Ministry of Public Health of Ukraine
National O.O. Bohomolets Medical University

METHODICAL GUIDE
to practical classes for students

Educational discipline	Propaedeutics of Pediatrics including nursing practice, basic medical skills in the pediatric department
Training direction	22 " Public Health ", II (master's) educational and qualification level
Specialty	222 «Medicine»
Department	Paediatrics # 2
Thematic module 2	Anatomical and physiological features of organs and systems in children, clinical examination methods. Semiotics of damage syndromes of each of the systems and the most common diseases.
Topic:	Anatomical and physiological characteristics, survey method, semiotics of diseases of the immune system in children.
Course	3

Approved on methodic meeting of department of pediatrics №2 from «24» august 2022., protocol №1

Considered and approved: CMC on pediatric disciplines from «25» august 2022., protocol №1

1. Goal: the student acquires knowledge about:
• anatomical and physiological features of the immune system in children;
• general semiotics of diseases of the immune system in children;
• main symptoms and syndromes of damage to the immune system in children, methods of clinical research in children;
• instrumental and laboratory examination methods for assessing the state of the child's immune system.
the student's acquisition of skills regarding:
• assessment of the results of instrumental and laboratory examination methods for assessing the state of the child's immune system system;
• analysis of the main symptoms and syndromes of damage to the child's immune system system.

2. Competencies:
• drawing up a diagnostic algorithm for children with immune system pathology;
• interpretation of the results of instrumental and laboratory methods of examination of children with pathology of the immune system.

3.Plan and organizational structure of the lesson

Name of the stage	**Description of the stage**	**Mastery Levels***	**Time (min)**
Preparatory stage	Organizational measures Setting educational goals, student motivation	*	10
The main stage	Test control on the subject of the lesson, checking and announcing the results. - theoretical survey; - demonstration of practical skills, clarification of the most important points regarding the semiotics of diseases of the immune system in children; - students' work on acquiring the skills of clinical examination of children with pathology of the immune system; - acquisition by students of the ability to assess changes in the state of the immune system in various diseases in children. Solving tasks according to the subject of the lesson.	** *, **, *** **, ***	20 55 20
Final	Analysis and evaluation of the results of students' work.	*	10

*	Announcement of the topic of the next lesson, an indicative map for independent work with literature.		
	Together	**2,5 academic hours**	**115**

Ознайомлювальний, **відтворювальний, *** реконструктивний, **** творчий рівні засвоєння.

4. Content of educational material

Features of the immune system in children.

The formation of immune competence begins at the early stages of embryonic development and is genetically determined.

The immune status of a newborn depends primarily on the immunogenetic characteristics of the mother and father, as well as on the characteristics of the course of pregnancy and childbirth, and only then on environmental conditions.

The following features can be distinguished in the development of the fetal immune system:

Unlike the formation of other organs and systems of the body, the development of immunocompetent cells and organs of the immune system occurs from different sources, independently of each other and initially they are not functionally related.

Thus, undifferentiated stem cells, which give rise to immunocompetent cells, appear first in the yolk sac at the 3rd week of intrauterine development, then in the embryonic liver at the 6th week, and from the 3rd month. gestational age in the spleen. Hematopoiesis in the spleen ends around the 5th month.

2. The central organs of the immune system are formed somewhat later. Thus, the bone marrow is laid down at the end of the 3rd month, but bone marrow hematopoiesis begins only from the 5th month.

3. The thymus gland is laid down in the 6th week, but Hassal's bodies (the place where thymocyte differentiation occurs) are formed only in the 12th week. Organopoiesis of the retrosternal gland during intrauterine development ends at 20 weeks. In the future, only its quantitative changes are noted.

4. The first peripheral lymphatic glands are formed from the third month of gestation, but their population with lymphoid cells begins from the 4th month.

5. Lymphatic glands of the gastrointestinal tract are formed only after the 21st week of gestation.

6. The first element of the immune system, which already appears in the 4th week of gestation, is a macrophage.

7. The first lymphocytes that assume the function of natural killers are found in the liver at the 6th week of gestation.

8. Lymphoid cells with T-L function are detected in human embryos at the 11th week.

9. At the 3rd month (12 weeks) of intrauterine life, the T-dependent population of lymphocytes is already capable of blast transformation under the action of a nonspecific mutagen, as well as adhesion

10. In the thymus gland, thymocytes appear on the 14th week and then only in the cortical layer.

11. From the 20th week, the differentiation of T-lymphocytes into killer, helper, and suppressor cells begins.

12. On the 6th week, histocompatibility antigens (HLA) appear on immunocompetent cells.

13. Maturation of B-lymphocytes from precursor cells in the fetus begins in the liver. As early as the 8th week, B-lymphocytes bearing immunoglobulin determinants on their surface are detected in the liver. At the same time, initially (at 9-10 weeks) cells with IgM receptors are detected, then lymphocytes with IgG receptors and only at 11-12 weeks with IgA receptors.

14. At the 14th week of embryogenesis, receptors for complement components appear on B-lymphocytes.

15. At the 20th week of intrauterine development, VL has the ability to transform into plasma cells capable of synthesizing IgM and IgG in the spleen.

16. IgA synthesis begins only from the 30th week.

Thus, on the 20th week of embryogenesis, that is, by the end of the first half of pregnancy, the formation of the organs of the immune system ends.

The noted features of the ontogenesis of the immune system have important clinical significance in terms of understanding the essence of congenital immunodeficiency states.

Ontogeny of the immune system

Organs of the immune system and immunocompetent cells	**Gestation term**
A primary stem cell first begins to function	**A) Yolk sac in the 3rd week** **B) Liver -3-6 weeks.** **C) Spleen for 3 months**
The bone marrow	It is established at the end of the 3rd month, but only from the 5th month, bone marrow hematopoiesis begins.
Thymus	**It is laid for 6 weeks** **Begins to function at 12 weeks.**
Lymph nodes: **a) peripheral** **b) Gastrointestinal tract**	 **3 - months** **5 - months**
Macrophages	**4- week**
NK	**6- week**
Tl	**11 weeks**
Differentiation of TL into killers, helpers, suppressors begins	**From the 20th week**
Synthesis of Ig	**12 weeks**
HLA system	**6 - week.**
Complement system	**20 weeks**

Features of the functioning of the immune system in the fetus.

The functioning of the immune system in the fetus has a number of features.

1. The early protective mechanism of the fetus - phagocytosis actively increases from the 20th week, but the neutrophils of the fetus have a low chemotaxic ability and also have a limited ability to adhere. Intrauterine infection rapidly depletes the neutrophil pool.

2. Until the 20th week, the blood of the fetus contains all the components of the complement system, but their concentration is not high. Thus, the concentration of C3 and C4 in the blood of a fetus at the time of birth is 50% of the concentration of an adult, and MAK, C8, C9 is only 10%. And only in the 3-month postnatal age, the concentration of the main components of the complement system reaches the concentration of adults.

3. The amount and activity of TL is insufficient, the cytotoxic function of T-killers is much lower than in older children, but the proliferative activity does not differ from that of an adult.

Clinical significance. The above-mentioned features include the fact that the insufficient concentration and activity of the complement system, NK, the T-chain of the immune system and the weak chemotoxic ability of neutrophils determine the high sensitivity of the fetus to viral (rubella, herpes, chicken pox, viral hepatitis B), microbial and protozoan infections (toxoplasmosis, listeriosis), which develop intracellularly.

4. The synthesis of immunoglobulins in the fetus is reduced. Thus, at the moment of birth, the concentration of IgM is only 0.1 g/l, and IgA is 0.03-0.05 g/l, while in adults, respectively, it is 0.5-1.8 g/l and 0.5-2.5 g/ l. Thus, the content of IgM is approximately 8-10%, and IgA is only 0.4% of the adult level.

Clinical significance. How much IgM and IgA do not penetrate the placenta, so their concentration in the blood reflects the fetus's own ability to synthesize these Ig. If the concentration of IgM in the umbilical cord blood of a newborn is more than 0.2 g/l, and IgA is more than 0.05 g/l, then this is a marker (evidence) of an intra-uterine infection.

5. The synthesis of own IgG in a small amount starts from the 15-20th week. At the same time, the concentration of IgG in a newborn is 10% higher than the level in the mother's blood serum, despite its insufficient synthesis by the fetus. This indicates that IgG crosses the placenta. Transplacental penetration of maternal IgG to the fetus during pregnancy is uneven. The most active transport of maternal IgG occurs in the last week of pregnancy. A low concentration of IgG in the umbilical cord blood of a newborn may indicate its prematurity.

Transplacental transfer of IgG from mother to fetus provides immediate passive protection of the fetus against infection by microorganisms.

As a result, during the first half of life, children do not get chickenpox, measles and some other viral infections.

6. During intrauterine development, alpha-interferon is determined in large quantities in all tissues of the fetus, placenta, and amniotic fluid. The embryo is completely impregnated with alpha-interferon. This endogenous interferon in the early stages of ontogenesis is primarily aimed at regulating the development of the immune system, and not at its stimulation. A sufficient amount of interferon begins to be produced only after the first year of life.

In the antibacterial protection of the fetus, amniotic fluid is of great importance. It contains a large concentration of lysozyme, transferrin and IgG

Features of the functioning of the immune system in newborns.

The functioning of the immune system in newborns in many ways resembles the functioning of the immune system in the fetus, but at the same time has some differences.

1. After the birth of a child, the lymphoid tissue receives a powerful push for development, because the body is affected by a flow of antigenic stimulation, through the skin, respiratory tract and especially the gastrointestinal tract, which are actively inhabited by microorganisms from the first minutes of life. And as a result of such stimulation, there is a rapid development of the body's lymphoid apparatus, which is manifested by the active population of peripheral lymph nodes (especially mesenteric) lymphocytes, an increase in their mass, intensive development of reproduction centers, and an increase in the number of plasma cells that produce antibodies. As a result, already in the first week of life, the absolute number of lymphocytes in the blood of a newborn increases sharply (the first cross in the white blood formula). Physiological lymphocytosis persists up to 4-6 years (the second cross in the white blood formula)

2. Newborns, as well as fetuses, have a reduced pool of neutrophils.

3. Migratory and phagocytic activity of microphages is reduced.

4. Decreased ability to form the main colonies of the stimulating factor and antitoxic immunity (factors that neutralize toxins).

Clinical significance

- Highly pronounced intoxication syndrome, especially for endotoxins.
- Reduced resistance to pustular pathogens.

5. Monocytes have a reduced ability to synthesize IL-1 (causes CRP synthesis by hepatocytes), IL-6 (enhances Ig synthesis) and tumor necrosis factor (inflammatory mediator). This leads to a violation of the inflammatory reaction, which explains the reduced febrile reaction in newborns.

6. Reduced digestive capacity of macrophages, especially for Haemophilus bacilli, Klebsiella - this explains the high frequency of diseases caused by these pathogens (sepsis, meningitis)

A feature of cellular immunity in a newborn

1. The proliferative response (the ability to produce cytotoxic T-L) to pathogens such as streptococci and pneumococci is reduced. As a result of this new population. very sensitive to diseases caused by these pathogens.

2. TL - memory in newborns is only 5%, while in adults it is 40-50%. These cells provide a quick response to repeated contact with an antigen, as a result of which newborns are not able to create a strong immunity after a viral infection, as well as to vaccination. And only repeated revaccination in children under one year causes persistent immunity.

3. T-Ls do not yet sufficiently produce IL-4 and IL-5, gamma interferon, CD 40L antigen is weakly expressed, which determines the interaction of T- and B-systems in the immune response. As a result, newborns produce mainly low-affinity antibodies in the form of Ig M. This causes a low response of B-L

to the production of antibodies against viruses, gram(-) microflora, and against protozoan pathogens, as well as a tendency to early generalization of viral and bacterial infections - this process (sepsis, meningitis and others).

Features of the functioning of humoral immunity

1. B-L have a low sensitivity to lymphokines produced by T-lymphocytes, as a result of which there is a weak interaction between T- and B - the immune system, and this, in turn, causes a low production of T-dependent (that is, against intracellular pathogens) specific antibodies.

2. B-L also have an insufficient ability to synthesize plasma cells, which explains the low production of all their own IG, especially secretory IgA. Thus, at the moment of birth, the concentration of Ig M is only 0.1 g/l, and IgA is 0.03-0.05 g/l, while in adults, respectively, it is 0.5-1.8 g/l and 0.5-2.5 g/l Thus, the content of IgM is approximately 8-10%, and IgA is only 0.4% of the adult level.

Clinical significance

As you know, Ig M is synthesized in the early stages of the immune response - it forms the first line of defense in case of bacteremia. And since Ig M acts mainly on gr(-) microflora, and secretory IgA protects mucous membranes from the penetration of antigenic material (including microorganisms) into the body, their insufficiency determines the high sensitivity of newborns to gr(-) pathogens and weak protection of mucous membranes. As a result, this category of children easily develops sepsis caused by gr(-) pathogens and especially often sepsis caused by Salmonella and Klebsiella.

3. IgM in newborns already effectively agglutinates antigens and triggers the reaction of complement binding in the classical way.

4. At the same time, newborns have a sufficient amount of IgG as a result of transplacental transfer of maternal IgG.

Clinical significance. As a result of the transplacental transfer of IgG, specific antibodies are transferred from the mother to the child, and this allows children in the first 2-3 months to be practically free from such diseases as measles, chicken pox, viral hepatitis A, polymyelitis, scarlet fever . At the same time, transplacental transfer of IgG does not protect the fetus and newborns from infections caused by staphylococcus, Escherichia coli.

5. Antibodies of the IgG class in a newborn are already able to activate the complement system by the classical way. However, the ability of newborns to respond to polysaccharide antigens is limited due to the low level of the IgG-2 subclass, which causes the high sensitivity of newborns to meningococci and pneumococci.

6. Significantly reduced number of natural killers, which weakens antiviral and antitumor protection.

7. In newborns, the Th/Ts ratio is 3.5:1, and in adults it is 2.5:1.

That is, according to the analysis data, newborns should have more helper than suppressor activity. In fact, this period is characterized by a suppressive focus of immunity. This contradiction can be explained by the fact that the new people have the suppressive function is carried out, in addition to CD8, also by immature T-L (CD-1, CD-10), NK, as well as the fact that so-called naive T-0 (immature) cells predominate among T-h. Biological expediency of the general suppressive focus of immunological reactions in newborns. due to the prevention of severe autoimmune reactions upon contact with newborns. with a large number of antigens at birth.

8. The barriers of the skin and mucous membranes are imperfect, which together with imperfect phagocytosis leads to increased vulnerability of the skin to pustular diseases, and this requires especially careful care of the skin and mucous membranes.

8. Among the factors of innate immunity, lysozyme is the most effective.

9. Reactions of complement activation are weakened and make up only 50% of the activity of adults.

10. The deficiency of the C-5 component remains, and this leads to a decrease in both complementary non-immune (activation by an alternative pathway) and immune (classical) lysis of bacteria and viruses. This also explains the reduced elimination of CIC from the body. All this, together with a reduced level of antibodies to microbes, leads to a weak ability of the newborn to effectively agglutinate some microorganisms, causes a tendency to excessive accumulation of inflammatory products and blockade of RES.

Thus, in healthy full-term newborns, there is a special, different from adults, biologically appropriate state of cellular and humoral factors of immunological reaction.

At the same time, after birth, the immune system is not yet functionally mature, and therefore its maturation, improvement and differentiation continue throughout childhood. With this statement, we emphasize that the state and strength of the immune response in the future depends not only on the course of the pre- and antenatal periods, but also to a large extent on the perinatal period.

After the end of the newborn period, maturation of the central organs of the immune system continues.

This is how quickly the mass of the retrosternal gland increases. If at birth its mass is 10-15 g, then before the onset of puberty - 30-40 g, after which it begins to decrease. This process is called age-related involution, but activity in parenchymal islets persists until old age.

In addition to irreversible age-related involution, the retrosternal gland has a unique ability to rapidly decrease in volume and mass under the influence of various environmental influences, such as severe infectious diseases, the action of glucocorticoids, sex hormones, cytostatics, starvation, radiation and other severe stress conditions.

This phenomenon was called "accidental transformation". The difference between accidental transformation and age-related involution, from a structural point of view, is a decrease in the lobes of the gland and, accordingly, its mass due to a decrease in the number of lymphocytes in the cortical layer of the gland and the subsequent collapse of the organ and, as a result, a decrease in its function. Due to the high regenerative capacity of the gland, this process is reversible. After the cessation of adverse factors, both the volume of the gland and its function are restored. Age-related as well as accidental involution of the thymus can be a factor in secondary immune deficiency.

Accidental transformation must be differentiated from congenital dysplasia of the organ.

In children, the opposite situation occurs - an increase in the retrosternal gland, the so-called ti-momegaly. The increase in the size of the gland is not due to an increase in the number of epithelial cells that synthesize hormones and lymphocytes, but due to the growth of fatty and connective tissue. That is, in this situation, despite the increased size of the gland, the excretion of thymic hormones is reduced.

Thymomegaly, in the appropriate clinic, should be differentiated from tumors of the retrosternal gland. A prednisone test is used as a screening test. For 7 days, the child is given prednisone at the rate of 1 mg. per kg of body weight. Then they compare the size of the gland before and after prednisolone. With thymomegaly, the size decreases, but not with tumor processes.

Epithelial cells of the thymus produce a number of hormones such as:

Thymosin - which increases lymphocytopoiesis, stimulates the production of antibodies, antitumor immunity, Tx function

Thymopoietin is an immunomodulator

Thymic humoral factor (THF) - stimulates the T-system, in particular: the reaction of transplants against the host, the reaction of blast transformation of lymphocytes to concavalin, the migration of T cells, enhances the function of T cells and Tx.

Thymulin or serum thymic factor (TSF) takes part in the differentiation of both prethymic and postthymic lymphocytes. The thymus also carries out censorial supervision (with the help of phagocytes, which are located at the border of the cortical and medullary layers) for T-lymphocytes that have not received class 1 or 2 GCHS receptors, thereby preventing the development of autoimmune diseases.

Critical periods of development of immunobiological reactivity in children.

1- the period of the newborn, we have just discussed.

2nd period - 3-6 months of life.

1. The suppressive focus of immune reactions is preserved.
2. Passive immunity is weakened due to catabolism of maternal IgG.
3. Primary immunologist. the response is still carried out due to IgM, which does not leave an immunological memory. As a result, whooping cough, chicken pox and other infections. have an atypical course. They can get sick twice

4. There is still insufficient amount of IgA, as a result of which children often get sick with RS-viruses, pneumonia, and repeated acute respiratory viral infections.

5. In children with intestinal infections (salmonellosis, choleenteritis, dysentery), antibodies to these pathogens are very rarely detected in children in the first 6 months of life, and only in 1/3 of patients aged 6 to 12 months. Hepatitis B virus rarely causes jaundice, but can cause acrodermatitis.

6. Primary and secondary IDS are manifested.

All this is due to the peculiarities of the formation of the immune system in young children, and in the literature such a clinical and immunological syndrome is called "physiological transient hypogammaglobulinemia", the consequences of which largely depend on the method of feeding.

The third period is the 2nd year of life.

1. The suppressive focus of immunity changes to the helper one, which leads to the appearance of minor abnormalities of immunity in the form of immune complex diseases - vasculitis, HUS and others. This feature of immunity explains the fact that children under the age of 2 rarely get sick with autoimmune diseases.

2. In the second year of life, B-lymphocytes become more sensitive to lymphokines, especially to IL-2, as a result of which the content of IgG and IgA in the blood increases and is, respectively, 80% and 40% of the concentration of adults. That is, humoral immunity is strengthened. An increase in the concentration of IgA, as already mentioned earlier, reduces the permeability of allergens through mucous membranes, as a result of which transient allergic diatheses can disappear.

3. The primary immune response to most antigens is preserved, but the differentiation of B lymphocytes, which produce IgG1 and IgG3, has already begun, although the synthesis of IgG2 and IgG4 is limited. What comes out of this? Insufficiency of the last two subclasses leads to the fact that pneumococcal polysaccharide antigens do not induce immunity, and 30% of patients do not develop immunity to the influenza bacillus, as a result of which children often get sick with pneumonia caused by these pathogens. Infectious mononucleosis is characterized by an asymptomatic course.

Lymphoid organs of a young child respond to infection with significant hyperplasia, which persists for a long time after the infection (lymph nodes and tonsils increase).

4. The system of local immunity is not yet developed, which causes sensitivity to viral infections and bronchopulmonary diseases, and at the same time, during this period, children's contact with the environment significantly increases.

The fourth period - 4-6 years of life

During this period, the second cross-check of the number of neutrophil granulocytes and lymphocytes in the blood is carried out

The ratio of Th to Ts reaches the adult level (conditions are created for the development of autoimmune diseases)

The average level of IgM and IgG reaches adults, but the level of IgA in the blood serum is still low, the level of IgE increases significantly, (meaning - a secondary immune response and immunological memory is formed, but the increased (or light) permeability of mucous membranes for micro-organisms still remains and allergens and as a result this period is characterized by a high frequency of atopic, autoimmune and parasitic diseases). Late immunodeficiency states, chronic organ diseases begin to manifest.

The fifth critical period - adolescence in girls - 12-13 years, in boys - 14-15 years.

1. The mass of lymphoid organs decreases
2. The production of sex hormones increases.
3. IgE concentration decreases, the severity of atopic diseases decreases.
4. Finally, a strong and weak type of immune response is formed.

As the effect of adverse exogenous factors on the immune system increases at this time (nicotine, alcohol, drugs, and others), there is an increase in chronic inflammatory processes, autoimmune and lymphoproliferative diseases

The structure of immunopathology

A group of diseases	Factors of inclusion in the immunopathology cohort
Immunodeficiency	Primary or secondary insufficiency of immune subsystems.

Allergy	Pathological or inadequate immunological response as a result of a congenital or acquired genetic defect in the cooperation of immunity subsystems, as well as genetically determined hyperproduction of biologically active substance, or insufficient production of their inhibitors.
Autoimmune diseases	Genetic defect of mechanisms of immunological tolerance, violation of recognition of "own" and "foreign".
Immunopathology of reproduction	A group of pathological conditions that arise as a result of an immunological conflict in the "mother-fetus" system (infertility, miscarriage, chronic kidney disease, etc.)
Transplantation immunity	The purely immune basis of transplant rejection, or the reaction of the transplant against the "host".
Immunoproliferative and tumor diseases	Violation of immune surveillance. Infections of the immune system with direct localization of the pathogen in lymphocytes (AIDS, infectious mononucleosis). Tumors of the immune system.

Immunodeficiency diseases (IDDs) are clinical and laboratory pathological processes that are manifested by persistent violations of one or more parameters of the immune response, as a result of which there is a high risk of the formation of protracted, often recurring, chronic diseases of various etiology and localization, and these diseases are resistant to traditional etiotropic and pathogenetic therapy.

Acquired IDS resemble the clinic of primary IDS, but they are not genetically determined (inherited), but arise as a result of adverse factors affecting the immune system in the prenatal and postnatal periods.

There are two degrees of immune deficiency.

1st degree - a decrease of individual indicators of the immune system by 50% from the lower age norm, which are not always accompanied by decompensation of the body's immune defense mechanisms.

2 degree - decrease of individual indicators of the immune system by more than 50% from the lower age norm, which are accompanied by frequent relapses of the disease.

DIAGNOSTICS

Identifying children with immune system dysfunction, including IDS, on the basis of clinical and anamnestic data is the task of pediatricians. Clinical immunologists confirm and clarify the diagnosis with the help of an immunological examination.

Diagnosis of immune system dysfunction is based on a combination of clinical and laboratory indicators.

Making a preliminary diagnosis of immune system dysfunction should be based primarily on clinical data and immunological anamnesis. The immunogram helps us to differentiate IDS from Immune deficiency, as well as to determine the nature and degree of immunodeficiency.

Clinical and anamnestic signs on the basis of which it is possible to suspect the presence of dysfunction of the immune system, and referral of children for consultation to a pediatric clinical immunologist.

I. Recurrent bacterial infections that have the following features:

- purulent otitis or sinusitis (sinusitis, frontitis, ethmoiditis) more than twice during one year;
- two or more pneumonias within one year, chronic endobronchitis, bronchiectasis,
- recurrent pyoderma and abscesses;
- two or more serious infections (meningitis, osteomyelitis, abscesses of internal organs, phlegmon or sepsis);
- chronic infection of the urinary tract without abnormalities in the development of the urinary system;
- chronic recurrent stomatitis;
- severe infections caused by unusual microorganisms (conditionally pathogenic bacteria, pneumocysts, etc.);
- low effect from repeated courses of antibacterial therapy.

II. Persistent oral thrush in a child older than 6 months - chronic recurrent stomatitis, generalized candidiasis.

III. Chronic diarrhea and malabsorption syndrome.

IV. Frequent recurrences of herpetic infection on the skin, mucous membranes, aphthous stomatitis with a long course, severe course of chicken pox, other opportunistic infections (immunodeficiency-associated).

V. The presence of primary immunodeficiency in the family (in the anamnesis, we find frequent deaths in this family, miscarriages, infertility, severe toxicosis of pregnancy, chronic and recurring diseases in relatives, endocrinopathy, malignant diseases.

VI. Adverse reactions to vaccination, vaccine-associated poliomyelitis, manifestation of a typical disease after vaccination with live vaccines (measles, tuberculosis vaccination).

VII Unusual course of some diseases - repeated measles, chicken pox, mononucleosis,

VIII. Recurrent viral respiratory infections of the upper respiratory tract, 8 or more episodes within one year; severe and/or long-term infections of the respiratory tract

IX Conditions associated with an infectious syndrome:

- growth and weight disorders;
- increased fatigue

* - absence of lymphoid tissue (lymph nodes, tonsil hypoplasia, thymomegaly or thymus aplasia) or its hypertrophy;

- combination of ataxia with blepharitis and telangiectasias, albinism, photophobia;
- rash, alopecia, eczema, warts all over the body);
- cartilage hypoplasia, hair, short stature;
- fever of unknown origin.

H. Hematological changes (not less than in two repeated analyses):

- neutropenia (< 1000 cells in 1 μl);
- lymphopenia (< 1500 cells in 1 μl);
- eosinophilia (> 10%);
- the sum of the amount of IgG, IgA and IgM < 6 g/l;
- IgG < 4 g/l
- CD4 < 0.5 x 109/l;
- NST = 0.

Laboratory diagnostics

When interpreting immuno-laboratory indicators, the following problems are solved:

Full health assessment.

Identify dysfunction of the immune system.

Confirm the presence of IDS or immune deficiency;

Determine the degree of severity of disorders in the immune system;

Find out in which chain of the immune system this defect is located;

Identify diseases in the pathogenesis of which immune disorders are possible.

Identify the state of the immune system before and after vaccination;

Prescribe the most adequate immune drugs;

Pre-evaluate the effectiveness of immunotherapy.

Рекомендації, якими необхідно керуватись при інтерпретації імунограми.

Повноцінну інформацію можна отримати при проведенні аналізу імунограми в сукупності з клінічною картиною в цього пацієнта.

Комплексний аналіз імунограм більш інформативний, чим оцінка окремих показників. Одні і ті же зміни в імунограмі при різних фазах гострого запального процесу можна розглядати як сприятливий так і негативний синдром.

Дійсну інформацію в імунограмі несуть тільки стійкі і проланговані зрушення показників.

Аналіз імунограми в динаміці більш інформативний як у діагностиці, так і в прогностичному відношенні ніж одноразово отриманий аналіз. Одноразовий аналіз імунограмі дає можливість зробити тільки орієнтовні висновки.

У висновку зробленому на сукупному аналізі клінічної картини та імунограми перевагу необхідно віддавати клінічним змінам.

Відсутність змін в імунограмі при наявності маніфестних клінічних проявів запальних процесів повинно трактуватись, як атипова реакція імунної системи і вказує на несприятливий перебіг захворювання.

У той же час при інтерпретації імунограм треба зважати на те ,що :

При вторинних ІДС відхилення імунологичних показників від норми в гострій фазі запалення може вказувати як на причину захворювання так і бути наслідком хвороби.

Імунокомпетентні клітини після контакту з АГ на деякий час зникають з крові і поселяються в лімфатичних вузлах - зрозуміло, що в цей час їх кількість у крові буде зменшена;

Необхідно враховувати вікові, індивідуальні, регіональні, сезонні, добові коливання функціональної активності імунної системи. Так максимальне збільшення Т-і В -ланцюга імунітету відмічається в зимовий період, зниження ТЛ відбувається восени, а ВЛ літом. Найбільша активність -в 24 години ,а найменша при пробудженні.

Recommendations that must be followed when interpreting an immunogram.

Full information can be obtained by analyzing the immunogram in combination with the clinical picture of this patient.

Complex analysis of immunograms is more informative than evaluation of individual indicators. The same changes in the immunogram at different phases of the acute inflammatory process can be considered both a favorable and a negative syndrome.

Only persistent and prolonged shifts in indicators carry real information in the immunogram.

The analysis of the immunogram in dynamics is more informative both in the diagnosis and in the prognostic relation than the one-time obtained analysis. A one-time analysis of the immunogram gives the opportunity to draw only tentative conclusions.

In the conclusion made on the combined analysis of the clinical picture and immunogram, preference should be given to clinical changes.

The absence of changes in the immunogram in the presence of manifest clinical manifestations of inflammatory processes should be interpreted as an atypical reaction of the immune system and indicates an unfavorable course of the disease.

At the same time, when interpreting immunograms, it is necessary to take into account the following:

With secondary IDS, the deviation of immunological indicators from the norm in the acute phase of inflammation can indicate both the cause of the disease and be a consequence of the disease.

Immunocompetent cells after contact with AH disappear from the blood for some time and settle in the lymph nodes - it is clear that at this time their number in the blood will be reduced;

It is necessary to take into account age, individual, regional, seasonal, daily fluctuations in the functional activity of the immune system. Thus, the maximum increase in the T- and B-chain of immunity is observed in the winter period, the decrease in TL occurs in the fall, and BL in the summer. The highest activity is in 24 hours, and the lowest when waking up.

It is also necessary to take into account that the immune system is a simultaneously working and mutually regulating system of immunocompetent cells and mediators, where a change in one indicator causes compensatory reactions of a number of other indicators, and these compensatory reactions can ensure the full functioning of the entire system. At the same time, in a completely healthy child, individual components of the immune system may be absent in the immunogram.

Currently, a 2-stage approach is used to assess a person's immune status.

At the 1st stage - with the help of simple, but quite accurate indicators, gross changes in the immunogram are detected.

Determination of non-specific protective factors

a) Determination of bactericidal activity of blood serum

b) Determination of the level of lysozyme in biological fluids

c) Determination of complement level (N =35-60)

d) Assessment of the functional state of phagocytic cells based on the determination of: phagocytic index (FI) and phagocytic number (FN), and the test with nitrotetrazole blue (NST test)

Phagocytic number - (total number of phagocytes participating in phagocytosis) = 60-80%

Phagocytic index - (the number of non-pathogenic microbes absorbed by one phagocyte) = 3-5

HST-test - determines the number of neutrophils and monocytes that can increase their digestive ability under the influence of infection (#-30%).

2. Assessment of acquired immunity:

a) Determination of the relative norm and absolute number of lymphocytes in peripheral blood

b) Determination of the relative number of T-Lymphocytes with the help of monoclonal antibodies (No.-55-60)

c) Determination of T-lymphocyte subpopulations (Th and Ts) no. - 40% and 20%, respectively) and the ratio of Th to Ts (Th/Ts in no. = 2/1,

d) proliferative activity (reaction of blast transformation) to FGA

e) evaluation of humoral immunity (relative and absolute number of B-lymphocytes; level of serum I.H.)

The second level is a deeper level of studying the immune status of a person and includes (determination of EC, HLA-phenotype, production of cytokines, presence of specific antibodies and others).

Classification of IDS.

Primary IDS are characterized by a decrease or absence of an immune response due to a genetically determined defect or as a result of a violation of the development of the immune system during ontogenesis.

1. IDZ with predominantly humoral immunological deficiency;

• Bruton's X-linked agamoglobulinemia;
• selective (selective) deficiency of certain I.G (IgG, IgA subclasses);
• transient childhood hypogammaglobulinemia);
• general variable immune deficiency • hyper-IgM syndrome;

2. IDS with predominantly cellular immunological deficiency:

• Lymphocyte dysgenesis, or Nezelof's syndrome or the French type of ID;
• Di-Georgie syndrome;
• Chronic mucocutaneous candidiasis);

3. Combined IDS:

• Swiss type or severe combined immunodeficiency (SCI);
• X-coupled ID;
• adenosine deaminase deficiency;
• Syndrome of naked lymphocytes;
• Vyskot-Aldrich syndrome;
• Louis-Bar syndrome.

4. Deficiency of the phagocyte system

(Chronic granulomatosis; Chediak-Higashi syndrome, familial neutropenias)

5. Deficiency of the complement system. Autoimmune diseases. Congenital angioedema occurs with C3 deficiency of the complement system.

Primary agammaglobulinemia - Bouton's disease.

Only boys get sick. Recurrent diseases of the bronchopulmonary system, ENT organs, and urinary system are characteristic of this disease.

Laboratory - there are no plasma cells, the number of circulating lymphocytes is normal, the number of all immunoglobulins is sharply reduced (IgG. less than 2.0 g/l, and IgA and IgM - less than 0.2 g/l), the number of gamma globulins is less than 3 g/l (No. -16 -18g/l), the number of T lymphocytes is normal.

Selective deficiency of serum IgA

This disease is often accompanied only by associated syndromes in the form of allergic reactions and especially to cow's milk, autoimmune diseases, malabsorption syndrome, dysbacteriosis, recurrent herpetic stomatitis, ulcerative colitis, celiac disease, Crohn's disease, tumor diseases. Almost half of children with this pathology have antibodies to immunoglobulin A in their blood. Therefore, in this category of children, transfusions of blood and protein preparations are often accompanied by complications.

Immunological characteristics - the total number of lymphocytes is normal, the relative number of B lymphocytes is normal, cellular immunity is normal, plasma cells that synthesize IgA are absent, secretory and serum IgA are absent.

Di-Georgie syndrome

A specific defect. Dysembryogenesis: disturbance of thymus development (aplasia or hypoplasia), absence of parathyroid gland. Some authors consider this disease to be congenital and due to a violation of embryonic differentiation in the area of 3-4 gill arches.

Clinical manifestations are the inability to resist both viral and bacterial pathogens. Hypocalcemic seizures.

Immunological changes: lymphocytopenia, reduced number and proliferative activity of T lymphocytes. The level of Ig in blood serum corresponds to the norm, but their ability to produce antibodies to some pathogens is reduced due to the absence of Th.

Wiskott-Aldrich syndrome (linked to the X-chromosome) is a disease characterized by a triad: a tendency to recurrent and chronic microbial-inflammatory diseases; allergic diseases of the skin, respiratory tract; thrombocytopenia The disease can manifest itself at any age, but usually with bleeding during the newborn period (purpura, melena, epistaxis), recurrent purulent infections. Children die early.

The immunological picture is characterized by a decrease in leukocytes and platelets, atrophy of the thymus and lymphoid tissue, a decrease in Ig M along with a normal level of IgG and increased IgA, IgE.

Louis-Bar syndrome

The type of inheritance is autosomal recessive.

Specific defects - impaired function of T- and B-lymphocytes, reduced level of IgG2 IgA, IgE, hypoplasia of thymus, spleen, lymph nodes, tonsils.

Clinical markers are cerebellar ataxia, which appears in 2-4 years, telangiectasias primarily on the mucous membrane of the sclera, chronic and recurrent inflammatory processes of the organs. In the future - damage to the endocrine, vascular system. In some children, it is possible to determine a delay in mental development. Manifestation of the disease at the age of 15.

Hereditary neutropenia

Hereditary neutropenias have the following variants:

- Infantile lethal agranulocytosis (Kostman's disease) is an autosomal recessive type of spasticity.

Clinical manifestations:

- chronic purulent infections of the skin, mucous membranes of the additional nasal sinuses, inflammation of the lungs, the mandatory presence of periodontitis, the development of osteomyelitis, sepsis is characteristic

Laboratory:

- neutropenia (the number of neutrophils is less than 300 in 1 μl) - monocytosis, eosinophilia

The prognosis is unfavorable.

Cyclic neutropenia is an autosomal dominant or recessive type of inheritance.

Clinical manifestations:

- periodically (with an interval of 3-4 weeks) there is fever with chills, pain in the joints, hepatosplenomegaly.

Laboratory:

- periodically neutropenia, leukopenia

The prognosis is favorable in the absence of septic complications.

Familial benign neutropenia may not manifest itself or may be manifested by a tendency to recurrent or prolonged banal infections.

Laboratory:
- leukopenia (in the range from 3.0 to 4.0 x 10'Ul)
neutrophils in the leukocyte formula 0-35%
The prognosis is favorable.

5. Theoretical questions that are considered in class.

1. What structures belong to the central organs of the immune system?
2. What structures belong to the peripheral organs of the immune system?
3. With the help of which cellular factors is acquired immunity carried out?
4. Name the main cellular and humoral factors of innate immunity.
5. Which cells belong to micro- and macrophages and what function do they perform in the body?
6. What function do components of the complement system and interferons perform in the body?
7. What subpopulations are lymphocytes divided into?
8. What is the main function of T-L and B-L?
9. Name the diversity of T-L and the function of individual subpopulations.
10. Know the classification of immunoglobulins and their function.
11. Know the ontogeny of the immune system.
12. Know the features of the functioning of the immune system in the fetus, newborn child, and in the second critical age periods.
13. Know the structure of pathology of the immune system.
14. Know the classification of immunodeficiency diseases.

Recommended literature.

Nelson textbook 21th Edition by Robert M. Kliegman, MD, Joseph St. Geme, Nathan J. Blum, Samair S. Shan, Robert C. Tasker, Karen M. Wilson, Richard E. Behrman Видавництво: Elsevier, 2019. P. 1911-1915.

Additional:

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2. Katilov O.V., Dmitriev D.V., Dmitrieva K.Yu., Makarov S.Yu. Clinical examination of a child. 2nd edition. Vinnytsia: Nova Kniga, 2019. 520 p.
3. Pediatrics: textbook. T.O. Kryuchko, O.Y. Abaturov, T.V. Kushnereva et al.ed. by T.O. Kryuchko, O.Y. Abaturov. Kyiv : AUS Medicine Publishing, 2016. 208 p. (p.39-49) ISBN 978-617-505-485-7.