Ministry of Health of Ukraine
Poltava State Medical University

Approved"
at the meeting of the Department of
of Internal Medicine No. 3, Phthisiology
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Minutes № from
Head of the Department
Associate Professor _____ PhD
Borzykh O.A.

METHODOLOGICAL RECOMMENDATIONS FOR CONDUCTING AND PREPARING FOR PRACTICAL CLASSES

Academic discipline	Clinical immunology and allergology
*Module **4***	Clinical immunology and allergology
Content module	Clinical immunology and allergology
*Topic **№5***	Acquired immunodeficiency diseases. AIDS, pathogenesis, immunodiagnostics, immunocorrection
Course	5
Hours	2

Poltava 2023

Methodological recommendations for the practical training for independent work of students in preparation for the practical training and during the class were prepared by:
Assistant of the Department of Internal Medicine №3 with phthisiology Bilko V.V.

Methodological recommendations were re-approved at the meeting of the Department of Internal Medicine of Internal Medicine №3 with Phthisiology_____
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1. Relevance of the topic.

The ability of the body's immune system to resist various infectious factors (bacteria, viruses, fungi) is an integral part of the human survival process. The ability of the human body to counteract various microorganisms is due to two mechanisms: non-specific anti-infective resistance, which is directed at many infectious agents, and the development of specific acquired immunity to specific microorganisms. Acquired population resistance occurs due to adaptive immunity in the majority of the population after vaccination or previous infection. Susceptibility to all infections is individual and always due to insufficient immunity to the infection. If there is resistance - immunity, then even particularly dangerous infections do not occur. Conditionally pathogenic bacteria and fungi induce an infectious process in an organism with normal protective mechanisms only when the ratio of infectious dose per unit of protective factor, for example, per phagocyte, exceeds a certain critical level, i.e. with relative immunodeficiency. In such a situation, the phagocyte is unable to absorb and digest the given number of microbes. Usually, infections caused by opportunistic microbes occur in people with deficiencies in the immune system, and for this, a small dose of microorganisms that do not infect people with a normal immune system is enough, i.e., we are talking about an absolute immunodeficiency. In this regard, elucidating the reasons for the weakening of the body's immunological protection, immunological characterization of conditions accompanied by a violation of the immune response, and the development of methods for their immunological correction is an important task in the diagnosis and treatment of secondary immunodeficiencies.

General goal: learn to diagnose, understand the causes and mechanisms of development, methods of immunological diagnosis and immunotherapy of secondary immunodeficiencies.

Specific goals:

1. Definition, causes, mechanisms of development, diagnosis of secondary immunodeficiencies.
2. Draw up a patient examination program.
3. Acquaintance with the classification of secondary immunodeficiencies.
4. Determine the severity of clinical manifestations and learn to differentiate the symptoms of one or another secondary immunodeficiency.
5. Diagnose and determine complications of primary immunodeficiencies.
6. Characteristics of the main types of secondary immunodeficiencies.

7. The role of secondary immunodeficiencies in the pathogenesis of various diseases.

Theoretical questions for practical training:

1. Acquired (secondary) immunodeficiencies.
2. Reasons for the development of secondary immunodeficiencies.
3. Forms, types of secondary immunodeficiencies.
4. Classification of secondary immunodeficiencies by clinical form.
5. Degrees of immune deficiency, classification by functional deficiency.
6. Diagnosis of secondary immunodeficiencies.
7. Clinical and immunological characteristics of secondary immunodeficiencies.
8. HIV infection: immunopathogenesis, immunodiagnosis, immunocorrection.

Approximate basis of action

Acquired (secondary) immunodeficiencies

Acquired (secondary) immunodeficiency is a disorder of the immune system that develops in the post-neonatal period or in adults and is not the result of genetic defects.

Thus, the term "secondary "immunodeficiency" should be understood as immunity disorders arising as a result of somatic and other diseases, as well as other factors, and having clinical manifestations (International Classification of Diseases, X revision).

Acquired (secondary) immunodeficiency is a clinical and immunological syndrome: a) that developed against the background of a previously normally functioning immune system; b) characterized by a persistent significant decrease in quantitative and functional indicators of immune status; c) is a risk zone for the development of chronic infectious diseases, autoimmune pathology, allergic diseases and neoplasms.

From this definition of the concept of acquired (secondary) immunodeficiency, the following features emerge.

1. Disorders in the immune system are really secondary and appear against the background of previously normal health, both clinically and immunologically. This can be found out by talking to the patient.

2. Disorders in the immune system must be persistent and pronounced. This is an important condition, since it is known that the indicators of the immune system

are labile, mobile, which allows its various links to complement each other and "insure" each other. Therefore, transient, temporary changes in immunity parameters may be caused by the peculiarities of situational response.

3. Disturbances in the immune system should not only be quantitative in nature. The function of certain cells should also be evaluated. There are known cases when the decrease in the number, for example, of NK cells, was compensated by their increased functional activity. If the decrease in the number of certain cells of the immune system is accompanied by a simultaneous violation of their function, this is by far the most important laboratory sign of immunodeficiency.

4. Disorders in the immune system can affect indicators of both specific (adaptive) immunity and non-specific resistance, that is, innate (natural) immunity.

Causes of the development of secondary immunodeficiencies

I. Infectious

1. Viral infections:

a) acute - measles, rubella, influenza, viral mumps (epidemic mumps), chicken pox, hepatitis, herpes, etc.;

b) persistent – chronic hepatitis B, subacute sclerosing panencephalitis, AIDS, etc.;

c) congenital – cytomegaly, rubella (TORCH complex).

2. Bacterial infections: staphylococcal, pneumococcal, meningococcal, tuberculosis, etc.

3. Protozoan invasions and helminth infections (malaria, toxoplasmosis, leishmaniasis, trichinosis, ascariasis, etc.).

II. Alimentary (eating disorders)

1. Protein-energy deficiency.

2. Deficiency of trace elements (Zn, Cu, Fe), vitamins - retinol (A), ascorbic acid (C), alpha-tocopherol (E), folic acid.

3. Exhaustion, cachexia, loss of protein through intestines, kidneys.

4. Congenital disorders of metabolism.

5. Excess nutrition, obesity.

6. Absorption syndrome in the intestines.

III. Metabolic

1. Chronic kidney failure, uremia, nephrotic syndrome.

2. Chronic liver diseases.

3. Diabetes.

4. Hypercatabolism of immunoglobulins.

IV. Conditions leading to the loss of immunocompetent cells and immunoglobulins (bleeding, lymphorrhea, burns, nephritis).

V. Malignant neoplasms, especially lymphoproliferative ones.

VI. Autoimmune diseases. VII. Exogenous and endogenous intoxications (poisoning, thyrotoxicosis, decompensated diabetes).

VIII. Immunodeficiency after various exposures

1. Physical (ionizing radiation, microwaves, etc.).

2. Chemical (immunosuppressants, cytostatics, corticosteroids, drugs, herbicides, pesticides, etc.).

3. Adverse environmental factors.

4.Immunosuppressive measures of treatment: medical drugs (immunosuppressants, glucocorticosteroids, cytostatics, antibiotics, nonsteroidal anti-inflammatory drugs).

4. Occupational hazards, including X-ray radiation, radioactive exposure, biologically active and chemically aggressive substances.

5. Different types of stress (emotional, mental trauma, physical, sports overload, etc.).

IX. Various serious diseases, surgical intervention, anesthesia, burns. X. Disorders of neurohormonal regulation. XI. Age factors: early childhood, old age, pregnancy.

Three forms are distinguished among secondary immunodeficiencies:

– acquired;

– induced;

- spontaneous.

An acquired form of secondary immunodeficiency is acquired immunodeficiency syndrome (AIDS), which develops as a result of damage to the immune system by the human immunodeficiency virus (HIV).

The induced form of secondary immunodeficiency arises as a result of specific causes that caused its appearance: X-ray radiation, cytostatic therapy, the use of corticosteroids, injuries and surgical interventions, as well as immune disorders that develop repeatedly in relation to the main diseases (diabetes, liver and kidney diseases, malignant neoplasms).

The spontaneous form of secondary immunodeficiency is characterized by the absence of a clear cause that caused a violation of immune reactivity. Clinically, it is manifested in the form of chronic, often recurring infectious and inflammatory processes of the broncho-pulmonary apparatus, additional sinuses of the nose, urogenital and gastrointestinal tract, eyes, skin, soft tissues caused by opportunistic (conditionally pathogenic) microorganisms. Therefore, chronic, often relapsing, delayed, difficult to treat with traditional means, inflammatory processes of any localization in adults are considered as clinical manifestations of secondary immunodeficiency.

Types of secondary immunodeficiencies (depending on the etiological factor):

- specified (infectious, toxic, metabolic, physical, psychogenic, post-traumatic, with indication of a specific diagnosis - the disease that caused it) (ICX-10 code D.84.8);

- unspecified (cryptogenic, or essential, or idiopathic, or spontaneous - presented in the absence of any etiological factor) (ICD-10 code D.84.9).

Types of specified immunodeficiencies.

Infectious immunodeficiency is formed as a result of the action of an infectious agent, including an opportunistic pathogen (viral, bacterial, protozoan, fungal, helminthic).

Toxic immunodeficiency develops under conditions of prolonged exposure to exo- and endotoxins, xenobiotics, etc. (exogenous, medicinal, occupational, endogenous, burns, etc.).

Metabolic immunodeficiency develops under conditions of long-term metabolic disorders, including disturbance of acid-alkaline balance (nutritional, metabolic, due to protein deficiency, malabsorption, etc.).

Physical immunodeficiency develops as a result of long-term effects on the human body of ionizing and ultraviolet radiation, the effects of high frequencies and fields, etc.

Psychogenic immunodeficiency develops under conditions of long-term effects of psycho-emotional overload, stress, diseases of the central nervous system, etc.

Post-traumatic immunodeficiency (including surgical) develops under conditions of severe extensive injuries, burns, extensive and long surgical interventions, blood loss, lymphorrhea, etc.

Classification of secondary immunodeficiencies by clinical form

The autoimmune form is characterized by appropriate clinical and laboratory data (hypergammaglobulinemia, elevated CIC level, etc.).

The allergic form (including IgE-dependent, reagin) is characterized by appropriate clinical (hypersensitivity of the skin and mucous membranes, primarily of the respiratory system and gastrointestinal tract) and laboratory data (eosinophilia, elevated IgE level, etc.).

The immunoproliferative form is characterized by the formation of tumors in various organs and systems with the accumulation of a tumor mass of lymphoid monocytic cell composition, an increase in the size of the spleen, tonsils, adenoids, thymus, Peyer's patches, etc.

The paraneoplastic form is characterized by a malfunction of the immune system in cancer patients due to the effect of the tumor on the body and damage to the immune system after the use of antiblastoma drugs (cytostatic therapy, radiation, etc.).

Neurogenic form (chronic fatigue syndrome, neuroimmunoendocrine syndrome, immunodeficiency in mental illnesses, etc.).

Mixed form - characterized by the presence of two or more forms in the patient; it is advisable to distinguish the leading form (for example, a mixed form with a predominance of autoimmune).

Variants of the course of secondary immunodeficiencies

Acute - clinical and laboratory signs of immunodeficiency develop and persist for 1 month.

Subacute - clinical and laboratory signs of immunodeficiency develop and persist for 3 months.

Chronic - clinical and laboratory signs of immunodeficiency develop and persist for 6 months.

Recurrent – clinical and laboratory signs of immunodeficiency re-form earlier than 6 months after successful treatment.

Degrees of immune deficiency (depending on the absolute number of lymphocytes; the norm of the absolute number of lymphocytes is 1.4-3.2 x 109 /l).

1st degree of immune deficiency - minimal (IN-1) - the absolute number of lymphocytes is 1.4-1.2 x 109 /l; laboratory indicators are reduced by 15-30% from the average normal value. Clinically, immunodeficiency may not be manifested (compensated form).

2nd degree of immune deficiency - medium (IN-2) - the absolute number of lymphocytes is 1.1-0.9 x 109 /l; laboratory indicators are reduced by 35-55% of the average normal value. Clinically, immunodeficiency can be manifested by one or a combination of several clinical syndromes, subacute or chronic course.

3rd degree of immune deficiency - high (IN-3) - the absolute number of lymphocytes is less than 0.9 x 109 /l; laboratory indicators are reduced by more than 55% of the average normal value. Clinically, immunodeficiency is manifested by pronounced clinical symptoms.

Classification of secondary immunodeficiencies by functional insufficiency

FI I – the patient retains working capacity, requires outpatient treatment without issuing a certificate of incapacity for work.

FI II – the patient temporarily loses his ability to work or his ability to work is limited, requires outpatient treatment with the issuance of a certificate of incapacity for work.

FI III – the patient loses working capacity temporarily or has persistent loss of working capacity, needs inpatient treatment and/or examination of working capacity.

Diagnosis of secondary immunodeficiencies

The first stage of diagnosis is the collection of anamnesis and clarification of the patient's complaints, which, depending on the type of immunopathology, can differ significantly. In the presence of secondary immunodeficiency in the anamnesis, recurrent infections are usually detected, the nature and localization of which may indicate the type of immunodeficiency. The allergic process has its own characteristics, and the correct diagnosis can sometimes be established only on the basis of the anamnesis. The anamnesis of autoimmune diseases has characteristic features that make it possible to distinguish them from other types of pathology. Lymphoproliferative and oncological processes also have their own characteristics.

The next stage is conducting immunological studies, which allow to assess the immune status of a patient with suspected immunodeficiency.

"Immune status" is the state of the immune system of a healthy or sick person at a certain point in time under specific environmental conditions. Immunological, or immune status (IS), is characterized by a complex of informative indicators that reflect the state of various links of the immune system at the time of research in a specific process or disease.

Assessment of immune status is a process of obtaining a complex of nonspecific and specific quantitative and functional indicators that reflect the state of the immune system. Reflecting the form and variant of the disease, IS indicators serve as the basis for creating an immunological "image" of the disease, that is, its immunological characteristics, identifying a defective link of immunity.

Immunodiagnostics is the application of a set of immunological methods to detect a disease or determine the causative agent of a disease in the researched material.

General non-specific methods characterizing the state of various links of the immune system: lymphocytes, granulocytes, macrophages, complement. They are usually used to detect a defect in the immune system, i.e. in immunodeficiencies.

Specific methods that allow detecting antibodies, immune T-lymphocytes, pathogen antigens in the human body or in the external environment. These methods are used to diagnose infections, allergies, and autoimmune diseases.

The diagnostic standard for secondary immunodeficiency states is represented by the following studies.

1. Mandatory laboratory examination:

a) study of immune status (determination of the total number of leukocytes, lymphocytes, subpopulations of T-lymphocytes, B-lymphocytes, the level of immunoglobulins A, M, G, phagocytosis);

b) control of detected violations after the course of therapy.

2. Additional research methods: special immunological studies depending on the clinical manifestations and defects detected during the initial assessment of the immune status, such as studies of the functional activity of classes and subclasses of lymphocytes, hemolytic activity of the complement system, nonspecific acute phase indicators, interferon status, immune control of opportunistic pathogens infections, etc.

3. Instrumental diagnostics.

4. Consultations of specialists.

The main signs of secondary immunodeficiency:

- lack of connection with heredity and genetic conditioning;

- occurrence against the background of normal reactivity in connection with the disease, the action of adverse physical and biological factors, methods or means of treatment;

- maintenance of deficiency during the treatment of the main disease and elimination of the factors inducing it;

- absence or long-term delayed normalization of the immune status.

Clinical and immunological characteristics of secondary immunodeficiencies

Mostly T-cell immunodeficiencies

1. T-lymphocytopenic syndrome

The paracortical zones of the lymph nodes become empty, the lymphoid tissue atrophies. Decreased number of T-lymphocytes by 15% or more. The diagnosis is established upon repeated confirmation against the background of remission of the underlying disease.

Variants: autoimmune (with the presence of anti-T-cell antibodies), stress, toxic (drug), viral, dysmetabolic, with sarcoidosis, lymphogranulomatosis, T-leukemia, etc.

Clinical picture: recurrent viral infections with a long course in combination with bacterial infections.

2. T-cell immunoregulatory imbalance syndrome

Immune status: Th-CD4/Ts-CD8 ratio is less than 1.4 (the lower the ratio, the more severe the secondary immunodeficiency). The diagnosis is established when these disorders are detected and confirmed during the period of remission of the main disease. Clinical picture: polymorphic recurrent infections of different localization.

3. Syndrome of T-cell immunoregulatory imbalance with increased cytotoxic reactivity

Immune status: relative lymphocytosis. The immunoregulatory index ThCD4/Ts-CD8 is less than 1.4 (the lower it is, the more severe the secondary immunodeficiency). Sharply increased levels of NK cells (CD16), IgM, IgG, increased NCT test. There are signs of the development of a cytotoxic reaction against the background of an intracellular infection, for example, herpes virus, cytomegalovirus infection. Clinical picture: polymorphic recurrent infections of different localization.

4. Syndrome of deficiency of lymphokines and their receptors

It is set with multiple confirmations.

Mostly B-cell immunodeficiencies.

1. Panhypogammaglobulinemia

Hypoplasia of lymphoid follicles, atrophic lymph nodes. Immune status: a decrease in the concentration of gamma globulins in the blood serum, a decrease in the level of natural antibodies, a decrease in the blood and other biological fluids (saliva, secretions) of IgA, M, G with a normal or moderately reduced level and functional activity of T-lymphocytes. Clinical picture: recurrent bacterial infections of the respiratory tract, lungs, and sepsis prevail.

2. Dysimmunoglobulinemia

Immune status: a change in the ratio between immunoglobulins with a mandatory decrease in the concentration of one of them against the background of normal and elevated levels of others.

3. Antibody deficiency syndrome

Immune status: lack of antibodies against detected infectious agents (for example, to staphylococcus, streptococcus). Clinical picture: recurrent infections.

8. Deficiency of secretory IgA Immune status: there is no (reduced) level of secretory IgA in saliva, tracheobronchial, intestinal and other secretions. Clinical picture: chronic bronchitis, inflammation of the mucous membrane of the oral cavity (periodontal disease), chronic tonsillitis, otitis, etc.

9. Secondary immunodeficiency in B-cell tumors (Waldenström plasmacytoma, lymphomas, B-cell leukemia)

10. Secondary immunodeficiency with dysimmunoglobulinemia phenomena and an autoimmune component. Immune status: neutrophilic leukocytosis, an increase in the level of plasma cells, B-lymphocytes, an increase in Th2 (CD4+), CD8+, the level of IgM, CYC, complement, ESR, CRP and an increase (less often a decrease) in the activity of phagocytes are characteristic. Deficiencies of macrophages and granulocytes.

11.Macrophage-monocyte hyperactivation syndrome

Immune status: monocytosis, increase of IL-1 in biological fluids. Clinical picture: febrile syndrome, arthritis and inflammation of various localization.

12. Pangranulocytopenia, deficiency of granulocytes

Immune status: agranulocytosis and neutrophilia. Variants are autoimmune, allergic, toxic, infectious. Clinical picture: purulent-septic diseases, ulceration of mucous membranes.

HIV infection is a disease caused by a retrovirus that affects the cells of the immune, nervous and other human systems and organs. It is characterized by a long, chronic, progressive course that culminates in the development of AIDS and accompanying opportunistic diseases.

Etiology. HIV belongs to the lentivirus subfamily of the retrovirus family. Two types of the virus are known: HIV-1 and HIV-2. Both types of virus have a

similar structure. At the same time, they differ in molecular weight of proteins and some additional genes.

Immunopathogenesis. Dendritic cells (Langerhans cells, specialized cells of the skin and mucous membranes) are among the first to encounter HIV in the mucous membranes and, according to their purpose, capture, process and transfer it to their surface.

After that, they migrate to the lymphoid tissue, where they present the antigen to T-lymphocytes, as a result of which the latter are activated. The envelope protein gp120 of HIV-1 binds to CD4, as well as chemokine receptors, and a complex biological process of interaction of the virus with the cell begins, ending with the synthesis of a new generation of virions.

The CD4-binding region of the membrane protein gpl20 binds to the CD4 receptor of the target cell. This step immediately leads to conformational changes, and individual parts of the proteins change their position relative to each other. As a result, the second site of gpl20, intended for binding to the CCR5 co-receptor, is opened and becomes available for interaction.

At the next stage, CCR5 interacts with the CCR5-binding site of gpl20. After this process is completed, conformational changes of gp41 begin.After fusion, the viral membrane loses the proteins gp41 and gp120. The RNA of the virus surrounded by nucleocapsid and capsid proteins enters the cell, and the virion "begins" the process of "undressing". As a result of the weakening of intermolecular bonds, the envelope of the virus is destroyed. Phosphorylation of the matrix protein occurs under the action of the MAP kinase enzyme.

After "undressing", the contents of the capsid, and above all the RNA, enters the cytoplasm of the cell, and the reverse transcription of the viral RNA begins with the participation of the reverse transcriptase enzyme. In the cytoplasm, information from viral RNA is transcribed into DNA using reverse transcriptase (revertase).

What distinguishes HIV-1 is its ability to transport its DNA across an intact nuclear membrane. This allows the virus to infect non-dividing cells, macrophages and microglial cells.

At the next stage, the proviral DNA is integrated into the chromosomal apparatus of the cell. The integrase enzyme at the three ends of the provirus molecule removes two nucleotides each, and also cuts the chromosomal DNA**.**

Cellular DNA repair enzymes "remove" excess nucleotides at the five ends of the provirus, complete the "missing parts" and use integrase to stitch together the ends

of proviral and chromosomal DNA. After incorporation, the proviral DNA serves as a template for transcription.

Cellular immune response. Depending on the secreted cytokines, T-helpers are divided into two types. Type 1 T-helpers mainly produce interleukin-2 (IL-2) and interferon-α. These cytokines support the effector functions of the immune system (cytotoxic T-lymphocytes, NK-lymphocytes, macrophages).

T-helpers of type 2 produce mainly IL-4, IL-5, IL-6 and IL-10, which activate the humoral response.

T-lymphocytes lose the ability to produce the T-cell growth factor - IL-2, as a result of which the differentiation of T cells into different functional subpopulations - CD4 and CD8, as well as the activity of NK cells - is disturbed.

IL-6 plays a major role in terminal B-cell differentiation into immunoglobulin-secreting cells. The envelope protein of the virus acts directly on CD4 clones of T cells, inducing the synthesis of IL-6 and increasing its production. A decrease in the subpopulation of T-helper type 1 is accompanied by a decrease in the production of α- and γ-interferon. In turn, the functional activity of NK lymphocytes is under the direct influence of such cytokines as IL-2 and interferon-γ.

During the development of HIV infection, not only lymphocytes with the CD4+ phenotype are affected, but also the function of lymphocytes with the CD8+ phenotype, i.e. T-suppressors, is impaired. The protein of the p15 virus has a suppressive effect on the production of IL-2 and γ-interferon by T cells. IL-2 and other cytokines are closely related to the function of cytotoxic T-lymphocytes, which are responsible for antiviral and antitumor protection of the body.

Humoral immune response. HIV affects the functional activity of B-lymphocytes, increasing the synthesis of immunoglobulins and especially the production of IgG.Most of the antibodies, despite the presence of the virus, are non-specific (only about 5% of all immunoglobulins are specific) and are produced much more than normal B cells. Such hyperproduction of immunoglobulins increases during the development of the infection.

Monocytes and macrophages. Tissue macrophages in HIV-infected people often contain the virus, and since they do not die from its action, they can act as a source of this virus in the body. In macrophages, chemotaxis, production of reactive oxygen species, and antibacterial toxicity decrease.

Clinical picture. The effect of the virus is the increasing suppression of the function of the immune system with the subsequent development of opportunistic infections (viral, bacterial, fungal, protozoal etiology). In its course, HIV infection goes through several stages, which have specific clinical manifestations and sufficiently clear laboratory criteria.

The incubation period can be from 3 weeks to 3 months, and in some cases from 2 to 5 years or more from the moment of infection.

The acute stage of the disease is characterized by the development of a "mononucleosis" symptom complex. At the same time, an increase in temperature to 38-38.5 °C, intoxication phenomena, pharyngitis, lymphadenopathy, enlargement of the liver and spleen, diarrhea (more than a week), small non-itchy rashes on the skin (lasting from 1-2 weeks to 1-2 months). Meningeal phenomena are possible. A transient decrease in the level of CD4+ lymphocytes and an increase in the number of CD8+ lymphocytes are registered in the blood. The duration of this stage is 2-3 weeks, after which the disease passes into one of two other stages - asymptomatic infection or persistent generalized lymphadenopathy (PGLA). Relapses of clinical manifestations of the acute stage are possible.

The asymptomatic carrier stage is registered in half of the patients and can last for 3-6 years. During this period, the patient does not complain, there are no clinical manifestations of the disease. Antibodies to HIV antigens are detected in the blood of patients. During all this time, a person is a virus carrier and can be a source of infection.

Stage of persistent generalized lymphadenopathy. In this stage of the disease, an increase in cervical, supraclavicular, axillary, elbow, inguinal lymph nodes is noted. The glands reach 1-3 cm in diameter (rarely up to 4-5 cm), are more often soft, but can also be dense, painful on palpation, mobile, not fused to the surrounding tissues and to each other.

Laboratory diagnosis of HIV infection and AIDS

Laboratory diagnostics is based on the detection of virus markers and specific antibodies in biological fluids.

The following techniques are used to make a diagnosis:

1. Polymerase chain reaction (PCR) is a highly sensitive method for detecting viral RNA.

2. Hybridization analysis (HA) – searching for certain nucleic acids and determining their quantity by binding to a DNA probe.

3. Immunofluorescence reaction (IF) - detection of antigens in blood leukocytes. The method is specific, but low sensitivity.

4. Enzyme immunoassay (ELISA) is a highly sensitive method of detecting HIV antibodies in the serum of a patient or a carrier.

5. Immunoblotting is a confirmatory test. The method detects antibodies to one or more membrane or core proteins of HIV. The result is considered positive if antibodies to any two of the three main HIV antigens - p24, gp 41 and gp 120 (or gp 160) are detected.

6. Flow cytometry - allows determination of subpopulations of lymphocytes and detection of phenotypic markers characterizing changes in the functional state of cells.

Determination of antibodies to HIV 1-2 in blood. Antibodies to HIV-1 and 2 are normally absent in blood serum. Determination of antibodies to HIV is the main method of laboratory diagnosis of HIV infection. The basis of the method is ELISA (sensitivity more than 99.5%, specificity more than 99.8%). Antibodies to HIV appear in 90-95% of infected people within 3 months. after infection, in 5-9% - after 6 months. and 0.5-1% - in later terms. In the stage of AIDS, the number of antibodies can decrease to the point of complete disappearance.When receiving a positive response of HIV antibody detection, in order to avoid pseudo-positive results, the analysis should be repeated 1 or 2 more times, preferably using a diagnostic of another series. A positive result is considered if both out of two or out of three tests clearly detect antibodies.

Immunoblotting for antibodies to HIV viral proteins in blood serum. Antibodies to HIV viral proteins are normally absent in blood serum. The ELISA method for determining HIV antibodies is a screening method. When a positive result is obtained, the Western-blot immunoblotting method is used to confirm its specificity - counter-precipitation in a gel of antibodies in the patient's blood serum with various viral proteins, subjected to separation by molecular weight using electrophoresis and applied to nitrocellulose. Antibodies to viral proteins gp41, gpl20, gpl60, p24, p18, p17, etc. are determined. Detection of antibodies to one of the glycoproteins gp41, gp120, gp160 should be considered a positive result. If antibodies to other proteins of the virus are detected, the result is considered doubtful, and such a person should be examined twice more - after 3 and 6 months. The absence of antibodies to specific HIV proteins means that the ELISA gave a false-positive result. At the same time,

in practical work, when evaluating the results of the immunoblotting method, it is necessary to follow the instructions attached by the company to the used research kit.

Antigen p24 in blood serum. Antigen p24 in blood serum is normally absent. Antigen p24 is a protein of the HIV nucleotide wall.The stage of primary manifestations after HIV infection is a consequence of the beginning of the replicative process. Antigen p24 appears in the blood 2 weeks after infection and can be detected by ELISA in the period from 2 to 8 weeks. After 2 months from the beginning of the infection, the p24 antigen disappears from the blood. Later, in the clinical course of HIV infection, a second increase in the content of p24 protein in the blood is noted. It falls on the period of the formation of AIDS. The existing ELISA test systems for the detection of the p24 antigen are used for early detection of HIV in blood donors and children, determination of the prognosis of the course of AIDS and control of the therapy carried out in these patients. The IFA method has high analytical sensitivity, which allows detection of p24 antigen in HIV-1 in blood serum at concentrations of 5-10 pkg/ml and less than 0.5 ng/ml in HIV-2, and high specificity. However, it should be noted that the level of p24 antigen in the blood is subject to individual variations, which means that only 20-30% of patients can be detected by this test in the early period after infection.

Antibodies to antigen p24 of the IgM and IgG classes appear in the blood starting from the 2nd week, reach a peak within 2-4 weeks and remain at this level for different times: antibodies of the IgM class for several months, disappearing within a year after infection, and IgG antibodies can persist for years.

Tasks for checking the initial level of knowledge

1. What factors can cause the development of secondary immunodeficiency?

A. Malnutrition.

B. Severe infectious diseases.

C. Long-term chronic recurrent infections.

D. Irradiation.

E. Administration of a large number of corticosteroid drugs.

F. Administration of cytotoxic agents.

G. None of the above factors.

2. The development of secondary immunodeficiency may be caused by:

A. Fermentopathies, including those due to insufficient entry into the body or impaired binding of iron ions in the body.

B. The immunosuppressive effect of viruses and their toxins.

C. A decrease in the functional activity of macrophages in chronic infections.

D. Damage to lymphatic vessels as a result of exposure to microbes and their toxins.

E. The appearance in the blood plasma of factors that block the blast transformation of lymphocytes.

F. Development of lymphoproliferative diseases.

G. None of the listed reasons can lead to the development of secondary immunodeficiency.

3. What clinical signs are characteristic of patients with insufficient T-cell immunity?

A. Increased sensitivity to viral infections.

B. Tendency to neoplasms of lymphoid or epithelial origin.

C. Change in indicators of T-cell immunity.

D. Change in indicators of humoral immunity.

4. What are the pathological conditions and diseases associated with immunodepression that should be differentiated from SNID?

A. With congenital immunodeficiency.

B. With a malignant tumor of the lymphoreticular system.

C. With severe protein-energy deficiency.

D. With none of the listed pathological conditions.

5.What is the systemic response to infection in sepsis?

A. In the uncontrolled release of a whole complex of mediators.

B. In a decrease in the number of lymphocytes.

S. In the release of a whole complex of pro-inflammatory and anti-inflammatory cytokines.

D. In inactivation of the complement system.

E. In the activation of the system of macrophages, lymphocytes and endothelium.

6. What protection factors can most often be disturbed in secondary immunodeficiency?

A. Mechanical protection against the penetration of an infectious agent into the body.

B. Humoral factors that destroy the pathogen that has entered the body.

C. Phagocytosis factors.

D. None of the listed options.

7. When examining patients to assess the immune status, it is necessary:

A. Study of cellular immunity.

B. Research of humoral immunity.

C. Studies of the complement system.

D. Study of all parameters.

8. Immunological examination of patients is carried out as:

A. One-time examination of the patient upon admission to the clinic.

B. Double examination of the patient.

C. Immunological monitoring during the course of the disease.

D. Immunological examination in dynamics when using immunotropic therapy.

9. Tasks of immunological examination of patients in the clinic:

A. Immunodiagnosis.

B. Forecasting the course of the disease.

C. Control over the quality of treatment.

D. Appointment of immunoregulatory therapy according to indications.

10. What environmental factors contribute to the development of secondary immunodeficiencies:

A. Long-term stress.

B. Adverse climatic factors.

C. Bacteria.

D. Viruses.

Correct answers to questions: 1 – ABCDEF; 2 – ABCDEF; 3 – ABC; 4 – ABC; 5 – A; 6 – ABC; 7 – D; 8 – CD; 9 – ABCD; 10 - ABCD.Sources of educational information 1. Clinical immunology and allergology: Textbook / [H.M. Dranik, O.S. Prylutskyi, Yu.I. Bazhora and others]; under the editorship Prof. AHEM. Dranika - K.: Zdrovya, 2006. - 888 p. 2. Kazmirchuk V.E. Clinical immunology and allergology / V.E. Kazmirchuk, L.V. Kovalchuk. – Vinnytsia: Nova kniga, 2006. – 504 p. 3. Andreychyn M.A. Clinical immunology and allergology: Textbook/Andreichyn M.A., Chopyak V.V., Gospodarskyi I.Ya. – Ternopil: Ukrmedknyga, 2005. – 372 p. 4. Clinical Immunology and Allergology: Textbook / Ed. A.V. Karaulova - M.: Medical Information Agency, 2002. - 651 p. 5. Nikulin B.A. Evaluation and correction of immune status / Nikulin B.A. - M.: GEOTAR-Media, 2007. - 376 p.