

ZAPOROZHYE STATE MEDICAL UNIVERSITY
DEPARTMENT OF CHILDREN'S INFECTIOUS DISEASES

INFECTIOUS DISEASES in CHILDREN

Educational aid for students in the 5 years of study having higher medical
education in English

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GENERAL INFORMATION

Infectious diseases are a group of diseases, which are caused by bacteria, viruses, Protozoa, etc. A common trait for the majority of infectious diseases is the possibility of transmitting them from one infected patient to a healthy person in certain conditions.

The ancient manuscripts and archives, excavations of ancient places give evidence of death of millions of people due to the infectious diseases, they accompanied such social disasters as wars, revolutions, famine, etc. Infectious diseases led and are still leading to great economic expenses. But is practically eradicated poliomyelitis, measles and others has considerably decreased.

In children's pathology, the infectious diseases draw the main attention. There is a great variety of acute respiratory viral infections and their numerous complications.

Nowadays, the evolution of infectious diseases in children is a problem that worries our scientists. We may point out *common clinical peculiarities of modern infectious diseases*: less severe clinical manifestations; rarity or decrease of malignant forms (dysentery, scarlet fever, etc); more frequent cases of mild forms, growth of the amount of atypical forms (scarlet fever, whooping cough, dysentery, etc); reduction of complication cases. There are changes in the epidemic process too; in the age structure of the disease, in periodicity and season, in spreading activity, reduction in epidemic districts (locations).

Periods of Infectious Disease Course

The essential feature of infectious diseases is their specificity conditioned by the peculiarity of the causative agent and protective reactions, first and **ibremost** the immunological reactions of the body. Clinically, acute epidemic diseases are characterized by a cyclic course and subsequent succession of disease periods and their more or less defined duration. There are the following periods of an infectious disease: incubation (latent), prodromal, full development and convalescence.

Incubation period begins from the moment of entry of the causative agent into the body and ends with the appearance of the first signs of the disease. In each infection, it has a certain duration, which may change depending on the individual peculiarities of body reactivity and, to some extent, on the dose of the infectious agent.

The precursor period (prodromal period) is observed in all infectious diseases. Nonspecific signs of the disease characterize it.

The period of full development of the disease is manifested by maximally marked causative agent activity, different physiological dysfunctions, and development of pathological changes in organs. Clinically this period of the disease is characterized by a complex of symptoms characteristic for each infectious disease that appear and follow in a definite sequence. Common signs (fever, development of dystrophic inflammatory processes, intoxication syndrome) are atypical syndromes, while there are typical syndromes as well (such as rash on the skin and mucous membranes, characteristic organ changes, biochemical disorders, etc.).

During the **period of convalescence**, there is a renewal of normal functions of the body and its homeostasis. This period may last for a long time.

Frequently there are mixed infections when two or more causative agents complicate the infectious process.

The clinical forms of infectious diseases are numerous. Manifestations and severity of the disease depend on the properties of the causative agent (its virulence), individual peculiarities of the human's reactivity (age, physical state, former diseases, and influence of the environmental factors).

A considerable decrease of most children's infectious diseases, their successful prevention depends on the clear understanding of the chain link in an epidemic process and skillful influence on the definite links. The **epidemic process** consists of three parts: 1) source of infection; 2) mode of transmission; 3) susceptibility of the human body.

1. Sources of infection are patients with clinically marked forms of infection like; also the patients with attenuated and atypical forms of infectious disease; virus and bacteria carriers.

2. Mode of transmission:

The most infectious diseases characteristic of children's age the transmission is by droplet route. These diseases are measles, rubella, whooping-cough, scarlet fever, epidemic parotitis, etc. The second big disease group is of enteric infection as the main route of contamination is a fecal-oral one. These diseases are dysentery, salmonellosis, typhoid fever, paratyphoid A and B types, escherichiosis, viral hepatitis A. The main syndrome in these diseases is dysfunction of the gastrointestinal tract. Subtypes of fecal-oral route of infection are alimentary, contact and water.

Mixed mode of transmission (droplet and fecal-oral) is observed in poliomyelitis, Coxsackie and ECHO-infections.

In some infections contamination occurs in direct entry of the causative agent into blood when the integrity of skin or mucous membranes is damaged (viral hepatitis B, C, D; HIV-infection).

3. Susceptibility of population depends on many factors connected with peculiarities of macro- and microorganism. Susceptibility is defined by the index of susceptibility or contagion that is correlation of the number of the all people with those in contact.

The condition of the microorganism, its susceptibility to infection is lastly determined, by individual factors of defense. *Specific immunity* is determined by the presence of antibodies specific to different antigens of causative agents in the child's body. Active immunity is formed after the disease is over or after the other form of the infectious process as well as after immunization with vaccines (active natural and active artificial immunity): a newborn gets his passive immunity from the mother via placenta (passive natural immunity). Besides, passive immunity may be forming by the introduction of γ -globulin, antitoxic serum (passive

immunity). Active immunity differs from the passive one by a greater stability, whereas passive immunity acts for a short time.

Age peculiarities of immunity formation are as follows:

1. The younger is the child, the slower and the less is the growth of specific antibodies. At first, antibodies of class M are formed. And later, in the 2nd-3rd month immunoglobulin of class B are formed.

2. Babies have not specific response to bacterial toxins. In the 5th-6th month, there is immunity to antitoxins. This is physiological hypo-activity.

3. Babies have more developed nonspecific factors of defense: systems of complement, properdins are higher than in adults; phagocytosis reaction is completely formed before birth.

4. Only babies have transplacental immunity.

These age peculiarities of immunity influence the course of the infectious disease, which are **differentiated peculiarities:**

a) Due to placental immunity babies are unsusceptible to most viral infectious diseases (measles, epidemic parotitis, poliomyelitis etc). At the same time therefore such diseases as dysentery, whooping-cough, diphtheria, meningococcal infection affect the babies from the first days after birth.

b) The younger is the child, the more frequently deviations from the typical picture of the disease may be observed.

c) Children of an early age have the course of the infectious diseases of a septic type more often due to poor ability to localize and separate an inflammatory process; toxic forms of the disease occur more seldom.

d) Frequent development of complications (otitis, pneumonia, etc).

e) The early age is characterized by prolonged and chronic diseases which are especially often observed in the enteric infections.

The **preventive measures** are of different volume taking into consideration all component parts of the epidemic process. Preventive measures may be specific and nonspecific.

The nonspecific prevention includes measures directed at the improvement of general resistance of the child's body: rational nutrition, physical training, prevention of rickets and hypotrophy. General prevention measures include teaching the sanitary-hygienic habits to children, conducting sanitary educational work with their parents.

Elaborated complex of emergency measures has been worked out for detecting an infectious patient. These **measures are directed at the four stages of the infectious process**: a) isolation of the patient; b) measures concerning the people in contact; c) disinfection; d) report to the sanitary-epidemiologic authorities.

Specific prevention is the most effective way to influence the epidemic process. It is aimed at the increase of insusceptibility to definite antigens – **vaccination**. Groups of diseases where the epidemic structure may be changed call controlled infections.

In a number of cases, specific prevention may be of a passive character. Various gamma-globulins are used mainly in those who are in contact with the patients.

WHOOPING-COUGH (H. PERTUSSIS)

The causative agent of whooping-cough is the Borde-Gengou bacillus *Haemophilia (Bordetella) pertussis*, gram-negative, strictly aerobic. Its resistance is very low, and it succumbs rapidly to the effect of high temperature, direct sunlight, desiccation and various disinfectants.

Epidemiology

The source of infection in whooping cough is a sick person. The disease is particularly infective in the initial stage, but gradually becomes less contagious. Patients continue to discharge *H. pertussis* up to the 28-30th day. Treatment with antibiotics shortens the period of infectivity.

Patients with abortive forms can also be sources of infection. Infection is transmitted by the aerial-droplet route, but is possible only by direct, more or less lengthy, contact with a patient. Isolation of patient in separate wards or

semicubicles prevents dissemination of infection. Susceptibility to whooping-cough is high (die index of susceptibility is 0.7).

Pathogenesis

The portal of entry of infection in whooping-cough is the upper respiratory tract. *H. pertussis* settles in the mucous membrane of the larynx, bronchi, and bronchioles, and also in the pulmonary alveoli, but no bacteriemia or penetration of the causative agent into the organs and tissues occurs.

The principal pathogenic factor is the toxin produced by *H. Pertussis*, which brings die cough reflex into play by its intense irritation of the nervous receptors of the respiratory mucous.

The continuous flow of impulses coming from receptors in the mucous of the respiratory tract leads to the development of stable focus of ex-citation in the central nervous system.

Owing to the inert character of the dominant focus, paroxysms can persist for a long time after recovery from the infection. The dominant focus becomes inhibited when other stronger centers of excitation arise.

Because of the frequent and prolonged paroxysms of coughing, and the circulatory disorders in the lungs, pulmonary ventilation becomes disturbed leading to hypoxemia and hypoxia. Inadequate supply of oxygen to the tissues and disruption of oxidation processes leads to the development of acidosis while hypoxia and acidosis, in their turn, aggravate the disturbed function of the nervous system.

Clinical manifestations

The incubation period of whooping-cough is 3 to 15 days. The course of the disease can be divided into three stages: catarrhal, paroxysmal and convalescent.

The first catarrhal stage is manifested by a moderate rise in temperature, but it may sometimes be subfebrile, or even normal. By the end of the catarrhal period, the cough progresses in severity and frequency acquiring the character of more or less prolonged paroxysms, occurring mostly at night. Chorizo is also often noted during the catarrhal stage, but the patient's general state is not much disturbed. The

catarrhal stage lasts for 3 to 14 days, but may sometimes be shorter especially in 1-year-old babies.

The transition to the second, paroxysmal stage is gradual. Paroxysms of coughing develop. At the height of the disease, paroxysms are unmistakable; they begin suddenly. The paroxysm consists of a series of short coughs following one another in rapid succession without a break. Then the child makes an inspiration, which owing to laryngeal spasm, is accompanied with a crowing sound (whoop). The paroxysm is then repeated in the form of the same successive spells with a subsequent whoop. There may be several whoops during a coughing bout. A coughing bout often ends in expectoration of a pellet of viscid transparent mucus and sometimes vomiting. In mild forms there may be no vomiting.

The outward appearance of the patient during a fit is characteristic: the face becomes red and sometimes takes on a cyanotic hue; the cervical veins become engorged; the eyes are bloodshot; the tongue is protruded to the limit, and its tip curves upward.

As a result of frequent paroxysms, the patient's face and eyelids become swollen and hemorrhages sometimes appear in the skin and conjunctiva.

When the oral cavity is examined a shallow ulcer on the frenulum of the tongue is found. The ulcer results from mechanical rubbing of the frenulum against the sharp edges of the lower incisors.

Signs of emphysema are often found on percussion of the lungs. Auscultation reveals dry rales and dull moist-ales in pneumonia complications.

The pulse rate is increased during paroxysms and there is an elevation of arterial and venous pressure.

In the patients blood counts reveal marked leukocytosis and lymphocytosis. The ESR is either lowered or normal.

During convalescence the cough is no longer paroxysmal and bouts gradually become less frequent. All symptoms of the disease subside gradually. This stage lasts from two to four weeks, so that the overall duration of the disease varies between five and twelve weeks.

Clinical forms

There are three principal forms of whooping-cough: mild, moderate, and severe. In the mild form, the frequency of coughing fits is between five and fifteen a day: they are typical but short and only rarely end in vomiting. The patient's condition is undisturbed. In the moderate form the number of fits varies between 15 and 24; with several whoops. In the severe form, there are numerous bouts of coughing (25 to 30, or more, a day). Paroxysms are severe and last up to 15 min, with 10 whoops, and always terminate in vomiting. Disturbed sleep, loss of appetite loss of weight, adynamia and often a long febrile state are noted.

An abortive form of pertussis is characterized by the absence of typical attacks with coughing relapses, and by a shortened course.

The *complications* most frequently met in whooping-cough are respiratory bronchitis and bronchopneumonia. This can be due to the secondary bacterial flora. Bronchopneumonia is a very common complication, especially in young children, and is the main cause of death in whooping-cough.

Spontaneous pneumotorax, emphysema of the mediastinum occasionally develop.

The nervous system is most often affected in small children suffering from the severe form of whooping-cough complicated by pneumonia. Epileptiform convulsions (clonic or clonicotonic) are especially dangerous (encephalopathy); when they occur they usually develop at the height of the cough paroxysm, and may be repeated several times a day.

In one year old babies whooping-cough has a number of special features. The incubation period is usually shorter (3 to 5 days), and so is the catarrhal stage (2-6 day). The fits of coughing often cause apnoea. Mental confusion, attacks of epileptiform convulsions, and twitching of the facial muscles are also more common. Respiratory complications (bronchitis and bronchopneumonia) are more frequent than older children.

Diagnosis

In diagnosis of whooping-cough the distinctive features of its clinical course must be considered: cyclic character, paroxysmal bouts of coughing with whoops, ending with expectoration of viscid mucus and vomiting, typical appearance of the patient. Important diagnosis symptoms are typical hematological shifts; the results of X-ray examination of the chest and analysis of the epidemiological situation.

Bacteriological tests can also be of great diagnostic aid. Testing for *H. pertussis* is usually done by means of "cough plates": an open petri dish of nutrient medium is held five to eight centimeters from the patient's mouth during a paroxysm.

Agglutination and complement – fixation reactions have also been suggested. But these reactions only become positive from the second week of the paroxysmal stage; they are often negative in one year old babies.

The catarrhal stage of whooping-cough has to be differentiated from influenza and ARVI, tracheobronchitis, tuberculous bronchoadenitis, foreign body in the upper respiratory tract.

Treatment

Properly organized regimen and nursing are very important in the treatment of whooping-cough. Bed rest is called for only when there is fever and severe complications. Cold fresh air has a wonderful effect on patients. Paroxysms become fewer and weaker.

Antibiotics are successfully used today as a specific (etiologic) therapy of whooping-cough. Erythromycin, ampicillin, amycacin, are given in the catarrhal or early spasmodic period.

In order to attenuate the pertussis attacks, neuroplegics are recommended: aminazine, propazone. The solution of aminazine is given intramuscularly, 1-3 mg/kg: propazine is given per os, 1 mg/kg a day. The daily dose is given for three intakes; the course continues for 10-12 days.

Oxygen therapy (oxygen tent) is especially valuable in pertussis, in particular in infants and neonates with marked signs of hypoxia.

Prophylaxis

Measures to be taken in an epidemic focus. The earliest possible isolation of the patient is imperative. Early diagnosis is therefore the success of the antiepidemic measures. The patient is usually left at home and put in a separate room or behind a screen.

Hospital!

Hospitalization is indicated in severe and complicated forms of whooping-cough, particularly in children under two years of age, children from families living in poor conditions, and from families where there are babies under six months of age. Patients are isolated for 30 days from the onset of the disease.

Active immunization against whooping-cough is given by pertussis - diphtheria - tetanus vaccine beginning from 3 months of age 3 times with 30 days interval and revaccination in the second year of age.

ACUTE RESPIRATORY VIRAL INFECTIONS

Acute respiratory viral infections (ARVI) is a group of diseases of various etiology, which are characterized by predominant affection of the respiratory tract and symptoms of intoxication which are expressed in various degrees.

Pathogens of ARVI include viruses of influenza, parainfluenza, adenoviral, respiratory-syncytial virus, rhino-and coronaviruses. The source of infection in all ARVI is a sick person or a virus carrier. The major route of spreading the infection is the air-droplet one, but fecal-oral (adenoviral infection) and contact (rhinoviruses infection) ones are not excluded. Susceptibility to infection is high especially in 1-year-old children.

General clinical syndromes that are observed in all ARVI are syndrome of intoxication and of lesion of the respiratory tract.

Intoxication is clinically manifested in weakness, sweating, headache, hyperesthesia, fever of various degree of expression.

Syndrome of lesion of the respiratory tract includes congestion or dryness in the nose, sore throat, cough, sneezing, lacrimation,

Different pathogens of ARVI affect different parts of the respiratory tract: rhinoviruses affect the nose, parainfluenza viruses — affect the larynx, influenza viruses — the trachea, adenoviruses — the pharynx, conjunctiva, lymphoid tissue, respiratory-syncytial virus — the lower respiratory tract. Due to that, each disease has specific clinical manifestations that allow to successfully differentiating the diseases of different etiology each from the other.

Influenza

Influenza is an acute respiratory disease of viral etiology, which is characterized by expressed symptoms of intoxication and affection of the upper respiratory tracts.

Etiology

Pathogen is the influenza virus, which is *Orthomyxoviridae*, and contains RNA. We distinguish 3 serotypes of influenza virus: A, B and C. They are alike in their morphology, but differ in their antigen content. Two antigens, hemagglutinin and neuraminidase provide easy changeability of the virus. Out of the 3 types of the virus the most changeable one is virus A. Changes of neuraminidase or hemagglutinin cause appearance of new subtypes of virus A. Changes of one antigen {antigenic drift), or two antigens (antigenic shift) are possible. Appearance of the new strains of a virus leads to an epidemic. The new subtype of virus A causes a pandemic.

All antigen variants of *type B* virus have similar types of neuraminidase and differ only in the structure of hemagglutinin, that provides more stability as compared to influenza A virus.

Influenza C virus differs in its stability of antigen structure. It causes neither pandemic, nor epidemic, it is a cause of sporadic diseases, especially in children.

Influenza viruses possess weak stability to the action of physical and chemical factors are easily destroyed at room temperature, or desiccation. In low temperature it maintains its infectious features during several years.

Epidemiology

The source of infection is the patient, who is particularly infective at the height of the disease, during pyrexia. The contagious period lasts from four to seven days.

The *aerial-droplet route* at relatively close distances from the infected patient chiefly conveys infection.

The susceptibility of man to influenza is very high. Only children in the first months after birth are relatively resistant to influenza because of passive immunity from mothers. Children are very susceptible to influenza from six months of age. Immunity against influenza A is effective in man for about two years, and against influenza B, three years. The postinfection immunity protects only from the corresponding antigenic variant of the virus.

Epidemics caused by the type A virus are repeated every one or three years, and by type B virus every three to six years.

Pathology

Reproduction of the influenza virus in the epithelium cells of the respiratory mucous is impotents pathology mechanism of influent. The development of marked inflammation is normally associated with secondary supervening of the infection. Catarrhal-desquamate tracheitis and bronchitis develop.

The pulmonary tissue is readily involved in the inflammatory process and segmental edema, focal and segmental pneumonia involves secondary bacterial flora.

Influenza is attended by pronounced circulatory disorders in various organs, the lungs and the brain. Grave affections of the nervous, such as encephalitis, meningoencephalitis, usually develop in the presence of mixed viral infections; the allergic mechanisms are very important in their development.

Clinical Manifestations

The incubation period of influenza is one or two days, but may be sometimes as short as a few hours.

The onset of the disease is acute, with elevation of temperature and chill. The febrile reaction may vary according to the severity of the disease; the temperature may be high, but it may remain sub febrile when the course of the disease is mild.

General toxemia is common, and is mainly expressed by the symptoms of the central nervous system involvement, namely: severe headache, vertigo, hyperesthesia, adynamia, and sleepiness or excitation. High fever often accompanied with mental confusion, delirium, and hallucinations. Frequent vomiting, convulsions and loss of consciousness (cerebral syndrome), and a syndrome of meningitis characteristic of the young children.

Influenza toxemia also produces marked changes in cardiovascular system. A brief period of hypertension is followed by a fall in arterial pressure, tachycardia or bradycardia, arrhythmia, and sometimes by cyanosis. There may be hemorrhage into the conjunctiva and mucous.

Catarrh of the upper respiratory tract is common in influenza. In some cases, it develops on the second or third day. The signs of catarrh of the upper respiratory tract are the following: fever, chills, dryness and irritation in the faces, a dry cough, and dyspnoea.

Laryngitis most frequently in children under two years of age. In some cases influenza laryngitis is accompanied by stenosis.

Croup in influenza patients develops mostly in infancy because of edema of the laryngeal mucous and the spasm of the laryngeal muscles. Its signs and course differ from those of diphtheritic croup. In most cases, its onset is sudden. Voice is hoarse; coughing is loud, coarse and barking. Signs characteristic of laryngeal stenosis develop noisy respiration, depressions in the yielding parts of the chest, tension of the auxiliary respiratory muscles.

Loss of appetite, a coated and often dry tongue, nausea, and sometimes vomiting and constipation are characteristic digestive disturbances. In young children, the stools are often liquid, dyspeptic.

The faces are often hyperemic. The mucous membrane of the soft palate has a granular character.

Blood findings at the beginning of the disease are transitory leukocytosis followed by moderate leucopenia, lymphocytosis, monocytosis, eosinopenia or aneosinophilia, and toxic granularity of neutrophils.

Complications

Respiratory tract complications are the most common:

- sinusitis, ethmoiditis, sphenoiditis;
- **Pneumonia** is a common and dangerous complication that develops there during the first days of the disease or later, as the result of mixed viral and bacterial infection. Microfocal, segmentary, or confluent pneumonia with involvement of interstitial tissue ;
- fibrinous or purulent pleurisy caused by secondary bacterial flora (mostly staphylococcus). Pneumonia sometimes results in abscesses in the lung;
- Various complications involving the nervous system, such as neuralgia, neuritis, or radiculitis, may occur. Clinical syndromes of encephalitis, meningo-encephalitis, and purulent meningitis;
- Catarrhal otitis is not uncommon in children;
- Other complications (stomatitis, purulent otitis, pyelitis, cystitis, nephritis, keratitis, phlebitis, etc.) may also occur.

Diagnosis

Diagnosis is made based on typical clinical manifestations.

The most widespread laboratory method is the method of direct immunofluorescent assay, based on detecting the antigens to influenza virus in the smears of cylindrical epithelium taken from the nose.

Virologist methods are time-consuming. Viral RNA may be discovered in the discharge from the respiratory tract and tissues by PCR method.

Serologic tests (HAIT and CFT) using in retrospective diagnostics. For serologic investigations, blood need to taken twice: in the beginning of the disease and in interval of 7-14 days. It is diagnostically important when the titer of specific antibodies increases 4 and more times.

Treatment

The patients with influenza are prescribed bed regimen and nutritive diet.

In influenza A the most effective etiotropic remedy are

remantadin (for 7-11 year old children: 0.05 g 3 times a day for 3 days, 11-14 year-olds: 0.1 g 3 times a day in the first day of the treatment, and 0.1 g 2 times a day in the second day, then 0.1 g 1 time in the third day). After the 5th day of the disease, remantadin is inexpedient;

arbidol (for 2-6 year old children: 0.05 g 3 times a day, 6-12 year old children: 0.1 g 3 times a day, after 12 year old children: 0.2 g 3 times a day);

osel'tamivir - after 12-year-old children: 0.1 g 3 times a day.

In influenza mild and average severe forms abundant liquid are recommended, in severe forms — infusion therapy is indicated with the use of 5-10 % solution of glucose, detrans, albumen, in total volume of 20-80 ml/kg/day. Specific antiinfluenza γ -globulin in a dose of 0.2-0.3 ml/kg the first days of the disease is also administered.

Symtomatic therapy includes antipyretics and analgetics. Antibacterial therapy is indicated for children under 2 years of age or if complications develop.

Prophylaxis is in isolation of the sick person for 7 days, keeping to the sanitary-hygienic regimen in children's institutions.

In epidemic focus, it is recommended to use leukocyte interferon 2 drops 4 times a day, lubrication of nasal passages with 0.25 % oxoline ointment 2 times a day for all children. One-year-old children may have antiinfluenza γ -globulin prescribed in the dose of 0.15 ml/kg/day. Live and inactivated influenza vaccines used according to epidemic indications have been developed. Now using polyvalent influenza vaccines, which have 3 type of influenza virus – Grippol, Fluorix, Influvak, Vaxygripp.

Parainfluenzal Infection

The causative agents are parainfluenza viruses. They have ribonucleic acid (RNA).

Epidemiology

Infants are particularly susceptible. Adults and older children, who usually have an attack of this disease in early childhood, contract the disease much less frequently; the disease runs a milder course.

Parainfluenza occurs either sporadically or in the form of outbreaks in organized groups of children, involving considerable part of them.

Clinical picture

Incubation continues from 1 to 7 days. The onset of the disease is moderate and in uncomplicated cases, it persists only for 2-5 days. A second rise in the body temperature sometimes occurs in the 1-2 day of apyrexia. The symptoms of pronounced intoxication, that are typical of influenza, are relatively rare. Most frequent and typical manifestation of the parainfluenza infection is the catarrh of the upper airways; hyperemia and swelling of the nasal mucosa, moderate hyperemia of the fauces. A permanent symptom is persistent coughing which is the manifestation of tracheitis or tracheobronchitis. Bronchitis in infants sometimes becomes asthmatic.

Laryngitis is typical of parainfluenza infection. It shows in dry coarse cough and a slight or moderate coarseness of the voice. It can sometimes be attended by symptoms of the laryngeal stenosis.

Laryngoscope reveals catarrhal laryngitis with edema of the anterior laryngeal and subglottic mucosa.

Pneumonia is the most frequent complication of parainfluenza in infants.

Blood findings are normal during the first days of the disease; leukocytosis occurs less frequently; moderate neutrophilia is possible; ESR is normal or slightly increased.

Diagnosis

The clinical picture of parainfluenza resembles that of influenza and other respiratory viral infections. In contrast to influenza, the onset of parainfluenza is less acute. The intoxication symptoms are absent or only slightly pronounced, the catarrhal symptoms are more pronounced, frequent laryngeal affections are typical. The diagnosis becomes less difficult in epidemic outbreaks.

Respiratory Syncytial Infection (RSV Infection)

The respiratory syncytial virus (RSV) belongs to the group of myxo-viruses. It contains RNA.

Clinical picture

The incubation period lasts for 3 to 7 days. The onset is usually gradual, with affections of the upper and lower respiratory tract.

The affection of the upper airways is manifested by rhinitis with scanty serous or seromucous discharge, cough, and sometimes-hoarse voice. The general condition is almost unaffected; the temperature is either normal or subfebrile.

The lower respiratory tract is very frequently involved in infants. A picture of diffuse bronchitis and bronchiolitis is observed. Bronchiolitis is characterized by a strong dyspnea of the mixed type with prevalence of difficult expiration. The examination of the lungs reveals fine or medium bubbling rales and symptoms of emphysema. The picture of respiratory insufficiency is supplemented by cyanosis. All these symptoms subside completely in 2-6 days. Pneumonia (microfocal, segmental) occurs in 25 % of cases on the average. The general intoxication is usually not pronounced. When pneumonia joins in the process, the changes are more marked. The overall length of an uncomplicated RSV infection is from 2 to 10 days (sometimes longer).

Most frequent complications are pneumonia and catarrhal otitis caused by secondary bacterial flora. Grave pneumonia in infants is the cause of lethal outcomes.

Diagnosis

During clinical diagnostication of the RSV infection in children, frequent affections of the lower respiratory tract (bronchiolitis), that are characteristic of the disease. In addition to isolation of the RSV, serological methods are also used in the laboratory diagnostication, namely: complement-fixation test and the neutralization test.

Rhinoviruses Infection

Rhinoviruses are very small; they contain ribonucleic acid, and are picornaviruses.

Epidemiology

Infection is spread from a patient or virus carrier by the aerial-droplet route. Contagiousness lasts not more than 5 or 7 days. All ages are susceptible. Seasonal elevations are noted in autumn and spring.

Clinical picture

The incubation period is between one and six days. Onset is characterized by the appearance of copious watery discharge from the nose and sneezing; later the discharge becomes mucous, or mucopurulent because of concomitant bacterial flora. The nasal mucous swells, obstructing the nasal passages. There are usually no constitutional symptoms, and temperature remains normal; a subfebrile temperature is met only in some patients. The illness lasts for six or seven days, rarely longer.

Secondary bacterial infection may cause various complications (sinusitis, otitis, pneumonia) sometimes supervenes.

Adenoviral Infection

Adenovirus particles are containing desoxyribonucleic acid (DNA). Adenoviruses are characterized by location inside the cell nucleus and marked stability to environmental effects.

Epidemiology

The source of infection is a sick person or a carrier of the virus. Excretion may continue for 2-3 weeks and even longer. Children from six months to three years of age are particularly susceptible to these infections. Children less than six months are still protected by passive immunity obtained from their mothers.

Pathogenesis and pathology

Adenoviruses infest the respiratory and intestinal mucosa. They are accumulated in the epithelial cells and regional lymph nodes.

Catarrhal inflammation of the nasal, pharyngeal, and tonsil mucosa with a marked oxidative component is almost constant. The trachea and bronchi are involved in the process. Focal and confluent, polysegmental pneumonias are frequent. The regional lymphnodes are affected by hyperplasia. Inflammation of the eye conjunctiva, often with formation of fibrinous coats, is characteristic.

Clinical picture

The incubation period is between four and seven days, sometimes longer. The principal **clinical forms** are

pharyngoconjunctival fever,
catarrh of the respiratory tracts,
and pneumonia.

Isolated or predominant affections of the pharynx or of the conjunctiva (adenoviral tonsil lopharyngitis and adenoviral conjunctivitis and keratoconjunctivitis), intestine (intestinal form) and mesenteric nodes (mesadenitis) are less frequent.

The onset of **pharyngoconjunctival fever** may be acute or gradual. Temperature rises to 38-39 °C, and there is usually moderate general toxemia. Headache, adynamia, loss of appetite are noted. Constant symptoms are rhinitis with copious serous or seromucous discharge, bronchitis or tracheobronchitis, pharyngitis, and conjunctivitis. An asthmatic syndrome and laryngitis sometimes develop. The fauces and posterior and lateral walls of the pharynx are hyperemic; lymphatic nodes are swollen. The tonsils are rather enlarged, and a film sometimes covers the lacunae.

Conjunctivitis may appear from the first day, but more often from the second or third. It usually starts on one side and may later spread to the other eye. Catarrhal, follicular, and membranous conjunctivitis are distinguished according to the character of the inflammation.

Enlargement of the cervical lymphnodes, and in infants liquid stool sometimes with mucus, are not uncommon. Sometimes there is enlargement of the liver and spleen.

Adenoviral catarrh of the respiratory tract is a frequent form of this infection, and the mildest. There is fever, moderate or mild disturbance of the patient's general condition and marked symptoms of catarrh of the respiratory tract, nasal discharge, bronchitis.

Pneumonia is the most severe form of adenoviral infection occurring mostly in infants. Pneumonia is of viral etiology with subsequent supervention of bacterial flora.

The intestinal form of adenoviral infection occurs mostly in infants. It is characterized by prevalent symptoms of acute gastrointestinal disorders. The body temperature is moderately elevated; catarrh of the respiratory ducts is a constant symptom. The gastrointestinal disorders are present for 3-4 days.

Mesadenitis (inflammation of mesenteric lymphnodes) is a rare manifestation of adenoviral infection which develops either against the background of another syndrome. Mesadenitis is characterized by an acute onset with abdominal pain, fever, nausea, and infrequent vomiting. The pain is felt predominantly in the lower part of the abdomen, often in the right iliac region. Peritoneal irritation is either absent or non-manifest. Appendicitis is often misdiagnosed and the patient is operated.

Complications (otitis, sinusitis, bacterial pneumonia, pleurisy) are caused by secondary bacterial infection. They are the most common in infants with a severe course of the disease.

For laboratory diagnosis isolation of the virus from gargling and feces, and serological examination (complement-fixation test, neutralization and hemagglutination inhibition reactions identifying the type of causative agent) during the first days and after two or three weeks, are performed; a four-fold minimal increase of antibody titer is considered as diagnostic of the disease.

Treatment of Acute Respiratory Viral Infections

The treatment and general prophylaxis of acute respiratory viral infections is largely the same as for influenza. The therapeutic effect of interferon has been

tested. Use of desoxyribonuclease by instillation into the nose or the conjunctivas sac (3-4 drops of fluid preparation, 3-4 times a day) has been suggested in adenoviral infection; good results were obtained in the treatment of adenoviral conjunctivitis.

MENINGOCOCCAL INFECTION

The *causative agent* of epidemic meningitis is meningococcus (*Neisseria meningitidis*). This microorganism has the form of a diplococcus, which stains well with aniline dyes, and is gram-negative. It grows on media containing human protein (blood serum), and is very unstable and perishes rapidly outside the organism. Several serotypes of meningococ (A, B, C, D, Z, X, and Y) have been discovered. Types A and B prevail in this country.

Epidemiology

The *sources of infection* are patient and carriers who expel the causative agent with the secretions from the nasopharynx and upper respiratory passages. Since there are more carriers than patients, the epidemiological role of the former is very great.

Infection is transmitted by the aerial-droplet route. There is not much danger in spreading the infection through objects because of the low viability of the causative agent.

The *susceptibility* of man to meningococcal infection is slight: the susceptibility index does not exceed 0.5 %: most infected persons become healthy carriers.

Children are mostly susceptible to the disease: about 70 % of cases are infants under 5. The meningococcal infection is characterized by *periodic rises* of the incidence every 10-15 year or longer.

Pathogenesis and Pathology

The *portal of the infection* entry is the nasopharyngeal mucosa. The carrier state develops frequently, while nasopharyngitis occurs significantly less frequently. The generalized form of infection occurs only in 0.5-1 % of cases: the causative agent

is carried by blood to various organs (soft cerebral meninges, joints, eye membranes, etc.). Meningococemia manifests itself sometimes as sepsis.

The important role in meningococemia belongs to marked *intoxication with the endotoxin* released during decomposition of the microbial bodies. Various organs are affected, in the first instance small vessels. Microcirculation is thus affected to provoke thrombosis and extravasates. Typical hemorrhagic eruption appears on the skin.

Necrosis in the adrenal glands with diffuse hemorrhages and decomposition of the glandular tissue occur in most severe fulminating forms of meningococcal infection attended by the *Waterhouse-Friderichsen syndrome*. Death occurs from acute renal insufficiency.

Purulent meningitis develops due to the ingress of the meningococcus into the soft meninges of the brain and the spinal cord. Purulent exudate is particularly abundant in the base, and also on the surface of the frontal and parietal lobes of the brain (a "purulent cap"). When the process involves the ependyma of the cerebral ventricles, the accumulating purulent fluid (ependymatitis) dilates the latter.

The matter of the brain and spinal cord is usually damaged to a greater or less extent (circulatory disturbances, edema, occasional hemorrhages, and the development of inflammatory foci). Acute swelling and edema of the brain can cause protrusion of the cerebellar tonsil into the great foramen, which often becomes the cause of death.

The inflammatory process can lead to obliteration of the orifices through which the cerebral ventricles communicate with the subarachnoid space. All these changes lead to hydrocephalus; the fluid accumulating in the ventricles dilates them, and atrophy of the brain matter develops consequently.

If the secondary focus is located in the joint, arthritis develops. Iridocyclitis and chorioiditis develop in metastasis affections of the eyes.

Clinical Manifestations

The *incubation period* lasts for 3- 10 days.

Classification

1. Location form:

- Nasopharyngitis;
 - Carriers;
2. Generalized form
- Meningitis;
 - Meningococemia;
 - Fulminating form;
 - Meningitis+ meningococemia.
3. Atypical form;
- Iridocyclochorioiditis;
 - Pneumonia.

The most frequent form of the manifest meningococcal infection is ***nasopharyngitis***. Its symptoms are headache, painful swallowing, subfebrile temperature in some patients, hyperemia of the nasopharyngeal mucosa and hyperplasia of lymphoid nodes, rhinitis with scanty discharge, and difficult nasal breathing. The clinical signs persist for 5-7 days.

Meningitis. The onset of the disease is usually violent, and a considerable elevation of temperature accompanied by chills is noted; severe headache, vertigo, and vomiting occur. Characteristic is hyperesthesia of the skin and increased sensitivity to light and sound. Mental disturbances are also frequent (lethargy, drowsiness, etc.). In young children clonic and tonic convulsions are not infrequent.

Meningeal symptoms are: ***stiffness of the occipital muscles*** develops very early (usually during the first 24 or 48 hours), and ***Kernig's*** and ***Brudzinsky's*** signs become positive. Anisocoria, strabismus, and paresis of the facial nerve are occasional. The patient's posture is usually typical: he is lying on his side with head tossed back and legs flexed to the abdomen.

The blood shows marked leukocytosis (up to $20-40 \cdot 10^9/l$), neutrophilosis with a shift to the left, aneosinophilia, the ESR is considerably increased.

In ***lumbar puncture*** spinal fluid flows under increased pressure. During the first day of illness, it may be transparent or slightly opalescent, but later becomes turbid and purulent. It displays marked neutrophilosis (from several hundreds to several

thousands of cells per mm³) and considerable protein content (up to 1-2 g/l); sugar content is lowered.

Bacterioscopy shows meningococci (diplococcus) within and out of cells; but microbiological investigation — culturing of spinal fluid — is a more reliable means of revealing meningococcal.

The gravity and course of meningococcal infection differ in various patients. The clinical manifestations are also quite varied. Especially grave are septic (meningococemia) and hypertoxic forms.

In the *rudimentary (abortive) form* all the symptoms are weakly expressed, including the meningeal. The changes in the cerebrospinal fluid may be insignificant and transitory.

The *septic form (meningococemia)* occurs in patients of all ages. Signs of meningococcaemia may be observed in the presence and less frequently in the absence of a pronounced symptom complex of meningitis.

The onset is acute and violent, with intermittent fever. This infection is usually attended by skin rash, which is the most frequent symptom. The rash is hemorrhagic, often with macular (measles-like) lesions. The hemorrhagic lesions are stellate formations varying in size; they are hard on palpation and are often elevated. Meningococcal are found in blood smears taken from the periphery of the lesions.

The **hypertoxic (fulminating) form** of meningococcal infection has a sudden turbulent onset and is characterized by severe toxemia (uncontrollable vomiting, convulsions, mental confusion, cardiovascular weakness). The patient soon becomes comatose. Meningeal symptoms are sharply pronounced or, on the contrary, rudimentary. Death usually ensues within 12 to 24 hours after the onset. Swelling of the brain and protrusion of the cerebellar tonsils into the great foramen is one of the frequent causes of death.

The **fulminating form** may develop as the Waterhouse-Friderichsen syndrome which is the sign of an acute renal insufficiency. Multiple petechiae and hemorrhage into the skin are characteristic. The arterial pressure falls progressively, the pulse is rapid and hard. Cyanosis, vomiting (often with blood) and convulsions are other signs.

The patient dies in 16-30 hours after the onset of the disease unless an urgent and effective therapy is given.

Significant hemorrhage into the skin is often followed by necrosis of the tissues with subsequent rejection of the necrotized tissue; scars remain on the skin. Arthritides in meningococemia are less frequent. Several joints are usually affected, with a purulent or a seropurulent exudates in the joint capsule. Inflammation of the chorioidea (iridocyclochorioiditis) is a less common, but very typical, complication of meningococemia; its first sign is a change in the colors of the iris, which becomes sort of rusty.

Along with these malignant forms, there also occur clinical variants of meningococcal infection characterized by very mild course.

Features peculiar to meningitis in infants.

Onset of the disease is accompanied with high temperature, general restlessness, vomiting, and refusal to suckle. There is marked hyperesthesia of the integuments and frequent dyspeptic disturbances. Infants cry loudly. Meningeal symptoms and red dermographism are often mild or absent. In the newly born the course of meningitis as a rule is atypical. High temperature, convulsions or tremor, and general muscular hypertension develop. Meningeal symptoms are absent or become apparent only with further disease course. Even with modern methods of treatment, mortality remains high.

Complications

Complications and residual phenomena are frequent and varied in meningococcal meningitis (pneumonia, purulent otitis, hydrocephalus, the symptoms of which appeared already at the height of the disease, paralysis, paresis, etc.).

Residual symptoms were observed in most children after meningitis: chronic hydrocephalus, deep mental retardation, epileptiform convulsions, stable paresis, etc.

Some patients develop complications associated with the bacterial superinfection.

Chronic hydrocephalus, motor disorders (paralysis, paresis), retardation in mental development are now rare. Asthenic syndrome, headache, and various functional disorders are observed.

Diagnosis

Diagnosis of epidemic meningitis is established from the distinctive features of the clinical symptomatology and its course (acute onset and rapid development of meningeal symptoms). The most important diagnostic aid is lumbar puncture and examination of the cerebrospinal fluid. The diagnosis is indisputable when meningococcus is detected by bacterioscopy or is found in a cerebrospinal fluid culture.

Examination of cerebrospinal fluid is particularly important in atypical forms and in meningitis in infants.

Errors in recognizing epidemic meningitis in children are not infrequent. Epidemic meningitis can be confused with other forms of meningitis, with various diseases accompanied with meningism syndrome. Meningeal symptoms are usually mild in *meningism* and the cerebrospinal fluid is unchanged.

Tuberculous meningitis starts gradually and is accompanied with moderate pyrexia; it is diagnosed from the anamnesis and the results of tuberculin tests. Miliary tuberculosis is often evident from the X-ray of the lungs. Cerebrospinal fluid is transparent or slightly opalescent; cell count is moderately increased due to an increase in the lymphocyte number. When cerebrospinal fluid is allowed to stand a delicate web-like fibrin film is formed on its surface. *Mycobacterium tuberculosis* is often found in the cerebrospinal fluid.

Acute serous meningitis differs in the cerebrospinal fluid findings (complete transparency; moderately increased cell count due to a higher number of lymphocytes; normal sugar content).

In the *meningeal form of poliomyelitis* the cerebrospinal fluid is transparent. A slight or moderately increased cell count and normal or slightly increased protein content (cellular-protein dissociation) is noted during the first five days; later the cell count drops, and a protein-cellular dissociation is observed from the tenth day. Lymphocytes predominate among the cells. Diagnosis is facilitated if tendon reflexes disappear, and even more so if flaccid paralysis or paresis develops.

In contrast to primary meningococcal meningitis, **purulent meningitis** caused by staphylococcus, pneumococcus, Afanasyev-Pfeiffer bacillus, and streptococcus usually develops secondarily to purulent otitis, pneumonia, sepsis, etc. Gram-positive cocci and diplococci are found in the cerebrospinal fluid, which is purulent.

Difficulties in differential diagnosis of *meningococemia* arise in cases where it has no symptoms of meningitis, and may be mistaken for septicemia of other etiology, thrombopenic purpura, and hemorrhagic vasculitis. It should be remembered that meningococemia is characterized by high temperature, pronounced intoxication, marked changes in the blood (hyperleukocytosis with the shift to the left); a stellate pattern of hemorrhagic eruption is typical. Accurate diagnosis is established bacteriologically. Meningococcus can be detected not only in the blood but also in the skin lesions.

Prognosis

Mortality from epidemic meningitis was very high (30 to 40 % on average) before the introduction of penicillin, but fell sharply with the application of highly effective chemotherapy. Mortality in infants younger than three months is still quite high. The worst outcome in meningitis is prognoses in cases with the Waterhouse-Frederickson syndrome and the hypertoxic clinical form.

Treatment

Penicillin was first given intramuscularly in moderately high doses administration of this preparation during the first 2-4 days. Now children are given a daily dose of 300 000-400 000 units per kilogram of body weight at intervals of 3 to 4 hours. Treatment lasts for 8-10 days without reducing the dose. Stopped antibiotic therapy need after sanayshin liquor: citosis is less then 100 cell of lymphocytes.

If the patient is hypersensitive to penicillin, levomycetin sodium succinate can be given (100 mg/kg for 6-8 days). Ampicillin (150-200 mg/ kg a day), cephalosporins, oxacillin or methicillin are also recommended.

In addition to etiotropic preparations, pathogenetic and symptomatic therapies are also important. Toxicosis can be controlled by administration of large amounts of liquids (water-based beverages, intravenous infusion of physiological solution of

glucose, plasma substitutes, and plasma); electrolyte balance and osmotic pressure should be watched closely. Dehydration techniques are also used: intramuscular injections of magnesium sulfate, diuretics (dichlothiazide, diacarb, furosemide, or lasix, mannitol). Dehydration therapy should be especially intensive in the presence of brain swelling (respiratory arrhythmia, convulsions, cyanosis, arterial hypertension). Corticosteroids should be given simultaneously.

In the presence of the Waterhouse-Friderichsen syndrome, 5 % glucose solution, or Ringer solution, plasma substitutes with hydrocortisone (not less than 5 mg/kg a day) should be infused by drip. Corticosteroids should then be given intramuscularly. To improve the cardiovascular function, strophanthin, ATP, and cocarboxylase are indicated.

The patient needs adequate care and supervision, and a good diet. Severe forms of meningococcal infection require urgent aid and should be treated at resuscitation and intensive therapy departments.

Prophylaxis

The following measures are carried out in an epidemic focus. The patient is hospitalized and isolated; he is discharged after the clinical manifestations of the disease subside and on condition that the results of two bacteriological studies of the pharyngeal mucus are negative.

It is advisable that contacts and virus carriers should be treated with sulfonamides or rifampicini for 3 days as a prophylactic measure, the standard dose being given 3 times a day. Terminal disinfection is carried out after isolation of the patient: regular concurrent disinfection is performed at the patient's bedside.

Polysaccharide meningococcal vaccines have been recently developed in some countries. They proved effective in the countries of Africa. But in many practical problems of their use have not been solved yet.

ACUTE EPIDEMIC POLIOMYELITIS

The *causative agent* of poliomyelitis (Poliovirus hominis), is a very small virus. It contains RNA. The virus is very stable in the external environment, and is resistant to low temperatures and desiccation. Three types of poliovirus (I, II, III) are known.

Epidemiology

Apart from patients with clinically manifest poliomyelitis, persons suffering from atypical and abortive forms are *sources* of infection.

The *infectivity* of patients is greatest during the acute stage. Most are free of the virus in 15 to 20 days after an attack, but the carrier state may last as long as 30 to 40 days, and even four to five months.

The mechanism of infection. Many facts have been accumulated pointing to the great importance of fecal mode of transmission. Individual patients become fecal carriers of the virus for three to five months. There is also evidence that milk and other foodstuffs can convey infection.

Judging from the recorded incidence, *susceptibility* to poliomyelitis is low. It is most prevalent in children aged under seven years of age (75 to 90 %).

Stable immunity is conferred by an attack, and repeated attacks are very rare.

Pathogenesis

The most probable *portal of entry* of the infection in poliomyelitis is the pharyngeal lymphoid ring and the intestinal tract. The poliomyelitis virus is isolated, as a rule, from lesions of the *nervous system*. The *most pronounced pathological* changes in poliomyelitis are in the ventral horns of the gray matter of the cervical and lumbar enlargements of the spinal cord. The nerve cells undergo dystrophic necrotic changes, and perish.

Clinical Manifestations

The *incubation period* of poliomyelitis averages from 5 to 14 days; it may sometimes be as short as 2 to 4 days or as long as 35.

Four stages are distinguished in the course of the disease: a) initial or preparalytic, b) paralytic, c) restitution, and d) the stage of residual phenomena.

Preparalytic stage.

The disease starts acutely with a marked rise of temperature. Catarrh of the upper respiratory tract (nasopharyngitis, angina, bronchitis) is present from the first days of the disease. In other cases the onset of the disease is characterized by gastrointestinal disturbances.

General symptoms of irritation and functional derangement predominate *on the side of the nervous system* (headache, vomiting, adynamia, lassitude, drowsiness or insomnia, sometimes delirium, tremor, muscular jerking, and convulsions).

General and local *hyperhidrosis* is a particularly frequent manifestation of vegetative derangement.

The preparalytic stage usually lasts from 2 to 5 days. Fever, catarrhal phenomena, or intestinal disturbances are noted lasting for several days; brief apyrexia follows, and then a second elevation of temperature accompanied with general cerebral and meningeal phenomena.

The changes in the cerebrospinal fluid are most constant and characteristic; the fluid is under considerable pressure and is transparent. Globulin reactions are positive, but protein content is normal or slightly elevated; cell count is increased due to lymphocytosis. Thus, a cellular-protein dissociation is characteristically observed during the first five days.

Paralytic stage.

The temperature falls at the end of the initial stage, and paresis and paralysis occur. *Paralysis* may develop at the height of the fever, usually suddenly; may wake up paralyses in the morning ("morning paralysis"). Careful examination will have revealed hypotonia, muscular weakness, and loss of reflexes several days previously. In the majority of cases paralysis sets in till the fifth day, but may develop much later, on the eighth-tenth day.

Various groups of muscles in the most diverse combinations become involved. The lower limbs are most often affected; the deltoid muscles come second in order of frequency of implication. Muscles of the trunk and neck, and abdominal and respiratory muscles are less commonly affected.

Signs of damage of the peripheral neuron characterize the paresis and paralysis in poliomyelitis: absence of tendon reflexes, cutaneous reflexes may also disappear, muscular appear one or two weeks after the onset of paralysis.

The paralytic stage may last several days or one or two weeks, but seldom longer.

Stage of restitution.

The stage of residual phenomena is characterized by stable flaccid paralysis, atrophy of definite muscular groups, and contractures and deformities of the limbs and trunk.

Clinical forms of poliomyelitis.

Depending on the localization of the principal lesions of the nervous system *paralytic poliomyelitis* is divided into the following forms: a) spinal, b) bulbar, c) pontine, d) encephalitic.

The *spinal* form is that most frequent and typical of paralytic poliomyelitis. It is characterized by flaccid paralysis of the limbs, trunk, neck and diaphragm.

The *bulbar* form, which is fraught with the greatest danger, is accompanied with swallowing, speech, and respiratory disturbances.

The *pontine* form is expressed in implication of the nucleus of the facial nerve with paresis of the facial muscles.

The encephalitic form is characterized by general cerebral phenomena and symptoms of focal lesions in the brain.

The visceral (or abortive) form shows symptoms of the initial stage of poliomyelitis. There are also signs of irritation of the nervous system. Sometimes there are no changes in the cerebrospinal fluid indicative of poliomyelitis.

In the *meningeal* form there are the same signs as in the visceral, with meningeal symptoms in addition. Findings in the cerebrospinal fluid are a moderate elevation of cell count (increase of lymphocytes) and a normal or slightly elevated protein content.

Diagnosis

Recognition of poliomyelitis is easy in the presence of typical manifestations of the paralytic form.

Now that poliomyelitis is a rare and sporadic disease, laboratory diagnosis has become of particular value. Even when it has a typical course diagnosis of poliomyelitis should be confirmed by virological studies. Patient's feces, and during the first week — nasopharyngeal washings, can serve as material for examination. Sera obtained during the first days of the disease, and in two weeks or later are used to detect progressive increase of the antibody titre in the complement-fixation test and neutralization reaction.

Treatment

In the acute period of the disease (the preparalytic and paralytic stages) a *regimen* based on the principle of protective inhibition should be maintained. Strict physical and mental rest in bed should be enjoined for two or three weeks.

Although no specific effective methods against the poliomyelitis virus have been evolved, gamma-globulin has been suggested for this purpose. The following are recommended: ascorbic acid (0.3 to 0.5 g twice a day); vitamin B₁; vitamin B₁₂.

Stimulants conduction (proserine, dibazol) are prescribed two weeks after the onset of the disease. Proserine is injected intramuscularly in the form of 0.1 to 1 ml (depending on age), or per os (0.5-1mg) two times a day for 10 to 15 days. Dibazol are given in doses of 1 to 5mg once a day for 20 to 30 days.

Prophylaxis

An important preventive measure is the earliest *isolation of poliomyelitis patient and suspected cases* - hospitalization in special departments is obligatory. After the patient is isolated (for 21 days from the onset of the disease) final disinfections is performed in his dwelling. Contacts are observed for 20 days after isolation of the patient.

The so-called vaccine-associated poliomyelitis occurs extraordinarily rare (1:1-4 million of vaccinated persons or those who had contacts with the vaccinated). The complication occurs more frequently in persons having immunodeficiency.

MEASLES (MORBILLI)

The pathogenic agent causing measles is the myxoviruses. The measles virus is very unstable and is soon destroyed outside the human body.

Epidemiology

The *source of infection* in measles is a sick person.

Infectivity is greatest in the initial catarrhal stage and during the first days after the appearance of the rash; and after the fourth day the patient is no longer a source of danger. In cases with complications, however (pneumonia), infectivity lasts longer and the patients are thought to remain contagious for as much as ten days from the appearance of the rash.

The aerial-droplet route usually *conveys infection*. The virus is *expelled* from the organism in the secretion of the mucous membranes of the nose, nasopharynx, and upper respiratory tract, particularly during coughing and sneezing. Infection can be spread considerable distances within dwellings and blocks of flats-along hallways and corridors and across landings to neighboring rooms and flats. There is no **transmission** of measles via articles or clothing, or through an intermediary.

The *susceptibility* of humans to measles is very high (**susceptibility index** 0.96).

Stable lifelong **immunity** is conferred by one attack of measles. Second attacks are very rare (0.5 to 1.0 %).

Infants under three months of age are immune to measles and those of three and six or eight months are relatively immune. This is attributed to immunity transplacentally transmitted from a mother who had previously had the disease.

Owing to mass-scale vaccination, the age structure of morbidity has changed significantly: the proportion of cases with measles among schoolchildren and adolescents has increased.

Pathogenesis

The *portal* of entry of measles is the mucous membrane of the upper respiratory tract, and possibly the conjunctiva.

The principal pathological changes attending measles are inflammatory processes in the nasopharynx, respiratory organs, and skin.

The *Belsky-Filatov-Koplik spots* scattered over buccal and labial mucosa in the initial stage are the result of an inflammatory process with small foci of degeneration and partial necrosis of the epithelium. Catarrh of the nasal and of the upper respiratory tract mucosa is a regular symptom in measles. The inflammatory process in the bronchitis and bronchiolitis in measles has a tendency to penetrate into the depth of the bronchial wall. Later inflammatory changes also appear in the alveoli with the foci of *interstitial pneumonia*. Purulent processes may also develop in the pulmonary tissue.

Intestinal lesions in measles, which occur later, have symptoms of catarrhal colitis, sometimes it is ulcerative, and less commonly fibrinonecrotic. In the *central nervous system*, cerebral circulation is disturbed, and early serous meningitis and encephalitis are sometimes encountered.

The altered reactivity of the child's organism during measles is expressed in the condition known as *measles anergy*; positive tuberculin reaction disappears, the immune body's falls, the complement decreases. As a result, measles can light up latent infection (tuberculosis, dysentery, etc).

Complications are caused by measles virus itself and by secondary bacterial flora. *Early pneumonia* is apparently an expression of the measles infection. The predominance of complications in the respiratory organs is associated with predilection of the measles virus for these systems.

The measles virus can persist for a long time in the *brain* tissue of man and cause chronic infection. Subacute sclerosing panencephalitis develops. This is a rare and a very grave demyelinating disease of the central nervous system with a lethal outcome.

Clinical manifestations

The period of measles:

- incubation period
- catarrhal period
- eruptive period
- period of pigmentation

The *incubation period* of measles is usually from nine to 17 days. In children who have been vaccinated, or were given blood or plasma transfusions, the incubation period may even be as long as 21 days.

The *catarrhal period* is characterized by a rise in temperature, headache, rhinitis, and cough. There is general malaise, adynamia, loss of appetite, and insomnia. Conjunctivitis expresses itself in conjunctiva hyperemia, lacrimation, and photophobia and blepharospasm.

Very typical alterations of the buccal and palatal mucosa occur. One or two days before the outbreak of the skin rash red irregular spots varying in size can be seen on the mucosa of the soft, and in part of the hard, palate. This eruption is known as *enanthema* is an important early diagnostic sign of measles. The typical initial symptom of measles is *Belsky-Filatov-Koplik's* spots.

Belsky-Filatov-Koplik's spots mostly break out on the buccal mucosa on the line of opposition of the molar teeth, and less commonly on the lip inner surfaces and on the gums, occasionally on the conjunctiva. Each element looks like a whitish papule, the size of a poppy-seed, surrounded by a narrow band of hyperemia, or areola. They adhere closely to the mucosa and cannot be removed by swabbing. The spots persist for two or three days. The presence of *Belsky-Filatov-Koplik's* spots is a pathognomonic measles symptom found in no other disease. The catarrhal stage of measles usually lasts for three or four days.

The eruptive period stage begins with a new rise of temperature. The appearance of the rash coincides with the rise of temperature. Its first elements are found behind the ears and in the centre of the face. Within 24 hours, it spreads rapidly over the whole face, neck, and upper part of the chest. On the second day, the exanthema rapidly spreads over the trunk and the proximal parts of the limbs, and on the third day covers the limbs. This order of succession in the spread of the eruption is typical of measles.

At first, the elements of the rash look like pink papules of a soft consistency, the size of a grain of millet or buckwheat. Soon adjacent maculopapules become confluent, forming large blotches of irregular outline. Large maculopapular elements have a tendency to fuse further. The rash exanthem persists for three days. Physical

examination of the chest often reveals symptoms of tracheobronchitis, and sometimes emphysema of the lungs.

The period of pigmentation - the rash on the face fades on the third day when it appears on the extremities. The subsiding rash becomes less prominent and assumes a cyanotic tinge; its elements, gradually fading, leave spots of a light-brown pigmentation, which persists for one or two weeks. Fine branny desquamation (on the face and trunk) sometimes following the decrease in eruption lasts around five to seven days. The catarrhal phenomena disappear with the rash decrease.

At the end of the incubation period, the ***blood*** picture shows mild leukocytosis and neutrophilosis, at the end of the catarrhal stage leukopenia and neutropenia, and at the eruptive stage leukopenia, often with a relative neutropenia, eosinopenia and thrombopenia.

Classification

Typical form:

- mild,
- moderately severe
- severe.

Atypical forms:

- measles with a toxic
- abortive
- rudimentary course
- mitigated.

Mitigated form of measles is in children who underwent serum prophylactic immunization: the incubation period is protracted to a maximum of 21 days, but the initial and eruptive periods are shortened, catarrhal symptoms in the mucous membrane are usually mild or absent; and the enanthema and Belsky-Filatov-Koplik's spots may not appear, rash is usually sparse and sometimes is represented by few macularpupular elements. Temperature is sometimes only subfebrile and lasts for two or three days. The patient's general condition is not severe. There are no complications or lethal issues.

Complications

Laryngitis - of measles croup

Pneumonia is one of the most common complications in measles, particularly in infants, and is a main cause of death from this disease: early pneumonia (in the catarrhal stage), secondary infection (pneumococcal, staphylococcal and streptococcal).

Complications of the alimentary tract are stomatitis (gangrenous stomatitis, or noma), dyspepsia is common, particularly in young infants, colitis.

Catarrhal otitis, purulent otitis, blepharitis and keratitis.

Nervous complications are serous meningitis, encephalopathy

Diagnosis

Measles must be identified as early as possible. The diagnosis is based on clinical symptoms, taking into account the epidemiological anamnesis. The diagnosis is verified by a serological test using the hemagglutina-don-inhibition test, neutralization and the complement-fixation test. The increasing titer (4 times and over), as determined during a repeated test in 7-10 days, is a more reliable diagnostic sign.

In the catarrhal stage can resemble influenza and other respiratory viral infections.

During the eruptive stage, there are usually no difficulties in recognizing measles, and errors can only occur when its course is atypical.

Measles is sometimes confused with Rubella; Scarlet fever, Serum rash, Drug rash.

Treatment

Properly organized hygienic conditions, nursing care of the patient and protection from secondary infections are of immense significance for the treatment of measles and prevention of complications.

Measles cases are hospitalized when they are severe and complicated; home conditions are unsatisfactory, or it is impossible to arrange due nursing care; when epidemiological signs are present. Patients should be isolated in cubicles.

Fresh and clean air is very important for the patient. The visible mucosa should be systematically cleansed.

The diet should be nourishing, easily digestible, and have a minimum of solid particles; liquids and soups should be preferred.

If measles is not complications, symptomatic means are taken if necessary. Antibiotics are given in case of complications, which are usually of bacterial nature.

Measles pneumonia should be treated in compliance with the general rules adopted in pediatrics: antibiotics, oxygen therapy, cardiovascular preparations. Corticosteroids and other preparations are indicated in severe pneumonia.

Prophylaxis

Carantin is during 21 days after contact. Gamma-globulin is only used for prophylactic purposes in a small number of children who were in contact with the measles patients and are 3-months to one year of age. Gamma-globulin is given not later than 6 days from the day of contact. The preparation is given in a dose of 1.5 ml (3 ml to infants who have already developed the disease).

RUBELLA

The agent that causes rubella is a microvirus, it contains a single-stranded RNA, and is sensitive to chemical agents and heat.

Epidemiology

The *source* of infection is a sick person, who probably becomes infective a few days before the disease becomes manifest. *Contagiousness* does not probably disappear two weeks (and over) after the rash resolves.

The aerial-droplet route *transmits* the infection. Pregnant women with manifest or symptomless rubella may become the source of intrauterine infection of the fetus.

Susceptibility to rubella is high. Life-long stable *immunity* develops as a rule, and a repeated infection is rare.

Clinical Manifestations

The *incubation period* lasts 15-21 days, sometimes up to 24 days.

A slight rise in temperature is noted, and occasionally slight malaise, cough, and reddening of the conjunctiva (conjunctivitis). *The typical symptom* is swelling of the post-auricular cervical, sub-occipital, and other lymph nodes, which develops 1-3 days before the eruption and disappears several days after it subsides.

The **rash** invades the face and neck, and covers the whole body within a few hours. It is localized mainly on the extensor surface of the limbs. Its elements are pale red, round or oval spots, sometimes slightly elevated above the surface of the skin, with no tendency to coalesce. The rash lasts 2 or 3 days and disappears rapidly without leaving any pigmentation. Subsequent desquamation is not observed.

With the skin eruption, an enanthem in the form of small red spots appears on the faucial mucosa; but Belsky-Filatov-Koplik's spots never occur.

Blood counts demonstrate leukopenia, lympho, and numerous plasma cells (10-15 %).

Complications (arthropathy, otitis, pneumonia, nephritis, polyneuritis) are exceptionally rare. Encephalitis and encephalomyelitis cases have been reported.

Clinical manifestations of congenital rubella:

microcephalic hydrocephalus, deafness, cataract, retinopathy, microphthalmia, glaucoma, cardiac defects, etc. ("congenital rubella syndrome" are cataract, cardiac defects, deafness). Depending on the term of pregnancy, a risk of various embryopathies arises in women with rubella: cataracts in the 5th-6th week, deafness in the 9th week, and cardiopathy in the 5th-10th week.

Diagnosis

Rubella has to be differentiated from acute exanthems: measles, scarlet fever, serum and various drug rashes.

Treatment and Prophylaxis

No treatment is required. The patient should be isolated until the 5th day from the outbreak of eruption. The current vaccine strategy is to immunize all infants at 12 to 15 months of age with measles-mumps-rubella (MMR) vaccine and to administer a second dose of MMR during childhood. Some specialists maintain that rubella during the first months of pregnancy is an indication for discontinuation of pregnancy.

SCARLET FEVER

Scarlet fever is an acute infectious disease, characterized by lesions of oropharynx with submaxillary lymphadenitis, fever toxemia, rash and then desquamation.

Etiology

The *pathogen* of scarlet fever is a β -hemolytic *Streptococcus group A*. Streptococci have considerable stability to the influence of physical factors. The streptococcus produces exotoxins, which cause toxemia. Erythrogenous exotoxin is principal among them. Stable antitoxic immunity is acquired against erythrogenous toxin. Bacterial antigens of streptococcus and antibodies against them are typospecific and antibacterial immunity is not stable. If the child has had scarlet fever, he will be able to contract other streptococcal infections (tonsillitis, nasopharyngitis).

Epidemiology

Scarlet fever is **anthroponotic**. The *source of infection* is a child with scarlet fever or with other forms of streptococcal infection.

The patients become *infectious* from the onset of the disease. Duration of infectious period may fluctuate from some days to several weeks or sometimes months. Antibiotics lead to rapid delivery of the patient from hemolytic Streptococcus and absolute removal bacteriocarriage in convalescence period.

The principal *route* of scarlet fever infection is an air-droplet one. Infection through toys and other things used by the patient may be caused in pre-school institutions. Alimentary route plays insignificant Milk is an exception.

The *contagious index* is about 40 %.

Pathogenesis

The principal *portal of entry* in scarlet fever is mucous membrane of oropharynx. The infection may penetrate through damaged skin (in bumps or injuries) or mucous membranes of the genitals (extrabuccal scarlet fever). After entering, the human body

hemolytic streptococcus leads to a complex pathologic process, which may be presented in the form of **three lines of pathogenesis**: toxic, septic and allergic ones.

The toxic syndrome is the result of influence of the toxic substances produced by the hemolytic streptococcus in the human body: the signs of toxemia in the form of fever, rash, headache, and vomiting, dystrophic changes in the myocardium, lesions of the vegetative nervous system.

The septic syndrome includes primary inflammation in the portal of entry and microbial streptococcal complications. There is purulent one and spreading of hemolytic streptococcus from the primary focus to the surrounding tissue and through lymphatic and blood vessels.

The allergic syndrome is caused by the sensitizing substances of hemolytic streptococcus, which are proteins. It reaches its peak on the 2nd -3rd week of illness. Clinically allergic syndrome is manifested by various eruptions on the skin, myocarditis, glomerulonephritis, synovitis and "Allergic waves".

Clinical Manifestations

The **incubation period** for scarlet fever is 2 to 7 days. The disease is started in fever, vomiting, sore throat and toxic symptoms such as headache and malaise. Within 12 to 36 hours after onset, the typical rash appears.

Tonsillitis is a typical sign of scarlet fever. Scarlatinal tonsillitis may be catarrhal, follicular or necrotic. **Tonsillitis** is accompanied by regional lymphadenitis. The pharynx is edematous and beefy red in appearance. The upper border of **hyperemia** is on the anterior palatal arches and on the base of the uvula (delimited hyperemia).

The **tongue** changes in appearance as the disease progresses. During the first 1 or 2 days the dorsum has a white "fur coat", and the tip and edges are reddened. By the fourth or fifth day the white coat has peeled *off*. The red, glistening tongue, studded with prominent papillae, presents the appearance of raspberry ("**raspberry tongue**"). This sign remains up to the 9th-10th day of the disease.

Exanthem. The rash usually appears within 12 hours after onset of the illness. Elements of rash are minute roseolas, closely situated with each other. The exanthema has the following distinctive features:

1. It becomes generalized very rapidly.
2. Patient face is typical in scarlet fever - cheeks are red, smooth and flushed, and the area around the mouth is pale (circumoral pallor), lips are crimson.
3. Rash is more intense in skin folds such as the axillae, cubital, inguinal, popliteal, and also on skin of the neck, breast, abdomen, buttocks.
4. Tiny petechiae occur in the creases of the folds of the joints and form transverse lines (Pastia's sign) that persist after the rash has faded.
5. Rash usually remains for 4-5 days.

Desquamation is one of the most characteristic features of scarlet fever. It becomes apparent initially on the face on the second week as fine branny flakes. Then it spreads to the trunk and finally to the extremities, becoming generalized by the third week. The desquamation skin of the trunk comes off in larger, thicker flakes. Sometimes a retrospective diagnosis may be made on the basis of peeling skin and a history of a sore throat associated with a rash several weeks before.

In acute period of scarlet fever, cardiovascular changes are characterized by tachycardia, increased blood pressure. Bradycardia, arrhythmia, decreasing of blood pressure, dull heart sounds, systolic murmur occur the 4th-5th day of illness. N. F. Filatov has described the so-called «scarlatinal heart». The bases of these changes are extracardiac disorders of vegetative nervous system.

There is leukocytosis, neutrophilia, increased ESR in the acute period of scarlet fever.

Classification

There are **typical** (mild, moderate, severe) forms of scarlet fever and **atypical** ones. The **indices of severity** of the disease are signs of toxemia and local changes (lesions of the tonsils and the lymph nodes). Extrabuccal forms (burn, injury, puerperal ones) are considered atypical too. They are characterized by a short-term incubation period, absence of mild tonsillitis. Rash appears near the portal of entry, it is more intensive there.

The forms with **aggravated signs** are atypical too; they are hypertoxic and septic ones.

Complications of scarlet fever may be divided into the infectious (septic) the early one (first week) and allergic ones the late one (2nd-3rd week). The principal *septic complications* are tonsillitis, lymphadenitis, otitis media. *Allergic complications* include lesions of kidneys (nephritis), heart (myocarditis) and joints (synovitis).

Myocarditis more frequently occurs on the 2nd-3rd week of the illness. Tachycardia, dull heart sounds, systolic murmur, enlarged liver, sometimes extrasystole appears.

Scarlet fever in 1-year-old babies occurs rarely, because they have trans-placental immunity. This immunity disappears by 6 months. At before 6 months the peculiarity of the disease is a mild expression of toxic syndrome, catarrhal tonsillitis, and scarce rash. "Raspberry tongue" and desquamation occur rarely. However, in 1-year-old babies, septic complications (otitis, lymphadenitis) occur more frequently and septicopyemia may appear.

Treatment Hospitalization takes place on the following indications:

1. Severe course of scarlet fever with various complications.
2. Children from boarding schools and other institutions.

Antibiotics should be administered even in a mild form of the disease because complications may later occur. Penicillin should be given in the dosage of 100 mg/kg/ day for 7-10 days. All patients must get antihistamine medications and polyvitamins.

Prophylaxis

Specific prevention of scarlet fever has not been devised. The patients with scarlet fever are isolated for 22 days. The children who had contacts with the patient should be observed for 7 days after the moment of the patient's isolation.

VARICELLA

Varicella is an acute infectious disease, characterized by vesicular eruption with transparent liquid on skin and mucous membrane.

The Varicella virus contains DNA. Varicella and herpes zoster were proved to be caused of varicella-herpes zoster virus.

Epidemiology

Patients are a source of infection from the last (1-2) days of the incubation period up to the ninth day from appearances of the elements of the rash. Infection is transmitted by air-droplet route, and can be conveyed over quite considerable distances. Susceptibility to Varicella is very high, practically universal. Stable lifelong immunity follows one attack; second attacks are extremely rare.

Pathogenesis and pathology

The portal of entry is the mucous membrane of the upper respiratory tract. After an incubation period, the virus circulating in the blood localizes by preference in the skin owing to its dermatropism. In very rare cases the lungs, liver, spleen, kidneys, pancreas, and other internal organs may be affected by the virus.

Many researchers think it possible that the Varicella virus may persist in the body of man for a long period of time in the cells of the intervertebral ganglia.

Clinical manifestations

The incubation period averages 11-21 days.

The outbreak of rash coincides with a rise of temperature or follows a few hours later. At first maculopapular, the elements are very quickly converted into vesicles, but some papules dry up without vesiculation. Vesicles are round or oval, differ in size, and are seated superficially on an uneducated base; their wall is tense, and they are lustrous and filled with a clear fluid. Vesicles dry up in one or two days, forming flat brown crusts. In some patients eruption is often seen on the mucous membranes of the mouth, nasopharynx, larynx, genital organs.

The rise of temperature in chickenpox usually coincides with appearance of the rash.

The chief *blood* findings in the eruptive stage are slight leucopenia, neutropenia, and a relative lymphocytosis.

When the contents of vesicles become purulent pustules are formed, and scars may then be left when the crusts are shed.

In the *bullous form* of varicella large flabby bullae develop (up to two or three centimetres in diameter, with turbid contents).

In the gangrenous form solitary vesicles assume a hemorrhagic character and are surrounded by inflamed zone.

A *hemorrhagic form* is encountered very occasionally in feeble children with symptoms of hemorrhagic diathesis.

Generalized or visceral form of Varicella with affections of the internal viscera is usually found on posthumous section.

Complications

Complications are rare in Varicella: keratitis, laryngitis, abscesses, phlegmons, stomatitis, otitis, lymphadenitis and bronchopneumonia.

Individual cases of encephalitis and serous meningitis have been described.

Treatment

The basic treatment of Varicella is hygienic measures aimed to prevent secondary infection. Vesicles are painted with a 1 to 2 per cent solution of potassium permanganate or aqueous solution of brilliant green. The mouth should be rinsed with a suitable weak disinfection.

Antibiotics (penicillin, erythromycin, tetracycline, etc.) are indicated for purulent complications. Antiviral medications (acyclovir in the dosage of 5 mg/day for 5 days) are administered of complications (encephalitis, pneumonia).

Prophylaxis

The patients are isolated (usually at home) for 5 days from the ending of the rash. Disinfection is not required because the virus is very unstable.

The patients who have contact with Varicella to it should be quarantined for a period between eleven and twenty-one days counting from the time of contact.

VIRAL HEPATITIS A

Viral hepatitis A (VHA) is an acute cyclical disease with a short-time, often insignificant, manifestation of intoxication, having a benign prognosis.

Etiology: its infectious is hepatitis A virus (HAV) which is an RNA containing. It taxonomically belongs to the *Picornaviridae* family, the *Hepatovirus* genus. There are 7 genotypes identified. All 7 genotypes have the same antigen and cause cross protective immunity.

The virus is characterized by **stability** in the environment

Antigen is found in feces of a patient (fecal antigen). In blood serum the anti-HAV **antibodies** are found, at first the M-class, and later in the disease the G-class which testify to the presence of protective immunity.

Epidemiology

The infectious **source** is a sick human. Very dangerous are the latent, inapparent and anicteric forms of the disease. The highest concentration HAV is observed in preicteric period. After the appearance of jaundice the viral level in feces is **significantly** decreased and the time of the HAV excretion does not exceed 6-7 days of icteric period.

VHA is a typical **intestinal** infection. Children **susceptibility** to it is much higher than in other patients, they form 70-80 % of all cases of VHA. The **highest morbidity** is registered in autumn and winter. Children **of the first year** of life are rarely ill with VHA.

Pathogenesis

VHA is called an **auto-restricted infection** that is caused by high viral immunogenicity. VHA enters the intestine. From here it spreads hematogenically to hepatocytes and penetrates into them. Owing to the interaction of the virus with biological macromolecules metabolic disorders appear in the membrane and other component parts of hepatocytes. This leads to **destruction of membrane structure**, and excretion of enzymes from hepatocytes - a cytolytic syndrome.

The anti-HAV **antibodies are virusneutralising** one and happen to be already effective in low titres. The **functional state** of liver is completely regenerated. There are no cases of chronic hepatitis development.

Clinical manifestations

The **incubative period** is 10-60 days.

Prodromal period (preicteric) of the disease begins acutely, the body temperature rises, there is **intoxication**, weakness, headache, nausea, vomiting, asthenia. Sometimes, there is a dull, acute or paroxysmal **abdominal pain**, a feeling of heaviness in the right hypochondrium, mild **catarrhal signs** (rhinitis, hyperemia of fauces). There may be **dyspeptic disturbances** (constipation, or diarrhea).

On **physical examination liver** enlargement, algesia and pain can be revealed. At the end of the preicteric period **dark urine and discolored excrements** (acholia),

According to the **laboratory findings** this is the period when enzymes (ALT, AST), thymol test increase, as well as bilirubin level.

Using the clinical characteristics we can discern **dyspeptic, astheno-vegetative, catarrhal and mixed** variants of the prodromal period.

The general **duration** of the preicteric period of the HAV is 3-7 days.

The icteric period frequently appears on the 3rd-5th day of the disease. After the appearance of icteric scleras and mucous membranes there is a rapid rise in the icterus of skin of the face, limbs, trunk. **Jaundice** increases for 2-12 days. The **significant sign** is that jaundice is not accompanied by aggravation, but just the opposite by an improvement of the general patient condition. Resumption of bile secretion begins with **clear urine** and darker feces.

The general **duration** of the icteric period often does not exceed 1.5-2 weeks. Hepatomegalia is retained during the whole icteric period and sometime it is enhanced. During **palpation** the liver border is smooth, somewhat painful. Frequently there is an enlarging of the **spleen**.

In the icteric the **general clinical manifestations** as asthenization, hypotension, bradycardia, weak cardiac tones, systolic murmur prevail.

In **blood** examinations there is leukopenia, lymphocytosis and eosinophilia, while ESR is normal. During the icteric period there are severe **biochemical disorders** demonstrating functional activity of the liver: the hyperbilirubinemia (a higher associated fraction), higher activity of the hepaticocellular enzymes, high thymol test findings and dysproteinemia.

The third disease period (*convalescence or posticteric*) is characterized by the absence of complaints, the patient feels better, but in some cases the enlargement of the liver is retained and the liver functional activity is gradually improving. Fatigability, hypomnesia, asthenovegetative disorders can remain.

Convalescence *duration* is 2-3 months.

The *main criteria of VHA severity* as well as other types of viral hepatitis, is the intoxication manifestation, its presence and degree of manifestation.

In the *light form* the general intoxication is not significant, jaundice is not intensive, liver may be enlarged up to 3 cm and be dense. The bilirubin level than 85 $\mu\text{mol/L}$ (unassociated up to 25 $\mu\text{mol/L}$), the hepato-cellular enzyme activity exceeds normal concentration 5-10 times.

The *moderately severe* form is characterized by moderate intoxication, (temperature rises up to 38-39 °C), anorexia and sometimes nausea continue. Jaundice is intensive, its duration is 2-6 weeks, liver is enlarged by 4-5 cm, spleen is also enlarged. The level of total bilirubin in blood serum is 86-200 $\mu\text{mol/L}$. There is a higher activity of the hepato-cellular ferments, but prothrombin index may decrease (to 70-60 %).

The *severe form* of the VHA is rare. The intoxication is considerable with CNS affection: high temperature, adynamia, weakness, anorexia, recurrent vomiting, sometimes excitement, insomnia, headache. There is hemorrhagic rash. Jaundice becomes very expressive, the feces are acholic, urine is dark. There is oliguria. Liver is considerably increased and dense. The jaundice progressing leads to severe intoxication: mental confusion, recurrent vomiting, nasal bleeding, bradycardia. Bilirubin level in blood serum is over 170-200 $\mu\text{mol/L}$. The prothrombin index is lower than 40 %, enzyme level is very high. Hypoalbuminemia is progressing.

Cholestatic syndrom occurs rarely, it has insignificant intoxication, prolonged hyperbilirubinemia accompanied with mildly higher activity of ALT and a higher concentration of alkaline phosphatase.

Atypical clinic form - without jaundice: the anicteric, latent and subclenic forms.

The *anicteric form* has no icteric skin and scleras. There is a short-time temperature rise, hyporexia, nausea, weakness, abdominal pain, liver enlargement. There is a higher activity of ferments (ALT, AST) and thymol test in blood serum. The bilirubin level is normal. The duration of changes is 3-7 days.

The *attenuated form* is characterized by the subfebrile temperature, transitory short-time jaundice (2-3 days), dark urine and acholic feces. The attenuated form is termed as "rudimentary" one being a variant of the mild type.

The *subclinical form* has no clinical manifestations, but there is higher activity of enzymes (ALT, AST) and IgM antibodies in blood serum are found.

The *course of the VHA* may be acute (up to 3 months) and protracted (from 3 to 6 months).

The *basic criteria for the primary VHA diagnosis* are:

1. Contact with a VHA patient during 35 days before illness.
2. Seasonal morbidity with a peak in spring and autumn. The patients are usually children, adolescents or young men.
3. The acute onset with manifested temperature rise and intoxication.
4. Enlargement of the liver.
5. Short preicteric period (4-6 days), mainly with dyspeptic disorders.
6. The general patient condition improvement with jaundice appearance.
7. Mild intoxication and short-time jaundice.
8. Rare development of severe forms.
9. Absence of chronization process.
10. And HAV (IgM) antibodies in blood during the initial period.

Differential diagnosis in the preicteric period.

More often doctors make a usually diagnosis of *ARVI* during that period. But in VHA, the catarrhal signs are not significant. But in ARVI there is no enlargement, density and painfulness of the liver on palpation. Dyspeptic disorders typical for the preicteric period of VHA, are absent in ARVI.

In VHA the dyspeptic signs differ from the *acute enteric infections*. The VHA manifestation has no inflammatory process in the gastrointestinal tract.

In the abdominal variant of the VHA prodromal period there may be *acute surgical diseases of abdominal cavity* (appendicitis and others). However, in VHA even in spite of the severe abdominal pain, muscular defence, the abdominal irritation signs are absent. The pain is mostly localized in the right subcostal region. In the blood is absence of inflammatory reaction.

In the icteric period doctors have to differentiate this state with the *suprahepatic jaundice* (hemolytic jaundice) which appears owing to an intensive hemolysis of erythrocytes. When making differential diagnosis you should take into account a case and life history (anemia, intoxication, hemorrhages), have vertigo, sweating, pale skin and mucous membranes, citric tint of jaundice, absence of acholic feces and dark urine. In case of suprahepatic jaundice there is no preicteric period. Laboratory examination shows a higher bilirubin fraction, biochemical factors of liver function are not changed, there is a drop in erythrocyte count and a lower level of hemoglobin.

Hepatic jaundice - different variants of hepatitis in infectious diseases (yersiniosis, infectious mononucleosis, herpetic infection, salmonellosis) develop on the background of the main disease with its typical clinical syndromes.

The main attention is paid to the making a differential diagnosis of VHA as other *etiology (B, C, D, E)*. The most decisive differential diagnostic significance have the indications of specific HAV markers (anti-HAV-IgM) in blood.

Treatment

The main, in VHA treatment is a *basic therapy*. It is a complex of measures directed at creation of favorable conditions for hepatic function. Patients *have to keep bed* (for 2-3 weeks). Improvement patient condition, better appetite, decrease in intoxication, normal color of urine and feces are basic indications for a more lenient regime.

During *diet* prescription the doctor should take into account the decreases functional activity of patient's liver. Proteins, fats and carbohydrates should correspond to the patient age. The patient must exclude meat extractive dishes, fried meat and fish, smoked and salty food products, tinned foods, cocoa, chocolate. The

patient may eat fresh and boiled fish or meat with exception of pork mutton and duck meat. Milk products should also be excluded from the diet. The fats in the daily diet must be oil in 60-70 % of instances. Carbohydrates are allowed while yellow, red and orange vegetables and fruits like carrot and tomato juice, oranges, tangerines, pumpkin which has a lot of carotene should be taken out of the diet. The carotene surplus may enhance jaundice and affect the body.

According to *Pevzner diets*, in the first and second disease period diet N 5A is prescribed while in the third period diet N 5.

It is necessary to make sure that the patient *drinks a sufficient quantity of fluid* (alkaline mineral waters, or tea, sweet-brier decoction).

After acholic feces stop *cholagogue drugs* ("Alochor", "Cholenzyme", herbal decoctions of cholagogue phytotherapy) are used.

In case of a severe course *intravenous dropper infusion* should be administered using Rheopolyglucinum, 5% solution of glucose for detoxication. Protracted illness needs a *prescription* of Essentiale, Legalon, Carsil.

Patients may be *discharged from the hospital* from jaundice appearance if intoxication, icterus, enlarged liver bilirubin and fermental activity levels in blood are absent.

The *convalescents* must go through prophylactic medical follow up examination during a 6 month's period (after 1, 3 and 6 months). Meals are the same as in the acute period. During the first 6 months physical exercises should be performed in special groups of physical exercise therapy.

Prophylaxys

The patients are *admitted* into the infectious departments. After hospitalization it is necessary to conduct *final disinfection*. *All contacts* must be found and supervised by medical professionals for 35 days. In all children *institutions* a quarantine of 36 days should be kept from the first disease case.

VIRAL HEPATITIS B

VHB refers to the parenteral hepatitis group. The VHB can be an acute or chronic hepatic disease which is characterized by a slow development and prolonged course. It often has severe and malignant (fulminant) forms.

Etiology

Contains DNA and consists of three antigens: "Australian" HbsAg, nuclear (HbcAg) and the infectivity antigen (HbeAg).

VHB is determined to an individual *hepatovirus* family. It is very *resistant*. There are eight known *subtypes* of VHB.

Epidemiology

The *source* of the VHB are patients with acute and chronic hepatitis.

In the VHB acute forms the patients *infectivity* appears from the moment of infection in the incubation and prodromal periods and it continues until complete sanation of the body in the convalescent period.

The virus is *contained* in blood, and also in different body fluids (saliva, urine, sperm, vaginal secretion, etc).

For the HBV appearance it is enough to inoculate a very *small volume* of blood (0.0005 ml).

There is a possibility of *transplacental route* of the VHB infection which occurs in placenta injury is not over 10 %. Most of the newborns are infected by *perinatal* way.

Children of the first year of life (86 %) suffer from VHB more often. After three years the morbidity is considerably decreased (because of reduced quantity of parenteral manipulations).

Pathogenesis

Infectious agent parenterally *penetrates* the body and with the blood flow spreads further into the *liver*. In hepatocytes the viral DNA is released, penetrates inside the nucleus of hepatocytes and inserts into the cellular genome. The Dane particles are blocked on the hepatocyte membranes. *Sensitized* killers attack the infected hepatocytes and cause their cytolysis. The disease course *depends* both on

the infection dose and infectivity of the virus, as well as on the character of genetically determined immune response of the body.

Clinical manifestations

Incubative period of the VHB lasts 6 weeks-6 months.

The disease ***progresses*** in stages: there appears weakness, patients easily get tired, their workability is low, there is loss of appetite, often the temperature rises. Often, these signs are weakly manifested and the disease ***beginning*** is manifested with dark urine and jaundice.

In the ***first-year-of-life children*** the prodromal period is shortened to 5-7 days, sometimes to 1-2 days.

When ***jaundice appears*** intoxication is not reduced (as in VHA): the patients complain of nausea, vomiting, high temperature, heaviness and pain in the epigastric part and in the right subcostal region.

Jaundice gradually increases during 5-6 days (sometimes 2 weeks). The general ***duration*** of icterus in VHB is 3-4 weeks (sometimes to 6-8 weeks).

In VHB ***different rash*** on skin can be observed, such as urticarial, papular like in measles and scarlet fever. The liver is enlarged, an enlargement of the spleen is observed in 40-50 % of cases. During the peak period of disease there is also a general depression of the nervous system, bradycardia, hypotension, acholic feces.

Classification of the VHB is similar to that of VHA, however, in VHB average-severe forms occur more frequently.

The most severe degree of the VHB, especially in the infants younger than 12 months, is the ***malignant form, hepatodystrophy*** (acute yellow hepatic atrophy, toxic hepatic dystrophy), which appears in cases of diffuse ***massive hepatic necrosis***.

Incubative period is shortened to 2-3 days, the onset is acute, temperature rises, apathy, adynamia followed by excitement. There are typical dyspeptic changes: regurgitation, vomiting, diarrhea.

Prodromal period is shortened to several days, sometimes there is no prodromal period and the disease begins from icterus.

From the *jaundice period* the child's general condition is quickly aggravated: severe intoxication, hemorrhagic syndrome, "saffron" color of skin, tachycardia, dull cardiac sounds, extrasystoles, adynamia, limb tremor, higher tendonal reflexes, psychomotor excitement, crying, depression with disorientation, hallucinations, delirium. In the day time these patients are drowsy, but at night they have insomnia. The recurrent vomiting and coffee-ground. Nasal bleedings, dermal and mucosal hemorrhages, hemorrhages around the injection places are possible (coagulopathy syndrome). The specific feature is a decreasing liver: decreased size, tympanis sound about the hepatic border, but in the severest cases the hepatic dullness absolutely disappears.

As *the time* goes an excitement is changed with depression, delirium, hallucination, convulsions, mydriasis, "raw liver" smell from the month, anuria, deep sleep.

In laboratory findings there is anemia, neutrophilic leukocytosis, thrombopenia, higher ESR levels. Bilirubin level gains high levels following important tests are *bilirubin-protein and bilirubin-enzymal dissociation* (a higher bilirubin level and lowering of prothrombin and protein-complexes, as well as an activity of hepatocellular enzymes). In the acute degeneration case there may be a lethal outcome in 1-2 days (in spite of all medical treatment).

Diagnosis of the VHB is based on clinical features, stable increase of hepatocellular enzyme level, presence of parenteral procedures in life history, also as a result of specific examination: HBV-markers and antibodies against (HbsAg, HbeAg and-antibodies, HbsAg-antibodies and Hbcor-antibodies, DNA HBV.

Treatment

All patients with VHB must be *hospitalized* for administering complex therapy. *Bed rest* is prescribed till complete recovery. *Diet* is similar to that one in VHA.

In fulminant forms, comatous patients, the patients in coma in the 1st year of life - prednizone is administered in doses from 1 to 5 mg/ kg body weight per day (4-6 times) during 7-10 days. For 3-7 days protein food is forbidden. The energetic requirements are provided by 5-10 % glucose solution, the plasma, albumen,

rheopolyglucinum, by dropper method according to the age and diuresis, Contrikal to 50.000 Un, cocarboxilase, Vicasol, Heparin (DIC-syndrome. In case of bacterial complication *antibiotics* are prescribed. *Substitutive hemotransfusion*, plasmapheresis, hemodialysis, hyperbaric oxigenation can be performed. *Hypoxia correction* using intensive therapy measures.

The patients are *discharged* when they get their clinical recovery and normal functional.

Prophylactic medical examination after 1, 3, 6, 9 and 12 months. Children are freed of *inoculations* during 1 year.

Prophylaxis

1. Obligatory *examination of donors* for HBsAg detection.
2. Use of *disposable instruments*.
3. Educating children in the *sanitary culture level*.

VIRAL HEPATITIS C

Viral hepatitis C is an infectious disease, which is transmitted parenterally, and characterized by not severe course and frequent development of chronic forms with following transformation into hepatocirrhosis and hepatocarcinoma.

The disease is *caused* by hepatitis C virus (HCV), which contains RNA. *Peculiarity* of HCV is heterogeneity of its genome.

The *source* of infection is an infected patient with viral hepatitis C. HCV may be *transmitted* from the mother to the fetus through the placenta.

The *incubation period* of viral hepatitis C is approximately from 6 to 8 weeks.

Fulminant forms do not occur. In spite of favourable course of the acute period of the disease, *forming of chronic hepatitis C* occurs in 20-50 % of the patients.

Etiologic diagnosis is made due to laboratory tests (in acute phase of the disease the antibodies of IgM class and RNA HCV).

Treatment is prescribed by general rules of treatment of viral hepatitis. The early therapy by *high doses of recombinant leukocyte interferons* (IFN-L) should be

administrated because the chronic process may result (3 million units of IFN-L three times weekly for 6-12 months).

VIRAL HEPATITIS D

Viral hepatitis D is an infectious disease, which is transmitted parenterally and characterized by clinic and laboratory signs of liver lesion, frequent development of *fulminant forms* of the disease or *chronic acute hepatitis* with rapid transformation into *hepatocirrhosis*.

The disease is *caused* by hepatitis D virus (HDV), which contains RNA. In absence of HBV, HDV cannot replicate.

Spreading of viral hepatitis D depends on the level of HBsAg carriage.

The *outcome of co-infection* (B+D) is less favourable, than viral hepatitis B: in 70% of the patients the disease has a severe course, fulminant form of hepatitis occurs in half of them.

In co-infection *the diagnosis can be confirmed* by the presence of active replication markers" of the two viruses

Steroid hormones should be given with special caution because HDV has a direct cytopathic influence on hepatocytes.

VIRAL HEPATITIS E

Viral hepatitis E (VHE) is an acute cyclic infection with fecal-oral transmission route and it is characterized by hemolytic syndrome with clinical laboratory findings of liver lesions, severe course and high mortality in pregnant women.

Hepatitis E *spreads widely* in tropical and subtropical countries.

A special sign, which has been discovered in viral hepatitis E, is *hemoglobinuria*. Its appearance is connected with hemolysis of erythrocytes. It is found in *women in 2nd and 3rd trimester of pregnancy*. Lethal outcomes in pregnant women fluctuate from 20 % (the 20th-21 st weeks of pregnancy) up to 75 % (the 40th week of pregnancy).

DIPHTHERIA

An acute, contagious disease caused by *Corynebacterium diphtheriae*, characterized by the formation of a fibrinous pseudomembrane, usually on the respiratory mucosa, and by myocardial and neural tissue damage secondary to an exotoxin.

Etiology and Epidemiology

Three biotypes of *C. diphtheriae* exist (*mitis*, *intermedius*, and *gravis*). Only toxinogenic isolates produce exotoxin; this ability is mediated by bacteriophage infection of the bacterium. Nontoxinogenic isolates may produce symptomatic diphtheria, but the clinical course is usually milder. Spread is chiefly by the secretions of infected persons, directly or via contaminated formats. Humans are the only known reservoir for *C. diphtheriae*. Sporadic cases generally result from exposure to carriers who may never have had apparent disease. Infection can occur in immunized persons and is most common and severe in those partially immunized.

Cutaneous diphtheria (infection of the skin) can occur when any disruption of the integument is colonized by *C. diphtheriae*. Lacerations, abrasions, ulcers, burns, and other wounds are potential reservoirs of the organism.

Pathology

Ordinarily, the organisms lodge in the tonsil or nasopharynx, and as they multiply, toxinogenic *C. diphtheriae* may produce exotoxins lethal to the adjacent host cells. Occasionally, the primary site is the skin or mucosa elsewhere. The exotoxin, carried by the blood, also damages cells in distant organs, creating pathologic lesions in the respiratory passages, oropharynx, myocardium, nervous system, and kidneys.

The myocardium may show fatty degeneration or fibrosis. Degenerative changes in cranial or peripheral nerves occur chiefly in the motor fibers. In severe cases, anterior horn cells and anterior and posterior nerve roots may show damage

proportional to the duration of infection before antitoxin is given. The kidneys may show a reversible interstitial nephritis with extensive cellular infiltration.

The diphtheria bacillus first destroys a layer of superficial epithelium, usually in patches, and the resulting exudates coagulates to form a grayish pseudomembrane containing bacteria, fibrin, leukocytes, and necrotic epithelial cells.

Symptoms and Signs

The incubation period ranges between 1 and 4 days, followed by a prodromal period of between 12 and 24 h. Initially, the patient with tonsil or faucial diphtheria has only a mild sore throat, dysphagia, a low-grade fever, increased heart rate, and rising polymorph nuclear leukocytosis. Nausea, emesis, chills, headache, and fever are more common in children.

The characteristic membrane, usually found in the tonsil area but sometimes in other areas (the nasopharynx), is dirty gray, tough, and fibrinous and may adhere firmly so that removal causes bleeding. Depending on the duration of infection, the membrane may be punctate or extensive and yellow-gray or creamy.

The disease may remain mild. When it progresses, dysphagia, toxemia, and prostration are prominent. Pharyngeal and laryngeal edemas obstruct breathing. If the larynx or the trachea and bronchi are involved, the membrane may partially obstruct the airway or suddenly detach, causing complete obstruction. The cervical lymph glands are enlarged. In severe cases, exotoxin may diffuse into the neck tissue, producing severe edema (bull neck).

The lesions of cutaneous diphtheria are not morphologically specific. Rarely, *C. diphtheriae* causes ocular infection, with or without cutaneous lesions.

Complications and Diagnosis

Severe complications are likely if antitoxin is not given promptly on the basis of clinical diagnosis, even before culture results are available. Insignificant ECG changes occur in 20 to 30% of patients; atrioventricular dissociation, complete heart block, and ventricular arrhythmias are associated with a high mortality rate. Myocarditis is usually evident by the 10th to 14th day but can appear any time

during the 1st to 6th wk. Heart failure may follow; sudden death may occur. Dysphagia and nasal regurgitation, from bulbar paralysis, may occur in the 1st wk of illness; peripheral nerve palsies appear from the 3rd to 6th wk. Spontaneous reversal occurs slowly over many weeks. Myocarditis and palsies do not abate with corticosteroids or delayed administration of antitoxin.

The clinical appearance of the membrane suggests the diagnosis, pending confirmation by culture. Gram stain of the membrane may reveal gram-positive bacilli with metachromatic staining in typical. Material for culture should be obtained from below the membrane, or a portion of membrane itself should be submitted. Loeffler's medium or tellurite agar is preferred for primary isolation of the organism. The laboratory should be notified that *C. diphtheriae* is suspected.

Prophylaxis and Treatment

Active immunization with diphtheria-tetanus-pertussis (DTP) vaccine should be routinely given to all children and all susceptible contacts. For previously immunized contacts, a booster dose of adult-type tetanus and diphtheria toxins, adsorbed (Td), is sufficient.

Symptomatic patients should be hospitalized in infection hospital. Diphtheria antitoxin must be given early, since the antitoxin neutralizes only toxin not yet bound to cells. Antitoxin must be given immediately upon clinical diagnosis, without waiting for culture confirmation.

Caution: *Diphtheria antitoxin is derived from horses; hence, a skin test to rule out sensitivity should always precede administration.* The first dose must be given 0,1 ml intraskin in solution 1:100. After 20 minutes, you must meter erythema and papule. If it smaller then 10 mm in diameter you must 0,1 ml antitoxin subdermaly. After 20 minutes, you must meter papule too, and if it smaller then 10 mm should be administered.

The dose, ranging from 20,000 to 100,000 U, is determined empirically. Patients with symptomatic diphtheritic pharyngitis require 20,000 to 40,000 U, whereas those with more severe symptoms or with complications require larger doses. Antitoxin may be added to 200 ml of 0.9% sodium chloride solution and

given slowly over 30 to 45 min to facilitate delivery of the large volume. For mild cases antitoxin have to given 40,000 U; moderate cases – 80,000 U; and severe cases – 120,000 U.

An urticarial wheal in response to the skin test indicates sensitivity and mandates *extreme caution* in giving the antitoxin. The patient must be desensitized with dilute antitoxin, given in graduated doses. If untoward symptoms appear, 0.3 to 1 ml epinephrine (adrenalin) 0.01 mL/kg should immediately be injected.

Antimicrobial treatment is required to eradicate the organism and prevent spread; it is not a substitute for antitoxin. Adults and children may be given penicillin G erythromycin, ceftriaxon, cefasolin 6 for 14 days. Elimination of organism should be documented by two consecutive negative throat cultures after 2 days for completion of antimicrobial treatment.

Recovery from severe diphtheria is slow, and patients must be advised against resuming activities too soon. Even normal physical exertion may harm the patient recovering from myocarditis.

Management of an Outbreak

All symptomatic patients should be isolated. Contact precautions (private room, use of gloves at all times, hand washing with an antibacterial agent, gowns worn at all times) are also recommended.

All *C. diphtheriae* isolates should be submitted to the local health department for biotyping and toxigenicity determination. Toxinogenic and nontoxinogenic biotypes may coexist in a community.

Nasopharyngeal and throat cultures for *C. diphtheriae* should be obtained for all close contacts of known diphtheria patients regardless of their immunization status. Asymptomatic contacts with positive throat cultures for *C. diphtheriae* (Carriers) should be hospitalization for the duration of therapy, and given erythromycin or rifampicin 6 days. Carriers should *not* receive antitoxin. Cultures should be rechecked at a minimum of 2 wk after completion of antimicrobials.

INFECTIOUS MONONUCLEOSIS

INFECTIOUS MONONUCLEOSIS is an acute disease which, characterized by fever, pharyngitis, and lymphadenopathy and cause Epstein-Barr virus.

Etiology and Pathophysiology

Epstein-Barr virus (EBV) is a ubiquitous herpesvirus with a host range limited primarily to B-lymphocytes and nasopharyngeal cells of humans and certain nonhuman primates. After initial replication in the nasopharynx, the virus infects B-lymphocytes, which are induced to secrete immunoglobulin.

The EBV-transformed B-lymphocytes are the target of a multifaceted immune response. There are atypical mononuclear resulting from primary EBV infection.

After primary infection, EBV remains within the host for life and is intermittently shed from the oropharynx. The virus is detectable in oropharyngeal secretions of 15 to 25% of healthy EBV-seropositive adults.

Epidemiology

EBV is relatively labile, has not been recovered from environmental sources, and is not very contagious. Only about 5% of patients have had recent contact with someone who has infectious mononucleosis. In most cases, the *incubation period* is believed to be 30 to 50 days.

Transmission may occur by transfusion of blood products but much more frequently occurs by oropharyngeal contact (kissing) between an uninfected and a healthy EBV-seropositive person who is asymptotically shedding the virus from the oropharynx.

EBV has also been associated with African Burkitt's lymphoma, certain B-cell neoplasm's in immunocompromised patients, and nasopharyngeal carcinoma.

About 50% of children have had primary EBV infection by the age of 5. In most, the infection is subclinical.

Symptoms and Signs

A tetrad of fatigue, fever, pharyngitis, and lymphadenopathy is common; however, patients may have all or only some of these symptoms. Usually, a patient presents with malaise lasting several days to a week, followed by fever,

pharyngitis, and adenopathy. Fatigue is usually maximal in the first 2 to 3 wk. The pharyngitis may be severe, painful, and exudative and may resemble streptococcal pharyngitis or tonsillitis. Lymphadenopathy may involve any group of nodes but is usually symmetric; anterior and posterior cervical adenopathy is often prominent. Enlargement of a single node or group of nodes may be the only manifestation.

Splenomegaly, observed in about 50% of cases, is maximal during the 2nd and 3rd wk and is usually confined to a splenic tip palpable just below the left costal margin. Mild hepatomegaly and hepatic percussion tenderness may also be observed. Less frequent findings include maculopapular eruptions, jaundice, periorbital edema, and palatal enanthema.

Complications

Although most cases resolve uneventfully, complications may be dramatic.

- ***Neurosis complications*** include encephalitis, seizures, Guieain-Barré syndrome, peripheral neuropathy, aseptic meningitis, myelitis, cranial nerve palsies, and psychosis. EBV-associated encephalitis may present with cerebellar manifestations, or it may be global and rapidly progressive, mimicking herpes simplex encephalitis. Unlike the latter, EBV-associated encephalitis is usually self-limited.
- ***Hematologic complications*** are usually self-limited and do not require specific treatment. They include granulocytopenia, thrombocytopenia, and hemolytic anemia. Mild granulocytopenia or thrombocytopenia is observed transiently in about 50% of patients. Splenic rupture, which requires splenectomy, can result from splenomegaly and capsular swelling. Most patients note abdominal pain, but splenic rupture is occasionally painless, and patients may present with hypotension
- ***Pulmonary complications*** involve airway obstruction or interstitial pulmonary infiltration. Airway obstruction due to pharyngeal or paratracheal lymphadenopathy is an indication for hospitalization and possible surgical intervention, if corticosteroids fail to control the process. Interstitial pulmonary

infiltrates are reported more frequently in pediatric patients, are usually found on radiography, and remain clinically silent.

- **Hepatic complications** are indicated by abnormalities in liver function tests. Elevated hepatocellular enzyme levels (about 2 to 3 times normal, returning to baseline over 3 to 4 wk) occur in about 95% of cases. If jaundice or more severe enzyme elevations occur, other causes of hepatitis should be investigated.

Laboratory Findings and Diagnosis

Although the clinical syndrome of infectious mononucleosis and its epidemiologic setting may be so stereotypical that the diagnosis seems certain, sufficient overlap with other illnesses warrants laboratory testing.

In most patients, a mild *leukocytosis* is observed, usually accompanied by a more pronounced relative and absolute lymphocytosis, resulting from reactive lymphocytes that are morphologically atypical to varying degrees. Atypical lymphocytes (*mononuclear*) may be absent or may account for up to 80%. Individual lymphocytes may have such extremely bizarre morphologic characteristics that a hematology malignancy may be suspected.

Antibodies to the EBV viral capsid antigen (VCA) IgM antibodies to VCA are present in all patients with primary EBV infection and disappear 2 to 3 mo after recovery; thus, demonstrating these antibodies is diagnostic of primary EBV infection.

Differential Diagnosis

The pharyngitis, lymphadenopathy, and fever may be clinically indistinguishable from that caused by *group A β -hemolytic streptococci*; however, detection of these organisms in the oropharynx does not rule out infectious mononucleosis. The mononucleosis syndrome may be due to **cytomegalovirus (CMV)** too. Diagnosis of primary CMV infection depends on demonstrating IgM anti-CMV antibodies or isolating the virus from peripheral blood. **Toxoplasma gondii, hepatitis B, or rubella infection** and atypical lymphocytes associated with adverse drug reactions may also cause heterophil-negative mononucleosis. A

mononucleosis-like illness has also been observed with primary *HIV infection*. In most of these cases, other clinical features help establish the correct diagnosis.

Prognosis and Treatment

Infectious mononucleosis is usually self-limited. The duration of the illness varies; the acute phase lasts about 2 wk. Generally, 20% of patients can return to school or work within 1 wk and 50% within 2 wk. In only 1 to 2% of cases, fatigue lasts for months. Death occurs in < 1% of cases and is mostly due to complications of primary EBV infection (encephalitis, splenic rupture, airway obstruction).

Treatment is largely supportive. Patients should be encouraged to rest during the acute phase but should be quickly mobilized as the fever, pharyngitis, and malaise abate. Because of the risk of splenic rupture, heavy lifting and contact sports should be avoided for 2 mo after presentation, even if there is no obvious splenomegaly.

Because of the rare association of EBV with Reye's syndrome, paracetamol is preferable to aspirin as an analgesic and antipyretic. Corticosteroids should be used only to treat specific complications such as impending airway obstruction. Their efficacy in treating thrombocytopenia and hemolytic anemia is less well established.

Antibiotic should be used to treat tonsillitis. Ampicillin should not be given to patients with mononucleosis. Penicillin, macrolides, cephalosporins should be used.

DYSENTERY (SHIGELLOSIS)

Dysentery is an infectious disease, accompanied by lesion of mucous membrane in the large bowel, especially its distal part.

Etiology

Pathogens of dysentery is *Shigella*, Gram-negative. Only the pathogen of species of *Grigoriev-Shiga Sh. dysenteriae* produces an *exotoxin*, other pathogens produce *endotoxins*.

Dysentery pathogens of various species have *different stability* in the environment. *Sh.dysenteriae* have the least stability. *Sh.Sonnei* are the most stable. Dysentery brought about by *Sh.Sonnei* is most spread these last years while *Sh.Flexneri* takes the second place.

Epidemiology

The *source* of infection is patients with acute dysentery and bacilli-carriers.

The *mechanism of infection* transference is fecal-oral. The *factors* of transference are dirty hands, contaminated food and water, flies. Water *route* of infection spreading is most typical for *Sh.Flexneri*, milk - *Sh.Sonnei*.

Morbidity in 1-year-old children is the lowest, and it is the highest among the children from 2 to 7 years of age.

Immunity in dysentery is typospecific that is why recurrent cases may occur.

Pathogenesis

The *portal* of entry is gastro-intestinal tract. The infectious dose has great importance due to its influence on the duration of the incubative period and severity of the disease course.

On getting into the stomach, the pathogens *perish* partially due to the influence of proteolytic enzymes and hydrochloric acid in the gastric juice. Remaining pathogens get into the small intestine and then they get into the *large intestine* where they reproduce.

The *Shigellae* have a *selective ability* to adhesion (sticking) to colonocytes of the large bowel. *Shigellae* strains have an ability to intracellular invasion. *Endotoxin* is the leading factor. It attacks the whole structure of intestinal wall: enterocytes, vascular and nervous structures. Entering *the blood*, endotoxin causes common toxic influence on the vascular and nervous systems of the body and its vegetative centers.

Clinical manifestations

The *incubative period* varies from several hours to 7 days. The onset of the disease vomiting may be present. The child becomes restless, loses appetite, complains of headache and abdominal pain. In the first hours after the onset of disease stool has *stercoral character*, but by the end of the day or the second day of the disease

stercoral masses disappear completely, stools become *poor and contain turbid mucus and blood* only.

In this period the children *complain* of abdominal painful cramps in defecation, drawing *pain on the side of the sigmoid colon* and anus.

Tenesmus is a typical sign of dysentery. Tenesmus appears due to the simultaneous spasms of the sigmoid colon and anal sphincters. In frequent tenesmus the rectum mucous membrane *prolapse* may result.

Symptoms of *toxemia, pallor and dryness of the skin* are found. On *abdominal palpation*, tenderness and hardening are found over the sigmoid colon. Moderate leukocytosis, neutrophilia with the change to the left, insignificant increase of ESR shows in the blood.

Clinical type classification of dysentery is based on the signs, which have been proposed by A. A. Koltupin (type, severity, course).

Typical and atypical forms are distinguished. In *typical* forms colitic syndrome is present constantly.

Obliterated, dyspeptic, subclinical, hypertoxic forms are referred to the *atypical* forms.

Typical forms of dysentery are divided into *mild, moderate and severe*. Such division depends on the presence and manifestation of *toxemia symptoms* (fever, convulsion syndrome, mental confusion, headache, weakness) and *local alterations from* gastrointestinal tract (number of stools per day, pain syndrome, tenesmus, rectum mucous membrane prolapse).

For 1-year-old babies dysentery has some peculiarities.

Colitic syndrome is not well expressed. Stools have enterocolitic or dyspeptic character. Stools always contain mucus; blood is not always present in feces. Abdomen is frequently moderately inflated. *Toxemia* at the early age is accompanied by high fever, recurrent vomiting. If frequent enterocolitic stools are present, *dehydration* with hemodynamic disorders may occur. Dysentery course is characterised by slow repair of the mucous membrane and delayed recovery. *Complications* can bring

about rectum mucous membrane prolapse. As a secondary infection, otitis, pneumonia, stomatitis, infection of the urinary tract may occur.

SALMONELLOSIS

Etiology

Pathogens of salmonellosis belong to the *Salmonella* genus. There are more than 2000 serologic types of *Salmonellae*. The *Salmonellae* groups are discerned due to the structure of O-antigen (A, B, C, D, E and others). The disease in 80-90 % of the cases is connected: *S.typhimurium*. *S.Heidelberg*. *S. anatum*. *S. derby*, *S.panama*, *S.enteritidis*.

Pathogens have high *stability* in the environment. They survive well at *low temperatures*. Salmonellae *live long* in the ground, water, food and even can reproduce (especially in butter, milk, meat).

Epidemiology

Salmonellosis is *anthropsoonosis*. The *general source* of infection is various animals. Besides, recently the sick people and bacilli carriers *present the main epidemiological danger*.

The *general route* of infection transference is alimentary; food (meat, eggs, fish, and milk) is the main *factor in spreading* of salmonellas. In babies, *the contact route* is the main one (soiled hands of the mother and the staff, various contaminated things).

Within the last years, *morbidity* of 1-year-old babies has considerably increased, particularly due to *nosocomial* (hospital) infection (neonatal departments, maternity homes).

Pathogenesis

In *per oral infection* much of the living pathogen is destructed intensively in the stomach and small intestine. At this time a lot of **endotoxin** is released. Due to the influence of endotoxins the *toxic signs* of the disease appear. Toxemia leads to gastrointestinal forms of the disease with an endotoxic shock.

A certain part of the pathogens **penetrates** into the mesenteric lymph nodes and enterocytes further getting into blood, and causing **bacteriemia**. In toxemia with bacteriemia **typhus-like form** develops, if an infectious component is present, then the **septic form** of salmonellosis develops (in neonates, premature neonates).

Salmonellae and their toxins **influence the nervous system**, causing paralysis of vasomotor centers causing thermoregulation disorders and development of diarrhea. Vomiting and diarrhea cause **dehydration** of the body with disorders in hemodynamics, electrolyte dysbalance, hypoxia and acidosis.

Clinical manifestations

The **incubative period** has duration from 2-3 hours (in the **alimentary** route of transference) to 5-7 days (in the **contact** route). Clinical manifestations of salmonellosis are characterized by extraordinary polymorphism.

Classification

Localization form:

- Gastrointestinal,
- flu-like,
- effaced
- asymptomatic

Generalization form:

- typhus-like,
- septic, forms

Acute (up to 1 month), **protracted** (1-3 months) forms are distinguished depending on duration of the disease.

Mild, moderate and severe forms are discerned depending on severity course of the disease.

Gastrointestinal form is diagnosed in 90 % of the patients and has the course of gastritis, enteritis, colitis, gastroenteritis, enterocolitis, gastro-enterocolitis. The disease has an **acute onset** with fever and chills. The main symptoms appear on the first day of the disease. Nausea and recurrent vomiting appear. **Abdominal pain** and diarrhea appear rapidly **stools** become more frequent up to 3-5 times daily. Stools

are watery, contain small admixture of mucus. The *tongue* is dry and coated. Besides, headache, general malaise and weakness appear. ***Duration*** of the disease is 5-7 days.

Typhus-like form of salmonellosis is found in 2-3 % of the children patients and clinically it may resemble abdominal typhoid or paratyphoid: duration of fever is 1-2 weeks, ***toxemia*** (headache, myalgia, arthralgia, anorexia), ***enlarged spleen***, roseolous or erythematous ***rash***, ***cardiovascular system disorders*** (bradycardia or tachycardia), ***gastrointestinal disorders*** (vomiting, diarrhea, abdominal distention).

Septic forms of salmonellosis are frequent in neonates and infants younger than 6 months of age. Septic forms are frequently accompanied by ***local lesions*** (meningitis, osteomyelitis, subcutaneous abscesses, arthritis, pyelonephritis). The diseases can have a very ***severe course*** with metabolic disorders of all forms, especially electrolyte dysbalance.

Diagnosis

Diagnosis of dysentery and salmonellosis ***is based*** on its clinical manifestations, the epidemiological history and bacteriological test results.

Clinical diagnosis of ***dysentery*** may be made if typical signs of distal colitis are present. For diagnostics of ***salmonellosis*** the pathogen should be isolated.

Stools is the ***material for bacteriological tests*** if suspicions of ***dysentery*** exist. Blood, stools, urine, vomiting mass, gastric water, pus from the inflammatory foci is the material for bacteriological tests if there is a suspicion of ***salmonellosis***. Material for bacteriological tests should be taken ***before the antimicrobial therapy*** is started.

Treatment

Diet has much significance in treatment of dysentery and salmonellosis. The babies should be recommended to reduce the volume of food in acute period of the disease. Breast milk is optimal nutrition. The ***volume*** and composition of the nutrition must correspond to the age norm by the 5th-7th day after the onset of the disease.

Antibiotics and nitrofurantoin medications accomplish ***Etiotropic therapy***. Antibiotics (ampicillin in dosage of 100 mg/kg/day, gentamycin sulfate in dosage of 3-8 mg/kg/day) should be administered in severe forms of dysentery and salmonellosis, in

moderate forms they should be administered to the children younger than 2 years of age. In 1-year-old babies and in generalized' forms of salmonellosis *cephalosporin* antibiotics should be administered (ceftazidime, ceftriaxone in the dosage of 100 mg/kg/day). *Furasolidone* in dosage of 8-10 mg/kg/day, *nevigramon* in dosage of 60 mg/kg/day, *bactrim* in dosage of 60 mg/kg/day may be given. Dysenteric and salmonellic bacteriophages may be used to.

Enzymatic therapy is administered in the reparation stage in a course from 2 to 4 weeks.

Bacteriological examination is made in all the patients alter 2 days when the antibacterial therapy is finished.

If epidemic **outbreaks appear**, all contact persons should be examined bacteriologically singly.

INTESTINAL COLI INFECTION (ESCHERICHIOSIS)

Escherichiosis is an acute intestinal infection caused by *E. coli*, which mainly affect 1-year-old babies.

Etiology

E. coli are Gram-negative pathogens. *Classification includes* enterohemorrhagic *E. coli* (EHEC), enterotoxigenic *E. coli* (ETEC), enteroinvasive *E. coli* (EIEC), enteropathogenic *E. coli* (EPEC).

The *EPEC group* of *E. coli* contains about 30 serotypes: O-111; O-55; O-25; O-44; O-119. They cause the *disease* in 1-year-old babies and have antigens similar to *Salmonellae*.

The *EIEC group* of *E. coli* contains 13 serotypes: O-124; O-151; O-144 and others. Their antigenic structure is similar to that of *Shigellae*. EIEC group cause the diseases in children and adults. The disease is similar to *dysentery clinically*.

The *ETEC group* of *E. coli* contains the pathogens which produce enterotoxin similar to *cholero-gen* by its effect. Enterotoxin causes considerable production of

liquid into the lumen of the small bowel. These diseases have likeness with the mild form of *cholera*.

The *EHEC group* was identified later.

Epidemiology

Escherichiosis of the *first group* is found all year round in the form of sporadic cases and small epidemic outbreaks. 1-year-old babies get ill most frequently. The *source* of infection is sick human in the acute period of the disease, sometimes the source of infection is a bacillus carrier.

Infection is caused by *contact and alimentary route*.

In *EIEC escherichiosis* infection is transmitted by alimentary route. The disease frequently occurs in *summer and autumn*.

ETEC eschcrichiosis is found among older children and adults. The main *routes* of infection are food and water.

Pathogenesis

E. coli enter the child's body through the mouth and then *get into* the lumen of the gastrointestinal tract. The pathogens reproduce in the *small bowel*. They produce *enterotoxins*, remaining on the surface of the mucous membrane. Epithelium of the small intestine *is affected*, and inflammatory changes appear. Besides *enterotoxins*, *endotoxins* are liberated due to the pathogen destruction.

Clinical manifestations

EPEC escherichiosis occurs in 1-year-old babies. The *incubative period* is from 3 to 8 days. The disease has an abrupt *onset*. The body temperature increases, weakness and anorexia appear. *Stools* occur frequently, they are watery, yellow or orange, contain transparent mucus. If such stools occur five to seven times daily, dehydration may occur. *Toxemia* is manifested by restlessness, recurrent regurgitation and vomiting. The disease has a protracted course.

The signs of the most severe *escherichiosis in 1-year-old babies* are neurotoxicosis and toxicosis with dehydration. *Neurotoxicosis* occurs rarely in the first days of the disease due to toxemia. It is characterized by the signs of the *CNS lesion*, which increase rapidly, such as hyperthermia, recurrent vomiting, acute

restlessness, mental confusion, tonic convulsions, occipital muscular stiffness, tachycardia, toxic breathing, protrusion of cranial fontanel.

Toxicosis with dehydration is the most frequent form of toxic condition in escherichiosis in the 1-year-old babies. It is **manifested** by the signs of CNS lesions, cardiovascular, electrolyte disorders. There are isotonic, salt deficient, water deficient types of dehydration.

Water deficit manifests itself by thirst, restlessness and excitement. The skin and mucous membranes are dry. Muscle tone is decreased, hurried breathing, low diuresis.

CHOLERA

Cholera is an acute especially dangerous infectious disease, caused by *Vibrio cholerae* and characterized by the signs of severe inflammation of intestine with fast development of dehydration due to loss of water and electrolytes, and hemodynamics disorders.

Cholera is one of the oldest human diseases. There were seven pandemics of cholera.

Etiology

The disease is caused by **two independent pathogens** — *Vibrio cholera asiatica* and *Vibrio El-Tor*. This is a Gram-negative curved bacillus.

Vibrios can produce **thermostabile endotoxin** and **thermolabile exotoxin** (cholera toxin).

Vibrios cholerae are divided into **3 serotypes** as to O-antigen: Ogawa, Inaba, Hikasima.

Vibrios cholerae are **stable** to the influence of the environmental factors.

Epidemiology

Cholera is an **anthroponotic disease**.

The **source** of the infection is a human with typical or subclinical forms of the disease, or vibriocarriers.

After the disease the convalescents and vibriocarriers may *excrete* vibrios from 2-3 weeks to 5-7 years.

Cholera spreads *by fecal-oral route*. Water, alimentary, contact and mixed epidemiologic outbreaks of cholera are **distinguished**.

Susceptibility to cholera is high. The outbreaks frequently appear in warm seasons (July-September). They neutralize the acid medium of the stomach.

Pathogenesis and pathology

Vibrios cholerae enter the human body *through the mouth*. *Exotoxin* activates adenylate-cyclase and catalyzes the formation of cyclic AMP. Resulting in the intensive secretion of fluid into the lumen of the intestinal tract.

In children dehydration appears more rapidly. Particular lability of water balance is connected with immaturity of neurohumoral and renal mechanisms of metabolic regulation. Children tend to get central nervous system lesions more frequently. They are manifested by adynamia, clonic convulsions, mental confusion, and coma. The early signs of cholera in children are sensory and cardiovascular disorders.

Clinical manifestations

Duration of the *incubative period* is from several hours to 6-7 days.

The disease has an abrupt *onset* with frequently passed stools without abdominal pain and tenesmus. The **feces** usually are clear and without odor, contain flecks of mucus that impart a "rice-water" appearance and have high concentrations of sodium and bicarbonate. **Vomiting** without nausea, described as effortless, usually follows the onset of diarrhea. Vomiting is plentiful; the quantity of vomitive mass may reach 5 L and more daily. The patient is thirsty, but the ingested liquid is excreted due to diarrhea and vomiting. If *dehydration* increases, the patient has emaciated appearance, his eyes fall in ("sun glasses" symptom), his nose becomes pointed. The *skin* of the hands may have a characteristic appearance resembling wrinkled "washer woman hands" in persons with severe dehydration. **Fever**, if present, is low grade, or the patient may develop hypothermia. The *mucous*

membranes are dry. The *voice* becomes hoarse, weak and even soundless. The *pulse* is weak, blood pressure is low. *Diuresis* decreases down to anuria. Convulsions occur.

The degree of dehydration is the basis of **clinicopathogenetic classification** of cholera. There are 3 degrees of dehydration. Their criterion is *body weight deficit*.

In dehydration of 1st degree (*mild*) the liquid deficit is up to 5 % of the patient's weight.

In dehydration of II nd degree (*moderate*) the liquid deficit is up to 10 % from the patient's weight, in dehydration of III rd degree (*choleric algide*) the liquid deficit is more than 10 % of the patient's weight. In *convulsions*, the muscles are rigid. Convulsions of diaphragm are manifested by hiccup. Condition of *hypovolemic shock occurs*: thread pulse, dull heart sounds, anuria, blood pressure decreases to zero. Erythrocyte count is $7 \cdot 10^{12}/L$ — $8 \cdot 10^{12}/L$. Leukocyte count is up to $15 \cdot 10^9$ — $60 \cdot 10^9/L$. There is neutrophilia, hypopotassemia, metabolic acidosis.

In babies cholera occurs rarely, it occurs more frequently in endemic foci. The disease has an acute onset with subfebrile temperature, *toxemia*, **dehydration**, and lesions of *cardiovascular and nervous systems*. Severe tonic spasms occur rapidly. *Mental confusion* and coma is typical. Disorders of **water-electrolyte metabolism**, the adjoining of bacterial and viral-bacterial infection may result in lethal outcome.

Fulminant form of cholera is atypical. There is abrupt onset with rapid dehydration. That is why hypovolemic shock, severe convulsions, signs of encephalitis, choleric coma are the result.

Diagnosis

Cholera is diagnosed *basing* upon the typical clinical manifestations and laboratory tests.

Bacteriologic tests are principal among laboratory examinations: isolation of *Vibrio cholerae* from feces and vomitus.

Serologic tests (diagnostic titer of antitoxic antibodies is 1:80 1:320; diagnostic titer of vibriocide ones is 1:1000 in the serum) have retrospective significance.

Treatment

Treatment of cholera should be started as early as possible.

The main condition of successful treatment is **rapid recovery of lost water and electrolytes**.

Antibiotic treatment plays an auxiliary part. The patient's weight should be registered before his hospitalization.

In the **first examination** of the patient with cholera, the degree of dehydration should be determined. When clinical manifestations of dehydration occur, the patient loses a lot of water and electrolytes. The main danger is underestimation of such losses.

If the patient has the signs of severe dehydration and *hypovolemic shock*; the liquid should urgently be administered intravenously. The liquid to the babies should be given in the dosage of 70 ml/kg during 3 hours. If clinical manifestations of dehydration persist, the liquid should be given in the dosage of 20 ml/kg during the next 3 hours. The liquid may be administered in the dosage of 100 ml/kg during 3-4 hours to older children and adults.

Vomiting is not a contraindication for giving liquid orally, the quantity of liquid should be reduced but it should be administered more often. Saline solutions "Regidron", "Oralit" are given.

Furazolidon in the dosage of 8-10 mg/kg/day or *chloramphenicol* in the dosage of 50 mg/kg/day should be given to children under 8.

The *diet* of the patients with cholera is the similar with the diet in other acute intestinal diseases.

The patient may be *discharged* on the 8th-10th day of illness after clinical recovery and three negative bacteriological tests. *Bacteriological tests* should be made not earlier than 24-36 hours after stopping antibacterial therapy 3 days in succession. Taking into consideration the ability of vibrio preservation in the upper part of

intestinal tract, *duodenal contents* of convalescents should be examined bacteriologically.

The patient should be *followed* up during 6 months after discharge from the hospital (fixes should be examined bacteriologically every 30 days).

Contact persons should be isolated and examined bacteriologically too.

TOXIC SYNDROME IN ACUTE INTESTINAL INFECTIONS

Toxicosis is *generalized reaction* of the human organism on the infectious agent, which is characterized by neurological disorders, failure of peripheral blood circulation and metabolic disorders. There are *two forms* of toxicosis in acute intestinal infections: toxicosis with dehydration and neurotoxicosis.

Pathogenesis

The pathogens of intestinal infections *attaching* to intestinal epithelium result in the lesion of enterocyte microvilli and their desquamation. The pathogens *penetrate* into cytoplasm, enter the lymph and the blood stream and result in generalization of infectious process.

The endotoxins of *Gram-negative pathogens*, entering into the lumen of the small bowel, quickly cause changes in cells and mucous membrane. The *microvilli* disappear under the influence of endotoxins, leading to disorders of *microcirculation* in the mucous membrane of the small bowel.

Enterotoxins get linked with the receptors of the enterocytic membrane and *activate adenylate cyclase*. That is why result in *increasing of water* and electrolyte secretion into the lumen of the small bowel.

Development of pathologic process in the intestine wall decreases its barrier function and allows the enteric pathogens and their toxins enter the blood stream.

Neurotoxicosis is characterized by hypertonic reaction of the human body to the infectious agent. It is accompanied by *neurologic lesions* (toxic encephalopathy), disorders of microcirculation, breathing, and metabolism.

There are *three periods in the clinical picture of neurotoxicosis*: prodromal, peak and reverse development.

Prodromal period is short. Its *duration* is from some hours to 1-2 days. This period is characterized by recurrent vomiting, increasing headache, sleep inversion, gradual increase of the body temperature.

Clinical manifestations *of the peak period are various* and characterized by multiple lesions of different organs and systems, but neurological and microcirculatory disorders are most important.

There are *such clinical signs* at the peak period in neurotoxicosis:

- acute mental excitement, monotonous crying;
- mental confusion, tonoclonic spasms;
- increased body temperature;
- disorders of blood circulation: tachycardia, striking pallor, cyanosis, cold limbs;
- disorders in breathing: tachypnea, toxic breathing;
- kidney failure: oliguria, anuria, azotemia, proteinuria;
- clinical and laboratory signs of DIC-syndrome (disseminated intravascular coagulation syndrome);
- decompensate metabolic acidosis.

Neurotoxicosis therapy consists in normalizing the blood microcirculation, coping with brain edema, hyperthermia, convulsions.

Antihistaminic medications, neuroleptics as droperidol (in the dosage of 0.04-0.1 ml/kg of 0.25 % solution) aminasine (in the dosage of 1-3 mg/kg/ day) peripheral vasodilators (papaverine in the dosage of 0.02g 3 times daily), glucocorticoid hormones (prednisolone in the dosage of 2-5 mg/kg/day) should be administered.

Treatment of brain edema consists of using diuretic medications (mannitol in the dosage of 1g/kg, lasix in the dosage of 1 mg/kg/day), steroid hormones (prednisolone).

Infusion therapy is administered in the dosage of 30-50 ml/kg with primary usage of 5-10 % glucose solution, rheopolyglucin.

For *arresting the convulsions*, seduxen in the dosage of 0.3-0.5 mg/kg should be administered. After the convulsions have been, arrested lumbar puncture should be made.

Toxicosis with dehydration occurs in secretory diarrhea. The period of various duration precedes its appearance. Loss of water through *gastrointestinal* tract up to 300 ml per day.

The *main signs of toxicosis* with dehydration are a decrease in body weight. Depending on the weight loss, *three degrees of dehydration* are distinguished.

First degree: loss of body weight is not more than 5 % of the primary one. The child is restless, drinks thirstily. Turgor of tissues decreases insignificantly. There is mild dryness of the mucous membrane in the oral cavity. Cardiovascular system functions satisfactorily.

IInd degree: loss of body weight up to 10 % of the primary one. The skin is dry and flabby. The mucous membranes are dry. Mental confusion can come to sopor. There are dull heart sounds, tachycardia, and hypotension, decrease in diuresis.

IIIrd degree: loss of body weight up to 15 % of the primary one. The signs of dehydration are severe. Turgor and elasticity of tissues decrease. The fontanel is sunken. Sclerema, dry mucous membranes, anuria, aphonia, acrocyanosis, and tachycardia are present. Hypovolemic shock occurs.

There are *three types of dehydration* depending on the clinical manifestations and laboratory tests: isotonic, water deficiency and salt deficiency.

Isotonic dehydration: is a condition when the loss of water and electrolytes is proportional. This type occurs most frequently and corresponds to dehydration of the 1st degree. This dehydration is mild and corrected easily.

Water deficiency dehydration (hypertonic, or cellular) occurs if the loss of water is more considerable than the loss of electrolytes. It occurs if diarrhea predominates over vomiting. The loss of liquid is not more than 10 % of the body weight. Dry mucous membranes in the oral cavity, severe thirst, manifest this type dehydration. Dry lips and dry warm skin, sunken eyes are too. The body temperature is high, rapid pulse and breathing is observed. Blood pressure is elevated.

Salt-deficiency dehydration (hypotonic, extracellular) occurs if the loss of electrolytes predominates over the loss of water. The child is languid, adynamic, refuses food and liquid. The child may fall into soporous or comatose condition. The skin is dry, flabby, "marmoreal", damp, and cold in the limbs. The body temperature and diuresis decreases. Muscular hypotonia, hyporeflexia, and enteroparesis result.

Treatment of AII with "*secretory*" **diarrhea** syndrome consists of a complex of measures: dietary regimen, etiologic and pathogenetic therapy. First at all, the physician should decide the question of patient hospitalization.

The patient **should be given to drink** by small portions in 2-3 teaspoons every 10-15 minutes peroral rehydration (Regidron, Oralit).

Version I of calculating the daily fluid intake (according to Velitishchev):

1. The existing water deficiency in the patient (**loss of body weight**).
2. **Replacement of the daily loss of fluids** through skin and breathing by 30 ml per kg per day and by 10 ml per kg per day if there is an increase of the body temperature per 1 °C.
3. If there is a **continuous loss due to vomiting and diarrhea** fluids should be rated at 20-30 ml per kg per day.

Calculation should be made on the **real weight** of the baby.

Version II of calculating the daily fluid intake (according to Dennis)

Degree of dehydration	ml/kg				
	1-3	4-6	7-12	1-5 years	6-10
I	170-180	150-160	130-140	100-130	75-100
II	190-210	175-185	150-170	130-170	110-150

Calculated **general volume of liquid** is administered through oral intake in drink, food and through intravenous infusions. The volume of intravenous infusions **depends**

on the quantity of food and fluid, which can be taken by the baby, but no more than 80 % of the calculated daily quantity of fluid.

In severe dehydration *with blood circulation disorders* the rehydration therapy should be begun from the macromolecular colloid medications for fluid retention in the blood stream.

The *correlation of glucose and saline solution* depends on the clinical manifestations, which are determined by the *dehydration type*. If it is difficult to evaluate the *dehydration type* and the laboratory tests are not available, then a 10 % glucose solution and saline solutions are administered in *correlation 1:1*, as in *isotonic* type of dehydration. In *water-deficient dehydration* (1:2-1 :3) of 10 % glucose solution may be given. In *salt-deficient dehydration* the correlation between saline and glucose solution is 2:1 -3:1.

Hypotassemic syndrome plays a leading part in pathogenesis and clinical manifestations of toxicosis with dehydration. There are some clinical symptoms in *potassium deficiency*: asthenia, muscular hypotonia, enteroparesis, dull heart sounds, systolic murmur, flattening of T waves, inversion of the ST segment, additional V waves, which appear after T waves.

The physician should *take into consideration*, that 1 ml of 7.5 % potassium chloride solution contains 40 mg or 1 mmol of pure potassium. The dosage of *potassium chloride* is 2 to 3 mmol/kg/day.

The following conditions for administration of potassium preparations are:

1. Potassium chloride solutions should be administered only if diuresis appears.
2. Intravenous infusion of potassium chloride solutions is made fractionally: *calculated dose is divided into portions* to be given 3 times daily every 3-3.5 hours.
3. Potassium chloride solutions are administered by intravenous drip only Potassium chloride solution is added to glucose solution in an ampoule.

The medications, which reduce liquid and electrolyte secretion into the small bowel, should be administered with rehydration therapy simultaneously; they are **Smekta**.