Ministry of Health of Ukraine
Ukrainian Medical Stomatological Academy

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PEDIATRIC INFECTIOUS DISEASES IN FAMILY DOCTOR'S PRACTICE

Study Guide

Міністерство охорони здоров'я України
Українська медична стоматологічна академія

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ДИТЯЧІ ІНФЕКЦІЙНІ ХВОРОБИ У ПРАКТИЦІ СІМЕЙНОГО ЛІКАРЯ

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Навчально-методичний посібник підготовлений співробітниками кафедри ендокринології з дитячими інфекційними хворобами (зав. кафедри проф. Л.Є. Бобирьова) Української медичної стоматологічної академії, доц., к.мед.н. К.В.Пікуль, доц., к.мед.н. В.І.Ільченко, к.мед.н. К.Ю.Прилуцьким.

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Рекомендовано Вченою радою Української медичної стоматологічної академії як навчально-методичний посібник для англомовних студентів медичних факультетів закладів вищої освіти МОЗ України (витяг з протоколу №4, від 26 грудня 2018 року)

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Навчально-методичний посібник складений згідно з типовим навчальним планом та програмою для підготовки іноземних студентів медичних закладів вищої освіти для циклу «Дитячі інфекційні хвороби». Цей навчально-методичний посібник написаний англійською мовою і присвячений питанням етіології, епідеміології, клініки та диференційної діагностики найбільш частих дитячих інфекційних хвороб, наведені алгоритми діагностики та терапії, згідно з протоколами лікування, що затверджені МОЗ України. Назви розділів автори підібрали у відповідності з тематичним планом для підготовки іноземних студентів медичних закладів вищої освіти. Посібник містить запитання для самоконтролю, тести, задачі та розбір історій хвороб дітей, що лікувались у дитячому відділенні ПОКІЛ для більш глибокого засвоєння матеріалу.

The teaching manual is compiled according to a typical curriculum and a program for the preparation of foreign students of medical institutions of higher education for the cycle "Children's Infectious Diseases". This teaching manual is written in English and is devoted to the issues of etiology, epidemiology, clinics and differential diagnostics of the most common infectious diseases of children, diagnostic algorithms and therapies are given in accordance with the treatment protocols approved by the Ministry of Health of Ukraine. The titles of the sections were chosen by the authors in accordance withthe thematic plan for thepreparation of foreign students of medical institutions of highereducation. The manual contains questions for self-control, tests, tasks and analysis of children's diseaserecords that were treated at the children's department for a deeper assimilation of the material.

CONTENTS

Introduction

The era of information society, which is based on knowledge, their production, tradition and acquisition, puts forward new requirements to the system of education. Implementation of the advanced technologies into teaching is crucial for contemporary medical higher education. One of the ways of integration and democratization of higher education in Ukraine is assimilation with European canons of education and ensuring the Bologna Process's educational objectives.

The implementation of these tasks is possible only on the condition of transition from the classical educational system, which aims to prepare the qualified future physician to a new system, which prepares a professional, who not only knows, but also is able to apply this knowledge in the Family Medicine practice.

Infectious diseases have always been virulent, proved by its mass character, rapid proliferation and high mortality, especially in child age. Numerous infections can lead to the development of complications, requiring proper diagnosis, therapy, taking into account the etiology of pathological process.

Hopefully, the present study guide will be useful in everyday practical work of pediatricians, pediatric infectiologist and family doctors, as well as for students of 5-6-year of study at medical HEIs.

The authors will gratefully accept all suggestions and criticisms.

List of Abbreviations

AS – acetonemic syndrome

BBB – blood-brain barrier

AEI – acute enteric infection

ASLT – acute stenosing laryngotracheitis

ABB – acid-base balance

CVP – central venous pressure

ITS – infectious toxic shock

ELISA – enzymoimmunoassay

BES – brain edema-swelling

EPEC – enteropathogenic Escherichia coli

ETEC– enterotoxigenic Escherichia coli

CIGD – complex immunoglobulin drug

IFA – immunofluorescence antibody assay

AR – agglutination reaction

CFT – complement-fixation test

PR – precipitation reaction

HAIR - hemagglutination-inhibition reaction

PHAT - passive hemagglutination test

CFR - complement-fixation reaction

NR - neutralization reaction

MA – membrane antigen

VCA – viral-capsid antigen

EA – early antigen-diffuse

SECTION 1.
PREVENTION OF PEDIATRIC INFECTIOUS DISEASES

Fighting infectious diseases is one of the major tasks for public health care and state. The non-specific and specific (vaccination) prophylaxis is distinguished. The system of nonspecific preventive measures is directed on strict observance of sanitary-hygienic regimen, early detection of the source of infection and its isolation, surveillance over the contact individuals and their control laboratory examination in the foci of infection, final disinfection in the foci of disease, etc.

Vaccination is the artificial creation of the immune response by administration of vaccine to the human body in order to form the immunity to the infection.

The beginning of successful fighting infectious diseases is considered the year of 1798, when English physician Edward Jenner invented a way of vaccination with the cowpox material to prevent the infection of smallpox. He called the procedure vaccination, and the material that was taken from smallpox of cows was vaccine (from Lat. "vacca"-cow).

Formation of post-vaccine immunity

Humoral immunity is the immunity of the body to infection which is caused by the presence of specific antibodies. Vaccine prophylaxis is aimed at creation of active artificial anti-infectious immunity by administration into the human body of antigens of infectious agent in the form of vaccine. In primary administration of the vaccine strain of the pathogen (vaccination) in a non-immune body, the JgM-class antibodies appear in the blood with the subsequent switching to the synthesis of antibodies of JgG-class, and cells of the immune memory are formed. In the repeated administration of antigen (revaccination) a "booster" effect occurs due to inclusion of memory cells. At the same time the producing of specific antibodies begins almost immediately and their level can be greater than in the initial administration of antigen. The third dose of antigen usually enhances the process of antibodies formation; however, the subsequent additional doses of antigen can lead to immunodepression, but not to enhanced production of antibodies.

Basic patterns of immune response in immunization:

- strong and long-lasting immunity is provided by revaccination;
- the immune response to vaccination is strictly specific and individual. Active immunization does not ensure the development of the same level of immunity in all vaccinated children;
- the highest level of artificial immune response can be obtained in the diseases that thereafter develop rather durable natural immunity (measles, rubella, mumps);
- active immunization causes the formation of immunity within the certain period of time, hence it is used for prophylaxis mainly.

Vaccine Types

1. Live-attenuated vaccines.
2. Inactivated vaccines:
   а) corpuscular vaccines;
   б) chemical vaccines;
   в) recombinant vaccines;
   г) toxoid vaccines.

Live vaccines

Live vaccines are immunoprophylactic agents produced on the basis of attenuated (weakened) strains of pathogens in the absence of virulence and preservation of antigenic and immunogenic properties of germs. Due to the ability of germs to multiply, in the body of the vaccinated individual the development of the vaccine infection is observed, which runs without marked clinical symptoms, but leads to the formation of a sustainable immune response.

Advantages of live vaccines:

- stimulate the formation of the strong and long-lasting immunity;
- single dose administration of vaccine (except for the polio) is enough for the development of protective level of antibodies;
- live vaccines are administered in different ways: subcutaneous, intracutaneous, intranasal, per os.

Limitations in use of live vaccines:

- need to be kept cold (from the moment of production to use the vaccine shall be kept and transported in the temperature of +4 - +8°C);
- during vaccination it is not recommended to use disinfecting agents with long-lasting contact with skin that can lead to vaccine inactivation (e.g. tincture of iodine);
- during vaccination it is not recommended to take corticosteroids and antibiotics that can affect the formation of the immune response;
- have much more higher reactogenicity compared to inactivated vaccines.

Currently, the following vaccines are used in Ukraine:

a) viral live vaccines to protect against polio, measles, mumps, rubella;
b) bacterial live vaccines to protect against tuberculosis, anthrax, etc.

Inactivated vaccines

1. *Corpuscular vaccines* are bacteria and viruses, inactivated by the effect of physical (heat, ultraviolet irradiation) or chemical agents (formalin, ethanol, phenol). Corpuscular vaccines contain integral cells of germs. They use the killed virulent strains with preserved antigenic and immunogenic properties (pertussis vaccine, as a DTaP (diphtheria, tetanus, and pertussis) component; leptospirosis, encephalitis vaccines, etc.).

Advantages of inactivated vaccines: low reactogenicity.

Limitations:

- are of lower immunogenicity as compared to live vaccines;
- need several doses (2 or 3) over time (booster shots) to get ongoing immunity;
- after vaccination they don't provide long-lasting immunity, requiring revaccinations.

2. *Chemical vaccines* are antigenic components, extracted from microbial cells (typhoid chemical vaccine, enriched by Vi – antigen; meningococcal polysaccharide vaccine; polysaccharide *Haemophilus influenzae* type B vaccine). Bacterial polysaccharides are thymus-independent antigens, so their conjugates with protein carrier (diphtheria or tetanus antitoxin in minimal amount, or protein of inner microorganism against which the vaccine is made) to form the T-cell immune memory. The important feature of chemical vaccines is low reactogenicity.

3. *Recombinant vaccines* are the product of genetic engineering. Recombinant vaccines are made by:

- gene cloning;
- introduction of genes into the cells-producers (viruses, fungi, bacteria);
- cell cultivation;
- antigen extraction and its purification.

Examples include the widespread vaccine, commonly used against Hepatitis B. The method of production involves introducing of subunit of Hepatitis B virus gene, which encodes the synthesis of surface antigen HbsAg), into DNA of yeast cells, multiplying fast and accumulate a considerable amount of HBsAg. The antigen is extracted, purified from the yeast debris and used as the vaccine against Hepatitis B.

Recombinant vaccines are safe and effective, can be used to produce mixed vaccines that provide immunity against several infections (vaccine against hepatitis B + DTaP, a five-component acellular vaccine against diphtheria, tetanus and pertussis, inactivated vaccine against polio and hemophilic infection, a six-component vaccine against Hepatitis B + acellular against diphtheria, tetanus and pertussis, inactivated against polio and hemophilic infection).

4. *Toxoids* are bacterial exotoxins with inactivated toxic properties (under the influence of formalin and high temperature), but with preserved immunogenic and antigenic properties. In the process of production, toxoids are purified from ballast substances (nutrient medium, remnants of microbial cell) and concentrated. Hence, the reactogenicity of toxoids is reduced and the volume of the injected agent is lowered. Toxoids are produced as univalent vaccines (diphtheria, botulinum, tetanus, staphylococcal, gangrenous antitoxin) and polyvalent vaccines (diphtheria-tetanus, botulinum trianatoxin). A strong anti-toxic immunity requires administration of several doses over time with subsequent revaccination. Prophylactic effectiveness of toxoids reaches 95-100% and persists for several years. An important feature of toxoids is the development of long-lasting immune memory; therefore the prescription of toxoids is quite reasonable in the prevention of diphtheria in the focus of infection and emergency prophylaxis of tetanus (rapid accumulation of antitoxin in blood serum in high titers).

Reactogenicity of toxoids is low. However, its limitation is considered the inability to create antibacterial immunity in population (only antitoxic is developed), not providing protection from infectioning and development of carriage.

Recommended guidelines for vaccinations

Preventive vaccinations are carried out in the rooms of vaccinations at medical facilities (hereinafter MF), medical offices of preschool and general educational institutions, medical centers of enterprises and the offices of vaccination of the subjects of entrepreneurial activities that are licensed to medical practice in accordance with the law of Ukraine "On the licensing of certain types of economic activity" (with amendments), as well as in the in-hospital conditions on indications. Vaccinations are allowed only to be registered in Ukraine by the vaccines in accordance with the indications and contraindications for their conduct keeping to the immunization schedule in Ukraine and the Instruction on the use of vaccines, approved by the Chief Medical Officer of Ukraine or his/her Deputy. Transportation, storage and use of vaccines is carried out with the mandatory observance of the requirements of the "cold chain" in accordance with the Procedure of providing proper storage conditions, transportation, and acceptance and accounting of medical immunobiological medications in Ukraine, approved by this Order. Preventive vaccinations are carried out by medical professionals, who are experts in organization and technique of vaccination, as well as in case of emergency in the development of vaccine reactions and complications. Responsible for organizing and conducting preventive vaccinations is the Head of the medical facility and individuals exercising medical practice as subjects of entrepreneurship and have a license for medical practice in accordance with sub-paragraph 26 Article 9 of the Law of Ukraine "On the licensing of certain types of economic activity" (with amendments). The procedure of preventive immunization is determined by the Order of the Head of the medical facility with a strict assignment of responsible individuals and functional duties of medical professionals who participate in vaccination process. The scope of preventive vaccinations shall be consistent with the territorial pediatric services in May and November of each year. In order to ensure the timely conduct of prophylactic vaccination a nurse invites individuals, subject to vaccination (parents or guardians in case of immunization of juveniles) in oral or written form on the designated day for vaccination and informs parents or guardians in advance in the child care centers. On the day of appointment for preventive vaccinations, immediately before its conduct, a medical examination with mandatory temperature measurement is made to exclude the acute disease and individuals subject to immunization, parents and guardians (in vaccination of juveniles) are informed about possible manifestations of the side effects after vaccination. The medical documentation has a relevant record of informing about possible manifestations of the side effects which is signed by a citizen and a doctor's record on permission to conduct vaccination. Preventive vaccinations shall be carried out in compliance with the sanitary and anti-epidemic rules and norms. The room for

vaccination shall be equipped with: refrigerator or a heat container (if the vaccine is stored in a different room, for temporary vaccination centers), a closet for armamentarium and medications, sterilizing cases with sterile material, baby changing table and medical couch, tables for preparation of medications for application, table (closet) for storing the documentation, the container with disinfecting solution. In the case of needle-cut off use for used syringes, it shall be placed next to the table for medications and a couch. It is strictly forbidden to conduct prophylactic vaccinations in surgical dressing rooms, manipulation rooms.

Prophylactic vaccinations are carried out only by disposable or self-locking syringes. Patients' safety of injections in immunization is guaranteed by self-locking syringes (accuracy of the dose, inability to be reused). Used syringes shall be decontaminated and disposed. In the case of using the cutoff for needles before decontamination, the collection of cut-off needles and syringes is made in separate hermetic containers. During disinfection and utilization of used syringes in order to avoid risk of infection of medical workers, resulted from microinjuries, manipulations with the prickly parts of injection equipment are prohibited. Vaccinations for tuberculosis prevention and diagnosis must be carried out in separate premises, and in case of their absence on a specially allocated table or on the other day. It is prohibited to use instruments intended for vaccination against tuberculosis for other purposes.

Training workshops for nurses on the theory of immunization and technique of preventive vaccinations and Mantoux tests with the compulsory conduct of pass/fail tests shall be organized by the territorial health care departments not less than once a year. The record of administered vaccination shall be done in the record books of medical documents approved by the Ministry of Health of Ukraine. Adult patients receive the appropriate certificate, specifying the following: type of vaccine, dose, series and control number. In the case of use of the imported vaccine the brand name shall be transliterated in Ukrainian. The data filled in into the immunization record are verified by the signature and seal of a doctor or individual who is engaged in private medical practice. After immunization the follow up medical surveillance must be provided within the time period specified by the instruction on application of the appropriate vaccine. In medical documents it is necessary to mark the nature and terms of general and local reactions, if they occurred, and to register them in compliance with the Instructions on the organization of epidemic surveillance of the side effects of immunobiological medications, approved by the order. In case of development of an unusual reaction after vaccination or suspicion of complications the Head of medical facilityor individual, engaged in private medical practice must be immediately informed and emergency notice of unusual post-vaccination reaction or suspicion of complications after administration of vaccine, completed according to the form of medical records, approved by the Ministry of Health of Ukraine, shall be disseminated to the territorial pediatric service.

Medical contraindications to the vaccinations of each particular child are established by the Commission on Immunization issues, created by the Order, issued for a medical facility, according to the list of medical contraindications for immunization, approved by this order. To solve difficult and contradictory issues concerning contraindications to vaccinations the Commission on Immunization issues at the Regional Children's Hospital is created. The fact of refusal from vaccination with the mark that the medical professional provides clarification on the consequences of such refusal is recorded in the medical record book approved by the Ministry of Health of Ukraine, and signed by both a citizen and medical professional. In each vaccination room there shall be instructions on the use of all the medications used for vaccination (including those that are not included in the list of mandatory ones). Immunizations within the immunization schedule can be conducted only by vaccines, which are registered in Ukraine. Vaccines of various manufacturers can be mutually replaced to prevent similar diseases.

Table1

NATIONALLY RECOMMENDED IMMUNIZATION SCHEDULE FOR CHILDREN AND ADULTS

(Order of the Ministry of Health of Ukraine No.947 as of 18.05.2018)

Age	Vaccine against					
1 day		Hepatitis B				
3-5 days	Tuberculosis					
1 month		Hepatitis B				
2 months			diphtheria, tetanus and pertussis	Polio IPV	Haemophilus infection	
4 months			diphtheria, tetanus and pertussis	Polio IPV	Haemophilus infection	
6 months		Hepatitis B	diphtheria, tetanus and pertussis	Polio OPV		
12 months					Haemophilus infection	measles, rubella, mumps
18 months			diphtheria, tetanus and pertussis DTaP	Polio OPV		
6 years			diphtheria, tetanus	Polio OPV		measles, rubella, mumps
14 years				Polio OPV		
16 years			diphtheria, tetanus			
Adults			diphtheria, tetanus once a 10 yrs.			

Reactions after immunization and complications

A. Codes of clinical manifestations of side effects after vaccination:

1. Fever to 39^0C.
2. Fever >39^0C (strong common).
3. Temperature not registered in the medical record.
4. Pain, swelling of soft tissues > 50mm, hyperemia at the site of the shot > 80mm, infiltration > 20mm (strong local).
5. Lymphadenopathy.

6. Headache.
7. Irritability, sleep disorder.
8. Non-allergic rash.
9. Loss of appetite, nausea, stomachache, dyspepsia, diarrhea.
10. Catarrhal events.
11. Myoneuralgia, arthralgia.

B. Codes of clinical manifestations of vaccine-associated complications:

12. Abscesses.
13. Anaphylactic shock and anaphylactoid reactions.
14. Allergic reactions (Quincke's edema, hives like rash on the body, Stevens-Johnson syndrome, Lyell's syndrome).
15. Hypotensive – hyporesponsive syndrome (acute cardiovascular inefficiency, hypotonia, decreased muscular tonus, dizziness or loss of consciousness, vascular disorders in the past history).
16. Arthritis.
17. Nonstop high-pitched crying (lasting from 3 hours and more).
18. Febrile seizures.
19. Afebrile seizures.
20. Meningitis /encephalitis.
21. Anesthesia/ paresthesia.
22. Acute flaccid paralysis.
23. Vaccine-associated paralytic poliomyelitis.
24. Guillain-Barré syndrome (polyradiculoneuritis).
25. Subacute sclerosing panencephalitis.
26. Mumps, orchitis.
27. Thrombocytopenia.
28. Subcutaneous cold abscess.
29. Superficial ulcer > 10 mm.
30. Local lymphadenitis.
31. Keloid cicatrix.
32. Generalized BCG-infection, osteomyelitis, osteitis.

Mode of reporting about the case of vaccine-associated side effect (complication)

Vaccine reactions and complications are impairment of health that arises following immunization. Health care facilities shall report to the Ministry of Health of Ukraine and Public Enterprise "Immunobiological Products Center" about each case of complication occurs after the use of bacterial, viral or humoral product, shock, death after administration of the drug, unusual reaction or high reactogenecity of the drug within 24 hours. PE "Immunobiological Products Center" informs the manufacture of IBP within 14 hours.

Each case of complication (or suspicions of complication) following vaccination shall be recorded and subject to investigation. Following the investigation the report of investigation of the side effect (complication) after vaccination shall be made, containing the following information:

1. Full name of the vaccinated individual. Date/month/year of birth. Place of employment (child care center). Place of residence.

2.Facility that investigated (reported) the case of side-effect (complication) following vaccination.

3.Information on the product.

Brand name. Serial number. Control number. Expiry date. Manufacturer. Amount of product received. Date received. Conditions and temperature mode of transporting and storage

on the region, district, city of use. Inappropriate use of vaccine (method of administration, dose, storage conditions, from the opened vial, etc.). Number of individuals, administered with vaccine of indicated series in the region, district or number of doses used. Occurrence of vaccine-associated unusual side effect in individuals.

4.Medical records on health state of vaccinated individual.

Date of vaccination. Position of health care provider who examined the individual before vaccination (physician, paramedic, nurse); temperature before vaccination. Individual features (prematurity, birth trauma, brain trauma, corticosteroid therapy prior vaccination, etc.). Diseases in the history (for children aged from 3 years old with recorded date and duration of the diseases); indicate the date and duration of the latest diseases. Allergy-associated diseases (including medications and food). Seizures in the history of a vaccinated individual, his/her parents, brothers and sisters, in the heighten temperature or without it, duration. Vaccinations made with records of the date of administration. Unusual vaccine-associated reactions in the history of vaccinated individual, his/her parents and siblings (details, nature of reactions). Additional data (contact with infected people in the family, child care center, exposure to cold, etc.).

5.Clinical course

Date of the onset of the diseases, complaints. Date of admission. On physical examination: signs of local and common reaction, diagnosis. Date and place of hospitalization. Progress of the diseases (brief description). Final diagnosis: main; complications; concomitant diseases. Date of discharge. Outcomes. Sequelae. In lethal case: date, postmortem diagnosis.

6. Report of the committee on reasons of complications

Positions and signatures of the members of the committee. Date of examination. Emergency report was sent on the telephone, telegraph (underline). Date. In the case when the Report of Investigation is sent to the Ministry of Health of Ukraine and Public Enterprise "Immunobiological Products Center" it is mandatory to specify name of the facility, reported the information and its location.

In many countries of the European Union and the United States people are protected from the following infections through **prophylactic vaccination**: chicken pox, hemophilic infection type B, human papillomavirus, Hepatitis A, Hepatitis B, influenza, diphtheria, pertussis, measles, meningococcal infection (serogroups A, C, Y, W-135), mumps, pneumococcal infection, polio, tetanus, rotavirus infection, tuberculosis, tick-borne encephalitis, multiple sclerosis. The following vaccines have been developed and are in use on epidemic indications: typhus, tularemia, hoof-and-mouth disease, brucellosis, leptospirosis, cholera, typhoid fever, yellow fever, Omsk hemorrhagic fever, Q fever, rabies, Japanese encephalitis, anthrax and plague.

In order to improve treatment and passive immunization the following **specific immunoglobulins** are used: anti-cytomegalovirus, anti-toxoplasmosis, anti-rotavirus, anti-chlamydia, anti-herpes viruses of 1, 2, 6 types, against the ureaplsma, mycoplasma, Epstein-Barr virus, chicken pox, anti-staphylococcal, anti-botulinum, influenza, anti- rabies, anti-tetanus, anti-hepatitis B, anti-leptospirosis, against tick-borne encephalitis, antiallergic. In rhesus incompatibility the immune globulin human antirhesus Rh_0 is used. In the secondary immunodeficiency state it is possible to use human immunoglobulin or triglobulin per os.

To treat bacteria-carrying and for combination with antibacterial therapy, bacteriophages (viruses that can infect bacterial cells and cause their lysis, not suppressing normal microflora) are used. The following bacteriophages are distinguished: dysenteric, salmonellosis, E.coli-Proteus, Staphylococcus, Klebsiella, Yersinia, Pyobacteriophage, polyvalent.

Treatment of bacterial infections, secreted exotoxin, involves foreign sera, administered according to Bezredki method (anti-diphtheria, anti-tetanus, anti-botulinum A, B, C, E, F, antigangrenous).

List of questions for final control:

1. Form the conception of “immunity”; types of immunity.
2. What are the common regularities of epidemiology of pediatric infectious diseases?
3. What are the epidemiological chain components? Give the description of its main constituents.
4. How can pediatric infectious diseases be prevented?
5. What is the classification of vaccines?
6. When do the vaccine-associated reactions and complications occur?
7. What are the conditions for vaccine transportation and storage?

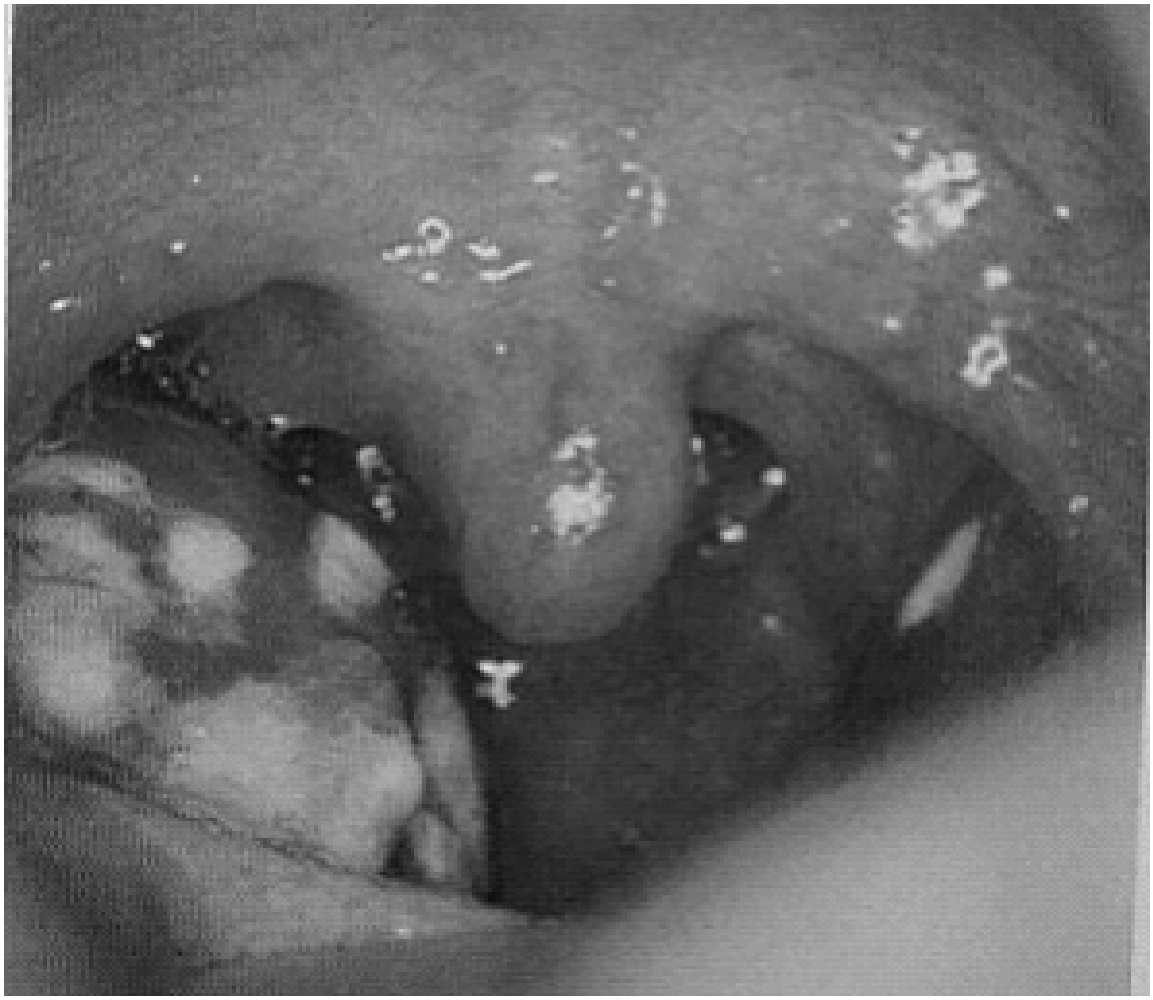

Fig.1 Koplik's spots in measles (a specific prevention of infection is vaccination)

SECTION 2.
EXANTHEMATOUS INFECTIONS IN CHILDREN

Exanthematous infections include measles, rubella, scarlet fever, chickenpox, sudden exanthema and infectious erythema.

Measles is a viral infection characterized by cyclic course, intoxication syndromes, catarrhal infection of the respiratory tract, conjunctivitis and exanthema. Measles is caused by the *Polinosa morbillarum* virus within the family *Paramyxoviridae* of the genus *Morbillivirus*, contains RNA but unlike other paramyxoviruses, it does not include neuraminidase.

Epidemiology:

1. Disease reservoir: infected person.
2. Way of transmission: respiratory droplets.
3. Susceptibility: common, susceptibility index is 98% from 6-8 months old.

Main chains of the pathogenesis

1. Entry of infection: mucous membranes of the upper airways (virus binding), spreads into regional lymph nodes.
2. Viremia (first waive).
3. Spreads into the organs of the reticulo-endothelial system; replicates.
4. The second wave of viremia.
5. Involvement of the CNS, mucous membranes of trachea, bronchi, bowels.
6. Inflammation, destruction, virus release.
7. Secondary immune deficiency, layering of bacterial flora.
8. Formation of complications.

Diagnostic criteria

The incubation period ranges between 9-17 days and 21 days in those individuals, administered with γ-globulin, blood products, immunodepressants following the contact. *The catarrhal period* lasts for 3-4 days. The period is characterized by the following manifestations: growing catarrh of the upper airways, subfebrile temeperature and intoxication syndrome. Occurrence of conjunctivitis, photophobia is recorded on day 2-3, appearance of enanthema (Filatov-Koplik's spots) 1-2 days prior the period of rash. *Period of rash* appears on day 4-5 and lasts for 3-4 days. Catarrhal events aggravate (laryngitis, coryza, conjunctivitis). Rise of temperature and intoxication syndrome is prominent. Rash is maculopapular and reddish-brown on the intact skin, often confluent, with typical staging:

day I – behind the ears, on the face;
day II – on the neck, shoulders, upper part of the body;
day III– spreads over the whole body, hands, proximal area of legs;
day IV – over all lower extremities.
Rash ends in pigmentation (the staging is preserved).

The period of pigmentation runs by stages, ends in defurfuration. Body temperature comes to normal, intoxication resolves, catarrhal events lessen and disappear (day 7-9 after rash appeared). *The period of reconvalescence* is characterized by asthenia and anergy (3-4 weeks).

Classification

***According to the form*:** typical, atypical, abortive, mitigated, hyperergic, latent, asymptomatic, measles in vaccinated individuals, measles in antibiotic- and hormonotherapy;

***According to severity**:* mild, moderate, severe (without hemorrhagic syndrome; with hemorrhagic syndrome)

***According to the clinical course*:** uneventful (non-complicated), eventful (complicated).

PARACLINICAL TESTS:

1. Complete blood count: leukopenia, lymphocytosis, eosinophilia, thrombocytopenia;
2. Cytological study (cytoscopy) of throat swabs to reveal the multinucleated giant cells, typical for measles;

3. Serological methods (indirect haemagglutination test (IHA) and passive haemagglutination test (PHAT): rise of antibody titer in dynamics by 4 times and more;
4. Immunoferment analysis (IFA): detection of antibodies to Ig M measles virus (acute period), growing of Ig G antibody titer by 4 times and more (resolved disease).

Treatment:

1. Homestay treatment mainly. Patients are hospitalized in case of: first year of life; severe forms of measles, complications; on epidemic indications.
2. Chemically and mechanically light food is recommended.
3. Oral hygiene.
4. Antisensitizers (younger than age 6: 5 mg/day edem; older than age 6: 10 mg/day edem; younger than age 3: 10-15 drops/day fenistil, from age 3 to 12: 15-20 drops/day fenistil; older than age 12: 20-40 drops/day fenistil; from age 6: 1 tab/day citrine).
5. Symptomatic therapy: antipyretics (10-20mg/kg paracetamol, Tylenol, eferalgan); nasal drops (galazolin, naftizin 0,05% 1-2 drops 2-3 times a day); eye drops (20% sulfacyl-sodium 1-2 drops 3 times a day); antitussives (5 ml tusuprex 3 times a day, stoptussin 8-10 drops 3 times a day, 7,5mg ambroxol 2-3 times a day).
6. Polyvitamins.
7. In the severe forms: short course of 1-2 mg/kg prednisolone once a day.
8. In bacterial complications: antibacterial therapy (penicillin, macrolides, cephalosporin).

Prophylaxis:

1. Limit interaction with patient for 4 days after the rash appears and in complications for 10 days after the rash appears.
2. Contact (unvaccinated) individuals, who did not receive γ-globulin, blood products, immunodepressants should avoid social activities for 17 days and for 21 days those who received the above.
3. Passive immunization with γ-globulin (unvaccinated; individuals without measles in the old history; those aged 3 month-2 years old; weakened) 3 ml within 3-5 days after the contact.

Active prevention:

Live measles vaccine of the L-16 strain at 12 months single dose, subcutaneous 0,5 ml, or MMR triple vaccine (against measles, mumps, rubella). Revaccination at the age 6.

Rubella

Rubella is the acute anthroponotic infectious airborne disease, caused by rubella virus and is characterized by fine macular rash, minor catarrhal events and swollen lymph nodes (posterior cervical and occipital lymph nodes mainly).

Etiology

Rubella is caused by the virus, containing RNA, of the genus *Rubivirus* within the family *Togaviridae*.

Epidemiology

The disease reservoir is an infected person (even in the absence of apparent clinical manifestations) and an infection carrier. The virus is released into the environment with nasopharyngeal mucus, sputum already in the incubation period 1-2 weeks before a rash appears. The release of the virus stops 2-3 weeks after the onset of rash, continuing in this way, and also when a person considers himself/herself healthy. The most intense release of the virus from the body of a sick person occurs in the first 5 days after the appearance of the rash.

The main path of infection is respiratory droplets; contact the mechanism of transmission is not excluded. In addition, there is another way of infection, namely, transplacental. The transmission of the virus by this route is possible during all periods of pregnancy, but the infection is particularly dangerous in the first trimester of pregnancy. Strict seasonality (winter and spring) is also characteristic for rubella, because at this time the virus is able to survive longer in the external environment, and it is more closely connected with the indoor communication of people. After a bout of rubella, a person gains immunity for the rest of their

life. In addition, children under 6 months of age are also unlikely to contact rubella because most of them have immunity inherited from the mother.

Pathogenesis

The virus penetrates the body through the mucous membranes of the upper respiratory tract and multiplies in the lymph nodes, and then is transmitted into the blood. The virus affects the endothelium of blood vessels, increases their permeability, swelling and haemodynamic disorders in the tissues. Clinically, it is manifested by the catarrhal syndrome and intoxication. In the vascular endothelium of the surface layers of the skin, the virus forms a focal inflammatory reaction that causes the appearance of rash. Within 2-3 days virus-neutralizing antibodies appear in the blood, and the body resolves from the virus which leads to the formation of long-lasting immunity. In addition, viruses can penetrate into leukocytes (lymphocytes), where they can be found a week before the onset of clinical symptoms. Affection of leukocytes is one of the reasons for the formation of characteristic leukopenia. But the bulk of the viruses lymphogenously spread into the regional lymph nodes, due to the specific tropicity of the virus to the lymphoid tissue, where their active multiplication and accumulation occurs. That is why at the end of the incubation period an increase in the posterior cervical and occipital lymph nodes occurs. The rubella virus has tropicity to embryonic tissue. Its teratogenic action is manifested by the local inhibition of mitotic activity of cells, which leads to a slowing down of their mitosis, resulting in the disturbance of the normal development of the body. In the early term of pregnancy, the virus causes various defects in the development of the fetus, depending on which organ develops in this period: 2-9 weeks of pregnancy: auditory defects, 3-11 weeks – brain defects, 4-7 weeks – heart defects, 4-10 weeks – ophthalmic defects, 10-12 weeks - hard palate. Thus, the most dangerous for the development of the fetus is the penetration of the virus into its tissue in the first trimester of pregnancy. Damage to the tissues of the fetus is amplified due to hypoxia due to the affection of the placental vessels and hemodynamic disorders in it.

Clinical classification according to Yu.V. Lobzin (2000):

А. Acquired: а) manifested form- typical (mild, moderate, severe clinical course); - atypical (without rash); б) unapparent (subclinical): - with complications; - without complications.

Б. Congenital: - nervous system lesions; - congenital heart diseases;

- auditory defects; - ophthalmic defects; - mixed defects; - residual events of the congenital rubella.

Clinical course

The incubation period of rubella ranges from 11-24 days (14-21). Two periods are distinguished in the clinical picture of rubella: catarrhal (prodromal) and period of rash.

Prodromal period can be very short, from several hours to 1-2 days. At this time, patients may feel a slight chills, drowsiness, sometimes there is a sore throat, coughing, a slight coryza. In most cases a careful examination can reveal light hyperemia of the conjunctiva, and sometimes small red-pink spots appear on the mucosa of soft palate (Forchheimer spots).

Subsequently, the period of rash begins, that is characteristic for rubella, and sometimes its first symptom. Rash appear on the face and spreads downward to the rest of the body within a few hours without any sequence. Their localization is characteristic on the extensor surfaces of the limbs, back, buttocks. The rash is fine-maculated, with a diameter of 2-4 mm, rarely maculopapular, pale pink, round or oval, with clear contours, a smooth surface on the intact skin, not confluent. It disappears within 1-3 (4) days, does not leave any pigmentation, nor desquamation. The pathognomonic symptom for the rubella is the enlargement of all peripheral lymph nodes, especially the occipital, parotid, and posterior cervical ones. No other disease is accompanied by such a significant enlargement, consolidation and often the pain of these groups of nodes. Swollen lymph nodes are the first long-lasting symptom of rubella, since it persists for 2-3 weeks after rash goes away, and in some cases longer. Any correspondence of the intensity of rash and lymphadenitis is not observed. Lymphadenitis is a permanent sign of rubella, although rash may not appear.

The peak of the disease can be manifested by the signs of catarrhal inflammation of the upper airways in the form of mild coryza and conjunctivitis. Unlike measles, photophobia is not observed; in the majority of patients with rubella enanthema (separate pink spots on the soft palate) occurs.

The course of rubella in children aged 2-14 is the most typical and mild.

Atypical forms of rubella are very diverse. Sometimes it starts immediately from rash, without any prodromal signs. Asymptomatic forms (unapparent) are also possible that are diagnosed only after laboratory tests.

Congenital rubella. In the case of rubella infection during pregnancy in the manifested or asymptomatic form, the risk of fetal abnormalities is close to 100% in the first weeks of pregnancy, 40% on the 2 months of gestation, 10% on the 3 months of gestation, 4% in the II-III trimesters. The congenital rubella syndrome is manifested by the triad of prevailing abnormalities: cataracts, heart defects, deafness (Gregg, 1941). Later, microphthalmia, buccal anomalies, craniocereal deformities (microcephaly, hydrocephalus), encephalopathy, cleft palate, hepatitis, myocarditis, glaucoma, genitourinary system defects, dermatitis, thrombocytopenia, hemolytic anemia, hypogammaglobulinemia was assigned to these anomalies.

In 40% of cases, fetal death and spontaneous abortion is observed. Some development defects caused by the virus may occur in a later period. Damage to the fetal brain leads to the development of chronic meningoencephalitis, it is clinically manifested in infants in the form of drowsiness, lethargy, or vice versa, increased excitability, fits. The microcephaly is then revealed.

The early neonatal signs of the congenital rubella include numerous hemorrhagic rashes along with thrombocytopenia that lasts for 1-2 weeks, hemolytic anemia with reticulocytosis, hepatosplenomegaly, hepatitis with hyperbilirubinemia, interstitial pneumonia, lesion of tubular bones. Most of the lesions disappear within 6 months. In addition, these children have low body mass and small height at birth. A physical and mental retardation may occur.

Diagnosis

In the acquired rubella:

- Complete blood count (leukopenia, neutropenia, lymphocytosis, plasma cells, normal ESR).
- Virological (the isolation of the virus from the washings from the nasopharynx, from blood, feces, urine.
- Serological method (RA, PHAT, IFR) – growth of antibody titers in dynamics by 4 and more times;
- Enzyme-linked immunosorbent assay (ELISA): identification of specific antibodies of the IgG class in the acute period of the disease and IgG after the infection in the blood, and in the cerebrospinal fluid, if necessary;
- PCR of blood, urine, saliva and cerebrospinal fluid, if necessary – the allocation of RNA virus.

In the congenital rubella:

- ELISA: detection of specific antibodies of Ig M class;
- Serologic method (PHAT): stable positive result;
- Detection of RNA of the virus (blood, urine, saliva, feces, cerebrospinal fluid) by PCR method.

Complications

The most severe rubella-related complication is encephalitis. Otitis, pneumonia and nephritis are also possible.

Treatment

Treatment of patients with uncomplicated course of acquired rubella is carried out at home:

- bed rest throughout the acute period;
- general hygienic measures;

- frequent room airing;
- symptomatic therapy: antipyretics in the rise of body temperature (paracetamol, ibuprofen), etc.

Management of patients with congenital rubella is dependent on the nature of major clinical syndromes in the specialized hospital in the separate ward.

Prevention

General prevention involves identification of patients, their isolation and treatment. Patients, if possible, are isolated at home for 5 days from the time of rash appearance; sometimes it is reasonable to extend the term. Disinfection is not carried out. The contact individuals are to be on the quarantine for 21 days. It is worth protecting pregnant women without rubella in the past history from communicating with patients for at least 3 weeks. In case of the disease of women in the first trimester of pregnancy, abortion is indicated (in the absence of antibodies to the rubella virus in her blood).

Specific prevention is vaccination. Different types of vaccines, including a live trivalent vaccine (against measles, rubella and mumps), are intended for mass vaccination the WHO plans to cope with this widespread and dangerous "childhood" infection in the nearest future. Because of the viremia, vaccination in pregnant is contraindicated, moreover, after vaccination, a woman should avoid pregnancy for at least 3 months.

In Ukraine, according to the vaccination schedule, specific rubella prevention is carried out by a live vaccine at the age of 12 months followed by revaccination of 6 years. Vaccination can be done both by monovaccine, and by a trivalent vaccine (measles, rubella, mumps).

Chickenpox

Chickenpox (also called varicella) is an acute viral disease caused by a virus from the family of herpes viruses, characterized by moderate fever, rash on the skin and mucous membranes that forms small, itchy blisters. Chickenpox is a contagious infection; susceptibility to it is about 100%. In young children, as well as in the weakened, who have been taking hormones for a long time, chickenpox has a severe course, often acquiring a generalized form, accompanied by various complications. Currently, a live attenuated vaccine is developing for active immunization; however, mass vaccinations against measles are not carried out, hence outbreaks of chickenpox are common. A physician of any specialization should be able to make a diagnosis and take measures to timely isolation of the patient. **Etiology** – DNA-containing Varicella-Zoster virus. **Epidemiology.** Diseases reservoir: patient with chickenpox, less commonly with herpes zoster. Ways of transmission: airborne respiratory droplets. Susceptibility is high: 90-100%, children are more likely to get sick, immunity is stable, possible recurrences are accounted for 3%.

Features of pathogenesis

1. Entry of infection – mucous membrane of the respiratory tract, primary multiplication of the virus.
2. Enters to blood by the lymph flow, causing veremia.
3. Spreads into epithelial cells of the skin, mucous membranes with the development of typical presentation of the disease.
4. Neurotropism: lesions of the intervertebral ganglia, cerebral cortex, subcortical area, cerebellar cortex.
5. Very rarely – generalization of an infection, affecting the liver, lungs, skin.

Classification of chickenpox clinical forms

1. Typical forms.
2. Atypical forms: latent (rudimentary), bullous, hemorrhagic, gangrenous, generalized (visceral).

Diagnostic criteria

Typical forms of chickenpox

The disease begins acutely with rise in body temperature, the rates of which is determined by the severity of the course of the disease, and the appearance of a rash.

Sometimes 1-5 days before rash starts to occur the prodromal phenomena in the form of low grade fever, malaise, loss of appetite and the appearance of a rash (scarlatiniform and morbilliform, erythematous) may appear. Chickenpox rash appears simultaneously with the temperature rise or a few hours thereafter. First small patches are developed, which quickly turn into papules and vesicles. Vesicles are usually unilocular. Rash covers the skin of the trunk, face, limbs, scalp, less commonly in the mucous membranes of the mouth, respiratory tract, eyes, external genital organs. Rash may be accompanied by itching. On the mucous membranes, the elements of rash quickly macerated with the development of surface erosions that resolve within 1-2 days. On the skin, the blisters cloud over and start drying out. A crust develops. After crusts fall off a slight pigmentation, in rare cases, scarring persists for some time. During the whole cycle, new waves of spots can appear with an interval of 1-2 days, within 2-4 days, in rare cases up to 7 days or more. Therefore, a false rash polymorphism occurs.

Atypical forms of chickenpox

Rudimentary form develops in children with hereditary passive immunity or after administration of immunoglobulins, plasma and blood in the incubation period. They experience a scarce papular rash with single small blisters along the normal body temperature. **A pustular form** is characterized by the typical development of purulent pustules on the top of the blisters. The disease is accompanied by a high level of intoxication. After crusts fall off scars often remain. **In bullous form**, along with typical vesicles large, up to 2-3 cm in diameter, blisters with soft top and cloudy contents. The blisters may burst with the formation of large erosive surfaces. After epithelization of the latter, brownish pigmentation often remain. **Hemorrhagic form** develops in immunocompromised children. On day 2-3 of the disease, the contents of the blisters becomes hemorrhagic, the crusts colored black. Hemorrhages in the skin, mucous membranes, internal organs, brain and nosebleeds are possible. **Gangrenous form** develops in immunocompromised children, with poor care. In this form of the disease, along with a typical rash, blisters with hemorrhagic contents occur with a marked inflammatory reaction around them. Subsequently, the sanguineous ("black") scab is formed; after falling off the scabs, orbicular ulcers with impure necrotic bottom and dented edges appear. **The generalized form** sometimes occurs in newborns or older children with immunodeficiency or with prolong exposure to glucocorticosteroids. Moreover, a specific damage to internal organs is observed. The diagnosis of chicken pox can be made based only on clinical diagnostic criteria. In cases of complicated clinical diagnosis, additional examinations are made.

Complications: encephalitis; myelitis; encephalomyelitis; polyneuropathy; neuritis of the optic nerve; serous meningitis; acute thrombocytopenia; hemorrhage in the adrenal glands; acute adrenal insufficiency; false croup; acute respiratory failure; pneumonia; bacterial complications (phlegmon, abscess, impetigo, bullous streptodermia, erysipelas, lymphadenitis, purulent conjunctivitis, keratitis, stomatitis); sepsis; arthritis; osteomyelitis; nephritis.

Paraclinical tests:

1. Complete blood count: leukopenia, relative lymphocytosis, normal ESR.
2. Fluorescence spectroscopy can detect the virus antigen in impression smears from the contents of vesicles.
3. For serological study, paired sera are used. Diagnostic is considered to increase the titer by 4 times or more during 10-14 days. Studies are conducted using RPC, IHA, ELISA, RIA.

Additional tests

- Immunofluorescent method.
- Serology: complement fixation test, ELISA.
- PCR.
- Virological method.
- Analysis of the liquor in the presence of the signs of meningoencephalitis.

Specific features of chickenpox in babies

1. Start from common infection manifestations, dyspeptic event.
2. Normal body t° or low grade fever, rise at the peak of rash.

3. Rash appears on day 2-5; widespread; occurs in successive waves.
4. Neurotoxicosis (fits, meningeal symptoms).
5. Possible visceral manifestations.
6. Bacterial infection overlap is frequent.

Treatment:

Basic therapy (used until the disappearance of clinical symptoms)

1. Generally hygienic baths with 0,05% permanganate potassium, decoction of herbs.
2. rash management with 1% "brilliant green" (antiseptic embrocation) or fucorcinum, silver nitrate, washing of mucus membranes with 2% of sodium bicarbonate or furatsillin (0,02%), eyes are digested with 20% sulfacetamide solution, applications with Zovirax ointmen.

Etiotropic therapy (5-7 days)

Antiviral therapy is not indicated for patients with chickenpox of mild and moderate severity. Indications for application of acyclovir are: severe forms; patients with oncohematological diseases; organ/ bone marrow recipients; patients receiving hormone therapy; children with congenital immunodeficiency or HIV infection; congenital chicken pox; nervous system-related complications; hepatitis; pneumonia; thrombocytopenia. In addition to acyclovir, effective are valacyclovir, famciclovir, ganciclovir, as well as erebra (sublingual tablet containing extract of dry hyporamine). In severe and recurrent forms of the disease, the minimum course of treatment is 2-3 weeks.

Acyclovir is administered intravenously at a dose of 10 mg / kg body weight 3 times a day. The course lasts 7 days or 48 hours following the last stage of rash. Immunocompetent children aged over 2 years and adolescents with the severe forms of the disease are administered with acyclovir intravenously at a dose of 80 mg / kg per day. In severe, generalized forms of chickenpox, especially in newborns and children of the first year of life, it is possible to use a specific Varicella-Zoster Immunoglobulin at a dose of 0.2 ml / kg body weight.

Antibacterial medications are used in bacterial complications (penicillins, macrolides, cephalosporins).

Intensification is carried out by interferon in case of generalized and severe forms.

Syndromal therapy (until the elimination of a life-threatening condition) involves:

- antipyretics (paracetamol, efferalgan, tylenol);
- disintoxication (5% glucose, 0,9% saline, rheosorbilact);
- antisensitizers (fenistyl, edem, erius, fenkarol, citrine at the age-related dose);
- dehydration (in neurotoxicosis) – lazix, mannit, mannitol.

Prevention:

1. Patient need to be quarantined for 5 days from the time of rash appearance.
2. Contact persons aged under 3 years without a past history of chickenpox need to be put in isolation from day 11 to 21 after contact.
3. Room airing and wet cleaning.
4. Active immunization on epidemic indications.
5. Passive immunization: donor 0,2-0,5ml/kg immunoglobulin during the first 2 days.

Scarlet fever

Scarlet fever (also known as scarlatina) is a severe anthropogenic infectious disease caused by the group A β-hemolytic Streptococcus bacteria, which has a predominantly airborne transmission mechanism, characterized by fever, intoxication syndrome, acute tonsillitis with regional lymphadenitis, punctulated rash, susceptibility to septic and allergic complications. The main way of transmission is respiratory droplets. The intensity of the spread of streptococcus increases significantly during coughing, sneezing. This is also due to the presence of dust in the air, close and prolonged contact with the infected patient. Contact-household way of infection transmission is possible through toys, personal items, home appliances, as well as through food, mainly dairy products. The lowest incidence is recorded in children of the first year of life (especially aged less than 6 months), in the blood of which antibodies from the placenta of mother's body circulate. The index of contagiousness of scarlet fever is 0.4 (40%). Most often

scarlet fever affects children aged 2 to 9 years. It is clearly seasonal: an increase in morbidity in the autumn-winter period of the year. The prevalence of scarlet fever is uneven. The highest incidence rates are recorded in countries with cold and temperate climate; in countries with hot climate it is rare.

Once contracted scarlet fever, two types of immunity are developed in the child's body: antitoxic and antibacterial. Antibacterial immunity has no typical specificity, it is homogeneous for all group A Streptococci. The specific feature of antitoxic immunity is its stability and expressiveness throughout human life. The erythropogenic exotoxin of streptococcus is the main pathogenetic chain of scarlet fever, as well as the features of antitoxic immunity; consequently, scarlet fever is experienced once in a lifetime. Antibacterial immunity is unstable, thus, local streptococcal diseases can be repeated.

The disease reservoir is mucus membranes of the palatine tonsils, sometimes it is damaged skin (wound or burning surface), mucous membranes of the genital tracts (in parturients). In the macroorganism streptococcus is spread by lymphogenous and hematogenous pathways, through canals (intracanalucularly) and through contact with adjacent tissues. Clinical manifestations of the disease are caused by septic, toxic and allergic effects of the pathogen (three syndromes of the pathogenesis of streptococcal infection).

Typical forms of scarlet fever are characterized by the presence of the initial focus in the pharynx and classical signs of the disease. There is a strict cycle of scarlet fever development with the successive change of 4 periods: incubation, initial, rash and reconvalescence. The incubation period ranges from 1 to 12 days, more often 2-4 days. Ordinarily, the onset of scarlet is acute. Intoxication, fever, acute tonsillitis with regional lymphadenitis is typical. The syndrome of intoxication manifests in malaise, headache, nausea and vomiting, tachycardia. The body temperature rises to 38°C and higher. The syndrome of acute tonsillitis is characterized by sore throat (especially in swallowing), bright red local hyperemia of the soft palate and palatine tonsils mucosa, sometimes punctulated enanthema appear on the soft palate, reaction of the anterosuperior cervical (tonsillary) lymph nodes (enlargement, moderate density and tenderness on palpation). Tonsillitis is more often catarrhal, though may be lacunar or follicular. Currently, necrotic sore throat is rare and assigned to complications.

Rash period. Along with marked severity of the syndromes of the initial period (intoxication, tonsillitis) punctulated rash appears. The syndrome of exanthema develops at the early stages, ordinarily, in the first 2 days of the disease. Morphologically, 1-2 mm fine macular erythema appears. The color of the rash on the first day is bright, sometimes bright red, within 3-4 days becomes pale to slightly pink. The rash is more often intense, rarely – scanty, localized mainly on the bending surfaces of the extremities, the anterior and lateral surfaces of the neck, lateral surfaces of the chest, on the abdomen, the lumbar region, the inner and the rear surfaces of the hips and legs, in the places of natural bending, i.e., axillary, elbow, inguinal, popliteal. In these areas, the rash is more intense, brighter, is located on a hyperemic background of the skin and persists for a longer time. As a result of mechanical injury of the skin vessels, small petechia often appear in isolation or form hemorrhagic strips (Pastia's lines), which persist some time after rash subsided and serve as one of the additional signs in the diagnosis of scarlet fever at a later date. The skin of the patient is dry, desquamated (due to hypertrophy of the hair follicles and the effect of the sympathetic part of the vegetative nervous system). Tongue alterations are typical for scarlet fever. On the first day of illness, it is covered with a white coating, from day 2 to 4-5 days, gradually cleansed, starting from the tip, and becomes bright red, with protruding fungiform papillae on the cleaned surface ("strawberry tongue"). In the acute period of scarlet fever, a characteristic face of the patient is observed: along with a bright blush on the cheeks and cherry or crimson lip color, a pale nasolabial triangle (Filatov's symptom) is markedly presented. Changes in other organs and systems in the acute period of scarlet fever are usually expressed insignificantly. There may be changes in the cardiovascular system.

The course of *phasis sympathicus* and *phasis vagus*, associated with affection of vegetative nervous system by toxin, is characteristic for scarlet fever. During the first 3-4 days

sympathic phase occurs: tachycardia, increased blood pressure, dry skin, negative Aschner's symptom, white dermographism slowly appears and disappears rapidly, and from day 5-6 vagus phase occurs: bradycardia, lowering blood pressure, sweating, Aschner's symptom is distinctly positive, white dermographism quickly appears and disappears slowly. The development of symptoms of scarlet fever is rapid; they are prominent already on day 1-2 of the disease. The follow up course of the disease is characterized by the consistent sequential subsidence of the scarlet fever symptoms. The first signs of intoxication start fading, and the body temperature in most patients comes to normal within 3-5 days of the disease. The rash persists for 2 to 6 days (an average of 4 days). Changes in regional lymph nodes disappear to day 4-5 of the disease, tongue – by the end of the 2nd week of the disease.

The period of reconvalescence begins from the 2nd week of the disease and lasts for10-14 days. It is characterized by the peeling of skin in some patients of. Scaled desquamation is typical for scarlet fever, especially on the fingers and toes. Minor branny desquamation is possible on the neck, trunk, and earlap. In the period of reconvalescence, the increased sensitivity to streptococcal superinfection is preserved, which can lead to the development of threatening infection-allergic and septic complications.

Atypical forms are extra-tonsillary (burn, wound, postpartum, postoperative). Extra-tonsillary scarlet fever differs from the typical form by the absence of complaints of sore throat, inflammatory changes in the oropharynx and reactions of tonsillary lymph nodes. The morphology and localization of rash is typical for scarlet fever, and accumulates around the entry of infection (wounds, burning surfaces). Intoxication is expressed moderately or significantly, other clinical manifestations do not differ from those with typical scarlet fever.

The severity can be classified as mild, moderate and severe forms of scarlet fever. Currently, ***the mild form*** is the most common and characterized by a slight syndrome of intoxication and the presence of catarrhal tonsillitis. The state of children remains satisfactory, body temperature does not exceed 37.5-38.5°C. There are no complaints, sometimes short-term headache, and sore throat during swallowing; one-time vomiting is also possible. Punctulated rash is not bright and intense, subsides following day 3-4 of disease. ***Moderate form*** is accompanied by significant intoxication and pronounced changes in the place of the infection entry. Children complain of fatigue, headache, loss of appetite, pain in swallowing. The body temperature rises to 38.6-39.5°C, vomiting is usually recurring. The events of tonsillitis with bright local hyperemia are markedly expressed in the oropharynx, often with purulent effusion in the lacunae, or purulent follicles. Spotted enanthema is sometimes noted on the mucous membranes of the soft palate. The rash is bright and intensive on a hyperemic skin and persists for 5-6 days. In all patients, changes in the cardiovascular system are detected: tachycardia, muffled heart sounds, increased blood pressure. ***A severe form*** of scarlet fever may occur with markedly expressed symptoms of intoxication (toxic form) or septic lesions (septic form). When combined with pronounced initial symptoms of toxicosis and septic manifestations, the form of scarlet fever is considered as toxic-septic. *The toxic form* of scarlet fever is characterized by the marked symptoms of intoxication. Frequent vomiting, headache, excitement, delusions, loss of consciousness, seizures are noted. The body temperature rises to 40°C and above. Characteristic look of the patient's face: bright blush on the cheeks with markedly pronounced pale nasolabial triangle, bright dry lips, injection of sclera vessels. Pharynx is bright, scarlet; hyperemia that reaches the edge of the soft palate, spotted enanthema of hemorrhagic nature. Rash on the body is bright, on the hyperemic background of the skin, often with hemorrhages. Symptoms of the lesion of the cardiovascular system are detected at the onset of the disease: marked tachycardia, muffled heart sounds, increased blood pressure. With the increase in toxicity, sometimes even on the first day, an infectious-toxic shock (ITS) may develop: cyanosis, cold extremities, frequent thready pulse, muffled heart sounds, sudden drop in blood pressure, oliguria. In the absence of adequate therapy, death occurs on the first day after the onset of the disease. *The septic form* of scarlet fever is accompanied by the development of severe inflammatory purulent and purulent necrotic processes that arise from the primary foci of inflammation. The state of the patient

progressively deteriorates. Body temperature rises, sore throat acquires necrotic nature, with the focus of necrosis manifest not only in palatine tonsils, but also in the arches, on the bottom of the uvula. Purulent lymphadenitis of tonsillary lymph nodes with involvement of the adjacent cellular tissue (adenophlegmon) to the pathological process, purulent otitis, ethmoiditis, mastoiditis are developing. In the absence of adequate etiotropic therapy, the disease progresses rapidly, a severe septic state develops resulting in lethal outcomes.

Treatment of scarlet fever. Regimen: bed rest throughout the acute period of the disease. The diet should correspond to the child's age and contain all the necessary nutritional ingredients. Etiotropic therapy: antibiotics: penicillins or macrolides are prescribed in the mild form; penicillins are prescribed in the moderate form; cephalosporins of the 1-3 generations, clindamycin, vancomycin are prescribed in the severe form. The course of antibiotic therapy: 10 days in case of the mild form; 10-14 days in case of the moderate and severe forms; the route of administration: per os in case of the mild form; intramuscularly in case of the moderate form; intravenously in case of the severe form. **Detox therapy:** in the mild form – drink plenty of water; infusion of glucose-saline solutions in case of the moderate and severe forms. Symptomatic therapy involves antihistamines; medications to strengthen the vascular wall (ascorutin, galascorbin), antipyretics (paracetamol, ibuprofen); gargling with disinfectant solutions, quartz tubes, etc.

Prevention. Specific prevention of group A streptococcal infection does not exist to date. The main preventive measures are the early detection and isolation of the source of infection. Isolation of a patient with scarlet fever is carried out in a hospital or at home. The discharge of children from the hospital is carried out not earlier than 10 days after the onset of the disease with a negative result of the bacteriological study on group A streptococcus. Convalescents of scarlet fever are not allowed in pre-school facilities and in the first two grades of schools for another 12 days. The same periods of isolation (22 days) are also recommended for patients with sore throat from the foci of scarlet fever. Influence on ways of transmission: conduct of daily and final (on the day of recovery registration) disinfection by the parents and attendants. Contact preschoolers and 1-2 grade-schoolchildren are to be put into quarantine for 7 days from the moment of isolation of a patient with scarlet fever with the conduct of the whole complex of antiepidemiological measures.

Fifth disease (Erythema infectiosum)

Fifth disease is a group of poorly diagnosed acute infectious diseases caused by the virus and manifested mainly by intoxication and erythematous rash. Children have the following forms of erythema: infectious Tschamer's erythema, infectious Rosenberg's erythema (more often in adults), sudden exanthema, nodular.

Infectious Tschamer's erythema

Infectious Tschamer's erythema was first described by A. Tshamer 1886 as "local rubella". The unresolved issue of the pathogen was apparently the reason for the inadequate study of this disease by both infectiologists and dermatologists, but it is the dermatologists who mainly decide the questions of its differential diagnosis. Patients with fifth disease often come to the dermatologists, as in the clinical course of the disease, skin symptoms are dominant, and it can simulate the pathology of the skin.

Etiology is practically unknown. Probably infectious Tschamer's erythema is a viral disease. The question of its existence as a distinct nosological unit has repeatedly been questioned. It was suggested that this is a clinical syndrome that occurs in various viral infections caused by multiple viral infections, as well as enteroviruses, but no single opinion has been developed. Some authors believe that the pathogen of fifth disease is Parvovirus B19 (HPV)

Epidemiology

This disease refers to diseases with minor contagiousness and is observed in the form of sporadic cases or minor outbreaks in families and children's facilities, but according to some

scientists, may take the nature of epidemics. Some authors report about large outbreaks of fifth disease occurred in Germany and the USA (up to 600-1000 cases).

Although the source of infection is not fully established, it is believed that it is a person contracted with fifth disease. Infection is transmitted by respiratory secretions, though the transmission through contact is not excluded. Children from 2 to 15 years old are mainly affected by the disease, adults are rarely contracted, and therefore, most authors consider infectious Tschamer's erythema as a childhood disease, which is more common in the spring or early summer. The disease leaves a stable life-long immunity.

Classification is not developed. However, the disease can be classified according to the severity of the course: mild, moderate and severe; some authors, depending on the presence and degree of manifestations of typical symptoms, distinguish inapparent (subclinical) form, which is especially common in epidemic outbreaks; however, this classification is rarely used.

Clinical course

Incubation period ranges from 2 to 20 days, on the average of 9-14 days, usually with mild clinical course. The onset is acute, without previous prodromal events; it is characterized by the appearance of chills, body temperature is normal or subfebrile, but sometimes it can reach 39°C. Symptoms of intoxication are absent or slightly expressed, but in older children they may be more pronounced. The duration of the subfebrile period usually does not exceed 1 -2 days, but in some cases (especially in older children) the temperature persists for 3-7 days.

The main symptom of the disease to make a diagnosis is rash. The rash appears on the first day of the illness, less often on the second one. First, rash appears on the face - mostly on the cheeks in the form of protruding elements of the maculopapular nature, sized 3-5 mm, disappearing when stretching the skin. Within a few hours, the spots are enlarged, become confluent, forming a common bright blush. A clear red membrane appears on the bridge of the nose, which resembling the "butterfly wings" on the face. The area of the nasolabial triangle, ordinarily, remains clean from the rash. No rash is developed on the scalp, though rash develops on the forehead and chin. During the rash period, complaints on sensation of skin burning and may appear, after 1-3 days the rash appears on the hands (mainly on the extensor surfaces), simultaneously or later on the buttocks, lower limbs and the trunk. Elements of rash are located symmetrically. It never develops on the palm and feet. From time to time rash becomes pale and then return its color to bright; in this diseases it is plentiful. On the limbs rash is macular, maculopapular, bright red with pale centers, though preserving purple shades, bright red edge, forming various shapes in the form of rings, garlands, coins, loops; lace-patterned rash. On the shoulders, buttocks, hips rash occupies most of the surface. On the trunk rash is in the form of individual roseolous or maculous elements of pink color, sporadic, resembling confluent erythema. Rash lasts for 3-13 days, rarely for 20 days. The disappearance of the rash, ordinarily, occurs gradually, through the stage of blurred mottled skin, minor pigmentation is less common, and in rare cases, gentle desquamation. No significant changes on the part of internal organs are observed.

Poleshko D.V. reports on mild, moderate and severe fifth disease.

Severe form is characterized by the body temperature of 39°C and higher, sometimes delusion, severe headache, sleep disturbances, plentiful rash.

Moderate form: rise of body temperature to 38-39°C, moderate agitation or adynamia, moderate headache, sleep disturbances, plentiful rash.

Mild form: body temperature is normal or subfebrile, disturbances in the general well-being are insignificant, sporadic and sometimes plentiful rash.

Sometimes catarrhal phenomena can be observed in the form of catarrh of the upper respiratory tract, conjunctivitis. Complete blood count shows normocytosis or leukopenia, eosinophilia, stab shift, elevated ESR.

Diagnosis

Since specific diagnostics has not been developed yet, the diagnosis of infectious Tschamer's erythema is based on the clinical picture and hemogram. The age of contracted child epidemiological data is taken into account.

Treatment

In mild form of the disease symptomatic treatment is advocated. In severe form, detoxification and bracing agents, as well as glucocorticoids are used.

Prevention

Specific prevention is not developed. Patients with infectious Tschamer's erythema need to be kept in isolation. Preventive measures in the focus of infection are not carried out. Quarantine for contact people is not established.

Exanthema subitum

The disease was first described in 1900 known as *roseola infantum*; later it was described as a three-day critical fever with exanthema. Exanthema subitum (also known as pseudorubeola, roseola infantum, sixth disease) is an acute infectious disease occurred in infants.

Most authors consider it a distinct disease with viral pathogen. Until recently, the virus causing this disease was unknown, later it was suggested that the sudden exanthema is due to adenoviruses, enteroviruses, but it has now been proven that in children this disease is caused by the herpes virus family. It affects about 30% of early age children. Most cases of exanthema fall at the age from 9 months to 1 year. It is caused by herpesvirus 6, and less frequently by herpesvirus 7. It is assumed that the transmission of the infection occurs by respiratory secretions or contact.

Clinical course

Incubation period ranges from 3-7 days. The beginning of the disease is acute: the body temperature rises to 39-40 ° C and above. Despite the severe fever, the state of health of children can remain satisfactory, but more often there are moderate manifestations of intoxication: headache, tearfulness, agitation, loss of appetite. Sometimes vomiting, diarrhea, abdominal pain and pain in the lower limbs, seizures occur. More severe course is seen in older children. The fever lasts for 3 days, in some cases up to 5 days, followed with rapid defervescence and simultaneously (on day 3-4) rash appears on the back (appearance of rash before defervescence or within 1-2 days is less common), spreading to the abdomen, chest, neck, head and limbs. Rashes are plentiful, blotchy, pale pink on intact skin, edges are uneven, often with pale halo, not confluent. The rash is mainly localized on the back, may also appear on the face and the flexion surface of the upper extremities. The process of rash development lasts for several hours; within 2-3 days exanthema disappears without peeling and pigmentation. The pulse is rapid; the heart sounds are weakened. Sometimes regional lymph nodes are moderately enlarged. Blood alterations are characteristic: from the first days of the disease leukocytosis is observed, followed by leukopenia due to elevated neutrophil granulocytes count, stab shift, relative lymphocytosis (up to 90%). In the urine, protein, leukocytes are detected. The course of illness is benign. In the fever period sometimes serous meningitis develops.

Diagnosis, treatment and prevention is similar to infectious Tschamer's erythema, infectious Rosenberg's erythema. Prophylaxis and actions in the foci of infection have not been developed.

Table 2

Differential diagnosis of infections that cause rash

Diagnostic signs	Measles	Rubella	Scarlet fever	Chickenpox
1	2	3	4	5
Onset	catarrh of the upper respiratory tracts, conjunctivitis 2-4 days	rash	acute onset, sore throat, vomiting, high grade fever, rash.	acute onset, fever, moderate catarrhal events, rash.
Period of rash appearance	on day 3-4 of the illness	1st day, less frequently the 2nd day.	1st day (20% on the 2nd day).	on day 1-2.
Rash description	maculopapular	fine macular, less commonly maculopustular	punctulate, on the flexion of the extremities, on the abdomen, lumbar, face, sides of the trunk.	polymorphous (spots, papules, vesicles, crusts).
Rash size	middle-sized, big on day 2-3 after rash appearance.	fine, middle-sized.	fine pink-colored rash, confluent.	middle-sized
Days and staging of rash appearance	day 1 – on the face. day 2-й день – on the face, trunk day 3 – on the face, trunk, extremities.	widespread, on extremities; no staging	widespread, on the face Filatov's symptom; no staging	all-over the body and mucous membranes, appearance of the new rashes throughout several days, evolution of the older ones.
Coloring	bright, pink-red	pale-pink	bright	pink papules; vesicles on the hyperemic base
Related rush outcomes	pigmentation starting from the face, branny desquamation	disappear on day 3-4	gradual subside on day 4-5 with desquamation on week 2.	insignificant pigmentation after crusts fall off
Catarrh	apparent in the first 5-6 days	insignificant, short-term (1-2 days)	local, bright hyperemia.	moderate, possible development of laryngotracheitis
Oral mucosa	hyperemic, loose; enanthema on the soft palate; Filatov's symptom on the cheeks.	clean, sometimes sporadic elements of enanthema	local, bright in the soft palate	on the pink background– polymorphous elements

Diagnostic signs	Measles	Rubella	Scarlet fever	Chickenpox
1	2	3	4	5
Intoxication	severe lasting for 5-7 days	mild or absent	corresponds to prominence of the local signs, short-term for 1-3 days	mild or moderate
t^0	low grade fever in the catarrhal period, high grade fever in the rash period.	normal, low grade fever, less frequently over 38-39˚c	rapid rise in body temperature in the first hours and on day 1-2	low grade fever, less frequently over 38-39˚c
Affection of other organs and systems	pneumonia, laryngitis, otitis	enlargement and tenderness of the posterior cervical and occipital lymph nodes.	sore throat, altered tongue (white coating, "strawberry tongue" from day 4-5), complications on week 2-3	rarely – laryngitis, generalized visceral forms, meningoencephalitis
Lab tests	leukopenia, lymphocytosis, aneosinophilia, HAI with coronary antigen (+); serological: ELISA, PCR	leukopenia, lymphocytosis elevated plasma cell count, HAI(+); serological: ELISA, PCR	leukocytosis, left shift, neutrophilia, ↑ ESR, streptococcus in the oral and nasal smears; serological: ELISA, PCR	immunofluorescent method; serological: ELISA, PCR

Differential diagnosis of exanthemas

The leading clinical manifestations of this group are exanthema and lymphadenopathy. First, rubella should be differentiated from measles.

Measles is identified by:

- extremely high contagiousness;
- acute, sudden onset, apparent intoxication and catarrh;
- scleritis, conjunctivitis, photophobia, lacrimation;
- absence of generalized lymphadenopathy;
- later (on day 3-4) appearance of rush with strict sluggish (about 3 days) staging of rashes;
- presence of Koplik's spots;
- pigmentation and branny desquamation after rash disappeared.

Differentiation from **scarlet fever**, characterized by:

- clinical course with apparent intoxication and fever;
- sore throat;
- enlargement of submandibular lymph nodes only;
- fine macular rash, located on the hyperemic background;
- presence of plentiful rash on the face with pale nasolabial triangle;
- "strawberry tongue";
- scaled desquamation on the spots of rush (day 6-9);
- tachycardia, possible myocarditis;

- neutrophilic leukocytosis, elevated ESR.

Rash, generalized lymphadenopathy can also occur in infectious mononucleosis. But unlike the rubella **mononucleosis** is characterized by:

- more severe generalized intoxication syndrome;
- sore throat, events of tonsillitis;
- rash occured along with medication therapy (more commonly);
- marked enlargement of the lymph nodes are significantly enlarged, sometimes in the form of packages, no predominant affection of the cervical and occipital lymph nodes occurs;
- marked enlargement of the liver and spleen;
- leukocytosis with lympho- and monocytosis, presence of > 10% of atypical mononuclear cells.

Enteroviral exanthema, in contrast to rubella, is characterized by:

- mainly summer-autumn seasonality;
- acute onset, intoxication with fever to 39°C and more;
- later appearance of rush (day 2-3);
- -absence of catarrhal events and conjunctivitis;
- absence of lymphadenopathy;;
- diarrhea, herpes angina, myalgia, meningeal signs;
- no significant changes in hemogram.

Medicamentous toxic exantemas are characterized by:

- clear correlation between medication taking and the appearance of rash;
- rash more often in the form of areas of hyperemia, although variations are possible;
- itching;
- medication-related rash appearance;
- generalized lymphadenopathy is less common;
- duration of the course is determined by the duration of the medication taking.

Regional lymphadenitis and rash is characteristic for **phelinosis (cat-scratch disease)**. However, it is characterized by:

- initial affect;
- within 10-20 days mainly groin glands, popliteal lymph nodes (on the side of the scratches) are enlarged;
- significant enlargement of the lymph nodes (up to 3-5 cm), can be suppurative;
- rash (scarlatiniform and morbilliform) appears within 1-6 weeks after enlargement of the lymph nodes;
- leucocytosis, elevate ESR.

The onset of **exanthema subitum** is acute: the body temperature rises to 39-40 ° C and above. Moderate manifestations of intoxication are common: headache, tearfulness, agitation, loss of appetite. Sometimes vomiting, diarrhea, abdominal pain and pain in the lower limbs, seizures occur. More severe course is seen in older children. The fever lasts for 3 days, in some cases up to 5 days, followed with rapid defervescence. Simultaneously rash appears on the back (appearance of rash before defervescence or within 1-2 days is less common), spreading to the abdomen, chest, neck, head and limbs. Rashes are plentiful, blotchy, pale pink on intact skin; edges are uneven, often with pale halo, and not confluent. The rash is mainly localized on the back, may also appear on the face and the front surface of the low extremities and back surface of the upper extremities. The process of rash development lasts for several hours. Sometimes regional lymph nodes and spleen are moderately enlarged. Blood alterations are characteristic: from the onset of the disease leukocytosis is observed due to elevated neutrophil granulocytes count, with subsequent leucopenia, relative lymphocytosis (up to 90%). In the urine, protein, leukocytes are detected. In addition, various diseases that cause rashes and lymphadenitis exist (AIDS, chronic toxoplasmosis, listeriosis, brucellosis, leukemia, etc.).

List of questions for final control:

1. What is the etiologic agent of measles, chickenpox, rubella, scarlet fever?
2. What is the epidemiology of measles, scarlet fever in children?
3. What are the components of the epidemiological chain and what is the characteristic of its main constituents in scarlet fever?
4. What is the etiotropic therapy of chickenpox in children?

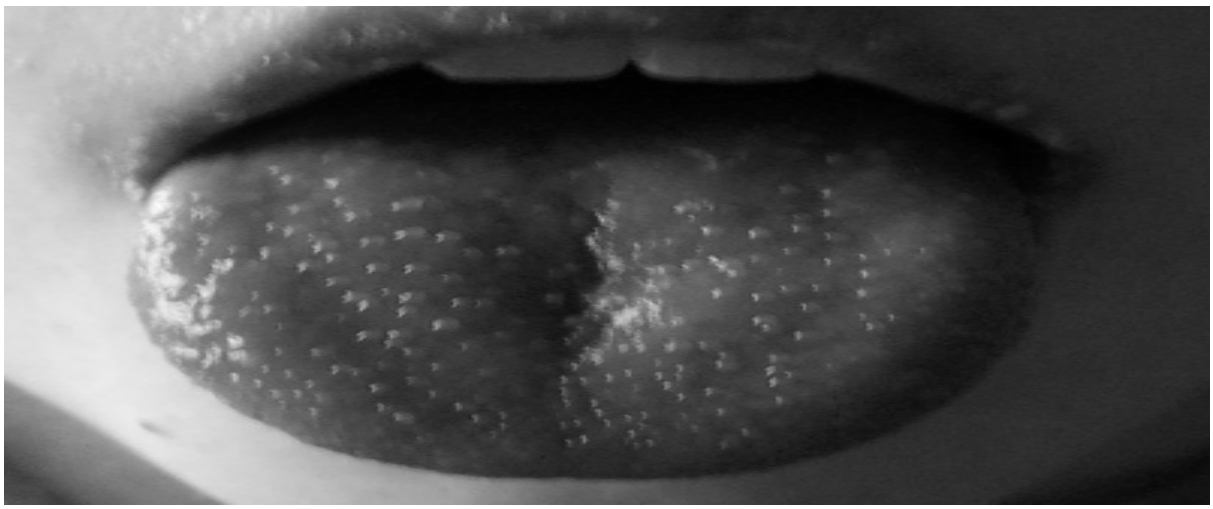

Fig. 2. "Strawberry tongue" in scarlet fever.

SECTION 3.
STREPTOCOCCAL INFECTION IN CHILDREN

Streptococcal infections continue to be among the most acute health problems worldwide. It is difficult to find a section of medicine in which there are no diseases caused by streptococci. Streptococcal infection is a group of diseases caused by streptococcus of different serological groups, differing in their morphological, pathogenetic, immunological properties.

The reservoir of the pathogen is stored due to the prolonged carriage of streptococci (up to a year or more). Within a group of people the presence of 15-20% of individuals with prolonged carriage determine almost permanent circulation of streptococcus among people. Periodic cyclicity is one of the characteristic features of the clinical course of the epidemic process in streptococcal infections. In addition to the well-known cycles with an interval of 2-4 years, periodicity with an interval of 40-50 years or more is noted. In the 20's and 40's of the 20^{th} century, diseases with streptococcal etiology were not only widespread, but also characterized by the severity of the clinical course. Scarlet fever and tonsillopharyngitis was frequently complicated by purulent-septic (otitis, meningitis, sepsis) and immunopathological (rheumatism, glomerulonephritis) processes. In the 50's, there was a tendency to decrease their number and up to 1987 streptococcal infections were not considered a significant health problem. In recent years, an increase in the incidence of streptococcal disease has been noted, and even outbreaks of this disease have been reported. Noteworthy, this tendency is observed both in developing countries and in developed countries, including the USA where outbreaks of rheumatism are noted in middle classes of population and military units. Streptococcal infections are common everywhere. In areas of temperate and cold climate, they are manifested predominantly in the form of pharyngeal and respiratory forms of diseases, accounting for 5-15 cases per 100 individuals per year. In the southern regions with subtropical and tropical climate, skin lesions prevail. The economic damage made by streptococcal infections is about 10 times higher than that of viral hepatitis. The most economically significant is sore throat (56%), followed by the acute respiratory diseases of streptococcal etiology (33%), erysipelas (9%), scarlet fever and active rheumatism (12%), acute nephritis (7%).

Streptococci - (from Greek *coccos* meaning "berry" and *streptos*, meaning "twisted chain"), the genus of spherical stationary bacteria. They are multiplied by cell division along a single axis, growing in chains. They are found in the soil, on plants, skin of animals and humans. Pathogenic streptococci cause streptococcal infection in humans and streptococcosis in animals. Some species are used to produce sour milk products. Streptococci are gram-positive microorganisms belonging to the family of lactobacilli. Depending on the ability to hemolize erythrocytes, streptococci are divided into β (complete hemolysis), α (partial hemolysis), and γ (no hemolysis). Streptococci are fairly stable in the external environment. Well tolerate drying and can be stored for months in dry pus, sputum. Tolerate heating to 60°C during 30 minutes. Under the influence of disinfectants are dying within 15 minutes.

Groups of Streptococci. Classified by Lancefield, streptococci are divided into groups of carbohydrates of the cell wall from A to V. The most well-known for general practitioners are group A streptococci, causing sore throat, scarlet fever, rheumatism, glomerulonephritis, group D streptococci, or enterococci, highly resistant microorganisms, causing the development of sepsis, endocarditis. At first, streptococci of groups B, C, G were considered as pathogens of animals and as part of normal human flora. However, recent years have clarified the pathogenic potential of these microorganisms. The mortality of the full-term newborns ranges from 2 to 8%, in premature neonates it is about 30%. Survived babies often have a neurological defect – deafness, hydrocephaly, motor and sensory impairments, developmental retardation. Early neonatal infection is transmitted vertically from the mother, and late (from the 7^{th} day to 3 months old) – horizontally, in some cases in the form of nosocomial infection.

Table 3

Classification of streptococci

Groupable	Species	Localization	Disease
A	S.pyogenes	pharynx, skin,rectum	pharyngitis, tonsillitis, sinusitis, scarlet fever, conjunctivitis, pneumonia, sepsis, meningitis, rheumatism, glomerulonephritis, skin infections
B	S.agalactiae	pharynx,vagina,rectum	neonatal sepsis, meningitis,osteomyelitis, osteoarthritis, pneumonia
C	S.equisimilis	pharynx, skin, vagina, rectum	pharyngitis, pneumonia, skin infections, sepsis, endocarditis, brain abscess
D	S.faecalis, S.faecium (enterococci)	large intestine	neonatal sepsis, intestinal infections, peritonitis, meningitis, urinary tract infection, endocarditis
G	S. canis	pharynx, skin, vagina	pharyngitis, pneumonia, skin infection, sepsis, brain abscess, endocarditis
L	S.salivarius	oropharynx	dental and gingival inflammatory diseases, mumps, neonatal sepsis, meningitis, brain abscess, endocarditis
Non-groupable	S.pnevmoniae (pneumococcus)	upper respiratory tract	otitis, sinusitis, pneumonia, meningitis, sepsis, endocarditis, purulent arthritis
Other groups	S.mitis, S.oralis, S.sanguis, S.gordonii, S.orista, S.anginosus, S.mutans, S.vestibularis, etc.	oropharynx	pneumonia, sepsis, dental and gingival inflammatory diseases, gums, hospital infections, endocarditis

Of all groups of streptococci, a special position is occupied by **Group A**, which involves *S.pyogenes*, β-hemolytic streptococcus. 80 serovars of β-hemolytic streptococcus are known. Their cell wall is represented by proteins with antigenic properties, which ensure the binding of the pathogen and its virulence. They have a wide range of superantigens: erythrogenous toxins A, B, C and D, exotoxin F (mitogenic factor), streptococcal superantigens (SSA), SpeX, SpeG, SpeH, SpeJ, SpeZ, SmeZ-2. These antigens can interact with antigen of the major histocompatibility complex class II, expressed on the cell surface by the variable sections of the ß-chain (α / ß-receptors) of the T-lymphocytes, causing their proliferation, thereby leading to a strong release of cytokines, especially tumor necrosis factor and interferon. This hyperproduction has a systemic effect on the body. Moreover, group A streptococcus is able to produce many other biologically active extracellular substances such as streptolysin O and S, streptokinase, hyaluronidase, DNA-ase B streptodornase, lipoproteinase, C5a-peptidase. In particular, the erythrogenous toxin has a cytotoxic, pyrogenic, and sympathotropic and allergenic effect on the human body. Streptolysin S has immunosuppressive properties; streptolysin O has cardiotropic effect and enterotoxin causes diarrhea.

Group B streptococci. *S.agalactiae* constitutes the majority of isolates. Group B streptococci colonize the nasopharynx, gastrointestinal tract and the vagina. Serovars la, lb, Ic, II and III are distinguished. Bacteria of the serovars Ia and III are tropic to the tissues of the central nervous system and respiratory tract, often cause meningitis in newborns, especially in preterms. When infecting a baby during maternal delivery, respiratory distress syndrome occurs in 55%; purulent meningitis, septicemia, osteomyelitis occurs in 15% and lethality accounts for 5%. Group B streptococci may not cause any symptoms, but are detected in the body. Such people are called carriers of these streptococci. The carriage of group B streptococci is not contagious, that is, it is not transmitted by human to human in contact. In most cases, B streptococci do not cause any problems.

Streptococci of groups C and G have many virulence factors that can cause both asymptomatic carriage and omphalitis in newborns, postinfectious glomerulonephritis, reactive arthritis, respiratory diseases, etc. Streptococcus, characterized by the presence of the antigen of the **group D**. Streptococcus (fecal) belongs to the genera *Enterococcus* and *Streptococcus*, possess high tolerance to adverse conditions of development. Streptococcus includes the following enterococcus species: *E.avium, E.casseliflavus, E.cecorum, E.durans, E.faecalis, E.faecium, E.gallinarum, E.hirae, E.malodoratus, E.munditiuse* and *E.solitarius*. Streptococci of this genus are enterococci of mainly fecal origin. Enterococci can in most cases be considered as specific indicators of water pollution by human feces. The source of fecal streptococci is mainly animal feces. Fecal streptococci rarely multiply in contaminated water and therefore can be used in the analysis of water quality as an additional indicator of the efficiency of water purification. Most cases of infectious diseases caused by enterococci are diagnosed in persons with a violation of physiological barriers (gastrointestinal tract, skin, urinary organs). In newborns it more likely causes sepsis (mortality to 15%), in older children - bacteremia, intracranial abscesses, affects the biliary tract and leads to cholecystoholangitis. Enterococcal bacteraemia in older children occurs in hospital infection.

Among other species, in the medical setting, the most important groups are **pneumococci (*S.pneumoniae*)**. Bacteria do not contain a group antigen and are serologically heterogeneous and, according to the structure of capsular antigens, 84 serovars are distinguished. They cause most cases of community-acquired pneumonia in human, which are polyfocal and destructive, may be complicated by pyothorax, empyema. Noteworthy, acute respiratory viral infection precedes the affection of respiratory tract by pneumococcus. Pneumococcal pneumonia is characterized by sudden onset, elevated temperature, chest pain, shortness of breath, fatigue, rust colored sputum excretion.

Pneumococcal meningitis (S. pneumoniae - Gr +) is one of the most severe forms. In primary infections, meningoencephalitis is developed starting from the first days, conjoined by the focal symptoms, paresis, paralysis, and ataxia

Currently, scientists have identified a relatively new **PANDAS** syndrome, i.e., pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections. Such children have an increased level of antibodies against the neurons of the caudate nucleus. This syndrome occurs after contraction or carriage of streptococcal infection in the first 3 months, as well as possibly within 1 year as a secondary affection of the CNS. In such children, more often in the puberty period, hyperactivity, emotional lability, various phobia, facial spasms, depression, obsessive thoughts occur.

Streptococcal bacteremia is one of the most common causes of **fever of unknown origin**. The antigen is activated in children who have long been carriers of streptococcus under certain stress, which leads to weakening of immunity, low grade fever more than 2 weeks or defervescence.

Pathogenesis of streptococcal infection

1. Entry of infection is palatine tonsils, the mucous membrane of upper respiratory tract, damaged skin, umbilical wound, mucous membrane of the birth canal.

2. The pathological process involves a **toxic syndrome** (intoxication, rise of body temperature, appearance of rashes); **septic syndrome** (inflammation in the site of the entry of infection: tonsillitis, otitis, lymphadenitis; purulent complications); **allergic syndrome** (infectious-allergic complications: glomerulonephritis, myocarditis, synovitis, etc.).
3. Development of the expressed antibacterial, antitoxic immunity; recovery.

Classification of streptococcal infection

1. Scarlet fever.
2. Erysipelas.
3. Streptococcal infection of different localization.

A. Local forms.

- ENT organs (tonsillitis, otitis, sinusitis);
- Skin, subcutaneous tissue (streptodermia, abscess);
- Lymphatic system (lymphadenitis, lymphangitis);
- Respiratory system (rhinitis, pharyngitis, laryngitis, tracheitis, bronchiolitis, pneumonia);
- Musculoskeletal system (osteomyelitis, arthritis);
- Cardiovascular system (endocarditis, pericarditis);
- Urinary system (pyelonephritis, cystitis, adnexitis);
- Nervous system (meningitis, brain abscess);
- Digestive organs (cholecystitis, pancreatitis, etc.).

B. Generalized forms

- Septicemia;
- Septicopyemia.

One of the common pediatric infectious diseases of streptococcal etiology is scarlet fever, erysipelas, strep throat (tonsillitis).

Acute tonsillitis is an acute infectious disease in which the local inflammatory process in the palatine tonsils is the leading clinical sign, less commonly in other components of the lymphoid pharyngeal ring. Primary tonsillitis (catarrhal, lacunar, follicular, ulcerative-filamentous) and secondary tonsillitis (in infectious diseases as diphtheria, scarlet fever, tularemia, typhoid fever, infectious mononucleosis, candidiasis, herpangina in enteroviral infection; in diseases of the blood as agranulocytosis, alimentary-toxic aleukia, leukemia) are distinguished. In addition, chronic specific tonsillitis in infectious granulomas (tuberculosis, syphilis, sclerema) occurs.

Table 4

Differential diagnostic criteria for diseases with signs of strep throat

Signs	Diphtheria of the oropharynx	Scarlet fever	Infectious mononucleosis	Strep throat
1	2	3	4	5
Onset	Acute	Acute	Acute	Acute
Leading symptoms	fibrinous inflammation in the oropharynx, intoxication.	tonsillitis, exanthema from day 1-2	hyperplasia of lymphoid tissue, sore throat not in all cases (secondary)	sore throat (follicular, lacunar)
Oropharynx mucosa color	cyanotic hyperemia tint, edema	bright scarlet hyperemia, separated from intact tissues	bright hyperemia	bright hyperemia
Characteristics of the exudate	gray-white, yellow patches can extend beyond the tonsils , dense,	purulent, white-yellow, encapsulated or in the lacunae, easy to be removed, non-	purulent, encapsulated or in the lacunae, white-yellow, easy to be removed, not	purulent, encapsulated or in the lacunae, white- yellow, easy to be

Signs	Diphtheria of the oropharynx	Scarlet fever	Infectious mononucleosis	Strep throat
1	2	3	4	5
	difficult to be removed, bleeding mucosa beneath them, recurrent, non-smeared	bleeding mucosa, smeared, not extended beyond the tonsils	extended beyond the tonsils	removed, non-bleeding mucosa, enlarged, not extended beyond the tonsils
Lymphadenitis	regional	regional	generalized enlargement of the lymph nodes	regional
Hepato-splenomegaly	absent	absent	typical	absent
Rashes	absent	punctulate	can be maculopapular, erythematous (in ampicillin)	absent
Intoxication syndrome	apparent	moderately apparent	can be apparent	moderately apparent
Neck swelling	in toxic forms	absent	on the area of the regional lymph nodes in severe cases	absent
Altered tongue	coated	coated; "strawberry tongue" from day 4-5	coated	coated

Diagnosis of the streptococcal infection

Prompt identification of the cause and timely follow up examination and therapy is crucial: **the first stage** – clinical examination, general clinical and biochemical laboratory methods, coprological examination, evaluation of immunograms, bacteriological and virological analysis of mucus, feces, urine, eye discharge, blood test for sterility, Mantoux reaction, X-ray examination of the lungs, thymus, ultrasound examination of the abdominal cavity, kidneys, heart, brain; **the second stage** is a repeated bacteriological and virological analysis of mucus, feces, urine, eye discharge, determination of markers of hepatitis, infectious mononucleosis, determination of intracellular pathogens-chlamydia, mycoplasma, DNA-viruses by ELISA and PCR. MRI of the brain is recommended; **the third stage** involves invasive methods, namely, puncture: sternal, spinal and articular and lymph nodes, hepatic biopsy, consultation of a surgeon, an ophthalmologist with eye-ground examination, a hematologist, an immunologist, a neurologist.

Treatment is carried out in accordance with the relevant protocols. Regimen: bed rest throughout the acute period of the disease. The diet should correspond to the child's age. **Etiotropic therapy** involves antibiotics: penicillins or macrolides are prescribed in the mild form; penicillins are prescribed in the moderate form; cephalosporins of the 1-3 generations, clindamycin, vancomycin are prescribed in the severe form. The course of antibiotic therapy: 10 days in case of the mild form; 10-14 days in case of the moderate and severe forms; the route of administration: per os in case of the mild form; intramuscularly in case of the moderate form; intravenously in case of the severe form. Disinfection therapy: in mild form - a significant amount of drinking, in moderate and severe forms - infusion of glucose-saline solutions. Also prescribed symptomatic therapy: antihistamines, drugs; which strengthen the vessel wall, antipyretic drugs; local remedies: rinse throat with disinfectant solutions, tubes-quartz and the like. **Detox therapy:** in the mild form – drink plenty of water; infusion of glucose-saline solutions in case of the moderate and severe forms. Symptomatic therapy involves

antihistamines; medications to strengthen the vascular wall, antipyretics; gargling with disinfectant solutions, quartz tubes, etc.

Specific **prevention** of streptococcal infection does not exist to date. The main measures are the early detection and isolation of the source of infection and other non-specific prophylaxis.

List of questions for final control:

1. What is the definition of the streptococcal infection?
2. What is the epidemiology of streptococcal infection in children?
3. What is classification and course of clinical forms of streptococcal infection?
4. What is the treatment of streptococcal infection in children?
5. What is the prophylaxis of streptococcal infection in children?

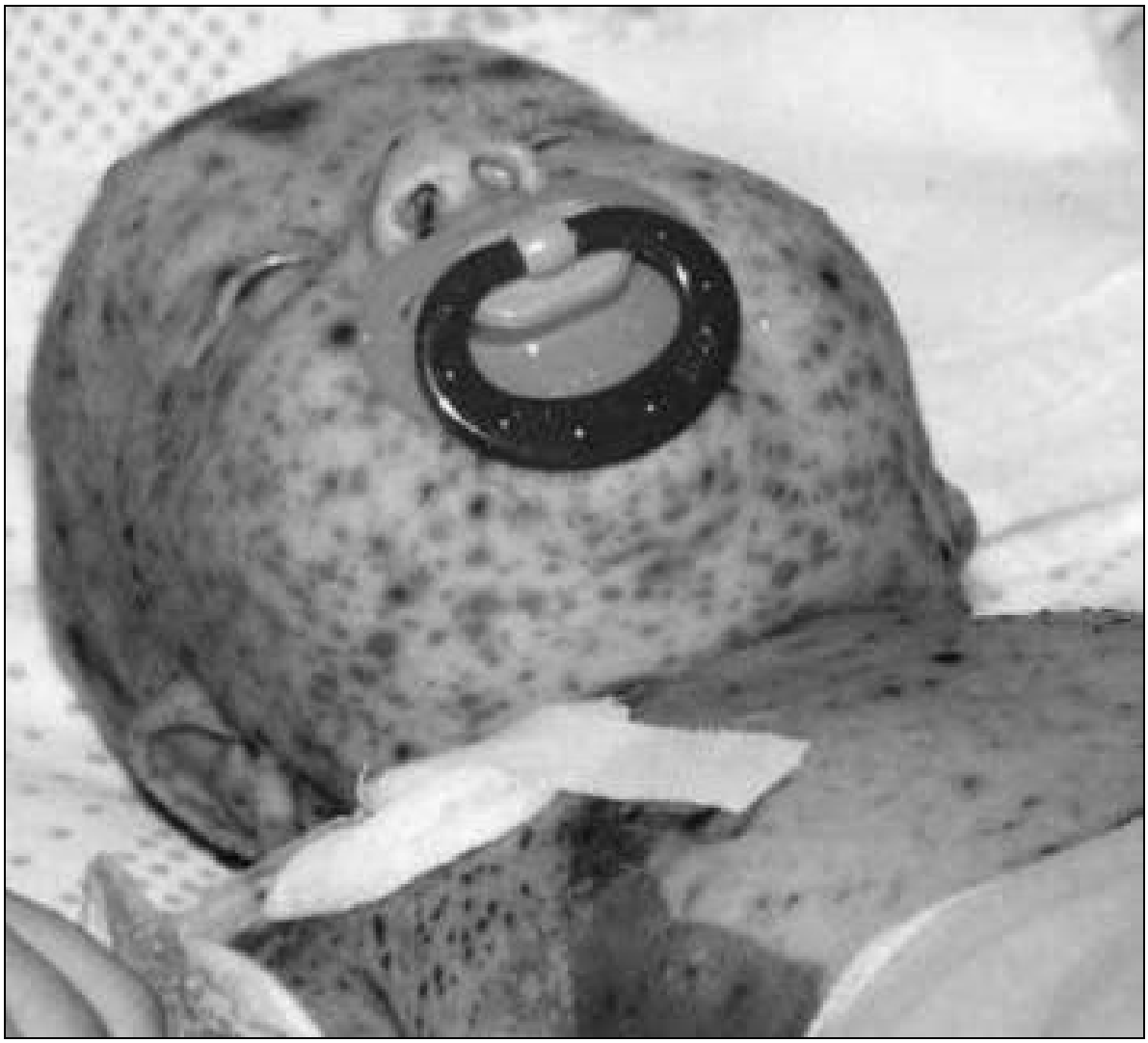

Fig.3. Chickenpox, hemorrhagic form, severe course in 10-month old baby.

SECTION 4.
HERPESVIRAL INFECTION IN CHILDREN

Herpes (from Greek *herpes* meaning "fever") is the most widespread human viral infection. 60-90% of the world population are infected with one or another herpes virus. The WHO reports that herpesviral infection (HI) ranks second, after the flu, as a cause of death from viral infections. This virus is part of the TORCH complex, which plays a significant role in the occurrence of reproductive losses. HSV was discovered by V. Gruter in 1912. It belongs to the *Herpesviridae* family. HI is often understood as a group of diseases caused by herpes simplex virus (HSV-1, HSV-2) and is characterized by primarily skin damage, mucous membranes and the nervous system. To date, eight types of herpes viruses are described: two types of herpes simplex (HSV-1, HSV-2), chickenpox and herpes zoster virus (VZV, HHV-3), Epstein-Barr virus (EBV, HHV-4), cytomegalovirus (CMV, HHV-5), HHV-b, HHV-7, HHV-8. According to the biological properties of viruses, α-herpesviruses, β-herpesviruses, γ-herpesviruses have been identified. α-herpesviruses (HSV-1, HSV-2, VZV) are characterized by a short cycle of reproduction with cytopathic effect in cells. β-herpesviruses involve CMV, HHV-6, HHV-7. They multiply slowly, causing an increase in the affected cells, capable to persist in the salivary glands, the kidneys, can cause congenital infections. EBV, HHV is assigned to γ-herpesviruses. They are characterized by tropism to B-and T-lymphocytes, in which they persist, can cause lymphoproliferative processes. Children are most susceptible to HI at the age from 5 months to 3 years. Type 1 herpesviruses are transmitted by air and contact paths; sexual, vertical, parenteral transmission is characteristic to Type 2 herpesviruses. HCV-3 causes genital and neonatal herpes. Depending on the mechanism of affection the following is distinguished: congenital and acquired forms. Acquired HI may be primary and secondary (recurrent), localized, generalized, latent.

The primary HI involves:

- neonatal infection (generalized herpes, herpesviral encephalitis, skin and mucosa herpes);
- herpesviral encephalitis;
- gingivostomatitis;
- Eczema herpeticum Kaposi;
- primary skin and eye herpes;
- herpes whitlow.

The secondary HI involves:

- skin and mucosa herpes;
- herpes keratitis;
- genital herpes, etc.

Etiology and epidemiology

The etiologic agent of this infection is large DNA-containing viruses with envelope, for a long time may persist at low temperatures and in a dried state, but destroyed at temperatures above 50^{o}C, ultraviolet and X-ray irradiation. The etiologic agent of HI is a sick person and virus carrier. Cross-immunity in people with the history of herpesviral infection is not observed. It is stored in the human body in a latent form, which, under the influence of various factors, transforms into clinically manifested forms. Seasonality and epidemic outbreaks of HI are not characteristic.

Pathogenesis

The entry of infection is mucous membranes of the lips, oral cavity, conjunctiva, genitalia. The primary affection by the virus occurs in cells of ectodermal and dermal origin, which leads to the destruction of epithelial cells. This phenomenon is accompanied by the appearance of blisters due to ballooning degeneration. It is hypothesized that the virus penetrates the dendrite of the neurons that innervate the skin, then into the sensory ganglia, where its main

replication occurs. If the child's organism cannot restrict replication, the virus spreads via hematogenous, neurogenic and lymphogenous pathway. In immunocompromised individuals disseminated infection occurs. Coagulation necrosis occurs in the internal organs in the generalized forms. The incidence and severity of recurrences depend on the child's immunity. Activation of the virus is associated with insufficient activity of macrophages, T-helper cells, cytotoxic lymphocytes, and decreased production of inflammatory mediators. Herpesviral infection is considered an indicator of AIDS' diseases due to immunosuppressive state.

Herpesviral encephalitis caused by HSV-1 occurs both in primary infection (30%) and in the reactivation of latent infection (70%). Ways of penetration of the virus into the brain: hematogenous or retroaxonal. The spread of the virus in the nervous system is due to its penetration into the cerebrospinal fluid. The primary replication of the virus occurs in the mesenchymal cells of the brain, ependymis of the ventricles with subsequent damage to the neurons and glia. HSV-1 affects all brain cells. In herpesviral encephalitis caused by HSV-2, the infection occurs more often when it passes through parturient canal or transplantation. After penetration of the virus into the skin and mucous membranes its replication begins with its subsequent spread from the cell to the cell, and then into the blood and lymph. In transplacental transmission the virus immediately enters the bloodstream and subsequently into the brain through the blood-brain barrier. HSV-2 belongs to cytolytic viruses. In infected cells, necrotic and inflammatory processes develop. In the brain, necrosis is localized in gray and white matter, often diffuse in nature and spreads to the deep layers of the brain, the cerebellum.

Clinical course

The incubation period ranges from 2 to 12 days. It is believed that more often HSV-2 is the etiological factor in newborns and during the first year of life, whilst HSV-1 is more common in older children and adults. The clinical presentations of the diseases are variable with specific characteristics in newborns and young children. Children of the first year of life have anti-herpetic antibodies transplacentally transmitted from their mother. Symptoms of primary herpes arose most frequently in the form of acute respiratory viral infections, aphthous stomatitis, which is characteristic of herpes simplex. Localized form of herpes manifests itself as a vesicular rash around the mouth, nose, on the ears, and on the face. Vesicles first have a transparent contents that gradually becomes cloudy, then the vesicles get dry, crust are developed, which subsequently disappear leaving barely noticeable pigmentation. This viral disease has a long latent course, is recurrent and can affect, apart from skin and mucous membranes, central nervous system and internal organs. In children with dermatoses with the presence of erosive skin lesions, herpetic eczema may develop. Acute onset with a rise in body temperature to 39-40°C and rapidly progressing symptoms of toxicosis are characteristic. The regional lymphadenitis is marked; repeated occurrence of rushes and superimposing of the secondary infection are possible. Skin damage may be zoosterform, hemorrhagic, hemorrhagic-necrotic or ulcerative-necrotic. Erythematous, papular, edematic are atypical forms of HI.

Lesions of the oral mucosa are the most common form of primary herpes in children, which occurs at the age of 6 months to 3 years. The causes are the inadequacy of mechanisms of antiviral defense by reducing the contents of natural killers, secretion of cytokines, interferon, interleukins, IgM, IgG. Persistent affection of the oral mucosa is caused by the impairment of its integrity during teething; injury by toys, household items also causes the occurrence of HI.

Genital herpes is more often diagnosed in adolescents and adults with sexually transmitted infections. In children of younger age groups, genital lesion is secondary to the appearance of other manifestations of herpesviral infection. In this case, the infection occurs through infected hands, towels, linen. Clinically, genital herpes is manifested by hyperemia and edema of the genital organs, vesicular rash on large and small labia in girls and skin of the penis and scrotum in boys. The vesicles desquamate quickly, forming erosive or erosion-ulcer surfaces. The disease is accompanied by itching, pain in the affected sites, and rise of body temperature.

The most typical course of **herpesviral encephalitis** involves 5 periods:

1. General-infectious period (1-21 days) is characterized by fever, upper respiratory tract catarrh, possible pustular rash on the skin and mucous membranes.
2. Encephalitic period (1-10 days) is characterized by headache, vomiting, altered mental state, delusion, hallucinations, aphasia, apraxia, agnosia, pyramidal disorders.
3. Encephalitic (comatose) period (1-50 days) is characterized by confusion, seizures, coma symptoms.
4. Early reconvalescence period (1-12 months) is characterized by retrograde and fixation amnesia, apraxia, agnosia, regression of physical development.
5. The period of residual effects is characterized by mental disorders, hyperkinesis, limb paresis (months, years).

Herpesviral meningitis develops as serous, aseptic and is often combined with primary genital herpes. Herpesviral meningitis has a protracted course, with the risk of complications such as enuresis, polyradiculoneuropathy, myelitis, recurrent meningitis; timely diagnosis and early specific etiotropic treatment is required.

Visceral forms of herpesviral infection are manifested by acute parenchymal hepatitis, pneumonia, and nephritis. They occur more often in newborns, but they can also be in older children.

Herpesviral hepatitis is more often a manifestation of primary herpetic infection in newborns and children of the first months of life. It is accompanied by high fever, severe symptoms of intoxication, vomiting, enlargement of the liver, spleen, jaundice, hemorrhagic syndrome. Clinicalcourse is often protracted with marked cholestasis and the development of acute hepatic encephalopathy, hepatic insufficiency; lethal outcome is possible.

Herpetic pneumonia and focal nephritis are not clinically different from the lesion of the lungs and kidneys of another etiology.

Herpes in HIV-infected patients develop more often as a result of the activation of latent herpesviral infection. In this case, the disease becomes generalized. Signs of generalization are the spread of the virus on the mucous membranes with the subsequent occurrence of herpetic pneumonia, the development of chorioetinitis, meningoencephalitis. Herpetic rash does not disappear, and ulcers are developed on their sites. Herpetic infection in HIV-infected patients has no tendency to spontaneous resolution.

Clinical symptoms of congenital herpetic infection depend on the time of infection, virulence of the virus and the state of the host defense of the pregnant woman and the fetus. Some researchers emphasize the possibility of development of defects in the case of infected fetuses in early pregnancy (microcephaly, microphthalmia, chorioretinitis, etc.). But most authors point out that HSV has no teratogenic effect.

The activation of HSV in pregnant woman following the 32 weeks of pregnancy leads to infection of the fetus in 10% of cases, and in the antenatal period in 40-60%. In this case, preterm labor may begin, or the baby becomes ill during the first hours after birth.

Forms of neonatal herpesviral infection:

1. localized;
2. herpetic affection of CNS (encephalitis);
3. generalized.

Laboratory studies

1. *Virological method.* Blood, liquor, saliva, scrape from the cornea, contents of the vesicles, cervical secretion on the chicken embryos is studied.
2. *Immunofluorescence method.* Intracellular aggregations of HI in the scrapes from the vesicles are in the form of specific fluorescence.
3. *Serological method.* The use of ELISA method to detect specific antibodies of the class IgG, IgM in the blood.
4. PCR.
5. *Cytological method.* Multinucleated giant cells containing eosinophilic intranuclear inclusion bodies are found in the impression smears of the affected area of the skin or mucous membranes.

Treatment

Stage 1 - treatment in the acute period or during relapse: Antiviral drugs (10 mg / kg acyclovir 3 times a day for 10 days; in herpesviral encephalitis 30-60 mg / kg acyclovir intravenous drop infusion for 14-21 days in combination with pathogenetic therapy according to the protocol of treatment of encephalitis, which is approved by the Order of the Ministry of Health of Ukraine). Compared with other antiviral drugs acyclovir is many times more effective. The specificity of its action is that it can only be used by the enzymes of herpesviruses. Importantly, the mechanism of action of the drug does not depend on the stage of the disease, which makes it universal for both prevention and treatment. The sensitivity of different types of herpes to acyclovir is not the same. Its antiviral activity decreases as follows: herpes simplex virus, herpes zoster virus, Epstein-Barr virus, cytomegalovirus.

Antiherpes medications: acyclovir, ganciclovir, virolex, heviran, valacyclovir, famciclovir, sorivudine, foscarnet, trifluridine, and isoxuridine.

In pediatric practice, medicinal products of natural origin with a high profile of efficiency and safety are particularly relevant. One of such medications is the medicinal product "Erebra" containing the hyporamine represented by the biologically active components isolated from the leaves of sea-buckthorn: haloelageletanins (not less than 60%), chlorogenic, eochlorogenic, kumar, ascorbic acids, catechins, epicatechinum, rutin, quercetin, isoramnetin, eleagnozide, carotenoids, essential oils, etc. The resulting analysis of the data of systematic reviews of the PabMed resource shows the high interest of scientists in the study of the clinical effects of substances isolated from the leaves of sea-buckthorn (Hippophae Rhamnoides L.) - about 20 studies confirming a big therapeutic potential with immunomodulatory, anti-inflammatory, protective, anti-tumor, antioxidant, cardio - and hepatoprotective, antimicrobial and antiviral activity. Researchers have shown by evidence the antiviral activity against different strains of influenza A and B viruses, adenoviruses, paramyxoviruses, herpes simplex virus, Varicella zoster, cytomegalovirus, respiratory syncytial virus. Hyperamine ("Erebra") is a plant antiviral drug, has effect on DNA viruses and enhances the induction of endogenous α- and γ-interferon. The drug is used at a dosage: children aged 3 years and more - ½tab. (10 mg) 2-4 times a day, from the age of 6 years - 1 tab. (20mg) 3-4 times a day, from the age of 12 years and adults - 1 tab. (20mg) 4-6 times a day. Duration is for 3 weeks.

- Natural antioxidants.
- In pronounced exudative component of inflammation: prostaglandin inhibitors (sodium diclofenac, indomethacin).
- Interferon drugs and inducers of endogenous interferon.
- Immunoglobulins.

Stage 2 - Therapy in the stage of remission (in the stage of early reconvalescence):

- Prolonged administration of antiviral drugs (0.1-0.2 g/day acyclovir for 2-12 months depending on the severity).
- Immunomodulators.
- Adaptogens of plant origin.

Stage 3 - in stable clinical and laboratory remission:

- Prevention of intercurrent diseases.
- Administration of the killed herpetic vaccine (0.1-0.2 ml in 2-3 days 5 times, at least twice a year).

Prevention

Children should be isolated in the individual wards in acute forms of herpesviral infection, common and generalized forms. Newborns, who were in contact with patients with herpetic infection should be examined for the presence of infection. In case of suspected herpesviral infection, antiviral therapy should be started.

Children with dermatitis, eczema, immunodeficiency states, AIDS, as well as those receiving immunosuppressive therapy, need to be isolated from patients with herpesviral infection.

Children who attend pre-school children's facilities and have the signs of skin herpes need to cover the affected sites with clothes, bandages, etc., or isolate them temporarily during exacerbation of the process.

In children born to mothers suspected of genital herpes, manipulations on the head should be avoided.

Pregnant women who have confirmed diagnosis of genital herpes, a Caesarean section is recommended, and children born to such mothers should be examined for herpesviral infection.

Ultraviolet irradiation can provoke relapses of herpes, so patients with recurrent herpes should avoid direct sunlight.

No antiepidemic measures are conducted in the focus of infection.

List of questions for final control:

1. What is the definition of herpesviral infection?
2. What is the epidemiology of herpesviral infection in children?
3. What is the classification and course of the clinical forms of herpesviral infection in children?
4. What is the treatment of herpesviral infection in children?
5. What is the prevention of herpesviral infection in children?

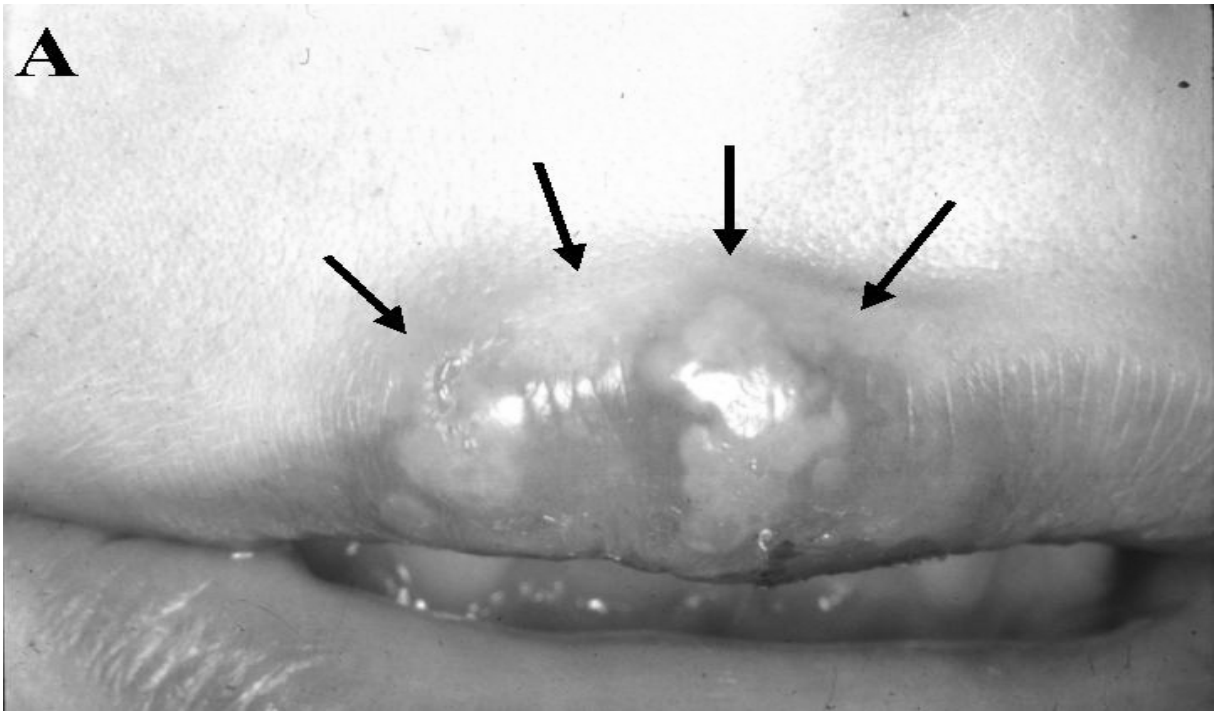

Fig.4. Herpesviral infection.

SECTION 5.
INFECTIOUS MONONUCLEOSIS IN CHILDREN

The urgency of the problem of infectious mononucleosis is due to the following main factors: incidence rise by 6 times in Ukraine over the past 5 years, a large variation in the clinical course of the disease, and the complexity of specific diagnosis, which causes a large percentage of diagnostic errors, the overall infection by the Epstein-Barr virus (EBV), capable of affecting the immune system. Antibodies to EBV are found in 15% of children under 1 year of age and 90% of adults. In Russia, the mandatory registration of cases of this disease has been introduced since 1990, and in Ukraine since 1992. The incidence of infectious mononucleosis is 28,47 cases per 100 thousand of children's population in the Poltava region for the last 10 years.

The disease was first described by Filatov N.F. in 1885 as “idiopathic lymphadenitis with fever”. The etiologic agent of infectious mononucleosis is the Epstein-Barr virus, isolated in 1964 by Epstein and Barr from Burkitt lymphoma cells (Isaakov, 1999). It has been proved by evidence that EBV is widespread, antibodies to the virus are found in all studied populations; the rate of infected people accounts for 80 to 90% of the world’s population. The findings of the studies have revealed a large variety in the time of primary infection and the degree of prevalence of infection. Representatives of the developed nations are infected more often at the age of 14-15 years, and 70-100% of the population of undeveloped nations has been already infected by age of 3-5 years (Zayats N. A., 1990, Isaakov V. A., 1999, Samaya C.V., 1985, Mohsen Z., 1990). However, despite the general prevalence and infectioning, in different regions the clinical diversity of the diseases caused by the virus is noted: in Europe the infectious mononucleosis is more common, in Asian countries the virus causes nasopharyngeal carcinoma, and in Africa the most common is Burkitt lymphoma (Berman N. E., 1987, Levine P.H. et.al., 1987, Wu H.C/ et al., 2003). A detailed description of the symptoms of the disease and their combination relates to 1970-1975 (Nisewich N.I., 1975). Treatment of infectious mononucleosis remains symptomatic to date. Acyclovir, which has been successfully used to treat other herpesviral infections, is ineffective. The appropriateness of the use of antibiotic therapy is denied by a number of contemporary domestic and foreign authors (Uchaikin V.F., 1998, Vashev Ye.A., 2001, Kramarev S.O., 2011, Levine P.H. et al., 1987, Andersson J., 2000). At the same time, methods of immunocorrection have been insufficiently substantiated (Khodak L.A., 2010, Chernyshova L.I., 2011).

Etiology and epidemiology. EBV belongs to the family of herpes viruses, the genus of γ-herpesvirus type 4. This is a DNA-containing virus. The mature virus has a spherical shape, contains a double-stranded DNA gene, capsid, protein, lipid outer membrane. EBV has specific antigens: capsid (VCA), nuclear (EBNA), early (diffuse EAD and localized EAR), membrane (MA). In the acute infection, antibodies first appear to the early antigens (EA, VCA), and, subsequently, to the nuclear (EBNA). Detection of antibodies to capsid (VCA) and nuclear (EBNA) antigens in the absence of antibodies to early antigens (EA) is a marker of long-standing infection, i.e., latent infection. The antibody spectrum is significantly different in various diseases associated with EBV. Thus, in patients with IM, antibodies belonging to the three classes of immunoglobulins, to different virus-specific antigens appear. In patients with Burkitt lymphoma, titres of IgG-antibodies to the EAR are elevated. In patients with nasopharyngeal carcinoma, titres of IgA antibodies to EAD and VCA are elevated. Antibody titers are correlated with an increase in tumor size and decrease in successful treatment.

The virus produces proteins that are analogues of interleukins that change the immune response and suppress cellular immunity. X-chromosome contains a marker of the lymphoproliferative process, and the Epstein-Barr virus has tropism to the lymphoid tissue. Incorrect immune response is caused by the abnormal genetic recombination, and can provoke tumor process, Burkitt lymphoma, lymphogranulomatosis, etc. The DNA virus penetrates into the cell where lymphocyte replication occurs: this process is called immortalization (immortality of lymphocytes). Up to 20% of B-lymphocytes are affected during the acute phase. In

generalization and chronization of the process T-lymphocytes, killers, epithelial cells of the vessels get damaged.

The routes of infection are air, sexual, vertical - from mother to child, hematogenous. **Contagiousness** in EBV-infection is moderate, which is due to the low concentration of the virus in saliva (the kissing disease). The common use of kitchen utilities, toys, linens by contracted and healthy children is crucial in transmitting the infection. Activation of the infection is facilitated by the factors reducing general and local immunity. The incubation period may range from several days to 1-2 months.

Pathogenesis, which is similar to all viral infections, the following stages can be distinguished:

1. inoculation;
2. primary-regional infection (entry infection reaction);
3. primary viremia;
4. parenchymal dissemination;
5. visceral focus phase;
6. immunity development phase;
7. reconvalescence.

Features of infectious mononucleosis in children are:

- Epstein-Barr virus activation may be caused by frequent acute respiratory diseases, seizure syndrome, neurological diseases, infectious diseases;
- after the initial reaction, may be asymptomatic and develop into chronic form; it is possible to detect by markers only;
- in the primary regional infection, enlargement of the lymph nodes, more frequently cervical and submandibular ones, and tonsillitis (from catarrhal to purulent inflammation) is characteristic. It should be remembered that infectious mononucleosis is not diagnosed when tonsillitis without lymphadenopathy ocuurs, though in case of vice verse it can be possible;
- parenchymal dissemination is detected at the end of 1 week with the characteristic hepatosplenomegaly, as well as possible alterations of the myocardium, blood vessels, kidneys, lungs, nervous system. Time periods are crucial only in 30% of children;
- in younger children, the disease can occur as an acute respiratory disease;
- when the clinical presentation is similar, but there is no serological confirmation, the syndrome of an infectious mononucleosis is suspected, caused by virus of measles, rubella, toxoplasmosis, hepatitis B; HIV-infection, adenovirus infection, cytomegalovirus infection;
- importantly, the presupposed simultaneous contraction of a person by several etiological agents of the family of herpesviruses, namely, co- and superinfection, should be considered. The disease is progressing in the form of combined EBV- and CMV-infectious mononucleosis in 2% of patients;
- Children with marked immune deficiency may develop generalized forms of EBV-infection with central and peripheral nervous system damage in the form of meningitis, encephalitis, polyradiculoneuritis. X-linked lymphoproliferative syndrome (Duncan syndrome) is assigned to a group of hereditary diseases that are manifested in males after contraction by EBV. The prognosis of the disease is very unfavorable, more than 70% of the patients die without reaching the age of 10 years. The survived individuals experience a severe hypogammaglobulinemia, lymphoblastic lymphoma, less frequently aplastic anemia and necrotic vasculitis with arterial and large vessel damage.

Classification of EBV-infection:

1. primary infection (seropositive and seronegative);
2. asymptomatic virus carriage or latent form of EBV-infection;
3. chronic reactive:
   - active form;
   - generalized form (myocarditis, pulmonitis, glomerulonephritis, meningoencephalitis);
   - EBV-related hepatophagocytic syndrome;
   - atypical reactive form (oncological process, autoimmune diseases: systemic lupus erythematosus (SLE), chronic vasculitis, chronic fatigue syndrome, etc.).

Clinical presentation: infectious mononucleosis is characterized by the triad of clinical symptoms: fever, sore throat, hepatosplenomegaly; hematological changes are expressed by leukocytosis with atypical mononuclear cells. The most characteristic blood-related manifestation of IM is the presence of atypical mononuclear cells. These cells vary greatly in size and shape. Such cells are called broad-plasma lymphocytes, mono-lymphocytes or virocytes. They appear in the bloodstream at the peak of the disease and are detected within 2-3 weeks, and sometimes several months, years. The amount of virocytes ranges from 5-10% to 50% and more. "Classical" gradual onset of the disease is noted only in 50% of cases; the number of patients with severe condition, prolonged fever (more than 10 days), jaundice and marked signs of hepatitis, high rates of cytolysis, cholestasis significantly increased. Rash is observed in 20% of patients, predominantly typhoid or maculopapular. Noteworthy, that infectious mononucleosis does not belong to mandatory exanthematous infections, thus, rash is not a permanent sign. Patients may experience vasculitis, myalgia, and disseminated intravascular coagulation (DIC)-syndrome in severe cases.

Differential diagnosis is made with other lymphadenopathies, caused by cytomegaloviral infection, herpesviral infection, as well as with oncologic diseases: leukemia, lymphogranulomatosis, Burkitt lymphoma, nasopharyngeal carcinoma, etc.

Burkitt lymphoma is a diffuse, undifferentiated malignant tumor. It is mainly located outside the lymph nodes - in the upper jaw, kidneys, ovaries, the liver, in the nervous system, etc. Depending on the localization of the lymphoma, a characteristic clinical symptomatology is observed. The affection of the jaw leads first to lymphoid infiltration of the soft tissues with subsequent bone lesions, resulted in disruption of teeth and deformation of jaw and nose. The process is prone to rapid generalization, which leads to the affection of the pelvic bones, vertebrae, thighs. This may be accompanied by a disturbance of the function of the pelvic organs, pathological fractures, compression of the roots of the spinal cord, paresis and paralysis, respiratory failure or swallowing disorders.

Nasopharyngeal carcinoma is a variant of a carcinoma that develops from epithelial cells. Three histological variants are distinguished: common, nonkeratinizing, undifferentiated. Leiomyosarcoma is a malignant tumor of smooth muscles. The disease is described in children with AIDS or after transplantation of organs. Patients with AIDS can also experience such **EBV-associated states** as non-Hodgkin lymphoma, lymphocytic interstitial pneumonia and hairy leukoplakia. In children, lymphocytic interstitial pneumonia is more common.

Congenital VEB infection. Publications report about the possibility of intrauterine EBV infection. Active EBV infection during pregnancy leads to early death of an embryo, premature birth or birth of a child with **developmental defects**: congenital cataract, cryptorchism, bone alterations of the "celery stalk" type. In the intranatal contraction, the disease may occur in a short period of time after child's birth, often in the form of encephalitis.

Diagnosis:

1. A specific method of laboratory diagnosis of EBV infection is an enzyme-linked immunosorbent assay (ELISA), which allows detection of antibodies to various EBV antigens.
2. PCR is a high-accuracy method (qualitatively and quantitatively) to detect the DNA of EBV in the saliva, blood, lymphocytes.

3. Complete blood count shows moderate leukocytosis, lymphomonocytosis with atypical mononuclear cells, thrombocytopenia or thrombocytosis.
4. Biochemical blood test reveals elevated blood transaminases, C-reactive protein.
5. Immunogram reveals antiviral immunity stress (elevated blood IF;elevated blood immunoglobulins (IgA, IgG, IgE, CIC), elevated natural killers (CD16 +), T-helper cells (CD4 +), cytotoxic lymphocytes (CD8 +); decrease avidity of antibodies, decrease in the number and functional activity of natural killers CD16 +, T-helper CD4 +, cytotoxic T lymphocytes CD8+, CD25+ -lymphocytes, functional activity of phagocytes).

Table 5

Identification of EBV-infection form

Interpretation	EA IgM	EA IgG	VCA IgM	VCA IgG	MA IgG
Incubation period	-	-	-	-	-
Very early primary infection	-	-	+	-	-
Early infection	+	+	+	+	-
Late reaction	±	+	±	-	±
Atypical primaty reaction	+	+	-	-	+
Chronic infection	±	+	±	+	-
Early postnatal infection	-	+	-	+	+
Late postnatal infection	-	-	-	+	+
Latent infection	-	-	-	+	+
Reactivation	+	+	+	+	+
Atypical reactivated infection	+	+	-	-	+

Note: MA – membrane antigen; VCA – capsid antigen; EA – diffuse early antigen.

Differential diagnosis of infectious mononucleosis with lymphadenopathies

Herpes Simplex. This infection is common in children. The disease occurs more frequently in winter. *H.simplex* infection is often accompanied by regional lymphadenitis, which can be both single-sided and bilateral, caused by disorders of lymphatic drainage from the affected area. At palpation lymph nodes are moderately painful, moving, not conjoined with adjacent tissues.

For differential diagnosis an important symptom of infection is the occurrence of pustular rash on mucous membranes and skin. Examination of the oral mucosa reveals bright hyperemia, swelling, herpetic rash (vesicles) in the size of 2-10 mm in diameter. First, the contents of rush is clear, then becomes yellowish, and subsequently areas of erosion are formed. Skin lesions are seen more often around the nose, mouth and ears and are itching, burning and painful. Within 1-2 days, blisters with clear contents appear against the hyperemic background, arranged in groups. On day 3-4, the blisters get dry, crusted and fall off on day 5-7. Scarring is usually not developed, but slight pigmentation of the skin is noticeable.

Herpesviral infection is sometimes accompanied by rise in body temperature to 39-40°C, weakness, chills, loss of appetite, especially in oral mucosa lesion. In younger children, body weight loss, the appearance of intestinal disorders with the development of even dehydration is possible. The consequence of toxicosis and hyperthermia may be CNS disorders, accompanied by headache, anxiety, febrile seizures. In case of viremia, CNS lesions are possible with the development of meningitis, encephalitis, meningoencephalitis, and meningoencephaloraditiculitis. Findings of the serological reactions in paired sera with the

determination of antibody titer in CFR, PHAT and specific IgM and IgG in ELISA, PCR are crucial for final diagnosis.

Cytomegalovirus infection (CMVI). Differential diagnosis is made taking into account that the acquired form of CMVI occurs in all age groups, but most often at the age 1 to 5 years; may occur in any season. In babies and younger children the acute onset of acquired CMVI manifests itself as a polymorphism of clinical manifestations. The disease begins with fever, symptoms of general intoxication, lymphadenopathy. Then pneumonia or obstructive bronchitis may develop, which can be accompanied by pertussis-like cough. Characteristic symptoms of CMVI are hepatosplenomegaly, anemia, hepatitis. Hemorrhagic syndrome often develops. In older children, CMVI often begins with mononucleosis syndrome, which is accompanied by lymphadenopathy, moderate fever, hyperemia of the oropharynx, enlarged palatine tonsils (sometimes with plaques), sore throat, hepatosplenomegaly. In addition, macular exanthema and sialoadenitis sometimes occurs in CMVI.

Complete blood count reveals leukocytosis with neutrophilosis or lymphocytosis, atypical mononuclear cells. In the formulation of a clinical diagnosis will help to conduct serological reactions by the methods of ELISA, CFR, NR, PHAT, immune blotting in order to exclude diseases occurring with similar symptoms.

Infectious lymphocytosis. It is believed that the disease is caused by various serotypes of enteroviruses and is benign. Ordinarily, clinical manifestations of the disease are absent or expressed insignificantly. In 50% of patients there is a slight increase in body temperature for 3 days, moderate catarrhal events, dyspeptic disorders and maculopapular rash on the face and extremities. The adenopathic form of the disease is characterized by a moderate enlargement of the peripheral lymph nodes, mainly cervical, retrocecal and bronchopulmonary ones, tonsils and spleen. Notably, lymphadenopathy can be the sign of infection of the upper respiratory tract or abdominal syndrome, progressing with acute abdomen, or pain in the muscles of the abdominal wall, intestinal colic, with the simultaneous development of enterocolitis. Encephalitis or meningeal syndromes are less common. Short-term appearance of rash on the skin (polymorphic erythematous, morbilliform or scarlatiniform rash) is possible. Complete blood count shows leukocytosis 30-40 to 100-150* 10^9/L with lymphocytosis (70-90% and more). The highest rates of lymphocytosis are observed during the first week of illness. Normalization of the leukogram occurs within 3 weeks to 3 months. The progress of the disease and prognosis is favorable.

Human herpesvirus 6 (HHV-6). The disease progresses both subclinically and with pronounced symptomatology. In most cases, HHV-6 infection is characterized by nonspecific clinical manifestations, namely, catarrhal syndrome and moderate intoxication that is accompanied by a lymphoproliferative reaction. In children younger than 2 years with respiratory viral infection, such symptoms as stuffy nose without rhinorrhea, lymphadenopathy, liver enlargement, gives reason to suspect HHV-6 infection. The average duration of the disease is 6 days. In the overwhelming majority of HHV-6 patients, latent infection is developed. However, the disease and clinical syndromes that are associated with the etiological factor of HHV-6 are described. HHV-6 is more often associated with the development of sudden rash, mononucleosislike syndrome and acute febrile illness. The development of chronic fatigue syndrome, which is characterized by acute influenza-like onset with the rise of body temperature up to 38°C, sore throat, minor enlargement of the cervical, occipital, axillary lymph nodes, unexplained generalized muscle weakness, migratory myalgia, arthralgia, sleep disorders, irritability, increased physical fatigue, followed by prolonged fatigue is considered HHV-6-associated infection. A possible manifestation of primary HHV-6 infection may be involvement of the central nervous system into the infectious process. Typhoid maculopapular rash can be combined with such manifestations as seizures, bulging fontanelles, meningoencephalitis or encephalitis, hemiplegia.

The association or interaction of HHV-6 and HIV is crucial. Clinical studies have shown that HIV-infected patients show HHV-6 viraemia, which correlates with HIV viral load.

Some researchers consider that HHV-6 may play a role in multiple sclerosis, multiple organ failure syndrome, pink zoster, hepatitis, viral hemophagocytosis, lymphomas, idiopathic thrombocytopenic purpura, drug-induced hypersensitivity syndrome, especially to antibiotics, histiocytic necrotizing lymphadenitis, fulminant encephalomyelitis in primary infection of persons with severe immune deficiency, Crohn's disease, Sjogren syndrome, autoimmune thyroiditis.

The clinical diagnosis is made on the basis of the following lab tests: neutralization, immunoblotting, ELISA, PCR, immunofluorescence.

Treatment and prevention

1. **Hospitalization** and bed rest is indicated in cases that are complicated for the diagnosis, in the severe progress and complications.
2. Pevzner diet No.5.
3. Vitamins and symptomatic means, gargling with antiseptic rinsing solutions are used in primary EBV infection is used. The disease does not require antiviral treatment. It has been reported that acyclovir therapy does not reduce the number of B-lymphocytes infected with EBV, and the rate of involution of pathological symptoms is not reliable.
4. In the pronounced necrotic changes in the pharynx, tonsillitis and superimposing of the secondary bacterial infection, benzylpenicillin is prescribed intramuscularly at the average age doses, followed by the transition to modern oral antibiotics for 7-10 days. Levomycetin and sulfanilamides, which suppress hematopoiesis, as well as hepatotoxic antibiotics, are contraindicated. Fluoroquinolones are not indicated for children under 12 years with the exception of severe course.
5. In severe cases glucocorticoids are effective. But it is necessary to consider the possibility of developing neurological and septic complications after their application. Publications report, that when it comes to diseases caused by DNA-containing viruses, hormones are not recommended. Exceptions are allergic dermatitis, obstructive syndrome and severe course of the disease.
6. Intramuscular administration of specific human immunoglobulin against the Epstein-Barr virus is reasonable. In case of severe forms of EBV infection, normal human immunoglobulin can be used for intravenous administration at a single dose of 3-4 ml/kg/day (0.15-0.2 g/kg/day) from 1 to 5 injections per course of treatment. Course dosage should not exceed 2g per 1kg of body weight. Treatment of the jaundice forms is similar to treatment of viral hepatitis with administration of hepatoprotectors: hepabene, silibor; ursofalk in cholestasis.
7. In EBV immunostimulants are not recommended, since health deterioration can be caused.
8. Treatment of chronic active EBV-infection (at the stage of reactivation) involve etiotropic medications, namely, ganciclovir, foscarnet, normomed, erebra. The efficacy of acyclovir in EBV- infection has not been proven. Ganciclovir is administered intravenously at a dose of 5-15 mg/kg 3 times a day for 10-15 days. The course can be extended to 21 days. The supportive dose is 5 mg/kg/day. The drug in such dosage is administered over a long period of time to prevent recurrence of the disease. The supportive therapy include per oral administration of 1g tablet ganciclovir 3 times a day. The antiviral effect of ganciclovir upon discontinuation is prolonged, but it should be remembered about the high toxicity of the drug. It can lead to the development of neutropenia, granulocytopenia, anemia, thus, blood indices should be monitored during treatment. Possible side effects of the drug include the disorders of cardiovascular, nervous system, digestive tract. Foscarnet is administered intravenously at a dose of 60 mg/kg 3 times a day. The course of treatment is from 10 days to 6 weeks. The use of the drug can lead to the development of thrombophlebitis, lowering of hemoglobin, and elevated blood creatinine.
9. Treatment of chronic active EBV-infection involves α-interferon drugs, which has an immunomodulating, antitumor and antiviral effect. Recombinant interferon (intron, laferon, roferon, viferon, laferobion, etc.) are prescribed at a dosage of 1mln IU per $1m^2$ of the body surface.
10. Burkitt lymphoma is highly susceptible to various types of cytostatic therapy. Surgical treatment in tumors of the jaw is contraindicated because of significant vascularization of the

tumor and the risk of hemorrhage. Radiation therapy causes local antitumor and analgesic effects.

11. Treatment of children under 1 year old should be careful due to the probability of a diagnostic error with leukemia, HIV-infection.

In the presence of residual changes in peripheral blood, reconvalescents are subject to outpatient surveillance for 6-12 months.

Prevention and measures in the site of infection. Patients are hospitalized in the infectious diseases unit or isolated at home. No specific preventive measures are conducted. Medical surveillance of contact persons from the epidemic site is carried out within 20 days. Some epidemiologists advocate the final on-site disinfection, but its effectiveness is not proven.

The following is the case report of the female 6 year-old patient A., admitted to Children's infectious diseases unit at the Poltava Regional Clinical Infectious Diseases Hospital in 2010 (medical history No.2756) with a **clinical diagnosis**: EBV-associated infectious mononucleosis with hepatitis; severe course. Nutritional anemia of the first degree. Complaints on hospitalization: malaise, high-grade fever, loss of appetite, pain in the abdomen, upper quadrant; dark urine. Physical examination revealed subicteric skin and sclera, polyadenia (enlarged cervical, submandibular, supraclavicular, axillary and inguinal lymph nodes), hyperaemia of the oropharynx; liver on the middle clavicular line was + 2.5 cm below the costal margin, the spleen was + 1.5 cm below the costal margin, dark urine. Diagnosis on hospitalization: Viral hepatitis A? Subsequently, during the period of stay in the hospital for 15 days the patient experienced fever 37,1-39^{0}C, polyadenia, hepato- (up to + 5-6 cm below the costal margin) and splenomegaly (up to + 3 cm below the costal margin), jaundice of skin and sclera, intoxication syndrome. Lab tests showed: **Complete blood count findings**: RBC-3,6*10^{12} / L, Hb:104 g / l, WBC:12,2 *109 / l, ESR-23 mm/h, stab:10%, segm:14%, lymph.:41%, mon:6%, plasma cells:2: 100, atypical mononuclears:30%, platelets: 360*10^9/l; **Blood biochemistry findings**: total bilirubin 102μmol / l, direct:50μmol / l, indirect:52μmol / l, thymol turbidity test: 4.0U, AlAT-2.30mmol / h: l, AsAT-1.20mmol / h: l; **Urine analysis findings**:specific gravity:1018, traces of protein, WBC:12-13 ppf, bile pigments: ++, **coprogram findings:** positive reaction to stercobilin, protozoa not found, other indicators are unremarkable. Blood screening for: RPR, leptospirosis; IHA with Yersinia pseudotuberculosis test; Vidal reaction; sterility; blood culture, anti-HAV IgM by the ELISA method, HBsAg, CMV DNA; in all cases, the result was negative; blood test for EBV markers: PCR method revealed EBV DNA; ELISA method revealed IgM to capsid antigen and early IgG antigen of Epstein-Barr virus. Medical advice of **ENT-physician**: catarrhal tonsillitis, adenoiditis; consultation of the **hematologist** after the interpretation of the **myelogram**: acute leukemia was excluded, nutritional anemia of the first degree, **ECG** showed sinus tachycardia. **Bacteriological study** revealed no pathogenic and opportunistic flora. **Management:** diet No.5, adequate hydration, infusion therapy: intramuscular 500 mg cefazolin twice a day for 10 days; 300 mg metragil once a day for 8 days; enterosgel, mesim-forte, intravenous 1 mg/kg dexazone according to the prednisolone scheme; diazolin, beriliton, glutargin, antipyretics, mildronate; intramuscular 3 ml human immunoglobulin against VEB in 2 days, no.5; acyclovir, viferon 500000 rectal candles. The condition of the child improved and on day 28 the girl was discharged from the department in the satisfactory state: skin and sclera were clear, liver on the middle clavicular line + 2cm, elastic, painless; spleen at the edge; light urine; colored feces, atypical mononuclear cells in the blood - 2 %.

Recommendations: «D» pediatrician diet No.5 and limited physical load for 1 year; berlition for 2 weeks; viferon according to the scheme; surveillance on the general health state and lab tests within 1, 3, 6, 9, 12 months.

List of questions for final control:

1.What is the definition of infectious mononucleosis?
2.What are the common patterns of the epidemiology of Epstein-Barr virus infection in children?
3.What are the links of epidemiological chain? Give the characteristic of the main stages of infectious mononucleosis clinical presentation?
4.What is the treatment and prevention of the disease in children?
5.What is the syndrome of infectious mononucleosis in children?

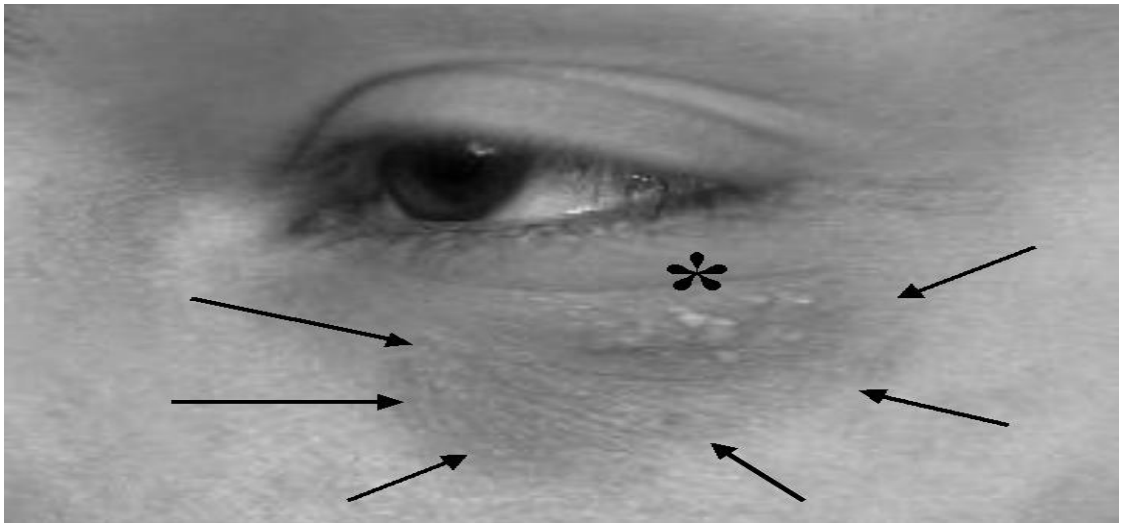

Fig.5. Vesicular exanthema.

SECTION 6.
PEDIATRIC ATYPICAL INFECTIONS

Currently, the urgency of the problem of atypical infections of childhood is a major concern for neonatologists, pediatricians and children's infectiologists. Data from domestic and foreign publications contain rather systematic information on TORCH-infection, namely, toxoplasmosis, rubella, cytomegalovirus infection, herpesvirus infection, but insufficient emphasis on clamidiosis, mycoplasmosis, and legionellosis both in children and their parents have been made. The WHO reports about 1 billion of infected people worldwide. Annually, 4 million newly registered patients with Chlamydia and 100 thousand neonates with manifestations of the disease are reported. The stillbirth and perinatal mortality is accounted for 15% and 35%, respectively. Publications report that mycoplasmosis is combined with other infections (chlamydial, viral, etc.) in 77,3% of cases. Legionellosis is generally called the disease of industrialization. Due to the fact that the diagnosis of atypical infections is made untimely, the latent and persistent progress, as well as the development of secondary immunodeficiency in children, is common.

Chlamydiae are a peculiar group of gram-negative microorganisms occupying an intermediate position between the virus and the bacterium, but closer to the latter. They are obligate intracellular parasites, do not independently synthesize ATP and depend on host cells. These microorganisms have a cellular wall containing DNA and RNA, but they do not have a nucleus, but a shell-free nucleotide. Multiply by binary fission. They are similar to the protozoa, because they have vegetative and reproductive forms. Toxins are not secreted, therefore adapted for use not only for the survival and development of epithelial cells but also for the cells of the immune system, in particular immature macrophages. This is an anthropozoonosis, because the source of the infection is a human being, cats, dogs, rats, rabbits, monkeys, some birds. The ways of infection are sexual, placental, contact, air-drop. The following varieties of the pathogen are distinguished: *Chl. pneumonia* is manifested in the form of pneumonia, bronchitis, Reiter's syndrome; *Chl. psittaci* causes ornithosis with lung, liver, spleen, myocardium, brain lesions; *Chl. trachomatis* is detected in eye lesions, urogenital and lymphotropic diseases.

The pathogenesis of chlamydiosis is based on destruction of the host's epithelial cells, the occurrence of hemodynamic disorders and the destruction of chlamydiae in phagolysosomes, at its best in spontaneous resolution, L-transformation and persistence. **Congenital chlamydial infection** is acute and persistent. Acute form is presented by meningoencephalitis, intrauterine pneumonia, respiratory distress syndrome, conjunctivitis, gastroenteropathy; in generalization: lethal outcome within the first hours after birth. The persistence of chlamydiae in neonates born to infected mothers is detected in 50-75% of cases, when the pathogen is isolated from the pharynx and vulva during the first year of life. **Neonatal conjunctivitis** is one of the most common forms of chlamydial infection. The incubation period ranges from 5-14 days; the duration of the disease is 3-4 weeks. Outbreaks of chlamydial hospital infection have been reported. Epidemic conjunctivitis occurs in the form of outbreaks in children aged 3-5 years. The progress is slow, unilateral; spontaneous resolution is possible. Uveitis has a recurrent nature with a tendency to chronicity and a rapid decrease in vision.

In the countries of the Middle East and North Africa a hyperendemic, primary-chronic **trachoma** occurs, manifested by the affection of the conjunctiva, cornea with frequent complications: blindness and scarring.

In neonates younger 6 months old **respiratory chlamydiosis** often develops along or after conjunctivitis. Ordinarily, no data on contact with a patient with acute respiratory viral infections are presented. Pneumonia, accompanied by obstruction of the bronchi is diagnosed more frequently. The first signs after an intranatal co ntraction can last from 5 days to several months. Late emergence of the disease is due to subclinical course and activation under the influence of various factors (stress, ARVI, secondary bacterial infection). Physicians detect a peculiar symptomatology: staged development, started from rhinitis, followed with dry pertussis-

like cough without reprises, accompanied by cyanosis. Auscultation reveals dry, disseminated rales with a zone of weakened breathing more often in the lower parts of both lungs. From the end of the second week, dry disseminated and fine- or medium moist rales with bronchial obstruction appear to be heard. X-ray pattern in the lungs reveals the phenomena of diffuse interstitial pneumonia. Without etiotropic treatment, chlamydiosis can last for many years.

Publications confirm the association of serologically verified chlamydial respiratory infections as a factor provoking the appearance of bronchial asthma. This is due to the fact that on the one hand, patients experience genetically determined hyperproduction of IgE and a number of cytokines that support allergic inflammation, and on the other hand, a low level of interferon-α and IL-5, facilitated by the persistence of the pathogen.

Ornithosis is assigned to respiratory chlamydiosis. The source is domestic birds, pigeons, ducks, parrots, etc. The transmission route is airborne respiratory droplets. Incubation period ranges from 7-15-30 days. Four variants of ornithosis are distinguished: influenza-like, pneumonia-like with signs of respiratory failure, typhoid with damage to the organs of the gastrointestinal tract, meningeal with the development of meningitis. The onset is more frequently sudden with prolonged fever for up to 2 weeks, followed by the events of tracheobronchitis with a dry cough. Maculopapular rach can appear with the development of hemorrhagic syndrome. Subsequently, the clinical symptomatology of the underlying syndrome is manifested. In timely treatment, the course of the illness ends within 1-1,5 months. Duration of humoral immunity is 2-3 years. **Reiter's disease** is defined as conjunctivitis in combination with urethritis and arthritis, which is more typical for adolescents and adults and is accounted for 1%.

Urogenital chlamydiosis is one of the serious problems of adolescent gynecology. Despite the low-asymptomatic course and prolonged inflammatory process, persistence results in scarring in the pelvic tissues. **Inguinal lymphogranulomatosis** is transmitted by sexual contact and is characterized by the appearance of ulcers at the place of chlamydia penetration, regional lymphadenitis with suppuration and scarring. Patients with the history of chlamydiosis may experience **nodular erythema** on the lower extremities. The long-lasting progress of chlamydiosis in a child leads to a secondary immunodeficiency, in particular, the T-cell link. Low level of IF-γ causes the persistence of the pathogen.

Discharge from the posterior wall of the pharynx, conjunctiva, vulva, urethra, as well as aspirate of tracheobronchial tree are subject to bacteriological study. Currently, ELISA and PCR methods are considered the reliable ones. At the acute stage, antibodies of IgM, IgA and IgG class appear, following the 5-7 days, 1 week and 2-3 weeks, respectively. Progression of the disease is characterized by high IgA rates, and reinfection is a spasmodic increase in IgG. Immunological examination is recommended.

Benign lymphogranulomatosis or **cat's scratch disease** is common in pediatric practice (is seen for differential diagnosis). The source is healthy cats-carriers, being contracted from the soil.

Bartonella henselae is the etiologic agent of the disease. The incubation period ranges 12 days (5-60 days). The localized stage has a rather simple clinical picture: dermal erythema, low-grade fever, enlarged regional lymph nodes. The most common atypical form is glandular-eye one. In generalization of the process follicular conjunctivitis develops; it can cause even serous meningitis.

Treatment of chlamydiosis includes complex therapy. The main means are macrolides (10 mg / kg azithromycin for 5-7 days, 50 mg / kg erythromycin for 10 days, 8 mg / kg roxithromycin for 14-21 days, etc.); tetracycline antibiotics are prescribed from the age of 8 years for 7-10 days at a dosage corresponding to the age. Fluoroquinolones are drugs of choice: ofloxacin, ciprofloxacin, flemoxin. Currently, chlamydial infection can be treated with intramuscular recombinant α_2-interferons in 10-15 000 IU / kg for 10 days, lipoferon rectally from the age of 3years at a diasage of 250 000 IU and inducers of interferons (6-10 mg / kg cycloferon for 10 days). It has been reported on the effectiveness of treatment with furazolidone at a dose of 8 mg / kg / day for 14 days. In conjunctivitis, 1% tetracycline or erythromycin

ophthalmic ointment is used. It is mandatory to make correction of dysbiosis and prescribe vitamin therapy, plant adaptogenes, antioxidants. In a chronic course, pulse therapy is used in 3 cycles of antibiotics for 10 days with a 10-day interval followed by the ELISA or PCR test. Outpatient surveillance with serological control in dynamics is carried out for 3 months.

Mycoplasma infection belongs to the *Mollicutes* class (no cell wall) and occupy an intermediate position between viruses, bacteria and protozoa. These gram-negative microorganisms are anthropozoonoses and have RNA and DNA. Researchers have discovered 80 types of mycoplasma, though pathogenic to humans are *M.pneumonia, M.hominus, M.genitalium, Ureaplasma urealificum*. Transmission routes are airborne respiratory droplets, domestic, sexual, transplacental. Characteristic seasonality is from October to February. The incidence increases in the first 3 months per 50% of children in the newly formed group. **Features of pathogenesis:** mycoplasma affects epithelial cells of the respiratory tracts, particularly involving alveoli, which leads to interstitial pneumonia. In severe cases, hematogenous dissemination with implantation in other organs and the development of the hepatitis, meningitis, and nephritis are possible**.**

Basic diagnostic criteria for mycoplasma respiratory infection:

1. Epidemic anamnesis, group morbidity, seasonality;
2. Acute onset with prolonged fever for 5-7days;
3. Characteristic lesion of all respiratory tracts, manifested by hyperemia of the mucous membrane of the oropharynx and its posterior wall, the presence of granular pharyngitis, laryngotracheitis, bronchitis, atypical pneumonia;
4. Dry cough with wheeze, transforming into productive coughing with mucopurulent sputum is typical;
5. The X-ray examination reveals the foci of pneumonia in the lower parts of the lungs;
6. Propensity to prolonged and chronic course;
7. In children of early age diarrhea is characteristic, and in schoolchildren, cramping abdominal pain, constipation is typical.

Newborns and premature neonates experience the most severe respiratory mycoplasmosis with a tendency to generalization of the process. **Signs of congenital mycoplasmosis** are respiratory distress syndrome, congenital pneumonia, sclerema, hemorrhagic syndrome, jaundice, meningoencephalitis after remission. About 15% of newborns have birth defects. In infants, minor catarrh events are noted, but prolonged a low-grade fever with hemorrhagic and hepatolial syndromes, anemia is typical.

The laboratory diagnosis is made based on the studies of the pharyngeal mucus, sputum, blood and liquor for bacteriological examination. Antibodies to mycoplasma are determined by ELISA and PCR. The study of paired sera in CFR and PHAT shows rise in titre of specific antibodies by 4 or more times (serological method). The immunological study shows the decline in activity of macrophages, C3 component of the complement, increase of IgM, decrease of IgA and IgG.

The drugs of choice for the treatment of various forms of mycoplasmosis are macrolides, namely, azithromycin, roxithromycin, clarithromycin, spiramycin in age-related dosage. For children over 8 years of age, doxycycline can be used. In case of damage to the nervous system tetraolean, benemitsin, levomitsetin are used. Detox therapy, anticonvulsants, antispasmodic, expectorants, aerosols with proteolytic enzymes, physiotherapy is recommended.

Follow-up outpatient surveillance is recommended up to 2 months.

In the era of industrialization such infectious disease as **legionellosis** occurs in 10% of the population of the developed countries. The novel highly contagious disease was first reported in 1976, which astonished the medical community and caused a high degree of alertness in the authorities of sanitary and epidemiological surveillance. Of the 440 participants of the convention of the American Legion, held in Philadelphia, 220 people were infected, 34 died. The disease was called “Legionnaires disease “. A year later, the bacterium *Legionella pneumophila* was isolated and identified from a pulmonary tissue of one of the deceased persons. The

serological and immunological examination of blood serum from previously infected people with similar illnesses in the United States and Spain has established their etiologic proximity. In 1982, the disease began to be called “legionellosis”. For the first time in our country a monograph on legionellosis was written by S.V. Prozorovsky, V.I. Pokrovsky, I.S. Tartakovsky (1984).

It is an acute bacterial sapronosis disease, affected the respiratory system, GIT, the central nervous system, kidneys with hyperthermia and intoxication syndrome. *Legionella pneumophila* is a gram-negative bacillus; secretes endotoxin and exotoxin. The *Legionellaceae* family consists of more than 40 species, among which 22 species include 35 serovars that are pathogenic to humans. It is persistent in the environment. It is found in stagnant water medium. Routes of transmission is water, inhalation. The main transmission factor is the water aerosol, formed during the operation of various systems of household, industrial, laboratory and medical purposes. The danger of being infected in everyday life is connected with the use of bath installations, room humidifiers, drinking tanks, faulty conditioners, underground and railway stations without adequate ventilation. *Legionella* can also be transmitted with dust that rises in the air during excavation and construction work. In some cases it is impossible to exclude infection when using infected drinking water. Currently, it is still the only disease among respiratory infections related to sapronoses and is transmitted by airborne respiratory droplets (from technical appliances: air conditioners, etc.). Continuous intra-hospital outbreaks with a permanent source of infection are characteristic. The incidence is usually low, but mortality among patients is high. The most common pathogen is *L. micdadei.* Typical manifestations: uni- and bilateral pneumonia with pleural effusion, cardiac and renal insufficiency. *Legionella* can be the cause of intra-hospital pneumonia among individuals with long-term intake of immunosuppressants and in patients with diabetes mellitus. Population susceptibility is 100%. Typical summer-autumn seasonality.

Specific pathogenesis involves the lesion of terminal bronchioles and alveoli, caused by the pathogen. Pulmonary infiltration consists of leukocytes, fibrin, alveolar cells; subsequently, it becomes necrotic that can be resulted in toxicoseptic shock and damage to other organs. Three forms of legionellosis are distinguished: pneumonic, Pontiac fever and Fort Bragg fever. Incubation period ranges from 2-10 days. **The respiratory form** has the following clinical picture: acute onset with febrile fever, dry cough and breast pain, transforming into productive cough with sanguineous sputum. The skin is pale, cyanosis of the nasopharyngeal triangle is noted, and the crackling fine moist rales are heard. Chest radiography shows patches in the lungs that are prone to consolidation. Commonly, unilateral pleurisy develops. Symptoms of cardiovascular and respiratory failure, dysfunction of the gastrointestinal tract, renal and central nervous system disorders, multiple organ insufficiency, DIC syndrome, and massive hemorrhages are noted. Once the disease resolved pneumosclerosis occurs in the lungs. Unfavorable prognosis can be cause by a massive dose of infection, its hypertoxicity and immune paralysis. **Pontiac fever** is caused by *Legionella pneumophila* , manifested by catarrh of the upper respiratory tract, with clinical signs similar to acute respiratory viral infection. Recovery occurs within 7-10 days. **Fort Bragg fever** is the acute disease with exanthema and catarrh of the respiratory tract. Polymorphic maculopapular rash appears on the skin of the abdomen, forearms, and the hips, accompanied by itching.

Basic diagnostic criteria for legionellosis:

1. Specific epidemic anamnesis: summer-autumn season, swimming in stagnant water, stay in rooms with air conditioning;
2. Catarrhal symptoms, unproductive cough with wheeze, intoxication syndrome, infiltrative changes in the lungs, pleurisy;
3. Ineffective antibiotic therapy with penicillins, cephalosporins;
4. Serological verification: 4-fold increase in antibodies in the studied paired sera, taken on day 6-7 of the disease with the interval of 15 days (IFA).

In the absence of adequate treatment of respiratory legionellosis, 20% of patients may have a fatal outcome.

Etiotropic therapy of legionellosis includes macrolides, fluoroquinolones. Particularly positive effect is noted after therapy with erythromycin phosphate at a dose of 20-40mg / kg for 14 days. Pathogenetic therapy includes infusion, anti-inflammatory, desensitizing agents. Hormonal therapy is ineffective. A course of immune correction, antioxidants, hepatoprotectors, probiotics and vitamins are recommended. Publications report that patients with the history of pneumonia, caused by legionellosis, develop life-long immunity.

Prevention and measures in the focus of infection. Outbreaks of acute pneumonia and respiratory diseases in the summer-autumn period are subject to thorough epidemiological analysis. The timely repair of faulty conditioners is crucial in the prophylaxis of the disease. Places of concentration of the pathogen are subject to disinfection by heat treatment of water (at a temperature of 80°C and more during the day). On industrial facilities, power plants and medical facilities, prophylactic cleaning and washing of the water system is carried out twice a year, and in the presence of legionella it is made quarterly with disinfection.

List of questions for final control:

1. What is the definition of chlamydiosis, legionellosis and mycoplasma infection?
2. What is the epidemiology of the infections in children?
3. What is the epidemiological chain and characteristics of the main links of the above infections?
4. What is the diagnosis, differential diagnosis and management of atypical infections in children?
5. What is the essence of the prevention of atypical infections in children?

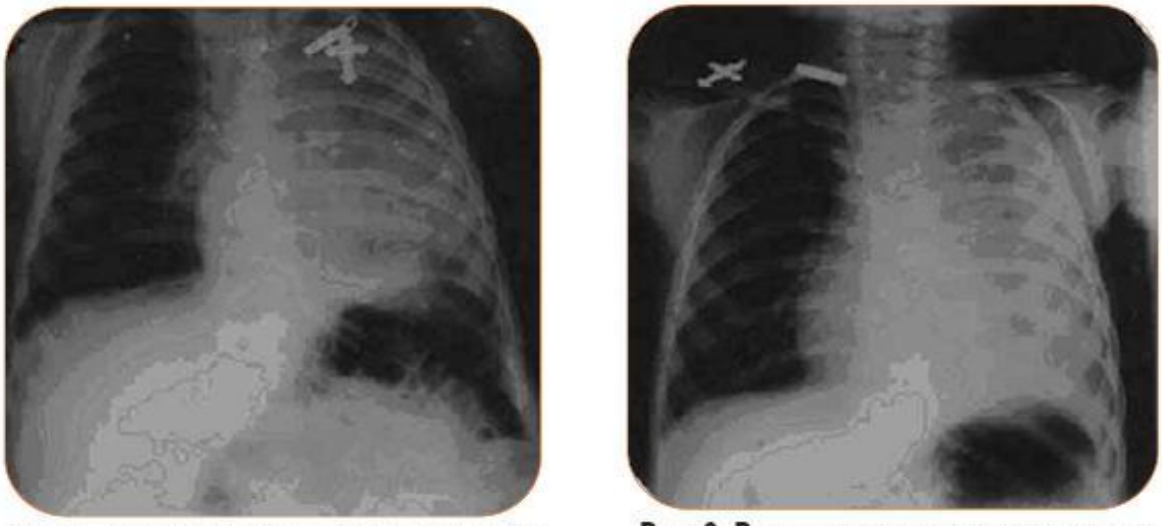

Рис. 1. Рентгенограмма легких ребенка при поступлении в стационар

Рис. 2. Рентгенограмма легких через 2 дня

FIG. 6. Hemophilic infection (AVAILABLE AT HTTP://WWW.HEALTH-UA.COM/PICS/TABL/186_37.JPG).

SECTION 7.
DIPHTHERIA IN CHILDREN

Diphtheria is an acute infectious disease caused by toxic strains of *Corynebacterium* and is characterized by an inflammatory process with the formation of the fibrinous membrane at the site of the pathogen intrusion, the events of general intoxication as a result of the exotoxin entering the blood, which causes severe complications by the type of infectious-toxic shock, myocarditis, polyneuritis and nephrosis. The causative agent is Loeffler *Corynebacterium diphtheriae*.

Epidemiology: the disease reservoir is the infected person, the bacteriological carrier of the toxigenic strain. The transmission route is airborne respiratory droplets, rarely contact-domestic (cutlery, food products). Susceptibility: contagiousness is 10-15%; occurs more often children aged 3-7 years. Immunity is short-term.

Pathogenesis

1. *The primary foci* are mucous membranes of the oropharynx, nose, larynx; less frequently eyes, genital organs, wounds, burns.
2. Multiplication of *Corynebacterium*, production of exotoxin and the action of antitoxin (recovery or formation of carriage) occurs.
3. Intracellular penetration of the toxin to the body occurs.
4. Fibrinous inflammation (necrosis, stasis, exudation), depending on the form of diphtheria occurs:
   a) diphtheritic (oropharynx, wound surface);
   b) croupous – (larynx, trachea).
5. Toxinemia (development of toxicosis) and lesions of the adrenal glands, kidneys, cardiovascular system, peripheral nerves, occurs.

Classification (according to localization)

Typical forms:

- Oropharyngeal diphtheria: local patchy, localized membranous, extended, toxic (Stage I, II, III), hypertoxic, hemorrhagic;
- Respiratory diphtheria: laryngeal diphtheria (localized croup); laryngeal and tracheal diphtheria (extended croup); laryngeal, tracheal and bronchial diphtheria (descending croup).
- Nasopharyngeal diphtheria (adenoiditis).
- Nasal diphtheria: localized membranous, extended.
- Eye diphtheria.
- Cutaneous diphtheria.
- Ear diphtheria.
- Genital diphtheria.
- Combined forms of diphtheria.

Atypical forms of diphtheria: subclinical; catarrhal oropharyngeal diphtheria.

Rare forms: diphtheria of the umbilical wound, lip, cheek.

Table 6

II. Classification of diphtheria according to severity of illness

1.Mild	Localized:	Patchy oropharyngeal diphtheria, diphtheria of the nose, eye, genitals, ear, skin.
2. Moderate	Localized: Extended:	Membranous oropharyngeal diphtheria, nasopharyngeal diphtheria, localized croup. oropharyngeal diphtheria, diphtheria of the nose, eye, ear, genitals.
3. Severe	Toxic and hypertoxic	Oropharyngeal diphtheria, diphtheria of the nose, eye, genitals, ear, skin. Extended and descending croup.

III. Forms of clinical course

Diphtheria with complications and without complications.

Complications

- early: at the end of the first-the beginning of the second week;
- late: at the end of the 3rd -7th weeks.

Early: nephrotic syndrome, myocarditis, peripheral paralysis of the cranial nerves.

Late: myocarditis, peripheral paralysis of the spinal nerves (polyradiculoneuritis).

IV. Bacterial carriage

1. Bacterial carriage of reconvalescents.
2. Transitory bacterial carriage (single-time production of *Corynebacterium diphtheriae*).
3. Short-term: up to 2 weeks.
4. Protracted: more than 1 month.
5. Chronic: more than 6 months.

Diagnostic criteria for oropharyngeal diphtheria

Localized: acute onset, unmarked intoxication, low grade fever, moderate sore throat in swallowing, moderate cyanotic hyperemia of the tonsils and oropharynx, without clear border, white-yellow, white-gray exudates, do not go beyond the tonsils in the form of isolated spots or coalesced, dense, adherent to surrounding tissues, bleed when removed or scraped, are tending to grow, regional lymph nodes moderately enlarged, not matted together, non-tender.

Extended: acute onset, moderate intoxication, fever of 39°C and higher, permanent moderate sore throat, cyanotic hyperemia of the mucous membrane of tonsils, oropharynx, swelling of the mucous membranes, exudates extend beyond the tonsils (pillars, posterior wall of the pharynx, uvula), regional lymph nodes are moderately enlarged, somewhat tender palpable.

Toxic: sudden onset, prominent intoxication, fever of 39-40°C, significantly enlarged lymph nodes, tender, diffuse hyperemia of the mucous membranes and edema of the nasopharynx, tonsils are coalesced, exudates extends beyond the tonsils (mucous membrane of the cheeks, hard palate), nasal tone in the voice, difficulty breathing (wheezing), swelling of the subcutaneous tissue.

Subtoxic: swelling of subcutaneous tissue over the regional lymph nodes: I degree - to the middle of the neck, II - to the collarbone, III - below the collarbone, foul odor.

Hypertoxic: sudden onset, highly severe intoxication (vomiting, seizures, loss of consciousness), hyperthermia>40°C predominate over changes in the oropharynx, fulminant development of infectious toxic shock, life expectancy unfavorable.

Hemorrhagic: along with the signs of toxic stage II-III diphtheria, exudates becomes hemorrhagic (4-5 days), hemorrhages at the sites of injection, bleeding from the mucous membranes, early evidence of myocarditis.

Diagnostic criteria of nasal diphtheria

Gradual onset, intoxication syndrome is minimal or absent, difficulty in nasal breathing, sanioserous discharges, followed by purulent serosanguineous ones, the appearance of excoriations at the entrance of the nose, rhinoscopy reveals erosions, ulcers, sanguineous crusts or dense, adherent white-grey membrane.

Respiratory diphtheria (true croup)

1. Localized diphtheritic croup (laryngeal diphtheria).
2. Extended diphtheritic croup:
   - laryngotracheitis,
   - laryngotracheobronchitis.

Diagnostic criteria of the respiratory diphtheria

Stage of croupous cough: 2-3 days: moderate intoxication, low-grade fever, dry, sometimes barking cough, loud, hoarse voice, gradual increase of clinical symptoms of laryngeal stenosis.

Stenotic stage: 2 hours - 2-3 days: moderate intoxication, aphonia, silent cough, stenotic breathing (shortness of breath, involvement of auxiliary muscles), hypoxia (cyanosis of the skin and mucous membranes, tachycardia), agitation.

Asphyctic stage: extremely severe condition, anemia, drowsiness, superficial and frequent breathing, reduced retraction of the intercostal spaces, pale gray skin, cyanosis, cold limbs, dilated pupils, no reaction to the surrounding environment, seizures, loss of consciousness, arrhythmia, hypotension, hypothermia, involuntary urination, defecation; death.

Laboratory verification: bacteriological: bacterioscopy of swabs from the oropharynx (on the border of the affected and healthy mucous membrane), nasopharyngeal and pharyngeal swab for culture; serological: AR, PHAT, ELISA.

In terms of differential diagnosis, consider false croup, which is much more common in the practice of the practitioner.

Acute stenosing laryngotracheitis (false croup) is a syndrome of a disease characterized by the airway obstruction, also known as croup.

Acute stenosing laryngotracheitis (ASLT) occurs only in childhood, mainly in children under 3 years of age, and then its incidence decreases from 3 to 6 years and from 7 to 14 years. In children under 6 months of age, this condition does not occur. Boys get sick three times more often than girls.

Etiology: the main cause of ASLT is: the viruses - 20%, the virus in combination with the bacterium - 45%, mycoplasma - 15%, chlamydia - 7%. Among the viruses, parainfluenza viruses are responsible for 45% of cases; other causes include the following viruses: influenza (18%), adenovirus (13,6%), respiratory syncytial virus (3%). In 2005, Human bocavirus was discovered, which causes ASLT in children aged 3 years and is associated with intestinal dysfunction (vomiting, diarrhea). The cause of acute stenosing laryngotracheitis is also pediatric infectious diseases: scarlet fever, pertussis and others. In children aged 3 to 7 years, ASLT can be also caused by a newly discovered metapneumovirus, which combines croup syndrome and inspiratory dyspnea in its clinical presentation.

Since epithelial tropism is characteristic to all viruses, 2 groups of viruses are distinguished:

1. with specific epithelial tropism (parainfluenza, influenza, rhinovirus, respiratory syncytial virus, bocavirus), which cause pathological process with the destruction of epithelial cells and cause gross morphological changes;
2. viruses for which epithelial cells are the primary foci of infection on the site of the entry (adenovirus, measles, rubella, herpes simplex virus).

Anatomical and physiological features of respiratory organs in children:

- small size of the larynx and soft cartilage, the plates converge at right angles;
- narrow, elongated epiglottis;
- vocal folds are short;
- lymphoid tissue is formed up to 6 months;
- presence of numerous glands in the mucous membrane of the upper respiratory tract;
- increased reflex excitability of the muscles closing the glottis;
- functional immaturity of the reflexogenic zones of the larynx.

Pathogenesis of croup syndrome involves:

1. edema of the mucous membrane of the larynx and trachea;
2. spasm of the larynx and trachea muscles;
3. hypersecretion of the glands of the airway mucosa.

Pathomorphological changes are manifested by hyperemia and swelling of the mucous membrane of the larynx and trachea, especially in the infraglottic cavity, the accumulation of pathological mass and its transformation into the crusts, especially in the hyposecretory form of the disease. During the microscopic examination of the mucosa, dystrophic changes in the epithelium, its desquamation, as well as necrotic-hemorrhagic and fibrinous-necrotic changes are detected, in case of secondary bacterial infection.

Main clinical manifestations:

- harsh barking cough;
- inspiratory stridor;
- hoarseness.

The clinical course of ASLT is staged. Compensated, subcompensated, decompensated and terminal (pre-asphyxia) stages are distinguished. The onset of the disease is sudden, at night, when stridor and dry high-pitched (barking) cough occurs. Overall agitation, restlessness, sleep disorder, loss of appetite occurs; but at the end of the night, the events of laryngeal stenosis disappear and appear again at night, lasting for several days in succession. However, occasionally, the events of laryngeal are growing at the daytime and laryngeal stenosis of I, II, III degree consistently appears. The occurrence of respiratory distress at night can be explained, perhaps, by the fact that due to the horizontal position of the child in the subglottic space, the swelling of the mucous membrane increases and accumulation of pathological mass in the larynx occurs, which contributes to laryngospasm.

Compensated stage is characterized by agitation, cry and sleep disorder. Stridor and inspiratory dyspnea is characteristic; inspiration is prolonged without the pause between inspiration and expiration in case of child's activity. At rest no inspiratory dyspnea occurs, though a marked increase in cardiac activity as a response to inspiratory dyspnea is noted. At this stage, the act of breathing is rearranging, providing the body with oxygen. Carbon dioxide irritation of the respiratory center is important.

Subcompensated stage is characterized by the growing respiratory distress, inspiratory dyspnea is observed at rest, and if the child is agitated, auxiliary muscles are involved in the act of respiration, which is manifested by the suprasternal, intercostal, and subcostal retractions. The events of heart failure are growing. Chest X-ray reveals enhancement of pulmonary pattern, indicating pulmonary circulation disorder.

Decompensated stage is characterized by the prominent respiratory distress. Sternal and *prelum abdominale* muscles are involved in the inspiration and, consequently, epigastric area is significantly retracted. The increased activity of the respiratory muscles contributes to the increased oxygen deficit, resulting in the development of deep acidosis and disorder of redox processes. Suboxidized metabolic products block enzyme systems, lading to worsening of oxygen disposal. Therefore, cyanosis of visible mucous membranes increases, the skin acquires a marble appearance, which is the ominous sign of circulatory collapse. Blood pressure abruptly declines, pulse becomes weak. On auscultation, respiration in the lungs is attenuated, sometimes even not audible that is caused by respiratory distress.

Terminal (pre-asphyxia) stage is characterized by superficial breathing of Cheyne-Stokes type, pliable areas of the chest and the epigastric area are not retracted, stridor is not audible. *Cough is not audible*. The heart tones are muffled, pulse is almost absent, blood pressure is not determined. Cyanosis is changing to sharp paleness, the patient is unconscious, the pupils are dilated, enophthalmia is observed, involuntary urination and defecation. Untimely medical care can lead to death due to impairment of tissue respiration, caused by hypercarbia, intoxication.

Clinical forms of false croup:

1. edematic form is characterized by growing severity, unproductive dry barking cough and hoarseness. Forced position of the body in children above 2 years of age is characteristic;
2. spasmodic form is characterized by stridor. During sleep, breathing is smooth, calm; loss of voice occurs upon wake up. Minor or no auscultatory changes;
3. hypersecretory form is characterized by the cough with viscous sputum, the state is worsening during sleep due to obturation that causes laryngospasm;
4. mixed form.

Croup severity assessment on clinical manifestations

1. Suprasternal retraction, signs of Type I respiratory failure, saturation is accounted for 90%;
2. Perioral cyanosis, respiratory rate is 25% higher the age norm, intercostal retraction, Type II respiratory failure, saturation is 90%-70%. The child requires emergency care.
3. acrocyanosis, sternal retraction, respiratory rate is 50% higher the age norm, saturation is lower 70%, Type III respiratory failure. The patient should be transferred to the intensive care unit;
4. asphyxia, total cyanosis, terminal state, arrhythmic respiration, jugular venous distention, respiratory rate is 70% higher the age norm, saturation is lower 50%.

Acute stenosing laryngotracheitis should be differentiated from **laryngeal diphtheria** (**true croup**), which is characterized by a slow onset, hoarseness, fibrinous membranes, growing respiratory distress; the events of toxicosis, cervical lymphadenitis and edema of tissues is observed. From the very beginning, a productive, but not a dry cough appears; it becomes dry after formation of the membranes. In laryngeal diphtheria aphonia is the hallmark. Finally, findings of bacteriological study are crucial.

Staging is characteristic feature of the progress of laryngeal diphtheria: catarrhal or dysphonic (croupy cough), stenotic (compensated, subcompensated and decompensated) and asphyxial. The initial stage lasts for 1-3 days, the beginning is slow, subfebrile therapy, cough is loud, hoarseness, laryngoscopy reveals swelling and hyperemia of the mucous membranes. The younger the child, the faster is the stenosis with aphonia and respiratory distress. Growing toxicosis, cyanosis, hypoxia. Laryngoscopy shows grayish membranes against the background of hyperemia of the larynx and vocal cords. This stage lasts for 2-3 days. The sub-compensated phase is characterized by persistent stenosis, shortness of breath, stridor at rest, respiratory insufficiency. Decompensated stenosis is characterized by a sudden agitation; pulse wave loss on the inspiration is observed. The asphyxial stage lasts for several minutes, the breathing becomes superficial, overall cyanosis, isolated breaths, bradycardia, respiratory arrest is observed.

Acute stenotic laryngotracheitis and diphtheritic croup should be **differentiated** from epiglottitis (edema and inflammation of the epiglottis), pneumonia, pediatric airway foreign body, allergic stenosis, laryngospasm in children with rachitis, spasmophilia. In this case, in addition to the anamnesis, dynamics of the disease, clinical and radiological studies, direct laryngoscopy and bronchoscopy are crucial.

The prognosis for ASLT and diphtheritic croup is serious with lethal outcomes in some cases, even if timely, comprehensive treatment is provided.

Treatment of ASLT

Therapy of acute stenotic laryngotracheitis is complex and dependent on the stage of the disease and its form. The treatment involves a pediatrician, otorhinolaryngologist, and resuscitation therapist. Children with stenotic laryngotracheitis should be **hospitalized** regardless of the clinical form and stage of the disease. During the first hours, warm drink, warm compresses around the neck, mustard plaster on the front surface of the neck and chest, warm

socks, filled with irritants (e.g, dry mustard) is imperative. These measures have a beneficial effect on the course of the disease and may even stop it at the beginning. In addition, cool mist administration is recommended, similar to acute catarrhal laryngitis.

Mixed form of false croup is most common. For **laryngeal stenosis of the first degree**, cool mist administration using the state-of-the-art "Nebulizer" ultrasound devices to inhale "Ventolin' (salbutamol with ambroxolum), "Relanza" (oseltamivir) for 5 days 2 times a day), hormonal therapy: hydrocortisone dosed at 3-5 mg per 1 kg body weight or prednisolone dosed at 1-2 mg per 1 kg body weight for 2-4 days, which can be discontinued without reducing the dose. Various decongestant mixtures in the form of aerosols, for example: 0.5% solution of 1ml ephedrine; 0.1% solution of 1ml adrenaline hydrochloride; 1% solution of 1ml dimedrol; 1 mg chymotrypsin in 1 ml; 1ml hydrocortisone (25 mg). 2 ml of the above mixture is administered for one inhalation 3 times a day. Other anti-inflammatory mixtures can be used. Antihistamines (Aerius®, edem, cetirizine, levocetirizine, fenistil, L-cet, etc.), multi-purpose drugs, sedative and vitamin therapy is recommended.

Laryngeal stenosis of the second degree requires the increase in the dosage of hydrocortisone from 5 to 10 mg / kg body weight, prednisolone up to 5 mg / kg for 5-7 days. The cool air in the ward is imperative for better activity of the ciliated epithelium. Currently, air humidifiers are widely used. Dehydration and detox therapy at a dose of 20 ml / kg, acritical mixtures to reduce the anxiety of the patient is advocated. Treatment should begin already on admission not to waste time. Prompt administration of spasmolytics to arrest swelling spread (2%No-Spa® 1-2 mg / kg, baralgin 0,2-0,4 ml / year of life) is imperative. In croup growing 30 mg / kg mucolvane in 0.9% sodium chloride is administered jet intravenously. The use of diazolin is contraindicated, since it increases hyperproduction of the mucous membrane.

Laryngeal stenosis of the third degree requires even more intensive anti-inflammatory, dehydration and infusion therapy. The dose of hormonal drugs is increased, for example, hydrocortisone from 10 to 25 mg per 1 kg, prednisolone up to 10 mg/kg; 2.4% solution of euphyllin at a dose of 0.1 ml/kg body weight for children under one year of age, and then 1 ml per each year of life. To reduce metabolic acidosis, 4% solution of sodium bicarbonate is administered at a dose of 4-5 mg/kg body weight intravenously. Symptomatic therapy is indicated. In the presence of hyperthermia, antipyretic drugs and cooling the child by applying cold to the projection of major vessels is recommended. In most cases, such intensive therapy gives a positive result within 2-4 hours. For agitated children intramuscular 0,5 ml aminazine or 1 ml droperidol are recommended for children from 6 months to 1 year of age; from 1 to 4 years of age intramuscular 1.0 ml aminazine or 2 ml droperidol; ½ tab of glycine sublingually 3 times a day can be used for older children. It should be remembered about biological role of calcium, which is the basis of osseous tissue, stimulator of nerve impulses, universal regulator of muscle contraction, an important component of coagulation system. Hypocalcemic state is noted in the genesis of laryngospasm in the viral ASLT. Reduce in calcium concentration in blood plasma is associated with the severity of the condition in spasmodic forms (Ca^{2+} is normally 2.25 mmol/L). Therefore, it is rational to use tablets of calcium gluconate dosed at 1 g per year of life 3-4 times a day.

The common treatment approach includes broad-spectrum antibiotics **on indications**. The "SMART" program recommends Flemoxin, Flemoclav Solutab® (for immunocompromised children), Josamycin, Sumamed®, Augmentin, Cefodox, Cefutil (from the prodrugs class) to start with in acute respiratory disease. In atypical pathogens Wilprafen® solutab is recommended. Combination with immunoprobiotics is mandatory, particularly in this case Fluvir® from 2 weeks to 2 months is warranted.

In case of viral etiology of the disease, Imustat, Arbidol is recommended in influenza or parainfluenza; "Amizonchik" in syrup, Amixin IC in ARI (from 2 years of age), 70-100 mg/kg

Novirin from 1 year of age; 50 mg/kg Groprinosin® up to 4 times a day from the first months of life, if necessary. Proteflazidum® and Immunoflazidum® that combines efficacy and safety and is produced in a convenient form (drops) is also recommended. The novel antiviral medication Erebra (Hiporhamin), an extract from the leaves of sea-buckthorn, showed high efficacy and safety in the treatment of children from 3 years of age and has a convenient form (sublingual tablets) with a pleasant taste that a child takes for a candy that facilitates the stage of drug administration.

In worsening of the overall condition, tracheobronchial toilet is conducted by direct laryngoscopy by inserting into the trachea proteolytic enzymes, hormonal medications, low concentration of antibiotics with their subsequent suction together with pathological mass of the trachea and bronchi. In the dry form of stenotic laryngotracheitis with obstructive crusts, this gives very positive effects. In case of ineffectiveness of the above intensive therapy, intubation is performed using general anesthesia for 3-4 days in children under the age of 3 years, for 5-8 days in children of school age. If the signs of **edema** are the forefront of clinical symptomatology, then the emphasis is placed on hormone therapy in age-related dosages as indicated above; in **spasmodic form** sedatives are beneficial; in **hypersecretory form** mucolytics (intravenous Mucolvan, Fluditec in syrup from 1 month of age, ACC, Prospan®, Ambroxol, Lasolvan®).

Table 7

Differential diagnostic criteria for diseases with croup-like symptoms

Symptoms	Parainfluenza	Respiratory diphtheria	Chicken pox	Measles
Onset	Acute, less frequently sudden	Gradual,sequential change of periods	Acute	Acute
Hallmarks	Catarrh of upper respiratory tracts, laryngitis	Barking cough, shortness of breath, respiratory failure	Exanthema	Catarrh of upper respiratory tracts, conjunctivitis, rush
Appearance	Unmarked	Unmarked, skin paleness, cyanosis in 3rd degree stenosis	Polymophous skin rush	Swollen; hyperemia of face, conjunctivitis, exanthema from day 3-5
Catarrh manifestation	Prominent, coryza,cough	Absent	Absent	Prominent
Lethargy, adynamia	Mild	Prominent	Absent	Absent
Coryza	Moderate or prominent	Absent	Absent	Prominent
Cough	Dry, harsh	Barking, followed by soundless	Less common	Dry, productive
Voice	Hoarse	Hoarse, followed by aphonia	Without changes	Could be hoarse
Oropharyngeal lesions	Moderate hyperemia	No	No	Moderate hyperemia, enanthema
Lymphadenitis	No	Regional	No	Often multiple
Patho-morphological sign of croup	Subglottic edema	Laryngeal obstruction by membranes	Subglottic edema	Subglottic edema

If diphterria was confirmed by the findings of differential diagnosis and laboratory studies then treatment is provided accoeding to the protocol.

Treatment (protocol)

Table 8

***Basic therapy* with antidiphtheritic serum (ADS) according to Bezredko (in 1000 IU)**

Clinical form	Initial dose	Booster dose	Cumulative dose (per course)
Patchy oropharyngeal diphtheria	10	—	10
Membranous	20-30	10	30-40
Extended	40-50	20	60-70
Toxic I	60-70	40	100-120
Toxic II degree	80-100	50	130-180
Toxic III degree	100-120	70-80	200-250
Hypertoxic	120-130	80	250
Localized nasopharyngeal diphtheria	20-30	10	30-40
Laryngeal diphtheria			
Localized croup	30-40	—	30-40
Extended croup	40-50	20-30	60-80
Localized forms of nasal, eye, cutaneous diphtheria	15-20	—	15-20
Genital diphtheria	20-30	10	30-40
Toxic forms of nasal, eye, cutaneous, genital diphtheria)	50-80	40	90-120

In toxic and hypertoxic forms, 1 dose of ADS is administered drip-feed together with corticosteroids (30-50 mg single dose similar to prednisolone regimen). In combined forms, the amount of ADS is added. For children in the first two years of life, the dose of ADS is half reduced, compared with older children; under 8 years 2/3 of the dose is administered.

1. Intensification. Antibiotics: erythromycin, rulid, penicillin, cephalosporins, lincomycin, (age doses) for 7-10-14 days.

2. Supportive therapy: desensitizes, vitamins B, C or ascorutin, irrigation of the oropharynx with disinfectant solution.

3. Syndromic therapy: detoxification, (5% glucose, 0.9% sodium chloride) cumulative dose 50-100 ml/ kg /day; 5-10 mg / kg hydrocortisone or 1,5-2,5 mg/kg prednisolone in toxic forms, protease inhibitors (10-20, 000 U contrycal, Gordox®), heparin 150-500 U/ kg (in hemorrhagic syndrome).

In infectious-toxic shock

- prompt administration of serum under prednisolone cover (30-50 mg single dose intravenously before serum administration);
- 10-20 mg/kg/day prednisolone or 20-75 mg/kg hydrocortisone (2-4 times a day, equally);
- infusion therapy with correction of acid-alkaline, water-electrolyte equilibrium;
- restoration of hemodynamics and renal function with dopamine, trental, corglicon.

In respiratory diphtheria, except for ADS:

- inhalation with decongestant mixture (2% $NaNCO_3$, hydrocortisone, mucolytic, euphyllinum);
- suction of membranes and mucus;
- moistured O_2;
- intubation in III degree stenosis;
- tracheotomy in extended croup, combined with toxic oropharyngeal diphtheria.

Management of complications according to the protocol.

Patients that are clinically healthy, with negative bacteriological test (twice 3 days after the completion of antibiotic therapy, at interval of 2 days) are **discharged** from the hospital on day 14-21 in mild and moderate forms and on day 30-60 in severe form. Surveillance by a pediatrician for 6 months.

Treatment of carriers: vitamin therapy, antibiotics: 30-50 mg/ kg/day erythromycin for 7 days. ultraviolet irradiation of the tonsils, immune modulators.

Prevention: hospitalization and sanation of patients and carriers, urgent notification of epidemiological center, quarantine at the sitr for 10 days (examination, swabs) and disinfection. *Specific* : DTaP vaccine from 2 months of age. Routinely administered at 2, 4, 6 months) at a doseage of 0.5 ml i/m; DTaP revaccination once a 1,5 years, following with DT - anatoxin at 6, 16, 26 years, then every 10 years**.**

List of questions for final control:

1. What is the epidemiologic and pathogenetic chain of diphtheria?
2. What is the common clinical presentation of diphtheria in children?
3. What are the clinical and laboratory characteristics of croup in scarlet fever, measles, acute respiratory viral infection, parainfluenza and other infectious diseases and in diphtheria?
4. What is the prevention of diphtheria in children?

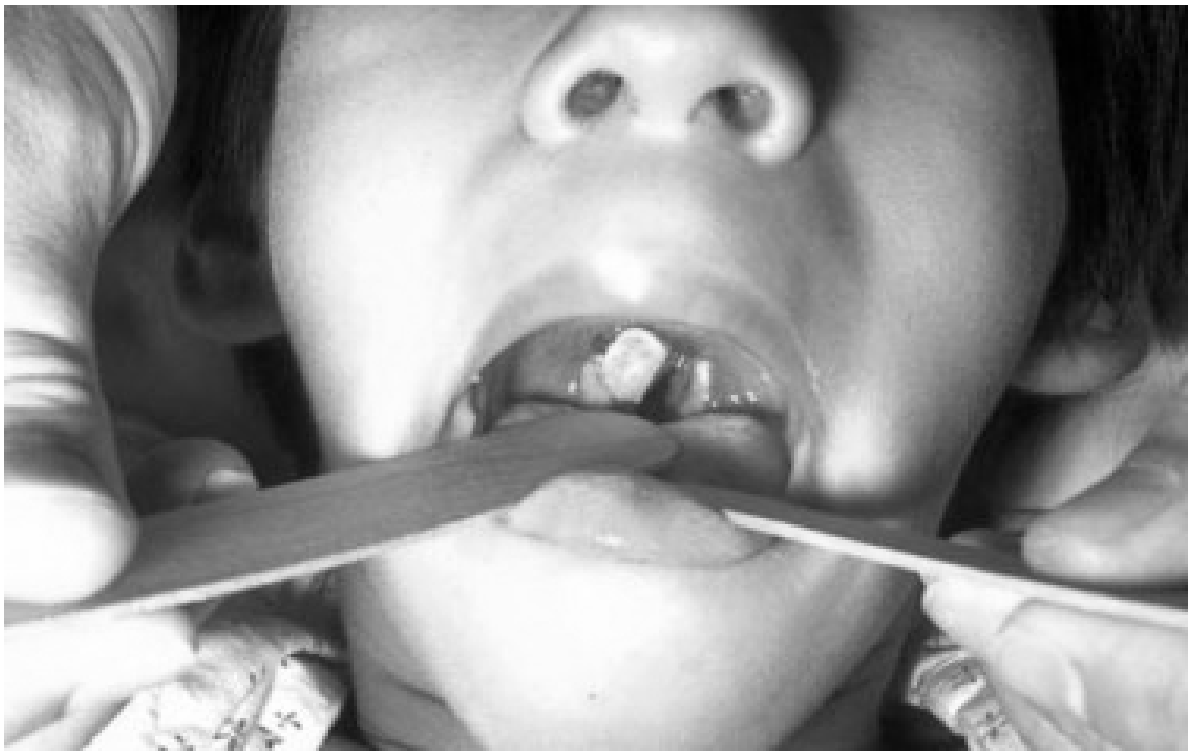

Fig. 7. Pharyngeal diphtheria.

SECTION 8.
WHOOPING COUGH

Whooping cough (pertussis) is an acute infectious disease caused by *Bordetella pertussis* bacteria and is characterized by paroxysmal cough with reprises and a possible respiratory arrest. Pertussis is the most severe in neonates and infants. Currently, the incidence of this disease has trended upward due to the lack of vaccinations among children on various factors**.**

Severity criteria:

- frequency of coughing and reprises;
- the nature of attacks of paroxysmal cough;
- apnea;
- vomiting after paroxysmal cough;
- specific and nonspecific complications;
- marked hematological alterations.

Clinical presentation of whooping cough in children

The pertussis incubation period ranges from 3 to 15 days on the average of 5-8 days. The course of the disease can be divided into three stages: catarrhal, paroxysmal, and convalescent phase.

The catarrhal (initial) phase is characterized by a moderate rise in body temperature: sometimes the temperature is subfebrile or even remains normal, high grade fever is less common. From the first days of the disease dry cough appears without specific features. Gradually, this symptom becomes more severe, becoming the major one in the clinical picture of the disease. Already at the end of the catarrhal period, the cough acquires the traits of paroxysmal cough with two characteristic features: it occurs mainly at night and ends with vomiting. Rhinorrhea is characteristic in the catarrhal phase. The overall sate of the patient is unmarked or worsens insignificantly; no loss of appetite is observed. This phase may last 3 to 14 days. The catarrhal period lasts 3-14 days. Sometimes, especially in infants, it is reduced to 5-7 days, and sometimes, on the contrary, may be prolonged.

The transition to the second, paroxysmal, phase occurs gradually. Typical attacks of spasmodic or convulsive coughing, which occur suddenly or after short precursors (aura): sore throat, chest compression, growing anxiety, are common. The attack consists of a series of short sequential coughs without a breath of exhalation. Then the patient makes a deep paroxysmal breath, which is accompanied by a whoop sound (reprise) due to spastic narrowing of the glottis. Subsequently, the attack continues in the form of the same cough impulses followed by whoops. During the cough attack there may be several reprises. The more severe form of the pertussis, the longer are the coughing attacks and the more reprises they are accompanied with. The cough attack ends with spitting of viscous clear sputum, sometimes vomiting. In severe cough, sanguineous sputum is characteristic. Posttussive vomiting is not an absolutely permanent symptom. The more severe form of the pertussis is, the more often it is observed. In the mild form of the pertussis, vomiting occurs less frequently or is absent at all.

During coughing attack, the patient has a very characteristic appearance: the face is becoming red or even cyanotic, the cervical veins swell, eyes engorge, lacrimation occurs, the tongue comes out, its tip bends upwards. During a severe attack, feces and urine may spontaneously excrete. Significant tension can lead to hemorrhages in the conjunctiva, nasal haemorrhage, and development of cerebrovascular accident. In severe coughing attacks, respiratory arrest can occur. Coughing attacks are caused by various external stimuli (examination of the pharynx, dressing and undressing, feeding, loud noise, child crying, etc.). Many clinicians have noted that coughing attack appear mainly at nighttime. At daytime, especially during outdoor walks, the child coughs much less often or does not cough at all.

Coughing paroxysm reaches its maximum at the end of the second week, and then gradually disappears. Frequent cough attacks accompanied by a circulatory disorder can resulted in swelling of the face and eyelids, skin and conjunctiva hemorrhages. Swelling can be observed not only on the face but also on the whole body (in severe cases), especially on the lower extremities. During the examination of the oral cavity, the sore is sometimes found on the frenulum of tongue, which is subsequently covered with a white coating in the form of the wart. The sore is a consequence of the mechanical friction of the frenulum on the sharp edges of the lower incisors. When pertussis cough fades, the sore gradually decreases and disappears. Even in the case of frequent coughing attacks in uncomplicated pertussis, the general condition of most patients does not deteriorate. Children with pertussis, in the intervals between coughing attacks, lead a routine life, play, have a good appetite. The body temperature, somewhat elevated in the catarrhal period, until the time of development of coughing attacks in most patients is reduced to normal, and only occasionally is subfebrile. Severe fever in the paroxysmal phase, ordinarily, indicates the presence of specific complication. Only in some patients, in uncomplicated pertussis, elevated temperature persists for a long time. Lung examination often reveals signs of emphysema, tympanic or dull sounds in percussion. Dry or moist rales are detected in auscultation. Radiographically, increased transparency of the pulmonary fields, low standing and flattening of the diaphragm, increased shadowing of both hili, enhancement of the reticular pulmonary pattern, the appearance of linear bands is noted. In the progress of the disease, mainly at the 5-7th week, intense bands emerge from the hilus and spread mostly down to the diaphragm. Sometimes these bands form a triangular figure with a peak near the spine with a diaphragm base. These X-ray alterations gradually disappear at the stage of illness resolution. From the side of cardiovascular system rapid pulse during coughing attack, rise of arterial and venous pressure is noted. Reduced capillary resistance, which causes hemorrhage in the skin and mucous membranes, is detected. In the severe form of pertussis, the heart is covered by emphysematic lungs or significantly enlarged due to the right ventricle. The second aortic tone (emphasis) sometimes is heard on the *a. pulmonalis*. From the side of the nervous system agitation of the patient, in severe cases - lethargy, adynamia, sleep disturbance, convulsive sprain of mimic muscle, dizziness is revealed. Blood tests show significant leukocytosis and lymphocytosis in most patients. The leukocytes count can reach 20-70 000 and more. The degree of leukocytosis depends on the severity of the disease. ERS is lowered or normal. These hematological changes are already observed in the catarrhal phase and disappear together with the elimination of the pertussis infectious process. In patients who have previously been vaccinated against pertussis, changes in the cellular composition of blood are observed less often, their severity is lower. The paroxyzmal phase lasts 2 to 8 weeks.

Gradually the frequency of coughing paroxysms decreases, their strength weakens, the disease transforms into the third phase. In the convalescence period, the cough becomes less paroxysmal and frequent. Sputum becomes mucopurulent. Gradually all symptoms of the disease disappear. This period lasts 2-4 weeks. Consequently, the total duration of the disease varies from 5 to 12 weeks. Sometimes the process persists for a longer period. At the convalescent phase , or even after the complete elimination of all symptoms of pertussis, resurrent of typical coughing sometimes occur (false relapses). They occur after the body is released from the *B pertussis* and is not accompanied by a typical blood response to the pertussis. These "relapses" occur in patients when they recover in the event of concomitant infectious disease (influenza, tonsillitis, measles, etc.). **Three basic forms of the pertussis are distinguished**: mild, moderate and severe. In the mild form, the frequency of attacks reaches 15 per day, the number of reprises is up to 5; attacks are typical, but short; vomiting is observed relatively rarely, the general health of the patient does not deteriorate. In the moderate form, the number of coughing attacks reaches 25 per day (each of them is sustained); the number of reprises is 5-10; posttussive vomiting is characteristic. General well-being is worsening, but moderately. In the severe form of pertussis, about 30-50 or more coughing attacks per day are observed; attacks are severe and sometimes last for up to 15 minutes, have more than 10 reprises and almost always end with vomiting;

Sleep disturbances, loss of appetite, lethargy, weight loss, prolonged fever is characteristic. Criteria for the severity of the pertussis by the number of attacks, suggested by N.F. Filatov, are rather conditional. Thus, in infants, even in the case of moderate frequency of short-term coughing attacks, the pertussis can be very severe. Recently, latent form of pertussis, characterized by the absence of typical coughing attacks with reprises and shortened clinical course has been observed more and more often. In these cases, tracheitis or tracheobronchitis is often diagnosed. Such forms are more commonly seen in the vaccinated children. Asymptomatic form of pertussis without clinical manifestations is also common, though cyclic immunological, sometimes hematological changes, radiological changes, blood filling of the lungs, changes in the system of capillaries occur. The study of cerebral hemodynamics in pertussis shows an increase in the peripheral resistance of the vessels of the brain, a decrease in systolic and diastolic velocity, increased pressure in the vessels, difficulty of venous outflow, slowing down of blood flow in the brain, which increases its hypoxia. Changes in cerebral hemodynamics in the moderate form of pertussis persist for 3-4 months, and in severe forms - up to 1 year. In children vaccinated against pertussis, mild and latent forms of the disease are common as compared to unvaccinated children; they have less pronounced hematological deviations, complications occur less often, the course and prognosis of the disease are more favorable.

Specific features of pertussis in children of the first year of life

Pertussis in infants is specific. Incubation period is reduced to 3-5 days, and catarrhal phase is reduced to 2-6 days; sometimes the disease progresses without the catarrhal phase, and paroxysmal cough appears from the first days of the illness. Coughing attacks in most infants are not accompanied by reprises. Vomiting, hemorrhagic symptoms and edema is less common than in older children. Coughing attacks often lead to apnoea. Gas exchange disorder is more pronounced than in older children; it is more frequent with more pronounced cyanosis. Infants and toddlers are especially sensitive to oxygen deficiency: hypoxia aggravates the course of the disease, promotes the development of complications. Infants, compared to older children, experience dizziness, epileptiform fits, seizure of mimic muscles more frequently. Pertusiss is the most severe in children under 6 months of age. Due to newborn toothlessness the formation of a sore on the frenulum of tongue in children aged 6-8 months is very rare. The duration of the paroxysmal phase can increase to 2-3 months. Pertussis complicated with bronchitis, bronchopneumonia occur more often than in older children. Pneumonia in infants is characterized by early development, confluent nature, prolonged course and high mortality; they are the main cause of death from pertussis.

Features of the current clinical course of pertussis

In the past 20-30 years, the clinical picture of pertussis has undergone significant changes in comparison with the data of previous years. The number of mild and latent forms has increased. The frequency of complications and mortality was dramatically reduced. However, among children under the 1 year of age, especially before 6 months, who did not undergo or did not complete active immunization, the pertussis remained a serious illness and is often the cause of death. The "relief" of the clinical presentation of pertussis is primarily due to mass prophylactic vaccinations. Probably, changes in biological properties of the pathogen are significant. Recently, *Bordetella pertussis* serotype has changed: 1.2.3 circulating serotype onto less virulent 1.0.3serotype.

Diagnosing pertussis. The most important condition for effective control of the pertussis is its early diagnosis at the catarrhal stage, when the patient is most contagious. However, the diagnosing pertussis in the catarrhal period is difficult, especially in the case of atypical course of the disease and in children under 6 months of age. Diagnosing pertussis requires taking into account the characteristic features of the clinical course (cyclicity, paroxysmal cough with reprises, viscous sputum and posttussive vomiting, typical appearance of the patient, sore on the frenulum of the tongue, etc.). Typical hematological alterations (lymphocytic leukocytosis with lowered or normal ESR that can last up to 5 weeks from the onset of the disease), X-ray findings (the presence of "pertussis triangles" - segmental or polysegmental atelectasis in the lungs) are

crucial. The epidemiological history: contact with contracted individual with a typical pertussis or with a person who coughs for a long time (atypical pertussis) is of great importance. Bacteriological studies assist in the diagnosis of pertussis, especially at an early stage. To isolate *B pertussis*, material from the nasopharynx is collected with a sterile cotton swab with a curved end, so that the material can be removed from the walls of the pharynx and from under the tongue. After culturing, a bacterioscopy is carried out and the cultural and agglutinating properties of suspicious colonies with specific serums are analyzed. The microbiological method is of great value for the diagnosis of pertussis. It should be noted that in the case of treatment with antibiotics the ability to culture *B pertussis* is sharply reduced. For the purpose of accelerated diagnosis, an immunofluorescence method, a PCR method, by which the *B pertussis* can be detected directly in smears of mucus from the nasopharynx.

Management of pertussis in children

Adequate regimen and patient care is crucial in the treatment of patients with pertussis. Bed rest is recommended only in the presence of fever and complications. Children of the first year of life are subject to mandatory hospitalization. It is recommended that children with severe forms of pertussis be kept in a darkened, quiet room, as they may be less likely to be disturbed, as the effects of external stimuli may lead to serious paroxysms of cough with apnea. Fresh, cool, moist air is very beneficial for patients with pertussis. Prolonged stay of the patient in the fresh air improves ventilation of the lungs, oxygen exchange and, possibly, reflex effect on the central nervous system. Coughing attacks are becoming less and less severe. In summertime, the child should spend most of the day in the open air, and in the cold months of the year only for several hours a day. In wintertime, avoid the drafts during the outdoor walks. Outdoor stay of patients is only possible at the temperature of ambient air not lower than -10°C. It is important to avoid exposure to cold; in addition, take into account the individual tolerance of such walks. It is also necessary to ensure continuous thorough ventilation of the room in which the patient is. Much attention should be paid to educational work with older children: organization of their leisure time, activities, games, etc. Children being involved into the game cough less frequently. It is necessary to exclude emotional and physical stimuli that can provoke coughing attacks. Nutrition of patient with pertussis is carried out taking into account the possible vomiting after coughing attack, which seriously impedes the digestion. High-calorie, wholemeal, concentrated, semi-liquid foods rich in vitamins are recommend. Patients are to be fed in small portions after coughing attack. After feeding, the child should be protected from the effects of stimuli that provoke the development of coughing attacks (various diagnostic and therapeutic manipulations, examination of the pharynx, etc.). In the event of vomiting shortly after feeding, the latter should be repeated. With very frequent vomiting, parenteral fluid is required. Antibiotic therapy (erythromycin, ampicillin) is a specific (etiotropic) treatment of pertussis. Antibiotics are used as the primary drugs in suspected diagnosis of pertussis or to prevent its spread. The use of antibiotics in the paroxysmal phase have no effect on the course of the disease, but can help in release the child's body from the *B pertussis* and prevent the spread of infection in the environment. The first-line antibiotics are erythromycin at a dosage of 50 mg / kg body weight (no more than 2 g per day), alternative drugs: ampicillin at a dosage of 100 mg / kg body weight per day, co-trimoxazole at a dosage of 8 mg / kg body weight similar to trimethoprim or 40 mg / kg body weight per day similar to sulfamethoxazole. The course of antibiotic therapy of pertussis lasts for 14 days. The main task of treating severe forms of pertussis is to eliminate hypoxia, which develops as a result of a decrease in the flow of oxygen through the respiratory tract during coughing attacks. The primary task is to prevent new coughing attacks using the protective regime: avoid of all possible external emotional stimuli, if possible - intramuscular injections, physiomanipulations, no bright light, no loud sounds, constant ventilation of the wards; in heavy frequent coughing attacks the patient is placed in an oxygen tent. To prevent and alleviate coughing attacks, 2.5% solution of chlorpromazine is administered at a dosage of 1-2.5 g / kg body weight twice a day before daytime and night sleep. In children of the first year of life, preference is given to the titrated solution of chlorpromazine, which is prepared at the rate

of 1 ml of 2.5% chlorpromazine to 3 ml of 0.25% solution of novocaine. Calculation of the dose is similar to chlorpromazine. Children aged 2-7 years are administered with salbutamol at a dosage of 1-2 mg 2-3 times a day; children aged 8-14 years - 2 mg three times a day. Most analgesics are ineffective in pertussis. However, mucolytic drugs are used to improve bronchial tubes in pertussis. Aminofilin is more appropriate to be administered per os in the form of a mixture of potassium iodide with marked mucolytic effect. In the case of respiratory arrest (apnoea), it is necessary to restore the patency of airways as quickly as possible. The nose and mouth of the patient should be relieved from mucus and vomiting masses. Normal respiratory movements are restored by means of rhythmic hand presses on the chest, and respirators. For frequent and sustained apnoea, the child should be transferred to the intensive care unit, in the most severe cases - for artificial respiration. It has been proved that the frequency and duration of apnoeic attacks in pertussis can be reduced by the administration of glucocorticoid hormones, especially hydrocortisone at a dosage of 5-7 mg / kg body weight for 3-5 days. The dose of hormones is to be reduced gradually, because its rapid decrease can lead to the recovery of apnoea and increased coughing attacks. Antitussives of the central action: Tussuprex, Sinekod, Stottusin, Tusin-plus, Libexin are also used.

Prevention

In practice, the diagnosis of pertussis is ordinarily made already in paroxysmal phase, therefore, the isolation of the patient is delayed, which, of course, reduces its epidemiological efficacy. Consequently, the most important condition for the successful implementation of antiepidemic measures against pertussis is early diagnosis. The isolation of the patient at home is carried out in a separate room or behind the screen. Patients with severe and complicated forms of pertussis, especially children under the age of 2 years, sick children from families living in unfavorable living conditions, as well as from families with children up to 6 months of age not being exposed to pertussis are subject to hospitalization. The isolation of the patient lasts until the 25^{th} day from the onset of the illness. Appropriate regimen in the hospital is crucial. It is necessary to ventilate the room and disinfect nasal handkerchiefs, towels, dishes of the patient. Careful protection of patients from joining the concomitant infection, which is the cause of exacerbations and complications, is required. For children under 7 years of age who have been in contact with patients with no history of pertussis and have not been vaccinated against it, are imposed to a quarantine for up to 14 days from the time of isolation of the patient. If the patient was not isolated and communication with him lasted throughout the period of illness, quarantine is imposed until the end of the infectious period in the patient. As a result of low resistance, the causative agent quickly dies, so there is no need for complete final disinfection after the patient's isolation. Medical supervision should be provided in the foci of the infection. In case of suspicion of pertussis, a bacteriological examination is carried out. It is advisable to carry out chemoprophylaxis of the pertussis with erythromycin at a dosage of 50 mg / kg body weight per day for 10-14 days in contact unvaccinated children. To prevent pertussis erythromycin is indicated for:

- all patients in the first 3 weeks from the onset of the disease to reduce the intensity of the spread of the *B pertussis* in the environment;
- newborn babies born to mothers contracted of pertussis;
- children with chronic diseases of the broncho-pulmonary system or heart regardless of the vaccination history
- Pregnant women contracted of pertussis for 3 days before delivery and 10 days postpartum.

For the purpose of active immunization in Ukraine a whole-cell pertussis (wP) vaccine, a suspension of the first phase of pertussis microbes, neutralized by formalin or mertiolate (2, 4, 6 months of age) is predominantly used. This preparation is used in association with diphtheria and tetanus toxoids (tetanus, diphtheria, pertussis or absorbed DTwP vaccine). It is known that absorbed DTwP vaccine is the most reactogenic due to the whole-cell pertussis component. To eliminate this disadvantage a new generation vaccine with acellular pertussis component –

absorbed DTaP (diphtheria, tetanus and acellular pertussis vaccine) was created. Absorbed DTaP contains only three purified pertussis antigens (detoxified pertussis toxin, filamentous hemagglutin and outer membrane protein pertactin). Diphtheria and tetanus toxoids and components of the acellular pertussis vaccine are adsorbed onto aluminum salts. The vaccine is made in a physiological solution, as preservative, it contains 2-phenoxyethanol (in contrast to other absorbed DTwP, where mercury salts are used as preservatives). According to the National Immunization Schedule, in Ukraine, acellular pertussis vaccine is used for follow up vaccinations in children who have had post-vaccination complications on previous vaccination with absorbed DTwP, as well as for all vaccinations in children at high risk of post-vaccinal complications, especially those with a history of perinatal pathology of the central nervous system. Absorbed DTaP is also used in Ukraine for revaccination against pertussis in children aged 18 months.

List of questions for the final control:

1. What age is pertussis most frequently registered?
2. What is the pathogenesis of pertussis?
3. What diseases should pertussis be differentiated with?
4. What emergency care should be provided in apnoea?
5. What is the prevention of pertussis?

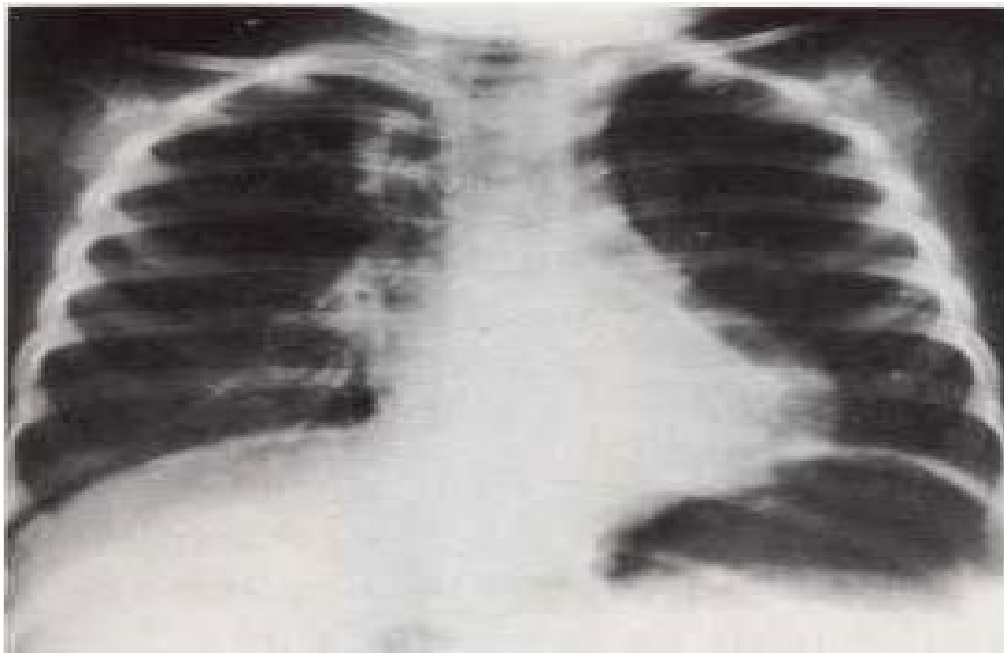

Fig. 8. Chest X-ray of patient with pertussis.

SECTION 9.
INFECTIOUS POLYNEUROPATHIES IN CHILDREN

The incidence of infectious polyneuropathies in comparison with other diseases is not high, however, it differs its severity of the course, frequency of disability (from 3 to 10%) and mortality (from 2 to 8%).

Polyneuropathy is often an undiagnosed and potentially curable disease with an average prevalence of approximately 0.5 cases per 100,000 children and 1-2 cases per 100,000 adults. They can be complications of common infectious diseases, and also occur as a primary affection of the nervous system.

Polyneuropathy is a polyetyological disease with a specific reaction and a multiple lesions of the peripheral nerve roots with marked pain syndrome, vegetative and motor disorders in the extremities and zones of the cranial nerves. Among the etiological factors of infectious polyneuropathy autoimmune processes are distinguished but the trigger mechanism is viruses and bacteria (Guillain–Barré syndrome).

Viral polyneuropathies are caused mainly by enteroviruses, herpesviruses, especially cytomegalovirus (CMV), Epstein-Barr virus (EBV), influenza viruses, adenovirus, HIV.

Bacterial polyneuropathy is provoked by *Campylobacter*, diphtheria, borreliosis, yersiniosis, botulism, leprosy, tetanus, etc.

It is appropriate to mention a number of structural and functional characteristics. The peripheral nervous system (PNS) is a part of the nervous system that consists of axons that form peripheral and cranial nerves, as well as *corpuses neuroni* located in the anterior and lateral horns of the spinal cord, motor and sensitive nuclei of the cranial nerves, spinal ganglions, and vegetative ganglions of the sympathetic and parasympathetic parts of the nervous system. In our opinion, it is worth mentioning 12 pairs of cranial nerves: I - Olfactory; II-Visual; III: Oculomotor; IV-Trochlear; V-Trigeminal; VI-Abducent; VII- Facial or Intermediate; VIII-Vestibulo-Cochlear; IX-Glossopharyngeal; X-Vagus; XI-Accessory; XII-Hypoglossal.

Under such structural features as myelin insulation, the fibers are divided into myelinated (thin and thick myelin membranes) and amyelinic ones. In amyelinic fibers, excitation is transmitted by so-called, wave-like path at a speed of about 2m/ sec. In myelinated fibers, the myelin insulation is interrupted through certain gaps called nodes of Ranvier, and the excitation transmission is speeded up (40-80 m/s) due to the salutatory conduction of nerve impulses, by jumping from one node to another. Pain sensitivity is also carried out by vegetative fibers. Myelinated cylinder has three layers: the upper - vegetative; medium-sensitive; internal - motor. Myelinated fibers with thick myelin insulation conduct proprioceptive, vibrational and complex types of sensitivity; motor fibers are also myelinated with thick myelin insulation. Myelinated fibers with a thin myelin insulation conduct superficial types of sensitivity (pain, temperature and tactile). Affected myelinated fibers provide the sensation of localized pain, and the affected amyelinic fibers provide the sensation of non-localized pain, respectively. Affection of peripheral nerves arises due to the development of Wallerian degeneration, axonal degeneration, segmental and primary affection of *corpuses neuroni*. Axonal degeneration (axonopathy) is a disorder of metabolic processes in the neuron and manifestations predominantly occur in the distal part of the axon. In segmental demyelination (myelinopathy), predominantly myelin and Schwann cells are damaged, which leads to the destruction of myelin and the nerve fiber's conduction blockade. The development of pathological changes in nerve cells, connective tissue interstitia, myelin insulations and axial cylinders is caused by numerous factors, including dystrophic, dysmetabolic, toxic, ischemic, immune and inflammatory ones.

Table 9

Classification of polyneuropathy

Type of polyneuropathy	Disease
Guillain–Barré syndrome	Acute inflammatory demyelinating polyneuropathy
Hereditary polyneuropathy	Hereditary motor-sensory polyneuropathies; hereditary polyneuropathy with susceptibility to pressor pareses
	Autosomal recessive hereditary polyneuropathies
Metabolic polyneuropathy	Diabetic polyneuropathy and polyneuropathy, associated with impaired glucose tolerance; uremic, hepatic and acromegalic polyneuropathy; hypothyroid polyneuropathy
Paraneoplastic polyneuropathy	Polyneuropathy associated with lymphoma or cancer
Polyneuropathy associated with monoclonal gammopathy	Polyneuropathy associated with osteosclerotic myeloma, monoclonal gammopathies and Waldenström's macroglobulinemia
Infectious polyneuropathies (major)	AIDS, influenza, enteroviruses, cytomegalovirus, herpesviruses
	Leprosy
	Borreliosis (including Lyme disease)
	diphtheria, botulism, tetanus
Polyneuropathies, associated with systemic inflammatory and immune diseases	Sarcoidosis; amyloidosis; vasculitis, including nodular periarthritis, Churg-Strauss syndrome, rheumatoid arthritis, Sjogren's syndrome, Wegener's granulomatosis, systemic lupus erythematosus, systemic sclerosis, giant cell arteritis, Behçet syndrome, cryoglobulinemia, Castleman disease
	Nonsystemic vasculitic polyneuropathy
Toxic polyneuropathies	Alcohol, industrial agents (e.g., acrylamide), metals (e.g., lead), medications (e.g., platinum-based drugs, amiodarone, perhexylin, tacrolim, chloroquine and suramine)
Nutritional polyneuropathy	Vitamine B_1, B_6, B_{12} or E deficiency
Critical illness polyneuropathy	Polyneuropathy associated with sepsis, multiple organ failure or prolonged intubation

Features of the pathogenesis of infectious polyneuropathies

In **bacterial** infections, exo- and endotoxins have a significant influence on the peripheral nervous system. Bacterial toxins, especially neurotoxins (botulism, tetanus), block the neuromuscular transmission, synapses of vegetative ganglia and penetrate into the central nervous system, leading to its disorder. The causative agent may be in the vessels of the perineurium and epineurium, in the structures of the spinal cord and the brain.

In **viral** infections, the occurence of polyneuropathies is associated with changes in the nervous and immune systems. Neuronal edema, vascular disorders, infiltration of the nerves by lymphocytes, accumulation of complement components on the membranes of the Schwann cells, accumulation of circulating antiganglioside and antiglycolipid antibodies on the peripheral nerves myelin insulations, leading to demyelination and axonal destruction, is characteristic. The immunological study reveals a dramatic increase in the concentration of IgM and IgA, hemolytic complement activity, the number of beta cells and circulating immune complexes.

According to ICD-10 the following forms of Guillain–Barré syndrome are distinguished:

1. acute inflammatory demyelinating polyneuropathy;
2. acute motor axonal neuropathy;
3. acute motor-sensory axonal neuropathy;
4. Miller Fischer syndrome.

4 variants of the neuropathies' clinical course are distinguished:

- acute (clinical progress for 1 week);
- subacute (duration of symptoms for 40-60 days);
- chronic (the diseases lasts more than 60 days);
- recurrent (repeated exacerbations for many years).

3 stages are distinguished in the development of the disease:

1. augmentation of paresis, paralysis and pain syndrome (3 to 25 days);
2. stabilization (1-2 weeks);
3. stage of reverse development of symptoms (1 month to 2-3 years).

Clinical presentation:

Common symptoms of infectious polyneuropathies:

- absence of intoxication;
- affection of the peripheral nervous system;
- motor disorders (**acute flaccid symmetrical distal paralysis**, muscular hypotension, tendon reflexes decrease)
- paresis of the III, IV, VI pairs of cranial nerves, les frequently, affection of the optic nerve;
- sensory disorder (pain along the nerve trunks path, paresthesia, hyperesthesia of socks/gloves-type);
- vegetative lesions (cold limbs, cyanosis, dry skin, hyperhidrosis);
- age of patients is 3 years and more;
- absence of pelvic disorders.

In 80% of cases **acute inflammatory demyelinating polyneuropathy** is common, which occurs mainly with proximal paresis, sensory disorder, affection of the cranial nerves, with possible paresis of respiratory muscles. In 15% of cases, **acute motor axonal polyneuropathy** occurs with characteristic more significant decrease in the speed of the pulse conduction on the nerve, without the involvement of cranial nerves. The **Miller Fisher syndrome** is associated with *Campylobacter jejuni*, which is characterized by damage to the oculomotor muscles, ptosis, cerebellar ataxia, orrexilation in the limbs.

Poliomyelitis is one of the polyneuropathy-related diseases. Poliomyelitis is an acute enterovirus anthroponotic infection, characterized by affection of the nervous system with the development of flaccid paralysis and paresis, inflammatory changes in the mucous membrane of the nasopharynx and intestines. Etiology: the pathogen - *Poliovirus* from the family of *Picornaviridae*, contains RNA, has a spherical shape. For polyoviruses, the special tropism to the motor neurons of the gray matter of the spinal cord is characteristic. Poliomyelitis is anthroponotic intestinal disease. The source of the infection is a sick person or the virus carrier. The main reservoir of wild (non-vaccine) strains of poliomyelitis viruses is the intestine of young children. The mechanism of transmission of infection is fecal-oral, which is implemented alimentary, but the airborne mechanism of transmission is also possible. The susceptibility to the virus is low. Paralytic form of the disease develops only in 0,2-1% of contracted individuals. The paralytic form **has 4 stages**: 1 stage - preparalytic, 2 stage - paralytic, 3 stage - convalescent, 4 stage – residual-paralysis (sequelae).

Asymptomatic form is virus carriage without clinical manifestations, which is diagnosed only on the basis of findings. After this form a stable immunity is developed.

The abortive form lasts 7-10 days. It begins with a sudden increase in temperature to 38.5-39.5°C, loss of appetite, general malaise, headache. Possible pain in the throat, hyperemia

of the mucous membrane of the oropharynx is characteristic. Possible symptoms of dyspepsia: nausea, vomiting. Neurological symptoms are absent. Resolves in recovery.

Meningeal form in the first 2-5 days does not differ from the abortive one. Subsequently, the temperature decreases to normal, and only the 1st phase has ended ("minor illness").

Within 1-3 days, and sometimes without an interval, the 2nd phase begins ("major illness"). Sudden headache, nausea, vomiting, which does not bring relief, occurs with the development of meningeal symptoms. Pain in the back and extremities, skin hyperesthesia, pain along the nerve stem path is characteristic.

The patient acquires a forced position, or a tripod sign (inability to sit without pushing his hands behind the buttocks, knee kissing sign (inability to touch the bent knee with lips).

Some patients experience simultaneous muscular weakness, but it does not reach the level of paralysis. During spinal puncture, which improves the patient's condition, it is possible to obtain a transparent fluid that leaks under pressure and has pleiocytosis of lymphocytic nature.

The course of this form is benign. Clinical recovery with cerebrospinal fluid rejuvenation occurs in most patients on 2-4 weeks, but asthenic syndrome can be preserved for a few more days.

Spinal polio develops as a result of damage to motor neurons in the anterior horns of the spinal cord.

The development of all paralytic forms is preceded by a preparalytic stage, which resembles a "minor disease". Decrease in temperature within 2-4 days, a period of fictitious well-being is observed in children. Paralysis arises suddenly and is formed very quickly, mainly in the proximal parts of the limbs, often in the lower ones.

Flaccide paralyses with low myotonus, hypo - and areflexia are asymmetric, mosaic, with atrophy of the muscles of some groups and spasm of the antagonists muscles leads to the formation of functional, and, subsequently, organic contractures.

Spinal forms with lesions of the intercostal muscles and the diaphragm are the most severe, accompanied by the development of respiratory failure and conjoint with secondary infection. If the cervical spine is affected, the patient is unable to keep the head upright.

The duration of the paralytic period is 1-2 weeks, followed by the recovery period. Muscles that were damaged earlier are restored first and more rapid. The maximum recovery lasts for 2 weeks. Low myotonus, areflexia, atony is prolonged. The affected extremity shortens from interference with growth, the ligamentous joint of the joints loses its tonus, articular cartilages is atrophied, which contributes to partial dislocation. The recovery stage actively lasts for 3-6 months, then slows down and lasts for 1-1.5 years.

At the residual-paralysis stage, kyphosis, lordosis, scoliosis, hernia of the abdominal wall, "horse" foot, residual flaccide paralyses, retardation of extremities in growth, sometimes deformation of extremities is characteristic.

Bulbar polio is the most severe. On the background of the clinical presentation of "minor" disease neurological symptoms occur: horizontal nystagmus, damage to the nuclei of IX-X pairs of cranial nerves, accompanied by disturbances of swallowing, phonation, voice becomes deaf, dysarthria, expiratory dyspnea, cyanosis. The condition is further aggravated when the respiratory and vascular-motor center is affected.

Pontile polio is characterized by lesion of the nucleus of the facial nerve. Complete or partial paresis or paralysis of mimic muscles up to amimia occurs.

The clinical picture is accompanied by the smoothness of the nasolabial fold, incomplete closure of the eye, and enlargement of the palpebral fissure on the affected side, with the displacement of the corner of the mouth in a healthy direction. Unlike neuritis of the facial nerve, no pain occurs, though tenderness is preserved.

Poliomyelitis in vaccinated children is characterized by mild progression. Often without prodromal period or it is not significantly expressed. The incidence of vaccine-associated cases of acute paralytic poliomyelitis is 3 cases per 10,000,000 doses of vaccines during the period of mass vaccination with the live Sebin vaccine.

Diagnostics:

- ✓ Virological study of feces (2 samples are taken, then stored in a refrigerator at low temperatures within 72 hours, re-take within 48 hours).
- ✓ Virological study of nasopharyngeal swabs (in the first 7-10 days).
- ✓ Study of liquor.
- ✓ Serological study (CFR, PHAT, ELISA).

Diphtheria is another illness, which can cause polyneuropathy. Its urgency was caused by the refusal of parents from vaccine prophylaxis of children.

Early diphtheria polyneuropathy occurs 3-4 weeks after the onset of the disease.

Clinically, paresis of the soft palate, reduce of the pharyngeal reflex at the 3-4 week, paresis of accommodation at the 4-5 week, paresis of oculomotor nerves at the 6-7 week, paresis of muscles of the pharynx, larynx, dysphagia at the 5-7 week, less commonly affection of the cranial nerves is observed.

Late diphtheritic polyneuropathy is observed at 6-12 weeks, more frequently on day 50 from the onset of the disease. In the history we mark the focus of diphtheria, and the clinical presentation will be: symmetrical motor disorders (paresis and paralysis), disorders of deep sensitivity of the ascending type. Heart rhythm disorder (affection of the X pair of cranial nerves), respiratory muscle weakness, bulbar disorders.

In toxic diphtheria, neurological disorders from the first days of the illness are characteristic. As a result, the patient can acquire nasal voice, choke on eating. At examination, the decrease or disappearance of mobility of soft palate, visual impairmentы due to accommodation paralysis, strabismus, ptosis is revealed. Later (at 4-5 weeks) polyradiculoneuritis (peripheral flaccid paralyses) occur. Their early sign is the reduction of tendon reflexes (primarily on the lower extremities), and sometimes their complete disappearance. Paralysis of muscles of the neck and trunk, in particular swallowing, intercostal muscles and diaphragm, may develop. Often, flaccid paralyses of the extremities are detected in the expansion of the motor regimen - the inability to walk, lurch, the weakness in the hands and feet due to partial atrophy of the muscles. Changes in the nervous system can lead to temporary disability and invalidization, the recovery process is slow.

Diagnostics:

1. Bacterioscopy of the secretion of the oropharynx and the nasal passages for isolation of *Corynebacterium diphtheriae* or similar.
2. Bacteriological diagnostics of mucus from the oropharynx, nose and other sites of affection to isolate the *Corynebacterium diphtheriae* and define its toxigenic properties.
3. Blood PHAT with diphtheria diagnosticum: an increase in the titre of anti-toxic antibodies in blood serum in the progress of the disease.
4. Indirect hemagglutination test with commercial diphtheria antigen: detection of diphtheria toxin in blood serum.
5. Blood PHAT with erythrocytic diagnosticum before administration of antidiphtheric serum to determine the level of diphtheria toxin in blood serum.

Studies to diagnose the complications:

1. Coagulogram: hypercoagulation or coagulopathy.
2. Urinalysis: possible proteinuria, cylinduria, microhematuria, increased specific gravity.
3. Renal tests: elevated residual nitrogen, urea, creatinine.
4. ECG: study in dynamics.
5. Examination made by otolaryngologist, cardiologist and neurologist in dynamics.
6. Direct and indirect laryngoscopy in laryngeal diphtheria.
7. Rhinoscopy.

The diagnosis is confirmed by detection of *Bacillus diphtheriae* in the pharyngeal or nasal smears.

Botulinum polyneuropathies commonly occur**.** The causative agent of botulism is C*lostridia*. Soil is a common habitat for *Clostridium botulinum*. In favorable conditions, spores sprout and secrete a toxin, which is the strongest neurotropic poison. The main routes of transmission are food and wound. Infants can be infected in the case of the use of milk mixtures, honey contaminated by botulism spores.

Peculiarities of **pathogenesis**: *Clostridia* enter through the mouth to the small intestine, where enzymes enhance the action of the toxin that has an effect on the cholinergic synapses of the vegetative nervous system, blocks the secretion of acetylcholine, suppresses the medulla and motor neurons, causes denervation of muscles with the development of all types of hypoxia.

Clinical presentation: primarily, gastrointestinal syndrome occurs due to the action of a toxin, no fever, vomiting without dehydration, dry sputum, single-time liquid stool, development of intestinal paresis and constipation. Within 1-2 days, neurological symptoms conjoin:

1. ophthalmoplegic syndrome (sensation of send in sight, visual impairment, mydriasis, nystagmus, anisocoria);
2. bulbar syndrome (swallowing disturbances, dysphagia, hoarse voice, choke on food);
3. paralytic syndrome (paresis and paralysis of the muscles, inability to walk, eat, keep the head straight).

The clinical course develops rapidly, the diaphragm paresis arises early. Particular attention is paid to neonatal and infant botulism, which can be the cause of sleep-related sudden infant death syndrome.

Diagnosis: detection of botulinum toxin by biological method using neutralization reaction. The material for study is blood, urine, stomach contents, feces, food product.

The peculiarity of the clinical course of the neuropathy in **campilobacteriosis** is marked motor disturbances and distal weakness. The development of paralyses occurs within 3-10 days after the infectious gastroenterocolitis.

Enteroviral polyneuropathies have a subacute clinical course with symmetrical flaccid pareses with motor-sensory disorders.

Herpetic neuropathies are severe with the clinical presentation of encephalomyelopolyradiculoneuropathy, affection of the cranial nerves, neuralgia and myalgia.

Umbilicus or wound aseptic care can result in severe infectious disease, **tetanus**. The causative agent of this disease is *Clostridium tetani*, which produce two toxins - tetanospasmin and tetanolysin. Tetanospasmin affects the motor centers of the spinal cord, medulla, reticular formation, causes a steady tonic contraction of the masticatory muscles (trismus) and occiput, back (opisthotonus). During the fit, spasm of the diaphragm, larynx may occur, which may lead to asphyxiation and paralysis of the heart. The consciousness in the tetanus remains completely clear.

Infectious polyneuropathies can occur in measles, rubella and mumps.

In the spring-summer period **Lyme disease (neuroborreliosis)** commonly occurs. The causative agent is *Borrelia burgdorferi*, spread by ticks of the genus *Ixodes. Borrelia* is intracellular pathogen with a tendency to chronize the process and can provoke an autoimmune disease. The source of the infection is rodents, some domestic animals. The transmission routes are transcutaneous, sometimes foodborne (not boiled milk). The symptoms develop within 1-3 weeks after the tick bite. The following stages of the disease are distinguished: **localized** (erythema migrans); **disseminated** (radicular pain with pain syndrome in the spine with signs of irritation and loss of sensory and motor functions, facial nerve damage); the **stage of organ lesions** (myocarditis, hepatitis, arthritis, keratitis, chronic dermatitis, multiple atherosclerosis). Diagnosis is performed by ELISA, PCR, samples for study (liquor, blood, synovial fluid).

The following is the case report of the female 9-year-old patient A., (medical history No.5140), hospitalized in the neurological unit at Poltava Regional Children's Clinical Hospital in January, 2012 with the diagnosis of Lyme disease (borreliosis), disseminated stage, severe course. Right-sided neuritis of the facial nerve, right-sided lagophthalmos, dry eye syndrome on

the right. HHV-4. Metabolic cardiomyopathy. Diagonal chord in the left ventricular cavity. Secondary immune deficiency. Acute bronchitis (convalescent).

Complaints on hospitalization: right-sided facial assymentry, inability to cover one eye, descended right mouth corner, inability to puff out the right cheek, malaise, productive cough.

The history of the disease: from the mother's words, 1.12.11 the child experienced subfebrile temperature, no clinical signs were detected. On 10, December, enlargement of the left axillary lymph node (sustained for 3-4 days) and sharp pain in this area was noted. She was admitted by the surgeon and the diagnosis was made: cat-scratch diseases. For treatment, a local semi-alcohol application with dimexidum was prescribed. The condition improved and lymph node disappeared. On the 5^{th} day a right-sided asymmetry of the face was noted. The girl was hospitalized in the diagnostic department at Children's Hospital in Kremenchug. At examination by the PCR method, HHV 1-2, EBV was not isolated. The treatment regimen: furosemide, asparcam, magnesia, traumeel C, neurovitinate, UHF the site of the mastoid process on the right, proserin, actovegin, nucleo-CMF forte, physical exercise therapy, massage of the right half of the face, electrophoresis with hydrocortisone on the right side of the face. On the background of a 10-day therapy, a poorly positive effect was noted. In order to clarify the diagnosis and further treatment, the child was hospitalized in the neurological unit at Poltava Regional Children's Clinical Hospital.

Life history: the child born to primigravida with placental insufficiency; timely cesarean delivery 1; weigh at birth-2970 g. Raised and developed corresponding to the age. Diseases in the history: acute respiratory viral infection, pneumonia, bronchitis, frequent manifestations of herpes on the lips, surgical extraction of papilloma.

Neurological status (29.12.11): moderate severity, weakness, bad mood. Palpebral fissure D> S, pupil D = S. The positive Bell's phenomenon on the right, the right cheek droops, in puffing out the cheeks, she does not hold the air. Descended right mouth corner, photoreaction is presented, no folds on the forehead. No motor disorders, muscle tonus is satisfactory. Arms' tendon-periosteal D = S, legs D = S. Abdominal reflexes D = S. Statics and coordination in the Romberg's position: the shakiness to the left is marked. Positive Chvosteck's sign, formation of face contracture on the right. Meningosigns are negative. No cramps. Intellectual and psychomotor development corresponds the age.

Lab tests: CBC– RBC-4,65*10^{12}/L, WBC-20,9*10^{9}/L, Нв-125g/L, ESR-10mm/h, platelets- 367*10^{3}/л, eos-2%, stab-11%, segm-58%, lymph-23%, mon-6%. IgG antibody to *Borrelia burgdorferi* (PCR method) - "+", HHV-6 "+" was detected. The examination of venous blood for toxoplasmosis and chlamydia is negative "-". Urinalysis is without pathology. Eggs of helminths not found. ECG: sinus rhythm, vertical position of the electric heart axis. Violation of the processes of repolarization on the posterior wall of the left ventricle. Ultrasonography of the abdominal cavity and MRI of the brain - no structural changes were found. The child was examined by specialists of various specializations. Ophthalmologist: Lagophthalmos on the right, right-sided dry eye syndrome. Neurosurgeon: Right-sided neuritis of the facial nerve. Cardiologist: Metabolic cardiomyopathy. Immunologist: Secondary Transient Immune Deficiency. Pediatric Infectionist: (Dr. K. Yu. Prilutsky, Ph.D.,) - Lyme disease, stage of dissemination.

Treatment regimen: cefatoxime, dexamethasone, nicotinic acid, midocalm, diacarb, asparcam, zovirax, heparin, valarvir, neurovitan, broth of sedative herbs, MRI on the right side of the face, ozocerite, facial massage, leukoprastic treatment.

After the treatment, the patient's condition improved but sequelae of neurological symptoms of the right-sided neuritis of the facial nerve to the right remained. Follow up course of therapy within 1 month in the neurological unit at PRCCH. Outpatient survelliance by a pediatrician, infectious disease physician, immunologist, cardiologist at the place of residence is recommended.

Features of diagnosis of polyneuropathies:

The diagnosis of acquired demyelinating symmetrical polyneuropathy is mainly based on clinical manifestations and findings of studies of conductivity of the nerves that correlate with demyelination. Elevated protein in the cerebrospinal fluid without pleocytosis and histological signs of demyelination and remyelination, often with inflammation based on the findings of the biopsy, provide additional information. In diagnostic doubts, nerve biopsy is performed, taking into account the iatrogenic consequences and serious side effects of prolonged immunomodulatory and immunosuppressive therapy. The analysis of neural conductivity is made by electromyographic study. Brain tomography and MRI is recommended.

Treatment of polyneuropathies.

Treatment of PNPs is a complex process, considering the polyethiologicity, the number of pathogenetic mechanisms of development and regenerative changes in the nerve fibers, clinical manifestations and variants of the progress of disease. The medical tactics should be based on the knowledge of physicians about the above-mentioned aspects, the features of the etiotropic, pathogenetic and symptomatic treatment, and also to be individualized, taking into account the peculiarities of the overall health state and the course of PNPs in a particular patient. In the acute period, bed rest, physiological stamping, minimum i / m manipulation, better i / v, catheterization are recommended.

In **infectious polyneuropathies**, it is necessary to prescribe antibiotic or antiviral therapy, taking into account the causative agent's etiology, sensitivity and mandatory follow up control to detect the pathogen by PCR, ELISA. In botulism, diphtheria, a specific serum is administered according to Bezredko's method.

The most common areas of therapy are intravenous administration of immunoglobulins, plasmapheresis and administration of corticosteroids (severe forms). It needs to be started at the earliest stages of the disease in order to prevent the intensification of demyelination and secondary axonal destruction, which leads to permanent disability. Nucleo-CMF-forte is used to restore myelin. To improve the nerve impulse conductivity, neuromedin, proserin is used. Vasodilators, angioprotectors, anesthetics, light antidepressants are also recommended; using of elastic golf, stockings and bandages with elastic bandages of the lower extremities (with cardiovascular autonomic neuropathy), physical exercise therapy, massage, dry heat is advisable.

List of questions for final control:

1. What is the definition of polyneuropathy?
2. What are the common mechanisms of the epidemiology of polyneuropathies in children?
3. What is the pathogenetic chain of polyneuropathies and its main links?
4. What are the methods of diagnostic, differential diagnostic and treatment of polyneuropathies in children?
5. What is the prevention of polyneuropathies?

SECTION 10.
MENINGITIS IN CHILDREN

The diagnosis of meningitis (of meningococcal etiology in particular), in children is made in 800 to 1200 cases (with approximately 100 fatal cases) annually in Ukraine. Moreover, in children who died of viral or bacterial affection of the central nervous system, in 46% of cases there was a discrepancy between clinical and postmortem diagnosis. The above index of mortality is almost zero in Scandinavian countries.

Meningites is a group of infectious diseases characterized by inflammation of the meninges. Leptomeningitis (inflammation of the arachnoid mater and pia mater) and pachymeningitis (inflammation of the dura mater) are distinguished. If meningeal symptoms are present, but the composition of the cerebrospinal fluid is unchanged, then this condition is called meningism, which occurs in various intoxications or infectious diseases and is caused by nonmeningitic irritation of the meninges, and not the true inflammatory process. All meningitis are divided into pyogenic and serous, depending on changes in the cerebrospinal fluid, the nature of the inflammation and the etiological factor.

Table 10

Classification of meningitis

No.	Pyogenic meningitis	Serous meningitis
1.	Bacterial: meningococcal, pneumococcal, Hiв-meningitis, staphylococcal, streptococcal, escherchia coli, salmonella, enterococcal, proteidae, klebsiella, pseudomonas, anthrax, leptospiral, listeria, mycoplasma, chlamydia, borrelia, etc.	Bacterial: tuberculous, Chlamidia psittaci, brucellar, syphilitic, listeria, leptospiral.
2.	Fungal: candidal, aspergillar.	Fungal: blastomycosis, cryptococcal.
3.	Parasitic: amoebic.	Parasitic: toxoplasmatic.
4.	----------	Viral: herpetic, enteroviral, parotid, influenza, parainfluenza, adenoviral, PC-viral, polioviral, measles, rubella, chickenpox, acute lymphocytic choriomeningitis (Armstrong's disease), bocavirus, metapneumoviral.

In the structure of neuroinfections, meningitis are rated second in the incidence, accounting to about 23%, among which 66% are recorded in children. In 12,3% of all meningitis, bacteria are the causative agents; viruses in 53.7%; unestablished etiology in 34%.

Table 11

Risk factors for meningitis development

Risk factor	Causative agent
Otitis, sinusitis, mastoiditis	*S. pneumoniae* *H. influenzae*
Cerebrospinal rhinorrhea	*S. pneumoniae*
Closed head injury	*S. pneumoniae* *H. influenzae*
Penetrating head injury	*S. aureus* Gram-negative bacteria
Sickemia	*S. pneumoniae* *Salmonella strains* *H. influenzae*
Asplenia (absence of the spleen)	*S. pneumoniae* *N. meningitidis* *H. influenzae*
Alcoholism	*S. pneumoniae* *Klebsiella* strains
Neurosurgical interventions	*S. aureus* Gram-negative bacteria
Immunosuppression	*L. monocytogenes* *C. neoformans*
HIV-infection	*C. neoformans* *Toxoplasma* strains *L.monocytogenes* *Cytomegalovirus*

The most common causes of bacterial meningitis, depending on the age, are as follows: in infants: *E. coli, B streptococci, L. Monocytogenes, S.Pneumoniae*; in children - *N.Meningitidis, S.Rneumoniae, H.Influenzae*; in adults *S.Pneumoniae, N.Meningitidis*, gram-negative bacilli, *Listeria* strains. Enteroviruses and herpesviruses are more commonly isolated in viral meningitis.

In newborns, perinatal pathology contributes to the onset of meningitis, namely, prematurity, maternal infection, adverse pregnancy and delivery.

Primary and secondary meningitis are distinguished. According to localization: diffusive and limited; brain-related: basal and convex. Depending on the progress, fulminant, acute, subacute and chronic meningitis are distinguished, that can be mild, moderate, severe and extremely severe.

The entry gate is the upper respiratory tract or the digestive system, then the infection gain access to the meninges through the bloodstream. The contact path of the spread is also possible.

The main pathogenetic links of meningitis are inflammation and swelling of the meninges, discirculation in the cerebral vessels, hypersecretion of the cerebrospinal fluid and delay in its resorption, which leads to increase in intracranial pressure. Cranial nerves, ventricles, vascular plexus are also involved in the pathological process. Exudate is contained in the brain sulci. In pyogenic meningitis the subarachnoid space is filled with fibrinopurulent exudate, which is subjected to phagocytosis by macrophages up to day 3 in proper treatment, and reparative changes occur within 2-4 weeks. From 5-6 days the “pus hat” is formed that covers the hemisphere of the brain. Pus aggregation leads to occurrence of commissures in the form of closed cysts, clogging of the foramen of Magendie, liquor outflow disorder, which leads to

increased intracranial pressure and the development of hydrocephalus. Thrombosis of the brain vessels and hemorrhages occur.

The clinical picture of meningitis was described in the VII century by Pavel Eginsky. However, one of the most predictive signs of meningitis was described by V.M. Kernig, the physician from the Obukhiv hospital, in 1884. He stated that "the symptom of knee joints contracture» is an early objective manifestation of inflammation of the meninges. The onset is most often acute with rapidly growing symptoms, fever. **Three main syndromes** in the clinical presentation of the diseases are distinguished:

liquor hypertension, which consists of the following symptoms: headache, vomiting, not related to food, bulging fontanelle, skin hypertension;

meningeal is a tonic muscle tension or muscle contracture (Kernig's sign, Brudzinski's sign). The cause of this syndrome is irritation with the inflammatory process of the III-IV ventricles of the brain, the roots of the spinal nerves and their reflex protection. In children under 3 months diagnostic errors are possible due to similarity with physiological reflexes, therefore, the Lesage's symptom should be checked, and from 6 months, the symptom of "landing" (in meningitis, the child will not be able to sit);

liquorologic: cytosis, blood pressure increase up to 200-300 mm Hg, elevated protein. Sugar and chlorides are normal or lowered, depending on the type of meningitis.

Indications for lumbar puncture: fever, headache, recurrent vomiting, positive meningeal symptoms. In pediatrics, the written consent of the parents to perform a puncture must be obtained.

Clonic tonic seizures occur before or after meningeal syndrome, or accompany it. Seizures are prone to recurrence (the smaller the child, the more frequently repeated), can occur similar to epileptic fits. Craniocerebral nerves are often affected similar to toxic or infiltrative neuritis. Most often, III, VI, VII, XII pairs of craniocerebral nerves are involved. Muscle tone is usually lowered, and tendon reflexes are elevated. Sometimes there is anisoreflection (on one side reflexes are higher than on the other side). In case of severe intoxication, reflexes may be absent, due to toxic effect on the reflex arc. Often, foot clones and pathological reflexes of Babinski, Rossolimo's signs are observed. Paralyses and pareses are rare, only if encephalitis conjoins.

Intoxication plays a significant role, creating a background and often causes circulatory, water-salt and hormonal disorders. In bacterial meningitis, the events of toxicosis are significantly expressed, which can cause an infectious and toxic shock. The clinical picture of meningitis of different etiology is different.

Table 12

Liquor composition in children

No.	Index	Standard
1.	color	colorless, clear
2.	pressure	100-150 mm Hg
3.	cytosis (neutrophils are absent, scarce lymphocytes)	normally, 25-20 lymphocytes/1mcl in neonates; 12-15 lymphocytes/1mcl in children aged 3 month to 1 year; older children: 1-5 lymphocytes/1mcl
4.	protein	0,1 – 0,3g/l
5.	chlorides	7-7,5g/l
6.	glucose	2,5-4,4mmol/L
7.	precipitation tests (Pandy's, Nonne, Appelt)	negative
8.	presence of bacteria (bacterial culture)	no

Meningococcal meningitis (Gram$^-$) is one of the generalized forms of meningococcal infection, characterized by the presence of bacteremia and severe endotoxinemia. A high mortality rate is observed due to hyaluronidase activity of the pathogen, which provides high invasiveness and virulence. Winter-spring seasonality is commonly present, sudden onset, rise of body temperature up to 40°C, the mother of a sick child can specify the exact time of the onset of the disease. In 70-90% of meningitis, the appearance of hemorrhagic rash is characteristic predominantly on the lower extremities; when it appears on the face, then it is a poor prognostic sign. The explanation for this phenomenon is the following: in the sites of meningococcal congestion blood clots are formed and a rash is observed. The difference between prominent toxicity and meningeal symptoms is detected, especially before 1 year of age. At the beginning of the disease, there may be changes in liquor which are characteristic in serous meningitis, which after a few hours present a picture of pyogenic meningitis with high cytosis, protein-cell dissociation. Recovery of liquor after a course of antibiotic therapy occurs within 7-10 days.

Pneumococcal meningitis (S. pneumoniae - Gram +) is one of the most severe forms. In primary infections, meningoencephalitis develops from the first days of the diseases with conjoined focal symptoms, pareses, paralyses, and ataxia. In fulminant course, meningeal syndrome delays in development. In secondary pneumococcal meningitis, which occurs along with otitis media, sinusitis, pneumonia, the onset is subacute with low-grade fever. In septic progress hemorrhagic rash is characteristic, without prolonged regress, liquor is green, dense, cytosis is not high. Relapses of pneumococcal meningitis are noted.

Hib-meningitis (Gram$^-$) occurs more often in children from the first months of life up to 2 years with frequent acute respiratory infections, in children with rickets, hypotrophy. The deficiency of antibodies to capsular antigens of the hemophilic sticks of type "b" from 3 months to 5 years was established. The onset is staged, low-grade fever, the first signs are lethargy, loss of appetite, meningeal symptoms are poorly expressed, the presentation of meningitis develops after 3 days, acute toxicosis is not observed. The peculiarity of the progress is the possibility of development of liquor hypotension, concave fontanelle; in lumbar puncture the fluid can only be obtained by suction with a syringe. Recovery of liquor is slow and can be delayed for up to 2 months.

Staphylococcal menigitis (Gram +) is most commonly seen in children under 3 months of the age with perinatal pathology and compromised immunity. The onset is acute, rapid growth of focal symptoms, the tendency to abscesses formation in the brain. The number of antibiotic resistant staphylococcal strains is great. Mortality can reach up to 20-60%.

Streptococcal megiditis (Gram +) occurs in infants with underlying sepsis, damaged skin, purulent lesions of the ENT-organs. During the development of septicemia, the liver, spleen, heart, lungs is often involved in the pathological process.

Pseudomonas meningitis (*Pseudomonas aeruginosa* Gram$^-$) is considered as an opportunistic disease. Preterm infants, children who receive glucocorticoids, cytostatics, infants with a burn disease are in the risk group. This type of meningitis is characterized by a subacute onset, a very severe course, a high mortality of up to 50-60%, gross neurological sequelae.

Salmonella menigitis (Gram$^-$) is mainly manifested in children during the first 6 months of life, combined with toxicosis, diarrhea syndrome, liquor hypotension. In the lumbar puncture, the liquor stays in the needle, not leaking. The course is severe, prolonged, often with a lethal outcome.

Escherichia coli meningitis (Gram$^-$) is a secondary pyogenic menigitis caused by enteropathogenic escherichiae. It develops more often along with intestinal infection, pyelonephritis, pneumonia with severe toxicosis and exicosis, and subsequent conjoining of meningal symptoms.

Serous meningitis is a non-purulent inflammation of the meninges, characterized by the benign course with rare complications. **Parotid meningitis** (first site) occurs more often with underlying mumps - an acute infectious disease of viral etiology with an air-drop mechanism of transmission with lesions of the glandular organs (salivary glands, pancreas and gonads) and the

nervous system. But it may also be the primary one, because the virus has adenoneurotropism. The onset is acute, with hyperthermia, headache, nausea, vomiting and meningeal syndrome. No signs of severe intoxication are noted. Sometimes the medulla is involved and then ataxia, deviation of speech occurs; cranial nerves, more frequently the VIII pair, can be affected with the development of encephalomyelitis. Liquor is characterized by elevated protein, lymphocytic cytosis, increased intracranial pressure. After lumbar puncture the state is improved, so it is a diagnostic and therapeutic measure.

Listeria meningitis in most cases occurs in newborns. It is marked by the severity of the clinical picture and the late timing of the onset of liquor sanation (up to 21 days).

Candidal meningitis occurs in children with immunodeficiency; the onset is subacute, torpid progress. Liquor sanation occurs only after the use of a specific antifungal antibiotic.

Enteroviral meningitis (**ECHO viruses, Coxsackie viruses**). The disease occurs in people of any age, but more often in children. The transmission paths are airborne, fecal-oral, transplacental. Seasonality - summer-spring period. During the outbreaks the high contagiousness and mass character of the disease is recorded. The major signs are hyperthermia, hypertensive-hydrocephalic syndrome (severe headache, cerebral vomiting). Meningeal syndrome on day 2-3 becomes moderate and short-term. In 40% of cases focal symptomatology is recorded. In younger children it starts with generalized seizures. In older children, confusion is characteristic. Typical appearance of the patient: pale nasolabial triangle (not to be confused with scarlet fever), hyperemia of the cheeks, in the pharynx - herpetic angina. Sometimes hemorrhagic rash may occur in enteroviral meningitis, as in meningococcal meningitis. Liquor is clear, colorless, leaks under pressure. Protein is normal, or sometimes elevated, but more often reduced ("diluted protein" due to excess of exudates), lymphocytic cytosis is detected. Glucose and chlorides are normal.

Lymphocytic meningitis (Armstrong's disease) was described in 1933. It is zoonotic widespread generalized viral disease of a human being. The infection reservoir is mice, Siberian hamsters. The causative agent belongs to the group of arenaviruses. Infection occurs through air or dust, possibly after bites of ticks, gnats, mosquitoes. It is not transmitted from person to person! Seasonality is winter, early spring. The disease more often occurs in children. The clinical presentation is polymorphous. The disease can have signs of flu, myocarditis, pneumonia, sore throat, mumps, orchitis, etc. The onset is acute, abrupt. Hyperthermia, meningeal syndrome appears from the first day and is dominant. The severe state is manifested by anxiety, agitation, hallucinations, loss of consciousness, possible infectious and toxic shock. Liquor usually leaks by pressure, is clear or opalescent. Protein can be diluted; lymphocytic cytosis, glucose and chlorides are normal.

Tuberculous meningitis occurs along with tuberculosis. Morphological process is exudative-productive. Meninges, brain parenchyma are mainly affected. The ventricles of the brain are usually enlarged and filled with liquor of jelly-like consistency of yellowish color (xanthochromia). Jelly-like consistency is associated with high protein content. The progress of the disease is gradual with a prodrome (about 2 weeks). In young children under 3 years of age it can be acute. Subfebrile temperature, malaise, fatigue, indifference, monotonous cry, hyperesthesia, hyperacusis, nausea, vomiting occurs. Vegetative dysfunction commonly occurs: red persistent dermographism, Trusso's spots, hyperhidrosis, tachycardia, drowsiness, loss of hearing, sopor. Meningeal syndrome is slightly pronounced at the beginning and slowly increasing with the occurrence of focal symptoms: strabism, ptosis, amimia, hemipareses, hyperkinesias, coordination disorders. On day 18-19 coma develops, and on day 21 death, if treatment has not been provided. Liquor is taken in 3 test tubes: glucose test, "spider's web clot" test (culture for *Mycobacterium tuberculosis*), protein test. Detection of *mycobacterium tuberculosis* is possible in Ziehl-Neelsen-stained liquor smear. The prognosis is made by the timeliness of the specific therapy.

If the liquor is left to stand, a fine clot resembling a pellicle or cobweb may form, the cytosis is mixed, the protein is elevated to 1-3 g / l, glucose and chlorides are lowered!

Herpesviral meningitis is often caused by HHV-1 and HHV-6, cytomegaloviruses. The onset is gradual, subacute; has a tendency to chronize the process. Liquor sanation occurs after antiviral therapy. Herpesviral meningitis may be associated with HIV-infection.

Diagnostic pattern of meningitis:

1. Complete blood count: neutrophilic leukocytosis with left shift (in pyogenic meningites), lymphocytosis (in serous meningites), elevated ESR;
2. Assessment of the liquor: neutrophilic pleocytosis (in pyogenic meningites), lymphocytosis (in serous meningites), elevated protein levels, lowered or normal sugar (in pyogenic meningitis), elevated or normal glucose (in serous meningites) and lowered glucose and chlorides (in TB meningitis);

3. Bacterioscopic study of liquor sediment and blood smears - "thick drop";
4. Bacteriological cultures on selective nutritional media: liquor, blood, mucus from the nasopharynx to isolate the pathogen;
5. Virological blood, liquor tests;
6.Serologic methods (latex agglutination test (LAT), counterimmunoelectrophoresis (CIEP)) to determine the antigen of the pathogen;
7.PCR;
8. Computer tomography to exclude the volume process;
9. Examination by an ophtalmologist with an assessment of the fundus.

Treatment

1. Strict bed rest until stable normalization of body temperature, the disappearance of the meningeal syndrome and normalization of blood, liquor parameters, an average of 10-14-21 days. Diet therapy: for children of the first year of life, breast milk or adapted milk mixtures are administered in the first day at the dosage of 1/2- /3 corresponding to age norm with subsequent increase to full amount for 2-3 days. Older children are prescribed with a dairy and plant diet (Pevzner diet No.5) in small portions 5-6 times a day with the subsequent transition to diet No. 2 or No. 15 (depending on the age) in the recovery period. The drinking regimem corresponds to the age daily need for liquid, taking into account the daily volume of solutions injected intravenously.
2.Antibacterial therapy. In meningitis of minor severity or associated with meningococcal infection, the starting antibiotic may be 100 mg / kg / day cefotaxime (penicillin 300-500 000 U/kg/day). In severe forms of pyogenic meningitis, at the first stage of therapy (before the pathogen is detected), **the drug of choice is 100 mg / kg / day ceftriaxone** or 200 mg / kg / day cefotaxime. Babies up to 1 month of age: 150-200 mg / kg / day ampicillin (brand new name-flemoksin) in combination with cephalosporins of the third generation or aminoglycosides (15-30 mg / kg / day amikacin, 6-9 mg / kg / day netylmicin). In severe cases, it is combined with fluoroquinolones (levofloxacin, flaccinum, ciprofloxacin, gatifloxacin) or carbapenems (imenem, meronem). Within 24-48 hours from the beginning of therapy, a control lumbar puncture is performed to estimate the effectiveness of the initiated therapy. The criterion of the effectiveness is the lowering of pleocytosis not less than 1/3. In case of identification of the etiological cause of the disease, starting antibiotics can be replaced by others, according to the sensitivity of the pathogen. However, in the presence of pronounced positive dynamics, namely lowering of intoxication syndrome, normalization of body temperature, disappearance of meningeal symptoms, significant lowering of pleocytosis, better complete blood count), it is advisable to continue the initial therapy. The reserve drugs in the absence of positive dynamics from the initial therapy within 48 - 72 hours is 120 mg / kg / day meropenem, 100 mg / kg / day cefepime, 60 mg / kg / day vancomycin. The duration of antibiotic therapy should be on the average: in meningococcal and Influenzae-meningitis - 7-10 days; in pneumococcus - 10-14 days; in streptococcal and listerial - 14-21 days; in meningitis caused by gram-negative bacilli - 21 days; in staphylococcal, enterococci - 28 days. **The criterion for withdrawal of antibiotic therapy is the liquor sanation.** Control lumbar puncture is carried out after sustained normalization of

body temperature, the disappearance of clinical signs of meningeal syndrome, normalization of the complete blood count. Antimicrobial therapy is discontinued if the number of cells in 1 ml of liquor does not exceed 50 due to lymphocytes. In the recurrence of pyogenic meningitis, a repeated therapy with reserve antibiotics (meropenem, ceftazidime, vancomycin, sulperazone) is performed. If the etiology of meningitis is established, then the anti-meningococcal gamma-globulin or anti-meningococcal plasma is administered (intramuscular, endolumbal). In staphylococcal etiology, antistaphylococcal plasma, gamma-globulin (obtained by immunizing the mother) is administered. Prolonged sulfanilamides (40-50 mg / kg/day sulfomonometoksin per os) are also advocated.

3. In serous viral meningitis ribonuclease is used - a 2-week-course 6 times a day; children under 1 year of age - 3 mg; 2-3 years old - 5-9 mg, 6-10 years old - 14 mg; 11-15 yrs.-20 mg; according to the protocol of etiotropic therapy, **10-15 mg / kg acyclovir** 3 times a day for 5-7 days intravenously; sometimes groprinozine, foscarnet, valacyclovir, erebra is recommended in age-related doses.

4. In TB meningitis various combinations of anti-TB medications are used: isoniazid, rifampicin and pyrazinamide for 2-3 months. The follow up 7 months: isoniazid and rifampicin. In case of poor effect, streptomycin is added. Duration of treatment is 18-24 months.

5. Detoxification therapy is carried out using 5% glucose solution in combination with 7.5% potassium chloride solution, saline solutions (isotonic sodium chloride solution, Ringer's solution), hydroxyethyl starch (refortan, stabizol, volekam). The total daily volume is no more than 2/3 of the physiological need (in normal diuresis and absence of initial dehydration). From it the volume of infusion should not exceed 1/2 of the physiological need (80 ml / kg). From the second day, the deficite of liquid is supported in the mode of zero water balance. Infusion volume is 1/3 - 1/2 of the physiological need. In case of oliguria or anuria occurs, the administration of the liquid is contraindicated until diuresis restoration. Angioprotectors (Actovegin, Trental, Instenon, Ceroxone) in combination with infusion therapy are indicated to improve the microcirculation.

6. Furosemide, manit is recommended for dehydration.

7. Dexamethasone is prescribed to prevent neurosensory deafness at a daily dosage of 0.15 mg / kg every 4 hours in the first 2 days. The first dose of dexamethasone should be administered 10-30 minutes prior to the administration of the antibiotic.

8. Anticonvulsant therapy (phenobarbital, diphenin, sibazon, gamma oxy-oil acid (GOOA). In case of fits in the past history, nootropic drugs are contraindicated.

Complications: infectious-toxic shock (ITS); acute brain swelling, acute intracranial hypertension, ependymitis; meningoencephalitis; brain abscess; syndrome of liquor hypotension, subdural exudate.

Outcomes: loss of hearing, vision, hydrocephalic syndrome, astenovegetative syndrome is possible.

Outpatients monitoring: monthly examination by the pediatrician; examination by the neurologist is twice a year. Physical activity is limited to 1 year; vaccination is advisable to be made in 1 year.

Prevention

1. Thorough room ventilation.

2. Daily wet cleaning of rooms where group of children is, using disinfectants, UVI.

3. Keeping to common hygienic activities. If meningococcal meningitis is diagnosed it is reported to the State Department of Health Services. If more than 5 cases are registered the report to the Ministry of Health of Ukraine is sent.

4. Meningitis patients are hospitalized initially into the intensive care unit, then pediatric infection unit. Discharge from the hospital after a clinical recovery and a single-time negative bacteriological test is no earlier than 3 days after the withdrawal of antibiotic therapy. Convalescents are allowed to stay in the child care facilities no earlier than 5 days after discharge from the hospital and after another bacteriological examination. Contact children are imposed on

quarantine for 10 days from the moment of registration of the last case. All bacteriological tests of contact people are performed twice with an interval of 3-7 days. The carriers are treated with levomitsetin. Contact children up to 5 years of age, not later than day 7, are administered with normal human immunoglobulin at a dosage of 2 ml; children aged 5-7 years - 2 ml (the other day 2 ml more) i/m. In case of an outbreak, if the etiology of meningitis is established, vaccination with a polysaccharide anti-meningococcal or anti-pneumococcal vaccine is performed. For prevention of parotitis and tuberculosis, Influence-meningitis vaccination is used. Prevention of lympho-choriocytic meningitis is the protection of premises, food from gray mice, rats and other rodents, to avoid bites of domestic and laboratory animals, gnats, mosquitoes.

For prevention of parotitic TB meningites, Influenzae-meningites vaccination is used. Prevention of lympho-choriocytic meningitis is the protection of premises, food from gray mice, rats and other rodents, to avoid bites of domestic and laboratory animals, gnats, mosquitoes.

The following is the case report of the male patient aged 1 year and 1 month (medical history No.1117), hospitalized in the intensive care unit at Poltava Regional Children's Clinical Hospital in June, 2012 with the diagnosis of the Acute serous meningoencephalitis, basal-stem form, severe course (mycobacterium tuberculosis were isolated). Convulsion syndrome. Congenital heart defect (open oval window) - "D" registration at the place of residence. Reactive changes of the liver.

Complaints on hospitalization: vomiting 4 times, weight loss, loss of consciousness. **The history of the disease:** from the mother's words it was found that the boy experienced the acute illness at night; the onset of vomiting triggered the growing atonia. Two weeks ago, the child had a low-grade fever for several days. He was hospitalized in a district hospital. The next day, the condition worsened, single vomiting, loss of consciousness, strabismus appeared, forced meningeal position of the body. He was delivered to the intensive care unit at Poltava Regional Children's Clinical Hospital by air medical service. **Life history:** the child has born to primigravida, 1 childbirth; weight at birth - 3050g. In the maternity hospital the diagnosis of cephalohematoma was made. Raised and developed corresponding to the age. Diseases in the history: acute respiratory viral infection. Breastfeeding was up to 6 months.

On examination: the state is severe, flaccid, forced posture. Palpebral fissures D <S, pupil D = S. Meningeal signs: rigidity of the occipital muscles, positive Kernig's symptom, high muscle tone. Convergent strabismus was detected. Inconstant myoclonia-typed seizures of the right lower limb were observed. Tendon periosteal reflexes D <S. The skin is pale, marked vascular net is on the temples. The pharynx is pink, a tongue without a covering. Foamy salivation from the mouth. Puerile respiration, cardiac rhythm is correct, the tones are somewhat muffled. Respiratory rate - 32 per minute, heart rate - 120 beats per minute, BP - 95-60 mmHg. The abdomen of the usual configuration, palpable. The liver was protruding from the edge of the costal margin to 2 cm, the edge is soft. The spleen was not palpable. Defecation was 2 times with shaped feces, urination was normal.

Lab tests: CBC – RBC-3,8*10^{12}/l, WBC-44,5*10^{9}/l, Нв-115g/l, ESR-8mm/h, platelets-220*10^{3}/l, eos-1%, stab-23%, segm-30%, lymph-40%, mon-6%, glucose – 4,9mmol/h. Blood biochemistry test: bilirubin 10,0μmol/L, whole protein – 64g/l, residual nitrogen 20mmol/L, urea – 3,4mmol/L, creatinine – 69μmol/l, ALT – 0,68mmol/h/L, AST – 0,45mmol/h/L, prothrombin index 80,6%; plasma fibrine – 3,55g/l. Urinalysis is without pathology. Eggs of helminths not found. ECG: sinus rhythm, vertical position of the electric heart axis. Violation of the processes of repolarization on the posterior wall of the left ventricle. Ultrasonography of the abdominal cavity revealed no structural changes were found. Liquor assessment: protein-5,87g/l, cytosis – 181 in 1μL, predominant lymphocytes, glucose – 0,6mmol/L, RBC – 20-30 per high-power field, after exposition for 15 minutes the membrane was detected. Brain CT revealed internal hydrocephalus, brain edema, dyscirculatory encephalopathy. Bacteriological study of saliva revealed isolated mycobacterium tuberculosis. Feces analysis on colibacillus revealed no pathogenic flora.

The child was examined by the specialists: ophthalmologist (convergent strabismus), neurosurgeon (no neurosurgical pathology), phthisiologist (confirmed acute tuberculosis meningoencephalitis), neurologist (internal hydrocephalus).

Treatment regimen: dehydration and detoxification therapy (25% magnesium sulfate, lazix, polyionic solutions, dexamethasone) and antibacterial and antifungal therapy (ceftriaxone, fluconazole) have been performed. Pentoxifylline was used in improving the microcirculation of the brain in 0.9% of the physical solution, heparin (to prevent DIC-syndrome). Specific therapy: izoniazid, rifampicin, ethambutol. Symptomatic therapy was also performed.

After the treatment in the intensive care unit the patient's condition improved; liquor sanation was detected, disappearance of meningeal syndrome, hypertension, temperature normalization, though follow up treatment at the regional T.B. prophylactic centre was indicated.

List of questions for final control:

1. What is the definition of meningitis, meningococcemia?
2. What are the common mechanisms of the epidemiology of meningitis in children?
3. What is the clinical course of the pyogenic and serous meningitis in children?
4. What is the laboratory diagnostics in suspicion of meningitis in children?
5. What is the treatment, prevention of meningites in children?

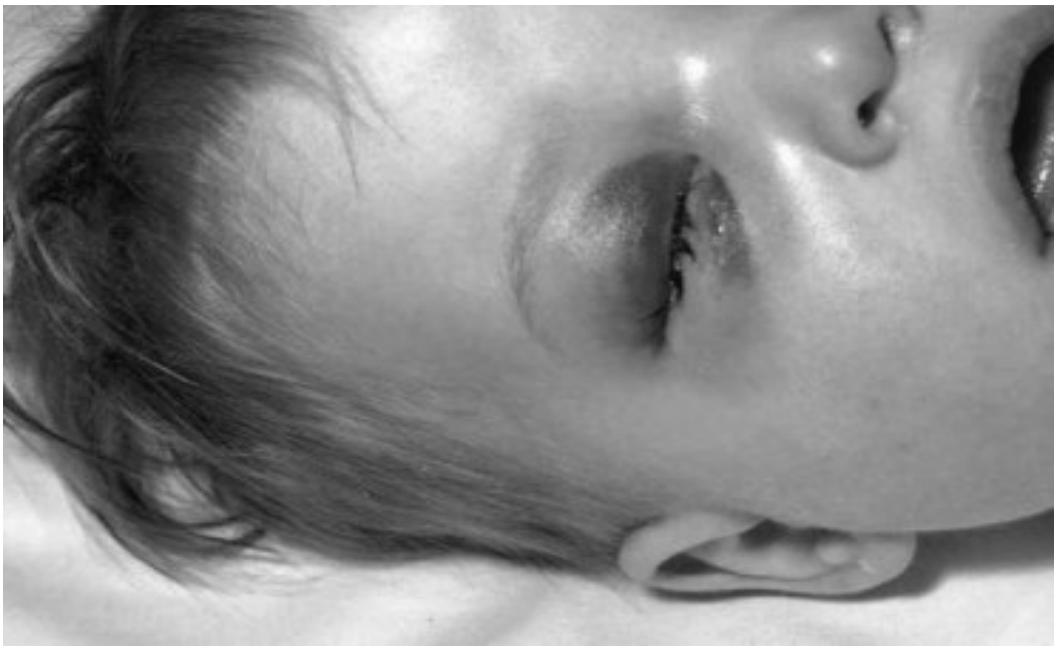

Fig. 9. Hemophilic meningitis.

SECTION 11.
HELMINTHOSES IN CHILDREN

Helminthoses remain an urgent problem to date that can endanger the health and life of children. The share of school-aged children and pre-school-aged children in Ukraine accounts for 90-95% and 65.1% of all patients with enterobiasis and ascariasis, respectively. Lamblia infection in children's care facilities can reach 50-80%. In the United States, cysts of lamblia are found in 21% of children attending children's care facilities. Every year in Ukraine 30-40 thousand of giardiasis cases are registered within 65% estimated for children. The WHO reports that helminth and parasite invasion in children population worldwide, in comparison with adults, predominates by 5-6 times. According to the World Bank estimate, the economic loss from intestinal helminthises ranks fourth among the losses that inflict all illnesses and injuries. Considering the importance of combating parasitic diseases in many countries, the 54th Session of the World Health Assembly approved a strategy to combat geohelminthoses.

In our domestic medicine, a paradoxical situation has arisen: if the host asks for a dog or cat to be vaccinated by a vet, then the animals will first be dewormed, as otherwise the effect of vaccination may be insignificant. On the other hand, when a mother appeals to a health facility for her child's scheduled vaccination, doctors do not even suspect a possible failure of immunization due to parasitic disease and therefore do not conduct an examination for helminths and subsequent deworming. Helminths have an immunosuppressive, carcinogenic effect on the body. The oncogenicity of parasites is becoming more and more relevant in connection with the pollution of the environment and food, as well as the expansion of the range of many parasites.

Helminthoses are a large group of diseases, caused by parasitic worms (helminths). Currently, more than 320 types of helminthes that are registered in humans. On the territory of Ukraine, they are very unevenly distributed and about 30 species are found. According to the three classes of parasitic worms, three groups of diseases caused by them are distinguished: nematodes, cestodes, trematodes. The group of **nematodes** includes: enterobiasis, ascariasis, trichinosis, dracunculiasis, toxocarosis, strongyloidiasis, filariasis (*Wuchereria bancrofti, Brugia malayi* infection), loiasis, trichocephalosis, onchocerciasis. **Cestodes** include: alveococcosis, echinococcosis, hymenolepiasis, diphyllobothriasis, taeniarchosis, Taenia infection. The group of **trematodes** involves *Schistosoma* infection, clonorchiasis, metagonimosis, opisthorchiasis, paragonimosis, fascioliasis.

Trematode infection is a group of diseases caused by flukes (trematodes). The common properties of this group are:

- a peculiar form of the body: flattened dorsoventrally;
- small sizes that do not exceed 10mm;
- trematodes are hermaphrodites;
- they are biogelminths whose development occurs with the involvement of an intermediate host (sometimes two);
- they all have a differentiated digestive system.

Opisthorchiasis, biogelmintosis, natureborn zoonosis are characterized by a predominant affection of the liver, gallbladder, pancreas, due to the features of localization of adult worms. The causative agent is a "cat fluke". Infection occurs in consumption of poorly heat-treated fish, as well as from sick cats and dogs. An ill person does not represent a risk for a healthy individual. The incubation period is 2-4 weeks. Depending on the progress of the diseases it can be acute, subacute (more than 2 months), chronic (several years).

Diagnostic criteria:

- Past medical history that shows living in the region at risk for opisthorchiasis;
- habit to consume raw, low salted, undercooked fish;
- "unmotivated" eosinophilia, sometimes combined with subfibrility, urticaria, dyspepsia;

- long-term signs of hepatitis in combination with eosinophilia;
- ineffective antibacterial, antiulcer therapy;
- in the presence of jaundice: obvious signs of cholestasis (elevated levels of alkaline phosphatase with low levels of ALT);
- prolonged course;
- the diagnosis is confirmed in the determination of helminth eggs in duodenal contents and feces.

Treatment: the main anti-helminthic drug is chloroxide at a dose of 0.2-0.3g / kg (three, five to ten day-course). The 5-day treatment schedule is optimal. In the morning after a light breakfast (tea, bread) the patient is given a chloxylum. In this case, the daily dose is divided into 3 portions, each of the portions is stirred in ½ cup of milk and drunk at an interval of 10 minutes. Within 2-3 hours the child can have breakfast, and within another 2-3 hours choleretic herbs and antispasmodics are taken. The effectiveness of the treatment is monitored within 4-6 months. Repeated course, if necessary, is carried out within 6 months (no more than 4-5 courses). 50-75 mg / kg Praziquantelum is also recommended for treatment per 3 times for 1 day. Dispensary supervision is 1 year.

Fascioliasis is a zoonotic biogelminthosis characterized by major affection of the liver and bile-excreting system with chronic course. Fascioliasis is classified as hepatic fasciolysis and gigantism, which occurs in countries with hot climates.

The causative agent of the hepatic fasciolysis is a liver fluke (*Fasciola hepatica*) with a length of 30 mm. Adult helminthes parasitize in the liver and bile ducts of domestic and wild herbivores. The human is the obligate final host of the parasite. An ill person and an animal do not represent epidemiological harm to the environment. A person is infected when eating different water plants and garden vegetables, irrigated by contaminated water. The peak of morbidity is summer.

Incubation period is 1-8 weeks. The onset of the is acute, manifested by fever (up to 40°C) permanent, wave, hectic, as well as myalgia, arthralgia, skin itching, rash. Pain in the epigastrium, enlarged liver, jaundice, unformed stool, eosinophilia is characteristic. At the subacute stage, the manifestations decreases and almost disappears. Within 3-6 months, organ damage to the liver and bile ducts is a major sign.

Diagnostic criteria:

- epidemic anamnesis (a habit of consuming unwashed vegetables, staying in a territory with a high risk of morbidity);
- rise of body temperature in combination with allergic manifestations (rash, arthralgia, eosinophilia);
- pain in the pancreatic-duodenal zone and the projection of the gall bladder;
- enlarged liver, sometimes jaundice;
- leukocytosis.

Into the chronic phase:

- prolonged course;
- recurrent attacks of abdominal pain with localization in the liver, gallbladder, pancreas;
- enlarged liver, jaundice;
- diarrhea, progressive weight loss;
- liver dysfunction (elevated ALT, AST, lowered protein, dysproteinemia);
- combination of leukocytosis, eosinophilia, anemia;
- the diagnosis is confirmed in the detection of eggs of helminths in duodenal contents, faeces, as well as specific antibodies.

Treatment is similar to opisthorchiasis. The peculiarity of pathogenetic therapy is the prescription of glucocorticoids.

Cestodes represent a group of helminthiases caused by cestodes with the following common properties:

- absence of stomach (absorb nutrients through the tegumen);
- structure of the body - head (skolex), short neck, hermaphrodite segments (proglottids);
- tape-shaped, flat, segmented body (strobila);
- high fertility (some spices of cestodes can produce up to 600 million eggs a year);
- the length of cestodes varies from a portion of millimeter to 30 meters;
- the cycle of development of cestodes occurs with the change of the host, i.e., they are assigned to oral biohelminthes.

Echinococcosis is a chronic helminthosis that can develop in the child's body for many years. The main source of invasion is domestic dogs, cats, wolves. Mature forms parasitize in the small intestine. Intermediate hosts are sheep, horses, pigs, hares, squirrels, and a human. Pathways of transmission are contact-houseborn, waterborn, alimentary. The uncomplicated form of illness lasts for years and can be detected by accident at scheduled fluorography. In rupture of echinococcal cysts the course is complicated by myocarditis, allergic affection of the lungs, liver, kidney, central nervous system. Swelling of the face, muscle aches, rash are characteristic. Less commonly is echinococcosis of the brain, mediastinum, mammary gland, intestines, subcutaneous tissue. In squeezing the vessels of the portal system the signs of portal hypertension, disability, fatal cases are possible.

Hymenolepiasis is anthroponose helminthoses with a predominant lesion of the gastrointestinal tract. Increased invasiveness of the population is promoted by uncontrolled trade in fish and meat. The source of helminthosis is a human. Children are affected in 67.5% of cases. Clinically, the disease is characterized by daily pain attacks with a few days interruption, diarrhea, weight loss, decreased hemoglobin and eosinophilia.

Diphyllobothriasis is helminthosis, which occurs with signs of gastrointestinal tract disorder and the development of megaloblastic anemia. The length of the tapeworm is up to 9 meters. The prevalence of diphyllobothriasis is associated with freshwater reservoirs, insufficiently salted caviar and raw fish. The final host of the parasite is a human, dog, cat, pig, fox, bear, and the intermediate host is freshwater crayfish and fish. The incubation period is up to 60 days. The clinical picture is manifested by moderate gastrointestinal disorders, development of B_{12} hypovitaminosis, anemia, disturbances of the cardiovascular and nervous system.

Nematodes are the most widespread in Ukraine, in particular enterobiasis and ascariasis. The causative agent of **enterobiosis** is a threadworm (*Enterobius vermicularis*) that infects about 90% of children. A human swallows the mature eggs with food, and the helminth parasites in the small intestine and inferior parts of the large intestine. In patients with enterobiasis, autoinvasia is often present - repeated infection by the pathogen already present in the body as a result of the contamination of the fingers with itching of the anus. The main symptom is itching in the anus at night that lasts for several days and is repeated after 3-4 weeks. The illness is manifested by sleep disturbance, fatigue, loss of appetite, dry mouth, cramping abdominal pain, faecal disorders. *Enterobius vermicularis* invasion can lead to acute appendicitis, pyelonephritis, cystitis, and nocturnal urinary incontinence.

Ascariasis is a widespread helminthosis, which manifests itself in itching, urticaria, eosinophilia, infiltration in the lungs, disorders of the digestive system. The causative agent is a human ascarid whose female has a body length of up to 25 cm. Ascariasis often occurs with less pronounced symptoms: dyspeptic disorders, weight loss, neurasthenia, and fatigue. But sometimes it manifests with the severe course in the form of focal lesion of the lungs, urticaria, fever, intestinal obstruction, liver abscess, appendicitis. Ascariasis promotes the transition of dysentery to chronic form, worsens the course of tuberculosis.

Diagnosis and treatment

The epidemiological history, clinical manifestations and data from paraclinical studies can only suspect helminthiasis. The final diagnosis is established in the detection of the causative

agent and the serological marker. The material for research is: faeces (repeat within 3-5 days), sputum, blood, urine, nasal mucus, vaginal discharge, body tissues. Immunological methods are informative only during the migration stage. However, currently, helminthiasis is a disease that is poorly diagnosed and sometimes requires instrumental examination methods (echinococcosis).

Common management is as follows:

1. Therapy should be individual;
2. Prophylactic administration of antihelmintic drugs is contraindicated;
3. Treatment must be controlled;
4. Uncomplicated forms are treated outpatient;
5. Severe and moderate forms are treated in the hospital, and sometimes require surgical intervention;
6. Necessary examination and preventive treatment of family members.

Table 13

Antihelmintic drugs

Medication	Indication	Contraindication
Albendazole	Ascariasis, ankylostomiasis, strongyloidiasis, trichinosis, trichocephalosis, toxocarosis, enterobiasis, echinococcosis, neurocysticercosis. Polyinvasion.	Hypersensitivity, pregnancy, breast-feeding, age under 2 years, retinopathy.
Diethylcarbazine	Lymphatic filariasis: brugiosis, Wuchereria bancrofti infection), loiasis, onchocerciasis.	Hypersensitivity, pregnancy, breast feeding, age under 6 years.
Ivermectin	Onchocerciasis, lymphatic filariasis: brugiosis, Wuchereria bancrofti infection; vucheriasis; strongyloidosis, lichen.	Hypersensitivity, age under 5 years.
Levamisole	Ascariasis, enterobiasis.	Hypersensitivity, pregnancy, agranulocytosis.
Mebendazole	Ascariasis, enterobiasis, ankylostomiasis, trichocephalosis, trichinosis, echinococcosis, polyinvasion.	Hypersensitivity, pregnancy, breast feeding, age under 2 years, nonspecific ulcerative colitis, Crohn's disease.
Niclosamid	Taeniarchosis,diphyllobothriasis, hymenolepiasis.	Hypersensitivity, pregnancy, stomach ulcer, duodenal ulcer, anemia.
Pyrantel	Ascariasis, enterobiasis, ankylostomiasis.	Hypersensitivity, pregnancy, breast feeding.
Prazikvantel	Trematodes:opisthorchiasis, clonorchiasis, paragonimosis, Schistosoma infection; cestodes: taeniarchosis, diphyllobothriasis, hymenolepiasis, cysticercosis.	Hypersensitivity, pregnancy, breast feeding, ocular cysticercosis, age under 4 years, liver damage, not associated with helminthiases.

Therapy of helminthic invasions consists of two stages: etiotropic treatment and correction of the sequelae (dysbiosis, colitis, anemia, hypovitaminosis, irritable bowel syndrome).

List of questions for final control:

1. What the definition is of helminthises?
2. What are the common mechanisms of the epidemiology of enterobiasis and ascariasis in children?
3. What is the characteristic clinical course of helminthiases in children?
4. What is the laboratory diagnosis in suspected trematodes and cestodes in children?
5. What is the treatment and prevention of helminthiases in children?

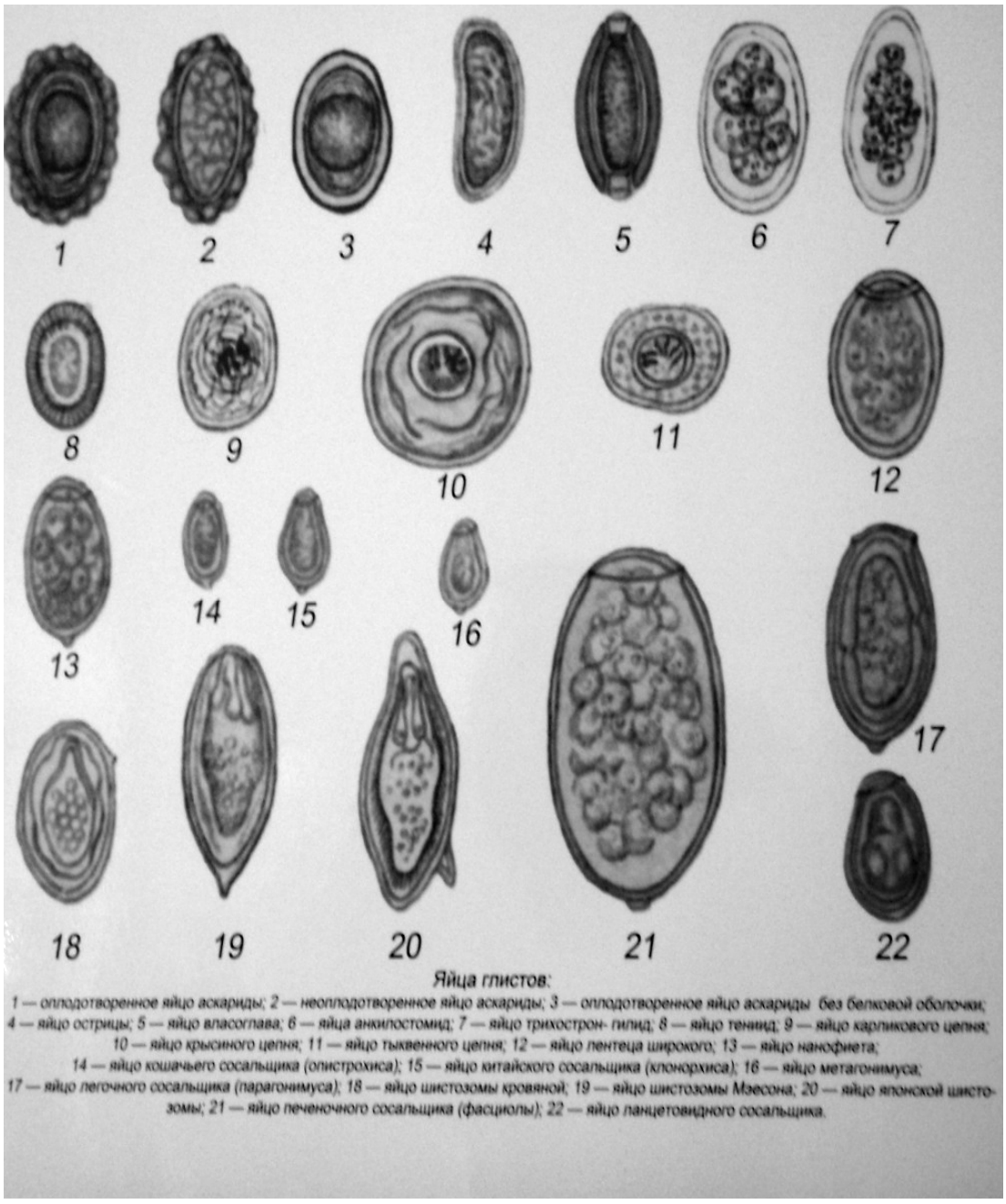

Fig.10. Eggs of helminthes.

SECTION12.
ACUTE INTESTINAL INFECTIONS

Acute intestinal infections (AII) are assigned to the group of infectious diseases of the viral, bacterial, fungal or parasitic etiology, which spread by the fecal-oral pathway and affect mainly the gastrointestinal tract.

AII are rated as one of the major infectious diseases of childhood. The WHO reports that the annual incidence of the acute intestinal diseases is accounted for more than 1 billion individuals worldwide, of which 65-79% are children under the age of 5 years. Annually in Ukraine, 60% of the total number of deaths from infectious diseases is children of predominantly young age. In the mortality structure of newborns, the proportion of AIIs ranges from 50 to 70%. In countries with high infant mortality, up to 15% of children under the age of 3 die every year from intestinal infections. Unfortunately, in our country, the etiological structure of AII changes annually and the tendency to increase the incidence of this pathology persists. A special place is occupied by AII among nosocomial (intra-hospital – derived form *nosos*, which means sickness, *nosocomialis* - hospital) infections, where their specific gravity reaches 60-80%.

According to the etiological principle, all acute intestinal infections can be divided into three groups:

1. **Bacterial intestinal infections**: *Shigella; Salmonella; Escherichiae; Campylobacter*, etc.
2. **Viral intestinal infections:** *Rotavirus; Adenovirus; Astrovirus; Norflokvirus; Coronavirus; Reovirus; Calicivirus*, etc.
3. **Fungal and parasitic intestinal infections:** *Cryptosporidium; Microsporidia; Balantidium coli; Isocpora; Giardia Lamblia; Entamoeba Histolitica*.

According to the WHO classification all diarrheal diseases are divided into:

I. Non-infectious diarrhea.

II. Infectious diarrhea:

1. Invasive AII: inflammatory; bloody
2. Secretory diarrhea: non-inflammatory; serous.
3. Diarrhea with immunodeficiency of the child's body.

Secretory diarrhea is caused mainly by viruses, bacteria and protozoa that produce enterotoxin: *Rotavirus, Adenovirus, Astrovirus, Norflokvirus, Coronavirus, Reovirus, Calicivirus*, enteropathogenic, enterotoxigenic and enteroaggregatory *Escherichiae coli, Cryptosporidium, Microsporidia, Balantidium coli, Isocpora*.

Invasive diarrhea is caused by the following bacteria: *Shigella, Salmonella*, enteroinvasive and enterohemorrhagic *Escherichiae coli, Campylobacter, Clostridium, Stapfylococcus, Giardia Lamblia, Entamoeba Histolitica*.

Secretory diarrhea is manifested by a combination of stomach lesion (frequent and repeated vomiting, pain in the stomach area) and enteritis (serous feces with residues of undigested food, rapid dehydration,). In invasive diarrheas, the pathogen penetrates into the intestinal wall, which causes inflammation of the small and large intestine (non-profuse feces with a large number of pathological impurities of mucus and blood with apparent colitis and intoxication syndromes). Pathogens of invasive diarrhea can enter the bloodstream, causing bacteremia and foci of the secondary infection. The etiological structure of AII in children of different age groups is different. In young children, this pathology is caused mainly by rotaviruses, enteropathogenic escherichiae, salmonella, staphylococcal, klebsiella, protein, citrobacter and other opportunistic pathogens. Less common are shigellosis, clostridios, cholera. In older children, shigellosis, food salmonellosis transmission, yersiniosis, typhoid fever and

paratyphoid are more common. Acute intestinal infections have many common epidemiological features. For children's population high contagiousness, spread among children groups, fecal-oral transmission mechanism, occurrence in both sporadic and epidemic outbreaks, summer-autumn seasonality, peculiarities of immunity (species-specificity and instability) is characteristic.

Features of the diarrhea pathogenesis in AII

1. For AII of viral etiology, the **osmotic** mechanism of diarrhea is characteristic due to increased osmotic pressure in the intestine due to the accumulation of disaccharidases in the villi of the affected epithelium, which leads to a violation of the absorption of water and electrolytes.
2. AII, caused by enterotoxin (enterotoxigenic escherichiosis, etc.) are characterized by a **secretory** mechanism that occurs in increased secretion of water and electrolytes into the intestinal cavity due to enzymatic disorders in the enterocyte membrane.
3. Invasive AII are characterized by **exudative** mechanism of diarrhea, caused by direct damage to the intestinal tract by the causative agent, activation of inflammatory mediators and excretion of a large amount of exudate (mucus, protein, blood), which increases the volume of fluid in the intestine.

All AII, regardless of **etiology**, have many similar manifestations. It manifests itself as a general infectious (general toxic) syndrome, as well as local symptoms associated with lesions of various parts of the digestive tract (gastritis, enteritis, colitis, gastroenteritis, gastroenterocolitis, enterocolitis). General toxic syndrome in AII in children is manifested in the form of intoxication or toxicosis (more commonly by toxicosis with exicosis), having the nature of non-specific reaction of the body to the infectious agent. Intoxication should be considered as the primary disorder of intracellular metabolic processes, concomitant with the inadequacy of functional state of physiological systems for the elimination of toxic products by the liver, kidneys, lungs, reticulo-endothelial system.

Clinical manifestations of intoxication are lethargy, fatigue, malaise, loss of appetite, sometimes anorexia, temperature reaction, impaired functions of various organs and systems. Intoxication is dominated by metabolic disorders and irritation symptoms of the parasympathetic nervous system. In toxicosis with exicosis, metabolic disturbances are associated with dehydration and electrolyte loss. Depending on the amount of water lost by the body, three levels of toxicosis with exicosis are distinguished:

- minor degree of dehydration, when loss of fluid is up to 5% of the body weight;
- moderate degree of dehydration, when loss of fluid is 5% to 10% of the body weight;
- severe degree of dehydration, when loss of fluid is greater than 10% of the body weight.

The degree of dehydration of the child is determined on the basis of two parameters: weighing the patient with the definition of mass deficiency (or relative to the mass that was on the day before the disease, or relative to that should be a child at this age) and based on clinical manifestations of dehydration.

According to the amount of electrolytes in the blood of patients with exicosis, in particular sodium, which is part of the extracellular fluid of the body and its osmolarity, three types of dehydration are distinguished:

- hypertonic, hyperosmolar, hypernatremic, water deficient type;
- hypotonic, hyposomal, hyponatremic, salt-deficient type;
- isotonic type, without electrolyte disturbances.

Table 14

Clinical evaluation of dehydration

Parameters	Degree I	Degree II	Degree III
Weight loss	0-4%	5-9%	10% та вище
Diuresis	insignificantly lowered	lowered	dramatically lowered
Thirst	moderate	dramatically manifested	absent
Skin	unchanged	atonic	folded
Turgor	preserved	lowered	significantly lowered
Mucous membranes	wet	dry	dry, hyperemic
Fontanelle	physiological	slightly concave	concave
Heart rate	according to the age	moderate tachycardia	embryocardia
Heart sounds	loud	weakened	significantly weakened
Blood circulation	unchanged	minor acrocyanosis	mottled
State of CNS	unchanged	lethargy, agitation	sudden lethargy, loss of consciousness

Monitoring of metabolic disorders is carried out in accordance with changes in acid-base balance parameters, electrolytes and gas composition of venous blood. Clinically, dehydration in each type of exicosis is manifested by the following symptoms, presented in the table.

Hypertonic (water-deficient, cellular) type develops if water loss predominates, which is due to vomiting and liquid serous feces along with hyperthermia and shortness of breath. Water loss is manifested by an increase in the concentration of electrolytes in the extracellular fluid (plasma and interstitial fluid), mainly due to hypernatremia, which leads to fluid transfer into extracellular space to equalize osmotic pressure and the occurrence of intracellular dehydration.

Hypotonic (salt-deficient, extracellular) type of dehydration develops gradually, at later dates in severe forms of AII with domination in the clinical symptoms of multiple vomiting along with diarrheal syndrome. In the increase in the degree of exicosis and loss of electrolytes (mainly potassium), the vomiting is not associated with eating or drinking, containing bile impurities of bubbles, sometimes blood (in the form of "coffee grounds"). Loss of salts is accompanied by a decrease in plasma osmolarity when water and sodium pass from the vascular bed to cells, intracellular hyperhydration develops, a significant increase in the amount of sodium in the cell and a decrease in the amount of potassium, hematocrit is elevated. The volume of plasma decreases, blood thickening occurs, blood circulation slows, hypoxemia, hypoxia, acidosis, microcirculation is disturbed.

In the presence of potassium deficiency in blood serum, lethargy, intestinal paresis, hypotension develops. The standard amount of potassium is 4.5 mmol / l. Metabolic acidosis manifests itself as a clinical symptom: mottled skin, hyperthermia, dyspnea, adynamia, oliguria, disturbance of peripheral circulation.

Isotonic (general) type of dehydration develops when the extra- and intracellular proportional loss of water and electrolytes. Most often occurs at the beginning of AII. Since water and electrolytes are lost in physiological proportions, this condition in the process of treatment is compensated faster than the two previous types of exicosis.

Findings of the study of the level of electrolytes are of differential and diagnostic significance. The degree of exicosis does not always correspond to the severity of the child's condition. Sometimes clinical symptoms in Degree II of dehydration of an isotonic type of exicosis caused hypovolemic disorders in the patient's body.

Rehydration therapy

The basis of treatment of AII in children is timely and adequate rehydration therapy, i.e., compensation of water and electrolyte losses. Proper rehydration therapy is a primary link in the treatment of AIIs, both in secretory and invasive diarrheas. Currently, rehydration is divided into oral and parenteral. To conduct rehydration it is necessary to determine:

1. Daily need in fluid.
2. Type and degree of dehydration.
3. Current pathological losses.
4. Total fluid deficit.
5. Determine the method of rehydration.

I. Determine the degree of exicosis. To do this, you need to know the fluid deficit, which is based on the percentage of weight loss from the moment of the disease to the time of examination (Degree I - reduction in body weight to 5%, Degree II - up to 10%, Degree III - up to 15%). If the mass of the body is not known before the disease, then the degree and type of dehydration are determined by clinical signs. Even easier, in this case, the shortage of fluids should be taken as 10%.

II. Determine the method of rehydration therapy. In exicosis of the Degree I-II. In the absence of uncontrollable vomiting and severe anorexia, the method of oral rehydration may be sufficient.

Oral rehydration (OR)

Oral (peroral) rehydration in AII is the mainstream of treatment, which is carried out at home in the onset of the disease. Timely OR enables effective treatment of most children at home, reduces the frequency of severe forms of exicosis.

1. The following solutions are used: “Glucosan”, “Oralit”, “Gastrolit” - I generation; “Rehydron” - II generation, “Rehidron-optim”; “ORS 200 HIPP” - III generation, “Biogaia-ORS”, “Electrolyte Humana”, “Hydrasek”. Fruit juices, sweet carbonated drinks are notrecommended.

2. Rehydration is carried out in 2 stages:

- Stage I - restoration of the volume of lost fluid: in exicosis of the 1st degree the volume of fluid - 50 ml / kg of body weight, in exicosis of the 2nd degree - 100 ml / kg body weight. Duration of the Stage I is 4-6 hours. Designed for 1 hour of the intake: the volume of the solution is poured into graduated glass; is given to the baby through the nipple, or using pipette, a teaspoon, every 5-10 minutes. In case of refusal to drink or vomiting, the solution is injected through a nasogastric probe drip with a system for intravenous administration at a rate of 10 ml / min. Length from ear to nose + from nose to xiphoid appendix.

Assessment of the efficacy, follow up tactics

a. Rehydration is effective (disappearance of thirst, improvement of tissue turgor, skin elasticity, moisturizing of mucous membranes, increased diuresis, disappearance of signs of microcirculatory disturbance): transition to the second stage (supportive therapy).

b. Rehydration is not sufficiently effective (signs of dehydration persist): continue the similar treatment for another 4-6 hours.

c. Rehydration is ineffective (dehydration increases, vomiting persists, profuse diarrhea, growing symptoms of toxicosis): infusion therapy (parenteral rehydration) by puncture of the peripheral vein or catheterization of the major vein is applied.

- II stage of PR: supportive therapy. If the amount of feces is less than once every 2 hours, or less than 5 ml of liquid feces per 1 kg of body weight per 1 hour, then the volume of the fluid is 5 ml / kg body weight / hour. In severe diarrhea, the volume of the liquid = 10 ml / kg body weight / hour. Estimated volume is distributed evenly within a day.

In order to avoid complications (edema of tissues, decreased diuresis), especially in children with concomitant pathology, neurotoxicosis, caused by colitis, it is reasonable to add strong sweetened (3% sugar) tea, better green tea, with lemon, wild rose decoction, raisin broth, rice, fruit (apple) broth to the half of the liquid intended for administration. During the day of oral rehydration, an increase in the body weight of the patient from 5% to 10% should be achieved.

Contraindications to oral rehydration

- Severe dehydration (body weight greater than 10% and 6% in younger and older children, respectively).
- Vomiting that cannot be stopped within 2 hours of oral rehydration.
- Paresis of the intestine.
- Stupor, coma, infectious and toxic shock.
- Oliguria and anuria that do not disappear during the first stage of rehydration.
- Metabolic alkalosis.
- Ineffectiveness of 24-hour oral rehydration.

In exicosis of the 3rd degree, uncontrolled vomiting, anorexia, refusal of drinking, rehydration therapy begins with parenteral (intravenous) administration of the fluid (infusion therapy), combined with oral rehydration.

Parenteral rehydration (infusion therapy).

1. Estimate the degree of exicosis. If the body weight is not known before the onset of the disease, then its loss due to dehydration is taken at 10%.

2. Determine the type of exicosis. The priority should be given to clinical manifestations prior to laboratory confirmation. Otherwise, the condition can be estimated as an isotonic type of exicosis.

3. Calculate the daily volume of the fluid required for baby (according to J. Dennis method): exicosis of the 1st degree: under 1 year of age: 140-170 ml / kg; 1-5 years of age: 100-125 ml / kg; older children: 75-100 ml / kg.

II degree of exicosis: under 1 year of age:160-180 ml / kg; 1-5 years of age: 130-170 ml / kg; older children:110 ml / kg.

III degree of exicosis: under 1 year of age: 200-220 ml / kg; 1-5 years of age- 170-180 ml / kg; older children: 120-150 ml / kg.

4. Calculate the daily volume of the infusate:

I degree of exicosis - up to 40% of the total daily volume of the fluid;

II degree of exicosis - up to 60% of the total daily volume of fluid;

III degree of exicosis - up to 80% of the total daily volume of fluid.

In case of pneumonia in a child, the volume of the infusate should not exceed 50% of the required daily volume.

5. Calculate the volume and duration of the first infusion (fraction). The calculated volume of the infusate should be administered within 24 hours. However, in the absence of access to the main (subclavian, etc.) veins, the fluid should be introduced into the peripheral veins by fractional method.

I degree of exicosis: the duration is not less than 4 hours, administration of the entire calculated volume (per day) is possible.

II degree of exicosis: duration of infusion (I fraction) is not less than 6 hours, 1/2 of the calculated daily volume of infusate is administered; within 8-12 II infusion (fraction) is performed.

III degree of exicosis: duration of infusion (I fraction) is not less than 8 hours, 1 / 2-2 / 3 of the calculated daily volume of infusate is administered; within 8-12 hours, II infusion is performed.

6. Calculate the rate of infusion.

Volume of fluid in ml / min. = total volume of fluid (ml): (3 × number of hours (minutes) of infusion).

7. Select the solutions, determine their ratio and sequence of their administration.

- The most optimal solutions of crystalloids for parenteral rehydration in young children are 5% glucose solution and 0.9% sodium chloride solution, reosorbilact, xylate, glucosil, stabilizol, refortan.
- Ordinarily, intravenous infusion begins with solutions, the volume of which is equal to

1/3 of the total volume of infusion. The daily volume of solutions is divided into the number of infusions. The dose of the medication for 1 admistration should not exceed 15 ml / kg body weight. Rehydratation of children with exicosis of the I-II degree, accompanied by multiple vomiting, is advisable to carry out with glucose-saline solutions without the use of colloids.

- Similarly, a daily solution of 5% glucose and 0.9% sodium chloride solution is distributed between the fractions.
- In isotonic exicosis, the ratio of 5% glucose solution to 0.9 NaCl solution is 2: 1 (the solutions can be mixed in one vial, and they can be administered simultaneously).
- In hypertonic type of exicosis, the ratio of 5% glucose solution to 0.9% NaCl solution is 3: 1 (if the solutions are not mixed in one vial, infusion begins with glucose solution).
- In hypotonic type of exicosis, the ratio of 5% glucose solution to 0.9% NaCl solution is 1: 1 (infusion begins with NaCl solution).
- The mandatory component of infusion therapy is potassium. In the hypertonic type of exicosis, potassium is introduced into infusion solutions in the form of 7.5 solution at a dosage of 1-2 ml / kg per day; in isotonic and hypotonic one: 3 ml / kg per day. Panangin (asparcam) at a dosage of 1 ml / kg per day can also be administered in such situations. The daily dose of potassium medications is evenly distributed between fractions during 24 hours. Concentration of potassium chloride in infusate is not more than 0,5%. Contraindications to intravenous administration of potassium medications is anuria or pronounced oliguria (less than 20 ml of urine/kg body weight per hour).
- 1 - 10 ml of calcium gluconate solution at a dose of 1-2 ml / kg / day is added in exicosis of the third degree; in pronounced disturbances of microcirculation, toxic, acidophilic breathing, metal disorders 4% solution of sodium bicarbonate at a dosage of 4 ml / kg / day is used. The calculated amount of sodium bicarbonate is divided into 3-4 indroductions and administered intravenously drip with glucose solution.

8. Estimate the effectiveness of the therapy. The correct infusion therapy is accompanied by:

- Liquidation (attenuation) of signs of exicosis in the first 24 hours (criterion is the gain of the body weight by 7-9% within 24 hours).
- Stable improvement of hemodynamics (criterion is normalization of blood pressure, pulse rate).
- Restoration of microcirculation (improvement of complexion, normalization of the body temperature, stabilization of hourly diuresis).
- Improving of the overall health state of the child.

9. Calculate the scope of rehydration therapy in the following days:

- Consider the residual nonrecoverable weight loss.
- Consider physiological **daily need for fluid and its current pathological loss**: in hyperthermia above 38°C a fluid is added at the rate of 10 ml/kg /day; extra 10 ml/kg/ day for every 10 breaths in dyspnea; in vomiting and diarrhea: 20-30 ml/kg/day; in decrease in dieresis: 30 ml/kg /day. Age requirement in water: under 6 months of age: 120-100 ml/kg; 6 months to 2 years of age: 100-80 ml/kg, above 2 years of age: 80-40 ml/kg.

Currently, oral medications, supplemented with Hydrasek at a dosage of 1.5 mg/kg/ body weight are recommended for restoration of the water balance.

Detox therapy

Detox tharpy is conducted in the marked intoxication syndrome and occurrence of infectious toxicosis. In mild forms, the use of solutions for oral rehydration is sufficient. In moderate and severe forms, intravenous administration of 5% glucose solution, 0.9% solution of sodium chloride, colloidal solutions (albumin, reopolyglucin, refortan, stabilizol) in addition to oral rehydration is used. Total volume of infusion is 50-100 ml / kg / day. The ratio of colloids to crystalloids is 1: 2. It is advisable to start infusion with the introduction of colloidal solutions at

single dose up to 20 ml / kg, followed by administration of glucose and sodium chloride solutions in 1:1 ratio. The total volume of fluid, including rehydration, should not exceed 150-160 ml/day.

Enterosorbtion

- ***Enterodes.*** The solution is prepared immediately before use (1 tea spoon of powder dissolves in 100 ml of cooled boiled water). Applied to children per os: under 1 year of age: 20 ml/day, 1-3 years of age: 30 ml/day, above 3 years of age: 50/ml/day. Daily dose is divided into 3-4 intakes.
- ***Polyphepan.*** Produced in powder in a moist form. Infants are prescribed for 1 tea spoon, older children:1 dessert spoon 2-3 times a day.
- ***Smecta.*** Produced in powder in sachets. Before use, dilute with water. Children under 1 year of age is prescribed by 1sachet per day and 2-3 sachets for older children.
- ***Enterosgel.*** Produced in powder. Infants are prescribed with 1 tea spoon and older children with 1 dessert spoon 2-3 times a day, pre-dissolving in 50-100 ml of cooled boiled water.

The above medications are most often used in domestic pediatric practice, rating Smecta the first drug for application, though Atoxil, white coal, etc., is also recommended. Duration of enterosorption in AII is 5-7 days. The criterion for early discontinuation is the normalization of defecation or constipation within 2 days.

Indications for antibiotic therapy in secretory diarrhea are:

- children above 1 year of age with immunodeficiency;
- HIV-infected;
- children who receive immunosuppressive therapy;
- hemolytic anemia;
- cholera in children, regardless the age.

Indications for antibiotic therapy in invasive diarrheas are:

1. All severe forms of the disease, regardless the age.
2. Hemorrhagic colitis, regardless the age of the child and the severity of the disease.
3. In moderate to severe forms in children under 1 year of age.
4. Children above 1 year of age with:
    - immunodeficiency;
    - HIV-infection;
    - immunosuppressive, long-term corticosteroid therapy;
    - hemolytic anemia;
    - shigellosis, amebiasis;
    - bacterial complications and extracellular foci of infection.

The course of antibiotic therapy is 5-7 days; currently, step-by-step regimen (parenteral route of administration for 3 days; enteral administration of macrolides or pro-drugs (cefix) for 2-5 days) is recommended. Antibacterial drugs in moderate to severe and severe forms in combination with sulfanilamides with trimethoprime, cephalosporins of III-IV generations (100 mg / kg cefotaxime, 20-80 mg / kg ceftriaxone) are advisable. In cholera, the drugs of choice are erythromycin, nalidixic acid, nitrofurans, combinations of sulfanilamides with trimethoprim; tetracyclines for children above 8 years of age. In cholera, antibacterial drugs are prescribed after the first stage of rehydration within 3-6 hours after hospitalization. Experts in treatment of diarrhea use immunoglobulins of enteral origin: lactoglobulin anticolitis, anti-rotaviral immunoglobulin, complex immunoglobulin preparation (CIP) for oral use, triglobulin instead of antibiotics or in combination.

Currently, the predominant etiological cause of diarrhea in children is the viruses (rotaviruses, enteroviruses, adenoviruses, etc.). Therefore, taking into account the epididamnesis, clinical presentation and virological study, antiviral drugs (laferobion, arbidol, proteflazid, erebra at a dosage corresponded to age) are required for 5-7 days.

Adjuvant therapy

Treatment of acute intestinal infections required correction of **dysbiotic disorders** of intestinal microbiocenosis with prebiotics, probiotics, symbiotics, prescribing them for 1-2 months, taking into account the coprogram data, the results of the examination of feces for dysbiosis. The most effective probiotics in the intestinal infections are: acidolact (baby, LGG, junior) enterogerminum, prema-kids, laktivit-forte, lactiale, lacticum, enterol, subalin, symbiter (symbiotic), and others.

Fermentotherapy should be conducted based on the coprogram. Detection of increased amount of undigested fiber, muscle fibers in the sample feces confirms the gastric insufficiency of digestion. In this case, medications, containing components of the gastric mucosa, are indicated: Pepsidil, Abomin 1 dessert spoon 3 times a day before meal. Increased amount of neutral fats in the sample feces confirms pancreatic insufficiency of digestion. It is recommended to use pancreatic enzymes: pancreatin at a dosage of 0,1-0,15; 0,15-0,2; 0,2 for children under 1 year of age, 3 years and older children, respectively, 2-3 times a day, within 1 hour after meal. Detection of excess starch, fatty acids in sample feces confirms enteritis insufficiency of digestion. In this case, the use of pancreatic enzymes, in particular, mesim-forte, creon, is reasonable. Unsplit fats and soap of fatty acids, detected in feces of the patient confirms insufficient bile secretion, therefore it is desirable to use medications, containing pancreatin, bile, hemicellulose (dihestal, cadistal, festal, kotazim-forte, panstal, rustal, enzystal).

In AII, induced by fermentation processes in the intestine, excessive gas formation is possible, therefore, in intestinal loops swelling and colics, a decoction of dill leaves, espumizan 25 drops 3-4 times a day after feeding, as well as simethicone, dimethicone, espicol bebi, colikid is recommended.

In invasive diarrhea, some scientists recommend Phosphalugel at a dosage of: from 0 month of age - ¼ of the packet up to 4-6 times a day; from 6 month of age - ½ of the package up to 6 times a day; from 1 year of age - 1 package 1-2 times a day with adsorption and **cytoprotective** purpose.

Symptomatic therapy if necessary.

Acetonemic syndrome (AS).

Acetonemic syndrome is a combination of symptoms caused by the elevated blood ketone bodies: acetone, acetoacetic and β-hydroxybutyric acids.

Pathological changes in the body that lead to the development of AS:

1. metabolic disorders;
2. decrease in glucose assimilation;
3. activation of gluconeogenesis;
4. enhanced lipolysis;
5. increase in the level of free fatty acids;
6. increase in the level of products of decomposition of fatty acids in the blood (acetone, acetone and β-hydroxybutyric acid).

Ketonemia is accompanied by: metabolic acidosis, vasoconstriction, hypovolemia, hypocapnia and hypoglycemia, which leads to irritation of the gastrointestinal mucosa in the form of spastic pain and toxic effects on the central nervous system.

The primary and secondary acetonemic syndrome is distinguished. Primary acetonemic syndrome occurs in children with neuroarthritic diathesis at the age from 2 to 10 years. The following diseases are assigned to the secondary AS: diabetes mellitus, Itsenko-Cushing disease, hyperinsulinism, thyrotoxicosis, infectious toxicosis, craniocerebral trauma, brain tumors.

Clinical presentation of acetoneemic syndrome: cyclic vomiting (1-5 days), dehydration and metabolic intoxication, pale skin, red cheeks, agitation changes with lethargy, drowsiness, signs of pseudomeningitis, haemodynamic disorders, spastic abdominal pain, nausea, constipation or liquid stool, liver enlargement by1-2 cm, low-grade temperature, in the acetone breath. Biochemical blood analysis shows elevated count of ketone bodies, hypochloremia, acidosis, hypoglycemia, hypercholesterolenemia, elevated β-lipoproteids; complete blood count reveals leukocytosis, insignificant increase in ESR.

Precursors of the acetonemic crisis:

1. anorexia;
2. lethargy;
3. agitation;
4. migraine headache;
5. nausea, pain in the parumbilical area;
6. acholic stool;
7. acetone breath.

Treatment of AS

- stomach and intestine lavage with 2% solution of household soda;
- oral rehydration;
- spasmolytics - 10-20 mg drotaverine 3 times a day(for children aged 1-6 years and 20-40 mg drotaverine for older children;
- enterosorbents;
- infusion therapy: 0.9% saline, 5% glucose (1:1), 10 ml / kg reosorbilact, 20 ml / kg xylate (acetone in urine 4+), 20-60 ml / kg glucosyl. The total volume of infusion is 50 ml/kg/day. Supplementary, 5% vitamin C solution 3 ml / day, 50-100 mg / day cocarboxylase; in hypokalemia: 5% potassium chloride 1-3 ml in 100 ml of glucose. In vomiting, 0.1 mg / kg metoclopramide 1-2 times a day for children under 6 years of age; 6-14 years - 0.5-1.0 ml;
- the follow up treatment involves the use of probiotics, enzymes, hepatoprotectors for 1-1,5; phytotherapy, strict diet.

List of questions for the final control:

1. What diarrheas are reffered to secretory ones?
2. What is invasive diarrhea?
3. How to calculate the daily amount of rehydration therapy in AII?
4. What is the physiological need for fluid in a child of 11 months of age?
5. What should be prescribed in salt-deficient dehydration in the child with AII?
6. What is acetonemic syndrome?
7. What are the pathological changes in the body in acetonemic syndrome?
8. What are the urgent measures in acetonemic syndrome in a 2 year-old child (acetone in urine 4+)?

SECTION 13.
VIRAL HEPATITIS

The situation in Ukraine with regard to viral hepatitis (VH) is complicated. The incidence of HAV in children per 100,000 of children population was accounted for 105.8 in the previous years; HBV - 2.95; HCV- 0,53 (data of the Ministry of Health of Ukraine). Mass outbreaks occur in areas where sewer and water supply systems do not meet the state-of-the-art requirements.

The term of viral hepatitis (VH) combines viral liver disease, in addition to hepatitis, caused by the viruses of cytomegaly, herpes, Epstein-Barr and adenoviruses.

Clinical classification of viral hepatitis (Ministry of Health of Ukraine)

1. Etiological types: A, B, C, Д, E, F, G, TT, SEN.
2. Forms: inaparant, subclinical, anicteric, icteric (cytolytic, cholestatic).
3. Cyclicity of the course: acute, subacute, chronic.
4. Degree of severuty: mild, moderate, severe.
5. Complications: acute hepatic encephalopathy (pre-coma, coma); aggravation and relapses (clinical, enzymatic, morphological); functional and inflammatory diseases of the bile ducts and bladder, induction of immunocomplex and autoimmune diseases.

Outcomes: recovery, sequelae (astenovegetative syndrome, posthepatitic hepatomegaly and hyperbilirubinemia).

Peculiarities of HAV pathogenesis

The entrance gate of the infection is the gastrointestinal tract. While penetrating into the small intestine, the virus enters the bloodstream, causing a short-term viremia. With the blood flow, the virus enters the liver, in particular in hepatocytes, where its replication occurs, which is accompanied by a disorder of intracellular metabolic processes and damage to the hepatocyte membrane. As a result of the direct cytopathogenic action of the virus on the liver parenchyma, a syndrome of cytolysis occurs, causing the disorder of all types of metabolism. The causative agent has a high degree of immunogenicity. Along with the auto-allergen protein complexes, isolated from cells, the virus stimulates the T- and B-immune system, causing the formation of specific antibodies, as well as enhancing the mechanisms of autoaggression. Noteworthy, in viral hepatitis A, the protective mechanisms predominate over the mechanisms of autoaggression, resulting in neutralization of viral activity followed up by recovery.

The main syndromes occurred on viral hepatitis:

1. **Cytolysis** occurs as a result of hypoxia, peroxidation on the membranes, activation of anaerobic pathways of metabolism, which leads to the death of hepatocytes (elevation of ALT, AST in blood, etc.).
2. **Hepatocellular insufficiency** is a consequence of hepatocyte deficiency, functional disorders of the liver, coagulopathy of consumption (hemorrhagic manifestations, changes in the coagulogram, proteinuria, lowered cholesterol, urea, prothrombin index, etc.);
3. **Mesenchymal inflammation** is accompanied by the formation of granulomas of productive inflammation, the appearance of coarse proteins (liver ultrasonography, increase of thymol turbidity test and decrease of corrosive sublimate test, dysproteinemia);
4. **Cholestasis** is manifested by jaundice, skin itching, intestinal dysbiosis, decreased fat-soluble vitamins (increased bilirubin, alkaline phosphatase, gammaglutamin transpeptidase);
5. **Portal hypertension** is the result of fibrosis in the portal vein system, which leads to blockage of detoxification function of the liver, the appearance of blood toxins (ELISA, PCR, liver puncture, alternative laboratory methods of fibrosis diagnosis).

Incubation period ranges 7 to 50 days. The onset of the disease is acute and is characterized by cyclicity. Conditionally it is assumed that the acute course of HAV lasts up to 3 months, prolonged course lasts 3 to 6 months and chronic course lasts for more than 6 months.

Inapparent form of viral hepatitis is diagnosed in cases when only specific markers of the pathogen and the corresponding immunological changes are detected.

The subclinical form is characterized by immunological, biochemical and pathological changes, but has no clinical signs.

In anicteric form, in addition to immunological, biochemical, pathological changes, various clinical symptoms appear, with the exception of jaundice.

Icteric form is accompanied by jaundice with marked hyperbilirubinemia.

The prodromal phase ranges 2 to 7 days. Several variants are distinguished: dyspeptic, asthenovegetative, flu-like, arthralgic and mixed.

The dispeptic variant manifests by complaints of loss of appetite, dull pain in the epigastrium and upper right quadrant, low-grade fever lasting for 3-5 days.

The asthenovegetative varian is characterized by mood change, sleep disturbances, headaches, irritability..

The flu-like variant is characterisized by fever lasting 5-7 days, headache, absence of catarrhal manifestations.

Arthralgic variant is less common in children and is manifested by pain in bones, joints and muscles.

An important diagnostic feature of the initial period is hyperfermentemia, as well as elevated ALT at the end of the incubation period, 5-7 days prior to the appearance of jaundice. At the end of the prodromal phase diuresis decreases, dark urine and light-colored stool develop. Almost all patients experience hepatosplenomegaly. The appearance of jaundice sclera indicates the transition to the **icteric phase**. The jaundice grows gradually. First, the sclera, the mucous membrane of the hard palate and the sublingual area, then the skin of the face and the trunk become jaundice. Improvement of the patient's health is observed from the first days after the appearance of jaundice. Children often have abdominal syndrome. The duration of the icteric period lasts 1-2 weeks, and on the average 7-10 days. In HAV infection, bilirubin exceeds the reference values not greater than 4-5 times, mainly due to the bound fraction. The amount of bilirubin in the urine increases in parallel with the increase in the level of bilirubinemia. On the contrary, the content of urobilin in urine, which was sharply elevated on the onset of jaundice, declines and even disappears at the peak of jaundice, and then increases again in its subsiding. At the peak of jaundice, the reaction of feces to stercobilin is negative. These data on changes in bilirubin metabolism are important for the icteric form of HAV infection.

The content of total protein in the blood decreases only on the peack of the severe form of illness (lowered albumin, but the concentration of gamma globulins increases). The presence of dysproteinemia can be established with sedimental tests: thymol and sublimate. In viral hepatitis, the rate of thymol test is increasing, while the rate of sublimate test decreases. The rates of alkaline phosphatase also increase. Complete blood count reveals leukopenia, lymphocytosis, eosinophilia, thrombocytopenia, and slow ESR. The final diagnosis of hepatitis A can be confirmed by specific immunochemical (ELISA, radioimmunoassay) or molecular-biological (PCR) methods. The main markers of the NAV-infection include antibodies to the classes of immunoglobulins M, G to the virus (anti-NAV-IgM, anti-NAV-IgG), NAV-Ag virus antigen, viral RNA (HAV-RNA).

In clinical practice, detection of the anti-NAV-IgM to the virus capsid is the most common. Its detection indicates a course or a recent infection. These antibodies appear in the blood serum even during the pre-icteric phase, 3-5 days prior the first symptoms that circulate for several months (sometimes 6-12 months, indicating delaying convalescence in hepatitis). Anti-NAV-IgG class antibodies appear later, but in significantly higher titres. Their appearance indicates the end of the infectious active process, the body's sanation and circulates for life, providing life-long immunity. Detection of NAV viral antigen is not commonly used in clinical practice. The peak of virus excretion is observed in the incubation and pre-icteric periods when it can be isolated in feces, less frequently in the blood. RNA of viruses can be detected in the blood and feces of patients. The detection of NAV-RNA indicates not only the presence of the virus, but also its active replication. The method is highly sensitive.

The period of convalescence ranges from 1-2 months to a year or more. The state of the patient is characterized by slow improvement and attenuation of clinical symptoms: appetite

appears, jaundice disappears, light urine, darkening of the stool, normalization of the size of the liver and the spleen. Sometimes the first sign of recovery is polyuria, when diuresis increases by 2-4 times. But in many convalescents, asthenic syndrome, heaviness in the right upper quadrant and epigastrium persist, especially after eating. Then the reverse dynamics of functional changes in the liver develops.

Viral hepatitis A can resolve with:

- recovery with full regeneration of liver structure;
- multiple complications in gastrointestinal tract and bile-excreting ducts.

Contact children are not subject to isolation, though medical surveillance is established for 35 days. For this period, children are not transferred to other groups or childcare centers. Newly come children are accepted only with the consent of the epidemiologist in timely introduction of gamma globulin.

Outpatient surveillance over convalescents lasts 6 months. 10 days after the discharge from the hospital, a biochemical study of blood on bilirubin and transaminases is conducted. Repeated check-up and lab tests are carried out within 3 and 6 months.

Specific prophylaxis in Europe and the USA is carried out with a recombinant and plasma vaccine for children aged 12 months or older. In Ukraine, vaccination against hepatitis A is not carried out. For prophylaxis by epidemic indicators, immunoglobulin with a high titre of antibodies to the hepatitis A-1 virus: 10000 and above is used. The drug is used no later than 7-10 days after contact with children over 1 year old and pregnant women.

VIRAL HEPATITIS B (HBV)

Viral hepatitis B is acute infectious disease of the liver caused by a DNA-containing virus from the family of hepatinaviruses, characterized by varying degrees of severity of the course, from asymptomatic to fulminant forms, has a tendency to exacerbation, cholestasis with a slower rate of recovery of the liver function and the possibility of formation of chronic hepatitis and liver cirrhosis.

Etiology and Epidemiology

The reservoir of infection is a sick person and virus carriers. HBV patients are infectious already in the incubation period, ranging from 1.5 to 6 months. The susceptibility to HBV is almost 100%. A stable life-long immunity develops after the past disease.

Features of the pathogenesis

The entry of infection is blood vessels, damaged skin, mucous membranes. The virus penetrates into the body and fixes on hepatocytes and cells of the reticuloendothelial system. Upon virus replication (reproduction), it enters the bloodstream. Hepatitis B is considered a disease of immunity. In HBV replication, cytolysis of hepatocytes, which carry T-lymphocytes and K-cells, occurs. The death of hepatocytes is associated with cytotoxic and humoral immune responses aimed at eliminating (destroying) the virus from the body. Destruction of infected hepatocytes is accompanied by a massive release of viral antigens, which leads to the accumulation of antibodies primarily anti-HBc and anti-HBe. The formation of immune complexes, phagocytosis by macrophages and excretion by kidneys occurs. The major patients experience detoxification of the body from the virus and recovery.

Clinical presentation

The incubation period lasts from 40 to 180 days. The initial (prodromal) phase lasts from 3 days to 3 weeks on the average of 7-14 days. The onset of the disease is usually staged. The most common variants of the prodromal phase of the hepatitis B are:

- dyspeptic (abdominal) (40-60%), characterized by anorexia, aversion to food, right upper quadrant and epigastric pain, flatulence, diarrhea or constipation;
- arthralgic (20-35%), manifested by pain in large joints, often at night and in the morning, without changing their configuration and skin color over the joints;
- allergic (10-12%) with appearence of urticaria on the skin, which is present for 1-2 days and accompanied by eosinophilia in peripheral blood;
- astenovegetative (malaise, fatigue, lethargy, sweating, headache);
- flue-like (low-grade fever, coryza, sore throat, dry cough).

Icteric phase lasts for 3-4 weeks and is characterized by the severity and stability of clinical manifestations. The transition of the prodromal phase into icteric phase is accompanied

by subictericity of the mucous membranes, primarily of the soft palate, sublingual area and sclera, with a threshold concentration of bilirubin in the blood of more than 20 μmol / L. Within 1-3 days, the skin gradually darkens, the urine becomes dark, the feces become acholic, which occurs in hyperbilirubinemia greater than 30-35 μmol / L. The jaundice reaches its peak at 2-3 week and late.

During this period in the clinical picture of the disease the following syndromes predominate: pain, dyspepsia, astenovegetative; approximately 20% of patients develop or intensify skin itching, hemorrhagic syndrome is possible. All patients experience moderate hepatomegaly. Liver is smooth, slightly dense consistency, moderately sensitive in palpation. Splenomegaly is possible; positive gall-bladder symptoms.

In the peripheral blood in the acute period, leukopenia is determined with lympho- and monocytosis, and sometimes with a plasma reaction. ESR is lowered to 2-4mm / h, during reconvalescence can accelerate to 18-24mm / h, with subsequent normalization in the absence of complications.

Hyperbilirubinemia is pronounced and persistent, often at the 2-3 week of jaundice, the level of blood bilirubin is higher than at the first one. Ordinarily, a rather manifested increase in the activity of aminotransferase in blood serum is observed in the declined sublimate test and prothrombin index. Normalization of the activity of aminotransferase commonly occurs at a in the mild course before the 30 -35 day of illness, in moderate form before 40-50 day, in severe form before 60-65 day.

In viral hepatitis B, all biochemical syndromes of liver damage can be observed: cytolytic, cholestatic, mesenchymal-inflammatory, in severe course, insufficiency of protein-synthetic function of the liver develops.

In HBV infection with cholestatic syndrome along with intensive cytolysis (high aminotransferase activity, dysproteinemia, positive thymol turbidity test, low values of the prothrombin index), in the course of the icteric period, signs of cholestasis (itching of the skin, hyperbilirubinemia, elevated alkaline phosphatase activity, biliary blood increase acids, phospholipids, B-lipoproteins, cholesterol.

The period of convalescence lasts for 3-6 months and more. Slow disappearance of clinical and biochemical symptoms of the disease is observed. From the functional tests, the blood bilirubin normalizes the fastest. ALT activity index normalizes slowly.

In severe course of HBV infection, signs of liver failure and progression of necrotic processes in the liver is growing. The severity of the course of acute hepatitis B can be determined by fulminant hepatitis, cholestatic syndrome, rarely by edema-ascites syndrome, aplastic anemia.

HBV should be differentiated from other viral hepatitis by the following criteria:

- short acute prodrom, possibly with fever;
- prominent intoxication, sleep disturbances, anorexia, nausea, repeated vomiting are characteristic in the initial phase of the icteric period;
- intense jaundice with rapid acceleration;
- “scissors”-symptom between the prominence of intoxication and jaundice and small dimensions of the liver;
- the liver is soft, small, tender (due to necrosis);
- prominent hyperemia in the incteric period without apparent cause;
- tachycardia, hypotension;
- early development of hemorrhagic syndrome (hemorrhagic rash, bleeding, hemorrhages);
- skin itching disappears (impaired bile acids synthesis);
- lab criteria: low prothrombin, low total protein and albumin, low cholesterol and β-lipoproteins, altered no-congugated/conjugated bilirubin ratio (1:1 and greater), neutrophilosis, aplastic anemia in the peripheral blood;
- presence of the HBs Ag, HBe Ag, Anti-Hbc IgM markers.

In prolonged forms of HBV clinical and biochemical manifestations of the severity of the disease, and especially the period of regression last from 3 to 6 months. These forms can be the pre-stage of chronic hepatitis. Chronic HBV infection in most cases has a clinically smooth

minor symptomatic course. The diagnosis is often initially established on the basis of laboratory results from non-specific biochemical parameters that reflect disorder of the functional state of the liver, moderate increase in ALT, diminished prothrombin index, dysproteinemia, minor increase in ESR. The severity of the cytolytic syndrome corresponds to the activity of viral replication.

An important criterion for assessing the course of chronic hepatitis is the characteristics and frequency of exacerbations, which may be caused by intercurrent illnesses, inadequate diet. The most common symptom of exacerbation is an increase in ALT ("biochemical exacerbation" in the absence of clinical signs).

The outcomes of the HBV can be:

- recovery;
- sequela: astenovegetative syndrome, posthepatitic hepatomegaly (hepatosplenomegaly), posthepatitic hyperbilirubinemia (manifestation of Gilbert's syndrome), prolonged convalescence;
- chronic hepatitis;
- dyskinesia and lesion of the biliary tracts;
- cirrhosis;
- primary liver cancer;
- chronic virus-carriage.

Specific prophylaxis

Active immunization is made using a recombinant hepatitis B vaccine: on the first day of life, on 1, 6 months, revaccination should be performed every 5 years.

Passive immunization is carried out using immunoglobulin with a high titre of antibodies to HBsAg (1:100000 – 1:200000). Passive immunization is recommended for:

- children born to mothers-carriers of HBsAg or with the history of HBV at the last trimester of pregnancy (postpartum, 1, 3, 6 months);
- within the first hours after infectioning and repeatedly following 1 month;
- in long-term threat for infectioning it is advisible to made following 1-3 months.

Outpatient surveillance should be provided for all convalescents with mandatory clinical and laboratory examination during 12 months. Biochemical and serological study (HBsAg) is made within 10 days after discharge from the hospital and following the 3, 6, 12 months.

VIRAL HEPATITIS C (HCV)

Acute viral liver disease caused by a RNA-containing virus from the family of Flaviviridae, genus *Flavivirus*, which has a gradual onset, with a variety of clinical forms - from the non-icteric to the malignant and frequent transition to chronic hepatitis.

Features of epidemiologic process

The source of infection is a patient with acute or chronic hepatitis C. The routes of transmission are parental, possible perinatal infectioning of a newborn from a HCV-infected mother.

Main chains of HCV pathogenesis

1. Virus entering through blood to hepatocytes and blood mononuclears.
2. Multiplication and persistence of virus in tropic organs.
3. Affection of hapatocytes with viral and immune cytolysis. HCV antigens have low immunogenicity; host defense is suboptimal, reinfectioning is possible.

Clinical presentation of HCV

The incubation period ranges from 2 to 52 weeks. *The pre-icteric period* lasts from 5 to 14 days. Initial signs are moderately expressed; signs of intoxication are characteristic; pain in the right upper quadrant pain; the liver is enlarged, tender on palpation and soft. *The icteric period* may last from 2 weeks to 1.5 months. At this time, the mild or moderate intoxication is sustained, liver and spleen are enlarged in 1/3 of patients, ALT rises by 5-10 times, a slight increase in AsAT and thymol turbidity test. A reliable and significant sign is the detection of RNA-HCV. Antibodies to HCV appear at 6-8 weeks from the onset of the disease: anti-HCV-

cor-IgM, HCV- cor-IgG, the latter are revealed by 6-7 years. Chronization of the disease is noted in 70-90% of patients.

VIRAL HEPATITIS D (HDV)

Hepatitis D, also known as "delta hepatitis, is a highly active inflammatory and dystrophic process in the liver, characterized by the moderate and severe course, often transforms into fulminant form, chronic hepatitis and cirrhosis.

Etiology and Epidemiology

Viral delta hepatitis is caused by a RNA-containing virus, the outer coat of which is a superficial antigen of viral hepatitis B HBsAg. This is a defective virus and its properties depend on the helper virus. It is more common in patients with chronic hepatitis B.

The source of infection is patients and carriers of delta infection. The routes of transmission are parenteral and transplacental, as well as through damaged skin.

Specific pathogenesis and clinical presentation

The delta virus has a direct cytotoxic effect on hepatocytes. Two variants of the course of the disease are distinguished: co-infection and superinfection. *Coinfection* is seen in case of simultaneous infectioning with the B and D viruses. The disease progresses in two phases: the first one is the replication and expression of the HB virus, and the second is the replication of the D virus. In blood serum, when coinfected, serological markers of hepatitis B and D are found.

Superinfection is seen when patients with chronic hepatitis B or HBsAg-carriers are infected with delta-positive pathogen. In this case, the combined action of HBV and HDV extends to the liver parenchyma, causing the chronic hepatitis and cirrhosis. Sometimes a chronization of the process occurs in immunosuppression and T-cells deficiency.

Treatment of the acute viral hepatitis

All patients with viral hepatitis should be treated in infectious hospitals. Partial bed rest and strict bed rest is advocated in minor/moderate and severe acute viral hepatitis, respectively. Dietary nutrition is recommended for all patients: diet No. 5 in minor degree; diet No. 5a in moderate and sever degrees. Diet No.5 contains 90-100 g protein, 80-100 g fat, 350-400 g carbohydrates, caloric content is 2800-3000 kcal. Warm dishes are allowed. It is recommended to take food 4-5 times a day, because eating in small portions helps normalize bile excretion and eliminate stagnation in the biliary tracts. To enhance the detoxification function of the body, the daily volume in liquid should be increased to 1.5-2L. Diet No.5a contains smoothed food; the amount of fats is reduced to 50-70 g, and the kitchen salt up to 10-15 g. The patient's diet should be changed after a substantial improvement in the general health condition and reduction of jaundice. During the reconvalescence the diet should be kept until complete recovery, at least 3-6 months after discharge from the hospital. Protocols recommended by the Ministry of Health of Ukraine are used in the treatment of viral hepatitis.

Minor form: basic therapy for 20 days, partial bed rest for 10 days. Diet No.5.

Moderate form: basic therapy for 20 days, bed rest upon the recovery of urine color, followed by the partial bed rest for 2-3 weeks; diet No.5. Peroral detoxification therapy in the volume of 40-50 ml / kg (5% glucose solution, table plain mineral water) with obligatory control of water balance. Enterosorbents for 2 weeks. Multivitamins are recommended. Use of choleretics is rational in the period of reconvalescence.

Severe form: basic therapy for 30 days; bed rest upon the recovery of urine color, followed by partial bed rest for 3 weeks; diet No.5a for 3-7 days (upon coloration of feces), followed by diet No.5. Detoxification therapy: intravenous drop administration of 50-100 ml/kg solutions, 5 ml/kg albumin , 5-10 ml/ kg rheopolyglukin, 5% glucose solution, Ringer's solution, 0.9% sodium chloride solution; enterosorbents for 2-3 weeks; in the presence of cholestasis: the course of 10 mg/kg deoxycholic acid; enzymotherapy for14 days; in the threat of development of fulminant form and children in the first year of life with an unfavorable premorbid background: 1-3 mg/kg prednisolone 4 times a day for 7-10 days. V.F Uchaikin in severe forms of the acute viral hepatitis recommends the following scheme of hormonal therapy with prednisolone: 2-3 mg/kg in 4 intakes for 3 days; 1-1.5 mg / kg in 4 intakes for 3 days; 0.5 mg / kg in 4 intakes for 3 days followed by withdrawal.

In severe cases, a polarizing mixture of 3.7 g potassium chloride, 6-8U insulin, 1 liter of 5% glucose solution is also used.

Taking into account the efficacy, safety, antiviral and immunocorrective effect, as well as antioxidant and detoxification properties, proteflazid at a dosage of 3-10 drops of 3 times a day is used.

Fulminant form: strict bed rest; diet No.5a with restriction of proteins up to 40% per day; intravenous prednisolone at a dose of 10-15 mg / kg per day every 4 hours in equal doses without a night break; detoxification therapy: albumin, rheopoliglukine, 10% glucose solution at a dose of 50-100 ml / kg per day under the control of diuresis; proteolytic inhibitors; 1-2mg / kg furosemide and 1.5g / kg mannitol; 100-300U / kg heparin in the threat of DIC syndrome; antibacterial therapy; preparations of lactulose: duphalac at a dose of 5-20 ml 3 times a day for 14 days; ursodeoxycholic acid 10 mg / kg body weight 1 time per day; extracorporeal methods of detoxification in the ineffectiveness of therapy: plasmapheresis at the rate of 2-3 CBV 1-2 times a day before the exit from the coma; hyperbaric oxygenation is up to 10 sessions; in edema-ascites syndrome: correction of water-electrolyte balance and protein composition of blood: administration of 10-20% solution of albumin, plasma, potassium-retaining diuretics (veroshpiron, triampur, spirolactones).

Interferon-based therapy in hepatitis B and C

Interferon takes a leading position among the antiviral drugs. The main purpose of interferon-based therapy in acute viral hepatitis is to prevent its transformation into chronic one. It is important to select patients for the treatment with interferon. This medication is indicated in children with a high risk of chronic process, in which blood HbeAg, HBV-DNA keep circulating for more than 30 days, as well as oncohematologic patients, HCV children with detected HCV-DNA in the blood, in which HCV-RNA is detected in the blood, high viral load, increased AlAT activity by 5 times and more. Currently, a therapy scheme is as follows: intracutaneous pegylated interferons at a dose of 1.5 mg / kg once a week in hepatitis B and hepatitis C of 2-3 types for 6 months and in hepatitis C of the 1 type for 1 year; immunomodulators: 15 mg / kg rebetol 2 times per day peros; inhibitors of transcriptase: 3-5 mg / kg cefix per day.

Chronic viral hepatitis (CVH)

Currently, the estimated 350 million people globally have chronic hepatitis B and about 200 million have chronic viral hepatitis C. Unfortunately, in Ukraine, the diagnosis of this diseases in children is an accidental discovery rather than a symptomatology, since non-icteric and icteric forms of CVH are accounted for 60-70% and 25-30%, respectively.

The pathogenesis of CVH is based on the inability of the body to eliminate the virus from the liver, the deficiency of the T-link of immunity, interferon is not produced fully, which leads to fibrosis, cirrhosis and portal hypertension. In the development of the clinical picture phases of replication and integration are distinguished.

The main syndromes that occur in CVH are: astheno-vegetative, general intoxication, pain, dyspeptic, icteric, hepatolienal, hemorrhagic, portal hypertension, cytolysis, hepatocellular, hepatic hyperazotemia, immune-inflammatory, pathological regeneration. The most common complications of CVH are cirrhosis, hepatocellular carcinoma.

Risk groups

1. Newborns with the diagnosis of acute viral hepatitis B.
2. Hemophilia.
3. Children with prolonged low-grade fever.
4. Astheno-vegetative syndrome of unknown etiology.
5. Prolonged increase of ALT, AST by 2 times.
6. Blood transfusion in the past history.

CVH can be suspected in children in case of: positive RNA (HCV) or DNA (HBV), patient's age above 2 months old, repeated positive findings within 2-3 months.

Screening of CVH:

- general clinical examination;
- biochemical blood test (liver tests, proteinogram), coagulogram, immunogram;
- alternative methods of fibrosis (fibro-test to detect serum markers of fibrosis);
- detection of antibodies to the antigen of viral hepatitis and viral RNA (ELISA, PCR);
- fibroscopy and liver puncture (4 stages of fibrosis have been established);
- liver MRI;

- abdominal ultrasound.

The findings can indicate about the *activity* of the process:

1. minor (increased ALT by 3-5 times);
2. moderate (increased ALT by 6-10 times);
3. high (increased ALT by 10 times).

The therapy can be postponed to 6 months in CVH genotype 1, absence hepatic inflammation, F_0-F_1 fibrosis, since self-recovery can occur in 40% of sick children. The treatment is mandatory in genotype 2, 3 regardless of ALT/AST indices.

Indication to α-IF in CVH

1. Signs of active replication of the virus.
2. High biochemical activity (increase of activity of AlAT by 1.5 times and more) during 6 months.
3. Histological picture of liver biopsies with signs of activity of the inflammatory process, which are characteristic in CVH.
4. No contraindications.
5. Age of children older than 3years.

Doses of IF-based therapy

In chronic viral hepatitis B combination therapy with lamivudine and IFN-α is prescribed. Lamivudine is prescribed once a day at a dose of 3 mg / kg for 6 months if it is combined with α-interferon, if isolated - within 12-18 months.

IFN-α is recommended for use in children from 12 months of age subcutaneously at a dose of 6.000.000 U/ m^2 three times a week; the recommended duration of treatment in HBeAg (+) hepatitis is 24 weeks, in HBeAg (-) hepatitis - 48 weeks.

IFN-related side effects and their correction in children:

- flue-like syndrome (mainly during the first weeks of treatment);
- leuko- and thrombocytopenia;
- alopecia;
- mental disorders;
- disorders of the thyroid gland (thyroidism);
- weight loss;
- growth retardation.

In cases of Peg-IFN-related hematologic complications (neutropenia less than 1,000 cells / μl; thrombocytopenia less than 50,000 cells / μl), monitoring of the safety of the treatment should be intensified and, if necessary, corrected or discontinued.

Upon completion of interferon therapy for 6 months, complete blood count, liver function tests, level of TTH, DNA HBV, HBeAg/anti –HbeAg should be made 12 weeks.

Lamivudine-based treatment should include:

- study of the liver function tests every 12 weeks;
- the level of DNA HBV monitoring every 12 weeks;
- in HBeAg+ hepatitis detection of HBeAg/anti –HbeAg every 24 weeks of treatment;
- in HBeAg- hepatitis and levels of DNA HBV that are not detected, PCR every 6 weeks
- HBsAg test every 12 mo.

Upon discontinuation of lamivudine, virologic relapse and exacerbation of hepatitis and HBeAg seroconversion may develop within 1 year. Therefore, such patients need to be provided with the control biochemical and virological blood test.

Currently, the **recommended therapy of chronic hepatitis C** in children is a combination of pegylated interferon alfa-2b and ribavirin. **Dosage regimen**: peginterferon α-2b (Peg-IFN) is administered at a dose of 60 μg / m^2 subcutaneously once a week; ribavirin is administered at a dose of 15 mg / kg / day intravenously, the daily dose is divided into two intakes.

Duration of treatment is determined according to the genotype of the virus:

- patients with genotype 2 and 3 chronic hepatitis C received antiviral treatment for 24 weeks;
- patients with genotype 1 chronic hepatitis C should receive treatment during 48 weeks.

Alternative regimens for treating chronic hepatitis C in children can be the use of standard (linear) interferons (IFN) - alpha 2a or 2b at a dose of 3.000.000 IU / m^2 3 times a week for 24 weeks (genotype 2 and 3) and for 48 weeks (genotype 1 and 4) in combination with ribavirin at a dose of 15 mg / kg. Treatment of chronic viral hepatitis C with Peg-IFN is preferable, since standard (linear) interferons - alpha is not always effective, characterized by worse tolerability and inconvenient treatment regimen.

The dosage of ribavirin is dependent on child's body weight:

- 25-36 kg: 200 mg 2 times a day;
- 37-49 kg: 200 mg in the morning and 400 mg in the evening;
- 50-61kg: 400 mg 2 times a day;
- > 61kg: adult dose is used (800-1200 mg/day).

Contraindications for interferon-based therapy of chronic hepatitis C in children

1. Age <3 years.
2. Psychosis, severe depression, epilepsy syndrome (even in the history).
3. Cytopenia (neutrophils <150 in mm^3, platelets <100000 in mm^3).
4. Autoimmune diseases with severe course (hepatitis, thyroiditis, etc.).
5. Renal and hepatic insufficiency.
6. State after transplantation of organs (exept for the liver).
7. Decompensated diabetes mellitus.

Contraindications to prescription of ribavirin

1. Age <3 years.
2. Hypersensitivity to ribavirin.
3. Acute liver and kidney disease.
4. Thyrotoxicosis.
5. Severe heart diseases.
6. Hemoglobinopathies (including thalassemia, sickle cell anemia).
7. Prominent depression.
8. Cirrhosis.
9. Autoimmune hepatitis.

Predictors of the effective antiviral therapy of chronic viral hepatitis C in children

1. Absence of viral genotype 1 and 4.
2. Relatively short (up to 3 years) duration of infection.
3. Increased ALT activity before treatment (1.5-2 of the normal values, but not more than 3 norms).
4. Low viral load (< 600,000 IU / ml).
5. Absence of immunosuppression.
6. Low level of iron in the liver tissue (up to 650 μg / g), normal levels of iron and ferritin in blood serum.
7. Early virologic response (absence or decrease in the level of HCV RNA by 2 log (100 times or more) after 12 weeks of treatment).

The use of an anti-aggregant **dipyridamole** at a daily dose of 1-2 ml of 0.5% solution (children above 12 years of age) intramuscular or intravenously reduces clinical and laboratory manifestations of cryoglobulinemia, regardless of its type. Prescription of **ursodeoxycholic acid** (10 mg / kg) has a poor effect on clinical and laboratory manifestations of cryopathy. In the general scheme of treatment hepatoprotectors (**Berlition, Geptral, Hepa-Merz, Essentiale Forte N, hepabene**), membrane stabilizers, choleretics, enterosorbents, probiotics are used.

Indices of the effective treatment of chronic viral hepatitis

1. Normalization of the AlAT level.
2. Sero-conversion of HBe Ag level to anti-HBe antibody.
3. Clearance of HBV-DNA-RNA.
4. At the same time, it is desirable to eliminate signs of immune imbalance, in particular, the level of total count of lymphocytes in absolute measurements and CD3 (mature T-cells), CD4 (T-helper), CD8 (T-suppressors), CD16 (natural killer), CD21 (B -cells) and changes in the humoral link, mainly IgA.

The following is distinguished in the efficacy of the chronic viral hepatitis therapy:

1. **Primary remission:** 2 subsequent normal rates of the AlAT level during the treatment with the interval of not less than 2 weeks, clearance of RNA HCV or DNA HBV at the end of the therapy.
2. **Stable remission:** normal AlAT, clearance of RNA HCV or DNA HBV within the 6 months after finishing the therapy course.
3. **Prolonged remission:** normal AlAT rates, clearance of RNA HCV or DNA HBV within the 24 months after finishing the therapy course.
4. **Relapse:** during 6 months of treatment after normalization of AlAT level and its increase (2 subsequent tests with the interval of 2 weeks), recurrent appearance of RNA HCV or DNA HBV after its clearance.
5. **Partial remission:** normalization of AlAT level, decline in viral load.
6. **Absence of remission:** elevated AlAT level, presence of RNA HCV or DNA HBV in blood at the end of the therapy, but not earlier than 3 months of treatment.

The side effects the interferon-based therapy: flu-like syndrome, loss of appetite, stunt, seizures, thrombocytopenia, leukopenia, alopecia, etc.

Outpatient surveillance should be provided for all convalescents with mandatory clinical-laboratory and instrumental examination. Biochemical and serological study is made within 10 days after discharge from the hospital and following the 1, 3, 6, 12 months for 5 years.

List of questions for final control:

1. What is viral hepatitis?
2. What are the main patterns of epidemiology of hepatitis A, B, C, D, etc. in children?
3. What is the clinical course of hepatitis A, B, C, D in children?
4. What is the lab diagnosis in suspicion of hepatitis A, B, C, D in children?
5. What are the treatment and preventive measures of hepatitis in children?

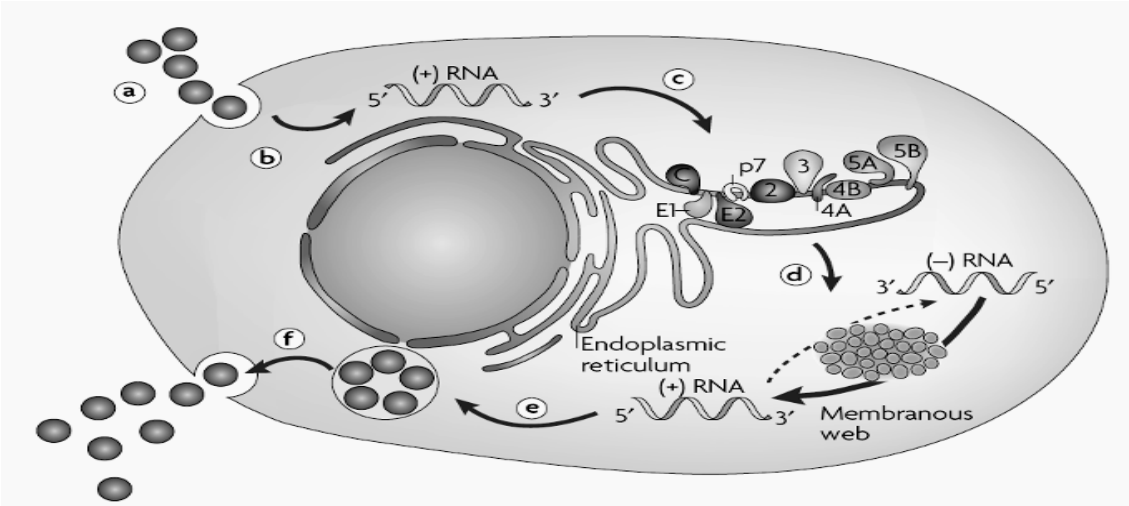

Fig. 10. HCV structure

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CONTROL TESTS

1. What is the pathogen of measles?
    a. Group A β-hemolytic streptococcus.
    b. Virus of the family *Flaviviridae*.
    c. The virus of the group of mixoviruses, contains RNA.
    d. Shigella flexneri.
2. Which complication is not characteristic for measles?
    a. Encephalitis.
    b. Pneumonia.
    c. Croup.
    d. Cholecystitis.
3. What type of vaccines does measles vaccine belong to?
    a. Killed bacterial.
    b. Living viral.
    c. Chemical.
    d. Combined.
4. What is the pathogen of chicken pox?
    a. Varicella-Zoster virus.
    b. Group A β-hemolytic streptococcus.
    c. Mycoplasma.
    d. Epstein-Barr virus.
5. What age do children not commonly have chicken pox?
    a. Under 3 months old.
    b. Under 6 months old.
    c. Under 1 year old.
    d. Under 1 month old.
6. What dynamics of the elements is characteristic for chicken pox?
    a. Roseola-papule-pigmentation.
    b. Roseola-papule-pustula-crust.
    c. Roseola-ecchymosis-necrosis-scar.
    d. Roseola-papula-vesicula-crust.
7. Which complication is not characteristic for chicken pox?
    a. Quincke's edema.
    b. Encephalitis.
    c. Erysipelas.
    d. Stomatitis.
8. What period does the chicken pox patient should be isolated?
    a. On day 21 from the onset of the diseases.
    b. Before day 3 after the appearance of the last elements of rush.
    c. Until complete crusts' fall off only.
    d. Until day 5 after appearance of the last elements of rush.
9. What is the pathogen for herpes zoster?
    a. Filtrating virus.
    b. Varicella-Zoster virus.
    c. Pneumocystis.
    d. Mycoplasma.
10. Which of the forms of poliomyelitis, listed below, is the mildest?
    a. Pontile.
    b. Bulbar.

c. Meningeal.
d. Inapparent.

11. What regions of CNS are mainly affected by the pathogen of poliomyelitis?
    a. Nuclei of motor cranial nerves.
    b. Meninges.
    c. Motor cells of the ventricornus.
    d. All listed regions.
12. What is the management of poliomyelitis in child care facilities?
    a. Immediate vaccination of children, not vaccinated against poliomyelitis.
    b. No immediate vaccination is carried out.
    c. Immediate single-time vaccination of all contact children.
    d. Immediate vaccination is made for children with low titer of specific antibodies.
13. What is the normal rate of protein amount in the cerebrospinal fluid?
    a. 0,5-1,1 g/l.
    b. 0,06-0,45 g/l.
    c. 1,0-3,3 g/l.
    d. 1,5 16,0 g/l.
14. Which of the rates of cytosis are characteristic for normal liquor?
    a. $0,001\text{-}0,01*10^9$ /l, neutrophils.
    b. $0,1\text{-}1,1*10^9$ /l, neutrophils.
    c. $0,001\text{-}0,01*10^9$ /l, lymphocytes.
    d. $0,03\text{-}0,06*10^9$ /l, lymphocytes.
15. What is glucose concentration is characteristic for normal liquor?
    a. 2,2-4,4 mmol/L.
    b. 1,1-2,2 mmol/L.
    c. 4,0-5,5 mmol/L.
    d. 3,5-4,5 mmol/L.
16. What is the normal pressure of the liquor (in mmHg)?
    a. 200-300.
    b. 200-500.
    c. 120-180.
    d. 220-410.
17. Which of the listed below is not characteristic for diphtheritic croup?
    a. Acute abrupt development of stenosis.
    b. Aphonia.
    c. Periodic whooping cough.
    d. Gradual development of laryngostenosis.
18. Which of the listed below is the most dangerous complication of diphtheria?
    a. Paresis of the soft palate.
    b. Myocarditis.
    c. Polyradiculoneuritis.
    d. Stroke.
19. Which of the listed below is not common in diphtheritic croup?
    a. Myocarditis.
    b. Hoarseness, transforming into aphonia.
    c. Whooping cough.
    d. Growing stenotic breath.
20. Which stage is not characteristic for the development of diphtheritic croup?
    a. Croupous cough (dystonic).
    b. Stenosis.
    c. Asphyxia.

d. All abovementioned are characteristic.

21. Which of the listed below regarding Simanovsky-Vincent's tonsillitis is not correct?
    a. It is necrotizing ulcerative tonsillitis.
    b. After sloughing a funnelform ulcer remains.
    c. One tonsil is affected.
    d. Prominent edema of the cervical cellular tissue is noted on the affected side.
22. Which of the listed symptoms is not common in scarlet fever?
    a. Prominent intoxication.
    b. Fine-maculated on hyperemic skin.
    c. Limited hyperemia of the pharynx.
    d. Prominent edema of the tonsils, subcutaneous cervical cellular tissue.
23. Which of the listed below is not the portal of entry in scarlet fever?
    a. Mucous membranes of the external genitalia in girls.
    b. Oropharyngeal mucosa.
    c. Wound surface.
    d. Burn surface.
24. Which disease occurs in child in contact with group A β-hemolytic streptococcus?
    a. Erysipelas.
    b. Tonsillitis.
    c. Scarlet fever.
    d. Pneumonia.
25. Which of the listed symptoms is the most characteristic at the onset of meningococcal meningitis in children of the first months of life?
    a. Significant rise in body temperature.
    b. Nuchal rigidity.
    c. Vomiting not associated with eating.
    d. Clonic-tonic seizures.
26. Which of the listed symptoms of meningitis is not characteristic in children of the first months of life?
    a. Opisthotonos.
    b. Bulging of fontanel.
    c. Kernig's symptom.
    d. Convulsions, tremor.
27. Which of the listed antibiotics is considered the most effective in treatment of meningococcal meningitis?
    a. Benzylpenicillin sodium salt.
    b. Levomycetin sodium succinate.
    c. Gentamicin.
    d. Ceftriaxone (longaceph, rocephin).
28. Which of the listed corticosteroids has a prominent mineralocorticoid activity (promotes fluid retention in tissues)?
    a. Prednisolone.
    b. Methylprednisolone.
    c. Dexamethasone Дексаметазон.
    d. Triamcinolone.
29. Which of the listed signs of rush is not characteristic for rubella?
    a. Extensor surfaces of the extremities, back and buttocks are mostly covered.
    b. Fine blotchy rush, pink-pale, 2-4 mm in the diameter.
    c. The staging is characteristic for rush appearance (day 1: on the face; day 2: on the trunk; day 3: on the extremities).

d. Appears on day 1-2 of the disease on the neck, face, proliferates on the whole body within few hours.

30.Revaccination against rubella is made:

a. At the age of 15-16 years for girls only.
b. Before school enrolment.
c. At the age of 15-16 years to all children without exception.
d. Within 1,5-2 after vaccination.

31.Which of the listed viruses is not assigned to the family of herpesviruses.

a. Respiratory syncytial virus.
b. Cytomegalovirus.
c. Chickenpox virus.
d. Epstein-Barr virus (causes infectious mononucleosis).

32. Which of the listed below is not characteristic for the typical form of infectious mononucleosis?

a. Puffy face and swollen eyelids.
b. Skin rushes of various etiology.
c. Rushes of various nature on the oral mucosa.

33.Which of the listed symptom are not involved into basic complex of symptoms of infectious mononucleosis?

a. Enlargement of all groups of lymphnodes, especially of the cervical group.
b. Edema of the cellular tissue of the neck.
c. Affection of the naso- and oropharynx.
d. Hepatosplenomegaly.

33. Which of the listed infections has the highest susceptibility in neonates?

a. Measles (Morbilli).
b. Rubella (Rubeola).
c. Whooping cough (Pertussis).
d. Chickenpox (Varicella).

35.What is the contagiousness index in pertussis?

a. 0,15 (15%).
b. 0,40 (40%).
c. 0,75 (75%).
d. 1,0 (100%).

36.Which is from the listed below is not characteristic for clinical presentation of pertussis in infants of the first year of life?

a. Shortened incubation period.
b. Shortened or absent catarrhal phase.
c. Significantly prolonged catarrhal phase.
d. Significantly prolonged spastic phase.

37.Which of the listed below is the most characteristic and common form of parainfluenza sequela?

a. Stenosing laryngotracheitis (croup).
b. Obstructive bronchitis.
c. Bronchiolitis.
d. Interstitial pneumonia.

38.Which of the listed below is not assigned to bacterial complications of, occurred mainly in children of the young age?

a. Otitis.
b. Pneumonia.
c. Myocarditis.
d. Pyelocystitis.

Situational task № 1

The boy is 14 years old. The disease began with fatigue, malaise, headache. The following day, the body temperature increased to 39.7 ° C, the overall health state became worse with nausea, vomiting, myalgia, severe pain in the scrotum with irradiation in the right inguinal region, which intensified in walking. Physical examination showed the severe patient's state with fatigue, severe headache, nausea, complains of pain, heaviness in stomach, severe pain in the scrotum. On examination: the skin on the scrotum is tense, shines, red cyanotic, vasodilation, swollen veins, the right testicle is significantly enlarged in size, sharply painful on palpation; at the same time, a dense, enlarged, painful epididymis is palpated. Additional examination revealed tenderness in chewing in the left parotid area. At the same site a swelling, located in front of the ear, under the earlap and behind the auricle was detected. The skin above the swelling is tense, moderately shiny, of normal color. Swelling is palpably tender. Filatov's pain spots are determined. Oral check up showed a positive Mursu-symptom. Internal organs showed no pathological changes. Meningeal signs are absent.

1. Make a working diagnosis.
2. Prescribe treatment.
3. What is the specific prevention of this disease?

Situational task № 2

The child is 1 year and 2 month-old. Day 1 of the illness. Acute onset with the increase in body temperature to 40°C. Mother relates the diseases to teething, as "the child always put the hands into the mouth." The child is very agitated, irritated, refuses to eat, more precisely, starts eating quite willingly, but immediately cries and pushes food. On examination: the skin is clean, of normal color. On the mucous membranes of the lips, cheeks, gums, tongue, against the background of hyperemia and edema, there are sporadic fine vesicles and erosions (aphthae). Salivation is significantly elevated. Enlarged and tender submandibular lymph nodes are palpable. Percussion over the lungs reveals pulmonary sound. Auscultatory: puerile breathing. Heart tones are rhythmic, clear. Abdomen is soft, painless on palpation. The liver, the spleen is not palpable. Feces are normal.

1. Make a working diagnosis.
2. Name the most probable source of infection and its rout of transmission.
3. Name the method of prompt diagnosis of this infection.
4. Make up the treatment regimen of the patient.

Situational task № 3

The boy is 15 years old. The disease began with an increase in body temperature to 37.3-37.6°C, malaise, headache, sore throat. The next day the health state deteriorated, the temperature rises to 38.5 º C, catarrhal events intensified, rash appeared on the skin. Physical examination of the patient (2^{nd} day of the disease) showed the moderate state of health, complaints of severe headache, myalgia, moderate weakness, loss of appetite, swelling and pain in the metacarpophalangeal joints of both hands. On the skin of the face, trunk and extremities is abundant rash. Its predominant localization is the face, neck, back, buttocks, extensor surfaces of the hands, and the outer surfaces of the thighs. Elements of rashes are red, blotchy, maculopapular, fine, equal in size, round or oval, have no tendency to fuse. Injection of vessels of sclera and conjunctiva is prominent. Oral mucosa is unchanged. Moderate hyperemia of the pharynx, elements of fine blotchy enanthema on the soft and hard palates is

detected. Occipital, parotid and posterior cervical lymph nodes are significantly enlarged and painful. Coryza and cough is insignificant. Internal organs revealed no pathological changes. Feces are normal.

1. Make a working diagnosis.
2. What hematological changes are characteristic for this infection?
3. Name the methods of prevention of this infection.

Situational task № 4

The baby is 7 months old. The onset of the disease is acute with a rise in body temperature to 40.3°C and worsening of the health state. The past history reveals abnormal constitution of the child from the first weeks of life in the form of exudative catarrhal diathesis with the phenomena of eczematization, mainly on the face, with frequent relapses. The condition of the child quickly deteriorated; listlessness, frequent vomiting, clonic seizures short-term loss of consciousness was noted. Skin of the face, neck, chest abundant vesicular rash appeared. Everything happened during the first day of the illness, in connection with which the child was urgently hospitalized. On examination: the child's condition is very severe; listlessness, lethargy, vomiting, short-term clonic seizures. On the skin of the face, neck, chest is abundant vesicular rash with the highest concentration in the sites of eczema. Vesicles are small in size (1-3 mm), filled with clear liquid, some even confluence. Enlargement of the submandibular, cervical and groin lymph nodes is apparent. Internal organs revealed no pathological changes. Feces are normal.

1. Make a working diagnosis.
2. Name the most probable source of infection and its rout of transmission.
3. Name the method of prompt laboratory diagnosis of the infection.
4. Make up the treatment regimen of the patient.

Situational task №5

A female child is 5 years old, attends a kindergarten, fell ill in the winter. The disease began with a low-grade fever, infrequent dry cough, coryza. During the next 2 days, the child's condition worsened, body temperature increased to 38.1°C, lethargy, loss of appetite occurred, catarrhal events intensified. Physical examination (on the 3rd day of illness), the child complains of headache, abdominal pain, heavy nasal breathing, coughing, "burning in the eyes". Skin is moderately pale and clean. The face of the patient is somewhat edematic, the eyelids are moderately swollen, with little purulent discharge from the right eye, abundant nasal mucous discharge; the mouth is almost always open. Submandibular, cervical, occipital, axillary, groin lymph nodes, enlarged to the size of the pea or bean, are palpable; they are elastic, painless. Oral mucosa is unchanged. Oropharynx checkup showed hyperemia and swelling of the front arches and palatine tonsils; the posterior wall of the pharynx is swollen and hyperemic, hyperplasia of the follicles, enlargement of the lateral cushions; tender whitish coatings, thick mucus draining from the nasal cavity are detected on the follicles. Conjunctivae are sharply hyperemic, swollen, even granular. Eyelashes of the right are stuck together from pus. The cough is quite frequent, productive. Respiration rate is 24 breaths per minute. Percussion findings revealed pulmonary sound over the lungs. Auscultatory: harsh breathing, minor scattered damp and dry wheezing. The chest X-ray data are presented in Fig.11. Heart rate is 96 beats in 1 minute. The heart borders are according to the age. Heart tones are sound, rhythmic. The abdomen is soft, painless on palpation. Liver + 1.5 cm, spleen + 1 cm, dense, painless. Urinary excretion is normal. Feces is up to 3 times a day: loose stool, without pathological impurities. Meningeal symptoms are not present.

1. Make a working diagnosis.
2. Name the method of express-diagnosis of this infection.
3. Prescribe the treatment.
4. Name the preventive measures of this disease for health care professionals.

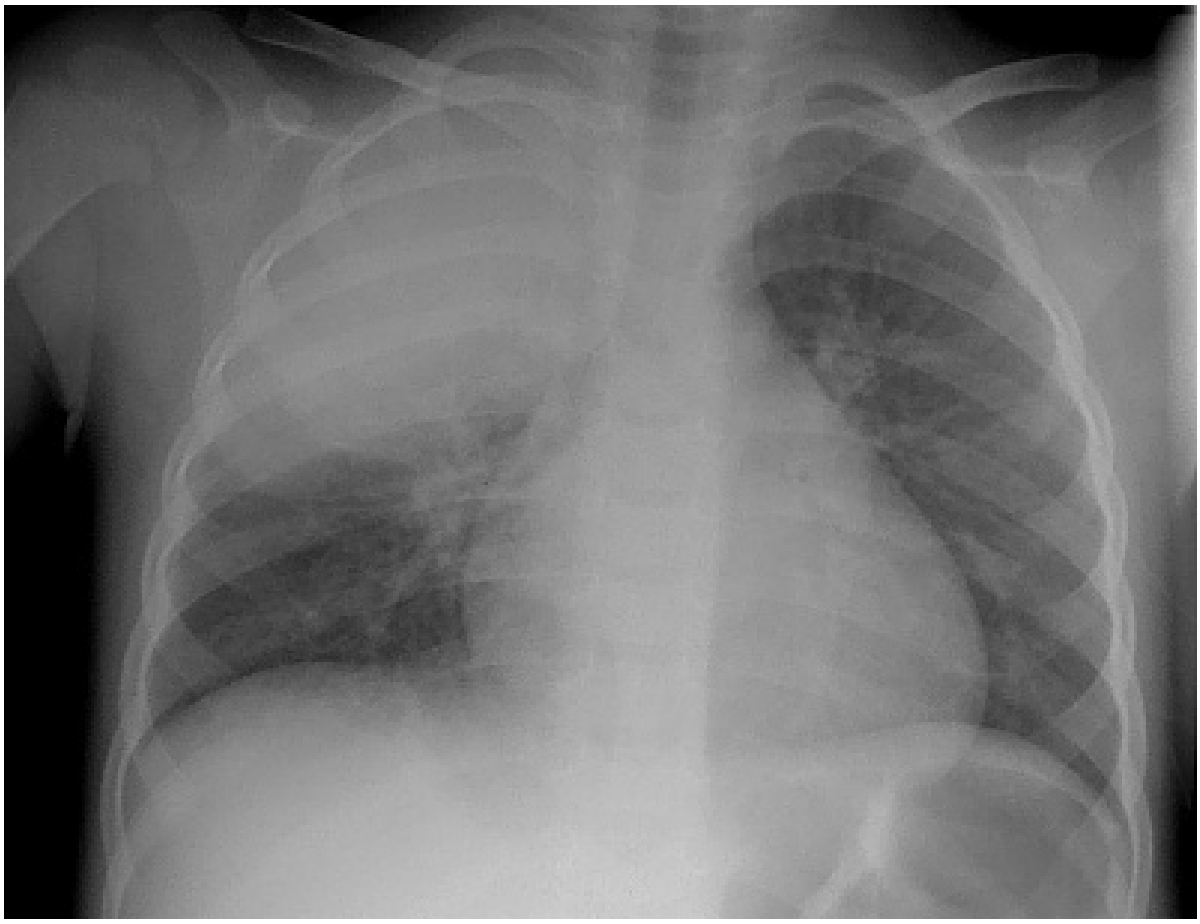

Fig. 11. What are the changes on the radiograph?