopathology. Based on deontological principles to teach a young specialist to establish psychological contact with the patient and his family.

And V . Interdisciplinary integration

p / p	Discipline	Know	Be able
2	Normal anatomy	Organs of the immune, sexual and endocrine systems	be able to examine the organs of the immune, sexual and endocrine systems
3	Histology and embryology	Tissues and cells of the immune system, reproductive system (egg and sperm); tissues of the ovary, zygote, trophoblast, amnion, chorion, fetoplacental complex, other organs and systems.	Microscopically distinguish between tissues and cells of the immune system, reproductive system and other systems.
4	Normal physiology	The main functions of the immune system, the functions of the reproductive systems of men and women Blood groups by ABO and Rh systems	Indicate the main methods of assessing the reproductive system of women and men To determine the blood groups according to the ABO, Rh systems to detect during testing
5	Endocrinology	Thyroiditis, Addison's disease, insulin-dependent diabetes mellitus: clinical and laboratory manifestations	be able to diagnose
6	Genetics	HLA system Genealogical anamnesis	be able to prescribe methods of genetic testing
7	Pathological physiology	Immunopathological reactivity, changes in the proteinogram, leukogram in ID. Structural changes of organs under the conditions of tumor processes Definition of the concepts "tumor" and "tumor process", chemical, physical, viral carcinogenesis, the interaction of tumors and the body. Causes and mechanisms of reproductive dysfunction in men and women associated with their immune system. Immune aspects of autoimmune pathology, tansplvntatsionnogo immunity.	interpret blood tests, proteinogram, immunogram for ID and tumors; microscopically evaluate the morphological signs of oncopathology. Assess diseases and syndromes of the reproductive systems of men and women that are associated with immune system disorders
8	Hematology	Autoimmune hemolytic anemia, thrombocytopenia, agranulocytosis: clinical and laboratory signs	be able to diagnose

7	Pulmonology	Exogenous allergic alveolitis, sarcoidosis, fibrosing alveolitis: clinic, diagnosis, treatment	be able to diagnose
8	Propaedeutic therapy	Know the approaches to the examination of organs and systems	Conduct palpation, percussion of organs
9	Rheumatology	Criteria for RA, SLE, SCD, rheumatism	to conduct a clinical examination of patients
10	Neurology	Criteria for multiple sclerosis, myasthenia gravis	to conduct a clinical examination
11	Obstetrics	Problems of infertility with immune mechanisms Immunoconflict syndromes	Detect immune-dependent diseases, complications, immunoconflict syndromes in women
12	Oncology	Features of examination of organs and systems of patients with suspected oncopathology	Evaluate the results of clinical, laboratory and instrumental methods of examination of patients with suspected oncopathology
thirteen	Pharmacology	The main groups of immunosuppressants, immunomodulators. Rules for writing prescriptions	prescribe prescriptions, prescribe adequate treatment

V . Contents of the lesson topic.

The teacher reminds students of the importance of a carefully collected history, talks about the influence of trigger environmental factors on the formation of immunopathology.

Educational questions:

5.1 Immunodeficiency

1. Classification of ID
2. Clinical-anamnestic and laboratory diagnostic criteria.
3. Treatment of immunodeficiencies

5.2 Tumor immunology

1. Tumor antigens
2. Mechanisms of tumor recognition of tumor antigens
3. Effector mechanisms of the immune response against tumor cells.
4. Immunological mechanisms promoting tumor growth.
5. Laboratory immunological diagnosis of tumor processes.
6. Immunotherapy of tumors.

5.3 Immunopathology of reproduction

1. Antigens of sperm and egg.
2. Immune status of pregnant women, immunology of lactation.
3. Immune-dependent forms of infertility in marriage and their immunodiagnostics.
4. Immunological mechanisms of miscarriage.
5. Immunological conflicts in the system "mother-fetus": diagnosis, treatment, prevention.

5.4 Transplant immunity

1. Phenotyping of the donor-recipient pair (determination of the histocompatibility index) in preparation for organ and cell transplantation.
2. The use of immunosuppressive therapy in the posttransplant period.
3. Clinical and laboratory signs of development of superacute, acute and chronic crises of rejection.
3. Differential diagnosis between rejection crisis and infectious complication in patients after organ transplantation.

5.5 Immune aspects of autoimmune pathology

1. Signs of autoimmune disease.
2. What is immunological tolerance, maintenance mechanisms and causes of its failure.

3. Congenital immunodeficiencies that contribute to the development of autoimmune pathology.
4. Principles of treatment of autoimmune pathology, new immunosuppressive drugs.

5.1 Immunodeficiency is a disease associated with persistent immune response disorders, which are characterized by an increased susceptibility to infectious and oncological diseases, especially in children and young adults. In most developed countries of the world, including Ukraine, there is a decrease in the level of immunological reactivity due to various reasons: genetic, environmental, social and so on. As a result of immunodeficiency, infections develop, which have a tendency to chronic the process, the formation of complications, which leads to high levels of disability and mortality, including among children. In addition, disorders of the immune system can be manifested by the formation of malignant tumors (primarily lymphoma), allergy, autoimmune diseases, especially in children and young people.

Immunodeficiencies are divided into genetic (primary) and acquired (secondary). Primary immunodeficiencies are formed as a result of genetic mutations, acquired as a result of long-term exposure to toxic factors (drugs, environmental factors, chemically contaminated water, food), lymphotropic infections (HIV, hepatitis B, C viruses, herpes virus group). They run under the guise of many chronic diseases in association with viral and polyvalent bacterial infections, often in a generalized form. It is necessary to emphasize the fact that if at the beginning of the century the ratio between chronic and acute diseases was 10:90, at the present stage this ratio is 90:10.

5.1.1 Classification of ICD-10:

Primary (congenital):

• hereditary (genetically determined **)** ***D 80-83 ;***

• congenital, formed antenatally ***D 80-83 ;***

Secondary:

• acquired immunodeficiencies (formed intra- and postnatally):

- HIV - associated,
- HIV - non-associated ***D 84.8; D 84.9;***

Other disorders involving immune mechanisms ***D 89.8; D 89.9.***

Immunodeficiency diseases can also be classified according to the defect of the corresponding immune system: macrophage-monocyte, complement system, cellular, humoral units or a combination thereof. The etiological factors of immunodeficiency diseases are genopathy, fetopathy and embryopathy. Unlike primary, secondary disorders of the immune system are not associated with genetic defects, but depend on the impact on the body of harmful environmental factors (ionizing and non-ionizing radiation, chemical pollution, unbalanced diet, stress, etc.), infections. Primary immunodeficiencies are characterized by persistent clinical (sometimes have characteristic clinical markers) and laboratory immunological features and are difficult to treat (pathogenetic, etiotropic). Acquired IDDs, especially immunodeficiency disorders, which are usually transient (unstable), may disappear after cessation of the harmful factor and / or adequate etiotropic, pathogenetic or immunotropic treatment.

The general practitioner can detect signs of IDD on the basis of clinical and anamnestic data (determination of causal factors, clinical signs, family, immunological, vaccine, somatic anamnesis), objective examination, results of skin tests with T-dependent antigens (tuberculin, fungal allergens) and laboratory immunological monitoring (determination of the absolute number of leukocytes, neutrophils, lymphocytes and platelets; serum immunoglobulins of the main classes IgA, IgM, IgG; hemolytic activity of complement CH50, which are screening laboratory tests). A summary analysis (3 or more signs) of these data may lead the physician to believe that the patient has signs of immunodeficiency (primary, secondary) or VIDS. Scientific

research and practical experience show that among IDUs there are more acquired immunodeficiency disorders than immunodeficiencies (primary, acquired).

5. 1 . 2 K line-anamnestic criteria IDZ

I . Etiological and pathogenetic factors of development: stress, infections, harmful factors of the external environment of physical and chemical nature, metabolic (alimentary, hypoxic, endocrine), depletion of antioxidant system as a result of chronic infection, radiation damage, diseases of internal organs - toxic effects radical oxidation: blockade of enzymes, their inactivation, intoxication of various genesis; iatrogenic factors of different genesis: long-term use of drugs that have immunosuppressive effects of hormonal drugs (glucocorticoids, contraceptives, etc.), cytostatics, antivirals, antibiotics, etc., surgery (especially on the immune system), injuries, burns.

II . The essence of the complaints of patients with signs of VIDS is diverse and depends on the leading clinical and anamnestic syndrome (infectious, allergic, autoimmune, lymphoproliferative), chronic fatigue.

The main complaints are fever for more than 12 days of unclear origin, constant fatigue, independent of physical and intellectual load, frequent respiratory diseases, enlargement of peripheral lymph nodes, rashes on the skin and mucous membranes, myalgia, arthralgia and more.

III . History and disease:

Infectious symptoms:

- increased frequency of uncomplicated infectious diseases caused by common pathogenic infectious agents: acute infectious diseases of the respiratory tract, oral cavity, bronchitis (6 or more cases during the year);
- frequent development of complications of acute inflammatory diseases of the ENT organs and respiratory tract: sinusitis, otitis, pneumonia (2 or more during the year);
- frequent development of complications of acute inflammatory processes of the genitourinary tract (4 or more times a year);
- atypical course of infectious diseases;
- infectious diseases caused by weakly virulent (low pathogenic), atypical and opportunistic pathogens;
- frequent recurrences of labial and / or genital herpesvirus infection;
- activation of sluggish (latent) infections with systemic clinical manifestations and a predominant predisposition to lesions of the nervous system and visual organ (Epstein-Barr virus, cytomegalovirus, toxoplasma);
- mixed forms of infections; change of the causative infectious agent during the disease;
- systemic mycoses;
- recurrent dysbacteriosis;
- development of purulent processes of the skin and / or internal organs: generalized pyoderma, furunculosis, carbuncles, phlegmons, deep abscesses, recurrent paraproctitis;
- urogenital infections (chronic purulent vulvitis, adnexitis, pyelonephritis with frequent exacerbations;
- gastroenteropathy with chronic diarrhea of unclear etiology, dysbiosis;
- protozoan and helminthic diseases (malaria, toxoplasmosis, trichinosis, leishmaniasis, trypanosomiasis, schistomatosis, etc.);
- bacterial infections (tuberculosis, ret. pneumo-, meningo-, staphylococcal, gonococcal, etc.);
- viral infections (measles, rubella, influenza, mumps, etc.);

- development of osteomyelitis, meningitis, sepsis, peritonitis (2 or more);
- resistance to standard schemes of etiotropic and pathogenetic therapy (for 2 or more months of treatment);
-need for "reserve" antibiotics, and / or the need for pre-existing infusions of anti-infective drugs;
Clinical immunological signs: prolonged hyper-, hypothermia; regional or systemic lymphadenopathy; chronic lymphadenitis; hyper-, hypo-, aplasia of the tonsils; splenomegaly, hypo-, asplenia; prolonged hepatomegaly, not associated with toxic factors and hepatotropic viruses (more than 1 month); cryopathy syndrome; chronic fatigue syndrome; autoimmune complications and exacerbation of infectious diseases after vaccination; increased fatigue, inadequate physical, intellectual and other loads for six months or more.
Other clinical signs: malabsorption syndrome; rapid change in body weight; signs of premature aging; long-term tissue regeneration; early formation of oncological diseases; autoimmune endocrinopathies; hypo / hyperpigmentation of the skin; focal or total alopecia; ineffectiveness of standard methods and treatment schemes.
Family history:
- unexplained cases of death of infants and young children associated with infection, cystic fibrosis, etc .;
- chronic and recurrent infections in relatives (tuberculosis, etc.);
- allergic, autoimmune, endocrine diseases and malignant neoplasms in the family;
-.blood relationship of parents.
Vaccine history:
1. The occurrence of a disease against which vaccination has been carried out (eg, measles).
2. Occurrence of post-vaccination reactions and complications (especially from the nervous system).
3. Low titers of specific antibodies 3 weeks after vaccination.
Clinical and anamnestic guidelines that allow to clarify the damaged part of the immune system:

- manifestations of **insufficiency of the macrophage-monocytic system:** recurrent chronic **purulent** infections of the skin, mucous membranes, lymph nodes, bones, joints, bronchi and other organs and systems; generalized infections (sepsis);
- manifestations of **cellular immunity:** recurrent chronic viral, fungal, parasitic infections; malignant neoplasms (lymphomas, lymphosarcomas, lymphocytic leukemia, lymphogranulomatosis, etc.);
- manifestations of **humoral immunity deficiency** chronic recurrent bacterial infections of the skin, conjunctiva, accessory sinuses, middle ear, bronchi, lungs, pleura, gastrointestinal tract, urinary and biliary systems; atopic dermatitis, bronchial asthma, hay fever; autoimmune pathology (rheumatoid arthritis, aggressive hepatitis, etc.).

Skin tests with T-dependent antigens

Normally, in response to intradermal injection of T-dependent hypertension (tuberculin, candida, etc.) after 24-72 hours at the injection site is registered papule (blister) up to 5 mm **Negative** skin tests for all administered antigens indicate a decrease in the functional activity of cellular immune factors. Local immunological reaction - 5-30 mm indicates **sensitization** (delayed type hypersensitivity) to the causative antigen and, thus, the preservation of the functional activity of the cellular immune system. Today in Ukraine it is possible to use the following T-dependent antigens: tuberculin, allergens of opportunistic fungi:

Alternaria, Aspergillus mixed, Cladosporium, Chrisonilla, Monilia, Penicillinum, Botrytis cinerea).

Laboratory signs

1. Long-term changes of blood cells and humoral immunological parameters common (more than 1 month): *leukopenia, lymphopenia, lymphocytosis, neutropenia, monotsitoz, hemolytic anemia, thrombocytopenia, hypogammaglobulinemia, hipoimunohlobulinemiya G , hypo / hiperimunohlobulinemiya M hipoimunohlobulinemiya A.*

2. Delayed ESR on the background of bacterial infections.

3. Lower protective levels titers of specific antibodies 3 weeks after vaccination.

4. Steady changes in cellular immunity (in vivo, in vitro).

5.1.3 Treatment of immunodeficiencies : 1) Immunoglobulins intravenously. **2)** Etiotropic: antibacterial, antiviral, antifungal. **3)** Bone marrow transplantation. **4)** Gene therapy. **5)** Cytokine therapy. **6)** Possible metabolic and thymic immunostimulants (based on persistent changes in the immunogram).

5.2 ***Immunopathology of tumors***

5.2.1 Tumor antigens - is pathologically changed (under the influence of physical, chemical, viral and other factors) avtoantyheny human body. Divided into groups:

- antigens present in both tumor and normal unaltered cells (eg antigen encoded by the CAMEL gene, presented by HLA-A2 particles, has the epitope MLMAQEALAFL, present on melanoma tumor cells and normal cells of the testis, placenta, heart, skeleton, tissue, pancreas);

- differentiated antigens that are present on tumor cells and on normal cells from which the tumor originates ;

- "common" antigens present in tumors of several types (eg antigen encoded by the MAGE-A1 gene, presented by HLA-A1 particles, has the epitope EADPTGHSY, present in melanoma cells, breast tumors, lung tumors);

- tumor-specific antigens present only on tumor cells (usually human tumors do not have specific tumor antigens, but there are exceptions, such as beta-catenin altered due to point mutation, presented by HLA-A24 particles, having the epitope SYLDSGIHF present only on the cells of some types of melanoma);

- antigens called oncofetal , present on embryonic tissues, normally disappear during the period of differentiation (alpha-fetoprotein, cancer-embryonic antigen).

- **Tumor-specific transplant antigens** play a significant role in tumor rejection by forming a cellular immune response, they are different in tumors that occur under the influence of carcinogens and identical in tumors that occur under the influence of oncoviruses.

A separate category of tumor antigens are **antigens present in tumors in the pathogenesis of which viruses are involved:**

5.2.2 **Mechanisms of immune recognition of tumor antigens :**

- p -lymphocyte recognition (for antigens , in most cases presented by MHC class 1 molecules to CD8 + T lymphocytes) (suppressors). It is known that reduced expression or absence of MHC class I molecules on tumor cells correlates with malignant neoplasms. which are also presented by MHC class II molecules to T CD4 + lymphocytes (helpers), tumor antigens were found, which are presented by different HLA-DR molecules);

- with the help of antibodies is the recognition of the following tumor antigens:

a / antigens of B-cell lymphomas with receptors CD 19, CD 20, CD 21, CD 22, CD 37;

b / cancer-embryonic antigen (CEA with CD 66e receptor, present in tumor cells of the colon, pancreas, stomach);

c / alpha-fetoprotein (on tumor cells and on normal cells of the liver, gallbladder);
g / tumor antigen CA-125 (present on tumor cells of the ovary, pancreas, lungs);
d / prostate-specific antigen (PSA) (present on both embryonic cells and prostate tumor cells).

5.2.3 Effector mechanisms of the immune response against tumor cells.

Immunological mechanisms of tumor suppression (anti-blastoma factors):

- activity of NK cells;
- action of T-lymphocytes-cytotoxic;
- the effect of cytokines synthesized by T-lymphocytes (including T-helpers);
- cytotoxic effect of activated macrophages and neutrophils;
- the effect of cytokines synthesized by macrophages;
- cellular cytotoxicity, dependent on antibodies;
- complement-dependent cytotoxicity of antibodies.

Natural antitumor mechanisms can be grouped into two directions of their action:

- activation of monocyte / macrophage functions (ie activation of T-helpers; synthesis of interleukin-12, which activates Tx1 and NK; secretion of proinflammatory cytokines IL-1, IL-6, TNF-alpha, increased inflammation and integration of protective forces)

- activation of T-helpers (their synthesis of IL-2, which stimulates the proliferation of T-helpers, T-cytotoxic, monocytes / macrophages, NK cells; their synthesis of IFN-gamma, TNF-alpha to affect the antitumor properties of monocytes-macrophages); synthesis of IL-3 and colony-stimulating factors to stimulate hematopoiesis).

5. 2.4 Immunological mechanisms promoting tumor growth .

Immunosuppression: exogenous origin (some drugs, viral infections); endogenous origin (suppressor cells and suppressor factors).

Immunoselection:

- reduced expression of MHC molecules, lack of costimulating molecules CD 80 and CD 86 on tumor cells;
- weak immunogenicity of tumor antigens, the presence of various tumor antigens on the primary tumor and metastatic cells
- formation of soluble forms of tumor antigens
- tumor cells, losing the receptor for TNF, become resistant to apoptosis
- on tumor cells, the expression of receptors for growth factors increases

Immunomodulation (avoidance of immunological surveillance): masking of antigens on tumor cells; formation of complexes of tumor antigens with specific antibodies and blocking of the corresponding effector cells; stimulation of tumor cell growth by specific antibodies present in small quantities; opsonization and destruction of cells capable of phagocytosis of tumor cells; activity of antiidiotypic antibodies; stimulation of tumor cell growth by lymphocyte synthesis products, etc.

A special immunological phenomenon that contributes to the development of a tumor is called **"immunological haste** ". It is implemented by the following mechanisms:

5.2.5 Laboratory immunological diagnosis of tumor processes

Before carrying out specific laboratory methods of determination of tumor antigens **it is necessary to define the general condition of immune system of the patient, and to consider age critical periods of development of tumors:**

1 / .Children's age (period of formation of the immune system)
2 / .Youth age (adjustment of hormonal regulation of the immune system)
3 /. Elderly age (period of reduced activity of the immune system)

According to the WHO, 60% -70% of the total number of tumors occur during these periods of life.

Laboratory markers of malignant growth are:

- tumor-specific antigens (PSA in the early stages of prostate cancer, CA 19-9 in cancer of the gastrointestinal tract, pancreas,

CA-125 for breast and ovarian cancer, CA 15-3 for breast cancer bets)
- other antigens (eg P-53 in bladder tumors, SCC in lung cancer, esophagus and rectum)
- cancer -embryonic antigen (is a marker of cancer of the colon, liver, pancreas, stomach, thyroid and breast, bladder)
- hormones (eg beta-chorionic gonadotropin in chorionomas, tumors of the uterus, testicles)
- enzymes (eg LDH)
- glycoproteins (eg alpha-fetoprotein in hepatocellular cancer)
- lipids
- proteins (eg acute phase: lactoferrin increases in Hodgkin's disease, lymphosarcomas, CRP- in all tumors)

5.2.6 Tumor immunotherapy. The main principle of immunotherapy in cancer patients is the support of traditional methods of treatment (surgical removal of tumors, chemotherapy and radiotherapy). **Only in some cases immunotherapy can be the first level of treatment.**
Tumors that can be treated with immunotherapy : melanoma, kidney cancer, non-Hodgkin's lymphoma, hairy cell leukemia, rectal cancer, ovarian cancer, glioma, soft tissue sarcoma.
Forms of tumor immunotherapy :
1 /. A ktyvna : specific - supply of patient tumor cells or antigens. Antitumor "vaccinations" - in the classical form the patient is given irradiated or killed autologous or allogeneic tumor cells or their extracts, in a modified form tumor cells or antigens are fed with adjuvants or cytokines (IL-2, IL-3, GM-CSF). Vaccinations are best for treating tumors that have well-defined antigens (eg, melanoma). The latest generation of "vaccinations" - the introduction of genetic engineering methods to tumor cells (for cytokines IL-2, IL-4, IL-7, GM-CSF, TNF, IFN-gamma for molecule B 7.1) and molecules of tumor-associated viruses .
- nonspecific - activation of the patient's immune mechanisms by immunostimulating drugs, including cytokines; This is achieved by administering to the patient immunostimulatory drugs (BCG, levamisole) or cytokines (TNF, IL-2, IL-4, IL-12, interferons in various combinations and as monotherapy); combination of cytokines and cytostatics
2 /. **P asyvna** : administering to a patient-specific **monoclonal antibodies** often specifically zmodyfikovanyh (modified monoclonal antibody structure reduces its molecular weight and immunogenicity).
3 / Adaptive : intravenous or topical administration to the patient of immune cells: a / TIL-lymphocytes (lymphocytes infiltrating the tumor), isolated and cultured with the addition of IL-2; b / LAC (lymphokine-activated killers themselves or with cytokines); in / monocytes of the patient.

5.3.1 Immunotology of reproduction.

Sperm antigens : superficial: provide interaction with the egg
- the main PH-20 (on the acrosome) binds to the corresponding receptor on the egg
- secondary PH-30 (fertilin) is responsible for the penetration of sperm into the egg, these processes are mediated by C1qR, CR3, FcR, CD46
acrosomal : participate in the further interaction of gametes (penetration of the transparent zone).
- TLX (trophoblast-lymphocyte-cross-reactive), it is also called protein membrane cofactor MCP or CD46 - binds and inhibits the complement component C3b and C4b
sperm nucleus antigens (internal): histones that are in the process of spermatogenesis transformed into protamines
HLA-system antigens : the surface of the sperm contains mainly classical HLA-A, B, C particles, and the cytoplasm contains non-classical E, F, G, which provide immunological tolerance (HLA-E).
Immunological properties of sperm:

- inhibition of sperm antigen presentation by monocytes and macrophages
- inhibition of the enzymatic activity of macrophages and neutrophils
- decrease in activity of T-l, B-l, NK-l
- attenuation of antibody- and complement-mediated cytotoxic reactions.

Egg antigens are mainly antigens of the transparent zone (Zona pellucida) ZP-1, ZP-2, ZP-3. Their main functions: **ZP -1** is a characteristic glycoprotein of the outer surface of the egg; **ZP -2** binds to trypsin-like proteinase, causes limited proteolysis and "hardening" of the transparent zone (inhibition of polyspermia); **ZP - 3** recognizes and binds sperm, induces an acrosomal reaction in sperm.

An acrosomal reaction is the destruction (under the influence of proteases, lipases, phosphatases, glycosidases) of the inner acrosomal membrane of sperm, which ensures the interaction of gametes, ie the penetration of the transparent zone of the egg.

The process of egg maturation occurs due to the immunoregulatory functions of the glandular cells of the ovary. Glandular ovarian cells:

- interact with factors of the immune system (cytokines synthesized by macrophages in ovarian tissue, promote the formation of stimulating factor SC, which accelerates the maturation of the follicle);
- IL-1 and IL-2, synthesized in macrophages in ovarian tissue, inhibit estriol synthesis 17 beta, luteinizing hormone and progesterone, are indirectly regulated menstrual cycle.

5.3. ***2. Immune status of pregnant women***

Adaptation mechanisms that help keep the fetus in the circumstances of physiological pregnancy:

- **immunologically prepared uterus** in connection with weakened reactions of T-cell immunity (suppressive effect of hormones: human chorionic gonadotropin, placental lactogen; steroid hormones: alpha-fetoprotein, proteins from the group of alpha-2-globulins, P protein of pregnancy; proteins from the group of beta-2-globulins: proteins SP-1,2,3, pregnancy-specific beta -globulin, beta 1-glycoprotein);
- **isolation of fetal-uterine circulation** with small penetration of cells in both directions
- **the presence on the trophoblast of nonclassical histocompatibility antigens** HLA-E, F, G (with a weak ability to present the antigen), especially HLA-G, which blocks the activity of NK cells;
- synthesis of trophoblast factors that contribute to the **resistance of the trophoblast** to the action of cytotoxic antibodies and antigen-antibody-complement complexes (such as MCP, DAF, protectin);
- **synthesis of suppressor factors** (prostaglandins) by **endometrial macrophages**
- **increase** in the endometrium of the uterus and placenta of **cells with regulatory / suppressive function**
- synthesis by endometrial cells and blastocysts of **immunoregulatory factors promoting implantation (LI F and mucin)**
- accumulation around the implanted blastocyst of **large granular lymphocytes** (with Fc R and CD56 receptors), which release suppressor factors similar to TGF-beta (which block the formation of T-cytotoxic lymphocytes and activation of NK cells, secretion of macrophages by macrophages).)
- **restructuring of systemic immunity** - change in the ratio between helper (downward) and regulatory / suppressor T-lymphocytes (upward), the predominance of 2nd-order T-helpers on 1st-order helpers

Based on modern knowledge about the cytokine regulation of fetal development, an **"immunotrophic hypothesis" has been** formed . This hypothesis is that the process of recognition of fetal and placental antigens by the maternal immune response (actually

T-lymphocytes) leads to the local release of cytokines such as IL-3 and G-CSF, M-CSF, which promote the growth of fetal and placental tissues. .
There are three options for the development of these tissues under the action of various cytokines: immunodystrophy, immuno-
trophy, immunosuppression . **Immunodystrophy** (inhibition of fetal and placental tissue growth) is observed in tissue infiltration by macrophages and cytotoxic cells and
synthesis of their corresponding cytokines), **immunotrophy** means the promotion of certain cytokines in the growth of fetal and placental tissues, **immunosuppression** means actually maintaining
immunodystrophy by cytokines, hormones and prostaglandins.

5.3.3 Immunology of lactation

Lactation is an energy-efficient mechanism that ensures the rational feeding of children in the 1st year of life, because breast milk contains active protective substances and is an ideal food for the newborn.

Colostrum is a sticky yellowish liquid that fills the alveoli of the breast during the last trimester of pregnancy and is produced for several days after birth. Its amount varies from 10 to 100 ml per day, gradually increases and reaches the composition of **mature milk** in 30-40 hours after birth. Colostrum contains less lactose, fat and water-soluble vitamins than mature milk, but has more protein and fat-soluble vitamins (A, E, K) and more certain minerals (sodium, zinc). It has a high content of immunoglobulins and other protective factors.

Antiviral factors contained in breast milk

Factor	Active until:
Secretory Ig A	Papillomaviruses types 1, 2, 3 Coxsackie viruses of types A9, B3, B5 Rotavirus, cytomegalovirus, reovirus type 3, rubella virus, herpes viruses, mumps virus, influenza viruses, respiratory syncytial virus
Ig M, Ig G, Ig G1	Rubella virus, cytomegalovirus, respiratory syncytial virus
Unsaturated fatty acids and monoglycerides	Herpes viruses, influenza viruses, encephalitis virus
Macromolecules of non-immunoglobulin nature	Herpes viruses, vesicular stomatitis virus, Coxsackie virus B4, reovirus №, cytomegalovirus, respiratory syncytial virus rotavirus
Alpha-2-macroglobulin (similar)	Influenza virus, mumps virus
Ribonuclease	Murin leukemia virus
Hemagglutinin inhibitors	Influenza and mumps viruses
The product of the synthesis of "milk" cells	Is interferon induced by rubella, herpes, measles, mumps, respiratory syncytial viruses

5 .3 .4 . Immune-dependent forms of infertility in marriage

The causes of infertility in marriage are:

- chronic inflammatory processes of the genitals (75%) (acquired immunodeficiency of infectious origin)
- imbalance of endocrine-immunological mechanisms, which leads to the development of acquired immunodeficiency (10%)
- causes of infertility of unknown etiology (10%)
- immunological causes of infertility (5%), mainly due to the formation of antibodies to sperm and increased histocompatibility of couples with the HLA system (relative infertility)

5.3.5 Immunological mechanisms of miscarriage:

***A)* Reactivity of maternal lymphocytes against hemisphere graft (embryo) with a high degree of histocompatibility between parents:**
- insufficient number of blocking antibodies to surface antigens of the embryo of paternal origin (these antibodies protect the embryo from attack by maternal reactive lymphocytes). Most often, their insufficient number occurs in the presence of common antigens of the HLA system in both parents;
- the mother and father have an identical set of TLX complex (trophoblastic leukocyte cross-reactive antigens), resulting in a lack of sufficient immunogenicity to induce a protective immune response from the mother;
***B)* Infertility due to an increase in the number of NK cells** with CD57 + molecules, and a decrease in the number of NK cells with the CD16- / CD56 + phenotype, which secrete cytokines that stimulate placental development;
***B)* Autoimmune reactions and inflammation in the mother:**
- the presence of antiphospholipid antibodies (can cause placental vascular thrombosis and its premature separation);
- the presence of a large number of immune complexes - the trigger of development systemic inflammatory response syndrome (SIRS) in late preeclampsia;
- the presence in the mother of specific Ig G antibodies in certain autoimmune diseases (eg type 1 diabetes, systemic lupus erythematosus, thrombocytopenia, autoimmune thyroid disease, Miastenia gravis) can induce disease in the fetus.

5.3.6 Immunological conflicts "mother-fetus": diagnosis, treatment, prevention
- **intergroup conflict** (in case of incompatibility of mother and fetus according to the ABO system, fetal erythrocytes immunize the mother and initiate the production of antigroup antibodies);

Most often, intergroup conflict is observed if the mother's blood group is 0 (1), and the fetus A (II). Other types of incompatibilities in the ABO system have no practical significance, as antigen B is not immunogenic, and, in addition, blood groups B (III) and AB (IV) are much less common. Clinically, the conflict is manifested by the threat of abortion or miscarriage. **Treatment** : intravenous infusions of maternal neohemodesis, polyglucin, reopolyglucin to reduce the titer of alpha-isoantibodies to antigen A1. **Prevention** : only the first pregnancy of this kind threatens the embryo, in re-pregnancy cytotoxic antibodies rarely have a negative effect on the fetus
- **rhesus conflict** due to incompatibility of the pregnant woman and the embryo on rhesus antigen (D)
and develops when the fetus is rhesus-positive and the mother is rhesus-negative; anti-D antibodies are cytotoxic. **Diagnosis** : performed by collecting medical history and detecting anti-D antibodies after childbirth and during subsequent pregnancies. **Treatment:** administration of anti-Rh-Ig G. **Prevention:** specific prevention is carried out by human anti-rhesus Ig G.

5.4 Transplant immunity, graft-to-host conflict
There are the following types of transplantation: autotransplantation - transplantation of own tissues; allotransplantation - transplantation of organs and tissues within the same biological species; xenotransplantation - transplantation of organs and tissues of different biological species; isotransplantation - transplantation between identical twins or between genetically identical animals.
And due to the fact that the donor cells carry on their surface, antigens that are different from the antigens of the recipient, the immune system of the latter develops an immune response to the graft. As a result, a **graft rejection reaction** is formed **.**
The way that a greater or lesser extent reduces resentment is **selection (selection) pairs for the donor-recipient antigens histosumis t ness** that humans are united in HLA (Human leucocyte antigens). They are also called transplant antigens.

To assess the degree of histocompatibility, a histocompatibility index was proposed. With one identical HLA antigen in the recipient donor, the histocompatibility index is 25%, with two - 50%, with three 75%, with four -100%. The degree of histocompatibility of antigens of the so-called classical HLA loci is evaluated. In fact, selection involves the selection of a donor-recipient pair, in which the donor differs the least from the recipient in antigens of the HLA system. In order to detect the HLA phenotype, the peripheral blood of the donor and recipient lymphocytes is typed.

Lymphocytotoxicity test in the micro modification of Paul Terasaki is used for typing of lymphocytes on class I antigens (HLA-A, B, C) . To detect class II antigens (HLA-DR, DP, DG) use a *prolonged lymphocytotoxic test with a suspension of cells enriched in B-lymphocytes* on the surface of which these antigens are present.

Selection of the donor-recipient pair, in addition to selection for HLA antigens, involves determining the degree of specific and nonspecific sensitization of the recipient to the donor HLA antigens. Also, determine the input immune status (absolute number of T-helpers and T-suppressors / killers), as well as their quantitative ratio - the IRI (immunoregulatory index) of the recipient, which usually affects the posttransplant period.

Allograft, endowed with foreign antigenic structures, initiates an immune response in the recipient. As a result, a **rejection reaction** develops **, which in the clinic is called a rejection crisis.** There are rejections: 1 *) subacute,* which develops immediately after connecting the graft to the bloodstream of the recipient; 2) **acute,** developing during the first three weeks after transplantation; 3) *chronic,* which is observed in a few months or years.

The modern **scheme of immunosuppressive therapy** in allotransplantation **for the prevention and treatment of rejection crisis** often includes: 1) azathioprine (imuran) - an antimetabolite of protein synthesis; 2) corticosteroids - prednisolone, dexamethasone, hydrocortisone, etc .; 3) cyclosporine A (sandimun).

5.5 Immune aspects of autoimmune pathology

5.5.1 Signs of utoimmune disease

- ▪Manifestations of the disease depend on the mechanisms underlying the immune response, namely: cytokine profile, the formation of specific antibodies or cytotoxic lymphocytes.
- ▪The disease is prolonged chronic with signs of self-maintenance.
- ▪Circulating autoantibodies and / or delayed hypersensitivity reactions should be detected in patients with autoimmune disease.
- ▪Autoantigens that cause this reaction should be identified .

5.5.2 Autoimmune tolerance is the inability to induce an immune response autoantigen. At maturation in a thymus autoreactive cells are destroyed (negative selection). Normally, there are a small number of autoreactive cells that are designed for elimination of own autoantigens of spent cells and their structures. Upon completion their function, they die by apoptosis, so do not cause autoimmune diseases, they are only "sanitarians" of the internal environment.

Mechanisms for maintaining auto tolerance:

- ▪Thyroid rejection of autoreactive T lymphocytes.
- ▪Anatomically sequestered organs (eye, CNS, testicles, thyroid gland) have mechanisms for the destruction of autoreactive cells.
- ▪Anergy signals from antigen-presenting cells and regulatory helpers (CD4 + CD25 +).
- ▪Antiidiotypic antibodies that block actoreactive antibodies.

Disruption of immunological tolerance underlies the emergence of autoimmune pathology.

The reasons are as follows : violation of anatomical barriers; thymus dysfunction; antigenic

mimicry; modification of autoantigens by viruses, chemical and physical factors, drugs;
loss of suppressive activity of regulatory helpers (CD4 + CD25 +); congenital mutations
immunodeficiencies, polyclonal activation by superantigens (herpes viruses, LPS bacteria),
excessive circulation of autoantigens, violation of phagocytosis.

5.5.3 Congenital immunodeficiencies that cause autoimmune pathology:

- Hypo-agammaglobulinemia: (selective IgA, hyper-IgM, total variable
immunodeficiency) - cause SLE, JRA, Sjogren's syndrome, scleroderma, DM, vasculitis, diabetes mellitus, myasthenia gravis, pernicious anemia, autoimmune hepatitis, polyendoctrinopathy, primary adrenal insufficiency, autoimmune.
- Defects of C2, C4 complement - cause SLE.
- Defects of phagocytosis - cause the formation of antinuclear, antineutrophil antibodies,
autoimmune arthritis.

5.5.4 Principles of treatment of autoimmune pathology

- Replacement of lost function (diabetes, hypothyroidism).
-Imunosuppression (cyclosporine, cyclophosphamide, mercaptopurine, gold preparations, penicillamine,
plaquenil, leflunomide, glucocorticosteroids, NSAIDs, heparin, pentoxifylline, antibiotics,
chloramphenicol, rapamycin, monoclonal antibodies, antilymphocytic sera).
- Immunomodulation (thymus preparations, cytokines, antibodies to cytokines and their immunoglobulin receptors).
- Efferent methods.
- Oral administration of antigens, which stimulates tolerance through the production of sIgA.

V I. Plan and organizational structure of the lesson

The main stages of the lesson, their functions and content	Levels of assimilation	Methods of control and training	Materials of methodical maintenance	Time in minutes
1	2	3	4	5
1. <u>Preparatory stage</u> : Organization of classes Educational tasks Control of the input level of knowledge, skills: - factors of innate immunity in antitumor protection - tumor antigens and antitumor antibodies - features of the immune response (local and systemic) in women and men - to determine the main immunological mechanisms in the development of autoimmune diseases; - to interpret the phenotyping data of the donor-recipient pair (determination of the histocompatibility index) in preparation for organ and cell transplantation.	1	Frontal poll Express survey Test control (input) Individual survey (control questions)	Tests Schemes	25
2. **<u>The main stage</u>** Formation of professional knowledge, skills, abilities: 1.- be able to diagnose immunodeficiency on the basis of early criteria - to find out the main factors of immunoresistance of tumors - to present the basic principles of immunodiagnostics of tumors	2 2 2 3	Professional training in solving typical situational problems ("Step-2")	Tables, diagrams, maps of immunological observation, typical situational tasks	180

- to form the main directions of tumor immunotherapy - know the immunological conflicts of pregnancy, immunology of pregnancy, lactation - to determine immune-dependent infertility - be able to use clinical and immunological criteria in the diagnosis of autoimmune pathology; - to determine clinical and laboratory signs of development of superacute, acute and chronic crises of rejection. . 2. To master the skills of examination of a patient with immunopathology, to interpret laboratory tests and additional methods of examination. 3. To supervise the patient with immunopathology studied in class	3 3			
3. <u>The final stage</u> Control and correction of professional knowledge, skills, abilities: - to generalize the basic knowledge about the mechanisms of antitumor protection - to form the causes of immunological resistance of tumors - to list perspective directions of immunotherapy of tumors - predict immunological conflicts; - characterize the immunogram of a pregnant woman; -be able to predict the risk of miscarriage according to the immunological examination. - justify the use of immunosuppressive therapy in patients with autoimmune pathology and in the posttransplant period.	3	Testing (initial level) Individual survey Professional training in solving atypical situational problems	Tests, atypical situational tasks	20
Conducting the results of the lesson Homework for the next topic				15

VII . Methods of organizing the educational process in a practical (seminar) lesson.

7.1. Preparatory stage.

After setting specific learning objectives, the teacher monitors the entry level knowledge of natural immunity factors in antitumor protection, tumor antigens, features of the immune response (local and systemic) in women and men, the main immunological mechanisms of autoimmune diseases, the ability to interpret phenotyping donor-recipient pair (determination of histocompatibility index) in preparation for transplantation organs and cells.

7.2. The main stage

This stage involves the performance of each student independently and under the supervision of the teacher below

these practical works.

Task 1

Students conduct a survey and objective examination of a patient with immunological pathology, using examination, palpation, auscultation, percussion.

Task 2

№	Task
1.	Which of the signs characterizes primary immunodeficiency (Bruton's syndrome)?
2.	What is the basis of the graft-versus-host reaction?
3.	A pregnant woman has the flu. What is the name of the newborn's developed influenza immu
4.	Which immunocompetent cells mainly provide nonspecific resistance to tumors?
5.	What sign is not characteristic of infectious diseases in patients with combined immunodefici
6.	Which of the signs of a hemogram is characteristic of acquired immunodeficiency?
7.	What signs characterize the autoimmune syndrome of immune system dysfunction?
8.	Cells that are not targets for natural killers…?
9.	The development of autoimmune pathology is not induced…?
10.	What are the signs of acquired immunodeficiency?
11.	In what period of treatment of cancer patients it is most expedient to appoint immunostimula
12.	What is the prognosis of subsequent pregnancies in immune rhesus conflict in the first pregna A. Without dynamics. B. Increasing signs of immune conflict. B. Weakening of immune conflict. D. Disappearance of signs of immune conflict.

Task 3

1. What causes a long period of latent development of the tumor process?

A. The phenomenon of cancer in situ
B. Mutational changes in malignant cells
B. Selection of antigens on malignant cells
D. Elimination of malignant cells by immunocompetent cells
D. Differentiation of antigens.

Answer - G. Elimination of malignant cells

2. The most immunogenic tumors are those that occur under the influence:

A. Pesticides
B. Nitrates, nitrites
B. Viruses
G. Ionizing radiation
D. Radionuclides

1. ***The answer is*** V. Viruses

3. The best evidence for the importance of immune surveillance in the development of tumors process is:

A. Hereditary nature of the tumor
B. The maximum incidence of tumors in the age group from 10 to 50 years
B. Rapid transformation of healthy (normal) cells into malignant ones in vitro (where there is no immune surveillance)
D. Significant increase in the incidence of malignant tumors among people with congenital or acquired immunodeficiency
D. Association of tumor process with violation of idiotype-anti-idiotic regulation of the immune response.

Answer - D. Significant increase in the incidence of malignant tumors among persons with congenital and acquired Immunodeficiency.

4 . Which of the following cells have antitumor activity regardless of the expression of HLA receptors?

A. T-cytotoxic cells.
B. Macrophages.
B. Natural killers.
G. B-lymphocytes.
D. T-helpers.

Answer - B. Natural killers

Task 4

№ / №	***Task***
1.	The child had a combination of otitis, eczema and thrombocytopenic purpura. What is imm
2.	Bruton's disease is…?
3.	What are the signs of lymphoproliferative syndrome of immune system dysfunction?
4.	Clinical signs of which primary immunodeficiency in a child 6 months, from the first preg 1 half of pregnancy), having a convulsive syndrome with hypocalcemia, malformations system, hypoplasia of the thymus?
5.	At the patient with an autoimmune syndrome of dysfunction of immune system the immu correct answer.
6.	In which cases can rhesus incompatibility be suspected in the mother-fetus system? A. Rhesus of mother (+), father (-). B. Rhesus of mother (-), father (+). B. Rhesus of mother (+), grandmother (-).

7.	15. Causes of habitual miscarriage: the presence of TORCH-infections; hormonal and gene disorders, immunological causes; all of the above.
8.	Which of the following can reduce the intensity of immunological conflict "mother-fetus" i Rh - and the fetus Rh +: A. Neglect of the introduction of globulins anti-D mother with Rh-. B. Introduction of maternal globulin anti-D regardless of the state of its sensitivity to anti-D B. The difference in ABO antigens between mother and fetus. D. Massive ingress of blood of the newborn mother, for example during caesarean section.
9.	Specify the main function of secretory IgA in local immune protection: A. Covers the mucous membrane of the genital system, where it binds bacteria and toxins. B. Stimulates the synthesis of acute phase proteins. B. Activates the complement system. G. Activates phagocytosis. D. Binds circulating immune complexes and promotes their excretion.
10.	What types of transplants do you know?

Second level tasks

Problem №1.

The patient is 14 years old for 3 years suffering from frequent respiratory infections (8-10 times a year), has chronic recurrent herpes simplex, chronic non-obstructive bronchitis with frequent recurrences, mycosis of the feet. For 7 years he has lived in the zone of enhanced radiation control. At laboratory inspection in the general analysis of blood the leukopenia, the lymphopenia delayed ESR during an exacerbation of chronic bacterial infections is observed. By the age of 5, the child developed according to age, did not get sick.

What can these data indicate?

Answer: Acquired immunodeficiency, infectious form

Problem №2.

The boy is 2 years old. At 4 months of age after vaccination against polio, he developed right-sided hemiparesis. At 6 months he suffered from bilateral purulent otitis, at 1.5 years - twice acute bronchitis with obstructive syndrome.

Objectively: the child is lethargic, pale, the shadows under the eyes, the mucous membrane of the pharynx is pale, the posterior wall is granular, the tonsils are not visualized. In the lungs auscultatory hard breathing, no wheezing. Percussion expansion of the root of the lungs.

Laboratory: 1. Hemogram: anemia, number of leukocytes, lymphocytes - N;

2. Immunogram: - T-lymphocytes; - B-lymphocytes - the number is reduced - the level of IgG <2 g / l; IgM, IgA are not determined.

Your diagnosis?

Answer: Primary hereditary immunodeficiency, X-linked agammaglobulinemia (Bruton's syndrome).

Problem №3.

Child V., 12 years old, has had eczema since childhood with frequent colds (4-6 times a year). He suffered from all children's infectious diseases. From the age of 12 he is worried about repeated nosebleeds, otitis, for which he is regularly treated by an ENT doctor. At inspection the

delay in physical development draws attention. Height 158 cm, weight - 50 kg. The skin is dry, there are areas of depigmentation on the back and chest, traces of itching on the skin of the elbow joints, popliteal fossae and legs, eczema: cracks with areas of hemorrhage, wetting, lichenization, crust. Regional peripheral lymph nodes of small size (d-0.3), but dense consistency.

General blood test: Er. - 3,0x10 ^{12}/ l; Hb - 120 g / l; KP-0.9; leukocytes - 4.2x10 ^{9}/ l; segments-68%; eosinophils-2%; monocytes-5%; lymphocytes-15%; ESR-20 mm / year; platelets - 110,000.

General analysis of urine: specific gravity -1018; protein-no; sugar - no; epithelial cells - single in the field of view; leukocytes -5-8 in the field of view.

Immune status: CD3 (T-lymphocyte) - 45% (N-50-75%); CD4 (T-helpers) - 30% (N-30-45%); CD8 (T c / k-suppressors) - 17% (N-18-35%); CD16 (NK cells) - 9% (N-10-20%); CD20 (B-lymphocytes) - 17% (N-15-30%); CD22 -16% (N-15-30%); CD25 (IL receptor) -18% (N-10-20%); IgG- 16 g / l (N-8.0-12.0 g / l); IgA - 2.3 g / l (N-1.4-2.0 g / l); IgM - 0.7 g / l (N-0.8-1.5 g / l); IgE - 220 IU (N-0-175 IU).

Preliminary diagnosis of the patient?

Answer: Immunodeficiency (congenital): Viscott-Aldrich syndrome, vaccinated with the X chromosome (only boys are sick), autosomal recessive type of heredity.

Problem №4.

Patient B., 13 years old, was admitted to the clinic with complaints of fever up to 38 C, generalized pyoderma with itching, a feeling of heat in the skin, neck, forearms, legs, soaking with an unpleasant odor in the damaged skin. In the anamnesis - flu, in 3 months a rubella cow. The above complaints appeared after the transferred diseases.

Examination revealed pyoderma in the neck and forearms, peripheral regional lymphadenitis. Pulse 100 beats / min., Rhythmic, heart sounds muffled, over the lungs hard breathing, abdomen soft, painless on palpation, liver enlarged by 1.5 cm, spleen increased by 2 cm In the study of blood for immune status the absence of IgM was detected, with normal values of other immunoglobulins.

1. Preliminary diagnosis of the patient?
2. Forecast?

Answer:

1. Acquired immunodeficiency: selective IgM deficiency with pyoderma.
2. The prognosis is favorable, provided adequate immunocorrection.

Problem №5.

Patient P., 17 years old, complained of weakness, fatigue, intermittent dry cough and nasal congestion. The patient is about 8 months old, when after undergoing community-acquired lower lobe pneumonia on the background of massive drug therapy, moderate splenomegaly was detected and there were periodic bouts of fever with the above complaints.

From the anamnesis it is known: grew and developed under normal conditions. At the age of 14, according to his mother, he suffered from rubella, after which he developed sinusitis, otitis and bronchitis, and often SARS and conjunctivitis. The doctor diagnosed chronic bronchitis, chronic rhinitis, chronic purulent bilateral sinusitis, X-ray examination of OGK - pneumosclerosis on the right (S8-9). Idiopathic splenomegaly. Aplasia of the right kidney. The patient was examined by a hematologist, oncologist, infectious disease specialist.

General blood test: er. - 4.3 x ^{10} ^{12}/ l; Hb - 136 g / l; KP-0.9; platelets - 253.7x10 ^{9}/ l; leukocytes - 6.2x10 ^{9}/ l; segments - 59%; eosinophils 1%; June -1%; sticks - 4%; monocytes -7%; lymphocytes - 28%.

Immune status: CD3 (T-lymphocyte) - 58% (N-50-75%); CD4 (T-helpers) - 46% (N-30-45%); the CD4 / CD8 ratio is 1.7 (N-1.4-3); CD8 (T-suppressors) - 32% (N-18-35%); CD20 - 20% (N-15-30%); IgG- 0.3 g / l (N-8.0-12.0 g / l); IgA - 0 (N-1.4-2.0 g / l); IgM - 0 (N-1.4-2.0 g / l). Phagocytic index - 75% (N - 4.0-9.0%), HCT - spontaneous 11% (N-5-12), HCT-stimulated - 41% (N-20-40%). Phagocytic number -15% (N-50.0-80.0%). At repeated (2) researches essential difference in immunological indicators was not revealed.

Blood culture for sterility - no growth was obtained. Inoculation of bronchial lavage fluid (bronchoscopy) - a moderate growth of Candida fungi. Sputum culture at the Office - not detected.

Bronchoscopy: catarrhal endobronchitis, inflammation of the first degree. Ro-graphy of additional nasal sinuses - cystic sinusitis on both sides.

PCR revealed DNA of Epstein-Barr virus, cytomegalovirus. DNA of the herpes simplex virus types I-II and VI was not detected.

1. Preliminary diagnosis of the patient? 2. Forecast?

Answer:

1. Secondary immunodeficiency: agammaglobulinemia with infectious syndromes of different localization (otitis, sinusitis, bronchitis, etc.).
2. The prognosis is favorable, provided adequate immunocorrection (appointment of immunoglobulins, thymomimetics)

Level 3 tasks

Problem № 6

Patient G., 36 years old, radiologist, participant in the liquidation of the Chernobyl accident, was admitted for the treatment of widespread dermatitis, onychomycosis of the hands and feet, regional lymphadenitis, prolonged subfebrile (3 months to 37.5C), general weakness. After prolonged physical activity and work in the night shifts, the patient's condition deteriorated and he applied for examination. Data from general analysis of blood, urine, biochemical analysis of blood within normal limits.

Total leukocytes - 2.5 x $^{10\ 9}$/ l; lymphocytes - 21%; CD3 (T-lymphocyte) - 40% (N-50-75%); CD4 (T-helpers) - 19% (N-30-45%); CD8 (T-c / k-suppressors) - 20% (N-18-35%); the ratio CD4 / CD8 - 0.9; CD16 (NK cells) - 9% (N-10-20%); CD20 (B-lymphocytes) - 10% (N-15-30%); CD25 (IL receptor) -23% (N-10-20%); IgG- 8.5 g / l (N-8.0-12.0 g / l); IgA - 0.2 g / l (N-1.4-2.0 g / l); IgM - 2.0 g / l (N-0.8-1.5 g / l).

1. Preliminary diagnosis of the patient?
2. Recommendations.

Answer:

1. Acquired immunodeficiency, combined immune disorders (decreased cell, impaired immunoregulation, changes in the receptor cytokine profile and dysimmunoglobulinemia with IgA deficiency). IN I-II centuries.
2. Dynamic clinical and laboratory immunological observation by a clinical immunologist, immunotherapy and immunorehabilitation are recommended.

Problem № 7

A 19-year-old patient who has been smoking since the age of 11 was transferred from a tuberculosis dispensary. From the anamnesis it is known: in the childhood of all infectious diseases, contact with the tuberculosis patient was not. At the age of 15, he was convicted and held in a juvenile prison. During the last year, while in prison 2-3 times suffering from COPD, sinusitis, otitis. Has recurrent herpes, candidiasis of the feet. Focal pneumonia of the upper lobe of the left lung was detected on the Ro-gram of OGK. The patient received drug therapy, but within 2 years the pneumonia recurred. After the next pneumonia, the patient was transferred to a

tube dispensary for specific therapy. The specific anti-tuberculosis therapy did not give the desired effect, clinical manifestations of inflammation (subfebrile, weakness, sweating), enlargement of peripheral cervical and axillary lymph nodes persisted. In the blood study there was no γ-fraction of immunoglobulins. The Office did not detect sputum analysis.

General blood test: er. - 3.9x10 12 / l; Hb - 111 g / l; KP-0.9; leukocytes - 6.8x10 9 / l; segments - 68%; monocytes -8%; ESR-40 mm / year; segments - 70%; sticks - 8%; lymphocytes - 30%.

General analysis of urine without pathology.

Immune status: CD3 (T lymphocyte) -52%; CD4 (T-helpers) -35%; CD8 (T-suppressors) -26%; CD20 (B-lymphocytes) - 20%; IgG- 2.0 g / l; IgA - 0.2 g / l; IgM - 0.9 g / l; phagocytic index - 80% .; phagocytic number - 4%.

1. Preliminary diagnosis of the patient?
2. Causal factors, prognosis?

Answer:

Immunodeficiency with hypoimmunoglobulinemia, exclude general variable immunodeficiency.

2. Causal factors: a number of immune stresses in a patient in adolescence

(Climate change, nervous stress, poor living conditions and malnutrition, smoking, massive anti-tuberculosis therapy. The prognosis is favorable under the condition of dynamic monitoring and immunocorrective therapy.

7.3. The final stage.

The current activity of each student during the lesson is evaluated, the analysis of students' progress is analyzed, the evaluation of each student's activity is announced and it is placed in the journal of attendance and student progress. The head of the group at the same time enters grades in the statement of performance and attendance of students, the teacher certifies them with his signature. It is advisable to briefly inform students about the topic of the next lesson and methods of preparation for it.

VIII . Additions

8.1. Theoretical issues of the preparatory stage:

1. Clinical and anamnestic criteria of immunodeficiencies
2. Laboratory signs of immunodeficiency.
2. Trigger factors of immunodeficiency.
3. Types of tumors-associated antigens
4. Mechanisms of antitumor protection.
5. Immunological factors of tumor resistance.
6. The main approaches to the appointment of immunotropic treatment in cancer patients.
7. Active, passive and adaptive immunotherapy of cancer patients.
8. Features of the immune response (local and systemic) in women / men.
9. Immunological tolerance of a woman to male sperm.
10. Immunology of normal pregnancy
11. Protective properties of human milk
12. Causes of miscarriage
13. Immunological conflicts of pregnancy, their diagnosis, treatment and prevention.
14. Types of immune-dependent infertility, their diagnosis.
15. The main immunological mechanisms of autoimmune diseases
16. Clinical and laboratory signs of development of superacute, acute and chronic crises of rejection.

I H. Conclusions:

1. Early criteria for the diagnosis of immunodeficiency have been identified
2. Generalized knowledge about the main types of tumor antigens.
3. The basic mechanisms of antitumor immune protection are formulated.
4. The basic principles of immunodiagnostics of tumors are formed
5. Indications for immunotherapy of tumor diseases are determined.
6. Mastered knowledge about the antigenic structure of male and female germ cells.
7. Formed understanding of the features of the immune response during pregnancy.
8. The main immunological causes of infertility are identified.
9. Generalized knowledge about the basic immunological mechanisms of autoimmune diseases
10. Mastered clinical and laboratory signs of subacute, acute and chronic rejection crises

Tasks for independent work on this topic :

1 / Make a list of the main groups of tumor antigens

2 /. Develop a table (scheme) of the functioning of the main parts of the human immune system in normal and oncopathology

3 /. Make a plan of immunological laboratory examination of a patient with suspected oncopathology

4 / Make a list of sperm and egg antigens

5 /. To make the scheme of inspection of married couple with suspicion of the raised degree histocompatibility for HLA system antigens

6 /. Develop a table for the differential diagnosis of different types of immunological conflicts "mother-fetus".

Practical skills:

The student must be able to:
- evaluate the data of clinical and laboratory immunological examinations in patients with immunodeficiency and other immunopathology;
- to determine indications for immunotherapy of cancer patients;
- to assess the immunological parameters of local and systemic immunity of men ages and women;
-predict immunological conflicts, the risk of miscarriage ;;
- characterize the immunogram of a pregnant woman;

X . LIST OF EDUCATIONAL AND METHODOLOGICAL LITERATURE

Basic:

1. Fundamentals of immunology / Functions and disorders of the immune system / Abul K. Abbas and co-authors. Scientific editor of translation Valentina Chopyak / 2020. - Medicine. - 327c.
2 . Clinical immunology and allergology.//GN Drannik: - K. - 2009.- 357p.

Additional:

1 .. Allergology and clinical allergology // ed. acad. Khaitova RM, Ilyina NI // GEOTAR "Media", 2018.- 352p.

2..Gavin Spickett. Clinical immunology and allergology. Oxford Directory. - 2019, 832 p.

3. Immunology.- Nat. textbook // ed. Kuznetsova LV, Babadzhana VD, Litus VI - Kyiv.- 2015.-584 p.

4 .. Clinical immunology and allergology (manual for practical classes // Chopyak VV, Potemkina GO, Gavrilyuk AM - 2017. - 224p.

5. Fundamentals of clinical immunology. Principles of diagnosis and treatment of immunopathology (manual for extracurricular work of students, interns) / Bondarchuk OB - 2016. - 52p.
6 . Allergy. Official Journal of the European Academy of Allergy and Clin Immunol.- 2019

7 . Singh AB Allergy and allergen immunotherapy new mechanisms and strategies.-2017., Edition 1, publ Apple Academic Press Inc. , pades 528.

16. Information resources

Website address: www.phthisiatry.at.ua / departments / departments of tuberculosis with a course of clinical immunology.

Libraries: library.vsmu.edu.ua

Training manuals:

1. A set of class presentations for multimedia use.
2. Test control Step-2 (computer version) and a collection of situational tasks for learning.
3. Methods of development for conducting practical classes.
4. Set of tables, slides

Methodical recommendations prepared
associate professor A. Bogomolov

Methodical recommendations were reviewed and approved at the meeting of the department
“28” 08 ”2022 Protocol № 1

Head of Department

Ph.D. Associate Professor Kulik LG