EPIDEMIOLOGY

and Fundamentals of Infectious Diseases

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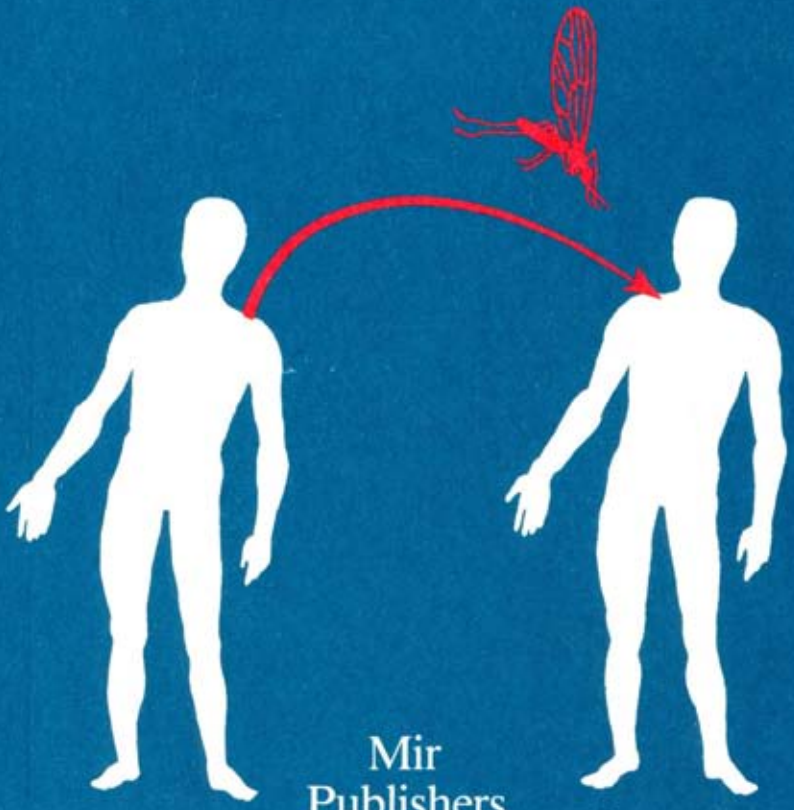

Mir
Publishers
Moscow

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Part One

General Epidemiology

The Subject Matter of Epidemiology

The word 'epidemiology' has been used since the time when most of the infectious diseases were epidemic. Today, when infectious morbidity has considerably decreased, the concept of epidemiology includes the study of objective laws of aetiology, distribution and control of infectious diseases in a human community, and also elaboration of methods to prevent and control these diseases.

The following definition of the term 'epidemiology' was formulated at the International Symposium of Epidemiologists in Prague (1960): "Epidemiology is an independent branch of medicine studying aetiology and spreading of infectious diseases in a human community and is aimed at prevention, control, and final eradication of these diseases".

General and special epidemiologies are distinguished. General epidemiology studies the laws of distribution of infectious diseases among people (characteristics of sources of infection, the mechanism of transmission, susceptibility to infection, and the like) and the general principles of prevention and control of these diseases. Special epidemiology studies epidemiologic characteristics of each particular infectious disease and the methods to prevent and control it.

History of epidemiology. Ancient people had their own concept of contagiosity of some diseases and took first prophylactic measures; they rejected people with infectious diseases from their community, used variolation (deliberate inoculation with smallpox virus), disinfection, etc. All these measures were empirical and their efficacy was low. At those times it was impossible to prove instrumentally that infectious diseases might be evoked by living microorganisms, but

numerous epidemics of black plague, smallpox and typhus, especially in the 14-15th centuries, aroused such suspicions in physicians. Fracastorius, an Italian physician (1483-1553), produced a theory that proved contagiosity of these diseases.

In Russia of the 11th century, they isolated people with contagious diseases and hurried the dead separately from the others. First quarantines were organized in the 16th century: patients were separated from their relatives, and funeral services over the dead were forbidden.

To prevent spread of plague epidemic into Moscow in 1552, posts were first organized in Russia to prevent penetration of people into the city from the outside. In the 17th century, quarantine piquets were organized during epidemics out at the entrance to the city and at the houses with the diseased. When a family died, the house with the dead and the utensils was burned. According to the law, any case suspected for a contagious disease had to be reported to the officials.

In the 18th century, Edward Jenner an English physician, (1749-1823) devised a safe and effective method to prevent natural smallpox by inoculating people with cowpox vaccine.

At about the same time, the Russian epidemiologist D. Samoilovich (1744-1805) was among the first who attempted to discover microscopically the causative factor of plague in excrements and various tissues of the diseased. He was also actively involved in control of plague in Moscow in 1771-1772. Samoilovich organized quarantines at the Black Sea coastal area and became world famous for his work in epidemiology.

Development of industry and trade between different countries stimulated advances in medicine, including sanitary, quarantine, and anti-epidemic services.

The second half of the 19th century was marked by vigorous development of physics (optics), chemistry, biology and other sciences, which all provided conditions for developing a new science-microbiology.

The scientific discoveries made by Pasteur, Mechnikov, Koch, Ivanovsky and many others promoted the study of aetiology, pathogenesis, course of infectious disease and also their epidemiology. The study of epidemiology of some infectious diseases and working out of prophylactic measures revealed the important role of social factors in the spread of epidemics. Inadequate labour and living conditions, poverty, and poor sanitation promoted the spread of contagious diseases.

A great contribution to epidemiology was made by Minch

(1836-1896) and Mochutkovsky (1845-1903), who inoculated themselves with the blood of patients with recurrent fever (Minch) and typhoid fever (Mochutkovsky). They proved by their experiments that the diseases could be transmitted by blood-sucking insects.

Gabrichevsky (1860-1907) made an important contribution to the study of diphtheria (serotherapy), scarlet fever (study of aetiology, manufacture of vaccines and vaccination), epidemiology of malaria, etc.

Zabolotny (1866-1929) is the founder of Soviet epidemiology. He is the author of numerous papers on epidemiology of plague, cholera, epidemic typhus, etc. and also of the manual entitled "Fundamentals of Epidemiology". Gromashevsky and Soloviev continued studies of their teacher.

Sysin (1879-1956), Semashko (1874-1949), Soloviev (1879-1928), Bashenin (1882-1978) and Martsinovsky (1874-1934) worked much to create anti-epidemic service in the young Soviet state. Further development of the theory of epidemiology is associated with the names of Pavlovsky (1884-1965) and Gromashevsky (1887-1980). Pavlovsky's works in the field of parasitology have won world repute. He developed also the theory of natural nidality of some infectious diseases.

Soviet epidemiologists Zabolotny, Vogralik, Bashenin, Gromashevsky, Pavlovsky and others have developed several theories in epidemiology. These are the first and second laws of sources of infection and the teaching of epidemic process. According to the law of infectious source, any infected person can be the source of infection; sometimes, this can be an animal. According to the second law, there exists agreement between location of the causative microorganism in a macroorganism and the mechanism of infection transmission. This law was used by Gromashevsky for classification of infectious diseases. The theory of epidemic process postulates that such a process develops and is maintained only through the interaction between the source of infection, the specific mechanism of transmission, and susceptibility of population with respect to a given disease. Teaching of natural nidality of infectious diseases and the effect of social factor on the course of an epidemic process are very important for a successful control of infectious diseases as well.

Advances in epidemiology are infeasible without improvement of labour and living conditions, adequate health care, and planned anti-epidemic measures.

The Concept of Infection

An infectious process is the interaction of a pathogenic microorganism with a macroorganism under certain environmental and social conditions. The concept 'infectious disease' means the condition manifested by a disease state of a patient and the so-called carrier state.

The specific properties of infective agents, various pathogenicity and virulence of these agents, as well as the quantity of microorganisms that enter the macroorganism, resistance of the macroorganism and duration of specific immunity account for the multitude of clinical manifestations of infection.

Infection can be clinically pronounced or it may be asymptomatic, which is known as the carrier state (parasite, bacterium, virus carrier state). A clinically manifest infection can run a typical or atypical course. Patients with a typical form of infection demonstrate all symptoms specific for a given disease. One or several symptoms of a given disease are absent from the clinical picture of an atypical form, or the symptoms can be modified. A disease can be acute or run a protracted or even a chronic course.

A clinically manifest disease is usually classed as mild, moderate, and severe; according to the duration, the disease can be acute or chronic.

An acute infection (smallpox, measles, plague) is characterized by a short stay of the causative agent in the body and development of specific immunity in the patient toward the given infection.

A chronic infection (brucellosis, tuberculosis) can last for years.

Asymptomatic infections can be subclinical and latent.

A person with a subclinical infection (acute and chronic) looks in full health, and the disease can only be diagnosed by detecting the causative agents, specific antibodies, and functional and morphological changes in the organs and tissues that are specific for a given disease. Such patients (or carriers) are a special danger for the surrounding people since they are the source of infection. At the same time, a repeated subclinical infection in poliomyelitis, diphtheria, influenza, and some other acute infections promotes formation of an immune group of people (herd immunity). Acute and chronic subclinical forms (carrier state) are more common in typhoid fever, paratyphoid B, salmonellosis, viral hepatitis B, etc.

Latent or persistent forms of human and animal infections are a prolonged asymptomatic interaction of macroorganisms with the pathogenic agents which are present in modified ('defective') forms.

These are defective interfering particles in latent viral infections, and L forms, spheroplasts, etc. in bacterial infections. Being inside the host cell, these forms survive for long periods of time and are not released into the environment. Under the action of various provoking factors (such as thermal effects, injuries, psychic trauma, transplantation, blood transfusion, various disease states), persistent infection can be activated and become clinically manifest. The microbe regains its pathogenic properties.

Persistence of virus has been studied best of all, but at the present time, persistence of other pathogenic factors has been intensively studied as well, e.g. of the L forms of streptococci, staphylococci, meningococci, cholera vibrio, typhoid fever bacilli, microbes causing diphtheria, tetanus, etc.

Protozoa and rickettsia can also persist. For example, latent epidemic recrudescent typhus infection is manifested by relapses of epidemic recrudescent typhus (Brill's disease).

The **Concept of Epidemic** Process

Microorganisms causing infectious diseases parasitize on host and persist due to continuous reproduction of new generations which change their properties in accordance with evolution of the environment conditions. Living inside its host, the microorganism persists for a definite period of time. Then the pathogenic microorganism can survive by changing its residence, i.e., by moving to another host via a corresponding transmission mechanism. This continuous chain of successive transmission of infection (patient - carrier), manifested by symptomatic or asymptomatic forms of the disease, is called an *epidemic process.*

According to Gromashevsky, the source of infectious microorganisms is an object which is the site of natural habitation and multiplication of the pathogenic microorganisms, and in which the microorganisms are accumulated. Since pathogenic microorganisms are parasites, only a living macroorganism can be such an object, L e., a human or an animal.

An epidemic focus is the residence of infection source including the surrounding territory within the boundaries of which, the source can, under given conditions, transmit a given disease through the agency of the pathogenic microorganisms. The focus of infection remains active until the pathogenic microorganisms are completely eradicated, plus the maximal incubation period in persons that were in contact with the source of infection.

The following three obligatory factors are necessary for the onset and continuous course of an epidemic process: the source of pathogenic microorganism, the mechanism of their transmission, and macroorganisms susceptible to infection.

Infectious diseases are classed according to their source as anthroponoses (the source of infection is man), zoonoses (the source of infection is animal), and anthropozoonoses (both man and animal can be the source of infection).

An infected macroorganism (man or animal), being the sole source of infection, can have either clinically manifest or asymptomatic form of the disease.

A diseased person is the primary source from which the infection spreads. A patient is the most dangerous source of infection because he or she releases a great quantity of the pathogenic microorganisms.

The danger of infection spreading from the patient depends on the period of the disease. During the incubation period the role of the patient is not great because the pathogenic microorganism resides inside tissues and is seldom released from the infected organism. The pathogenic agents are released into environment during the late incubation period only in measles, cholera, dysentery, and some other diseases. The greatest quantity of microbes are released during the advanced stage of the disease which is associated with some clinical manifestations of the disease such as frequent stools (dysentery), frequent stools and vomiting (cholera), sneezing and cough (airway infections). The danger of infection spreading during the early period of the disease depends on pathogenesis of a particular infectious disease. For example, in typhoid fever or paratyphoid A and B, the patients are not dangerous to the surrounding people during the first week of the disease, while in respiratory infections, the patient is a danger to the surrounding people from the moment when the clinical symptoms of the disease become apparent.

Severity of the disease is of great epidemiologic importance for determining "the source of infection". If the disease is severe, the patient remains in bed and can only infect his relatives. But it is difficult to diagnose the disease if it runs a mild course; besides, the patient often does not attend for medical aid and continues performing his routine duties (at the office, school, and the like) thus actively promoting the spread of infection.

Carrier of infection is another source of morbidity. According to modern views, carrier state is an infectious process that runs an asymptomatic course. But those who sustained an infectious disease,

convalescents, and also healthy persons (transition) can also be carriers of infectious microorganisms. True, carriers release pathogenic agents into the environment in a smaller quantity than patients with clinically manifest diseases, but they are danger to community too since they actively associate with healthy people and spread the infection.

Recovery from some infectious diseases, e.g. dysentery, typhoid fever, paratyphoid, diphtheria, meningococcal infection, viral hepatitis B, is not always attended by complete destruction of the microbes in the patient. Carrier state can persist in persons who sustained diphtheria or meningococcal infection after their clinical recovery: acute carrier state can last from several days to several weeks. Persons who sustained typhoid fever or paratyphoid B can be the source of spread of the pathogenic microorganisms for months. Carrier state can persist for years or even for the rest of life (chronic carrier state) in 3-5 per cent of cases, which can be explained by defective immune system.

Various concurrent diseases can promote persistence of carrier state: diseases of the bile ducts and urinary system in typhoid fever and paratyphoid, chronic diseases of the nasopharynx in diphtheria, helminthiasis in dysentery, etc.

Healthy carriers are persons with asymptomatic infection. Transitory carrier state is characterized by rapid withdrawal of the pathogenic microorganisms from a subject; foci where these microorganisms might multiply are absent. From 30 to 100 carriers can be detected among people surrounding one patient with meningococcal infection of poliomyelitis. Healthy carriers are less dangerous for those who surround them because the pathogenic microorganisms are not usually detected in them during subsequent tests.

The danger of carrier state depends on hygiene and occupation of a carrier. If a carrier of typhoid fever, paratyphoid B, salmonellosis, or dysentery agents is employed at a food catering establishment or a children's institution, he or she is especially dangerous for the surrounding people. Infected animals are the source of infectious diseases that are common for man and animal. Infection of a human with zoonosis by another person occurs in rare cases. Domestic animals and rodents are dangerous in the epidemiologic aspect. The degree of their danger as the source of infection depends on the character of relations between people and the animals, on the socioeconomic and living conditions. People can get infected during management of diseased animals, cooking and eating their meat (anthrax, brucellosis, Q fever, etc.). Rodents are the source of

tularaemia, plague, leptospirosis, rickettsiosis, encephalitis, leishmaniasis and some other diseases.

Main and secondary sources of infection are distinguished in zoonosis. The main source are animals which are a harbour of pathogenic microorganisms and they create natural nidi of tularaemia, plague, and other diseases. Secondary sources of infection become involved periodically in epizootic.

Humans can be infected by wild animals when hunting, during stay in wild environment contaminated with excrements, when drinking water or eating food that may be contaminated with excrements of wild animals. Birds can also be transmitters of infection (ornitosis, salmonellosis, etc.).

Mechanism of transmission. For the epidemic to break out it is not sufficient to have a source of infection alone. The causative agent can survive only if it is transmitted from one host to another, because any given macroorganism destroys the pathogenic microorganisms by specific antibodies that are formed in it in response to the ingress of these microorganisms. Death of an individual host terminates the life of the parasitizing microorganisms. The only exception are spore-forming microbes (causative agents of anthrax, tetanus, botulism). The combination of routes by which the pathogenic microorganisms are transmitted from an infected macroorganism to a healthy one is called the *mechanism of infection transmission.*

Four mechanisms of infection transmission are distinguished according to the primary localization of pathogenic agents in macroorganisms: (1) faecal-oral (intestinal localization); (2) air-borne (airways localization); (3) transmissive (localization in the blood circulating system); (4) contact (transmission of infection through direct contact with another person or environmental objects).

Three phases are distinguished in the transmission of infection from one macroorganism to another: (1) excretion from an infected macroorganism; (2) presence in the environment; (3) ingress into a healthy macroorganism (Fig. 1).

The method by which microbes are excreted from an infected macroorganism (the first phase) depends on the locus of infection in the infected individual or a carrier. If pathogenic microorganisms reside on respiratory mucosa (influenza, measles, pertussis) they can be released from the patient only with expired air or with droplets of nasopharyngeal mucus. If the infection is localized in the intestine, the pathogenic microorganisms can be excreted with faeces (dysentery). The pathogenic organisms in the blood infect blood-sucking arthropods.

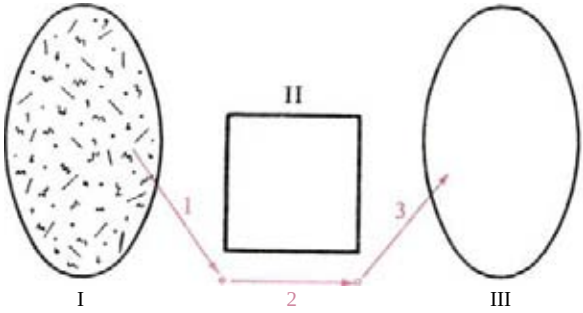


Fig. 1. Transmission of infection:
/-source of infection (diseased human or animal; carrier of the causative agent); //-transmission factors: contaminated fomites (dishes, toys, bedding, clothes), foodstaffs, water, air, soil, living transmitters; ///-healthy macroorganism; / -excretion of the causative agent from an infected macroorganism (1st phase); 2-life in the environment (2nd phase); *3*-entrance to a healthy macroorganism (3rd phase)

The presence of the causative agents outside a macroorganism (the second phase) is connected with various environmental objects. Pathogenic microorganisms excreted from the intestine get on soil, linen, household objects and water, while those liberated from the airways are borne in air. The environmental elements that transmit the pathogenic agent from one person to another are called *transmission factors.* The pathogenic agent can sometimes be transmitted by direct contact with an infected individual or a carrier (venereal diseases, rabies).

Microorganisms causing infectious diseases (viral hepatitis, rubella, toxoplasmosis, syphilis, etc.) infect the foetus through the placenta (transplacental transmission of infection).

Pathogenic microorganisms can be transmitted mechanically during transfusion of blood or its components (plasma, erythrocytes, fibrinogen, etc.). Infection can be transmitted through inadequately sterilized medical tools (viral hepatitis, hepatitis B, AIDS).

The following main factors are involved in transmission of infection: air, water, foods, soil, utensils, arthropods (living agents).

Air is a factor of transmission of respiratory infections. Contamination occurs mostly in an enclosure where a patient is present. From the source of infection, microorganisms get into air together with droplets of sputum. They are expelled in great quantities during sneezing, cough and conversation. Droplets of sputum containing the

pathogenic microorganisms often remain suspended in the air for hours (smallpox, chickenpox, measles) and can sometimes be carried from one enclosure to another with air streams and precipitate on environmental objects. After drying, sputum droplets infect dust which is then inhaled by a healthy person. Dust infection is feasible only with those microorganisms that persist in the environment and can survive in the absence of water. Tuberculosis mycobacteria, for example, can survive in dust for weeks, and virus of smallpox for years. Agents causing Q fever, anthrax or tularaemia can be transmitted with dust.

Water is another very important medium by which infection can be transmitted. Pathogenic microorganisms can get into water by various routes: with effluents, sewage, with runoff water, due to improper maintenance of wells, laundry, animal watering, getting of dead rodents into water, etc. Spontaneous purification of water depends on ambient temperature, chemical composition, aeration degree, exposure to sun rays, the properties of the microorganisms, and other factors. Infection is transmitted by drinking contaminated water, using this water for domestic purposes, bathing, etc. Water can be the medium for transmission of cholera, typhoid fever, leptospirosis, dysentery, viral hepatitis A, tularaemia, and other diseases. If potable water gets contaminated with faecal sewage, water-borne infection can become epidemic with rapid spreading.

Transmission of infection with *food* is especially important since pathogenic microorganisms can multiply in foodstaffs. Food can be infected by contact with an infected person or a carrier, by insects or rodents. Food can be infected during improper transportation, storage, and cooking. The form in which a given food is taken is also epidemically important (uncooked natural foods, thermally processed foods, hot or cold foods). Consistency of foodstaff and its popularity are also important factors. Milk and meat are common transmission media. Dairy products (curds, sour cream), vegetables, fruits, berries, bread and other foods that are not cooked before use are important transmission factors as well. Milk, dairy products can transmit dysentery, typhoid fever, brucellosis, tuberculosis, etc. Meat and fish can be an important factor in development of salmonellosis. Intestinal diseases are often transmitted through vegetables, fruits and baked products.

Soil is contaminated by excrements of humans and animals, various wastes, dead humans and animals. Contamination of soil is an important epidemiologic factor because soil is the habitat and site of multiplication of flies, rodents, etc. Eggs of some helminths

(ascarides, *Trichuris trichiura*, hookworms) are incubated in soil. The pathogenic microorganisms of soil can pass into water, vegetables, berries that are eaten by man uncooked.

It is especially dangerous to use faecal sewage to fertilize soil where cucumbers, tomatoes and other vegetables are grown. Tetanus, gangrene, and anthrax are transmitted through soil.

The role played by various *environmental objects* in transmission of diseases depends on contact with the source of infection, probability of transfer of a contaminated object to a healthy person, and also on the character of chemical and physical effect that a given object can produce on the pathogenic microorganism.

The objects at patient's room can be the transmitting factor for influenza, tuberculosis, children's infections, dysentery, typhoid fever, and other diseases. Domestic animals can be the source of infection, while arthropods can transmit infection.

Utensils and household objects such as dishes, cups, plates (in hospitals, canteens, etc.) can become a transmissing factor for tuberculosis, scarlet fever, typhoid fever, diphtheria. Soiled linen and underwear can promote the spread of infection such as scabies, intestinal or droplet infections.

Toys, pencils, and other objects in children's use are important transmitting factors.

Living objects that transmit infection (Fig. 2) can be divided into two groups: specific and non-specific (mechanical). Specific carriers are lice, fleas, mosquitoes, ticks, etc. They transmit infection by sucking blood (inoculation) or contaminating human skin with their excrements. Inside specific transmitters of infection, the pathogenic microorganisms multiply, accumulate, and with time become dangerous to the surrounding. A louse, for example, sucks blood of a typhoid fever patient and excretes the pathogenic microorganisms with faeces only in 4-5 days. Non-specific carriers transmit the pathogenic microorganisms by purely mechanical method. Flies, for example, carry microbes of dysentery, typhoid fever, viral hepatitis and some other diseases that are found on their bodily surfaces, on the limbs, in the proboscis and the intestine. Gadflies transmit microbes causing anthrax and tularaemia by their stinging apparatus.

Transmitting factors determine also the third phase of transmission mechanism-inoculation of the successive biological object (host). The pathogenic factor is inhaled with air, ingested with food and water, or is transmitted into the blood by arthropods.

The forms of realization of the transmission mechanism, including

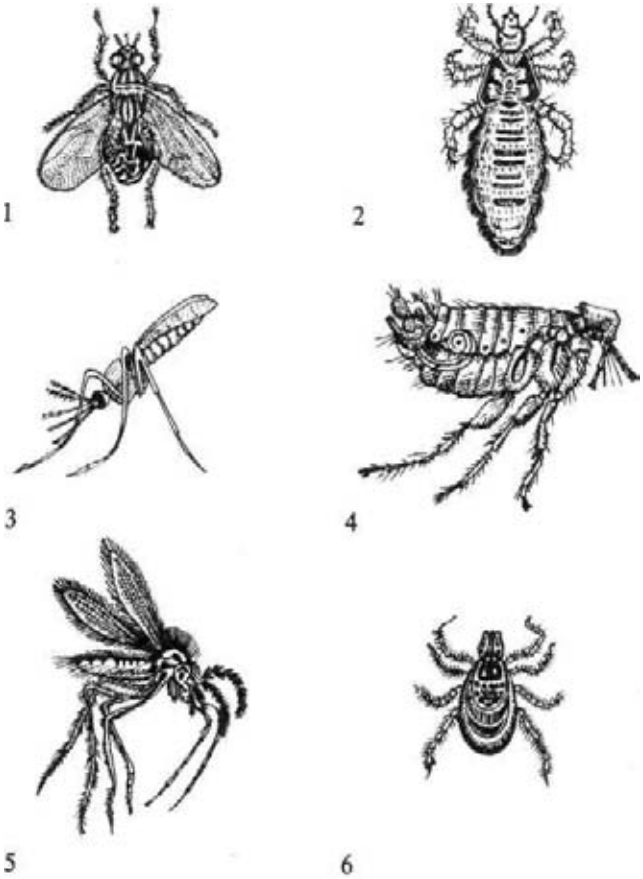


Fig. 2. Arthropod-vectors of the causative agent:
/-house fly; 2-body louse; J-mosquito *(Anopheles);* 4-flea; 5-sandfly; 6-ixodes (female tick)

the combination of factors involved in spreading of a corresponding disease, are known as the *transmission routes* of the infective agents.

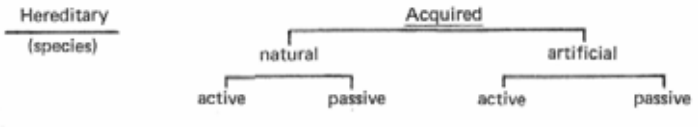
The following transmission routes are distinguished: contact, air-borne (or dust-borne in some diseases), food- and water-borne, transmission by arthropods and soil, through the placenta, by medical parenteral and other manipulations.

Susceptibility and immunity. Susceptibility of people to a given

infection is a very important factor in infection spreading. Susceptibility of an individual or of a community are distinguished. Susceptibility to a disease is a biological property of tissues of a human or an animal, characterized by optimum conditions for multiplication of pathogenic microorganisms. Susceptibility is a species property, that is transmitted by hereditary trait. Many infectious diseases can affect only a certain species of animals. Some anthroponoses, e.g. typhoid fever, scarlet fever, gonorrhoea do not affect animals even after artificial inoculation, because the animals are protected by *hereditary (species) immunity*.

But hereditary immunity is not an absolute property. Under some unfavourable conditions, immunity of a macroorganism can be altered. For example, overheating or cooling, avitaminosis, or some other unfavourable factors can promote the onset of a disease that would not, under normal conditions, affect man or animal. Pasteur, for example, exposed hens to cold to artificially provoke anthrax in them (the disease that does not affect hens under normal conditions).

The following kinds of immunity are distinguished



Acquired immunity, both natural and artificial, is specific because specific antibodies are produced in an infected macroorganism in response to the ingress of foreign antigens.

Natural active immunity is formed in a macroorganism as a result of a sustained disease (postinfection or acquired immunity). Duration of such immunity varies from several years (measles, chickenpox, plague, tularaemia) to a year (brucellosis, dysentery). Natural active immunity can sometimes develop without apparent illness. It is formed as a result of an asymptomatic disease or multiple ingress of the pathogenic microorganisms that are unable to provoke a clinically manifest disease. (For example, only 0.2-0.5 per cent of the infected, develop meningococcal infection; the percentage is even lower in poliomyelitis.)

Natural passive immunity is acquired by a foetus from his mother through the placenta (intrauterine immunity). A newborn acquires it with mother's milk. This immunity is not stable and persists only for 6-8 months to protect the nursling from some infectious diseases (measles, rubella, etc.).

Artificial active (postvaccinal) immunity is created by inoculation with bacteria, their toxins, or virus (antigen) attenuated or inactuated by various techniques. After administration into a macroorganism, they undergo active re-organization which is aimed at production of substances that destroy the pathogenic microorganisms or their toxins (antibodies, antitoxins). Artificial active immunity develops during 3-4 weeks and persists from 6 months to 5 years. The effect of postvaccinal immunity on the course of an epidemic process depends on the scale of vaccination of population, especially of children (against tuberculosis, diphtheria, pertussis, measles, poliomyelitis, and other infections). Vaccination is considered successful if at least 80 per cent of the vaccinated develop adequate immunity (according to WHO experts).

Artificial passive immunity is created by administration of antibodies (sera, immunoglobulins). It persists for 3-4 weeks and then the antibodies are destroyed and excreted from the body. Passive immunization is necessary in situations where the danger of infection exists or if the macroorganism is already infected (in foci of measles, pertussis, etc.).

Depending on a particular antigen, the following types of immunity are distinguished: antimicrobial, antitoxic, and antiviral.

Depending on the period within which the infectious microorganisms are removed from the body, immunity can be sterile (the macroorganism is freed from the pathogenic agent after cure) and non-sterile (immunity persists until the pathogenic microorganism remains in the macroorganism).

Apart from individual immunity there also exists *community (herd) immunity.*

Community immunity is non-susceptibility of a community to a given infection. This type of immunity is created by specific prophylactic and other measures that are taken by health-care services, and also by improvement of well-being of population. Susceptibility to a disease, the course of infection, and duration of immunity depend on diet (that must be rich in proteins and vitamins), ambient temperature, physiological condition of an individual, pre-existing or attending diseases.

Non-susceptibility to smallpox, for example, was formerly attained by compulsory mass-scale immunization. After eradication of smallpox in the world, smallpox vaccination is no longer necessary.

The immunologic structure of population is the ratio of the number of people susceptible to a given infection to the number of those non-susceptible to the disease. This ratio is determined by

various immunologic, serologic, and allergic reactions. If the number of susceptible people is not great, they are surrounded by the majority of non-susceptible persons and the disease is thus not spread.

For example, practical eradication of poliomyelitis in the USSR is due to compulsory planned vaccination of children and adolescents.

Some features of epidemic process. An epidemic develops and is maintained only by the interaction between the source of infection, specific mechanism of its transmission, and susceptible population under given natural and social conditions. The role of these motive forces during subsequent infection is different. The most active is the source of infection, the carrier of the infective factor, the pathogenic microorganisms multiply in it with subsequent release into the environment. The mechanism of infection transmission is decisive. It can be active ingress of the pathogenic factor into a healthy macroorganism through the agency of living carriers, inhalation with air, ingestion with food and water, or persistence of viable pathogenic microorganisms on various non-living objects before they enter another living organism. Susceptibility plays a passive role. In the presence of susceptibility, a person gets infected, while in the absence of such susceptibility a person is not afflicted.

The intensity of an epidemic process can also be different. Three stages of quantitative changes are usually distinguished in the epidemic course: sporadic incidence, epidemic, and pandemic.

Sporadic incidence is a normal (minimal) morbidity characteristic of a given infection for a given country or region. Many infectious diseases occur as single cases.

Group incidence of infectious diseases in a community is assessed in everyday medical practice as an epidemic outburst.

An *epidemic* is characterized by morbidity that 3-10 times exceeds the sporadic occurrence of a given disease in a given locality; it is also characterized by development of multiple epidemic foci.

Pandemic is characterized by widespread epidemic throughout large territories.

*Endemic** characterizes an epidemic qualitatively. An endemic disease constantly occurs among population of a given area. Long existence of any infectious disease in a given country or area can be due to the presence of some natural factors.

Exotic disease is an opposite notion. It is used to designate an infectious disease that does not normally occur in a given country or area and can only be brought from a foreign country.

* From the Greek *endemos* dwelling in a place.

In veterinary the terms epidemic, pandemic, and endemic are replaced by epizootic, panzootic, and enzootic, respectively.

A focus of infection is a site or area where cases of an infectious disease can occur or has already occurred.

The quantitative and qualitative changes in the epidemic process depend on the natural and social conditions that can activate the source of infection, the transmission factor, or susceptibility of population, thus increasing their epidemiologic activity, or on the contrary, decreasing it.

The effect of *natural conditions* on the transmission mechanism of infection is especially marked when the pathogenic microorganisms are transmitted by living carriers. Absence of living transmitters (ticks, mosquitoes) during a certain season or reduction of their population reduces the human infection rate, and hence is important for the course of the epidemic process.

Pavlovsky has worked out a theory of natural nidality of transmissible diseases. He showed that many infectious diseases exist in nature independently of man, in a certain combination of natural conditions in a given locality, in the presence of warm-blooded animals and arthropods that are depots of the pathogenic micro-organisms. For example, ticks transmit encephalitis from diseased animals to healthy ones. Besides, ticks transmit the virus to their posterity.

According to Pavlovsky, naturaljiidality of transmissible diseases is characterized by indefiniteIy~long existence of the pathogenic microorganisms, their specific transmitters and animals (reservoirs of the pathogenic microorganisms) during renewal of their generations independently of man in various biocenoses, both during the course of their evolution and at a given period of time.

Natural nidi of non-transmissible diseases can exist as well. For example, carriers of leptospirosis are not involved in circulation of the pathogenic microorganisms. Spread of this disease is confined within a certain geographic area where a particular rodent lives. Diseases with natural nidality are characterized by seasonal morbidity which is associated with biology of the carriers.

Many animals give posterity in spring; hence vernal rises in brucellosis morbidity. Plague exists in its latent form during hibernation of gophers and marmots. As rodents return to active life in spring, the infection activates and rapidly spreads among the young generation.

Natural processes have their effect on non-living transmission factors as well. Open water bodies get contaminated more easily with

effluents and serve as the source of water-borne epidemic of typhoid fever during the cold season when spontaneous purification of water is slowed down and the microorganisms causing intestinal infections survive for longer periods of time.

Presence of people in enclosures promotes transmission of air-borne infections, while wearing warm clothes without proper hygiene of individuals promotes multiplication of lice, carriers of louse-borne and recurrent fever. The effect of the *natural factor* on susceptibility is insignificant. It only increases or decreases non-specific body resistance (barrier function of the skin, mucosa, blood, bile, etc.).

The *social factor* is more important epidemiologically. It includes the concept of living conditions of population: the quality of dwelling, density of population in residential buildings and areas, conveniences (water supply and sewage system), well-being of population, nutrition, cultural standards, sanitation, health-care system, social structure of a community, etc.

The course of an epidemic depends strongly on the living conditions, i.e., on population density, intensity of association between the source of infection and the surrounding people, the character of occupation, traffic, time of detection of carrier state or developing disease, and time of hospitalization or isolation in home conditions. Poor ventilation, overcrowded residence, inadequate insolation and ventilation of rooms and suboptimal sanitation promote spread of tuberculosis and other infectious diseases.

Domestic animals, poultry, and wild animals can be the source of infection. Man can be infected by a domestic animal due to inadequate veterinary control, untimely detection of diseased animals and their isolation, slaughter or treatment. Rodents and wild animals are regularly reduced in their number which decreases considerably their epidemiologic danger.

The condition of water supply and sewage systems, rational and timely cleaning of settlements are important for the spread of intestinal infections such as typhoid fever, paratyphoid, dysentery, cholera, poliomyelitis, viral hepatitis, etc.

Inadequate control and poor organization of food catering is responsible for spread of infectious diseases. Food can be infected by carriers among those who work in food catering, food shops, children's and medical institutions. People can be infected by meat of diseased cattle and milk and dairy products manufactured from the milk of infected animals.

Labour conditions are often important for the development and

spread of infectious diseases. Animal breeders, veterinary workers, those engaged in handling and processing animal materials (leather, wool, etc.), get infected by diseased animals (anthrax, brucellosis, etc.). These diseases can thus be occupational. Besides, factors decreasing resistance of people (hard labour, overcrowded dwellings, cooling and other debilitating factors) can also promote spread of infection.

Migration of population during social conflicts (famine, war), disasters, such as earthquake, flood, or fires, that are associated with destruction of dwellings and worsening of the living conditions and cause mass-scale migration of the victims, intensify the epidemic spread of infectious diseases, that previously occurred as single cases.

The method of epidemiology. A complex epidemiologic method is used to study the laws of infection spread among population. The method includes epidemiologic observation and experiment.

Epidemiologic *observation,* in turn, includes epidemiologic study of the focus of infection (incidental case) and outbursts; statistic analysis of morbidity; study and description of epidemic process on the whole within a given district or area.

Epidemiologic inspection of an infectious focus is necessary to reveal the source of infection and determine the mechanism of its transmission, to estimate the environmental factors and the living conditions that might promote the spread of the infection. Inspection includes analysis of the incidence of a given infection within its focus (residence, office, children's institution) during 2-3 previous months.

In order to reveal the source of infection and the routes of its transmission, the patient and the surrounding people are inquired, and laboratory tests and experiments carried out. In accordance with the findings, concrete measures are taken to prevent further spread of the infection (see "Prevention of Infectious Diseases and Measures to Control Them").

An epidemiologic examination of an outburst includes the study of morbidity before the outburst, the dynamics of morbidity during the outburst (by days and longer periods of time), the analysis of morbidity by its main signs, epidemiologic findings in separate foci, clinical course of the disease, the laboratory findings, examination of various objects, isolated strains of the causative agents, materials characterizing the sanitary and technical condition of food catering and other establishments. This complex examination gives information about the type of infection outburst (water-borne, food infection) and causes of its development, which facilitates conduction of rational measures to eradicate the infection outburst.

Analysis of morbidity on the basis of statistic findings is necessary for the study of epidemiology of infectious diseases by some indices during the course of a year, or several years. The infectious process is characterized by numerous indices. The most important of them are distribution of the incidence by age, sex, occupation, season, area, source of infection, nidality, etc.

Statistic data are usually absolute or relative figures, but they can also be presented in the form of tables, graphs, diagrams, and the like.

Primary material for a statistic presentation of an epidemic process is the material collected for each particular case of the disease which is entered into a chart of epidemiologic examination. Statistic analysis gives a summary in absolute indices, which are not, however, convenient for comparison of morbidity in various cities, areas or countries. In order to enable such comparison, absolute figures are converted into mean or relative values. Intensive and extensive indices are usually used in epidemiology.

Intensive indices characterize the distribution of a given infection. The coefficients are calculated from proportions reducing absolute figures to one base (1000, 10 000, 1 000 000 of population). Intensive indices include morbidity, mortality, and lethality.

Morbidity (incidence or sick rate) is the ratio of the diseased during a given period of time (e. g. a year) to the number of residents of a given city or country during the same period. Morbidity is expressed by the following ratio:

$$\frac{\text{sick persons}}{\text{average population}} \times 100\,000$$

Mortality (death rate) is the number of dead expressed by a coefficient per 100 000 of adult population, and 10 000 of children. The death rate is expressed by the ratio:

$$\frac{\text{number of dead}}{\text{average population}} \times 100\,000$$

Lethality is the percentage of the dead due to the given infection. Lethality index is expressed by the ratio:

$$\frac{\text{number of dead}}{\text{number of sick persons}} \times 100$$

Lethality index is used to estimate severity of infection and efficacy of treatment. Statistic analysis enables their comparison with the

previous experience and thus to draw conclusions concerning the increase or reduction of morbidity, efficacy of therapeutic measures, and hence to plan further measures.

Description of an epidemic process within a confined area makes it possible to demonstrate the effect of separate elements of social conditions on morbidity.

Experiment includes microbiologic and serologic examinations, entomologic, physical and chemical studies, experiments on humans and animals. Microbiologic and serologic methods are used to study aetiology of infectious diseases, stability of causative agents in environment, inside the macroorganism and resistance to desinfectants; experiment is also used to diagnose infectious disease, to assess treatment efficacy, to reveal acute and chronic carrier state. Microbiologic tests are used to detect pathogenic microbes in food and water. These tests are also used to locate accurately the source of infection, its transmission routes, time during which a sick person remains dangerous to the surrounding people, and to determine the immunologic structure of population.

Entomologic studies are concerned with ecology of the arthropods, the living carriers of the pathogenic microbes, multiplication of these microbes in the macroorganism in various environmental conditions, and establish the carrier type in a particular disease.

Chemical studies of water, food and other objects are necessary to solve disputable questions (e.g. in order to exclude chemical poisoning).

Single and mass-scale experiments can be carried out on animals and people. Experiments on animals are usually used for diagnostic purposes. Besides, they are used to assess harmlessness and efficacy of new vaccines, sera, immunoglobulins and therapeutic preparations.

New vaccines, sera, or immunoglobulins can be used in experiments on humans only after they have been tried in laboratory (experiments on animals included).

Classification of Infectious Diseases

In the 19th century, infectious diseases were classed as contagious (transmissible from person to person), miasmatic (transmitted through air), and contagious-miasmatic. Late in the 19th century, in view of advances made in bacteriology, the diseases were classified according to their aetiology. These classifications could not satisfy clinicians or epidemiologists since diseases with different pathogene-

sis, clinical course and epidemiologic characteristics were united in one group. Classifications based on clinical and epidemiologic signs proved ineffective too.

The classification proposed by Gromashevsky seems to be more reasonable than many others. It is based on the location of infection in the macroorganism. In accordance with the main sign, that determines the transmission mechanism, all infectious diseases are divided by the author into Jour groups: (1) intestinal infections; (2) respiratory infections; (3) blood infections; (4) skin infections. According to Gromashevsky, each group is subdivided into anthroponoses and zoonoses; their epidemiology and prevention differ substantially.

Intestinal infections. Intestinal infections are characterized by location of the causative agents in the intestine and their distribution in the environment with excrements. If the causative agent circulates in the blood (typhoid fever, paratyphoid A and B, leptospirosis, viral

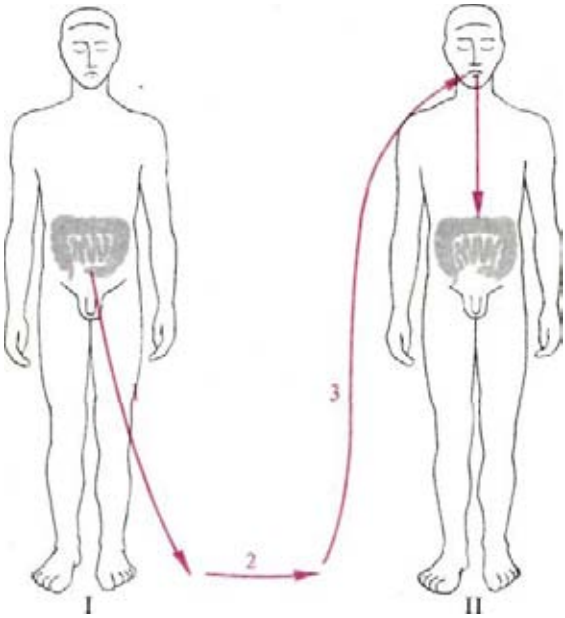


Fig. 3. Transmission of intestinal infection (after Gromashevsky):
/-infected macroorganism; //-healthy macroorganism; /-excretion of the causative agent from an infected macroorganism; 2-life in the environment; *3*- entrance to a healthy macroorganism

hepatitis, brucellosis, etc.), it can also be withdrawn through various organs of the body, e. g. the kidneys, lungs, the mammary glands.

As a microbe is released into the environment with faeces, urine, vomitus (cholera), it can cause disease in a healthy person only after ingestion with food or water (Fig. 3). In other words, intestinal infections are characterized by the faecal-oral mechanism of transmission.

Maximum incidence of intestinal infections occurs usually during the warm seasons.

The anthroponoses include typhoid fever, paratyphoid, bacterial and amoebic dysentery, cholera, viral hepatitis A, poliomyelitis, helminthiasis (without the second host). The zoonoses include brucellosis, leptospirosis, salmonellosis, botulism, etc.

The main means of control of intestinal infection are sanitary measures that prevent possible transmission of the pathogenic microorganisms with food, water, insects, soiled hands, etc. Timely detection of the diseased and carriers, their removal from food catering and the like establishments is also very important.

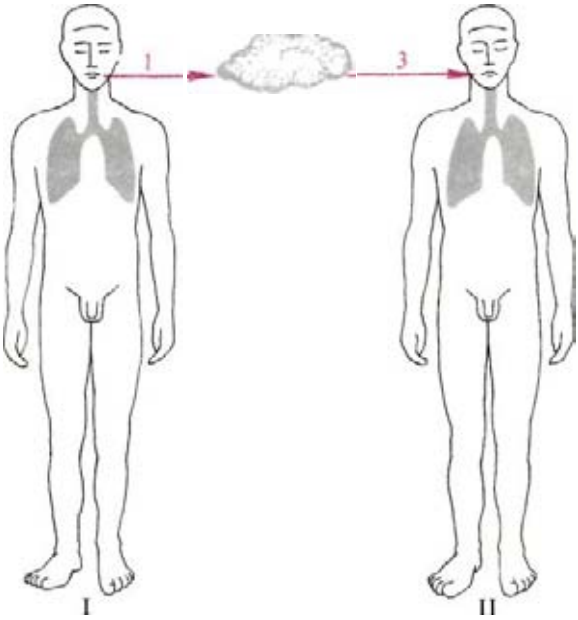
Specific immunization is only of secondary importance in intestinal infections.

Respiratory infections. This group includes diseases whose causative agents parasitize on the respiratory mucosa and are liberated into the environment with droplets of sputum during sneezing, cough, loud talks, or noisy respiration.

People get infected when the microbes contained in sputum get on the mucosa of the upper airways (Fig. 4). If the causative agent is unstable in the environment, a person can only be infected by close contact with the sick or carrier (pertussis).

Pathogenic microorganisms causing some diseases can persist for a period of time in an enclosure where the sick is present. Infected particles of sputum or mucus can dry and be suspended in the air. Some diseases of this group can spread through contaminated linen, underwear, utensils, toys, etc.

Since susceptibility of people, and especially of children to respiratory infection is very high, and since the infection is easily transmitted from the diseased (or carriers) to healthy people, almost entire population of a given area usually gets infected, and some people can be infected several times. Some diseases of this group form a special subgroup of children's infections (diphtheria, scarlet fever, measles, pertussis, epidemic parotitis, chickenpox, rubella). A durable immunity is usually induced in children who sustained these diseases. The main measure to control respiratory infections is to



1 ig. 4. Transmission of air-borne infection (after Gromashevsky):
/-infected macroorganism; *II* healthy macroorganism; *1* -excretion of the causative agent from an infected macroorganism; *2*-life in the environment; *3*-entrance of the causative agent to a healthy macroorganism

increase non-susceptibility of population, especially of children, by specific immunization.

It is important to timely reveal the sick and carriers, and also to break the mechanism of infection transmission: control of over-crowding, proper ventilation and isolation of enclosures, using UV-lamps, wearing masks, respirators, disinfection, and the like.

Blood infections. The diseases of this group are transmitted by blood-sucking insects, such as fleas, mosquitoes, ticks, etc., which bite people and introduce the pathogenic agent into the blood (Fig. 5).

Tick-borne encephalitis, Japanese B encephalitis and some other infections are characterized by natural nidality which is due to specific geographic, climatic, soil and other conditions of infection transmission. The morbidity is the highest during the warm season which coincides with the maximum activity of the transmitters - ticks, mosquitoes, etc.

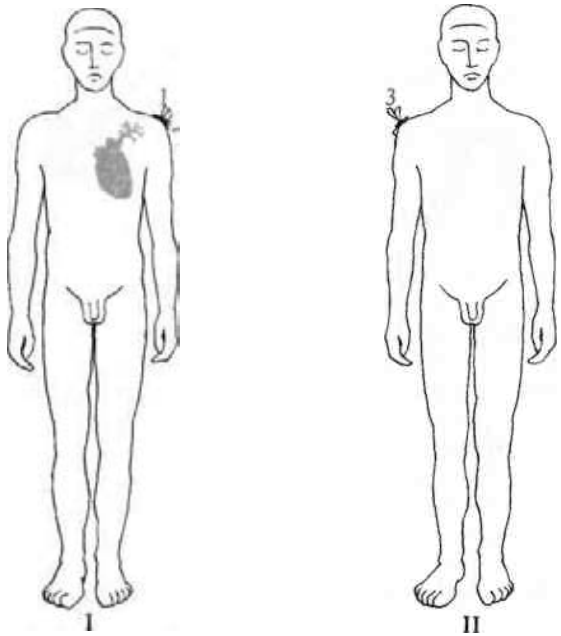


Fig. 5. Transmission of blood infections (after Gromashevsky):
/-infected macroorganism; //-healthy macroorganism; /-excretion of the causative agent from an infected macroorganism; *2*-life in an arthropod; *3*- entrance to a healthy macroorganism

Control of blood infections includes altering natural conditions, improvement of soils, draining swamps, destroying sites where the insects multiply, disinsection measures against mosquitoes, ticks, etc., detoxication of sources of infection by their isolation and treatment, carrying out preventive measures.

If the source of infection are rodents, measures to control them are taken.

Active immunization is also effective.

Skin infections. The diseases of this group occur as a result of contamination of the skin or mucosa with the pathogenic micro-organisms (Fig. 6). They can remain at the portal of infection (tetanus, dermatomycoses), or affect the skin, enter the body and be carried to various organs and tissues with the circulating blood (erysipelas, anthrax). The transmitting factors can include bed linen,

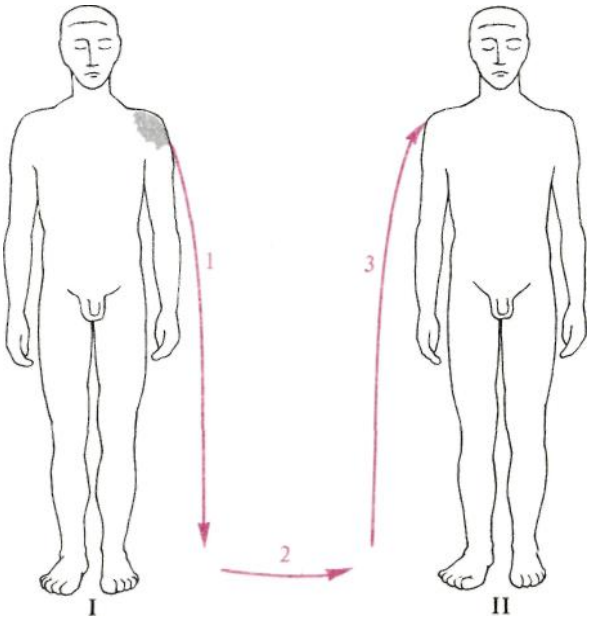


Fig. 6. Transmission of skin infections (after Gromashevsky):
/-infected macroorganism; //-healthy macroorganism; /-excretion of the causative agent from an infected macroorganism; 2-life in the environment; 3-entrance to a healthy macroorganism

clothes, plates and dishes and other utensils, that can be contaminated with mucus, pus or scales. Pathogenic microorganisms causing venereal diseases, rabies, AIDS, and some other diseases are transmitted without the agency of the environmental objects. Wound infections are characterized by damage to the skin as a result of injury (tetanus, erysipelas).

The main measures to control skin infections include isolation and treatment of the source of infection, killing diseased animals, homeless dogs and cats, improving sanitation and living conditions of population, personal hygiene, control of traumatism, and specific prophylaxis.

Prevention of Infectious Diseases ak.d IVkasuics to Control luuu

Prevention and control of infectious diseases include the following:

(1) mass-scale measures aimed at improvement of public health, prevention and spread of infectious diseases;

(2) medical measures aimed at reduction of infectious morbidity and eradication of some diseases;

(3) health education and involvement of population in prevention or restriction of the spread of infectious diseases;

(4) prevention of import of infectious diseases from other countries.

Improvement of peoples' well-being, adequate housing, medical aid, and health education should be adequately planned and carried out. Preventive sanitary supervision is also necessary. Industrial objects, residential houses, children's and medical institutions should be constructed with strict adherence to the special sanitary requirements that are intended to improve labour and living conditions, prevention of onset and spread of infectious diseases.

Preventive measures aimed to control infectious diseases taken by medical personnel are divided into *preventive* and *anti-epidemic.* Preventive measures are carried out regardless of the presence or absence of infectious diseases at a given time and locality. These measures are aimed at prevention of infectious diseases.

Anti-epidemic measures are necessary when an infectious disease develops. It has already been said that the following three basic factors are necessary for development of an epidemic: the source of infection, transmission mechanism, and susceptibility of population. Exclusion of any of these factors terminates the spread of an epidemic process. Prophylactic and antiepidemic measures are therefore aimed at control of the source of infection, disruption of the route by which infection spreads, and strengthening of non-susceptibility of population.

Control of infection source. Patients with some infectious diseases, e. g. measles, pertussis, dysentery or cholera, liberate the pathogenic microorganisms into the environment during the last days of the incubation period or during the first day of the disease. Timely *revealing of the sick* is thus very important. Active detection of the sick is performed by medical personnel at hospitals, polyclinics, medical posts and the like. Health education of population by medical personnel promotes early attendance of the sick for medical aid and thus helps timely detection of infectious patients. Examination of population in outpatient conditions (in residential districts) is helpful in this respect.

An infectious disease is diagnosed on the basis of clinical findings, epidemiologic anamnesis and laboratory tests. All patients with the diagnosis of an infectious disease should be entered into a special record. The record should be made by a physician or a medical nurse. All cases of infectious diseases or suspected cases should be entered into the record, and higher epidemiologic authorities should be informed not later than within 24 hours. In cases of plague, cholera or other disease that requires quarantine measures, local medical personnel must inform higher authorities of the health system.

The *infectious patients must be isolated* in proper time. Patients with plague, cholera, viral hepatitis, typhoid and paratyphoid fever, diphtheria, and similar contagious diseases should be immediately hospitalized. The patients should be handled in special ambulance cars that should be disinfected after transportation of each patient (See *Disinfection).* The patient delivered to the hospital must be given appropriate sanitary treatment before placing in the appropriate ward or an isolated room, if the diagnosis is not clear, or infection is mixed by its character. Special measures should be taken in order to prevent spread of infection within the hospital. In order to remove the danger of spreading infection, the patient should be given appropriate therapy. Patients with scarlet fever, escherichiasis, dysentery and the like diseases can remain at home where they must be isolated from the other family. The family must be instructed how to prevent infection and to disinfect the household utensils. Observation of the patient by the medical personnel must be constant.

Persons cured from infectious diseases should be discharged from hospital after alleviation of all clinical symptoms, and examination for the carrier state, specific for each particular infection; for example, person who sustained diphtheria, can be discharged from hospital after a complete clinical cure and two negative bacteriological tests of the faucial and nasopharyngeal smears. Persons who recovered from typhoid fever, paratyphoid, salmonellosis, dysentery should be observed in outpatient conditions. The term of observation depends on each particular disease.

Carriers of infection should be revealed and isolated for medical examination and treatment. Since it is impossible to screen the entire population, only those who can be a danger for the surrounding people (personnel of children's institutions, food catering, and the like establishments) should be inspected.

If the epidemiologic situation requires, the following groups of people should be examined for the carrier state: (a) persons who can

be in contact with typhoid fever patients, patients with dysentery, paratyphoid, diphtheria, and meningococcal infection; (b) persons with a history of sustained typhoid fever, paratyphoid, and dysentery; (c) persons suspected for being a source of infection in the focus of infection. The carriers must be immediately withdrawn from their occupation at food catering or children's institutions till they are completely cured and given multiple tests for the absence of the carrier state. Chronic carriers should be moved to other jobs that are not connected with food or children. Infection carriers must be regularly treated and observed according to special instructions.

If *animals* are the source of infection, measures differ. Veterinary measures should be taken with respect to domestic animals. Animals with brucellosis should be slaughtered. Horses with glanders should also be killed. Food and materials obtained from diseased animals must be given special treatment. Farms where infection is revealed, must be disinfected and quarantine established. Wild animals that are not the object of quarry must be destroyed, and measures for their isolation from man should be taken.

Disruption of infection transmission pathways. The pathways by which infection can be transmitted are disrupted by acting on the transmission factors. Since intestinal infections are transmitted by the faecal-oral route, all preventive measures are aimed to preclude contact of the infected material with water, food, or hands. General sanitary measures should be taken constantly and universally, regardless of the presence or absence of infection in a given locality.

Community hygiene is very important in prevention of infection spread. Layout of settlements, housing conditions, the presence or absence of water supply and sewage systems are important factors in this respect. Permanent control of water supply system, a correct selection of water body and the site of water intake, protection of the water intake zone, purification and decontamination of water are important preventive measures. Soil protection from contamination with domestic wastes and sewage and timely cleaning of settlements are decisive measures against flies.

Almost all intestinal infections can spread by ingestion of food. The anti-epidemic role of sanitary supervision over foods consists in prevention of contamination of food during all stages of its preparation, cooking, handling and storage, and during final dressing before serving. Neglected rules of cooking and storage of food at catering establishments, shops, and in food industry result in mass-scale spreading of salmonellosis, dysentery, typhoid fever, paratyphoid, etc.

Health education of population is decisive too.

Respiratory infections are easily transmitted from the source of infection to susceptible population. The main measure is prevention of overcrowding, adequate insolation and ventilation of enclosures, use of ultraviolet radiation for disinfection of air at medical and children's institutions. Respirators are necessary in special cases.

In blood infections, the pathogenic agent resides in the blood supply system, in the lymphatic system and sometimes in various bodily organs. The pathogenic agent is transmitted to another susceptible macroorganism through bites of the blood-sucking arthropods. Besides, inoculation is possible during transfusion of blood from an infected person, through wounds during autopsy of the infected dead, during removing skin from infected rodents with valuable fur; transmission of infection is possible during medical manipulations that can be associated with damage to the blood vessels.

Most blood infections are characterized by natural nidality, except those transmitted by lice.

Irrigation of land, drying of swamps, cultivation of new soils and other measures taken in combination with medical ones have considerably decreased morbidity of tick-borne encephalitis, tularaemia, malaria and many other infections.

Control of arthropods (disinsection) is important for prevention of blood infection. Improved living, labour and leisure conditions of population and sanitary control at hairdressers', etc. promote eradication of recurrent fever and louse-borne typhus.

In skin infections, each particular disease is characterized by specific routes of transmission of the causative agent which depend on the living and labour conditions. The transmission mechanism can be broken by improving general health of population and the living and labour conditions. In addition to the mentioned general sanitary conditions, disinfection is another important factor for the disruption of the transmission pathways. Measures to break the transmission mechanism during wound infections include prevention of industrial injuries, traffic and domestic trauma.

Measures to increase non-susceptibility of population. Non-susceptibility of population is increased by improving general non-specific resistance of population by improving the living and labour conditions, nutrition, physical training, health envigorating measures and by creating specific immunity through preventive vaccination. The ancients noted that people who had sustained many infectious diseases became non-susceptible to repeated infection with the same

disease. In the Orient (China, India) they believed that if a person could sustain a mild form of an infection, it could protect him from dangerous diseases during epidemic outbursts. They protected themselves from smallpox by rubbing the content of smallpox lesions into the skin or ingested crusts (variolation), or put contaminated underwear of smallpox patients on healthy children, etc.

In Europe, first attempts to create artificial non-susceptibility to infectious diseases were made in the 18th century. Variolation was practiced in England, Germany, Italy, France, Russia and some other countries. Samoilovich, for example, suggested that population could be immunized by the bubonic contents of plague patients.

The discovery of the English physician Edward Jenner has become a turn point in the teaching of artificial immunity. In 1796, Jenner developed a process of producing immunity to smallpox by inoculation with cowpox vaccine.

Louis Pasteur produced a live vaccine against anthrax by attenuating the causative agents at high temperature. His principle was used successfully by other investigators who also manufactured live vaccines. Virulence of tuberculosis bacteria has thus been decreased by multiple cultivation of the starting culture on bile-potato media.

Most effective proved the method of controlled variability of microbes and selection of low-virulence and highly immunogenic strains. Artificial active immunity is now induced by vaccines (from Latin *vacca*, cow and *vaccina*, cowpox); the method is known as vaccination.

The following preparations are used to prevent infectious diseases: live vaccines prepared from attenuated non-pathogenic microorganisms or viruses; inactivated vaccines prepared from inactive cultures of pathogenic microorganisms causing infectious diseases; chemical vaccines (antigens), isolated from microorganisms by various chemical methods; toxoids, prepared by treating toxins (the poisons produced by microorganisms causing infectious diseases) with formaldehyde.

Vaccines can produce immunity against a given infectious disease or can be polyvalent, i. e., effective against several infectious diseases. Adsorbed vaccines are popular. Aluminium hydroxide is used as an adsorbent. Adsorbed vaccines induce active durable immunity in the vaccinated macroorganism by creating a depot at the site of administration of the antigen, which is slowly absorbed.

Live vaccines are used to create specific immunity against poliomyelitis, measles, influenza, tuberculosis, brucellosis, plague, tula-

raemia, anthrax, Q fever, skin leishmaniasis, epidemic parotitis, and some other diseases.

Live vaccines prepared from attenuated vaccine strains of microorganisms are more effective than inactivated chemical vaccines. Immunity induced by live vaccines is about the same as produced by normal infection. Live vaccines are given in a single dose intracutaneously, subcutaneously, per os, into the nose or by scarification. The disadvantage of live vaccines is that they should be stored and transported at a temperature not exceeding 4-8 °C.

Inactivated vaccines are prepared from highly virulent strains with adequate antigen properties. They are used to prevent typhoid fever, paratyphoid, cholera, influenza, pertussis, tick-borne encephalitis, and some other diseases. Depending on the microorganism species, various methods are used to inactivate them. The microorganisms can be treated with formaldehyde, acetone, alcohol, merthiolate, or at high temperature. Efficacy of inactivated vaccines is lower than that of live vaccines although there are some highly effective inactivated vaccines as well. Inactivated vaccines are injected subcutaneously. Adsorbed vaccines are given intramuscularly. Inactivated vaccines are more stable in storage. They can be kept at temperatures from 2 to 10 °C.

Chemical vaccines are more active immunologically. These are specific antigens extracted chemically from microbial cells. Adsorbed chemical vaccines are used for active immunization against typhoid fever, paratyphoid and other diseases.

Toxoids are formaldehyde-treated exotoxins of the microorganisms causing diphtheria, tetanus, cholera, botulism, and other diseases. Diphtheria and tetanus toxoid is used in the adsorbed form. Toxoids are highly efficacious. When administered into a macroorganism, the vaccine induces an active immunity against a particular infection. Live vaccines produce an immunity that lasts from 6 months to 5 years. Duration of immunity produced by inactivated vaccines is from a few months to a year.

Immune sera and their active fractions (mainly immunoglobulins) induce passive immunity. Immune sera and immunoglobulins are prepared from blood of hyperimmune animals and from people who have sustained a particular disease or have been immunized otherwise. Passive immunization is used for urgent prophylaxis of people who are infected or supposed to be infected, and also for treatment of the corresponding infectious disease. The effect of immune sera and immunoglobulins lasts from 3 to 4 weeks. They are given intramuscularly.

Bacteriophages are used to prevent and treat some infectious diseases. Bacteriophages are strictly specific toward separate species and even types of.bacteria.

The preparations can be given parenterally (percutaneously, intracutaneously, subcutaneously, intramuscularly, intravenously) or enterally (per os), intranasally or by inhalation (aerosols).

When giving vaccines parenterally, it is necessary to observe sterile conditions and to adhere to the rules specified for injection of a particular vaccine. Jet injections are widely used now: the preparations are administered into the skin, subcutaneously and intramuscularly using various syringes.

When given in the liquid state or in tablets, the vaccine should be taken together with water.

Live vaccines are usually given in a single dose, while inactivated vaccines are given in two or three doses at intervals from 7 to 10 or from 30 to 45 days.

Revaccination is used to maintain immunity induced by previous vaccination. The terms of revaccination depend on a particular disease and vary from several months to 5 years. Efficacy of immunization depends largely on regularity of revaccination performed in due time with adequate doses. Quality of the vaccine, and the condition of its storage and transportation are also important.

When selecting persons for immunization, contraindications should be considered. Individual contraindications depend on the route of vaccination, the presence of concurrent diseases, the stage of recovery, previous vaccinations, and the like.

Vaccination should be performed by a physician or secondary medical personnel after thorough examination of persons to be vaccinated in order to reveal possible contraindications, the presence of allergic reactions to medicines, food, etc.

The main contraindications to prophylactic vaccination are as follows: (1) acute fever; concurrent diseases attended by fever; (2) recently sustained infections; (3) chronic diseases such as tuberculosis, heart diseases, severe diseases of the kidneys, liver, stomach or other internal organs; (4) second half of pregnancy; (5) first nursing period; (6) allergic diseases and states (bronchial asthma, hypersensitivity to some foods, and the like).

Vaccination can induce various reactions. These can be malaise, fever, nausea, vomiting, headache and other general symptoms; a local reaction can develop: inflammation at the site of injection (hyperaemia, oedema, infiltration, regional lymphadenitis). Pathology can also develop in response to vaccination; such pathologies are

regarded as postvaccination complications. They are divided into the following groups: (1) complications developing secondary to vaccination; (2) complications due to aseptic conditions of vaccination; (3) exacerbation of a pre-existing disease.

Prevention of postvaccination complications includes: strict observation of aseptic vaccination conditions, adherence to the schedule of vaccination, timely treatment of pathological states (anaemia, rickets, skin diseases, etc.), timely revealing of contraindications to vaccination, and screening out the sick or asthenic persons. All cases with severe reactions to vaccination should be reported to higher authorities. If vaccination is performed by scarification, the results are not always positive, and the vaccine must therefore be tested. The results of vaccination should be assessed at various terms, depending on a particular disease against which a person is vaccinated. The result of vaccination against, e. g. anthrax, should be assessed in 2-3 days.

Vaccination should be performed according to a predetermined plan, or for special epidemiologic indications. Planned vaccination is performed against tuberculosis, diphtheria, tetanus, pertussis, poliomyelitis, measles, epidemic parotitis, and against some other infections within the confinement of separate districts or population groups, regardless of the presence or absence of a given disease. Vaccination for special epidemiologic indications are performed in the presence of direct danger of spreading of a particular infection. Vaccination reports must be compiled and special entries made in histories.

The results of vaccination (efficacy of vaccination) are assessed by comparing morbidity rates among the vaccinated and non-vaccinated groups of population. The number of the diseased and severity of cases must be assessed (agglutination test, complement fixation test, test for allergy).

Sanitary and epidemiologic posts and stations must supervise the work of vaccination posts.

Complex prophylactic and anti-epidemic measures. In case of infectious outbreak it is necessary to take a complex of anti-epidemic measures aimed at eradication of the source of infection, disruption of the transmission mechanism, and increasing non-susceptibility of population. The main measure should be selected depending on the character of infection and a particular condition in a given area. Other measures are only secondary in importance, although their role is also great. For example, only systematic vaccination of the entire population has made it possible to eradicate smallpox all over

the world. The main measure in louse-borne and recurrent typhus is control of the source of infection and eradication of pediculosis among population.

Anti-epidemic measures in the focus. The efficiency of anti-epidemic measures taken in the focus of infection depends largely on the time when the source of infection (patient) is revealed and isolated from the surrounding people.

Regardless of the character of the focus (family, community) measures should be taken toward the patient, the persons who were in contact with the diseased, and the surrounding objects. As the diseased person is revealed, the following measures should be taken: the disease diagnosed, appropriate record made and the authorities informed, the patient hospitalized or isolated in out-patient conditions and given specific therapy.

The focus should be examined by an epidemiologist or a rural physician. The results of examination should be entered into a special chart (record). The purpose of the epidemiologic examination is to reveal the source and ways of infection transmission, to establish the boundaries of the focus, to determine the scope of disinfection and reveal contacts; a plan of immediate measures aimed to control and eradicate the focus should be made out.

Epidemiologic examination of the focus should begin with the study of morbidity at a given locality in the past (flat, hostel, institution, etc.), acquaintance with disease rate among animals and contamination of surrounding objects.

Questioning of the patient, the family and contacts helps reveal the source of infection. Questioning usually begins with asking the patient if he or she had contact with the diseased within his family, among the relatives or acquaintances. If a zoonotic focus is examined, possible contacts with the diseased people or animals must be established. Information about previous travels to other city or village, visits of relatives or acquaintances from other districts should be revealed. It is very important to establish occupation of the diseased, conditions of his labour, living and nutrition conditions.

The value of epidemiologic examination depends on the skill and form of questioning. It is recommended that the results of questioning should be recorded at the end of the talk. The physician must plan his questions beforehand.

Depending on a particular disease, the corresponding objects must be examined. For example, the source of water supply and rooms where food is cooked and stored should be examined in intestinal

infections. If sewage is absent, waste receptacles should be examined. Places where refuse is collected must be examined as well. It is necessary to establish if^ flies were the transmitters of the infection. Cleaning of the surrounding territory must be inspected. Sanitation and hygiene of persons residing in the focus of infection should also be taken into consideration.

Material for microbiologic studies should be taken from the patient, his contacts, and, if necessary, animals and the surrounding objects (water, food, washings from equipment, various materials of animal origin, etc.).

Immunity tests, skin allergy tests, experimental inoculation of susceptible animals should be performed if necessary.

Persons who had contacts with the patient (in the family, house, institution) should undergo a thorough medical examination in order to reveal, as early as possible, new cases of the disease. The terms and character of observation depend on a particular infection. For example, a typhoid fever focus is visited by medical personnel every day (during 25 days), the residents are questioned, examined, and their temperature taken. A viral hepatitis focus should be visited once a week (for 45 days). Stools must be examined in the focus of dysentery. If bacteria carriers, are found in the focus of infection, all contacts must be examined microbiologically to reveal possible carriers.

Workers and other personnel engaged in food catering and the like establishments (i.e., persons engaged in handling foods, their processing and cooking, maintenance of equipment used for food processing and cooking, staff of medical institutions dealing with nutrition of people, workers engaged in water supply and those responsible for storage of water), children at kindergartens and schools should be isolated for various terms depending on a particular infection. All persons who had contacts with plague or cholera patients should be isolated, observed, and given preventive treatment.

The room where the patient is kept before hospitalization should be disinfected (see *Disinfection).* After taking the patient to hospital, or after his or her recovery from the disease (if the patient remained at home), the focus should be disinfected again. If the disease is transmitted by living transmitters (lice in louse-borne and recurrent fever, fleas in plague), disinsection must be carried out. Rodents must be exterminated in the focus of plague or tularaemia.

Health education of population must be carried out in the focus of infection. Medical personnel must acquaint population with the first

signs of the disease, the measures that people must take if the signs of the disease develop, and preventive measures.

In order to stop the spread of infection and eradicate the focus of infection, specific preventive measures must be taken. Depending on indications, the entire population in a given region, or only separate persons who had contacts with the diseased must be vaccinated. For example, if there exists a danger of repeated cases of tularaemia, the entire population of a given area must be immunized.

Review Problems

1. Name the epidemic factors and characterize them briefly.
2. Name the phases of transmission of pathogenic microbes from one macroorganism to another.
3. What major factors are involved in the transmission of pathogenic microorganism s?
4. What measures are necessary to control the source of infection and to disrupt the route of infection transmission?
5. What measures are taken to strengthen insusceptibility of population to infectious diseases?
6. What vaccines are used to prevent infectious diseases?
7. Name the methods by which vaccines are administered. What is vaccination and revaccination? Name the main contraindications for prophylactic vaccination.
8. Who can perform vaccination? What are the causes of postvaccination complications?
9. Name anti-epidemic measures that should be taken in a focus of infection. Name the measures that should be taken to persons who were in contact with the diseased?

Disinfection Measures

The subject matter of disinfection are methods and means of control (or eradication) of the causative agents of infection in various objects and substrates of the environment, and also means of accomplishment of these means and measures.

Disinfection includes three concepts: (1) disinfection proper; (2) disinsection (control of the arthropods transmitting infection); (3) deratization (rodent control).

Depending on the mechanism of infection transmission, it may be necessary to perform disinfection alone (respiratory infections); disinfection and disinsection (intestinal infections); disinsection (louse-borne fever, malaria); disinfection, disinsection and rodent control (plague).

Besides, sterilization is also used. Sterilization implies complete eradication of pathogenic and non-pathogenic microorganisms (spores included) in the environment. Sterilization is used for treatment of surgical, gynaecological, stomatological and other fools, apparatuses, dressing materials, linen, needles, syringes, etc. Nutrient media, laboratory ware, tools and instruments are sterilized in microbiology.

Before sterilization, all objects are first disinfected and cleaned with detergents, hydrogen peroxide and similar solutions.

Several disinfection methods are known. Glass, metal, thermally stable polymers and rubber articles can be sterilized by boiling for 30 minutes, by treatment in special sterilizers at a temperature of 110 + 2°C and elevated pressure of steam.

Special sterilization units must be provided for regular sterilization of tools, instruments and other materials.

Disinfection

Disinfection includes focal and preventive disinfection.

Focal disinfection is necessary if infection develops in a family, children's institution, or any other public institution. It implies current and final disinfection.

Current disinfection includes regular disinfection measures taken during the entire period of presence of a patient or a carrier in a given enclosure. The object of current disinfection is to prevent the spread of the infection.

If, for some reason, the patient is not hospitalized, he must be isolated in a separate room or his bed screened from the other family. Only indispensable objects may be left in the room where the patient remains. The patient must use a separate towel, dishes, bed-pan and the like. In intestinal infections, excrements of the patient (urine, faeces, vomitus) must be mixed with l/5th volume of dry lime chloride, or the excrements should be poured over with two volumes of a 10-20 per cent lime chloride solution or a 5 per cent chloramine or lysol solution. The room must be cleaned 2 or 3 times a day using a moist cloth and aired properly. A 2 per cent soap-soda or 0.2 per cent chloramine solution should be used for the purpose. The concentration of chloramine solution depends on the sensitivity of the pathogenic microbes to disinfectants. Glass ware and dishes used by the patient should be boiled for 15 minutes. Disinfection should be done by a person who takes care of the patient (after being properly instructed) or medical personnel.

Final disinfection is carried out in the focus of those infections

whose causative agents are stable in the environment (typhoid fever, viral hepatitis, cholera, diphtheria, poliomyelitis, plague, etc.). Final disinfection in the focus of paratyphoid and quarantine infection should be performed simultaneously with evacuation of the patient. In the focus of other infection, disinfection should be done not later than in 6 hours (in towns and cities) or 12 hours (in rural areas) after evacuation of the patient. In addition to disinfection, disinsection should also be carried out in foci of intestinal infections (flies should be destroyed). This measure should be taken after hospitalization of the patient, after his recovery or death (if the patient remained at home). Final disinfection is also necessary after discharge of the patient from the hospital, after removal of the diseased from children's or other institution. Final disinfection should be performed by representatives of a sanitary-epidemiologic post or station.

As soon as the disinfection brigade has arrived at the site of disinfection, the scope of work must be determined and a solution of required concentration prepared. If flies are found in the enclosure, disinsection should be performed after the windows and the doors are closed tightly. After disinsection has been performed, the window can be opened, and the patient's belongings (linen, clothes, carpets, toys) are put into special bags for disinfection in special chambers.

Disinfection should be done in the following order: objects that were used for care of the patient, and his excrements are disinfected first, then follows disinfection of remaining food, linen, toys, pieces of furniture. After decontamination of all objects in the room, the floor and the walls are sprayed with the disinfectant in the room of the patient and the adjacent premises. In 30-50 minutes, the rooms are treated with a disinfectant solution. Depending on pathogenicity of the causative agent, disinfection can be done by the family themselves after being properly instructed by the medical personnel.

Preventive disinfection is necessary in all cases regardless of the presence or absence of infectious diseases in a given district or area. Examples of preventive disinfection are daily cleaning at medical institutions, hospitals, schools and other children's institutions, public establishments using a 0.5 per cent chloramine solution. Pasteurization of milk, chlorination of water, washing hands before meals, and the like are also preventive disinfection measures.

Mechanical, physical, chemical, and biologic methods and means are used for disinfection.

Mechanical methods include laundry, washing hands, wet cleaning of floors, removal of dust with wet clothes or using a vacuum cleaner. Pathogenic microbes are partly removed by all these methods.

A common *physical* method of disinfection is boiling. It is used to treat linen, utensils, drinking water, food, toys, surgical tools, and the like. The bactericidal effect increases when boiling is done in a 2 per cent sodium hydrocarbonate or soap-soda solution for 15 minutes and over. The time of boiling depends on stability of a particular pathogenic microorganism to high temperature. Contaminated linen or dishes used by an anthrax patient should be boiled for 60 minutes. Dead animals, wastes, cheap materials, used dressing, etc. should be burned. Dead people should also be burned.

Steam is also used for disinfection. It penetrates into the depth of tissues to destroy the microbes and their spores. Steam is used in special disinfection chambers and autoclaves. Saturated water vapour is very effective.

Treatment at a temperature of 70-80 °C for 30 minutes (pasteurization) kills vegetative forms of microbes, while spores survive.

Linen and other textile articles can be disinfected in home conditions by hot ironing on both sides. It is even more effective if textile fabrics are first sprayed with water.

U-V lamps are used to disinfect air in enclosures (in hospitals, children's institutions, in food industry, etc.). If people are present in the enclosure, the radiation must be directed only into the upper or lower layers of air.

Direct sun rays kill many pathogenic microbes. This simple method must be utilized as much as possible.

The *chemical* method of disinfection includes the use of various chemicals that destroy pathogenic agents found on the surface and inside various objects of the environment and in various substrates, such as faeces, pus, sputum, and the like.

Chlorine- and oxygen-containing substances, phenols, acids, alkalis, hydrogen peroxide, formaldehyde are commonly used as chemical disinfectants.

Chlorine-containing chemicals. *Lime chloride* is a white substance with a pungent odour of chlorine, insoluble in water. The active chlorine content varies from 36 to 28 per cent (minimum 25 per cent). When stored, the substance loses part of its active chlorine and it should therefore be kept in tight containers in the dark. The concentration of clarified solution of lime chloride varies from 0.2 to 20 per cent, depending on the properties of the objects to be treated and stability of the pathogenic microorganisms. A 10 per cent clarified solution of lime chloride is prepared by dissolving 1 kg of dry lime chloride in cold water to make 10 litres. The solution is stirred with a wooden stick, then it is allowed to stand in a tightly

closed glass or enameled container for 24 hours. The clarified solution is passed through a dense cloth and the sediment is discarded. Thus prepared solution should be kept in a dark air-tight bottle for not more than 6 days.

If lime chloride contains less than 25 per cent of active chlorine (not less than 16 per cent), the amount of this substance necessary to prepare a 10 per cent clarified solution should be determined using the following formula:

$$x = \frac{a \times 25}{b}$$

where x is the necessary amount of lime chloride, in kg; a is the quantity of lime chloride containing 25 per cent of active chlorine which is necessary to prepare a 10 per cent solution, in kg; and b is the content of active chlorine in lime chloride, in per cent.

Dry lime chloride is also used for disinfection of faeces (200 g of powder per 1 litre) and urine (10 g per 1 litre).

Commercial lime chloride can be stored for years in a dry place (used as 1-3 per cent solution).

Chloramine (monochloramine, dichloramine) contains from 24 to 28.4 per cent of active chlorine. The substance is soluble in water. Chloramine solutions are widely used for preventive and focal disinfection (0.2-5 per cent solution). Aqueous solutions are prepared immediately before use. They remain active for 15 days.

Activated solutions of chlorine-containing substances are widely used for disinfection. These are prepared by mixing lime chloride and chloramine with ammonium chloride, ammonium sulphate or ammonium nitrate taken in the ratio of 1:1 or 1:2. Ammonia water (10-20 per cent) can also be used as an activator (added in the ratio of 1:8 or 1:16). The reaction is vigorous. Nascent chlorine kills the microorganisms and their spores. Activated solution can thus be used in lower concentrations and the time of exposure can be shorter.

Sulphochlorantin (thermally stable) is a creamy powder with an odour of chlorine. It contains 15.6 per cent of active chlorine; remains active for more than a year if stored in a dark dry place. The activity of sulphochlorantin is 5-10 times higher than that of chloramine. The preparation is used as 0.1-0.2 per cent solution for current and final disinfection in foci of intestinal and air-borne infections of viral and bacterial aetiology.

A *Soviet-made preparation DP-2* is a white powder with an odour of chlorine. It contains 40 per cent of active chlorine. The expiration term is 3 years. Aqueous solutions of the preparation remain active

for 24 hours. DP-2 is used as 0.02-0.08 per cent aqueous solution. The amount of the preparation (in grams) required to prepare one litre of the working solution depends on the concentration of active chlorine. If, for example, the active chlorine content is 40 per cent, 0.5 g of the preparation is necessary to prepare 1 litre of a 0.02 per cent solution; 1.0 g of the preparation should be dissolved in 1 litre of water to prepare a 0.04 per cent solution, etc. DP-2 is used for current, final and preventive disinfection in intestinal, and air-borne infections of bacterial and viral aetiology, fungal diseases, anthrax, plague, etc.

The DP-2 preparation irritates mucosa of the eyes and the upper airways. Measures of individual protection should therefore be used: overalls, gloves, goggles, respirators and the like equipment.

Calcium hypochlorite (neutral salt) is a white powder containing 50, 60 and 70 per cent of active chlorine, depending on commercial grade. It is used as 1-5 per cent aqueous solution for disinfection of buildings.

Chlordesin is a white powder with a faint odour of chlorine. The active principle is a potassium salt of dichloroisocyanuric acid. The preparation contains from 10 to 12 per cent of active chlorine. It is used as a 0.5-2 per cent solution; it acts as a detergent and disinfectant; does not spoil the treated objects.

Oxygen-containing chemicals. *Hydrogen peroxide* is produced as 27.5-40 per cent solution. It is a colourless liquid decomposing spontaneously into water and oxygen. Its 0.5-6 per cent solution is used as disinfectant. In order to prepare a 3 per cent solution, 9 parts of water are mixed with one part of commercial hydrogen peroxide. A 6 per cent solution is prepared from 8 parts of water and 2 parts of hydrogen peroxide. Concentrated solutions of hydrogen peroxide can cause burns on the skin; overalls, goggless and rubber gloves should therefore be worn.

Desoxon is a colourless liquid with a specific acetic odour; readily soluble in water, alcohol and other solvents. Aqueous solutions are prepared immediately before use because the active principle is rapidly inactivated in solution. The preparation is used for preventive, current and final disinfection in hospitals and other medical institutions, in foci of intestinal and air-borne infections of viral and bacterial aetiology. It is used for sterilization of plastic, glass, and corrosion-proof articles. The concentration of the working solution varies from 0.05 to 0.1 per cent.

Phenol (crystalline carbolic acid) is usually stored as aqueous solution (90 parts of the acid in 10 parts of water). The acid is used as

a 3-5 per cent solution to disinfect contaminated materials in clinical and microbiological laboratories.

Lysol is a brown-red oily liquid. Its commercial solution contains not less than 47.5 per cent of soluble cresols, about 50 per cent of soft potash soap and water. It is used as a hot 3-10 per cent aqueous solution.

Hydrochloric acid kills pathogenic microorganisms and their spores. The acid is used to decontaminate hide and pelt of anthrax animals.

Nitric acid is used as a 2 per cent solution to disinfect shaving tools by keeping them in the acid at a temperature of 40 °C for 2 hours.

Sodium hydroxide is readily soluble in water. It is used as a hot 1-10 per cent solution to disinfect rooms, stores, and other enclosures where food or animal raw materials are processed. The solution is effective against anthrax.

Formalin is a 40 per cent solution of formaldehyde. It is used to prepare a 2 per cent solution to disinfect chemical fibres and textiles, instruments, and the like.

Biological disinfection is commonly used in laboratory during cultivation of microorganisms (causing pertussis) in nutrient media (casein-carbon agar). In order to inhibit the growth of extraneous flora, penicillin is added to the nutrient medium.

Disinsection

Insect control includes preventive and destroying measures.

Preventive measures are used to control multiplication of the arthropods and their penetration into residential houses and other buildings. Individual hygiene and sanitation of enclosures are very important. Food or wastes should be kept closed as not to attract flies, cockroaches or other insects.

Destroying measures are aimed to kill insects at the sites of their possible multiplication or habitat, in human environment, on human body, in residential houses, household articles, furniture, and the like. Disinsection can be mechanical, physical, biological, genetic and chemical.

Mechanical disinsection includes removing insects from the walls, flood sweeping, cleaning yards with subsequent destruction of the insects in the wastes. In order to prevent insect bites, the workers must wear overalls, and masks, the doors and windows must be closed with wire gauze, etc.

Winged insects can be killed in special traps, on sticky paper, and

the like primitive appliances. Mechanical disinsection can be combined with other disinsection methods.

Physical methods include burning wastes and inexpensive articles, using hot air (moist or dry), steam, boiling, hot ironing pressing, and the like.

Biological methods are mainly used to kill agricultural and forest pests. Biological means also include infection of the arthropods with bacteria, viruses, fungi, protozoa and helminths. Microbiologic 'insecticides' are widely used; they are prepared from toxins produced by microbes (dendrobacillin, insectin, toxobacterin, entobacterin, and others). A Soviet-made preparation bactocumicid kills the larvae of mosquitoes when applied to the surface of water bodies (0.5-2 kg/ha). Residual effect of the preparation persists from 2 to 10 days. The toxicity of the preparation with respect to warm-blooded animals is low. Spores of *Beauvaria* fungus are used in the preparation boverin which is used to kill larvae of mosquitoes and agricultural pests. Studies are now carried out on viruses that are pathogenic to the arthropods.

Microsporidia are used to control insects. They parasitize on cockroaches, fleas, bed bugs, mosquitoes, gnats, etc. Fishes feeding on larvae can be cultivated in open water bodies. It should however be remembered that predatory fishes can eat eggs and offspring of other useful fishes.

The *genetic* method consists in restriction of arthropod multiplication by radiation or chemical sterilization of insects using x-rays, gamma rays of cobalt-60 or cesium-139, and chemical sterilants which partly or completely sterilize insects. Chemical sterilants are added to baits, or used to treat surfaces, pupa, etc. Investigations are carried out to provide chemical sterilants to kill cockroaches, fleas and other insects. It should however be remembered that chemical sterilants must be used with great precautions since they are highly toxic.

Pheromones secreted by female arthropods are now used to attract insects to traps.

The *chemical* method of insects destruction is based on the use of insecticides and acaricides. Chemical substances killing the larvae of arthropods are called larvicides; chemicals used to destroy the eggs are known as ovicides.

The common forms of pesticides are dusts, granules, wettable powders, emulsifying concentrates, solutions, aerosols, soaps, baits, etc.

Chlorine and phosphorus organic compounds, carbamates, pyre-

thrins, synthetic pyrethroids, and other chemical substances are now used for disinsection.

Chlorine organic compounds are contact and intestinal poisons. They act on the nervous system of the arthropods to cause their paralysis and thus kill them.

Dilor (dihydroheptachlor) is a low-toxic yellowish crystalline substance with cumulative properties. It is manufactured in wettable powders (80 per cent) and dusts (10 per cent).

Phosphorus organic compounds are less stable in the environment, but some preparations are highly toxic toward the warm-blooded animals. Most phosphorus organic compounds act when ingested by or come in contact with the insect. Some compounds are used as fumigants.

Diphos is a white crystalline substance, produced as a wettable powder (50 per cent), emulsifying concentrates (30-50 per cent), and granules (10 per cent). The preparation is effective against fleas, flies, and bed bugs. When used in the form of liquid soap it is effective against lice and mosquito larvae (20-40 g/ha).

Diazinon is an oily liquid, produced in the form of wettable powders (40 per cent), emulsifying concentrates (60 per cent), and granules (5-10 per cent). It has a broad spectrum of action and is highly toxic.

Dichlorophos is a colourless powder, produced as emulsifying concentrates (50 per cent) and granules (20 per cent). Solubility in water is 1 per cent, in liquid petrolatum, 2.3 per cent. Highly toxic. It is an active ingredient in various aerosols that are effective against flying insects.

Dibrom is a white crystalline substance produced as emulsifying concentrate (50 per cent) that is used against cockroaches, flies, bed bugs and some other insects.

Carbophos is a colourless or yellowish liquid produced as emulsifying concentrate (30-50 per cent) and dust (40 per cent). It has a strong characteristic odour: soluble in water (150 mg/1). Its toxicity is moderate. The preparation is used against two-winged insects and ticks *{Ixodes).* The consumption rate of a 1 per cent emulsion is 2-5 1 per sq.m.

Methylacetophos is a colourless liquid. Commercial product is a 5 per cent dust. It is effective against cockroaches and is an active ingredient of 5 per cent liquid soaps, ointments and shampoo used to kill lice, nits and larvae.

Sulphidophos is a colourless soap produced as emulsifying concentrate (50 per cent), poorly soluble in water; its toxicity is

moderate. The preparation has cumulative properties and is used to control larvae of winged blood-sucking insects, cockroaches and lice.

Trichlormetaphos-3 and *trollen* are produced as emulsifying concentrates. Both preparations are effective against larvae of flies, bugs, cockroaches, winged blood-sucking insects, and ticks *(Ixodes).* The consumption rate of a 0.1-0.2 aqueous emulsion is 50-100 ml/sq.m.

Chlorophos is a white odourless crystalline substance, soluble in water (15 per cent at a temperature of 20 °C). The preparation is used as a 5-10 per cent powder, 1-4 per cent aqueous solution, suspension, aerosols, or in baits. Residual action lasts from 7 to 30 days. The preparation is used against flies, bed bugs, fleas, cockroaches and other insects and ticks; it kills the eggs of the arthropods.

Carbamates are derivatives of carbamic acid: dicresyl, dioxacarb, sevin, etc. Some of them should be used with restrictions.

Ficam is commonly used against cockroaches, ants, bed bugs, fleas, flies, and some other insects. Surfaces treated with ficam preserve their insecticide activity from several weeks to a few months. Ficam is produced as 20 and 80 per cent wettable powders.

Pyrethrins and synthetic pyrethroids (neopinamine, permethrin, decamethrin, etc.) are strong neurotropic poisons for the arthropods; their toxicity towards warm-blooded animals is low.

Neopinamine is a white crystalline substance. It is produced commercially as 1 per cent powder (neopin) and as aerosol. The preparation is effective against bed bugs, flies and cockroaches.

Decamethrin is a white crystalline substance produced in the form of wettable powder (2.5 per cent), emulsifying concentrate, and aerosol. Remains active on the surfaces for several months; it is a broad-spectrum preparation.

Permethrin is a viscid yellowish-brown liquid; produced commercially as wettable powder (25 per cent), emulsifying concentrate (25 per cent) and aerosol. Residual effect on the treated surfaces persists for 6 months; the preparation is used against flies and cockroaches.

Among other chemicals used for medical disinsection are borax, boric acid (to control cockroaches and house ants), butadion (against lice), liquid petrolatum (against fleas and bed bugs), etc.

In order to increase the insecticide effect of the said preparations, sesame oil, piperonyl butoxide and some other substances are added as synergists.

Repellants (chemical preparations) and mechanical means (overalls, goggles, and the like) are used to protect humans from blood sucking arthropods (gnats, ticks, fleas, mosquitoes).

Repellants manufactured as aerosols or emulsions are applied to the skin or clothes, gauzes, masks, etc.

Disinfection equipment. Disinfectants and disinsectants are applied by means of various mechanical apparatus that can be driven by electricity or engines; hand-operated apparatuses can also be used.

Rodent Control

Rodents are the source of infection such as plague, tularaemia, leptospirosis, haemorrhagic fever, leishmaniasis, etc. House mice, field mice, black and brown rats, marmots, and water rats are especially dangerous epidemiologically. Preventive and destroying measures are used to control rodents.

Preventive measures include correct storage of foods and wastes, observation of special requirements for building residential houses, stores, etc., aimed at prevention of rodent penetration into them.

Destroying measures include mechanical, chemical and biological means.

The *mechanical* method can be used alone or in combination with chemical and biological methods. Traps of various design are used for the purpose.

The *chemical* method implies in the use of poisons that kill rodents when they are inhaled or ingested. Gases are used to treat stores, ships, railway cars and also sites of natural habitat in field conditions. The consumption rate for various poisons are as follows (with reference to one cubic metre): sulphurous acid anhydride 60-100 g, chloropicrin 45 g, carbon dioxide 700 g. The time of exposure varies from 2 to 12 hours. Ingested poisons are used in baits. Bread, porridge, dough, boiled vegatables, grain, flour and other foods can be used as baits. Sunflower seed oil, chopped meat, fish and sugar are used to attract rodents to baits.

Raticides, zoocoumarin, barium sulphate, zinc phosphide, thiosemicarbazide, arsenic and other preparations are used to poison baits and to dust burrows and water. Zinc phosphide and arsenic preparations are dangerous for man. The amount of poison added to 1 kg of bait depends on a particular poison and the conditions under which the bait is used. Zoocoumarin, thiosemicarbazide, or zinc phosphide are, for example, added in the quantity of 50 g per kg of bait. Poisoned baits are prepared in special rooms by specially trained personnel.

The *biologic* method includes destruction of rodents by bacterial cultures and by their natural antagonists, such as cats, dogs,

predacious animals (weasels, foxes), and wild birds (eagles, owls, etc.).

lsachenko and Merezhkovsky cultures causing typhus among rats and mice are now widely used in the Soviet Union. The bacterial cultures are used in the form of food baits. It is prohibited to use bacterial cultures against rodents at children's institutions, hospitals, industry or food catering establishments, or in buildings where food is stored.

Disinfection in Various Infectious Diseases

Intestinal infections. Final disinfection should be carried out in foci of typhoid fever, paratyphoid, salmonellosis, bacterial dysentery, gastroenteritis and colitis, infections caused by yersinia and escherichia, viral hepatitis, poliomyelitis and other enteroviral infections.

1. The following objects should be disinfected in foci of typhoid fever, paratyphoid, salmonellosis, dysentery, gastroenteritis and colitis, yersiniosis, escherichiasis and cholera:

patient's excrements (faeces, urine, vomitus) should be treated with dry lime chloride taken in the ratio 1:2 (one part of the preparation per two parts of excrements). The time of exposure is 30 minutes. This time should be doubled if the ratio of the disinfectant to excrement is 1:5. Thus treated excrements should be discarded to sewage. If the excrements contain little moisture, water should be added (1:4). Excrement containers (bed pans, pails, bottles and the like) should be treated in the following solutions: (a) 3 per cent chloramine solution (30 minutes), 3 per cent clarified lime chloride solution, 0.5 per cent activated chloramine solution; (b) 1 per cent clarified solution of chlorinated lime, 1 per cent solution of thermally stable chlorinated lime, 1 per cent chloramine solution (for an hour); (c) 0.1 per cent sulphochlorantin solution (for 2 hours). After disinfection, the articles should be washed in water;

the walls at the patient's bedside and in the lavatory (to the height of 1.5 m) should be sprayed with a disinfectant solution (250-300 ml/sq.m) or rubbed with a cloth wetted in the disinfectant. The disinfectant solution should be removed in an hour after treatment with a 1 per cent chloramine solution, 1 per cent clarified chlorinated lime solution, 0.2 per cent sulphochlorantin solution; if a 3 per cent chloramine solution (0.5 per cent of activated chloramine), a 3 per cent clarified chlorinated lime solution is used, final treatment should be terminated in 30 minutes;

polished pieces of furniture should be treated with vaseline oil or other suitable material;

doors, walls, and lavatory pans in toilet rooms should be treated with one of the mentioned disinfectant solutions (500 ml/sq.m) and, in 30 minutes, rubbed with cloth wetted with the disinfectant;

if the lavatory is situated out-of-doors, the surface of the receptacle pit should be treated with dry chlorinated lime (0.5 kg/sq.m); the walls and the floor should be sprayed with a 10 per cent solution of chlorinated lime;

dishes (cups and plates) should be boiled in a 1 per cent sodium hydroxide solution for 15 minutes or they can be placed for 60 minutes (after removing food traces) into one of the following solutions: 0.5 per cent chloramine solution, 0.5 per cent clarified chlorinated lime solution, 0.5 per cent of hydrogen peroxide, or (for 15 minutes) a 0.04 per cent DP-2 solution. Two litres of solution are necessary to treat one set of dishes (2 plates, a spoon, fork, knife, cup, and a saucer). The amount of the solution must be sufficient to cover the dishes. After disinfection, the articles should be washed in hot water;

food remnants should be boiled for 15 minutes or mixed with dry chlorinated lime taken in the ratio of 5:1 and allowed to stand for 30 minutes;

linen, towels, underwear and the like articles should first be laundered in disinfectant solution and then kept in one of the following solutions: 0.5 per cent chloramine solution, 0.5 per cent clarified chlorinated lime solution, 3 per cent lysol solution, 0.04 per cent DP-2 solution, or boiled in a 1 per cent soap-soda solution for 15 minutes. Underwear having no visible traces of contaminants should be boiled in a 1 per cent soda-soap solution for 15 minutes and then treated in a disinfectant solution;

toys (rubber, metal, plastic or wood) should be boiled for 15 minutes in a 2 per cent sodium hydrocarbonate solution or a solution of another detergent (except plastic articles), or kept for 30 minutes in one of the following solutions: 0.5 per cent chloramine solution, 0.5 per cent clarified chlorinated lime solution, 0.1 per cent sulphochlorantin, or for 15 minutes in a 0.04 per cent DP-2 solution;

pillows, blankets, mats, clothes and carpets should be treated with steam or formaldehyde vapour in special chambers, or cleaned with brushes wetted in disinfectant solution.

2. Final disinfection in hepatitis A, poliomyelitis and other enteroviral infections is the same as in intestinal infections, except that:

dishes should be boiled in a 2 per cent sodium hydrocarbonate solution for 15 minutes, or, after removing food remnants, the dishes can be kept in one of the following solutions: (a) for an hour in: 0.5 per cent activated chloramine solution, 3 per cent chloramine solution, 3 per cent clarified chlorinated lime solution, 0.04 per cent DP-2 solution, 1.4 per cent hydrogen peroxide solution; (b) for 2 hours in: 1 per cent chloramine solution, 1 per cent clarified chlorinated lime solution, 1 per cent clarified sulphochlorantin solution;

linen, underwear, towels and other personal belongings should be boiled for 15 minutes in a solution of any detergent or in a 2 per cent soda-soap solution, or soaked for 30 minutes in a 0.5 per cent activated chloramine solution, 3 per cent chloramine solution, hot (50 ^{C}C) 3 per cent hydrogen peroxide solution containing 0.5 per cent detergent solution, or for 2 hours in a 0.04 per cent DP-2 solution. The rate of solution consumption is 4 litres per kg of dry material to be disinfected. Heavily soiled articles should first be laundered in any of the mentioned solutions and then soaked or boiled in this solution;

toys (rubber, metal, plastic, wood) should be boiled in a 2 per cent sodium hydrocarbonate solution for 15 minutes, or placed for 30 minutes in any of the following solutions: 3 per cent chloramine solution, 0.5 per cent activated chloramine solution, 3 per cent clarified chlorinated lime solution, or placed in a 0.04 per cent DP-2 solution for an hour;

hot-water or ice bottles, inflatable rubber cushions or other similar articles should be treated with a cloth wetted in a disinfectant solution or washed in a 2 per cent hot soda-soap solution and rinsed with hot water;

oil cloths, napkins should be treated in the same solutions as used for treatment of linen and underwear, and then washed in hot water;

pillows, mats, blankets, clothes and carpets should be treated with steam or formaldehyde vapour in special chambers.

Current disinfection should be carried out every day: the floor and utensils should be treated with cloths wetted in disinfectant solution. Patient's excrements, the linen and other personal belongings should be disinfected as in final disinfection.

Respiratory infections. Obligatory final disinfection should be carried out in foci of diphtheria, meningococcal infection and ornitosis. The following objects should be treated:

dishes (free from food residue) should be boiled in a 2 per cent sodium hydroxide solution for 15 minutes or kept for an hour in one

of the following solutions: 1 per cent chloramine solution, 1 per cent clarified chlorinated lime solution, 0.1 per cent sulphochlorantin solution, or for 15 minutes in a 0.1 per cent activated chloramine solution, or 0.04 per cent DP-2 solution;

dishes with residues of food on them should be boiled for 15 minutes in a 2 per cent sodium hydrocarbonate solution or kept for 2 hours in one of the mentioned solutions;

toys (plastic, rubber, wood or metal) should be boiled for 15 minutes in a 2 per cent sodium hydrocarbonate solution, or kept for an hour in one of the following disinfectant solutions: 1 per cent chloramine solution, 1 per cent clarified chlorinated lime solution, 0.2 per cent sulphochlorantin solution, or kept for 15 minutes in a 0.1 per cent activated chloramine solution, or a 0.04 per cent DP-2 solution;

underwear, linen, towels, etc. that are not soiled with excretions of the patient, should be boiled in a 2 per cent sodium hydrocarbonate solution for 15 minutes, or kept for an hour in one of the following solutions: 1 per cent chloramine solution, 1 per cent clarified chlorinated lime solution, 0.1 per cent sulphochlorantin solution, or for 15 minutes in a 0.1 per cent activated chloramine, or 0.04 per cent DP-2 solution;

linen and underwear of the patient soiled with patient's excrements should be boiled for 15 minutes in a 2 per cent sodium hydrocarbonate solution or soaked in one of the mentioned disinfectant solutions for 2 hours with subsequent common laundry. The consumption of disinfectant solution is 4 litres per kg of dry linen.

Room where the petient is kept, utensils, and the adjacent rooms where the patient does his private hygienic procedures (lavatory and the like) should be sprayed with one of the following solutions: 0.5 per cent chloramine solution, 0.5 per cent clarified chlorinated lime solution, 2 per cent hydrogen peroxide solution with an additive of a 0.5 per cent of a detergent, 0.1 per cent sulphochlorantin solution. After a 1-hour exposure, the walls coated with an oil paint and all pieces of furniture should be treated with a cloth soaked in a disinfectant solution. The consumption of the disinfectant is 0.5 litre per square metre of the floor area.

Cloths and other materials, that were used for disinfection, should be boiled in a 2 per cent sodium hydrocarbonate solution for 15 minutes or soaked in one of the mentioned disinfectant solutions for 2 hours; later procedures are the same as those used for disinfection of the linen and underwear. Linen, clothes, textile toys and books should be treated in formaldehyde vapour chambers.

In cases of an air-borne infection, the room should be treated with cloth wetted in one of the following disinfectant solutions: 0.5 per cent chloramine solution, 0.1 per cent sulphochlorantin solution. Dishes and toys should be boiled in a 2 per cent sodium hydrocarbonate solution or kept in one of the mentioned disinfectant solutions as described above.

Skin infections. Final disinfection in foci of anthrax should be carried out in the house (after hospitalization or death of the patient) or in enclosures where raw materials and products manufactured of the animals with anthrax were stored.

The floor, the walls, the ceiling, pieces of furniture, and utensils should be sprayed two times (at 30 minutes interval) with one of the following solutions: 5 per cent clarified chlorinated lime solution, or 4 per cent activated chlorinated lime or chloramine solution, hot (55-60 °C) 5 per cent solution of formaldehyde with an additive of a 5 per cent soap, 6 per cent hydrogen peroxide solution with a 0.5 per cent detergent solution.

Linen, underwear, overalls of the medical personnel, who take care of the patient, should be boiled in a 2 per cent sodium hydrocarbonate solution for an hour or kept in a 0.1 per cent sulphochlorantin solution for 90 minutes, or in a 1.2 per cent DP-2 solution for 30 minutes.

Garments, blankets, mats and the like articles should be disinfected in steam and formaldehyde chambers.

Dishes should be boiled in a 2 per cent solution of sodium hydrocarbonate for an hour, or kept in a 1 per cent activated chloramine or 6 per cent hydrogen peroxide solution containing 0.5 per cent detergent solution at a temperature of 50 °C, or in a 1.2 per cent DP-2 solution for an hour.

Food remnants should be boiled in a 2 per cent sodium hydrocarbonate solution for an hour, or mixed with dry chlorinated lime (200 g/1, or 1:5) and allowed to stand for 4 hours.

Patient's excrements should be mixed with dry chlorinated lime (200 g/1, or 5:1). Bed pans, urine receptacles, sputum receptacles should be cleaned and kept in a 20 per cent clarified solution of chlorinated lime for an hour. Excretions of the patient are taken in the ratio of 10:1 (100 g/1) and allowed to stand for 4 hours after which they are discarded to sewage. Dressing material, wastes, and inexpensive articles should be burnt.

Final disinfection in a focus of plague should be performed by a disinfection brigade headed by a physician. Special antiplague overalls should be worn.

All rooms and objects in them should be sprayed with ample 3 per cent chloramine solution or 10 per cent lysol solution (at 60 °C). Disinsection and deratization should be carried out in an hour, then disinfection is repeated in 4 hours and the house kept locked for 3-4 days.

Quarantine Measures

Protective measures against import of and spreading of infectious diseases from other countries were specified by the World Health Organization in 1969 and 1973. Each country must have special system of measures aimed at prevention of import of infectious diseases from abroad, and if an infection is taken into a country, measures should be taken to prevent its spreading. Quarantines should be organized in cases of plague, cholera, yellow fever. (Smallpox has been completely eradicated in the world by 1982).

Quarantines measures should be taken in international sea and river ports, airports, and at posts of international highways, on the border posts on highways. The following measures are necessary at border intersection points:

(1) medical examination of persons who arrive into or depart from a given country, their vehicles and belongings;

(2) availability of special medical documentation (international certificate of vaccination, certificate of deratization, and the like) must be checked;

(3) revealing and isolation of persons with infectious diseases, and isolation of persons who require medical observation;

(4) disinfection, deratization, disinsection of means of transportation, of cargo and luggage (for special indications).

Special measures should be taken to protect import and spreading of infectious diseases such as plague, cholera and yellow fever. Preventive measures should also be taken against haemorrhagic fever, louse-borne and recurrent fever, malaria, anthrax, brucellosis, foot-and-mouth disease, glanders, myeloidosis, rabies, and psitaccosis, that can be imported from other countries.

Review Problems

1. Methods and means used for disinfection in intestinal infections according to this form:

Object of disinfection	Methods and means of decontamination during final disinfection
Example. Excrements of the patient (faeces, urine, vomitus)	Mix with dry chlorinated lime or dry thermally stable lime or taken in the ratio of 1:2; time of exposure, 30 minutes

2. Methods and means used for disinfection in droplet infections. Make out a table as hinted above.

Part Two

The Concept of Infectious Process

The Course of Infectious Diseases

Diseases of man due to pathogenic microorganisms are studied by a special branch of medicine. In the middle of the 19th century these diseases were given the name of infectious, from Latin *inficere*, which means to stain or to taint with morbid matter, i.e., to contaminate.

As distinct from other human pathologies, infectious diseases are characterized by specificity of the living microorganism causing the disease, its transmissibility from a diseased human or animal to healthy people, epidemic dissipation among population under certain conditions, the cyclic character of the clinical course with specific symptoms characteristic of a given particular disease, development of immunity in those who sustained the disease, development of allergy to a given causative agent, and persistence of the carrier state in some infectious diseases after clinical recovery.

As a rule each particular disease is caused by its specific causative agent. Besides, many pathogenic microorganisms can be retained in certain organs or tissues (tropism), where they find beneficial conditions for their multiplication. Accordingly, the clinical picture of some infectious diseases is characterized by specific symptoms of involvement of separate organs and systems. For example, dysentery (shigellosis) is characterized by the presence of mucus and blood in the stools which is due to inflammation of the mucosa of the large intestine; catarrh of the airways is characteristic of measles and influenza.

The site of entry of the pathogenic microorganism to the body is called the portal of infection. In some infectious diseases, such as dysentery, or cholera, the causative microorganisms enter the body

only through one certain gateway, while in other infection they can enter the microorganism through various portals, e.g. in brucellosis, tularaemia, or plague.

As the microorganism enters the human body it can multiply at the site of its entrance (i.e., in the portal of infection) to evoke a pathology. The microorganisms produce toxins which act on the infected body. Besides, the causative agents can be disseminated inside the macroorganism by various routes, e.g. with lymph, blood, or by nervous fibres. From the foci of their multiplication, the agents enter the blood to cause bacteraemia (circulation of bacteria in the blood), virusaemia (the presence of virus in the blood), or toxaemia (the presence of microbial toxins in the blood).

Toxins are classed as endotoxins and exotoxins. Agents of botulism, tetanus or diphtheria produce exotoxins which act selectively on various tissues and organs, while endotoxins are liberated during destruction of microbial cells; the latter toxins are less specific.

Infectious diseases are characterized by the staged character of their course and by a certain sequence of its stages, in which the symptoms increase or decrease. The following periods are distinguished: incubation (latent) period, prodromal period (the period of precursors), the main clinical manifestations of the disease, and the recovery phase (convalescence).

The *incubation period* lasts from the time of ingress of the infection into the macroorganism till the time when the first clinical symptoms become manifest. Each disease has its specific incubation period during which the clinical symptoms are absent. The pathogenic agent multiplies and disseminates in the body during the incubation period, the length of which varies from few hours (food poisoning) to several days (plague, cholera, typhoid fever), weeks (viral hepatitis A), months (viral hepatitis B, rabies), and even years (leprosy).

The incubation period is superseded by the *prodromal period*, which lasts from several hours to several days. The first symptoms of the disease develop during this period. These symptoms are, e.g. headache, malaise, slightly elevated body temperature, myalgia, loss of appetite, catarrh, gastrointestinal dysfunction, and the like. A correct final diagnosis cannot be established at this stage.

The *period of main clinical manifestations* lasts from several days (measles, influenza) to several weeks (typhoid fever, brucellosis). This period is divided into the following phases: increasing clinical symptoms, the period of advanced disease in its full swing (development of the symptoms specific for a given disease), and decreasing clinical manifestations of the pathology.

The clinical symptoms can decrease gradually, during 4-5 days (lysis), or terminate suddenly with an abrupt fall of body temperature within few hours or 1-2 days (crisis). Exacerbations can develop during the period of decreasing clinical symptoms.

The period of the main clinical manifestations is followed by the *recovery phase (convalescence).* The length of this period depends on the immune reaction of a given patient, the severity of the disease, efficacy of treatment, and on some other causes. Recovery can be complete or incomplete. Residual phenomena can be seen during incomplete recovery.

Relapses of the disease can occur in some infectious diseases after recovery: the entire clinical picture can be repeated in 5-20 days, but the course of the relapse will be shorter than of the main disease. Some diseases, e.g. tuberculosis, brucellosis, or dysentery can run a protracted and sometimes chronic course, and persist for years.

Infectious diseases can be followed by specific complications. Otitis, lymphadenitis or nephritis can complicate scarlet fever, while typhoid fever can be complicated by intestinal haemorrhage or perforation of the intestine; some complications can be non-specific, i.e., caused by some other microorganisms. The most dangerous complications of infectious diseases are shock, renal encephalopathy (viral hepatitis), acute renal failure (meningococcal infection), brain oedema (meningitis), etc., which require intensive therapy.

Infectious diseases caused by one agent are called monoinfections, while infections due to several agents-mixed infections.

Mixed infection should be differentiated from secondary infection. In the latter case, a new infection is superimposed upon the existing infection (e.g. an infection due to staphylococcus).

Reinfection is a repeated disease state due to new invasion of the same causative agent (scarlet fever). If a patient is reinfected before his convalescence by the same causative agent but belonging to another type, the case is referred to as superinfection (dysentery, malaria).

Symptoms of infectious diseases. The clinical manifestations of infectious diseases are varied, but some clinical symptoms are common for all of them. The main symptom that can be seen in almost all infections is fever, that develops due to the upset thermal regulation caused by toxic substances of bacterial and tissue origin. Body temperature can be subfebrile, from 37 to 37.9 °C, moderate, from 38 to 39 °C, high (pyrexia), from 39 to 39.5 °C, hyperpyretic, above 40 °C, and subnormal, below 36 °C.

Fever can also be different by its character (Fig. 7): it can be

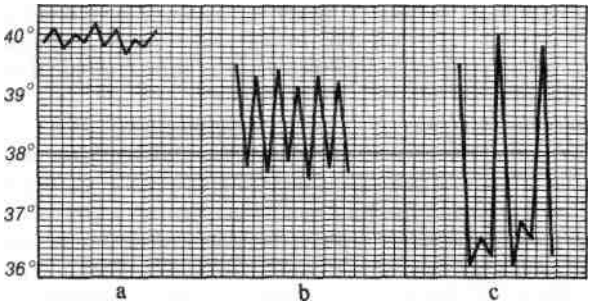


Fig. 7. Temperature curves:
a-continuous fever; *b*-remittent fever; c-intermittent fever

continuous, with variations not exceeding 1 °C in twenty-four hours; *remittent*, with diurnal variations over 1 °C (sometimes 2-2.5 °C); *intermittent*, with alternation of paroxysms of fever with periods of normal body temperature; *undulant*, with wave-like rises and falls of the temperature curve within several days or even weeks; *recurrent* or *relapsing* fever, with alternation of 4-7 day long periods of fever arid apyrexia.

Many infectious diseases are attended by changes in the skin and visible mucosa. The skin becomes dry or, on the contrary, covered with sweat. Various rash can also develop (exanthem). The morphology of skin eruptions is different and classed as follows.

Roseola is a rose-coloured rash, with elements sizing from a millet grain to the size of a pea. Roseola disappears when pressure is exerted but reappears in 2-3 seconds after release of pressure. This is dilatation of a minutest blood vessel.

Petechia is a pinpoint brown-red spot: it does not disappear when pressed, because it is due to intradermal haemorrhage.

Bulla is formed due to exudation into the surface layer of the skin. It occurs in serum disease and urticaria.

Erythema is a large rose-coloured or red spot, often raised over the skin surface.

Papule is a red nodule raised over the skin surface due to infiltration of cell elements.

Vesicle is a small bladder filled with clear serous fluid.

Pustule is a vesicle filled with purulent fluid circumscribed by a red rim.

After resolution of some forms of rash, the underlying skin may

remain pigmented, while in other diseases, e.g. scarlet fever or measles, the skin scales off due to cornification of epidermis.

Polymorphous rash often includes various morphological types, e.g. papules, vesicles, or crusts in chickenpox.

Eruption on the mucosa is called *enanthema.*

The character, the time of development, and location of eruption are specific in some diseases. In scarlet fever, for example, fine rash develops by the end of the 1st day and covers the whole body on the second day. In louse-borne typhus, the skin rash is first roseolous (on the 4-5th day) and then turns to roseolous-petechial.

Involvement of the cardiovascular system is manifested by hypotension (typhoid fever, louse-borne typhus) and lesion of fine vessels (upset capillary permeability). Toxaemia, e.g. in scarlet fever or diphtheria, affects the heart muscle.

The haematologic changes are leucopenia (in viral diseases), leucocytosis (bacterial infections), or accelerated or slowed ESR (hypochromic anaemia).

The spleen, liver and lymph nodes are enlarged in many infectious diseases. Gastrointestinal symptoms are also characteristic. These are loss of appetite, nausea, vomiting, intestinal dysfunction (diarrhoea, constipation, flatulence and the like).

The central nervous system is involved in almost all infectious diseases. This is manifested by deranged sleep, adynamia or excitation, headache, loss of consciousness, delirium, hallucinations and the meningeal symptoms.

Main methods of diagnosis. Despite the specific character of infectious diseases, their diagnosis is difficult, especially during the early period. Only combination of all diagnostic methods makes it possible to establish a correct diagnosis.

Anamnesis is an important step in identification of an infectious disease. Together with the findings of the examination, a correctly collected anamnesis helps reconstruct the clinical picture of the disease. When taking history (anamnesis), it is necessary to find out if the disease began acutely or gradually, if the patient vomited, the time of appearance of skin eruptions, the character of stools, etc.

Epidemiologic anamnesis is also important. It helps establish the fact of association with the diseased person, an infection carrier, or a sick animal; to determine the site where a person could be infected; it is necessary to find out the occupational hazards, labour and living conditions, to obtain information about former operations, injuries, arthropodal bites, transfusions of blood or serum, other medical interventions associated with disruption of integrity of the skin or

mucosa, and also infectious diseases and vaccinations of past history.

The patient should preferably be inspected in natural light, because the yellow colour of the mucosa or skin, or else cyanosis, rash and the like can be overlooked in inadequate illumination conditions. The skin of the patient must be inspected thoroughly and the patient must therefore be stripped of his clothes. If rash is found on the skin, its character must be determined; it is necessary to inquire the patient if he complains of pruritus, etc. The mucosa of the mouth, fauces, pharynx and the tongue should also be examined. The respiratory organs, the cardiovascular and the gastrointestinal systems, and also the lymph nodes should be examined by auscultation, percussion and palpation. The nervous system and the psychic activity of the patients must also be examined.

Depending on the results of examination, a set of *clinical and laboratory tests* should be conducted. These include examinations of the blood, cerebrospinal fluid, sputum, duodenal content, faeces, urine, and vomitus. Changes in the blood, especially in leucocyte count and ESR, are very important diagnostically. For example, leucopenia with relative lymphocytosis is quite specific for typhoid fever, while leucocytosis and neutrophilosis with a shift to the left are characteristic of louse-borne typhus.

Additional methods, such as x-ray examinations, rectoromanoscopy, or ECG help establish the diagnosis.

Special *laboratory examinations* are also very important for establishing a diagnosis of an infectious disease. Depending on the character, form and period of the disease, blood, vomitus, faeces, urine, cerebrospinal fluid, contents of ulcers, pustules and vesicles, materials obtained by puncture and biopsy, mucosal washings, and cadaveric material are examined in the laboratory. Materials for laboratory examinations should be properly labelled and sealed.

Specific laboratory examinations include microscopic, bacteriologic, virologic, serologic and biologic analysis and allergic tests.

Bacterioscopic study of specimens of blood, urine, cerebrospinal fluid, contents of vesicles, pustules, ulcers, and the like is necessary in many infectious diseases. Bacterioscopic study of the blood is necessary in malaria, recurrent typhus, and leptospirosis; urine should be examined in leptospirosis; cerebrospinal fluid in meningitis; faeces in amoebiasis; vesicular or pustular content in anthrax.

Direct microscopy of the sputum, faeces, or nasopharyngeal discharge is used much less frequently because the pathogenic agents in these materials are scarce and difficult to detect. Besides, saprophytes, that are identical to the true agent by their morpho-

logical signs, interfere with diagnostication, because they are contained in great quantities.

Bacteriologic studies are used to isolate the causative agent from blood, e.g. in typhoid fever, paratyphus A and B, salmonellosis, plague; from the cerebrospinal fluid in meningitis; from urine in typhoid fever and leptospirosis; from faeces in intestinal diseases; from nasopharyngeal discharge in diphtheria, and pertussis; from lymph node content in plague and tularaemia.

The time when the result of laboratory tests is ready depends on the time required to grow cultures. The pathogenic agent can be detected bacterioscopically during the first day of the disease; when grown on culture medium the agent can be detected in the laboratory in few hours. Bacteriologic study gives a preliminary result in 24 hours and the final result in 2-4 days. In brucellosis, leptospirosis and some other diseases the result is ready in one or more weeks.

Virologic diagnosis is more difficult and labour-consuming because the virus can multiply only in tissue cultures or chick embryo. Bacteriologic and virologic studies can be complete, accelerated, and rapid, depending on the character of the infection.

Serologic studies include reaction of agglutination, e.g. in typhoid fever or paratyphus (Vidal's reaction), Wright reaction in brucellosis, rickettsia agglutination reaction in louse-borne typhus and tularaemia, etc. These tests are based on the interaction of the antigen with antibody. Using a known antigen one can determine the presence of antibodies in the serum of the patient, while in the presence of known antibodies in the serum it is possible to determine the presence of the antigen in the material taken from the patient. At the present time, more sensitive tests are used for the diagnosis of these diseases. These are reactions of indirect (passive) haemagglutination which is based on the ability of red blood cells, upon which specific antigens are adsorbed, to agglutinate with the patient's serum.

The complement fixation reaction is used to diagnose louse-borne typhus, brucellosis, seasonal encephalitis, and other diseases. Inhibition of haemagglutination and neutralization reactions are also used for the diagnosis of viral diseases.

Immunofluorescent methods are now widely used. They are based on fluorescence of antigen-antibody complexes. In order to induce specific fluorescence, the preparation of material taken from the * patient is treated with specific fluorescent serum.

Accelerated reaction of enzyme-labelled antibodies is used for specific diagnosis of viral and parasitary diseases. In serologic diagnosis, it is very important to determine the specific class of

immunoglobulin (IgA, IgM, IgG) to which a particular antibody belongs. This helps differentiate between inoculated persons and carriers, primary and secondary infection, the transition of an acute disease to a protracted and chronic form (viral hepatitis B), etc.

Tests on animals are used to diagnose plague, tularaemia, foot-and-mouth disease, leptospirosis.

Skin allergic tests are used in brucellosis (Burnet's reaction), tularaemia (tularin test), ornitosis (ornitosis diagnosticum).

Skin tests are based on the increased sensitivity of the body to re-entry of the antigen (microbe, its metabolite).

Allergic reaction tests are performed by epicutaneous or intracutaneous application of the allergen on the inner surface of the forearm. The results are estimated in 48 hours, and if the reaction is doubted, in 72 hours. The test is positive if hyperaemia or oedema specific for a given disease develop at the site of administration of the allergen.

Infectious Department and Hospital

Infectious departments and hospitals are intended for isolation of infectious patients for the time during which they remain dangerous to the surrounding people, and also for treatment of such patients after the diagnosis is established.

An *infectious hospital* has two major divisions: the diagnostic unit and the therapeutic department. An infectious hospital must be provided with units for intensive therapy and reanimation (resuscitation), a surgical department, laboratories for clinical, bacteriologic, serologic, virologic and biochemical studies, a pathologico-anatomic department and mortuary.

Each hospital must also have a unit where all medical tools and instruments can be sterilized.

The admittance unit must have separate cubicles, with their separate entrances and exits, for patients with different infectious diseases. Each cubicle should be provided with separate conveniences, such as cloak-room, showers, baths, etc.

During admittance to an infectious hospital, after establishing a tentative diagnosis, material should be taken from the patient for its laboratory examination. The ambulance car in which the patient was brought to the hospital and the cubicle should be disinfected with a 0.5-1 per cent chloramine solution.

Patients with mixed infections or dubiour. diagnosis, should be placed in isolated wards or rooms provided with all facilities and conveniences.

In order to prevent nosocomial infections, infectious patients of general hospitals should be kept in a separate building. (Patients with similar diseases should preferably be placed in separate buildings.) Rooms for critical patients should be provided. Medical and paramedical personnel should have all facilities separately from the patients (lavatories, canteens, etc.).

Rooms, where infectious patients are kept, should be regularly aired and treated with ultraviolet rays (3 times a day for 40 minutes)..

Rooms should be cleaned with a 0.5 per cent chloramine solution at least three times a day. Lavatories should be cleaned at least 4 times a day with a 0.5 per cent solution of chlorinated lime. Soiled lavatory pans should be cleaned immediately.

Table dishes should be boiled in a 2 per cent sodium hydrocarbonate solution for 15-30 minutes after each meal; chloramine solution can also be used, but after such treatment all dishes should be rinsed in hot (100 °C) water. Food residue should be treated with dry chlorinated lime.

Only rubber or plastic toys can be given to children since these are easy to disinfect. Medical personnel must see to it that the patients observe individual hygiene rules.

Critical patients should be given a separate nurse for 24-hour observation. A signal button must be provided at bedside of each patient in all wards.

A patient can be discharged from an infectious hospital only for special indications (favourable results of laboratory examinations, termination of therapeutic course, normal body temperature, etc.).

Before leaving a hospital, the patient takes bath or shower and puts on clean and disinfected clothes.

The room where the patient remained during his stay in the hospital should be given a final disinfection. Soiled linen should be sent in a special bag to the disinfection chamber. The concentration of chloramine solution by which the room is disinfected depends on a particular infection.

Hygiene requirements for medical personnel. Medical and paramedical personnel of an infectious hospital must keep their clothes in separate boxes. The personnel must wear special overalls and keep them clean. Nails must be cut short.

Materials for laboratory examinations (blood, urine, faeces, vomitus, cerebrospinal fluid) should be taken and handled in conditions that exclude infection of the personnel or other patients.

After inspection and examination of the patient, or after any other

manipulation associated with patient's care, the personnel must wash their hands with a 0.5 per cent chloramine solution and then with warm water.

Prevention of nosocomial infection. A nosocomial infection is an infection that develops in a patient inside a hospital in a lapse of time that exceeds the duration of the incubation period of a given infection, or an infection that develops in a patient after his discharge from the hospital in a period of time that is shorter than the incubation period for a given infection.

Extrahospital infection implies cases of infection before hospitalization (the patient is admitted to the hospital during the incubation period of a given infection). Among nosocomial infections, most common are air-borne infections, such as influenza and acute respiratory diseases, chickenpox, rubella, epidemic parotitis, scarlet fever, or measles.

Nosocomial infections result from admittance to the hospital of patients with unrevealed diseases.

Anti-epidemic measures should be taken in cases of development of nosocomial infections. These measures are aimed at prevention of infection spread. Quarantine should be established whenever necessary. During this period, only those patients can be admitted to the hospital who have already sustained this particular disease.

The first patient with a nosocomial infection should be isolated from the others or placed in a mixed-infection ward, while the room and objects that were used by this patient must be disinfected.

Other patients and personnel who had contacts with the nosocomial infection patient should be observed during the incubation period. Depending on the disease, they should be given immunoglobulin (prophylactic therapy) and tested for the carrier state.

Care and Nutrition of Infectious. Patients

Proper care is an important curative and preventive factor. It is decisive in children and critical patients. Considerate care strengthens the patient's belief in his recovery and restoration of the working capacity.

The medical and paramedical personnel should take care of patient's hygiene and the condition of his bedding. The patient must be given a bath at least once a week. If the patient's condition is critical, his body should every day be rubbed with a wet towel. Patient's underwear and linen should be changed each week or, if necessary, every day or immediately. All patients must be washed in

the morning. Children and critical patients should have their faces and hands washed with warm water.

To prevent bedsores, the skin of patients with severe diseases should be coated with vegetable oil or camphor alcohol at sites where bedsores are more likely to develop. The patient must be helped to turn from side to side; inflatable cushions should be placed under the patient, if necessary.

Body temperature should be taken twice a day. The configuration of the temperature curve is important diagnostically. Great temperature variations indicate complications or change in the course of the disease.

If symptoms of toxaemia develop (headache, delirium, high body temperature), ice should be applied to the patient's forehead for 20 minutes (at 25-30 minute intervals).

If the patient complains of insomnia, he should be given a hypnotic an hour before night sleep. The condition of the patient must be constantly observed. His cardiovascular system should be controlled (pulse frequency and strength). The function of the respiratory system (frequency of respiratory excursions per minute, the character of respiration, the presence of cough, expectoration of sputum), of the alimentary system (inflation of the abdomen, constipation, diarrhoea, vomiting), and of the urinary system (frequency of urination, the character of the urine, its colour and other properties) should be controlled.

Nutrition is an important curative factor. Patients and convalescents should be given at least 4 meals a day. Food must be adequate, i.e., contain all necessary nutrients, salts, vitamins; it must be caloric. The patient must be given fresh vegetables, fruits, berries, fruit juices.

When prescribing a diet, it is necessary to consider the pathogenesis and the course of the disease. For example, a patient with typhoid fever should be given a sparing diet because df the ulceration in the intestine. Food must be liquid or semiliquid. Meat broth, kissels, dried bread, curds, kefir, boiled steamed-cured chopped meat, porridge rubbed through a sieve, and fruit juices should be given. Dietary restrictions should be gradually removed in shigellosis and typhoid fever patients during the recovery phase; the caloric value of the diet should be increased. Food must be sparing mechanically. All dishes should be chopped or rubbed through a sieve. Dietary habits and the appetite of the patient must be considered as well. The appearance of food is also important.

Liquid must be given in adequate amount in order to ensure

withdrawal of pathogenic microbe metabolites from the patient's body. Patients must be given tea with lemon, stewed fruits and berries, and juices.

Treatment of Infectious Patients

Complex therapy should be given along with specific treatment, that must be pathogenetically substantiated and individual for each particular patient, depend on the severity of the patient's condition, and the period of the disease.

Specific therapy is used to eradicate or neutralize the infective agent and its metabolites, and to strengthen the defensive forces of the patient. Chemotherapy, serotherapy, and immunotherapy are indicated.

Chemotherapy. Chemical drugs that produce a specific action on the pathogenic agent can be synthetic or vegetable by their origin. Synthetic antibiotics are also used.

When a chemical drug is administered, it inhibits multiplication and vitality of the pathogenic microorganisms. Further eradication of the agent is ensured by the defense force of the patient.

Sulpha drugs include prolonged-action preparations such as sulphapyridazine, sulphadimethoxin, and other preparations. Limited use of these preparations is explained by development of resistant strains and the irritating effect on the gastric mucosa (nausea, vomiting, gastric hyposecretion). Allergic rash and stones in the kidneys are also possible. Taking great amount of alkaline drinks prevents formation of such stones.

Derivatives of 8-oxyquinoline (intestopan, mexaform, mexase, 5-NOK) are used to treat intestinal infections. These preparations do not inhibit normal intestinal flora, decrease putrefactive and fermentative processes in the intestine. Prolonged use of 8-oxyquinolines can cause peripheral neuritis and impair vision.

Nitrofurans (furadonin, furacin, furazolidone, furagin) are effective against intestinal infections.

Antibiotics are efficacious in infectious patients. They shorten the course of the disease, prevent complications and decrease the mortality rate. When prescribing antibiotics, it is necessary to consider the type of causative agent, its sensitivity to a given antibiotic, duration of antibiotic therapy, the dose and route of administration (oral, intramuscular, intravenous), duration of treatment and toxicity of the antibiotic. Antibiotics give prompt therapeutic effect. The patient's condition improves in 1-2 days (less

frequently in 3 days) and the body temperature normalizes. In the absence of improvement, it is necessary to change the antibiotic.

Chloramphenicol has a broad spectrum of its action and is effective against intestinal infections (typhoid fever, paratyphus A and B), rickettsiosis, spirochaetosis.

Penicillins (salts of benzylpenicillin, bicillin, ampicillin) are highly effective against meningococcal infection and anthrax.

The tetracyclines (hydrochlorides of tetracycline and doxycycline, rondomycin) are effective against rickettsiosis, intestinal infections, tularaemia and plague.

Allergic and endotoxic complications, and also dysbacteriosis can develop following chemotherapy. Allergic reactions occur regardless of the dose or time during which a preparation is given. They manifest by capillarotoxicosis, catarrhs of the mucosa, oedema, skin rash, and shock (loss of consciousness, arterial hypotension, respiratory distress). The endotoxic reaction occurs after administration of priming doses of antibiotics and is explained by liberation of great amount of endotoxin from the dead microorganisms. Dysbacteriosis occurs mostly in treatment with chloramphenicol and the tetracyclines, which inhibits the normal intestinal microflora. Autoinfection develops due to multiplication of staphylococci and yeast-like fungi *(Candida)* which are a part of natural intestinal flora. Biosynthesis of vitamins, especially of vitamins B, is upset. Another disadvantage of antibacterial therapy is development of resistance of the infective agent to a given preparation.

In order to prevent the allergic response in the patient, a thoroughly collected history is important. Desensitizing preparations should be given whenever necessary (dimedrol, dimedryl, diazolin, diprazin, suprastin). In order to lessen endotoxic reactions, detoxicating and antihistaminic preparations should be given together with antibiotics. Dysbacteriosis can be prevented by nystatin, biologically active bacterial preparations, e.g. colibacterin, lactobacterin, bificol, bifidobacterin.

Serotherapy. Serum of immune animals and people is used to treat infectious diseases. The preparations are classed as antitoxic (containing antitoxins) and antibacterial (containing bactericidal antibodies). Antitoxic sera are highly effective. They are prepared by hyperimmunization of animals (e. g. horses, bulls and other animals) with specific exotoxins. Antitoxic sera are used to treat diphtheria, botulism, tetanus, gaseous gangrene, etc. The serum should be administered as early as possible, before the toxins produce irreversible changes in the organs and tissues. Antitoxic serum should be

given in various doses depending on severity of the disease. It can be administered intramuscularly and, in exceptionally rare cases, intravenously.

Antibacterial sera are prepared by hyperimmunization of animals with bacterial vaccines. They are given in millilitres (50-100-150 ml) depending on severity of the disease.

Administration of heterologic serum can evoke various reactions. They can be immediate, early (developing in 4-6 days after administration), and late (in two and more weeks). Immediate complications can develop as specific anaphylactic shock characterized by a fall of arterial pressure (collapse), dyspnoea, convulsions, low body temperature, involuntary defaecation and urination; non-specific fever and chill; hyperaemia of the face, cramping, skin rash; local reaction (hyperaemia developing at the site of injection immediately or few hours following the injection, oedema, less frequently necrosis).

Early and late reactions are manifested by development of serum disease that is evoked by the administration of large doses of serum, especially in repeated injections. In 1-12 days after the injection, the patient develops rash in the form of erythema or urticaria, which is especially intensive at the site of injection, oedema of the face, diarrhoea, swollen and tender joints, enlarged lymph nodes, elevated body temperature.

The serum disease lasts from several days to 3 weeks. Treatment includes dimedrol (dimedryl) and calcium gluconate.

In order to prevent anaphylactic shock, individual sensitivity of the patient should first be determined by an intracutaneous test. To that end, a horse serum (diluted 1:100) is given intracutaneously in a dose of 0.1 ml. The test is considered negative if the diameter of the resultant papule does not exceed 0.9 cm in 20 minutes after the injection and erythema is limited. The horse serum can then be given without dilution in a dose of 0.1 ml. If the reaction is absent within 30-60 minutes, the whole dose of the serum can be injected intramuscularly or intravenously. If the skin test is positive, or anaphylactic reaction develops, the serum may be administered only for very important clinical indications. The dilute serum is injected three times at a 20-minute interval (doses: 0.5, 2 and 5 ml, respectively), then 0.1 ml of serum without dilution is injected. In the absence of reaction, the remaining dose is injected in 30 minutes. Human (homologous) serum almost never evokes anaphylaxis or serum disease.

In order to prevent allergic complications, it is necessary to find out if the serum was administered to the patient before or if the

patient had allergic diseases (bronchial asthma, urticaria, eczema). If signs of anaphylactic shock develop, the administration of the serum should be discontinued, the patient placed in bed with his legs in the elevated position. Noradrenaline or ephedrine (or mesatone) should be given intravenously; atropine or glucocorticoids (prednisolone) should be given for bronchial spasm.

Immune globulins (polyglobulins, gamma-globulins) should be used to treat infectious patients. Gamma-globulins and polyglobulins are obtained from serum, placental blood, immunized donors (homologous) or animals (heterologous). No side reactions are evoked after administration of homologous gamma-globulin or polyglobulia Heterologous gamma- and polyglobulins should be administered after an intracutaneous test. To that end, 0.1 ml of gamma-globulin (diluted 1:100) should be injected into the flexor surface of the forearm. If the test is negative, 0.1 ml of the solution diluted 1:10 is administered in 20 minutes, and then, in an hour, the whole dose, intramuscularly. If the test is positive, the preparation should not be injected, or it may be given in divided doses. Gamma-globulins are used for therapeutic and prophylactic purposes in influenza, pertussis, measles, seasonal encephalitis, anthrax, leptospirosis, staphylococcal infections. Treatment of infectious patients with immunoglobulins is often combined with chemical drugs.

Immunotherapy acts on the immune system of a patient. Specific and non-specific therapies are differentiated. Specific immunotherapy produces effect on the systems of cell and humoral immunity, intensifying formation of specific immunity to certain antigens. Biologic preparations such as vaccines, antigens, bacterial lipopolysaccharides, and anatoxins are used for this purpose. Autovaccines prepared from the causative agent isolated from the patient are most efficacious. Vaccine therapy should be combined with antibiotics, usually when acute manifestations of the disease decrease, in long-standing and chronic cases (tularaemia, brucellosis, dysentery). For therapeutic purposes, the vaccine is given intravenously, intramuscularly, subcutaneously, and intracutaneously. The vaccine therapy is contraindicated to patients with lesions of the cardiovascular system, of the kidneys or the liver.

Blood and its components, vitamins, pyrimidines or their derivatives (methyluracil, pentoxyl) are used for non-specific stimulation. Pyrimidines are component parts of nucleic acids that are involved in the biosynthesis of protein, both specific and non-specific, they stimulate cell and humoral mechanisms of immunity, and produce anti-inflammatory effect. Pyrimidines are used for complex treatment

of typhoid fever, dysentery, brucellosis, and viral hepatitis. Non-specific immunotherapy also includes bacterial lipopolysaccharides (pyrogens), most popular of which are pyrogenal and levamidol. Other pyrogens that are isolated from various cells and tissues of macroorganism, are also used. Pyrogens intensify the activity of antibody-forming cells; they stimulate leucopoiesis and increase non-specific resistance of the body to toxins of bacteria and viruses.

Pathogenetic therapy includes many medical measures aimed at elimination of toxaemia by detoxicating or infusion-detoxicating therapy, and glucocorticosteroid therapy, depending on the clinical form of the disease; restoration of water-salt equilibrium by rehydration therapy; normalization of the cardiovascular and nervous function; and also increasing the impaired bodily functions by stimulation therapy.

Detoxicating therapy is given in mild and moderate forms of infectious diseases. It is sufficient to give the patient ample drinking: juice, stewed fruits, mineral water, boiled water, tea, etc.

Patients with pronounced toxaemia are given infusion-detoxicating therapy directed at neutralization and elimination from the body of microbial toxins and metabolites. To that end, haemodez is given intravenously; polyglucin, rheopolyglucin, blood plasma, and 10 per cent albumin solution should be given for severe hypotension. A 5 per cent glucose solution and isotonic sodium chloride solution should also be administered. The solutions can be infused separately or, wherever possible, in mixtures (drip infusion).

Depending on the degree of toxaemia, from 500 to 1000 ml of fluid are infused. Infusions should be repeated 2-3 times a day with strict control of the infused volumes, body weight, and of the diuresis, that must ensure withdrawal of excess liquid from the body.

Glucocorticosteroid therapy is given to patients in septic shock and acute adrenal failure (meningococcal infection, influenza, haemorrhagic fever, poliomyelitis, typhoid fever, louse-borne typhus, salmonellosis, dysentery, diphtheria, plague, cholera).

Glucocorticosteroids (prednisolone, dexamethazone, triamcinolone, cortisone, hydrocortisone) are given in large doses, better intravenously. For example, a daily dose of prednisolone is 120-300 mg and more; after recovery of the patient from shock, the daily dose of the preparation is decreased 2-4 times and is given intramuscularly or per os with control of arterial pressure.

Rehydration therapy is directed at restoration of the water-salt equilibrium and is used in gastrointestinal forms of intestinal infections attended by incoercible vomiting, frequent stools (profuse

diarrhoea), dehydration of the body and accordingly decreasing volume of circulating blood (hypovolaemia), and development of hypovolemic shock.

The amount of repleted salts, their composition and the way of administration depend on the rate and degree of dehydration and the character of the water-salt disbalance. Four degrees of dehydration are differentiated.

Dehydration, degree I. The patient loses water in the amount of 1-3 per cent of body weight. The patient develops moderate thirst, dryness of the mucosa, and moderate fatigue; stools are semiliquid or watery, 3-10 times a day; vomiting is rare.

Dehydration, degree II. The loss of liquid is 4-6 per cent of body weight. Stools are ample, watery, or resembling rice water, 10-20 times a day; vomiting is frequent (5-10 times). The patient develops thirst, the skin and mucosa are dry; the lips, fingers and feet are cyanotic; fatigue is marked. Muscular cramping in the calves, wrists, and feet; signs of blood thickening develop; tachycardia, hypotension and oliguria are seen.

Dehydration, degree III. The loss of liquid is 7-9 per cent of body weight. Stools are frequent and ample; vomiting and cramping of limb muscles are seen; the skin and mucosa are dry, washerwoman's hands symptom develops, hypotension is pronounced; oliguria or even anuria develops.

Dehydration, degree IV(the algid form). The liquid loss is 10 per cent of body weight. The disease begins acutely. Diarrhoea and vomiting discontinue at the beginning of the disease. The body temperature falls to 35-35.5 °C, peripheral pulse and arterial pressure are absent; anuria and aphonia develop. Cyanosis is intensive, the muscles are cramping, the facies are pinched, the eyes and the cheeks are retracted.

In I and II degree dehydration the patient is given gastric lavage and then one of the following solutions (to drink in small portions): glucose-salt mixture (3.5 g of sodium chloride, 2.5 g of sodium hydrocarbonate, 1.5 g of potassium chloride, and 20 g of glucose dissolved *ex tempore* in 1 litre of drinking water); a solution containing 4 g of sodium hydrocarbonate, 5 g of sodium chloride, and 1 g of potassium chloride; a solution containing 2.6 g of sodium acetate, 1 g of sodium hydrocarbonate, 6.2 g of sodium chloride, and 0.3 g of potassium chloride; or Locke-Ringer solution containing glucose or sweet tea. If vomiting continues, the liquid should be administered through a nasogastric tube.

In II and III degree dehydration, and especially degree IV, the

patient should be given intravenously polyion buffer solutions preheated to 38-40 °C. In addition to the mentioned solutions, used also are solutions containing 2 g of sodium acetate, 5 g of sodium chloride, 1.0 g of potassium chloride, or a solution containing 3.6 g of sodium acetate, 4.75 g of sodium chloride, and 1.5 g of potassium chloride, or a solution containing 3.3 g of sodium lactate, 4.75 g of sodium chloride, and 1.5 g of potassium chloride. Treatment includes two states: primary rehydration (repletion of the liquid lost before rehydration therapy is started) and compensatory (replenishment of the liquid lost during treatment).

In III degree dehydration the solution is given intravenously at a rate of 100 ml/min. In IV degree dehydration, and if hypovolaemic shock develops, one of the specified solutions is infused at a rate of 100-120 ml/min, 5-7 litres during 60-90 minutes. After the patient's condition is no longer critical, the second stage of treatment begins. The solution is now infused by drip at a rate of 100-150 drops per minute with a gradual reduction of the rate to 60 and then 20-10 drops per minute. Liquid infusion can be suspended depending on the degree of improvement of the patient's condition and normalization of the water-salt metabolism. If necessary, the glucose-salt solutions are given per os, by small portions at short time intervals.

Salt solutions, especially their large volumes, should be administered under constant laboratory control of the water-electrolyte metabolism, blood counts, and diuresis.

Stimulating therapy is aimed at normalization and intensification of dysfunctioning organs and systems. Cardiovascular dysfunction develops due to the action of toxins liberated by the pathogenic agent on the myocardium and the vessels. Dehydration of the body causes thickening of the blood, evokes circulatory and haemostatic disorders. Cordiamine, caffeine, ephedrine, and norepinephrine are given to neutralize the action of toxins.

Vitamin therapy is useful from the very beginning of the disease; especially important this therapy is in long-standing and chronic diseases and in the presence of complications. Vitamins given together with hormones and enzymes catalyze the metabolic processes.

Vitamin B_t facilitates correction of some nervous disturbances, vitamins A, C and $B_:$ decrease the toxic effect of antibiotics, vitamins C, B_{ls} PP and P produce an anti-inflammatory and detoxicating action, vitamin P decreases brittleness and permeability of vessels, vitamin K promotes blood coagulation. Depending on the nature of a given disease, vitamin complexes are prescribed; the dose should

3-4 times exceed normal one; during the recovery phase, the dose should be 2-3 times higher than normal. Vitamins are given per os or intravenously with glucose solutions (vitamin C as a 5 per cent solution of ascorbic acid; vitamin B_x as a 6 per cent solution).

Blood transfusion produces a neuroreflex effect on body reactivity, stimulates resistance to infections, and performs a haemostatic and replacement role in haemorrhages. Blood is transfused in protracted and chronic diseases, in the presence of complications (typhoid fever, scarier fever). Two or three transfusions at 3-4 day intervals are necessary.

Plasma can be infused instead of blood. Plasma is available in the dry form in ampoules. Before use, it is dissolved in distilled water. Plasma is infused intravenously in a dose of 50-100 ml to children with protracted and chronic dysentery and with other infections.

Autohaemotherapy, polyglobulia and interferon (in viral infections) are also used.

Symptomatic therapy is aimed at elimination of separate symptoms that usually develop as a result of toxaemia: amidopyrin with phenacetin are given for headache, hypnotics are effective against insomnia.

Review Problems

1. Name the periods of infectious diseases and describe them. What patients present the greatest danger as the source of infection?
2. What are the main symptoms of infectious diseases?
3. What serologic reactions are used for the diagnosis of infectious diseases?
4. Name the specific features of regimen in infectious hospitals and departments.
5. What are the specific features of care of infectious patients?
6. Name the prophylactic measures that should be taken to prevent nosocomial infection.
7. What cases can be referred to nosocomial and extrahospital infections?
8. A child developed chickenpox in 5 days after admittance to a paediatric department (for gastrointestinal infections) of an infectious hospital. Is this a case of nosocomial infection?
9. A child developed epidemic parotitis in 24 days after admittance to a gastrointestinal department of an infectious hospital. Is this a nosocomial infection?
10. Name the main principles of treating infectious patients.
11. Name the methods of specific therapy of infectious patients and characterize each method.
12. Name the main methods of pathogenetic therapy and characterize them.
13. What are the principles of nutrition of infectious patients?

Part Three

Special Epidemiology

Intestinal Infections

Typhoid Fever (Typhus abdominalis)

Aetiology. Typhoid fever is caused by *Enterobacteriaceae*, genus *Salmonella.* The microorganism is motile, it is pathogenic only toward man. It is stable in the environment: in running water it persists for 5-10 days and in stagnant water for a few months. It can survive over winter in ice. In fruits and vegetables it lives for 5-10 days, in other foods from 2 to 8 weeks. On some objects of the environment it persists from several hours to a month and even longer. When dried in direct sun rays the pathogenic microorganism is rapidly destroyed. Boiling kills it instantaneously. A 3 per cent solution of lysol and a 3 per cent chloramine solution kill the bacteria within 2-3 minutes.

Epidemiology. The source of infection is a typhoid patient or a carrier. Patients with mild or abortive forms of the disease are especially dangerous because they often continue performing their routine duties and thus promote the infection spread. Patients with typhoid fever are contagious for the surrounding people beginning with the first week of the disease, but they are the greatest danger during the second and third week of the disease, when the maximum amount of pathogenic microorganisms are excreted with the urine and stools.

Chronic carrier state is a chronic form of typhoid infection. The microorganism persists in the cells of the macrophague system in the L form. Under certain conditions, it can be reactivated into the initial pathogenic form and cause bacteraemia with development of secondary foci in the absence of clinical symptoms.

Beginning with the first week of the disease, specific immunity

develops in most patients. It helps the patient to free from the pathogenic microorganisms and to terminate toxaemia.

The leading role in the spread of infection belongs to chronic carriers, especially if they are engaged occupationally in handling of food that is not cooked before use. Chronic carriers are dangerous not only as the source of infection, which cause disease in other persons and epidemic outbreaks, but also as depots of typhoid infection.

The epidemiologic importance of healthy (transitory) carriers, compared with chronic carriers, is not great because they release the microbes only for a short period of time and in small amount.

The mechanism of transmission. Typhoid fever is characterized by the faecal-oral mechanism of infection. The pathogenic microorganisms are released from the patient or carrier with faeces and urine, and enter the body of a healthy person with water or food. The transmission factors are water, food, soiled hands, environmental objects such as dishes, toys, linen, towels, flies, and the like. If infection is transmitted with water, the morbidity rate depends on a particular source of water: water supply system, river, well, pond.

Water-borne epidemics of typhoid fever can be classed as: (1) acute, that develop periodically and last over a comparatively short period of time; (2) chronic, that last for a few months and even years.

Acute water-borne epidemics result from breakdown in the water supply system or neglected rules of their maintenance. Epidemics are characterized by a sudden onset and a relatively rapid termination after eradication of the cause that has promoted the spread of infection with drinking water.

Chronic water-borne epidemics develop as a result of systematic contamination of water with surface pollutants through maintenance wells or some other routes. The morbidity rate remains high over a prolonged period of time in such cases.

Food-borne transmission is characterized by ingestion of contaminated milk and dairy products, and dishes, not cooked before serving. Besides, the pathogenic microorganisms find a beneficial nutrient medium for their multiplication. The character of food epidemics depends on the scale of use of a particular food. Usually they are short-lasting.

During transmission of infection by *person-to-person* contact the microorganism is transmitted from the patient or a carrier to a healthy person directly through soiled hands or infected environmental objects. Spread of infection is facilitated by suboptimal sanitation and poor socio-economic conditions.

If sanitation is inadequate and disposal of wastes in towns is below standards, flies promote the spread of typhoid fever.

Typhoid fever occurs in various countries but the incidence is never pandemic, because typhoid fever is characterized by a prolonged incubation period and the maximum amount of pathogenic microorganisms are released by the patient in 2-3 weeks after the onset of the disease, that is, when the patient is already hospitalized. Besides, the absence of conditions for microbe spreading with water and food are sometimes absent.

The incidence is the highest during the warm season (summer and autumn). During recent years the incidence of typhoid fever is mostly sporadic; local outbreaks are not significant.

It is believed that susceptibility to typhoid fever is universal but many people are not afflicted by the disease in the focus of infection. Immunity that is induced in persons who sustained typhoid fever is rather durable but it weakens with years.

Pathogenesis. The pathogenic microorganisms enter a human through the mouth. If the defensive function of the stomach is adequate, the microorganism is killed in the stomach and the person does not develop the disease. If the defense function is impaired and the number of microorganisms that enter the stomach is great, they can reach the lower portions of the small intestine where they get into the aggregations of lymphatic follicles (Peyer's plaques) and solitary follicles, and into the nearest mesenteric lymph nodes, where they multiply. At the end of the incubation period, the pathogenic microorganisms are released from the mesenteric nodes into the blood to cause bacteraemia. The pathogenic microorganisms are thus carried throughout the entire body and precipitate in the spleen, bone marrow, lymph nodes and the liver. As the microbes die, they release endotoxin that poisons the human body. The endotoxin acts on the central nervous system to induce *status typhosus*, which is characterized by dimmed consciousness, inhibition, sleepiness alternated by insomnia, headache.

The rate of bacteria removal from the patient depends largely on the function of the excretory organs and systems (the liver, the intestinal glands, the intestine, the kidneys) and formation of specific antibodies. From the liver, the microbes are released with bile into the intestine and are partly excreted from the patient. The remaining microbes precipitate in aggregated and single lymphatic follicles, primarily sensitized by the microbes, in the lower portion of the small intestine. The re-entrance of the microbes into the presensitized aggregated and solitary lymphatic follicles causes an allergic inflam-

mation with ulceration and necrosis of tissues (Plate I).

Involvement of the sympathetic nervous system induces meteorism (inflation of the intestine), diarrhoea, bradycardia, and hypotension.

Endotoxin affects also bone marrow and induces leucopenia.

Clinical picture. The incubation period lasts from 7 to 25 days (usually 14 days).

The disease begins with a prodromal period. The patient gradually develops weakness, malaise, chills, headache; his appetite is impaired. The period lasts from a few hours to 2 days. The symptoms then gradually intensify. The subjective condition impairs. The patient develops adynamia, indifference, headache, and suffers from insomnia. Weakness makes the patient keep his bed. The body temperature rises in steps, and by the 4th or 5th day it is 39-40 °C. For a period of time it remains constantly high and then undulant fever develops (Botkin's type of the disease). In the absence of specific treatment high fever can persist for 2-3 weeks and then body temperature decreases to normal in 4-5 weeks.

Examination of the patient reveals pallor of the skin and visible mucosa, the tongue is thick, with imprints of the teeth by its edge; the tongue is white, while the margins and the tip are free from the coat and are crimson. If the disease runs a severe course, the tongue becomes dry, its surface is cracked, the coat is stained with blood and turns brownish.

The abdomen is inflated due to accumulation of a great amount of gas. Constipation develops (diarrhoea is less common). The spleen becomes enlarged by the end of the first week; the liver is enlarged later. The pulse rate does not agree with the body temperature (relative bradycardia); arterial pressure falls.

At the height of the disease, beginning with the 5th or 7th day, as the fever intensifies, the nervous system is involved and the status typhosus develops. The patient becomes indifferent, delirium develops, headache intensifies along with increasing meteorism and insomnia. In severe cases stupor develops which can transform into sopor.

Rose spots occur on the abdomen, less frequently on the chest in 8-9 days of illness (Plate II). The rash persists for 4-5 days and then regresses. Fresh spots develop on new sites of the skin. In severe cases the rash can bleed.

A transient moderate leucocytosis is followed by leucopenia with a relative lymphocytosis (40-60 per cent), aneosinophilia and thrombocytopenia; ESR is moderately accelerated.

Bronchopneumonia and pharyngitis ulcerosa can develop at the height of the disease; protein and casts can be found in the urine. Oliguria develops. Bacteriuria is associated with lesions of the urinary tract (pyelitis, cystitis).

As the clinical manifestations abate, toxaemia lessens, body temperature gradually drops, sleep is normalized, appetite improved, the tongue clears of the coat, and the amount of urine excreted increases. After normalization of body temperature, the patient begins recovering.

Typhoid fever can recur. After several fever-free days, the body temperature can rise again; characteristic rash develops along with other clinical signs of the disease, but a new attack is usually milder and lasts shorter.

Uncomplicated typhoid fever can be mild, moderate, and severe.

Deviations from the normal course of the disease are possible. The disease can begin acutely with hyperpyrexia, intestinal disorders, and other symptoms; mild, obliterated and abortive forms of the disease are also possible.

An abortive form of typhoid fever runs a typical course with all specific symptoms, but ends by a sudden critical fall of body temperature and rapid recovery. Fever lasts 5-7 days.

Atypical cases are characterized by a short-lasting fever (6-9 days) superimposed upon meagre clinical symptoms. The patient may remain out of bed.

Complications. Severe complications can develop following even a mild form of the disease, and the patient must therefore always remain in his bed during illness, regardless of the subjective condition.

Intestinal haemorrhage and perforation are the most dangerous complications. They usually occur during the 2nd or 3rd week of the disease and are associated with ulceration of the small intestine. A septic shock is another possible complication.

Intestinal haemorrhage can be mild. If bleeding is severe, pallor develops, the body temperature falls, the pulse accelerates, arterial pressure falls abruptly, the face becomes pointed. Collapse develops in severe cases.

Ulcer is usually perforated in 3-4 weeks; it is a danger to the patient's life. Meteorism, increased peristalsis, rough food and heavy exercise can provoke perforation of the intestine. Abrupt abdominal pain is not obligatory, and even mild abdominal discomfort must therefore be considered by the physician. The abdomen is first retracted and later becomes inflated; the anterior abdominal wall is

strained, the pulse is fast, the leucocyte count in the peripheral blood increases. Vomiting and persistent hiccup develop. Only a surgical operation performed within 6 hours following perforation can save the patient.

If septic shock develops, the body temperature abruptly falls, the patient perspires, his arterial pressure drops, tachycardia develops, oliguria transforms into anuria.

Other complications are also possible: pneumonia, parotitis, cholecystitis, myocarditis, pyelocystitis, thrombophlebitis, involvement of the nervous system (meningo-encephalitis, etc.)

Diagnosis. The diagnosis of typhoid fever is based on the clinical picture of the disease, epidemiologic anamnesis, and the laboratory findings. The main method of laboratory diagnosis is bacteriologic study. The blood, urine, faeces and bile (duodenal contents) are examined in the laboratory.

The blood culture method is rapid and accurate for early diagnosis. A sterile syringe is used to take 10-15 ml of blood from the patient's ulnar vein. The blood specimen is placed into a vial containing Rappoport medium or 10-20 per cent bile culture medium (1:10). The flask is kept in a thermostat at 37 °C and then Endo agar and Ploskirev medium are inoculated in 1, 2 and 7 days. Blood cultures are mostly positive during the first days of the disease, before antibiotic therapy is started.

The immunofluorescence method is also used for early diagnosis of typhoid fever. It reveals the typhoid bacillus in 10-12 hours after inoculation, but this does not exclude confirmation of the diagnosis by the classical blood culture method.

Stool and urine cultures are less important because they are positive only beginning with the second week of the disease. Cultures are inoculated from the first day of the disease.

In order to take a specimen of faeces, a disinfected pan is used; 3-5 g specimen is transferred into a test tube containing a 30 per cent glycerol mixture. The test tube is handled to the laboratory where the taken material is used to inoculate Endo or Ploskirev medium and an enriched culture medium.

A urine specimen shtmld be better taken by a sterile catheter. If a catheter is not available, the outer orifice of the urethra should be washed with an isotonic sodium chloride solution, the first portion of the urine discarded, and then a 20-50 ml specimen taken into a sterile flask. In the laboratory, the urine is centrifuged or settled, and the sediment is used to inoculate the medium.

In order to reveal carriers, the duodenal contents should be

examined not earlier than 5-10 days following the fall of temperature. Bile is taken from a fasting patient using a duodenal tube. A, B and C biles are taken in separate sterile test tubes.

Serologic studies are used to confirm the diagnosis. Widal's test is used along with passive (indirect) haemagglutination test with erythrocytic diagnosticum (O, H and Vi antigens). Widal's test is performed with 2-3 ml of blood taken from the ulnar vein of the patient on the 8-9th day of the disease. Indirect haemagglutination reactions with H, O and Vi antigens are more specific than the Widal reaction, and they are used to reveal antibodies from the 4th or 6th day of the disease. The reaction is positive with the titre of 1:200 and over.

In order to differentiate acute carriers from chronic ones, and also vaccinated persons from carriers, indirect haemagglutination tests with cysteine are used. Of the known immunoglobulins of five classes (IgA, IgM, IgG, IgD and IgE), immunoglobulins IgG (cysteine-resistant antibodies), which are not destroyed by cysteine, are of greatest diagnostic importance.

Treatment. Chloramphenicol is used to treat typhoid fever. It is given in doses from 0.5 to 0.75 g four times a day until the body temperature normalizes, and then for another 8-10 days (0.5 g three times a day). Chloramphenicol is given per os, 20-30 minutes before meals. If vomiting develops, chloramphenicol sodium succinate should be given intramuscularly or intravenously, 1.0 g three times a day.

Ampicillin in doses of 1 g four times a day (for 14 days) is also effective.

Bactrim (biseptol), 2-3 tablets two times a day (for 3-4 weeks), or nitrofurane preparations in doses of 0.15-0.2 g four times a day are given to patients with antibiotic-resistant bacilli.

Antibiotics combined with vaccines decrease the incidence of relapses and prevent carrier state. Treatment with Vi antigen is more effective. It is given subcutaneously twice in 1 g doses at 8-10 day interval during any stage of the disease. In order to lessen toxaemia in severe course of the disease, a 5 per cent glucose solution (500-800 ml) is given by intravenous drip or haemodez (400 ml) in combination with cocarboxylase and ascorbic acid. Furosemide is given per os, 0.04 g in the morning, for 1-2 days; vitamins B_u B_6, B_{12} and rutin are also given. Cardiovascular preparations are given in cases of medium severity.

An immediate surgical operation is necessary in intestinal perforation. Patients with intestinal haemorrhage must remain in bed,

and an ice bag should be placed on the abdomen. Blood of the appropriate group should be transfused in haemostatic doses (75-100 ml). Vikasol should be given in a dose of 0.01 g twice a day. A 10 per cent solution of calcium chloride should be given intravenously in a dose of 5-10 ml. In profuse bleeding, 1-2 litres of blood, polyionic and colloid solutions (polyglucin, gelatinol) should be transfused. During the first 10-12 hours the patient is allowed only to drink tea or water. Thin (5 per cent) milk semolina and fruit jellies can be given later until stools normalize.

Patients must remain in bed regardless of severity of the disease. The patient is allowed to assume a sitting position only in 7 or 8 days after normalization of body temperature. The patient is allowed to leave the bed and walk only in 10-11 days (provided there are no contraindications). In 21 day after normalization of body temperature the patient can be discharged from hospital, provided his condition permits. If the patient did not receive antibiotics, he can be discharged from hospital in 14 days after normalization of temperature.

Care of typhoid patients is important. Sanitation of the mouth, ears, nose and skin is of great significance. If the disease runs a severe course, the patient's tongue should be treated with a piece of gauze wetted with a 2 per cent boric acid solution; dry lips can be treated with vaseline oil. In order to prevent congestion in the lungs and bedsores, a critical patient should be helped to turn from one side to another. Cleansing enema is necessary in constipation. If the abdomen is inflated, a tube should be passed into the intestine to release gases. Careful attitude to the patient and his complaints, control of his pulse, etc. help timely reveal possible complications.

Food must be easily assimilable, rich in vitamins and caloric. It is recommended that food should be cooked by steam and contain no solid ingredients (thin porridges, broth, minced meat, omelette, puree, fresh fruits, rubbed through a sieve, and juice. Food that might evoke meteorism should be avoided.

Prevention and control. Sanitation is of prime importance: control of water supply, control of food production and sale, destruction of flies. Towns, villages, and other settlements should be cleaned daily, the condition of sewage must be supervised and wastes decontaminated.

Timely revealing and isolation of patients and typhoid bacilli carriers are very important. Convalescents should obligatory be examined for the carrier state before discharge from the hospital.

For epidemiologic indications, all persons who were in contact

with typhoid patients, and also personnel of food catering and the like institutions should be examined for the absence of the carrier state. Persons who are hired for work in food catering and the like institutions should be examined as well. The examination begins with the cysteine test (indirect haemagglutination reaction) and bacteriologic study of faeces.

Specimens of stool and urine are taken either at special medical posts or straight at the job, or at hospitals.

All chronic carriers should be regularly examined regardless of their occupation. Chronic carrier may not be admitted to work at food catering and the like institutions. Health education of population is obligatory.

Specific prophylaxis is of secondary importance. It can be regular (laundry, cleaning of settlements, etc.) and for epidemiologic indications. Sorbed typhoid-paratyphoid vaccine is used against typhoid fever and paratyphoid. A typhoid vaccine enriched with Vi antigen of S. typhi, typhoid-B-paratyphoid and other vaccines are also used to prevent the disease.

Before vaccination, a person must be examined by the physician for possible contraindications (with obligatory thermometry).

Measures in the focus. If an epidemic focus has been revealed, measures should first of all be taken to eradicate the infection source, i.e., to reveal as early as possible, and isolate the typhoid patient, with a subsequent report to the local health authorities, and epidemiologic examination. The revealed typhoid patients must obligatory be hospitalized. Prior to hospitalization of the patient, current disinfection should be performed, and after hospitalization final disinfection with decontamination of the garments, clothes and linen in disinfection chambers.

Convalescents should be discharged from hospital after clinical recovery and three consecutive negative stool and urine cultures obtained at 5-day intervals, and after one examination of the bile performed 10 days after abatement of the clinical manifestations. In order to reveal carriers, faeces and urine of convalescents should be examined five times at 1-2 days intervals not later than ten days after discharge from hospital.

Convalescents must be regularly observed within two years. If carrier state has been detected in a convalescent, he must be observed for a longer time. Workers of food catering and the like establishments must be employed at jobs where their danger for the surrounding people might be minimal. By the end of one month, their stool and urine must be examined five times. If cultures are

positive these carriers may not be employed at their former jobs for three months after recovery. Then their faeces and urine are tested five times at 1-2 day intervals, and the bile examined once. If the cultures are negative, these persons can be admitted to their former occupation, but their stools and urine must be examined at 3 month intervals during two years. By the end of the second year, an indirect haemagglutination test with cysteine must be performed. If the test is positive, the person must be observed for the rest of his employment with two yearly examinations of faeces and urine.

If typhoid bacilli are revealed in a person three months after recovery, he is considered a chronic carrier and dismissed from occupation where he may contact food.

If carrier state is revealed in a child, he is allowed to visit school but dismissed from any job that may be associated with preparation of food or its handling. If carrier state is revealed in a child of preschool age, the child is not allowed to attend kindergartens and the like children's institutions. Carriers of this age must be taken to a hospital for examination.

Persons who were in contact with typhoid patients must be under daily medical examinations for 25 days with obligatory thermometry, questioning and inspection. In case of fever, the patient must be hospitalized and his blood culture grown in order to verify the diagnosis.

Stools and blood serum must be examined (indirect haemagglutination reaction with cysteine) in all persons who were in contact with the patient. If the results of bacteriologic or serologic tests are positive, stool, urine and bile should be examined once in order to determine the character of the carrier state.

Paratyphoid Fevers A and B

Paratyphoid fevers A and B are acute infectious diseases with clinical manifestations, pathological changes and epidemiologic features similar to those of typhoid fever.

Aetiology. The disease is induced by Schottmuller's bacilli which are similar morphologically to the typhoid bacillus and differ only with respect to their antigen structure. They belong to the *Salmonella* genus.

Epidemiology and pathogenesis of paratyphoid are the same as those of typhoid fever. As distinct from typhoid fever and parathyphoid A, the source of paratyphoid B can sometimes be animals.

Clinical picture. The clinical symptoms of paratyphoid are similar

to those of typhoid fever, and an accurate diagnosis can therefore be only established in the laboratory (blood cultures, serologic tests). There are, however, some features in the course of A and B paratyphoid fever.

Paratyphoid A occurs much less frequently than typhoid fever or paratyphoid B. The incubation period of paratyphoid A is shorter, from 3 to 14 days. The disease usually begins acutely. The onset is characterized by hyperaemia of the face, injection of the scleral vessels, rhinorrhoea, cough, herpetic lesions on the lips. The temperature curve is irregular. Fever lasts to 2 weeks. Toxaemia is less pronounced than in typhoid fever. Rash is polymorphous and develops earlier. Complications and relapses are as frequent as in typhoid fever. Leucocytosis and lymphomonocytosis can occur.

Paratyphoid B runs a milder course than typhoid fever although severe forms are not uncommon either. The onset of the disease is acute, as in gastroenteritis, less frequently as in catarrh of the upper airways with later superimposition of the symptoms characteristic of typhoid fever. The temperature curve is characterized by great circadian variations. Rash is ample; it develops on the 5-7th day of the disease. Neutrophilic leucocytosis occurs. Relapses and complications are less common than in typhoid fever and paratyphoid A.

Complications, treatment, prevention and control are the same as in typhoid fever.

Salmonellosis

Aetiology. The disease is caused by a large group of microorganisms -*Salmonellae*, counting about 2000 serotypes. *Salmonellae* include two antigen complexes; O (somatic) and H (flagellar) antigens. The international classification of *Salmonellae* is based on the antigen structure. About 700 serotypes have been isolated in man. Most common of them are *S. typhimurium, S. Heidelberg, S. london, S. cholerae-suis, S. derbi, S. enteritidis, S. anatum.*

Salmonellae are stable to low temperatures, and survive over winter in field conditions in animal faeces. They withstand absence of moisture and survive in dry dung for 90 days, in home dust for 80 days, in dry animal faeces for 4 years. A 0.5 per cent chloramine solution kills salmonellae in one hour; a 3 per cent solution, in 30 minutes.

Epidemiology. The source of infection is man and animal. The main epidemiologic role belongs to animals in which the disease is clinically manifest or is characterized by the carrier state. From an

infected animal the microorganisms are released with faeces, urine, milk, saliva, and nasal discharge. Infected cattle and pigs are the greatest danger. Horses, sheep, cats, dogs and rodents (mice and rats) can also be the source of infection. Birds, especially waterfowl, in which the salmonellae can be found not only in flesh but in the eggs as well, are also important epidemiologically.

Examination of animals and their meat reveals salmonellae in cattle (from 1 to 5 per cent), in pigs (from 5 to 15 per cent), in sheep (from 4 to 30 per cent), and in ducks and geese (to 50 per cent). Mice and rats are carriers in about 40 per cent of cases, and about 10 per cent of cats and dogs are carriers too.

Human patients and carriers are also the source of infection. People working at kindergartens, food catering and the like establishments are a special danger for the surrounding people.

The transmission factors are foods in which salmonellae not only survive but also multiply. Man is usually infected by ingestion of meat, milk, fish, etc. heavily infested with salmonellae as a result of inadequate handling, cooking, and storage. Meat can be infected during slaughter of the diseased animals, as a result of neglected sanitary rules at slaughterhouses (intestinal contents of the diseased animals can get on meat of slaughtered healthy animals), during transportation, improper cooking and processing, and storage.

Contact infection is possible during intimate association with a patient or a carrier, less frequently with animals. Infants are mostly infected by contact. Nosocomial (intrahospital) outbreaks of salmonellosis are possible in children, who are weakened by coexisting diseases, especially premature infants, neonates, infants under two years of age, asthenic persons, patients with other diseases and the aged.

Since salmonellae are stable in the environment, they can be distributed with water and dust.

People are quite sensitive toward toxins produced by salmonellae, and outbreaks of the disease are therefore possible among people who ingest food infected with salmonellae and their toxins.

The incidence of salmonellosis is higher during the warm (especially hot) season since the conditions for multiplication of salmonellae are most favourable during this seasons, and besides, the incidence of the disease among cattle is also the highest in summer.

Pathogenesis. An infectious process can begin only after living salmonellae (not only their toxins) reach the gastrointestinal tract. Part of the microorganisms are killed in the stomach, while the surviving salmonellae enter the small intestine and multiply in tissues

(localized form). By the end of the incubation period, the macroorganisms are poisoned by endotoxins that are released from the dead salmonellae. The local response to the endotoxins is enteritis and gastrointestinal disorder.

In the generalized form of the disease, salmonellae pass through the lymphatic system of the intestine into the blood of the patients (typhoid form) and are carried to various organs (liver, spleen, kidneys) to form secondary foci (septic form).

Endotoxins first of all acts on the vascular and nervous apparatus. This is manifested by increased permeability and decreased tone of the vessels, upset thermal regulation, vomiting and diarrhoea. In severe forms of the disease, much liquid and electrolytes are lost to upset the water-salt metabolism, to decrease the circulating blood volume and arterial pressure, and to cause hypovolaemic shock. A septic shock can develop. Shock of mixed character (with signs of hypovolaemic and septic shock) are more common in severe salmonellosis.

Oliguria and azotaemia develop in severe cases as a result of renal involvement due to hypoxia and toxaemia.

Clinical picture. The incubation period varies depending on the mechanism of infection and lasts from 6 to 24 hours, when salmonellae are ingested, and for 2 and more days if infection is transmitted by contact. The following forms of salmonellosis are distinguished: (1) gastrointestinal (localized), that runs a course similar to that of acute gastritis, gastroenteritis, or gastroenterocolitis; (2) generalized form, that runs a typhoid and septic course; (3) carrier state (acute, chronic, transient).

The gastrointestinal form. The onset is acute. The body temperature rises; weakness, headache, chill, nausea, vomiting develop; the appetite impairs, and the patient complains of epigastric pain. When the disease is at its height in 1-2 days, diarrhoea begins. Stools are usually ample, with admixtures of mucus, or watery, without pathological admixtures. The duration of the disease and its symptoms depend on severity of the disease.

In mild forms the body temperature is normal or subfebrile, vomiting occurs only once, abdominal pain is not severe, stools are watery, five times a day. The patient recovers in 2-3 days. The liquid loss does not exceed 3 per cent of the body weight. The onset of salmonellosis of moderate severity is acute, the body temperature rises to 38-39 °C and persists for 4 days; vomiting is repeated, stools are ample and fetid, to 10 times a day, cramps in the limbs are common.

The gastroenterocolitic form is characterized by mucous stools, sometimes with streaks of blood. Diarrhoea persists for 7 days. Tachycardia and dehydration of the first and second degree (liquid loss to 6 per cent) are possible.

In severe cases, the symptoms manifest to their maximum extent already during the first hours of the disease. The temperature rises to 39 °C, the patient develops chill, repeated vomiting, that rapidly becomes incoercible, and frequent (10-20 times a day) ample, fetid, watery stools. Diarrhoea lasts 6-7 days and more. If water-salt metabolism is upset (dehydration of the second or third degree), the patient develops cramps, pallor with a cyanotic hue, skin dryness, and hoarse voice that transforms into aphopia. The loss of moisture is from 7 to 10 per cent of body weight. The amount of urine excreted decreases; pathological admixtures appear, such as protein, erythrocytes and casts. Arterial pressure falls, tachycardia develops.

The generalized form. The disease can begin with gastroenteritis or fever without signs of this disease, whose clinical manifestations are similar to those of typhoid and paratyphoid fever. The septic form, which usually occurs in infants, is characterized by acyclic character, prolonged and severe course, remittent fever, chills and profuse sweats, tachycardia, spleno- and hepatomegaly. Secondary septicopyemic foci of various localization (pneumonia, pleurisy, osteomyelitis, arthritis, tonsillitis, cervical purulent lymphadenitis, meningitis) are formed.

Carrier state. Acute and chronic carrier state occur in convalescents. Acute carrier state probably lasts to 3 months, chronic over three months. A transient carrier state is characterized by the absence of clinical symptoms of the disease, the bacillus is isolated only once or twice at 1 day interval with subsequent negative cultures and reactions of indirect haemagglutination with salmonellous diagnosticum.

Complications. Pancreatitis, cholecystitis, cholangitis, chronic colitis, abscesses of the brain, liver or kidneys are among possible complications. Localized forms can be complicated by septic shock, acute heart failure, and renal failure.

Diagnosis. The diagnosis is based on clinical findings, a thoroughly collected epidemiologic anamnesis and laboratory findings. Bacteriologic studies should be performed as early as possible (before commencement of treatment). Blood taken from the ulnar vein in sterile conditions in quantity of 5-10 ml is cultivated in 50-100 ml of bile culture medium or Rappoport medium. Vomitus (50-100 g) and gastric washing water (100-200 ml) are taken in sterile flasks;

excretions (4-5 g) are taken into a sterile test tube containing a glycerol mixture; urine (20-50 ml) is taken in a sterile bottle or a test tube; pus (in septic form of the disease) is taken from secondary foci. Suspected food (in the quantity of 50-60 g from various portions, taken in a sterile bottle) should also be delivered to the laboratory. A preliminary result is ready in 2 days and the final result in 4 days.

Direct and indirect haemagglutination reactions can be performed in a week (1 ml of blood). The result of the indirect haemagglutination reaction is ready in 4-6 days of the disease. The test is positive if the serum dilution is 1:160 and over.

Immunofluorescence test is used for rapid diagnosis.

Treatment. Mild forms of the disease can be treated at home. For detoxication, it is necessary to perform gastric lavage with ample warm water (2-3 litres) or a 2-3 per cent sodium hydrocarbonate solution.

If salmonellosis is of mild or moderate severity, and vomiting or marked toxaemia are absent, the patient is given salt solutions per os. The amount of liquid given must comply with the amount of liquid lost. If toxaemia is marked while dehydration is mild, these solutions must be given by intravenous drip (40-60 drops per minute). If the course of the disease is severe (dehydration of the 3rd or 4th degree) a polyionic solution should be given at a rate of 80-120 ml/min. The volume of the solution that is given to replenish the liquid lost, depends on the degree of dehydration (4-8 litres and over). After haemodynamic stabilization, termination of vomiting, and restoration of the excretory function of the kidneys, the patient can be given liquid per os.

If adrenal insufficiency develops, the patient should be given prednisolone (60-90 mg) or hydrocortizone (125-250 mg) intravenously; later (in 4-6 hours) these preparations can be given by intravenous drip. Desoxycorticosterone acetate should be given intramuscularly (5-10 mg at 12-hour intervals).

In order to restore the gastrointestinal function, the patient can be given festal, panzynorm, cholenzyme, etc., and also preparations restoring the intestinal microflora (bifidumbacterin, colibacterin, lactobacterin, etc.). Antacids, e.g. white clay, bismuth preparations, should also be given.

In typhoid forms of salmonellosis the patient should be given (in addition to detoxicating, rehydrating and desensitizing therapy) chloramphenicol sodium succinate (30-50 mg per kg of body mass a day) or chloramphenicol (0.5 g 4 times a day for 10-12 days), and ampicillin (1 g 4-6 times a day for 8-10 days).

Septic forms should be treated with ampicillin in combination with surgery of purulent foci. It is important to prescribe a proper diet to the patient. Vitamins are also necessary.

The patient is recommended to eat oat and rice porridges (without milk), boiled fish, steam-cooked minced meat, fruit jellies, curds and sweet cheese during the first days of the disease.

Prevention and control. Prevention of salmonellosis includes veterinary and medical measures with respect to the source of infection and ways of infection transmission. Veterinary service acts to improve the condition of animals by timely isolation of the diseased animals and their treatment, decontamination of milk and other animal materials obtained from the diseased animals. It is prohibited to the affected animals slaughter (in case of emergency) together with healthy animals. Healthy cattle should be slaughtered immediately after delivery to the slaughterhouse. Meat obtained from diseased cattle can be utilized only after a prolonged thermal treatment. Veterinary inspection must be effective at all stages of handling of animal materials, beginning with the slaughterhouse, transportation, thermal and other treatment, and storage of cooked food at low temperatures. Roddent control is another requisite condition.

In order to locate the source of infection, all persons with acute intestinal diseases of unknown aetiology should be examined for carrier state. Those who develop intestinal dysfunction during their stay in hospital, all infants under two years of age that are admitted to somatic hospitals, should also be tested for carrier state. All persons who are hired for work in food catering and similar establishments, and also children who are prepared for admission to children's institutions should be tested for carrier state as well.

Salmonellosis patients may be isolated at home conditions or taken to hospital. Persons working at food catering and the like establishments, children visiting kindergartens, and infants under two years, who may or may not attend preschool children's institutions, should be hospitalized.

Convalescent persons who work in food catering and the like establishments should be discharged from hospital after a complete clinical recovery and three successive negative stool cultures. (The first test should be performed in 3 days after completion of the specific therapy, the other two tests follow at 1-day intervals). If cultures are positive, the person may not be admitted to perform his routine duties for 15 days after discharge from hospital. Meanwhile they are employed at jobs that do not present epidemiologic danger. Their faeces are tested three times. If a new examination reveals

carrier state again, the tests should be repeated at 15-day intervals. If carrier state persists for more than 3 months, the person is considered a chronic carrier and must change his occupation for a year. Three stool cultures and one bile culture (1-2 days later) should be cultivated a year later. If the cultures are positive again, the person should be dismissed from food catering and similar establishments.

Children-carriers of antibiotic-resistant salmonellae should not be admitted to kindergartens. Schoolchildren can be allowed to attend school, but they are not allowed to help their mates in canteens.

Measures in the focus. Current disinfection should be performed at home before the patient is hospitalized or if the patient remains at home till recovery. After hospitalization or recovery of the patient, his apartment should undergo final disinfection. Persons who took care of the patient must be observed for 7 days. Persons who had contacts with the patient, or persons who work at food catering and similar establishments, and also children attending kindergartens and schools should be tested (once) for carrier state.

Measures **taken in a collective body** (office, school, etc.). If a group of persons are all taken ill, they are given medical aid and epidemiologic studies are undertaken to reveal the particular food that caused the disease outbreak. Circumstances under which this was contaminated should be established. Preventive measures against salmonellosis should be performed by epidemiologists and sanitary physicians.

Pseudotuberculosis

Aetiology. The disease is caused by *Yersinia,* the bacteria of the family *Enterobacteriaceae,* that causes plague and yersinosis. Six serotypes are distinguished, among which type I, and less frequently types **III** and IV, cause disease in human beings. The bacteria are stable in the environment: on vegetables they survive for 2 months, in milk for 18 days, and in water for more than a year. *Yersinia pseudotuberculosis* can multiply at temperatures maintained in a refrigerator (0 to 8 °C); they can withstand multiple frost-defrost cycles. The bacteria are sensitive to the absence of moisture, ultraviolet radiation, and disinfectants.

Epidemiology. The source and reservoir of infection are rodents (mice and rats). Cats, cattle, sheep, goats, some wild animals and birds can also be afflicted by the disease. Rodent-infected vegetable stores can be especially dangerous, since the bacteria can multiply on vegetables at temperatures from 4 to 10 °C.

The role of humans as a source of infection has not been proved. Yersinia can be ingested with foods that are taken without cooking (vegetables, milk, dairy products), less frequently with water. Pseudotuberculosis is characterized by group infection which usually outbreaks in the army, boarding schools and similar isolated collective bodies. Sporadic incidence occurs also. Morbidity is the highest in spring, which is associated with activation of rodents and increased incidence of epizootics among them, accumulation of the bacteria in the vegetable stores.

Pathogenesis. After ingestion, yersinia get into the lymphatic apparatus of the intestine, where they multiply and enter the blood that carries them throughout the body. Bacteraemia develops with subsequent toxaemia, allergy, possible involvement of all organs and systems, especially those containing reticulo-endothelial cells. The living macroorganism is slowly freed from the bacteria, and exacerbations and relapses of the disease are therefore possible.

Clinical picture. The incubation period lasts from 3 to 18 days, usually from 8 to 10 days. Pseudotuberculosis usually begins acutely. The body temperature rises to 38-40 °C, with repeated chills. Nausea, vomiting, abdominal pain and sometimes diarrhoea develop. The face and neck are hyperaemic, hyperaemia of the hands and . feet is limited; the sclera is injected and the conjunctiva hyperaemic. The fauces are scarlet and oedematous. After the tongue is freed from the coat, it is crimson, granular and looks like a strawberry tongue in scarlet fever.

Punctate roseola-like ample rash appears in 60-70 per cent of patients in 2-4 days of the disease. The character of the rash and its location (mostly on the flexor surfaces of the arms, the flanks, and the inguinal folds) are similar to those in scarlet fever. On the 5th or 7th days papules, maculae, and mixed papulomacular lesions develop. This is followed by scaling (beginning with the 2nd or 3rd week of the disease). Seizures of abdominal pain occur in the right hypochondrium. Palpation reveals tenderness in this region. The liver is enlarged, some patients develop jaundice. The height of the disease is marked by pain in the large joints and their swelling. Catarrh and lesion of various organs are possible.

The leucocyte count increases (with the shift to the left in the leucocytic formula); monocytosis, and lymphopenia develop; ESR accelerates. Depending on the involvement of organs and tissues, the following clinical forms of the disease are distinguished: abdominal, icteric, catarrhal, mixed, generalized, abortive, and subclinical. The disease can be mild, moderate, and severe.

Pseudotuberculosis is characterized by exacerbations and relapses, which occur with less pronounced toxaemia and more frequent involvement of the internal organs, especially of the terminal portion of the small intestine, the proximal portion of the large intestine, and mesenteric lymph nodes. The disease lasts from 10 days to several months, usually for a month.

Diagnosis. The diagnosis of pseudotuberculosis is established by the clinical, epidemiologic findings, and the results of bacteriologic studies. Blood, faeces and faucial washings are examined in the laboratory. Faucial washings are taken during the first days of the disease; stool cultures are grown several times. Smears are prepared from the patient's material; they are stained and studied by microscopy and immunofluorescence. Cultures are grown on common or special nutrient media (Peterson and Cooke methods). The method is based on the ability of microbes to multiply in cold in a phosphate buffer. Agglutination and indirect agglutination tests are performed beginning with the end of the first week. The tests are repeated in 5-6 days. Agglutination tests are positive with titres of 1:200, and indirect haemagglutination reaction, 1:100.

Treatment. The patient is given chloramphenicol, 0.5-0.75 g 4 times a day for 5-7 days, or, in severe cases, for 10-14 days. The tetracyclines are given in doses of 0.3-0.4 g 4 times a day, nitrofuranes in 0.1 g doses 4 times a day, for 7 days, if necessary, detoxication therapy is given: haemodez, rheopolyglvtcin, polyglucin. They are given intravenously.

In order to prevent exacerbations or relapses of the disease, stimulating immunotherapy is indicated: nv$_e$thyl uracil 1-2 g 4 times a day, pentoxyl 0.2-0.4 g 3-4 times a day for 15-20 days. Vitamins, oxygen therapy, antihistaminics (suprastin, pipolphen, dimedrol, etc.) and cardiacs are also given.

Prevention and control. Deratization J$_s$ necessary. It includes destruction of rodents that transmit infection. Vegetable stores and other storehouses should be protected from penetration of rodents. The stores must be disinfected before loading them with vegetables. During the storage period, vegetables must be tested bacteriologically for the presence of yersinia every month. The condition of storage and treatment of foods, especially of those that are not cooked before serving, must be controlled.

If infection spreads among people who attend the same canteen or other food catering establishment, the rooms and equipment of this establishment must be disinfected. Serving uncooked food is prohibited.

The patients must be hospitalized, and discharged only after clinical recovery and two successive negative stool cultures.

Measures in **the focus.** The focus must be disinfected. Persons who were in contact with the diseased and who ate food suspected for infection with pseudotuberculosis microbes should be observed for 21 day.

Remainders of suspected food should be sent to the laboratory for examination.

Yersiniosis

Aetiology. The disease is caused by *Enter-obacteriaceae,* the genus *Yersinia,* which causes also plague, intestinal yersiniosis, pseudotuberculosis, etc. Bacteria causing intestinal yersiniosis do not differ morphologically from intestinal bacteria and are similar to those causing pseudotuberculosis.

The bacteria causing intestinal yersiniosis occur widely in nature. They remain viable for long time at low temperatures and can multiply at temperatures from 0 to 9 °C, the optimum multiplication being at 25 °C. Boiling kills them instantaneously. The bacteria are sensitive to chloramphenicol and the tetracyclines.

Yersiniae are divided into 5 bio types and 10 phagotypes; by the O antigen they are classed into 30 serotypes. Serotypes 03 and 09 are more common in Europe, and 08, in America.

Epidemiology. The source of infection are usually pigs; humans can also be infected by dogs, cats, cattle, rodents, and also by human beings (patients or carriers). The causative agent enters man with ingested food and is discharged with stools.

The main route of infection is with food (pork, milk, vegetables contaminated with the microbes). Transmission of infection is also possible by contact with domestic animals and human beings. Familial foci of yersiniosis have been reported. Outbreaks of the disease are possible at collective bodies served by one canteen, restaurant, etc.

Yersiniosis is now common in all countries. The incidence is the highest in the Northern Europe. The maximum morbidity is observed during the cold season.

Pathogenesis. Depending on severity of infection, yersiniae cause catarrh of the mucosa or haemorrhage, deep ulceration and necrotization in the distal portions of the small intestine and the ileum. The bacteria are carried by lymph to the mesenteric nodes to cause their inflammation and suppuration. The vermiform process is often

afflicted. From the lyrnph nodes, the bacteria can pass into the blood and cause bacteraemia with lesion of the organs and systems, especially the liver and the spleen. Destroyed bacteria provoke toxic and allergic reactions with subsequent development of hepatitis, cholecystitis, arthritis, otitis, myositis, nephritis, etc.

Clinical picture. The incubation period lasts 1-2 days (variations are possible from 4 to 15 days). The onset of the disease is acute, with chilis and fever to 38-39 °C; in severe cases the body temperature rises to 39-40 °C. The patient complains of headache, weakness, myalgia and arthralgia. In 2-3 days the patient develops nausea, vomiting, severe attacks of abdominal pain, frequent and ample stools, sometimes with streaks of blood (from 3 to 15 stools a day), symptoms of hepatitis, and rash. Severe yersiniosis is characterized by toxaemia and dehydration of the body, changes in the cardiovascular and nervous system. Mild yersiniosis terminates in few days; a severe course lasts 2 weeks and more.

Blood changes: neutrophilic leucocytosis, accelerated ESR (to 20 mm/h).

The pathology usually resembles gastroenteritis, enteritis, gastroenterocolitis; appendicular, arthritic, septic and abortive forms are less common.

The appendicular form can begin as gastrocnterocolitis, but palpation of the abdomen reveals pain mainly in the right hypochondrium. Abdominal muscles can be strained, and the symptoms of peritoneal irritation are possible.

The haematologic picture is characterized by neutrophilic leucocytosis (to 20 x 10^9 1 and over), and very high ESR (to 30 mm/h and over).

The septic form is more common in infants, in patients with chronic concurrent diseases, and in the elderly. In addition to the gastroenterocolitic symptoms, the disease is also characterized by elevated body temperature with circadian variations of 2-3 °C, repeated chills alternated by profuse sweats, enlargement of the liver and spleen; jaundice and anaemia develop.

Abortive forms of yersiniosis occur only occasionally, during examination of population for other diseases.

Complications. Patients with severe yersiniosis can develop infectious-allergic complications -myocarditis, polyarthritis, iritis; surgical complications, such as appendicitis or acute cholecystitis can also occur.

Diagnosis. The diagnosis is difficult because of similarity of yersiniosis to many intestinal infections. Only laboratory studies can

verify the diagnosis. Blood (in septic forms), faeces and vomitus are studied in the laboratory. Agglutination and indirect haemagglutination reactions are used. Four-fold and greater increase in the titres of antibodies are diagnostically important.

Treatment. Severe and moderate forms are treated with chloramphenicol and the tetracyclines (normal doses) during 5-7 days (see "Pseudotuberculosis").

Prevention **and** control. Measures to control yersiniosis include eradication of the source of infection and destruction of *the* transmission mechanisms. Measures to control yersiniosis are the same as against salmonellosis.

Intestinal Infections due to Conventionally Pathogenic Microbes

Aetiology. The group of pathogenic agents includes *Proteus, Clostridium perfringens, B. cereus,* etc., which cause proteosis, clostridiosis and cereosis, respectively. The mentioned bacteria are common in nature. *Clostridium perfringens* and some *B. cereus* form spores under adverse environmental conditions.

Epidemiology. The pathogenic microbes are contained in great amounts in soil, open water bodies, on vegetables, which are contaminated by human and animal faeces; the microbes are also contained in air and dust.

The main route of infection is ingestion with food. Infected food (meat, fish, canned food exposed to air, milk and dairy products, etc.) is the substrate on which the microbes propagate and accumulate. The optimum temperature for their multiplication is from 20 to 37 °C. Outbreaks of the diseases are therefore more common in the warm season.

Spread of infection is facilitated by employment of patients at food catering establishments (proteosis, clostridiosis), negligence of the rules for storage of cooked food and subproducts. The infected food does not as a rule change its organoleptic properties.

Pathogenesis. The diseases develop after ingress of a large number of the microbes into the macroorganism. Endotoxins released after the death of the microbes cause inflammatory changes in the intestine. They enter the blood and produce a toxic effect on the entire body; the cardiovascular system is especially vulnerable to endotoxins. The presence of the microbes in the blood causes bacteraemia. The microbes are released into the environment with faeces and other excrements (in cereosis in rare cases and in small amount).

Clinical picture. The incubation period lasts from 3 to 24 hours, more frequently 5-6 hours. Duration of the incubation period and the severity of the disease depend on the condition of the infected person, the amount of ingested microorganisms and their toxicity.

The onset of the disease is acute. The patient develops weakness, lassitude, vertigo, and headache. Elevated temperature and chills are characteristic of moderate and severe forms of the disease. Soon the patient develops nausea, repeated vomiting and diarrhoea (2-10 stools a day; 20 and more stools in severe cases). Pain localizes in the epigastrium and the periumbilical area.

Severe disease is manifested by incoercible vomiting, frequent stools dehydration, cardiovascular dysfunction. Severe proteosis can be manifested by stabbing abdominal pain, vomiting, strong diarrhoea, dehydration, cramps, and confusion. Severe forms of clostridiosis can be attended by signs of general toxaemia and anaerobic sepsis (cholera-like gastroenteritis and necrotic enteritis). Cereosis is usually mild and lasts several hours. Moderately severe disease lasts 1-2 days, and severe, 4-5 days. Duration of moderate proteosis is 2-4 days, and of severe, 5-7 days.

Diagnosis. The diagnosis is based on clinical and epidemiologic (group incidence) findings. Bacteriologic and serologic studies in the laboratory are also necessary. Vomitus and gastric washings (200-300 ml), faeces (20-30 g), blood (10 ml), and food remnants (200-400 g) are examined in the laboratory.

Agglutination tests are performed with blood serum beginning with the second week of the disease. Autocultures isolated from the patient are cultivated at least 4 times. Microbes isolated from suspected food are also cultivated. Revealing the pathogenic microbes in the patient's blood is an indisputable diagnostic proof.

Treatment. Repeated lavage of the stomach is required. Patients with the septic course of the disease should be treated with antibiotics (kanamycin 0.5-0.75 g 4-6 times a day, neomycin 0.125-0.25 g two times a day, tetracycline 0.2-0.3 g 4-6 times a day, etc.), nitrofurans (furadonin and furazolidone 0.1-0.15 g 3-4 times a day, furacin 0.1 g 4-5 times a day for 4-5 days). Cardiacs, rehydration and detoxication preparations should be given whenever necessary.

For pathogenetic and symptomatic treatment see "Salmonellosis".

Prevention and control. Strict observation of sanitary and hygiene requirements at food catering and manufacturing enterprises, correct observation of the conditions for food processing are necessary. Food should be stored at a temperature of 2-4 °C. Patients with

intestinal disorders should not be admitted to work at food catering and manufacturing enterprises. Veterinary supervision of cattle is necessary.

Staphylococcal Toxaemia

Aetiology. Staphylococcal toxaemia is due to some staphylococcal strains, that invade humans with ingested food, and the toxins produced by these microorganisms. Staphylococcal toxins are stable to heat (boiling of contaminated food for an hour does not destroy the toxin).

Epidemiology. The source of infection are usually patients with suppurative foci (acute tonsillitis, conjunctivitis, abscess, phlegmon, furuncles, carious teeth, and the like) and carriers. Diseased animals (cows, goat and sheep with mastitis) are another source of infection.

People usually get infected by ingesting milk, diary products, cream, fish or meat invaded with the bacteria that have multiplied on them due to improper storage.

Pathogenesis. The disease is due to ingestion of food containing enterotoxin that produces a pathologic effect on the gastrointestinal tract.

Clinical picture. The incubation period lasts from 2 to 5 hours. The onset is characterized by nausea, followed by vomiting and epigastric pain. Diarrhoea afflicts about 50 per cent of patients (10-20 stools a day). The body temperature is either normal or 39-40 °C for 10-15 hours with subsequent reduction to normal. Headache, vertigo, cold limbs, cold sweat, and pallor appear. A severe course of the disease is characterized by cyanotic lips, cheeks and the wings of the nose, and fast (flaccid) pulse; cramps and collapse can develop.

The disease lasts 1-2 days, less frequently more than three days.

Diagnosis. The diagnosis is based on the clinical findings and results of epidemiologic examinations. Biologic tests can be performed on animals (kittens and adult cats).

Treatment. Enterotoxin should be eradicated from the patient by gastric lavage with large amounts of a 2 per cent sodium hydrocarbonate solution or a 0.1 per cent potassium permanganate solution; water can also be used. In moderate and severe forms of the disease, detoxication can be attained by rehydration and replenishment of the lost electrolytes by intravenous infusion of plasma substitutes (2-3 and more litres). Vitamins and cardiacs are also indicated.

Prevention and control. Persons with pyodermitis or acute ton-

sillitis cannot be admitted to work at food catering and manufacturing establishments. Food may not be sold after the expiration date. Storage temperature should not exceed 2-4 °C. Strict veterinary supervision of animals during the lactation period is necessary. Diseased animals should be isolated. Their milk should be boiled and utilized for nutrition of other animals.

Botulism

Aetiology. Botulism (from Latin *botulus* sausage) is caused by spore-forming Clostridia *(Clostridium botulinum).* Seven serologic types of these motile anaerobes are distinguished by the structure of the antigen and exotoxin: A, B, C, D, E, F, and G types. Types A, B and E are commonly found in soil; these are responsible for the onset of botulism in humans.

Clostridial spores withstand boiling for 5-6 hours; if treated in an autoclave, the Clostridia are killed in 10-20 minutes. As the vegetative forms of the microbes propagate in anaerobic conditions in food, they produce exotoxin, it is destroyed completely by boiling for 5-15 minutes.

Epidemiology. Botulism microbes are widely distributed as they are stable in the environment because they can form spores that are distributed with air-borne dust and water, and also by humans and animals. The intestinal contents of healthy people and animals are not suitable for multiplication of the microbes and formation of toxins. The spores are therefore released from the macroorganism with faeces and contaminated soil. From soil, the spores get on vegetables, mushrooms or other plant materials that are used for canning. Accumulation of the causative agents and their toxins in food occurs in anaerobic conditions at a temperature not below 4-10 °C (depending on the type of the microbe). The optimum temperature for production of toxins is 28-37 °C. The disease develops after ingestion of food contaminated with the toxin and live microbes, which multiply and intensify toxaemia. A form of the disease known as wound botulism is also known. The disease is caused by infection of a wound.

The disease is usually associated with ingestion of pickled or salted mushrooms, or home-canned vegetables, home-smoked meat, and other foods infected with botulism spores. Industrially canned food is safe because it is treated in autoclaves in which the spores are quickly killed. Botulism microorganisms and their toxins propagate in separate foci rather than in the whole bulk of smoked meat, fish or

sausage. This explains the fact that only few people may be infected, v/hile others, who took the same food, may remain healthy.

Botulism occurs sporadically; group morbidity is less frequent.

Pathogenesis. *Clostridium botulinum* and its toxin are ingested with food. In the gastrointestinal tract, the toxin is rapidly absorbed and is carried by blood throughout the whole body to affect, in the first instance, the nervous system. Motoneurons of the medulla oblongata and the bone marrow are more sensitive to the toxin. This explains development of bulbar paralysis. The toxin inhibits the release of acetylcholine in the nerve synapses thus interfering with normal transmission of the impulses from the nerve to the muscle. Specific paralysis of the chest musculature, dysphagia, and vision disorders develop as a result. The toxin constricts the blood vessels, increases their permeability, and causes their paresis and ruptures. Humans are more sensitive to toxins of serotypes A, B and E. Simultaneous effects of several serotypes are additive by their character.

Clinical picture. The incubation period lasts from 6 to 30 hours; it can vary from 2 hours to 12 days, depending on the amount of the toxins and the microorganisms ingested. The shorter the incubation period, the severer is the course of the disease.

Severe, moderate and mild (atypical) forms of botulism are distinguished.

The onset of the disease is acute: nausea, vomiting, abdominal pain, muscular debility, lassitude, headache, and vertigo. Diarrhoea is rare. More characteristic are constipation and flatulence due to atonia and paresis of the gastrointestinal tract. Simultaneously with dyspepsia, or 3-4 hours later, the specific symptoms of botulism develop. The body temperature is usually normal but it can rise to 37.7-38 °C.

The muscles of the eye are affected and the patient complains of dimmed vision, indistinct contours (especially in the near sight) and diplopia. Examination reveals ptosis of the upper eyelid, strabismus, anisocoria, and stable mydriasis (morbid dilatation of the pupils). Speech and swallowing are difficult due to lesion of the 9th and 12th pairs of the cranial nerves. The voice first becomes hoarse, then it weakens and becomes whispered. Speech becomes inarticulate and nasal (rhinolalia); aphonia is possible.

Secretion of the saliva and mucus can be upset. The mucosa of the mouth, nose and throat becomes dry. Thirst develops. The muscles of the throat may be paralyzed to cause difficult swallowing. The soft palate can also be paralyzed and liquid food then returns through the nose; the tongue movement is upset.

The motor function of the stomach is terminated. Pylorospasm is followed by a complete relaxation of the pylorus; gastric secretion decreases.

Respiratory distress develops in severe cases. The patient experiences compression of the chest; dyspnoea develops (tachypnoea of 40-50 per minute); inspiration is difficult, asphyxia and complete cessation of respiration occur. Respiratory disorders develop due to lesion of the intervertebral muscles and the diaphragmatic muscles. The pulse is first slow but later it accelerates and becomes small; "cyanosis and pallor develop. Combination of tachycardia with low body temperature are characteristic. Consciousness is normal. The blood is characterized by neutrophilosis with a shift to the left.

If the disease is mild, only several symptoms of botulism can be observed and the patient recovers in 2-3 weeks. The severe course of the disease is characterized by the presence of all symptoms and the patient recovers only in 2-3 months.

Death from botulism is due to respiratory paralysis.

Diagnosis. The diagnosis is based on clinical and anamnestic (epidemiologic) findings (ingestion of canned food, sausage, home-smoked ham), and also on the laboratory examinations.

Blood from the ulnar vein (6-8 ml, prior to administration of therapeutic vaccine) taken into a test tube containing 1 ml of a 4 per cent sodium citrate solution is sent to laboratory. Vomitus (100 g), gastric washings (50-100 ml), faeces (50-60 g), liver specimens (50-60 g, taken from the dead), pieces of the small intestine and the stomach with its contents, and cadaveric blood (8-10 ml) are examined in the laboratory. Besides, specimens of suspected food are taken from different places (100 g). Bottles and test-tubes with the collected material are stoppered with rubber or cork plugs and labelled. Preservatives may not be added to the specimens. Since the toxins produced by the bacteria are partly destroyed at room temperature, the specimens should be kept at low temperatures (not below zero). The specimens should be examined as soon as possible.

Detecting the causative agent is a difficult and time-taking operation. The diagnosis is often confirmed by the neutralization reaction on albino mice. One pair of mice is inoculated intraperitoneally with 0.5-0.8 ml of the patient's blood, filtrate of the vomitus, gastric washings, extract of the suspected food or of the biopsied specimens. Another (control) pair of mice is given a mixture of the material with antibotulism vaccine (A, B, C, E, F), 0.05 ml of each type. If the experimental pair of mice dies, while the controls survive, a reaction

of neutralization is performed with separate monovalent vaccines.

Besides, cultures of each material are grown on casein-mushroom, casein-acid and other culture media.

Treatment The stomach of the patient should be lavaged as soon as possible with a 5 per cent sodium bicarbonate solution; the patient should also be clysterized (siphon). The specific treatment includes early administration of antitoxic vaccine after determination of sensitivity to equine protein (skin test). If the causative microbe has not been identified, a polyvalent vaccine containing A, B, C and E antitoxins is used. The vaccine is given intramuscularly or intravenously (10000 U of types A, C and E and 5000 U of type B). Patients with moderately severe botulism are given a single dose of the vaccine once a day for 3-4 days. In severe cases, or if the treatment begins late after the onset of the disease, the vaccine is administered at 6-8 hour intervals for 2-3 days, and then 2 times a day. The course of serotherapy should not exceed 4-6 days. After identification of the causative microorganism, monovalent vaccine should be used. Chloramphenicol (0.5 g 4 times a day), and the tetracyclines (0.3 g 4 times a day) should be additionally given for 7-8 days.

Antitoxin types A, B, C and E are used to produce active immunity. The preparations are given as follows: 0.5 ml of each type for the first injection, 1 ml of each type for the 2nd and 3rd injections. (The second and third injections should be separated by a 5-7 day interval.) Monovalent antitoxin should be used after identification of a particular type of the causative agent.

In order to lessen toxaemia in moderate and severe forms of the disease, neocompensan or haemodez should be given intravenously; 2000 or 3000 ml of a 5 per cent glucose solution with an equal amount of sodium chloride solution should be infused. Vitamins B and ascorbic acid, cocarboxylase, ATP, cardiacs (cordiamine, camphor, cardiac glycosides) and hormone preparations are indicated. Patients with severe respiratory distress should be taken to an intensive care unit and artificial respiration given.

Prevention and control, Since Clostridia widely occur in the environment and their spores are highly resistant to environmental effects, measures should be taken against their multiplication and against contamination of food. These measures include:

strict observation of sanitary and hygiene requirements in food canning industry and plants processing vegetables and fish. Only fresh and high-quality foods can be canned;

observation of sanitary and hygienic requirements at slaughterhouses and meat processing plants, prevention of contamination of animal carcasses with intestinal contents during processing. Meat and fish should be processed at shortest possible time in order to prevent passage of the pathogenic microorganisms from the intestine to the flesh;

foods that do not require thermal treatment (sausage, ham, fat, salted and smoked fish) should be stored at temperatures not above 4°C.

Population must obligatory be educated how to can food (vegetables, mushrooms and fruits) in home conditions. Vegetables, fruits, mushrooms and other foods should be freed from soil before canning, polyethylene caps must be substituted for metal, canned food should be stored at low temperatures and treated thermally for 30 minutes before serving.

Laboratory workers, who contact infected materials, should be vaccinated with purified sorbed polyvalent antitoxins. The preparation should be given in a dose of 0.5 ml twice, subcutaneously at 25-30 day interval. Revaccination is necessary in 6-9 months. Subsequent revaccinations should be performed at 5-year intervals.

Measures in the focus. The diagnosis must be established at shortest possible time; higher authorities must be informed and the case officially recorded; epidemiological examination should be carried out, the patient hospitalized, and the infected food identified and destroyed (mixed with dry chlorinated lime or burned).

All persons who took the suspected food should be given gastric lavage with a warm 2 per cent sodium bicarbonate solution; they should be given laxatives and 1000-2000 U of antitoxins types A, B, C and E for prophylactic purposes.

Dysentery

Aetiology. The disease is due to *Enterobacteriaceae,* the genus *Shigella,* that includes more than 100 types.

According to the international classification, 4 groups of shigellae are distinguished: A, B, C and D. Group A includes 10 serotypes of *Shigella dysenteriae* among which are *S. shigae, S. schmitzii;* group B includes *S. flexneri* (6 serotypes); group C includes *S. boydii* (15 serotypes); group D includes *S. sonnet*

Shigellae are released from the patient or carrier with the excrements. The microorganisms can survive in soil for 3 months, on soiled utensils, dishes, moist linen for weeks or even months, for

several days on food (bread, meat); in milk they persist for 30 days and longer; in running water they can survive from several hours to 5-9 days.

Epidemiology. The source of infection are humans, either patients with acute or chronic dysentery, or carriers. The patient is contagious from the very first day of the disease till complete recovery. Patients with mild forms of the disease are especially dangerous because they often remain out of hospital. Clinical recovery of patients does not always coincide in time with bacteriologic convalescence. If a convalescent carrier continues excreting shigellae for more than 3 months, he (or she) is considered a chronic carrier (for 2 years). Chronic dysentery patients are the habitat for the pathogenic microorganisms and they excrete them (either constantly or periodically) into the environment.

Like other intestinal infections, dysentery is transmitted by the faecal-oral route. The main transmitting factors are food, water, soiled hands, linen, toys, dishes and the like articles. Depending on the transmitting factor, the conditions for infection spread are different. The number of infected people is the decisive factor. Food that is not cooked before eating (milk and dairy products, salads, stewed fruits, berries, etc.), in which the bacteria multiply and accumulate, is an important factor in dysentery due to *S. sonnei.* Ingestion of infected food is often responsible for group morbidity.

Outbreaks of food-borne dysentery can be due to negligence of sanitary and technical requirements in food and milk industries, at food catering and similar establishments. If the shigellae multiply and accumulate in food, food-borne epidemic toxicoinfections occur. This is especially characteristic of dysentery due to *S. sonnei.* Food-borne outbreaks can occur during the whole year but their incidence is more common in the warm season.

Water-borne dysentery is explained by the fact that water is easily contaminated with the microorganisms that persist in it for long periods of time. Water in open bodies is polluted by surface effluents (run-off), untreated sewage, faecal sewage included (ship sewage), by leakage of faecal sewage into the open water bodies from lavatories and other sites of refuse accumulation. Tap water can be contaminated during breakdown in the sewage system, through maintenance wells, etc.

The character of morbidity with water-borne infection can be different. For example, if tap water is polluted with sewage (breakdown), the morbidity curve rises suddenly due to instantaneous

development of the disease in a considerable number of people simultaneously.

If water is used for domestic purposes, such as for bathing, epidemic can be local and the disease is characterized by protracted and sluggish course.

Transmission of the disease through contact with domestic articles contaminated with shigellae is common for children (soiled hands are the decisive transmitting factor). Besides, the infection can be transmitted through contaminated toys, linen, door handles, switches and other objects of common use. Flies can also contaminate food and water.

Dysentery is characterized by intensive spread in the presence of the source of infection, the mechanism of transmission and susceptible population. The spread of infection is promoted by suboptimal socio-economic conditions, inadequate sanitation in food industry and food catering establishments, and inadequate sanitary health education of population.

Children's morbidity remains high compared with the incidence of the disease in adults. Infants under 3 years of age are the most susceptible group of children (under 14). Acquired immunity and different resistance of population are also important.

The incidence of the disease is the highest during the warm season (summer and autumn). Flexner dysentery occurs mostly in summer and Sonne dysentery in the autumn months.

Pathogenesis. Dysenteria bacilli penetrate the mucous and submucous layer of the large intestine and the regional lymph nodes where they multiply and partly die to release endotoxin that passes into blood. As the endotoxin re-enters the tissues with blood, it attacks the sensitized colonic mucosa to render its vessels brittle and permeable, Grigoriev-Shiga microbes also produce exotoxin. Lesion of the mucosa (necrosis, oedema, haemorrhage, erosion, ulcers) is also connected with trophic disorders which develop due to the action of the toxin on the peripheral nervous system.

Some symptoms of the colitic syndrome in dysentery are associated with disordered innervation of the large intestine. This causes its dysfunction.

In addition to the toxins, the invasive properties of shigellae are also very important for the development of pathology in the intestine. Intracellular parasitizing causes degenerative changes, desquamation, and destruction of the epithelial cells.

Toxaemia affects the cardiovascular and nervous system, causes disorders in the alimentary tract and, in the first instance, upsets the

secretory, motor and absorption functions; water, mineral, protein, carbohydrate, fat and vitamin metabolisms are also upset.

In most cases, the causative microorganisms are eradicated from the patient due to the defensive response of the body and medication; the patient recovers.

If the immune response is decreased and some other diseases concur (especially chronic gastrointestinal pathology or helminthiasis), or else if treatment does not begin in due time, while the living conditions of the patient are suboptimal, the acute disease can transform into its chronic form.

Clinical picture. The incubation period lasts 2-3 days (with extremes 1-7 days).

The onset of the disease is usually acute. Less frequently the disease is preceded by a prodromal period which is manifested by lassitude, malaise, poor appetite, inflation of the abdomen, rumbling, chills, etc. Weakness progresses, appetite is completely lost, Headache, nausea, vomiting, spinal and articular discomfort develop, the temperature rises from subfebrile to 40 °C and remains high for several days. Abdominal pain soon develops. First it is dull, permanent and diffuse over the entire abdomen, then cramps occur (usually on the left side).

Stools are liquid and frequent, first formed, several days later pathological admixtures (mucus and streaks of blood) appear in the faeces. Faecal mass abruptly decreases or faeces are absent altogether.

Spastic contractions of the muscles in the lower portions of the large intestine can cause tenesmus. Only a small amount of mucus with streaks of blood is excreted after a strong effort; the act of defaecation becomes long and the feeling of incomplete defaecation develops.

Toxaemia can cause secondary attacks of vomiting, cramps, especially in infants.

Examination reveals bradycardia, low arterial pressure, dry coated tongue. Palpation reveals spasm and tenderness of the large intestine, especially in the left iliac region.

The following forms of dysentery are distinguished by the clinical manifestations: (1) acute dysentery with the following clinical variants: colitic (mild, moderate, severe), gastroenterocolitic (mild, moderate, severe), gastroenteric (mild, moderate, severe); (2) chronic dysentery with clinical variants: recurrent and permanent; shigella carrier state.

Acute dysentery. The clinical *colitic* variant can be mild, moderate

or severe. Mild course of the disease has become more common during recent years: signs of toxaemia are weak, the body temperature is either normal or only subfebrile, pain is noted by the course of the sigmoid colon, stools are liquid, sometimes with admixtures of mucus, 3-5 (less frequently 10) stools a day. All these symptoms subside in 3-5 days without treatment.

Moderate form of the disease is attended by marked toxaemia and chill: the body temperature rises over 39 °C (for 2-3 days). The patient complains of headache, nausea, vomiting, prolonged attacks of abdominal pain; stools contain mucus and blood (from 10-15 to 20 stools a day); tenesmus develop. The acute period lasts 5-7 days. If treatment is timely, the patient recovers by the end of the second weak.

The severe form of the disease is characterized by high body temperature (39 °C and above), delirium, nausea, vomiting, anxiety, cramps. Stools are frequent: 20-40 a day, and even more. Abdominal pain is attended by painful tenesmus with extension of the urge onto the urinary bladder. The faeces contain much mucus and blood in the form of spots or streaks.

If treatment is not energetic, toxaemia increases, pulse becomes frequent, and arterial pressure drops. Some patients develop septic shock. The severe condition can persist for 7-10 days.

The *gastroenterocolitic* variant of acute dysentery is characterized by a short incubation period (6-8 hours), a vigorous onset with prevalence of gastroenteric symptoms and toxaemia. The symptoms of enterocolitis develop later. Depending on the severity of the disease, repeated vomiting and profuse diarrhoea with copious watery stools can cause dehydration (moderate, I and II degrees, or severe, III-IV degrees).

The *gastroenteric* variant of acute dysentery is not attended by the symptoms of colitis. Rectoromanoscopy reveals less marked changes in the mucosa of the large intestine. The leading symptoms are those of gastroenteritis and dehydration of various degrees (moderate, I—II degree; severe, III-IV degree), depending on the severity of the disease.

Abortive and protracted courses of the disease are common now in some patients. Patients with obliterated clinical symptoms usually do not attend for medical aid and the disease can then only be revealed during purposeful clinical and bacteriologic examination.

Patients with uncomplicated dysentery usually recover clinically in 2-3 weeks. The gastrointestinal function and morphology of the gastrointestinal tract are completely restored only in 1-3 months (and

even later). In this connection, relapses are possible within the course of the first 2-3 months following acute dysentery. Relapses are provoked by concurrent diseases, suspended treatment, dietary disturbances during the recovery period, etc. During the relapse, toxaemia is less marked.

Chronic dysentery. It can be recurrent or continuous. In the *recurrent* form of the disease, the patient develops relapses in 3-5 months after discharge from hospital. The relapses follow at various intervals. Exacerbations are attended by less marked toxaemia but the clinical picture only slightly differs from that of acute dysentery.

The *continuous* form is characterized by a gradual onset and the absence of improvement. Stools are liquid or semiliquid, often containing mucus and pus; 5-6 stools a day. The function of the liver, pancreas and the intestine is upset.

Postdysenterial intestinal dysfunction persists for years in many patients. It is the result of stable achylia and atrophic changes in the intestine, which cause chronic colitis and are among the causes of non-specific ulcerative colitis.

Complications. Severe cases can be complicated by rectal prolapse and secondary infection: pneumonia, otitis, parotitis, pleurisy (usually in children). If the disease is protracted, infants under the age of 1 year can develop hypotrophy, hypovitaminosis and anaemia due to metabolic disorders.

Diagnosis. The diagnosis is based on the clinical, epidemiologic, instrumental and laboratory findings. Whether or not a particular patient should be taken to hospital should be decided on the basis of the clinical and epidemiologic picture. If any diagnostic doubt arises, the patient must be examined in the diagnostic department of the hospital. The epidemiologic anamnesis helps reveal contacts with the diseased or persons suspected for dysentery, carriers in the family, house, or at a children's institution.

Laboratory diagnosis includes bacteriologic, serologic and immunofluorescence studies.

Freshly taken mucus, pus and other pathological admixtures (not blood) obtained by natural defaecation or by tampons are used for cultures.

Best results are obtained with cultures of fresh excrements taken directly at patient's bedside. If this is infeasible, the material is placed in a sterile tube containing a preservative (glycerol mixture, or the like) and delivered to the bacteriologic laboratory not later than in 2 hours. If the material cannot be delivered to the laboratory within

this time, the test tube should be kept in a refrigerator (not longer than 12 hours). Cultures are more informative if the material is taken during the early stage of the disease, before treatment is started. A preliminary result is ready in two days, while the final result, in 4 days.

Indirect haemagglutination reaction is additionally performed using an erythrocytic dysentery diagnosticum beginning with the 5th day of the disease. The minimum diagnostic titre of indirect haemagglutination test is 1:160.

The immunofluorescent technique is used for rapid diagnosis.

The diagnosis can also be established rapidly by adding a suspension of native faeces to a mixture of carbon and serum containing shigella antibodies. If the test is positive, large dark flakes precipitate in few minutes (agglomeration). The test is performed on glass.

Coprologic analysis (microscopy of the patient's faeces aimed to detect the pathologic admixtures such as mucus, leucocytes, or erythrocytes) is used as an additional diagnostic method.

Another additional method is rectoromanoscopy by which the mucosa of the large intestine can be observed to a distance of 25-30 cm from the anus. This method helps follow the changes in the pathology inside the intestine. Rectoromanoscopy is contraindicated to pregnant, infants under 1 year, and in the presence of acute processes in the intestine.

Treatment. This should be complex and begin as early as possible. Patients with mild and moderate forms of dysentery attended by marked symptoms of colitis should be treated with nitrofurans (furazolidone, furazolin, etc.), 0.1-0.15 g 4 times a day after meals for 3-5 days. Derivative of 8-oxyquinoline can be given: mexase, mexaform, 2 tablets 4 times a day after meals for 3-5 days. Nitrofurans and 8-oxyquinolines act aetiotropically on shigellae and do not kill the normal intestinal flora.

Aged patients with moderate shigellosis superimposed upon other diseases, and also patients with severe forms of shigellosis should be treated with antibiotics: ampicillin 0.5 g 4 times a day after meals for 2-3 days.

If this treatment fails, neomycin sulphate should be given in 0.1-0.2 g doses 2-4 times a day, or kanamycin 0.5 g 4 times a day for 3-5 days. Prolonged-action sulpha drugs can also be given: sulphadimethoxine, sulphapyridazine, phthazin. Sulphadimethoxine should be given per os: 2 g in a single dose on the first day, and then 1 g a day for the following two days; colibacterin, lactobacterin, bificol,

bifidumbacterin should be given 5-6 times a day for 3-4 weeks to prevent intestinal disbacteriosis.

If toxaemia is marked and the signs of dehydration are obvious, isotonic salt solutions should be given intravenously (1-2 litres). If the disease is severe (in the absence of dehydration), colloid solutions are also indicated: haemodez, rheopolyglucin, or polyglucin to 400-800 ml a day.

In addition to vitamin C (500-600 mg/day), nicotinic acid (40-60 mg/day), thiamine and riboflavin (9 mg/day) are also prescribed.

Symptoms of cardiovascular pathology and collapse should be managed with subcutaneous injection of cordiamine, caffeine, etc. In order to prevent relapses of dysentery, the concurrent diseases should also be treated.

Patients with chronic dysentery should be treated if they excrete shigellae or the disease is exacerbated. Nitrofurans or sulpha drugs and antibiotics should be supplemented with vaccines.

Nutrition is important. Hunger is indicated during the first 10-12 hours in the presence of vomiting. Mechanically and chemically sparing diet is prescribed: strong tea with lemon, dried bread (300 g/day), 2- or 3-day old kefir, curds, rice soup, rice porridge rubbed through a sieve.

Since gastric secretion is inhibited, hydrochloric acid with pepsin, acidin-pepsin, abomin, pancreatin, cholenzim, festal and other preparations should be given. As acute symptoms subside and appetite improves the patient can eat meat soups, steam-cooked chopped meat, boiled fish and vegetables, butter, fruit juice, apples, dry bread, etc.

The patient should be kept clean. Measures should be taken to prevent bedsores on the buttocks and intertrigo around the anus. Spasmolytics (papaverine, nospanum, belladonna preparations, warm baths and water bottles) should be given for abdominal pain.

Prevention and control. Sanitation and hygienic measures are decisive. They are aimed at disruption of the infection transmission routes and include observation of sanitary and process requirements in food industry, food catering establishments, and food sales. Special attention should be given to sanitary control of enterprises engaged in manufacture, storage and transportation of food. Health education of food industry workers, personnel in children's establishments and of the entire population is also very important.

The sanitary condition of settlements, the condition of water supply and sewage systems, disposal of wastes and their deconta-

mination, and control of flies are decisive. Sources of water should be protected from pollution. Tap water should be purified and decontaminated.

Measures that are taken against the source of infection include revealing and isolation of patients and persons suspected for dysentery.

Patients should be hospitalized for clinical and epidemiologic indications. The patient should obligatory be hospitalized if it is impossible to provide the necessary anti-epidemic conditions at patient's home or if the regimen cannot be properly observed.

Patients with an acute intestinal disease (without bacteriologically confirmed diagnosis) may be discharged from hospital not earlier than in 3 days after clinical recovery, normalization of stool and body temperature. Workers of food industry and public catering should be examined bacteriologically not earlier than in 2 days after termination of treatment. If dysentery has been confirmed bacteriologically, the convalescents should be discharged not earlier than in 3 days after normalization of stool and body temperature, and after an obligatory examination (negative result) that should be carried out not earlier than in 2 days after termination of treatment, while workers of food industry and public catering should be examined two times.

All workers of food industry and public catering who sustained dysentery (bacteriologically confirmed diagnosis), carriers and persons with prolonged deranged stools should be observed in outpatient conditions. Of the other groups of population, only patients with chronic dysentery should be observed. All persons who are observed in outpatient conditions should be examined every month and studied bacteriologically for three months. Persons with chronic dysentery who are engaged in food production and public catering, should be observed in outpatient conditions for 6 months with monthly bacteriologic examination.

In order to detect possible sources of dysentery, all persons who are hired to work in food producing and catering establishments should be examined bacteriologically.

Measures in the focus. Prior to hospitalization, or before the patient recovers at home, current disinfection should be performed in the focus of infection. After the patient recovers or is taken to hospital, final disinfection is required.

Persons who had contact with dysentery patients should be observed for 7 days (thermometry, inspection of stools, palpation of the intestine, and the like). Persons working in food industry and

public catering in the focus of infection should be examined bacteriologically for the carrier state (faecal cultures).

Whenever necessary (or when required by the sanitary and epidemiologic service), prophylactic measures should be carried out in the focus of infection: water wells should be inspected and maintained, lavatories should be repaired, flies controlled, etc. Health education is also necessary.

In order to reveal patients and carriers among children at preschool institutions, their stools should be daily tested, frequency of defaecation noted, and the character of stools estimated.

In the presence of intestinal dysfunction or suspected intestinal infection, the patient must be isolated. Children who had contact with the suspected person should be observed medically: their body temperature should be taken twice a day and stools inspected. If another case is registered, all children and the personnel of the institution should be examined bacteriologically.

If the disease occurs simultaneously in several groups of a children's institution, persons engaged in cooking food should be examined bacteriologically.

Bacteriophage treatment can be given only for preventive purposes at preschool children's establishments. Specific antidysenteric immunization of population is unnecessary because of its low efficacy.

Amoebiasis

Aetiology. Amoebiasis is caused by *Entamoeba histolytica* that exists in the form of the motile trophozoite and the cyst. The former is subdivided into forma magna, or the tissue form which is found in the ulcers of the intestinal wall (it can phagocytize erythrocytes), and forma minuta that inhabits the lumen of the upper portions of the large intestine. Cysts are formed from the forma minuta in the lower portions of the large intestine; they contain from 1 to 4 nuclei. The disease is produced only by a mature cyst containing 4 nuclei. The tissue form is found in faeces of patients during the acute period and during exacerbation; the forma minuta can be found in convalescents and in cyst carriers.

Outside a human body the trophozoites are rapidly destroyed. The cyst is encased in a dense coat that protects it from the environmental changes. The cyst can survive in water for 8 months, in moist faeces-to a month; it readily withstands low temperature, but is rapidly killed at a temperature of 85 °C and above. The cyst is more stable against chlorine preparations; it is sensitive to lysol and phenol solutions.

Epidemiology. The source of infection is man, either an amoebiasis patient or a carrier. Cyst carrier state in epidemic areas can last from several months to years. The transmission mechanism is the same as in shigellosis (faecal-oral). The main route of amoeba transmission is by water (by drinking infected water from open sources such as a river) and by contact (soiled hands or domestic objects). If the sanitary conditions at food catering or children's establishments are below standards the infection can be transmitted with food contaminated by soiled hands of patients or carriers. Foods served without preliminary cooking (vegetables, fruits) are of special importance in transmission of amoebiasis. The highest incidence is during the warm season. The disease is common for countries with hot climate.

Pathogenesis. The cyst of *Entamoeba histolytica* is ingested with food or water. In the lower portion of the small or in the upper portion of the large intestine the cyst is dissolved and the trophozoite is released into the lumen, where it multiplies, descends to the lower portion of the large intestine in the form of cysts, and is released into the environment. In the patient, the trophozoite is embedded into the submucous layer of the upper portion of the large intestine; it increases in size and converts into the pathogenic form. As the microorganisms multiply in the submucous membrane, they form abscesses which rupture into the intestinal lumen and form ulcers. The caecum and the ascending colon are usually involved. Ulcers can be deep and reach the serous coat which may result in perforation of the intestinal wall. Blood can carry amoeba to the liver, lungs, brain, kidneys and other organs, where abscesses can be formed.

Clinical picture. The incubation period varies from several days to 3 months (usually 20-30 days). The disease usually begins gradually. The patient complains of malaise, poor appetite, abdominal pain and headache. Stools are liquid, 4-5 times a day. As the disease progresses, stools become more frequent (10-20 a day) and the vitreous mucus is contained in large amount. Streaks of blood can be found. The mucus is sometimes uniformly mixed with blood, and the faeces look like raspberry jelly. Frequent stools are attended by cramping; sometimes tenesmus develops. The abdomen is inflated and tender to palpation on the right side and in the region of the sigmoid colon.

The acute symptoms last 4-6 weeks. Abdominal pain then subsides and stools normalize. The condition of the patient improves.

If the disease is not treated, relapses develop and the disease is transformed into a chronic process that persists for years. Chronic disease causes nutritional disorders, anaemia and cachexia.

Mixed amoeba and shigella infection is characterized by high body temperature, toxaemia and frequent stools leading to dehydration.

Complications. Complications of amoebiasis are associated with ulceration of the intestinal walls and hence with adhesions, constriction of the intestinal lumen, perforations, and subsequent peritonitis.

Among other complications it is necessary to indicate abscess of the liver, less frequently of the brain, kidneys or other organs.

Diagnosis. The diagnosis is based on laboratory studies. From 4 to 6 smears of fresh warm faeces or material taken during rectoromanoscopy are examined to reveal amoeba. The discovery of the trophozoite with ingested erythrocytes (haematophagous trophozoites) indicates an active disease in the intestine. The enzyme-linked immunosorbent method is also used. Serologic tests (indirect haemagglutination test, immunofluorescent antibody test) are used for the diagnosis of amoebic abscess of the liver and abscesses of other organs.

Rectoromanoscopy is an additional diagnostic technique by which specific deep ulcers can be revealed in the lower portion of the intestine.

Treatment. Specific treatment of patients with intestinal and extra-intestinal forms of amoebiasis includes metronidazole (trichopol, flagil), 0.6-0.8 g 3 times a day for 5-10 days. The trophozoites are more readily killed by entamizole, the preparation that includes metronidazole and diloxanide. Two tablets of the preparation are given three times a day for 5-7 days. Acute amoebiasis can be treated with emetine hydrochloride (1 per cent solution, 1.5-2 ml intramuscularly) 2 times a day for 5-7 days. The course is repeated in a week. Dihydroemetine is less toxic than emetine. The preparation is given as 1-2 per cent solution intramuscularly (1-1.5 mg per kg body weight) for 5 days; the maximum dose is 90 mg/day. Chingamin (delagil, chlorochin) 0.25 g three times a day, quiniofon (yatren) 0.5 g three times a day and antibiotics (tetracyclines, monomycin) should be given in the intervals of the emetine therapy.

After the specific treatment, the patient should be given colibacterin, bificol or other preparations for 20-30 days.

In the presence of vast abscess of the liver, surgical treatment is indicated in addition to medication with metronidazole in combination with tetracycline and monomycin.

General envigorating therapy (vitamins, repeated transfusions of blood or dry plasma) is indicated. (For dietary restrictions see "Dysentery").

Prevention and control. Amoebiasis patients should be hospitalized until the course of therapy is complete. Convalescents are discharged after three negative tests for the cyst carrier state. Convalescents should be observed in outpatient conditions for 6-12 months (clinical and laboratory examinations at 3-months intervals).

In 1-3 months after discharge from hospital, the convalescents should be given antirelapse treatment. Diloxanide furoate should be given to persons who release amoeba into the environment; the preparation should be given in a dose of 0.5 g three times a day. Quiniofon (yatren) should be given in a dose of 0.5 g three times a day for 10 days.

Current and final disinfection with a 3-5 per cent lysol solution should be performed in the focus of infection.

Prophylactic measures against transmission of infection are the same as in other intestinal infections.

Escherichia Coli Infections

Aetiology. The infections are produced by *Escherichia coli*, a group of microorganisms belonging to the family of *Enterobacteriaceae.*

Enteropathogenic bacilli are differentiated by their antigen structure: K antigens (capsular antigens types A, B, L and M), O antigens (somatic) and H antigens (flagellar). A hundred variants of K antigens (mainly B type) are known; the quantity of O antigens is 163, and of H antigens, 56. Depending on the result of agglutination test with sera containing K, O and H antigens, the antigen composition of an isolated culture (the antigen formula or serotype) is determined, e.g. 026:B4:H11, OHl:B6:H4. For the sake of convenience, only the serotype of the microorganism is indicated, e. g. 026, 025, Olll.

Infections due to escherichia are numerous. Conventionally they are divided into two categories.

The organisms belonging to category I cause diseases in infants. Since they affect predominantly the small intestine, they are called enteropathogenic bacilli (026, 055, Olll, 0127, etc.).

Microorganisms of category II are divided into two groups, which can cause dysentery-like and cholera-like diseases in children older than 1 year and adults. Escherichia causing dysentery-like diseases invade the intestinal epithelium and are therefore called enteroinvasive bacilli (0124, 0136, 0143, 0144, 0151, etc.). Escherichia causing cholera-like diseases produce enterotoxin and are therefore called enterotoxigenic (Ol, 06, 08, 015, etc.).

Enteropathogenic escherichia coli are sufficiently stable in the environment. They survive for a long time in enclosures and remain viable for several weeks and months in river, well and tap water; they propagate in various foods.

Epidemiology. The source of infection are patients who liberate the microorganisms with their faeces during the acute period of the disease; carriers are another source of infection. Less frequently, infected animals (calves, pigs, poultry) are the source.

The infection is transmitted by the faecal-oral mechanism. The following transmitting factors are involved: food, water, household objects. Coli infection among infants (enteropathogenic bacilli of category I) is mostly transmitted by soiled hands of adults (nurses). Newborns, premature and asthenic infants are most susceptible to coli infections. Dysentery-like infections caused by category II enteropathogenic bacilli are transmitted mainly through ingestion of infected food, such as milk, potato puree, sour milk, kefir, curds, sour cream, chopped meat, fried fish, etc., upon which the bacilli can readily propagate.

The incidence is either sporadic or epidemic. The spread of the infection is facilitated by improper sanitation and hygiene in food and milk processing industry, food catering establishments, children's institutions; untimely isolation of the diseased also promotes infection spread.

The peak of morbidity is observed during the warm season.

Pathogenesis. When ingested, the enteropathogenic microbes pass into the small intestine where they propagate violently on the epithelial surface. As the bacilli die they liberate endotoxin that acts on the endothelial vessels and the nerve centres thus upsetting permeability of the vascular wall and changing their tone. The secretory function of the epithelium intensifies and large amounts of water, salts of sodium and potassium are liberated into the lumen of the intestine. These phenomena are especially pronounced in infection with enterotoxigenic bacilli.

In cases with frequent enteric stools and vomiting, the volume of circulating blood decreases and the blood thickens. Hypovolaemia and low intravascular pressure, and also increased permeability of cell membranes upset the renal function. Protein and formed blood elements can be seen in the urine; oliguria and anuria develop.

Clinical picture. The incubation period lasts from several hours to 3 days (usually from 18 to 24 hours). The intestinal forms of escherichiasis in children run the course similar to those of enteritis and enterocolitis. In mild cases, the body temperature is normal or

subfebrile. Stools are liquid (5 a day), without pathological admixtures. Moderate forms of the disease are attended by elevation of body temperature to 38-39 °C, stool frequency rises to 10; stools are liquid, watery, with admixtures of mucus; appetite is poor; the abdomen is inflated. Severe course of the disease is characterized by high body temperature (39-40 °C), stools are frequent (to 20 times a day), watery, with admixtures of mucus and green substance, appetite is absent, the abdomen is inflated and tender to palpation. The disease lasts from several days to 2 weeks; a protracted course is also possible.

Dysentery-like disease begins fulminantly with chills, severe abdominal pain, weakness, vertigo, nausea, and fever. Depending on severity, stool frequency is from 5 to 10 a day; stools contain mucus and sometimes blood. Tenesmus is less common than in dysentery. The disease lasts from 5 to 7 days but can run a longer course. If the disease runs a severe course, toxaemia is marked; it is manifested by cramps and loss of consciousness. The body temperature is normal if the disease is mild, stools are liquid (3-5 a day), free from admixtures. The overall duration of the disease is 3-5 days.

Cholera-like infections are similar to mild forms of cholera by their clinical course. The incubation period is 1-3 days. The onset is acute; the disease begins with weakness, malaise, headache, and nausea; body temperature is usually normal. Epigastric pain and vomiting develop. Frequent watery stools without mucus or blood occur in several hours. If the disease runs a severe course, symptoms of dehydration develop due to loss of liquid with vomitus and faeces.

Diagnosis. A final diagnosis can only be established in the laboratory (bacteriologic and serologic tests).

Faeces for a bacteriologic analysis are taken into a vessel washed preliminarily with hot water. A specimen weighing 3-5 g is placed into a test tube containing an isotonic sodium chloride solution or a 30 per cent glycerol mixture. The specimen should preferably be taken from the last portions of stools because the small intestine is involved in enteritis due to coli bacteria. Faeces of newborns are taken from the cloth into which the baby is wrapped. Vomitus (3-5 g) is also sent to the laboratory in a sterile test tube containing an isotonic sodium chloride solution. Endo and Levin media are used. The isolated culture is identified by its biochemical and serologic properties. Blood should be analyzed in 3-5 days after the onset of the disease. Indirect haemagglutination tests are used to follow changes in the antibody titres.

A highly sensitive immunofluorescent antibody test and carbon

agglomeration reaction are widely used for diagnostic purposes.

Treatment. Dysentery-like infections are treated as dysentery, and cholera-like diseases like cholera (see below).

Prevention and control. See "Dysentery".

Patients with escherichiasis should be either hospitalized or isolated at home. Besides, in order to reveal the source of infection, infants under 2 years, puerperal and parturient women with acute intestinal diseases should be examined for diagnostic purposes. In order to reveal carriers, workers of food industry and food catering establishments should be examined before hiring (and for epidemic indications). Infants under 2 years should be examined before admitting to preschool children's institutions, or to somatic and infectious hospitals. Means of specific immunization against escherichiasis are unknown.

Cholera

Aetiology. The disease is caused by *Vibrio cholerae.* The bacillus has a single polar flagellum due to which it becomes motile.

The vibrio is divided into two subspecies: the classic one and El Tor vibrio. Each biotype is in turn subdivided into three serotypes: Inaba, Ogawa and Hikojema.

Non-agglutinating (NAG) vibrios, that can produce cholera-like diseases, are sometimes isolated from water and humans.

Cholera vibrio is sufficiently stable in the environment. It can survive for 150 days in faeces in the absence of light, for 60 days in soil, for several days in milk, for 20-30 days in butter, and from 3 to 10 days on fruits and vegetables. Cholera vibrio withstands low temperature. Under equal conditions, El Tor vibrio survives in the environment longer than the classic biotype. Vibrios are sensitive to the absence of moisture; they are killed immediately on boiling. Even weak hydrochloric and sulphuric acids (1:10000) kill them in few seconds.

Epidemiology. The only source of infection is a diseased human or a carrier. Humans with the disease in full swing are especially dangerous for the surrounding: they liberate from 7 to 30 litres of liquid daily with stools and voinitus that contain large amounts of the vibrio.

The degree of danger depends on the clinical form of cholera. If the disease runs a severe course, the patient attends for medical aid immediately and the spread of the infection is usually confined to a family. Patients with atypical and obliterated course are a great

danger. They continue performing their routine duties and diffuse the infection among their coworkers and mates thus promoting the infection spread over a large area.

Convalescents, chronic and healthy carriers can also be the source of infection. Convalescents usually stop being carriers during the first 1-2 weeks after recovery; healthy carriers, in few days. Chronic carrier state is rare in cholera; the state persists from several months to years. Especially it concerns El Tor cholera. It can also run an asymptomatic course; healthy carrier state is possible too.

Like other intestinal infections, cholera is mainly transmitted by the faecal-oral mechanism. The vibrios are ingested with infected food or water. Infection is also possible through direct contact with the patient: the vibrios are then carried into the mouth with soiled hands.

Depending on the transmission factor, water-borne, food-borne and contact epidemics are possible. Water in open bodies (sea, river, pond, lake, canals, etc.) that can be contaminated with effluents is important transmission factor. The vibrio persists and multiplies in water for long periods of time. It has been established that the vibrio can multiply in neutral and alkaline effluents, provided the temperature conditions are optimal. During the hot season people use much water, they bathe, and have other contacts with water and thus maintain vibrio circulation not only in the endemic areas (India, Indonesia, Burma, etc.) but also in other areas, in a closed human-water-human circle. Epidemic spread depends on intensity of using water from an infected source (for drinking, bathing and domestic needs), and also on the degree of water contamination with faecal effluents. Water-borne epidemics are characterized by an abrupt rise in the morbidity due to massive infection of population through water.

Epidemics due to direct contamination (soiled hands, domestic objects) spread because of late diagnosis. The course of epidemic depends on the social factor. Sanitation of populated areas, socioeconomic conditions of population and hygiene standards, availability of medical aid and some other factors are important for cholera contagion rate.

Population is highly susceptible to cholera. After recovery, a convalescent acquires a sufficiently stable immunity, although repeated infection is also possible.

Cholera morbidity in countries with temperate climate is the highest during the hot season. In countries of the torrid zone the seasonal variation in the attack rate is less apparent. El Tor cholera

is characterized by revival of epidemic from season to season due to prolonged carrier state and unrevealed atypical cases.

Pathogenesis. The microorganisms are ingested. Since the cholera vibrio is highly sensitive to dilute hydrochloric acid, it can survive only in an empty stomach in the absence of gastric secretion, inside a food lump, or when ingested with ample water, or else if gastric secretion is inhibited. The vibrio multiplies in an alkaline medium intensively, mainly on the surface of the intestinal mucosa and in the intestinal lumen.

As die vibrio multiplies, its great quantities are accumulated and a great amount of cholera toxins (endo- and exotoxins) is found inside the small intestine. The clinical symptoms of cholera develop due to the general effect of the cholera toxins. The symptoms depend on the lesion of the central and vegetative nervous system, gastrointestinal tract, and the parenchymal organs (kidneys, adrenal glands, liver, etc.). Due to the effect of exotoxin (choleragen), large amounts of water and electrolyte, especially of sodium and potassium chlorides are released through the membranes of epithelial cells of the small intestine. Water is not absorbed in the large intestine and excess liquid in the intestine stimulates peristalsis to cause profuse diarrhoea, which is attended by vomiting.

In severe cases (dehydration of degrees III and IV), a considerable amount of liquid and salts is lost. As a result, exsiccosis develops along with salt depletion. Blood thickens, the activity of the cardiovascular system becomes deranged, hypothermia develops (the body temperature drops below 36 °C); the condition is also attended by acidosis, hypoxaemia and deranged gas metabolism (to asphyxia). The liver function is also upset: the mucosa and the skin become icteric; renal function is deranged with subsequent development of oliguria and possibly anuria. Acidosis and saline depletion cause muscular cramps.

Clinical picture. The incubation period lasts from several hours to 5 days, more frequently 2-3 days. Cholera can be mild, moderate or severe.

The onset of the disease is fulminant, without prodromal symptoms. The disease begins with diarrhoea that develops suddenly. Stools are watery from the very beginning of the disease. Less frequently stools are first faecal, but very soon they become watery and profuse. During the first day of the disease the stool frequency is 3-10 a day (and more). The patient is thirsty, his appetite is impaired, weakness develops.

A mild cholera runs its course in 2-3 days and the patient can

completely recover. The liquid loss does not exceed 2-3 per cent of the body weight (I degree dehydration). If the disease progresses, stool frequency increases to 15-20 a day; stools resemble rice water.

In moderate cases, profuse vomiting can develop in few hours following the onset of diarrhoea. The vomitus first contains food remnants and bile, but soon becomes watery. The patient complains of vertigo, weakness, thirst, and dry mouth. The skin is pallid and dry, the turgor is low; the lips and the fingers become cyanotic; the voice is hoarse. Limb muscles are attacked by short-lasting cramps; twitching of the masticatory muscles occurs. Tachycardia, moderate hypotension and oliguria develop. The liquid loss is 4-6 per cent of body weight (II degree dehydration).

The severe form of cholera is characterized by III degree dehydration (liquid loss 7-9 per cent of body weight). The onset is acute, with frequent and profuse watery stools and early repeated vomiting. Thirst and painful cramps of the abdominal and limb muscles develop. The skin is cyanotic, its elasticity is lost; the skin of hands and feet is wrinkled (washerwoman's hand). The voice first becomes hoarse and then inaudible; the facies is pinched, the eyes and the cheeks retracted (Fig. 8); the lips, ears and nose become cyanotic. The heart sounds are dull; tachycardia develops; arterial pressure falls.

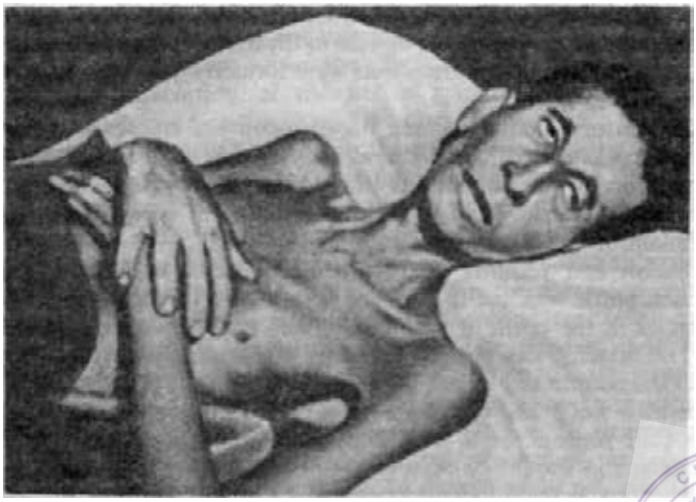


Fig. 8. Choleraic algid

The body temperature can be below normal. Active therapy can rapidly restore the metabolic equilibrium in the patient.

Inadequate treatment or its absence can cause transition of the disease to its most severe form: IV degree dehydration (liquid loss over 9 per cent of body weight); vomiting and diarrhoea discontinue, the body temperature is low. Further progress of the disease results in a hypovolaemic shock. The algid state can sometimes develop in 3-12 hours after the onset of the disease. In connection with thickening of blood, the leucocyte count increases to 20-60 x 10^9/1, the number of juvenile and rod neutrophils increases too. The erythrocyte counts increase to 6-8 x 10^{12}/1. Azotaemia increases along with potassium, chlorides and carbonates depletion. Decompensated acidosis develops. In the absence of active treatment, the patient loses consciousness; coma and asphyxia develop.

Severe forms of cholera usually occur in persons with achlorhydria, chronic enterocolitis, and tuberculosis. According to WHO, the ratio of severe cholera cases to subclinical infection varies from 1:5 to 1:10 with the classic cholera, and from 1:25 to 1:100 with El Tor cholera.

Complications. Complications usually occur in hypovolaemic shock due to secondary infections (pneumonia, thrombophlebitis, sepsis).

Diagnosis. Diagnosis of cholera is established on the basis of anamnestic, epidemiologic, clinical and laboratory findings. It is more difficult to identify the disease in the first victims of an epidemic outbreak, especially in areas that were formerly safe with respect to this disease.

Laboratory studies include bacterioscopy of smears of vomitus and faeces of the patient, and also bacteriologic studies. The material for laboratory examinations should be taken before antibiotic therapy is started and not sooner than in 36-48 hours after termination of the therapy.

Faeces and vomitus (10-20 ml) are collected in a sterile wide-mouth bottle which is then closed with a glass or cork stopper. The stopper in the bottle is wrapped in wax paper (two layers).

The material can also be taken by introducing a cotton tampon into the rectum to a depth of 5-6 cm (the material is taken from the intestinal wall). The tampon is then placed in a vial containing a 1 per cent peptone or a preservative solution. Excess length of the wooden rod should be removed.

Faeces and the duodenal contents are examined in convalescents and vibrio carriers. In 15 minutes after taking the duodenal content,

50 ml of a 30 per cent magnesium sulphate solution are administered through the gastric tube. B and C bile samples are placed in separate tubes and examined in the laboratory.

Cultures of native material are grown not later than in 3 hours after taking the specimen (solid and liquid culture media are used). If the material should be sent to a remote laboratory, it is recommended to place it in a preservative solution. If faeces are taken from persons who had contacts with cholera patients, or from convalescents after taking laxative (20-30 g of magnesium sulphate), the material should be delivered to the laboratory only in a 1 per cent peptone solution.

Specimens of the upper, middle and lower portions of the small intestine (about 10 cm long, between double ligatures) should be taken from the dead who presumably died of cholera. The gall bladder should be extirpated after ligation of the bile duct. Organs of the dead should be placed separately in sterile bottles, packed and labelled.

Beside classical bacteriologic examinations which give results (final) in 36 hours, there exist rapid methods of investigation.

The rapid methods to diagnose cholera include the following:

1. Immunofluorescent method; a presumptive result is ready in 30-60 minutes.

2. Immobilization and micro-agglutination of the vibrio using anticholera O vaccine; examination in a phase-contrast microscope gives the tentative result in few minutes.

3. Macro-agglutination under the effect of specific anticholera O vaccine with cultivation of the native material on peptone; a presumptive diagnosis is ready in 3-4 hours.

Treatment. Treatment depends on the pathogenesis of the disease and includes restoration of the lost fluid and electrolyte. Patients with a severe form of cholera are examined for determination of heart and respiration rate, arterial pressure, body weight, body temperature, and also the physicochemical indices (plasma density, concentration of electrolytes in the plasma and in the red blood cells, degree of acidosis, and the haematocrit). This done, treatment can begin. To replenish the lost water and electrolyte, polyion solutions (sterilized and warmed to a temperature of 38-40 °C) are usually infused intravenously at a rate of 40-48 ml per minute in the II degree dehydration, and 80-120 ml per minute for III and IV degrees of dehydration. After administration of 2-4 litres of solution, the rate of subsequent infusion should be gradually slowed to 10 ml/min. The volumes of stools and vomitus are measured at 4-hour interval; the

physicochemical properties of blood are also determined. After termination of vomiting and recovery of the patient from the dehydration state (III and IV degree), the polyion solution should be continued per os. Depending on the amount of lost liquid, 120-200 ml/kg (to 1000 ml/h) should be given during the first 6-8 hours and then the intake should be decreased to 15 ml/kg per hour until diarrhoea has stopped. Patients with I degree dehydration and also patients with II degree dehydration (depending on their condition) can be given the polyion solutions per os from the very beginning of rehydration therapy (primary rehydration).

After vomiting discontinues, tetracycline (0.3 g 4 times a day for 5 days) should be given per os; the preparation shortens the duration of diarrhoea and eradicates the pathogenic microorganisms from the patient.

The diet should be sparing during the first days of the disease, but beginning with the 3-5th day, dietary restrictions are unnecessary.

The patient should be given a thorough care. Hot water bottles should be placed to keep him warm. The ambient temperature in the room must be adequate.

Rehydration should be performed in an intensive care unit or in a special ward provided with the necessary equipment: a special bed with an aperture to collect faeces, volumetric receptacles for excrements, etc.

The patient should be discharged from hospital after clinical recovery (usually in 10-11 days) and three negative bacteriologic tests that are carried out not earlier than in 24-36 hours after suspension of antibiotics. The tests should be performed during three successive days. The duodenal contents should be examined only once. Faeces should be collected after administration of a laxative salt.

Vibrio carriers are given tetracycline for 3-5 days. If the vibrio is detected repeatedly, chloramphenicol should be given.

Prevention and control Prevention of cholera import from other countries is substantial. In the Soviet Union, all persons who arrive from countries where cholera is endemic, are observed for 5 days. Means of transport are also given sanitary inspection.

Preventive measures are especially important in areas adjacent to countries or regions where cholera is reported. Inspection of potable water, decontamination of effluents, observation of sanitary requirements in food industry and public catering, timely revealing of first cholera cases and vibrio carriers are all important for timely prevention of infection spread.

In order to ensure timely detection of an infection source, it is

necessary to ensure permanent epidemiologic analysis of incidence of acute intestinal diseases. Special attention should be given to the aetiological structure and dynamics of morbidity, to the detection of areas with increased cholera incidence, etc. Whenever necessary, all patients with acute intestinal infections should be examined for cholera. All fatal cases with acute gastrointestinal diseases or with unknown diseases should be thoroughly considered with obligatory postmortem section and bacteriologic examination of the intestinal contents.

Water in open bodies, sources of potable and industrial water supply, sewage (especially sewage of infectious hospitals, baths, laundry, food industry) should be examined bacteriologically. Besides, hydrobionts and silt should be examined in open water bodies.

Specific preventive measures against cholera are of secondary importance. Corpuscular cholera vaccine and choleragen-anatoxin are used for epidemic indications. These are given in single doses by needle or jet injections. Children aged over 7 years should be vaccinated in the absence of contraindications. The adult dose is 0.5 ml. Postvaccinal immunity persists for 4-6 months.

When revealing a cholera patient or a vibrio carrier, the boundaries of the focus should be determined by the results of epidemiologic examinations and by considering the transmission factors.

The complex of anti-epidemic and control measures includes:

1. Timely detection, diagnosis, hospitalization and treatment of patients and vibrio carriers. Hospitalization, treatment and examination is necessary for all patients with intestinal diseases caused by NAG vibrios. All patients with gastrointestinal diseases should be revealed, hospitalized and examined in the focus.

2. Detection, isolation, examination and prophylactic treatment of all persons who had contacts with cholera patients or vibrio carriers. These persons should be observed for 5 days. During the first day, they should be examined three times for cholera and given preventive treatment with antibiotics (tetracycline, 0.3 g 3 times a day for 4 days).

3. Epidemiologic examination of the focus in order to detect the source of infection and persons who had contacts with the patients or carriers, and in order to reveal the transmission factors (water, food, etc.). The entire complex of anti-epidemic measures should also be taken.

4. Current and final disinfection (see "Disinfection").

5. Regular (at 2-week intervals) examination of persons working in food industry, public catering, transport, children's establishments, water supply system.

6. Examination of environmental objects (once a day until the infection focus is eradicated).

7. Restriction measures and quarantine in order to prevent infection spread inside the focus and beyond its boundaries: bathing and fishing in open water bodies are prohibited; use of water from such open bodies for other purposes is also prohibited.

8. Sanitary and hygienic measures including permanent control of water supply, adequacy and timely cleaning of populated places, sanitary condition of market places, food shops, food catering establishments and food industry; control of sanitary condition and prophylactic disinfection of public laundries, hotels, baths, etc. Besides^ potable water should be treated with excessive percentage of chlorine; water used for industrial purposes should also be chlorinated; faecal effluents should be acidified to pH 5.5-6.0.

9. Health education of population.

10. Emergency vaccination and antibiotic therapy of population for prophylactic purpose (for indications).

The focus of infection is considered eradicated in 10 days after hospitalization of the last cholera patient (carrier) and after final disinfection.

Convalescents and also persons in whom the carrier state was detected, should be observed in outpatient conditions.

Prophylactic and sanitary-hygienic measures in populated places after eradication of the focus should be carried out during 12 months until the end of the next epidemic season, provided no new cholera (or carrier state) cases are detected.

Rotaviral Gastroenteritis

Aetiology. The disease is due to rotavirus (the family of *Reoviridae).* Human rotavirus is difficult to cultivate on cell cultures or by inoculation of animals. The virus is shed with faeces and is stable in the environment. Rotavirus of calves and lambs is similar to human rotavirus, but does not cause pathology in people.

Epidemiology. The source and reservoir of the infection are only humans who liberate the virus into the environment with faeces. The patient releases rotavirus from the very first day of the disease, the maximum release being in 3-5 days. Liberation of the virus ends by the 7th or 8th day of the disease. Rotaviruses can be liberated by people who are apparently healthy but who sustained an asymptomatic disease. The route of infection is faecal-oral. The virus can be ingested with food and water.

People of all ages can be afflicted by viral gastroenteritis but infants and young children (from 6 months to 24 months) are most commonly affected. Outbreaks of the disease are more common for the cold season in collective bodies, hospitals, maternity houses, and the like establishments.

Pathogenesis. As the virus is ingested, it multiplies and accumulates in the mucosa of the small intestine and its lumen. The epithelial villi of the small intestine are destroyed, the digestion and absorption of the nutrient is upset, and much water and electrolytes are lost from the body.

Clinical picture. The incubation period lasts 1-2 days (in some cases from 15 hours to 7 days). The onset of the disease is acute. Nausea, vomiting, diarrhoea and abdominal pain develop. In mild disease, the stool frequency is to 5 a day, in moderate and severe forms-10-15 stools a day. Loud rumbling in the abdomen is characteristic. Stools are watery and profuse, with pungent odour, without mucus or blood. The faeces are sometimes cloudy whitish, resembling cholera stools.

Dehydration is possible in the presence of profuse diarrhoea and vomiting. The body temperature rises to 37-38 °C in rare cases. Toxaemia, debilitating weakness and adynamia are characteristic. Arterial pressure is low.

Diuresis during the acute period is low. Pathologic admixtures (protein, leucocytes, erythrocytes) can be seen in the urine of patients with severe course of the disease.

Gastroenteritis due to rotavirus can last 5-7 days and end in complete recovery provided bacterial infection does not interpose.

Complications of rotaviral gastroenteritis are absent.

Diagnosis. Diagnosis is established on the basis of clinical, epidemiologic and laboratory findings.

Laboratory diagnosis includes detection of rotaviruses by electron microscopy (in faeces), immunofluorescent and other methods; viral neutralization, haemagglutination inhibition, complement fixation tests are also used. Antibodies belonging to various classes of immunoglobulins (IgA, IgG, IgM) can be detected using radio-immunologic, immuno-enzyme and immunofluorescent methods. Detection of antibodies immune to rotavirus (IgM) during the course of the disease indicates early infection.

Treatment. See "Salmonellosis", except that antibiotics or other specific preparations are not prescribed to patients with rotaviral gastroenteritis.

Prophylaxis. General preventive measures common for other

intestinal infections are recommended: environmental improvement, proper sanitation and hygiene of populated places, waste disposal and decontamination. Isolation of patients for 10-15 days.

If the disease is mild, the patient can be isolated in home conditions under observation of the physician. Current and final disinfection are necessary in the focus of infection. In order to prevent nosocomial infection, it is necessary to separate patients, to perform current disinfection, and observe personal hygiene rules (by patients and the medical personnel). Final disinfection is required after discharge of the patient from the hospital.

Viral Hepatitis

Several forms of hepatitis are designated by the collective term 'viral hepatitis'. The main forms are viral hepatitis A and hepatitis B. A group of viral hepatitides that are clinically similar to hepatitis A and B have been recently separated and given a conventional name of non-A, non-B hepatitis. The epidemic characteristics of non-A, non-B hepatitis are similar to those of hepatitis B.

Aetiology. Hepatitis A virus (HAV) contains RNA and is similar to enterovirus by its physicochemical properties. It is completely destroyed at a temperature of 100 °C for 5 minutes; it is also sensitive to U-V radiation.

Hepatitis B virus (HBV) contains two-spiral DNA. In addition to Dane particles (mature viral particles), the blood serum of a hepatitis patient contains also other viral particles: small oval (or spherical) and tubular (subviral) forms that are the main antigen carriers. Three antigens are distinguished: surface antigen HBsAg (it is also known as Australia antigen); it appears in liver cells, biological fluids, in the faeces of hepatitis patients and HBV carriers in 2-6 weeks following the infection, and persists over the entire period of the disease or the carrier state); antigen E, designated HBeAg (it is present not only in the Dane particle but is also found to circulate in the blood; in the free form or bound with immunoglobulin; persistence of HBeAg over 3 weeks indicated transition of the disease into its chronic form (infectivity antigen); and antigen C, or core antigen, designated HBeAg; it is contained inside Dane particles. It can only be detected in the liver cell nuclei during infection.

Hepatitis B virus is stable to physical and chemical factors and is inactivated only by treatment in an autoclave at a temperature of 120 °C for 45 minutes, by sterilization in dry air at a temperature of 180°C for an hour, or by boiling for at least 30 minutes.

Epidemiology. Humans are the only source of hepatitis A infection. Patients with a typical (icteric) or atypical (anicteric) forms of hepatitis are the reservoir of infection. Patients with atypical forms of hepatitis are more dangerous for the surrounding people. Their percentage varies from 56 to 90 (with respect to the total hepatitis morbidity). The virus is liberated with the faeces. At the end of the incubation period and during the entire pre-ieteric period the patients are the greatest danger for the surrounding because they excrete the greatest amount of the virus into the environment. The virus is found in the blood after development of the first signs of the disease (from 2 to 10 days) and it disappears from the blood during the first days of the clinical jaundice.

Liberation of the virus with faeces determines the transmission mechanism, which is thus faecal-oral. The following factors are involved: food, surrounding objects, water, and soil. Since virusaemia is short-lasting, the parenteral transmission mechanism is unimportant. Outbreaks of food-borne hepatitis A are characterized by revealing several cases within a short period of time, which is measured by the time of the incubation period (not more than 2-3 weeks) and the presence of a common source of food (usually simultaneous infection). If the virus contaminates food occasionally and in small amounts, hepatitis A occurs as sporadic cases.

Faecal contamination of water sources and soil, especially during irrigation or fertilization of soil, evokes water-borne epidemics and transmission of infection through vegetables, berries, etc. Soiled hands, dishes, or toys are important factors of infection transmission.

Stable immunity is acquired by people who sustained hepatitis A. It is presumed that this immunity is life-long.

Children from 1 to 14 years and young adults are more susceptible to viral hepatitis A.

The high contagion rate among children, compared with adults, is explained by infection through environmental objects, while a considerable number of adults have already sustained the disease in their childhood.

Certain periodicity (3-5 years) is observed in hepatitis A incidence; the incidence increases in the autumn and winter.

Chronic HBsAg carriers, patients with acute and chronic forms of hepatitis B and convalescents are the source of infection.

Hepatitis B virus can be found in the blood 2-8 weeks before the onset of the disease during the prodromal period and during 2-3 weeks of the clinically manifest jaundice. Hepatitis B virus persists in the organism for a long time after convalescence (from 4 months to

13 years and longer). Hepatitis B virus is usually transmitted parenterally during transfusion of blood or its preparations (plasma, erythrocytes, fibrinogen, prothrombin prepared from the blood of donors who are virus B carriers). The disease can be transmitted through inadequately sterilized medical tools. Medical personnel can be infected through minor injuries (surgeons, obstetricians, dentists, nurses, laboratory workers, etc.). Infection can be transmitted during nail finishing or shaving. It is supposed that infection can be transmitted through the placenta from the mother to the foetus, or during contact of the newborn with amniotic fluid during labour.

Virus B can be found in the saliva, urine, semen and other biologic fluids or faeces, and the infection can thus be transmitted through sexual and other intimate contacts. Susceptibility to hepatitis B is high.

Immunity acquired after hepatitis B is less active. Infants under 1 year of age and adults are mostly afflicted. This can be explained by more frequent transfusions and other medical manipulations in this age. No seasonal variations or periodicity of hepatitis B are observed.

Pathogenesis. As virus A is ingested, it multiplies in the gastrointestinal mucosa and then in the regional lymph nodes (incubation period). During the pre-icteric period, the virus invades the blood (virusaemia), and is carried to the parenchymatous organs, mainly to the liver, where it multiplies in the macrophage and liver cells to destroy them. Growing immunity promotes eradication of the virus from the patient by the end of the second or third week of the icteric period. Transition of the disease into its chronic and protracted form is more frequent in hepatitis B than hepatitis A.

When infection is transmitted parenterally, virus B gets into the blood and is rapidly eradicated from the body (short-lasting virus carrier state), provided immunity is sufficiently active. If the virus is retained in the body, it is carried to the liver and other organs. Ingress of the virus into the macrophage and liver cells evokes the cytolysis, cholestasis and mesenchymal inflammatory syndromes. The virus alters the antigen composition of the hepatocyte plasma membranes, arouses the immune response to the hepatocytes containing the virus, and causes their subsequent cytolysis. Secondary and subsequent invasions of the virus in the blood accounts for the unduiant course of the disease, its exacerbations, and transition into the chronic form. Increasing specific immunity eradicates the virus from the patient.

The cholestatic syndrome is associated with disturbed liver architecture, upset production of bile and its excretion. Intralobular

cholestasis, dilatation of the bile capillaries with cholestasis and formation of thrombi dominate other disorders. Gall pigments and acids are carried with blood to account for the yellow colour of the skin and mucosa, and, in some cases, itching. Hyperbilirubinaemia, choiuria, hypercholesterolaemia and increased transaminase activity in the blood are noted.

The mesenchymal inflammatory syndrome is manifested by infiltration of and damage to the stroma and cells of the macrophagic system, their proliferation, hypoproteinaemia, low albumin and high globulin levels.

Clinical picture. The clinical forms of viral hepatitis are differentiated by their type, severity, and course. Typical forms include all icteric cases and atypical (abortive), anicteric and subclinical forms. According to the severity of the disease, typical forms can be mild, moderate and severe. Acute, protracted and chronic viral hepatitis are also distinguished. The course of the disease is divided into pre-icteric or prodromal, icteric period (clinical jaundice) and convalescence (recovery phase).

The incubation period of hepatitis A lasts from 7 to 50 days, more commonly from 15 to 30 days. The pre-icteric period lasts from 7 to 14 days on an average, but can last longer (to 30 days). The onset of the disease is usually acute. The body temperature rises to 38 °C. The patient develops chill, headache, lassitude, and catarrhs (influenza-like syndrome). Dyspepsia, arthralgia, asthenovegetative and other syndromes can develop.

Dyspepsia is characterized by poor or completely lost appetite, nausea, vomiting, discomfort, distension in the epigastrium or dull pain in the epigastrium and right hypochondrium. The asthenovegetative syndrome of the prodromal period is less common. A patient gradually develops lassitude, the working capacity decreases, the patient becomes irritable, his sleep deranges, he develops headache. Still less frequent is arthralgia, it occurs mostly in the elderly. The patient complains of myalgia, pain in the bones and joints in the absence of visible deformations, erythema or swelling.

An insignificant leucopenia (without changes in the leucocytic formula) is common. Activity of serum transaminases (alanine- and aspartate transaminase) is high during the entire pre-icteric period.

In the end of the pre-icteric period, the liver is enlarged, the urine becomes dark (beer-coloured) due to increased urobilinogen content. Faeces are sometimes discoloured (clay-coloured), the bilirubin (especially conjugated bilirubin) in the blood serum increases. Clinical jaundice begins when the sclera turn icteric.

The icteric period is characteristic for the advanced disease. The sclera, the visible mucosa and the skin become icteric; some symptoms of the pre-icteric period lessen or disappear. Enlargement of the liver continues. Its edge is tender to palpation and extends from under the costal arch to 2-4 cm; the spleen is often enlarged as well.

The arterial pressure usually falls; bradycardia develops. Leucopenia with lympho- and monocytosis are characteristic. ESR slows down to 2-4 mm/h in the acute period. As jaundice subsides, ESR can accelerate to 18-24 mm/h with subsequent normalization. As jaundice intensifies due to upset liver function, the bilirubin of blood serum increases (not above 100 uM/1 in mild form, 100-200 uM/1 in moderate and above 200 uM/1 in severe form of the disease). The thymol turbidity test becomes more positive. The icteric period lasts from 7 to 15 days. The transition to the recovery phase begins with lessening and then disappearance of jaundice, normalization of the faecal colour and excretion of a great amount of light urine.

The clinical symptoms of the disease rapidy subside with the onset of the recovery phase. The serum bilirubin and the activity of alanine transaminase normalize. The index of the thymol turbidity test remains high for a long time. Relapses of the disease are usually provoked by physical strain, negligence of regimen and prescriptions, dietary violations, etc. If a relapse occurs at late terms, the patient must be examined for possible infection with hepatitis B, or non-A, non-B virus.

The incubation period of hepatitis B is usually 60-120 days (minimum 6 weeks, maximum 6 months).

The pre-icteric period lasts from 1 day to several weeks, or can be absent in some patients. Body temperature rises in some patients. Dyspepsia, arthralgia and the asthenovegetative symptoms are more common for hepatitis B. The liver is enlarged, some patients complain of pruritus and urticaria-like allergic itching rash.

Serum transaminases (alanine and aspartate transaminases) are increased.

The icteric period (clinical jaundice) begins with a yellow colouration of the sclera, visible mucosa, and skin. Jaundice is longer than in hepatitis A; it attains its maximum in 2-3 weeks. The clinical symptoms of the prodromal period intensify. The liver enlargement continues, its edge is tender to palpation. The spleen is also enlarged in many cases.

The changes in the peripheral blood are basically the same as in viral hepatitis A.

Serum alanine transaminase is higher than aspartate transaminase in severe disease. The result of the sublimate test is low (1.4 ml against normal 1.8-2.2 ml), albumin content decreases to 45-47 per cent, gamma-globulins increase to 26-29 per cent; hyperbilirubinaemia develops. The thymol turbidity test is 2-4 U (as determined absorptiometrically); it increases in 90-95 per cent of cases. The course of the disease is characterized by increasing toxaemia with vertigo, weakness, adynamia, nausea, repeated vomiting, euphoria, development of haemorrhagkf diathesis and tachycardia.

The recovery phase is longer than in hepatitis A. The disease is more severe and is likely to transform into a protracted (from 3 to 6 months) chronic active hepatitis or chronic persistent hepatitis.

Non-A, non-B hepatitis is similar to hepatitis B as regards its clinical course, but it is milder, though often transforms into the chronic form. The transition to the chronic disease is manifested by high ALT (5-10 times higher than normal), that persists more than 3 months, and hypergammaglobulinemia.

Complications. The severe forms of hepatitis B can end with acute hepatic encephalopathy. The onset of this condition is heralded by increasing dyspepsia (nausea, vomiting), lassitude, sleepiness, apathy or excitement, flapping tremor, haemorrhagic syndrome, occasional deep inspirations or yawning. Bradycardia or normal pulse is followed by tachycardia; the liver is diminished or its edge is thinned; pain develops in the presence of intensifying jaundice. The specific symptom is the hepatic breath (resembling the smell of rotten apples).

As the disease progresses, consciousness is dimmed. This is manifested by loss of orientation in space and time, monosyllabic answers, interjections, motor excitement. If the precoma state is impossible to terminate, coma develops. It is characterized by the absence of verbal contact; the patient still reacts to pain stimuli. If coma is deep the patient does not respond to pain and is lost in profound sleep. The pupils are dilated, the reflexes are absent or decreased, muscular twitching can be seen; urination and defaecation are involuntary. The liver shrinks, hyperbilirubinaemia increases, **ALT** level decreases. The result of the sublimate test, the prothrombin, cholesterol, and free heparin levels are very low; the serum potassium decreases and the acid-base equilibrium is upset. The prothrombin index is low (less than 55 per cent).

Diagnosis. The diagnosis is based on clinical and epidemiologic findings.

Hepatitis B is diagnosed on the basis of the epidemiologic anamnesis (operative intervention, blood transfusion and other

manipulations connected with disruption of integrity of the skin or mucosa 2-32 weeks before the onset of the disease), clinical and laboratory findings.

The specific method of laboratory diagnosis is based on the determination of marker antigens to hepatitis B virus (HBsAg, HBcAg and HBeAg) and the corresponding antibodies in the serum of patients (anti-HBs, anti-HBc and anti-HBe).

The reaction of precipitation in gel, counter immunoelectrophoresis, and a more sensitive reaction of passive haemagglutination are of greatest practical importance in the detection of hepatitis B markers. Among other highly sensitive methods are radio-immune and immuno-enzyme methods. HBeAg is detected in blood simultaneously with HBsAg during the incubation period. They are eliminated from the blood after the onset of clinical jaundice. Disappearance of HBeAg and of HBsAg 3 and 6 weeks after the onset of the disease, respectively, and also detection of anti-HBe and anti-HBs in the blood of patients suggest acute form of viral hepatitis and the prognosis is good. Persistence of HBeAg in the blood and liver of patients for more than 3 weeks, and of HBsAg for more than 6 weeks indicates transition of the disease into its chronic form.

Treatment. Specific therapy is unknown. Mild viral hepatitides in their acute phase should be treated by adequate regimen, diet, and sparing conditions for the liver. During the first 7-10 days of clinical jaundice, the patient must remain in bed but later he can occasionally leave his bed. The diet should be sparing but adequate. The daily ration must include at least 100 g of protein, to 30-40 g of butter, and carbohydrates. Fried, smoked or pickled food, and also alcohol should be excluded. Food must be rich in vitamins.

Taking much liquid (2-3 litres a day) as stewed fruits, tea with lemon, fruit juices, and the like, is recommended. Daily evacuation of the bowels is necessary.

Patients with moderate disease attended with signs of toxaemia, who are unable to drink great quantity of liquid because of nausea, should be given detoxicating therapy. A 5-10 per cent glucose solution, Ringer-Locke solution (250-500 ml each) with an addition of 10 ml of a 5 per cent ascorbic acid solution should be given by drip infusion. Nicotinic acid (60 mg), thiamine (6 mg), riboflavin and pyridoxine should also be given. If necessary, haemodez or rheopolyglucin (200-400 ml), plasma (100-150 ml) or the like should be administered.

Patients with severe forms of the disease should be moved to an intensive therapy unit or other ward where they can be properly

observed by a neurologist (twice a day). Their acid-base and water-salt equilibria should be controlled; coagulograms should be taken, and daily diuresis measured. Detoxicating preparations should be given. Oliguria should be treated with furosemide (0.02-0.04 g) in combination with verospiron (0.025 g 3-4 times a day). In order to eliminate hypokalaemia, panangin (10-20 ml) should be administered. Vikasol (1 per cent solution, 2-5 ml) should be given intramuscularly for haemorrhage. Prednisolone is indicated of encephalopathy.

Patients with acute hepatic encephalopathy should be restricted in protein; they should be given cleansing enema with subsequent intestinal lavage with a 4 per cent sodium bicarbonate solution. Complications are prevented by antibiotics. If signs of brain oedema develop, dehydration therapy is indicated in addition to detoxicating treatment. Inhibitors of proteolytic enzymes (gordox, trasylol) in mean therapeutic doses (10000-30000 U) give a positive effect.

Prevention and control. Control of viral hepatitis includes revealing the source of infection and its isolation, and also disruption of the infection transmission routes.

Patients in the end of the incubation period, and during the prodromal period, are the greatest epidemiologic danger. In this connection, it is very important to reveal and isolate hepatitis patients as soon as possible. Early detection should be ensured by the medical personnel during outpatient examinations, visits to patient's families, and also during regular examinations of various cohorts of population.

All patients with acute viral hepatitis and also with exacerbated chronic form of the disease should obligatory be taken to infectious hospital. Persons suspected for viral hepatitis should be placed in a diagnostic department. Patients with hepatitis A and B should be placed in separate wards.

Convalescents should be discharged from hospital after jaundice subsides, the pigment is no longer detected in the urine, and the blood bilirubin normalizes.

Since acute forms of viral hepatitis can transform in chronic, convalescents should obligatory be observed in outpatient conditions after their discharge from hospital.

Hepatitis A convalescents should be examined in one month after their discharge, and then in 3 months.

Persons who sustained hepatitis B should be examined regularly during one month after discharge from hospital. If the results of examination are beneficial, repeated examinations should be carried

out in 3, 6, 9, and 12 months. In the absence of chronic hepatitis and if two tests for HBsAg performed at a 10-day interval are negative, the convalescent needs no further examination.

Persons who sustained viral hepatitis, who suffer hepatitis of unknown aetiology, who were given blood or plasma transfusions during recent 2 years, and also alcoholics or drug addicts may not be regarded as potential donors. Blood taken from a donor must be examined for the determination of its biochemical properties and the presence of HBsAg. Those in whom HBsAg has been detected may not be used as donors. Carriers of HBsAg should be examined immediately after the carrier state has been detected, then in 3 months, and later twice a year, until 4 successive tests are negative (during 2 years of observation).

Viral hepatitis can be prevented by proper sanitary control of food industry, water supply system, by adequate cleaning of residential districts, proper maintenance of sewage system and waste contamination; and by control of flies, and the like.

In order to prevent parenteral infection, medical *^ols should be kept sterile. All manipulations on patients should be performed with separate sterile syringes, needles, scarifiers, etc. Non-reusable syringes or systems for blood transfusion should be preferred.

Hospitals and other medical institutions should be provided with special centres where tools must be sterilized.

Children aged from 1 to 10 years attending children's establishments should be given 1 ml immunoglobulin to prevent viral hepatitis A during the pre-epidemic season.

Measures in the focus. In all cases, patients with viral hepatitis A and B should be registered separately and examined epidemiologically. It is necessary to examine all people who associate with viral hepatitis patients or persons suspected for hepatitis (with acute respiratory diseases, influenza, cholecystitis, etc.).

It is necessary to find out if a patient was, during the past 6 months, treated at any hospital or other medical institution, if he had blood transfusions or infusions of other blood components. In the latter case, it is necessary to collect information about the donor.

It is necessary also to find out if the patient had intracutaneous, subcutaneous, intramuscular, intravenous or other injections, if his blood was taken from the finger or vein, if the patient was a donor, etc.

Current disinfection should be performed in the focus of viral hepatitis before hospitalization and a final disinfection after hospitalization of the patient.

All persons who had contacts with the patient should be examined medically not less than once a week for 35 days after separation from the patient and disinfection in the infection focus.

Children who attend children's institutions and who had contacts with hepatitis A •patients can be allowed to visit these institutions only on special permission of an epidemiologist after administration of immunoglobulin, provided a regular medical observation over such children is ensured, and provided a child with the first signs of infection is isolated and hospitalized.

If a case of viral hepatitis is revealed at a preschool institution, all persons who had contacts with the diseased should be observed daily; once a week they should be given a thorough medical examination during 35 days after isolation of the last patient. No child can be admitted to the institution, where cases of hepatitis were detected, unless immunoglobulin is administered to the newly admitted child after a special permission of an epidemiologist. A child who had viral hepatitis A in past history can be admitted to such an institution.

In the presence of indication (increased acute respiratory morbidity, especially diseases attended with hepatic enlargement, non-motivated elevation of temperature, etc.), enzyme level in the blood should be determined at 10-15 day intervals. Immunoglobulin should be given for prophylactic purpose to children aged from 1 to 14, and to pregnant women. The preparation should be given during the first 7-10 days from the onset of the disease. The dosage: 1 ml for children from 1 to 10 years, and 1.5 ml for children aged over 10 and to pregnant women.

Planned vaccination, diagnostic tests and stomatologic examination should not be carried out during 2 months after isolation of the last patient from other children.

Health education is necessary in the focus of viral hepatitis.

Poliomyelitis

Aetiology. Poliomyelitis (Gr. *polios* gray and *myelos* marrow) is caused by a virus belonging to the family of *Picornaviridae,* the genus *Enterovirus;* coxsackievirus and echovirus also belong to this group. Three separate serotypes of the poliovirus are distinguished: I, II, and **III.** The poliovirus is sufficiently stable in the environment: it withstands absence of moisture and cold; in water it can survive for 100 days and in milk to three months; in faeces it remains viable for 6 months; the virus is sensitive to disinfectants. The virus is also

pathogenic for monkeys. Albino mice and cotton rats are sensitive to some strains of type I virus.

Epidemiology. Humans are the source of poliovirus; these can be patients with manifest clinical symptoms and also persons with asymptomatic forms of the disease. According to some authors, the ratio of clinically manifest cases to asymptomatic cases can (before prophylactic vaccination) be from 1:100 to 1:1000.

Patients in the acute period of the disease are of greatest danger for the surrounding people. The virus is eradicated from the convalescent in 15-20 days after recovery. This period is sometimes longer: 30-40 days or even 4-5 months.

The infection is transmitted by the faecal-oral route. Infected dishes, toys and other objects in common use are the transmitting factors. The causative agent can be transmitted with food (milk, etc.), thus accounting for the epidemic spread of the disease. Water-borne epidemics have also been reported.

Poliomyelitis can be transmitted by droplets borne in air.

Children aged under 5-7 years are mostly susceptible to the infection. Older children and adults are less susceptible, which is explained by the fact that they might have already sustained this disease (or carrier state) in an abortive form. Those who sustained the disease, develop a stable type-specific immunity.

The incidence of poliomyelitis is often sporadic. Epidemic outbreaks and seasonal variations (maximum incidence during the warm season) were characteristic of poliomyelitis in the past.

High poliomyelitis contagion rate is now seen in countries that do not practice vaccination. Meanwhile, Sabin's vaccination (live vaccine) has decreased considerably the poliomyelitis morbidity.

Pathogenesis. The portal of infection is the mucosa of the mouth, alimentary tract and the upper airways. From mucosa the virus passes to the regional lymph nodes where it multiplies and is carried with the lymph to the blood to cause virusaemia. Blood carries the virus to the cells of cornua of the spinal cord. The cervical and the sacrolumbar enlargements are mostly involved. About one fourth or third of the nerve cells in the enlargements are destroyed to cause paresis. A complete paralysis occurs in cases where three thirds of the cells die. The virus also damages the cells of the macrophagic system, respiratory mucosa, lung, gastrointestinal tract, etc.

Clinical picture. The incubation period lasts from 5 to 14 days; variations from 2 to 35 days are possible. The following forms of poliomyelitis are possible: (1) inapparent, asymptomatic; (2) visceral (abortive) without involvement of the nervous system; (3) forms with

involvement of the nervous system: non-paralytic poliomyelitis (meningeal form) and paralytic poliomyelitis.

Inapparent form. Since the disease runs an asymptomatic course, it can only be diagnosed in the laboratory.

Visceral form. It makes about 80 per cent of poliomyelitis morbidity. The temperature elevates, the patient develops headache, lassitude, weakness, catarrh of the respiratory tract, pharyngitis, rhinitis, bronchitis, and tonsillitis. Some patients have gastroenteritis or enterocolitis symptoms. The patient recovers in 3-7 days. The diagnosis of poliomyelitis in this form can only be established in the laboratory.

N on-paralytic form. Symptoms of general infection, that are seen in the visceral form of the disease, intensify. Meningeal symptoms develop beginning with the second or third day of fever. These are stiff neck and positive Kernig and Brudzinski's signs. The cerebrospinal fluid is clear, it issues under normal or slightly elevated pressure. The number of cells in the cerebrospinal fluid is high: from 100-300 x 10^6 per litre during the first days of the disease (due to neutrophilosis) to 900 x 10^6/1 and over (due to lymphocytosis) during subsequent days; the protein content does not exceed 1 g/1. The meningeal form is benign: the patient recovers in 2-4 weeks.

Paralytic form. This form of the disease runs several stages: preparalytic (initial), paralytic, restorative, and the stage of residual phenomena.

The *preparalytic* stage begins acutely with elevation of body temperature to 38.5-40 °C, catarrh of the upper airways (tonsillitis, bronchitis, rhinitis, nasopharyngitis), gastrointestinal disorders (vomiting, diarrhoea, abdominal pain), headache, lassitude, somnolence or insomnia, delirium, and convulsions. The spinal symptom is positive: the sitting patient is unable to rich his knees with the lips because of severe spinal pain. In order to release the load on the spinal column, the patient has to lean against his both arms in the sitting position. The meningeal symptoms are common; general hyperaesthesia (increased sensitivity of the skin) develops.

The quantity of protein and the number of cells in the cerebrospinal fluid increase; the globulin reactions are positive.

The stage of *paralysis* begins on the 2-5th day of the disease. Paresis and paralysis can be seen immediately following the drop of body temperature, or at the height of fever. The muscles of the legs are usually affected (58-82 per cent of cases). Combinations of paralysis of the arms with paralysis of the muscles of the trunk, neck and other parts of the body are less frequent. Paralyses are flaccid

Fig. 9. Poliomyelitis. Residual phenomena. Paralysis and muscular atrophy of the extremities and trunk with severe spinal and chest deformities

and asymmetric; restricted movement and decreased muscular tone are seen; the tendon reflexes are diminished or absent. Muscular atrophy develops in 1-2 weeks after the onset of paralysis. The quantity of protein in the cerebrospinal fluid increases and cytosis decreases beginning with the 5th day of the disease.

The *restorative* stage begins in few days after development of paralysis. The motor function is restored in the initial period of this stage in separate groups of muscles due to lessening of oedema and normalization of function of the nerve cells that were not severely damaged. In 4-6 months, the process of restoration is slowed down, but it can continue to 2-3 years.

The stage of *residual phenomena* in characterized by atrophy of some muscular groups. In this connection, deformations and contractures of the extremities and trunk develop (Fig. 9).

Depending on location of the foci of nervous system lesions, the following forms of poliomyelitis are distinguished: spinal (flaccid paralysis of the muscles of the extremities, neck, diaphragm and trunk); bulbar (the most dangerous form due to lesion of the organs

of respiration, speech and swallowing); pontine (the nuclei of the facial nerve are damaged with paresis of mimic muscles); encephahtic (symptoms of the general and focal lesions of the brain). Mixed forms are more common: spinobulbar, bulbospinal, etc.

Diagnosis. The diagnosis is based on clinical, epidemiologic and laboratory findings. The diagnosis of non-paralytic forms and of the preparalytic stage of poliomyelitis is especially difficult. Only a thoroughly collected anamnesis (contact with poliomyelitis patients, the seasonal factor) helps establish a correct diagnosis.

Faeces (15-20 g), pharyngeal washings, and smears are sent to the laboratory where cultures are grown. The answer is ready only in 10-15 days. The serum samples obtained from the patient during the first days of the disease, in two weeks and later are used for serologic tests.

Treatment. Specific therapy of poliomyelitis is unknown. Immunoglobulin (0.3-0.5 ml per kg body weight) is given intramuscularly during the preparalytic period. In order to lessen oedema of the brain and its meninges, 20-40 ml of a 40 per cent glucose solution are given intravenously. Vitamins (vitamin C, B, B_{12}) should be given. Anaesthetic and amino acids are also used.

An apparatus for artificial respiration should be used in patients with respiratory failure. The patient must remain in bed for 2-3 weeks. When paralysis develops, it is necessary to see that the paralyzed extremities are in normal position; this helps prevent deformation, contractures, etc. (Fig. 10). Medical exercises, massage, physio- and stimulation therapy are prescribed in the restorative period. The orthopaedist should observe the patient. Sanatorial treatment is recommended in the stage of residual phenomena.

Prevention and control. Sabin's live attenuated vaccine is the most effective prophylactic preparation. Children aged from 3 months to 16 years are given planned antipoliomyelitis vaccinations in the absence of contraindications.

The first vaccination is given at the age of 3 months. The vaccine is administered in three portions at 45-day intervals. Revaccination is carried out at the age of 1-2 year and 2-3 year (at a 45-day interval). During revaccination at the age of 7-8 and 15-16 years, the vaccine is given in a single dose. The vaccine against poliomyelitis is given simultaneously with vaccination against pertussis, diphtheritis, and tetanus.

It is important to reveal and timely isolate patients with poliomyelitis and those suspected for the disease. Patients with mild forms of the disease and with steadily improving health should be isolated

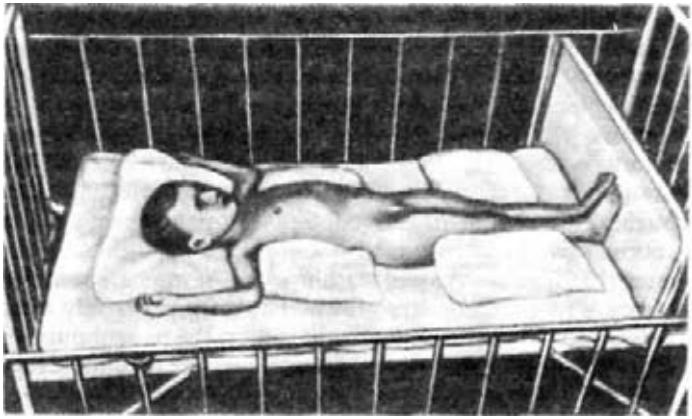


Fig. 10. Poliomyelitis. Patient's posture

in an infectious hospital for at least 20 days; patients with moderate and severe forms (paralysis) should be kept in hospital for at least 40 days.

The sanitary and prophylactic measures include supervision of cleaning and waste disposal, supervision of food industry, food catering, and water supply system, control of flies, improvement of populated places, observation of hygiene at children's institutions, and control of overcrowding.

Measures in the focus. Current disinfection is necessary before hospitalization of the patient. After the patient is hospitalized, a final disinfection should be carried out and flies eradicated.

Persons who had close contacts with the poliomyelitis patient (healthy children aged under 15 years and all adults working at children's institutions, workers of food industry and catering) should be vaccinated with a single dose of Sabin's vaccine. If a case of acute poliomyelitis is reported from a school or preschool children's institution, all children in the group where the patient belongs should be vaccinated. Planned vaccination against polyomyelitis should be performed later according to the existing schedule.

If a poliomyelitis case is revealed in a general hospital, all patients, who contacted the poliomyelitis patient in the ward, and the medical personnel should be given a single dose of Sabin's vaccine. If vaccination is infeasible for some reason, quarantine (20 days) should be established. Persons who contacted the poliomyelitis patient should be observed for 20 days.

Non-poliomyelitis Enteroviral Infections (Coxsackievirus and Echovirus Infections)

The enteric virus *Coxsackie* (coxsackievirus) was first isolated in 1948 at the village of Coxsackie (USA) from faeces of children with the disease, the clinical picture of which resembled that of poliomyelitis. The echovirus was isolated in 1951. Since its relationship to disease remained to be established at those times, the virus was called *orphan* (ECHO stands for: E-enteric, C - cytopathic, H-human, and O - orphan).

Aetiology. The pathogenic microorganisms are enteroviruses *Coxsackie* and echovirus which belong to the family of *Picornaviridae*, the genus *Enterovirus.* By the present time, 32 serotypes of coxsackievirus and 30 serotypes of echovirus have been isolated. They are stable in the environment. They can be revealed in faeces, nasopharyngeal discharge, and blood of patients. Coxsackievirus is pathogenic for experimental animals while echovirus is not.

Epidemiology. The source of infection are patients and virus carriers who shed the viruses with faeces and with the nasopharyngeal discharge (air-borne infection). The infection is characterized by the faecal-oral transmission mechanism. Since the viruses can persist in water, soil, milk, on vegetables and environmental objects, the infection can be transmitted through water (during bathing in open water bodies or swimming pools), food, and by direct contact. Since the viruses are present in the nasopharyngeal mucus, the infection can be transmitted by air-borne route, which is considered the main route in this group of diseases.

Susceptibility to enteroviral infection is especially high in children aged from 3 to 10 years. The incidence increases during the summer and autumn.

Pathogenesis of the infection is similar to that of poliomyelitis.

Clinical picture. The diseases due to coxsackievirus and echovirus are characterized by great variability of their clinical symptoms. The incubation period varies from 1 to 7 days (usually from 2 to 4 days). The onset of the disease is acute. The body temperature rises to 38-40 °C and persists from 2 to 5 days (less frequently to 7 days). Fever is often undulant (with two peaks). The patient develops headache, vertigo, weakness, vomiting, abdominal pain, difficult swallowing, hyperaemia of the face and fauces, injection of the scleral vessels.

The quantity of leucocytes increases, but the condition is rapidly followed by normocytosis or leucopenia.

Depending on a particular causative agent of the disease, and on the presence of particular symptoms, the following clinical forms of the pathology are distinguished.

Epidemic myalgia. This is characterized by the known symptoms, attacks of severe pain in the chest muscles, epigastric and spinal pain, and pain in the muscles of the extremities. Pain is cramping; it persists from several hours to 1-2 days. Signs of serous meningitis can develop in some patients.

Herpetic tonsillitis. The onset of the disease is acute. Papules and vesicles with scarlet hyperaemic margins develop on the mucosa of the anterior folds of the fauces, uvula or palate. The vesicles and the hyperaemic margins can increase in size in 2-3 days and later turn into greyish yellow ulcers.

Serous meningitis. It begins with elevation of body temperature and severe headache. Meningitis symptoms develop in 2-3 days. The neck is stiff, the Kernig and Brudzinski's signs are positive. The cerebrospinal fluid issues under high pressure; it is clear and contains to 200 (and more) lymphocytes in a microlitre. The quantity of protein is either normal or slightly increased.

The leucocyte count is either normal or increased to 10×10^9-$15 \times 10^9/1$. During the recovery phase, the quantity of eosinophils can increase to 15-20 per cent.

Poliomyelitis-like form. This form of the disease resembles poliomyelitis by its clinical manifestations. The onset is marked by paresis and paralysis without preceding catarrh. The disease is much milder than poliomyelitis. Flaccid paresis and paralysis usually abate completely in 2-8 weeks.

Encephalomyocarditis of newborn runs a severe course; the mortality is high due to lesion of the brain and heart.

Other forms also occur: enteroviral fever, enteroviral exanthema, enteric (intestinal) and catarrhal forms (the names are self-explaining).

Diagnosis. The diagnosis is based on clinical, epidemiologic and laboratory findings. The virus is isolated during the acute period from faeces, nasopharyngeal washings (lavage during the first three days of the disease), and blood. In the presence of meningitis, the cerebrospinal fluid should be examined. Paired serum samples are tested: the first test is performed during the first days of the disease and the second during the recovery phase. These sera are examined for the presence of neutralizing antibodies to the virus or for their increasing titre (compared with the onset of the disease). The immunofluorescent method is used for early diagnosis.

Treatment. Treatment is symptomatic. Cerebrospinal puncture is

indicated in serous meningitis. During the first days of the disease the patient is treated with analgesics, a 25 per cent magnesium sulphate solution intramuscularly, intravenous infusion of a 40 per cent glucose solution, and vitamins. Care of patients depends on the clinical form of the disease.

Prevention and control. The patient is isolated for at least three weeks. Diseased workers of children's institutions and food enterprises, or of other organized collective bodies, should be hospitalized.

Convalescents are admitted to their jobs not sooner than in 30 days following the onset of the disease. Duration of quarantines at preschool institutions is 12 days.

Brucellosis

Aetiology. This infection is caused by microorganisms of six species. Human brucellosis is due to the following three species: *B. melitensis* (goats), *B. suis* (hogs) and *B. abortus* (cattle). The microorganisms were discovered by the English physician David Bruce in 1886 in preparations of human cadaveric spleen. (Hence the names of the pathogenic microorganism, *Brucella,* and the disease due to these causative agents, brucellosis.)

The causative agent of brucellosis in goats, *B. melitensis,* is the most pathogenic to humans.

Brucella is sufficiently stable in the environment. In soil it survives for 3 months, in milk for 10 days, in sheep cheese to 45 days, and in wool to 3 months. It is sensitive to high temperature and boiling kills it instantaneously; heating to 60 °C for 30 minutes is also detrimental. The microorganisms are sensitive to disinfectants (3 per cent lysol solution, 5 per cent solution of lime chloride).

Epidemiology. Brucellosis is a typical zoonosis because the reservoir of infection are domestic animals. It has already been said that goats and sheep are the commonest source of infection in man. Cattle and swine are less important. If healthy and diseased animals of various species are raised together, brucella migrates from goats to cattle and other animals. Outbreaks of the disease in man thus become possible.

Cats, dogs, camels, deer, horses are a secondary reservoir of the infection.

A diseased man presents no danger to the surrounding people.

Diseased animals shed the pathogenic microorganisms with amniotic fluid, abortus, urine, dung, and milk. Besides, the organisms are contained in the blood and flesh of the animals. The infection is

usually transmitted by direct contact with the animal excrements and objects infected by these excrements. Humans get infected when taking care of the animals, during milking, shearing, etc. Another route of infection transmission is through infected foods, such as raw milk, curds, sheep cheese prepared from raw milk, and also through meat of the diseased animal. There is still another, although rare, route of infection transmission: by air-borne droplets. Humans get infected during processing wool of the diseased animals. Since brucella survives for a long time in water, water-borne infection should not be excluded either.

Brucellosis is an occupational disease of animal breeders and farm workers. Immunity, that is produced in those who sustained the disease, is unstable.

The highest incidence of the disease is during the spring and summer. The first wave of morbidity is seen in the early spring. It is associated with bearing the young and miscarriages. The infection is spread by direct contact due to intensive liberation of the organisms with miscarriages, placenta, amniotic fluid, and the like. Another wave of seasonal morbidity occurs during maximum lactation in domestic animals; the main mechanism is alimentary. The incidence of brucellosis among the workers of slaughterhouses and meat processing plants coincides with the time of mass-scale slaughter of cattle.

Pathogenesis. When the pathogenic organism gets inside a human through a damaged skin or mucosa, it passes with the lymph to regional lymph nodes where it multiplies during the entire incubation period. By the moment when the disease becomes clinically manifest, brucella enters the blood and is carried to various organs and systems: the liver, spleen, bone marrow, and the lymph nodes. Secondary foci of infection thus develop. In a considerable number of persons the acquired immunity does not ensure elimination of the causative agent. Retention and multiplication of brucella in the infection focus, repeated release of the organisms into the blood, and endotoxaemia account for the sensitization of the person to various allergens. If untreated, the disease converts into its chronic form with periodic exacerbation and remissions.

Allergic changes are manifested by systemic lesion of the vessels, inflammation in the organs, arthritis, fibrositis, etc.

Clinical picture. The incubation period lasts for 2-3 weeks, with variation from one week to two months. The clinical manifestations of brucellosis are varied. The disease is sometimes asymptomatic and can only be diagnosed in the laboratory. Acute brucellosis (lasting to

3 months from the onset of the disease), subacute (from 3 to 6 months), chronic brucellosis (longer than 6 months) and residual phenomena following clinical recovery are distinguished.

According to severity, the disease is classed as mild, moderate and severe. An acute form of brucellosis often begins with a prodromal period. The patient complains of malaise, lassitude, depression, deranged sleep, lumbar pain, myalgia and arthralgia, chills. The prodromal period lasts from several days to a few weeks. The period of precursors is followed by a manifest clinical picture of brucellosis. The body temperature suddenly rises to hyperpyrexia. The elevation of temperature is attended by chills. The fever then lessens and sweating is profuse. Despite fever, the patient's general condition remains normal and his working capacity is preserved. The patient then complains of rapid fatigue, headache, irritability, transient pain in some large joints. Fever can be undulant, remittent, intermittent, or, less frequently, continuous.

Lymph nodes, usually submandibular and cervical, less frequently axillary and inguinal lymph nodes are enlarged in some patients. The spleen and liver are enlarged from the first days of fever; the condition persists for a long time. These organs become firm.

Among permanent symptoms of brucellosis in man is pain. By the end of the second week of the disease the patient develops pain in some large joints. Pain comes in attacks (undulant). It is due to arthritis and periarthritis, periostitis, bursitis, myositis, fibrositis, cellusitis, etc.

Headache and pallor are due to the lesion of the central nervous system. Excitability and whining are characteristic. Leucopenia ($3 \times 10^9/1$) with relative lymphocytosis, aneosinophilia, neutropenia, thrombocytopenia and high ESR are seen.

Late treatment of patients with weak reactivity facilitates the transition of the disease to its subacute and chronic forms.

Subacute brucellosis, in addition to the mentioned symptoms, is also characterized by focal allergic lesions in the form of arthritis, neuritis, plexitis, etc.

Subacute brucellosis can gradually transform into chronic brucellosis which is characterized by a further reconstruction of allergic response with involvement of other organs and systems. The body temperature is usually subfebrile or normal during weeks and months (remissions). The chronic form of the disease is usually characterized by stable changes in the locomotorium (arthritis, bursitis, tendovaginitis, periostitis, perichondritis) and in the nervous system (radiculitis, ischioradiculitis, plexitis, neuralgia). The genital

system is also involved: orchitis (inflammation of the testes), orchiepididymitis (inflammation of the testes and the epididymis) in males and oophoritis (inflammation of the ovaries and the tubes), endometritis, and abnormal menstrual cycle in women.

Chronic brucellosis proceeds with relapses and remissions and can last 2-3 years.

After the patient recovers, residual phenomena are possible: pain in the joints and muscles, headache, irritability, organic changes in the locomotorium with deformation of the joints, etc.

The clinical picture of the disease has lately somewhat changed. Severe forms of brucellosis are rare.

Complications. The commonest complications are orchitis and epididymitis, salpingitis and oophoritis, bursitis, pneumonia, acute and subacute endocarditis, plexitis and neuritis of the peripheral nerves, etc. *

Diagnosis. The high variability of the symptoms complicates the diagnosis of brucellosis. A properly collected epidemiologic anamnesis and laboratory studies help establish a correct diagnosis. Isolation of brucella from the blood, bone marrow, urine, and the lymph nodes is diagnostically decisive although these studies take much time. Blood cultures are inoculated with 5-10 ml blood specimens taken from the ulnar vein of patients before the antibiotic therapy is started. It is recommended to cultivate specimens of blood, bone marrow and lymph nodes of patients with chronic brucellosis during exacerbation before treatment begins (test for the presence of the L forms of *Brucella).* The result is ready only in 5-10 days, and sometimes in 29-30 days. Serologic tests, the immunofluorescent method, Coombs' test, direct haemagglutination test, and intracutaneous allergic test are used for serologic diagnosis of brucellosis. Wright and Huddleson tests are positive beginning with the 8-9th day of the disease, while the Burnet test in 7-8 days and later. A specimen of blood taken from the finger or the vein (1-2 ml) is tested (Wright's reaction) and result is considered positive with serum dilution of 1:200 and more. The Huddleson test can be carried out at patient's bedside (1 ml of blood). But this reaction is qualitative and the agglutination titres remain unknown. The test is suitable for screening of population before prophylactic vaccination.

The reaction of direct haemagglutination is more specific. It is positive with the dilution of 1:100.

The Burnet intracutaneous test is performed after the 10th day of the disease. Brucellin is injected into the skin on the palmar surface of the middle third of the forearm. A painful oedema develops in

24-48 hours (positive test). The size of the oedema is measured: if the oedema is from 1 to 3 cm in diameter, the reaction is weakly positive, if 4-6 cm-positive, and greater than 6 cm-highly positive.

Coombs' test is used in chronic forms of infection. The reaction is based on the detection of incomplete antibodies using antiglobulin serum.

The luminescent serologic test consists in applying a fixed smear of labelled serum in the working dilution. The smear is examined in a luminescent microscope.

Treatment. Patients with acute brucellosis and exacerbated chronic brucellosis should be taken to hospital.

Antibiotics are given to patients with acute, subacute and exacerbated chronic brucellosis with signs of marked toxaemia and high fever. The tetracyclines and terramycin are most efficacious. They are given in a dose of 0.3 g 4 times a day. Chloramphenicol (0.5 g 4 times a day) and other antibiotics are also useful. The mentioned preparations are given per os for 5-7 days. The course is repeated at a 5-day interval. Vaccine therapy is indicated after 2-3 courses. The vaccine should preferably be given intravenously. In the presence of contraindications it can be given intracutaneously.

The dose of the vaccine depends on the patient's condition, the route of administration, allergization of the patient (the result of the Burnet test), and on the response to the previous vaccination. In order to lessen the response, the vaccine is administered intravenously in two steps. The daily dose of the vaccine is administered not by a single injection but in two portions at a 90-120 minute interval. From 7 to 10 administrations are necessary at 3-5 day intervals between the injections. The sensitivity is determined by administering 1-2 million microbes at 2-3 day intervals, and then subsequently 5, 10,25, 75, 100 and 125 million microbes. In 2-3 hours following the administration, the patient develops chill, arthralgia intensifies, and the body temperature rises to 38-40 °C in 6-8 hours. The temperature normalizes in 1-2 days, the patient sweats profusely, the liver and the spleen are enlarged. Subsequent administration of the vaccine is attended by desensitization of the body, lessening of pain, fall of body temperature, and improvement of the patient's condition.

Especially severe cases of brucellosis with involvement of the joints, the central and peripheral nervous system, orchitis, etc., are treated with prednisolone and prednisone (in addition to antibiotics), given in a dose of 20-30 mg for 4-6 days. The corticosteroid therapy is combined with butadione and other anti-inflammatory preparations. Symptomatic treatment should also be given: invigorating

measures, preparations improving appetite, vitamins B and ascorbic acid, cardiacs and analgesics. To release arthralgia, 3, 5 or 10 ml of a 0.25 per cent novocaine solution are injected intravenously.

Physiotherapy is widely used in brucellosis. Residual phenomena should be corrected by medical exercises and massage. Health-resort therapy is indicated in 6 months after recovery.

Prevention and control. Measures to prevent brucellosis in humans should be directed at eradication of the infection among agricultural animals and decontamination of environmental objects, foods and raw materials of animal origin, and protection of people against contamination. The intracutaneous Burnet test and serologic reactions should be performed in areas where brucellosis cases are reported in order to reveal timely the diseased animals. People should be protected by taking general sanitary measures and also by using means of individual protection. These include observation of disinfection requirements at animal farms and in industry where animal materials are processed; observation of sanitary requirements during slaughtering the diseased animals with subsequent disinfection of enclosures, equipment, etc.; observation of rules for handling animals, and provision of means for individual protection of the personnel (overalls, rubber gloves, special footware, aprons, etc.). The workers must be provided with detergents, disinfectants, hot water, and the like.

Materials obtained from diseased animals should be decontaminated: milk should be boiled or pasteurized, dairy products should be prepared only from pasteurized or boiled milk. Meat should be treated thermally. Sheep cheese should be cured for 60 days.

Prophylactic vaccination is necessary in endemic areas. Quarantines are also necessary to prevent the infection spread. In order to prevent brucellosis in humans, planned vaccinations (revaccinations) should be performed in people who are exposed occupationally to the risk of infection with goat brucellosis.

Single epicutaneous vaccination, and revaccination in 8-12 months (also epicutaneously) should be carried out. Vaccinated and revaccinated are people with negative serologic and allergic tests for brucellosis at the age over 18 years, and also people to whom vaccination is not contraindicated.

Dry live vaccine *(B. abortus)* is used. Vaccination and revaccination are performed 1-2 months before hiring for jobs associated with possible danger of infection, before intensive seasonal work begins (sheep shearing, mass-scale slaughtering, etc.). Persons exposed to the danger of brucellosis infection (animal breeders, slaughterhouse

workers, etc.) should be observed regularly in outpatient conditions. The observation includes inspection by the general therapist and laboratory testing.

Health education of population is necessary in areas where brucellosis cases are reported.

Measures in the focus. Patients with acute brucellosis are not dangerous for the surrounding but they should nevertheless be treated in hospital. Those who sustained brucellosis should be regularly examined in outpatient conditions for 2 years after recovery.

Leptospirosis

Aetiology. The causative agents of leptospirosis belong to the family of *Spirochetaceae*, the genus *Leptospira. Leptospira* contains two complexes: *interrogans* and *biflexa.* Each complex has antigenic variations, serovars. Serotypes with common antigens are arranged in serogroups: *Icterohaemorrhagiae, Autumnalis, Canicola, Australis, Pyrogenes, Javanica, Pomona, Ballum, Cynopteri, Celledoni, Semaranga, Andamana.*

Leptospiras survive in moist environment. In water bodies they remain viable for 30 days and more, in soil for 3 months, on foods for several days. Leptospiras withstand low temperatures but are sensitive to high temperature and absence of moisture. Boiling kills them instantaneously.

Epidemiology. The main reservoir of the infection are roddents: common rats, voles, harvest mice, etc. Another source of infection are leptospirosis cattle, swines, horses, sheep, goats, dogs, and also clinically recovered animals. Human patients are practically safe for the surrounding people. Natural, anthropurgic, and mixed foci of infection are distinguished.

Natural foci of leptospirosis usually occur in the vicinity of rivers, lakes, swamps and moist soils. The infection is transmitted from roddents (which are chronic carriers of the infection) to humans by direct contact and through water or food during agricultural work, fishing, picking mushrooms, drinking water from occasional open sources of water, bathing, walking barefoot, or eating food contaminated with the leptospiras.

Leptospirosis incidence rises in the end of summer and early autumn.

Cattle, hogs, dogs, and rats are the reservoir of infection in the anthropurgic foci. Poultry and wild birds can also be involved in

epizootics. Leptospirosis usually runs a severe course in cattle, especially in calves. In swines, leptospirosis is usually characterized by mild clinical symptoms. The animals shed leptospiras in their urine. Leptospira carrier state can persist from a month to a year and longer.

The main factor transmitting the infection from the diseased animals to man is water. Humans (especially persons with an empty stomach) get infected by drinking contaminated water, or when bathing in an open water body infected with the animal excrements. Leptospira penetrates through the mucosa of the mouth, eyes, nose, and through abraded skin during bathing, when working barefoot on rice plantation, etc. Less frequently man is infected by drinking milk of diseased animals or by ingesting food contaminated with the infected urine. Man is also infected by contact with the infected objects, when taking care of diseased animals, during slaughtering diseased animals, and processing their tissues. Common brown rats are the source of infection in large cities, especially in sea ports. Deratizators and sanitary workers are especially exposed to the danger of infection. Outbreaks and sporadic infection cases are possible among stevedores and miners.

In anthropurgic foci, leptospirosis occurs during the whole year in the form of sporadic cases.

Pathogenesis. Motility of leptospiras helps them overcome the defense barriers and enter the blood circulating system. Blood carries them to various organs, mainly to the liver, kidneys, spleen, lungs, etc. This process is actually the incubation period. The onset of the disease is characterized by re-entry of the decayed leptospira and their metabolites into the blood which carries them to various organs and tissues, especially to the kidneys, the adrenal glands, the liver, and the meninges. Beginning with the second week of the disease, in connection with marked toxaemia, the capillaries are damaged, their permeability increases to cause the haemorrhagic syndrome (bleeding into the internal organs and the skin). Lesion of the liver cells and, to a lesser degree, red cell haemolysis due to the effect of leptospiral haemolysins, evoke jaundice. Complications in the kidneys, the nervous system and the eyes can develop during this period. Leptospiras are liberated into the environment with urine for several weeks. They can be detected also in the liquor. Recovery begins with the production of immunity to the specific serotype.

Clinical picture. The incubation period varies from 6 to 20 days (usually from 7 to 12 days). Anicteric and icteric forms of leptospirosis are differentiated. The onset of the disease is sudden and

acute. The patient complains of chill, his temperature quickly rises to 38-40 °C. The common symptoms are weakness, lassitude, persistent headache, insomnia, myalgia (especially in the calves and the neck). The face is hyperaemic, the scleral vessels injected, with haemorrhage into the sclera, the tongue is coated and dry. Scarlatina-like and measles-like rash develops in 4-5 days. Roseolas and petechiae are less frequent (usually in severe cases). Rash appears instantaneously on the chest, abdomen and the limbs. The liver is enlarged and tender to palpation. Some patients develop the haemorrhagic syndrome at the beginning of the second week: petechiae on the skin, ecchymosis at the sites of injection, nasal, gastric, intestinal, and uterine haemorrhages, blood spitting, haemorrhage in the brain, myocardium and other organs. The platelet count is low.

Symptoms of nephritis can develop. In mild cases, the urine of patients contains small amounts of protein, single red cells, white cells, and hyaline casts. In anicteric cases, jaundice is either absent or mild. Severe disease is characterized by high body temperature that persists for 6-10 days. In the icteric form of the disease, the sclera and then the skin turn yellow in 3-5 days of the disease. The urine is also dark. The conjugated bilirubin of blood is high. After jaundice develops, the body temperature decreases critically or by an accelerated lysis. The patient's condition improves. Oliguria develops from the very first days of the disease, and becomes especially marked in 7-10 days. The protein level in the urine is high; the quantity of red and white cells, of hyaline and granular casts is also increased. Rest nitrogen of blood increases too. If the disease runs a benign course and treatment begins in due time, oliguria is superseded by polyuria in the end of the second week; the pathological changes in the urine gradually subside. If the course of the disease is unfavourable, death is possible due to renal failure and uraemia.

Haematologic changes include hypochromic anaemia, low haemoglobin (to 64-80 g/1), thrombocytopenia, leucocytosis (10-12 x 10^9/1), neutrophilosis with a shift to the left, aneosinophilia, and lymphopenia; ESR accelerates to 50-60 mm/h. In 5-6 days after normalization of body temperature, some patients develop an exacerbation. Fever during the relapse lasts from 3 to 9 days.

Complications. Severe leptospirosis can be complicated by renal failure, acute hepatorenal failure, acute cardiovascular failure, haemorrhage, myocarditis, meningitis, encephalitis, pneumonia, otitis, and diseases of the eye.

Diagnosis. The diagnosis is based on clinical and epidemiologic

findings. It is necessary to examine blood taken from the ulnar vein during the first 4-5 days of the disease; 2 ml should be used for microscopy, and 4 ml for cultivating a blood culture on a water-serum medium (distilled water and rabbit serum).

Nutrient medium (5 ml) should preferably be inoculated with the patient's blood straight at the bedside. From 5 to 10 drops of the material should be added to each test tube. A 4-ml specimen of blood is defibrinated and injected to guinea pigs and 2-3 week-old rabbits (0.5-2 ml).

Cerebrospinal fluid is examined in the presence of indications. The urine is taken in sterile conditions (0.5-1 ml) on the second week of the disease and later. Nutrient media are inoculated with the urine in 3-4 test tubes. Blood (2 ml) is tested in the laboratory on the 7-8th day: microscopic agglutination and lysis reactions are carried out with live leptospira cultures; the complement fixation test is also performed. Paired serums should be tested because the specific antibodies persist in convalescents from few months to several years. Direct haemagglutination test and the immunofluorescent method are also used.

Treatment. Treatment should be early and complex. Mild forms can be treated symptomatically and by proper diet and vitamins. Mild and moderate diseases should be treated with penicillin (3 000000-4000000 U daily intramuscularly until body temperature normalizes and then for 2-3 days more). Detoxication therapy is also necessary. Severe forms should be treated with penicillin in doses to 10-16 million U daily. Polyvalent leptospiral immunoglobulin containing antibodies to common leptospiras, that are pathogenic to man, should also be administered. Immunoglobulin is first tested for tolerance by the patient and then administered intramuscularly in doses of 3 ml for children from 8 to 13 years of age, and 5-10 ml for older children and adults. Treatment continues for 3 days. In the presence of symptoms of cardiovascular insufficiency, cardiotonics and glucocorticoids are prescribed. In cases with acute renal failure and oliguria, a 20 per cent mannitol solution (300 ml), a 20 per cent glucose solution (500 ml), and a 4 per cent sodium bicarbonate solution (150-200 ml) should be administered by drip infusion in two sessions. The anuria stage of acute renal failure should be treated with haemodialysis (artificial kidney apparatus).

Prevention and control. Prophylactic measures should be taken against all epidemic factors: the source of infection, transmission routes, and susceptibility of population.

Health care and veterinary supervision systems are responsible for

the detection and isolation of diseased animals and leptospira carriers, for vaccination of the animals in the anthropurgic foci.

The condition of the water supply system should be supervised. Sources of drinking water should be protected against contamination with animal excrements. If leptospirosis cases are revealed among people or animals, it is prohibited to use water from open reservoirs for drinking or other domestic needs if these water bodies were the watering place of the diseased animals. Water from these open bodies can be used again only in 3-4 weeks after elimination of the cause of infection. If water is suspected for being infected with leptospira, it can be used only after boiling.

All agricultural workers should be instructed how to prevent abrasion or other minor damage to the skin of the legs and arms (wearing rubber boots, gloves, etc.).

Swamps should be irrigated in areas where leptospirosis is revealed. Deratization should be carried out in cities and towns.

Milk of leptospirosis cattle containing the yellow pigment or traces of blood should be decontaminated by boiling and then used for feeding animals. In the absence of visible changes, boiled milk can be used as food. When milking and taking care of leptospirosis cattle, rules of individual protection should be observed. Animals may not be slaughtered during the acute period of the disease. If any changes are found in the organs of slaughtered animals (jaundice, haemorrhage), meat should be used for technical purposes only or after adequate thermal processing. Hides of the dead or slaughtered animals should be processed with observation of all precautions and then used without any restrictions after drying for 10 days.

All persons habitating the areas where there is a danger of leptospirosis infection should be immunized with specific inactivated vaccine; the vaccine is administered in two doses-2 and 2.5 ml (for adults) with a 7-10 day interval between the injections. Children aged over 7 years can be vaccinated too. Revaccination with a single 2 ml dose is necessary in 12 months.

Vaccination produces immunity against the commonest pathogenic agents. An attenuated leptospiral vaccine has been recently developed.

Measures in the focus. Each detected or suspected leptospirosis case should be reported to the higher authority in a given locality. All patients should be registered and hospitalized. Disinfection measures are the same as for intestinal infections.

Review Problems

1. Patient B., female, developed typhoid fever on Nov. 10. She had been married on Oct. 30. According to medical information sendee, 4 other cases of typhoid fever were reported from different districts of the city; all those patients were present at the wedding party on Oct. 30. They developed the disease on Nov. 9, 11, and 12. Salads for the wedding party were prepared by a person who had had typhoid fever in the past. Before serving, the salads (containing meat and fish) were kept at room temperature for 5 hours.

What should be undertaken to reveal the source of infection? Describe the rules of taking specimens, their delivery to the laboratory, and specify the terms within which the results can be attained. Indicate the mechanism by which the diseased were infected and specify the measures to be taken in the infection focus in order to prevent further spread of the infection.

2. What is substantial for differentia! diagnosis of typhoid fever and paratyphoids A and B? What laboratory methods should be used for the purpose, and what are the terms within which the examinations should be carried out? What is decisive for the time of taking specimens of material for laboratory studies in typhoid and paratyphoid patients?

3. A routine examination of water from an open water body (river *K* in the town M) revealed the presence of El Tor cholera vibrio. At the same time, six patients suspected for cholera were hospitalized. They are residents of different towns. They bathed in the same river *K* and were fishing two days before the onset of the disease. Sewage is discarded into the river upstream.

What anti-epidemic measures should be taken in the town M in connection with the detection of the cholera vibrio in the river *K"!* What laboratory examinations should be carried out in order to verify the diagnosis? Describe the rules of taking material specimens, and specify the terms and conditions for delivery of the material to the bacteriologic laboratory and the time of presumptive and final answer?

Establish the cause and route of infection spread, plan the necessary anti-epidemic measures in order to localize and eliminate the cholera focus.

4. Subject A., a railway worker, was found dead near a railway line. On the second and third day after the funeral party 4 persons were hospitalized with complaints of weakness, impaired vision (indistinct outlines of objects, especially of near ones, diplopia), dry mouth, nose and throat, thirst, difficult swallowing, compression of the chest, and oedema. The body temperature was normal.

Epidemiologic study established that the dead had taken home-smoked ham for his lunch. None of the family had eaten this ham, but his mates ate it at the funeral repast and developed the unknown disease.

What is a suggested diagnosis? What material should be sent to the laboratory for examination? In connection with a suggested diagnosis, what treatment is necessary? Indicate the mechanism by which the patients were infected and the measures that should be taken in the focus of infection.

5. 22 children with dysentery were hospitalized within two days from various groups of a kindergarten. Epidemiologic examination of the focus

revealed that children had eaten vegetable salad on the day before the first cases were revealed. The salad was prepared on the eve of the day of the suspected infection. The cook reported that she had liquid stools but did not attend her doctor. Indicate the measures that are necessary to verify the source of infection, the mechanism of infection, and the measures that should be taken in the focus of infection.

6. From a sanatorium for rheumatic children, 32 (out of 85 children) were hospitalized for salmonellosis within 6 hours. Epidemiologic investigation established that warm milk (after boiling) was placed to cool in a refrigerator on a shelf beneath frozen meat. As the meat defrosted, liquid dropped into the milk which children later took for breakfast.

Indicate the cause and mechanism of the outbreak. What measures are necessary in the sanatorium? Name the anti-epidemic measures that are necessary in the focus of infection in order to prevent the infection spread; specify the conditions for discharge from hospital of the recovered children and for their observation in the sanatorium.

7. Patient Z., female, a nurse at a day nursery, was hospitalized on Sept. 21 for viral hepatitis. Her last working day was 19th of September.

Name the clinical forms of viral hepatitis, its periods and the main symptoms. What period of the disease is the most dangerous for the surrounding? What are the mechanisms of infection transmission, and what measures are necessary to carry out at the patient's residence and the day nursery?

Respiratory Infections

Influenza

Aetiology. The disease is caused by the virus belonging to the family *Orthomyxoviridae.* Three serotypes of the influenza virus are distinguished: A, B, and C. Virus A is of greatest epidemiologic danger. Its antigen structure is constantly changing. Four subtypes of virus A have been established: AO, Al, A2 and A3.

Virus B has a more stable antigen structure. Virus C is the most stable influenza virus.

Two various antigens are contained in the outer envelope of the influenza virus: haemagglutinin (H) and neuraminidase (N). Haemagglutinin (H) has four independent subtypes: HO, HI, H2 and H3, which relate to viruses AO, Al, A2 and A3, respectively.

The other antigen of the influenza virus of the envelope, neuraminidase (N), has two subtypes: Nl (common for viruses AO and Al) and N2 (common for viruses A2 and A3). Depending on the presence of particular surface antigens, influenza A virus is designated **A(HONl), A(H1N1),** A(H2N3), A(H3N2), etc. Influenza

viruses are intracellular parasites. The virus is unstable in the environment, is rapidly destroyed on heating, drying, and by various disinfectants; it withstands frosting.

Influenza viruses are cultivated and isolated on chick embryo. Among laboratory animals, hamsters, mice and pole cats are most susceptible to the influenza virus.

Epidemiology. Diseased humans, especially during the first days of the disease, are the main source of infection. The virus is released from the patient during sneezing, coughing and talking till the 4-7th day of the disease. If influenza is complicated by pneumonia, the virus is liberated for 10-12 days. Patients with abortive and asymptomatic diseases are dangerous for the surrounding, because the quantity of such patients is much greater than of patients with clinical symptoms, and they continue actively infecting people. Infection is transmitted by air-borne route in enclosures where an influenza patient is present.

Infection spread is facilitated by inadequate living conditions, overcrowding that promotes close contacts with the patient, inadequate labour conditions, intensive migration of population. Since the influenza virus is unstable in the external environment, fomites (dishes, toys, towels, etc.) are not substantially important. Influenza occurs as sporadic infections and epidemic outbreaks, pandemics. Influenza A epidemic is characterized by a rapid spread, which is due to generation of new antigenic variants of the virus. During an epidemic outbreak, the number of influenza cases and acute respiratory diseases increases 10-20 times. Within a short lapse of time (1-1$^1/_2$ months) residents of many cities and countries become involved (the sick rate from 30 to 40 per cent). People of almost all age groups are equally involved. The duration of circulation of all new virus A serotypes is 10-11 years. During this period, each serotype gives 3-4 antigenic variants, which, in turn, become the cause of new epidemic outbreaks of influenza every 2 or 3 years.

During the past seventy years, virus A changed its antigenic structure five times. One virus type superseded the other: A0-A1-A2-A3. Late in 1977, when cases with influenza A3 were still reported, a new influenza appeared due to serotype A(H1N1). Since the last pandemic caused by this serotype was in 1956, people aged under 25 years were mostly afflicted.

Stable immunity to serotype A(H1N1) in persons who sustained this infection in the past was thus discovered.

Epidemics due to virus B develop slowly and involve to 10-25 per

cent of population; they occur every 2 or 3 years. Virus C causes sporadic infections mostly among children.

The spread of influenza is thus promoted by the instability of the antigenic structure of virus A under the influence of immunity in those who sustained the disease in the past. The spread is also promoted by high natural susceptibility of population, by a considerable proportion of asymptomatic (abortive) forms of the disease, by the short-lasting incubation period, and by the easiness of infection transmission through the droplet mechanism. The influenza incidence increases during the autumn and winter, and also in the spring.

Pathogenesis. The portal of infection is mucosa of the upper airways. Columnar epithelium of the trachea is afflicted selectively. As the virus multiplies in the epithelium it causes its degeneration and necrosis. The underlying tissues are affected by oedema, the vessels become permeable to cause epistaxis, blood in the sputum, etc. Toxaemia evokes the lesion of the nervous and cardiovascular system. Suppressed immunity facilitates development of secondary complications due to exogenic and endogenic microorganisms; chronic diseases are exacerbated. Miltiplication of the virus is inhibited by interferon that is formed from the very first hours of the disease in the infected cells. By the end of the first week, the titre of the specific antibodies increases. The type-specific immunity after the sustained disease persists for 20 years.

Clinical picture. The incubation period lasts 1-2 days with variations from a few hours to 3 days.

Influenza can be mild, moderate and severe. The disease can have a typical or atypical clinical manifestations.

A typical influenza begins acutely with elevation of body temperature and chilliness. In 4-5 hours the body temperature can be as high as 38.7-40 °C. If the disease is mild, the body temperature can be subfebrile. The condition of the patient worsens. He complains of headache, mostly frontal and retro-ocular, which is accentuated by the movement of the eyes, pain in the muscles and bones, insomnia, cough, nasal obstruction, dry throat, sneezing, sweating, and weakness.

Examination reveals hyperaemic face and neck, and injected scleral vessels. There are also tachypnoea and arterial hypotension; the heart sounds are dull; the pulse is slow (disagrees with body temperature). Nosebleed is possible. Among the respiratory symptoms are catarrh of the upper airways: stuffy nose, sneezing, hoarse voice, dry cough. The fauces are hyperaemic, the tongue is coated.

Cough can persist in the young for 10-12 days, and in the elderly for longer time. The influenza virus and its toxins affect the peripheral nervous system and bone marrow, which is manifested by neuralgia, neuritis and symptoms of encephalitis.

If influenza is not aggravated by complications, fever persists for 2-4 days, less frequently 5 days, or it may be as short as 1 day.

A severe (toxic) form of influenza is characterized by marked symptoms of toxaemia: severe headache, hyperpyrexia (to 40 °C), dyspnoea, cyanosis, hypotension, weak and fast pulse, insomnia or somnolence, sometimes delirium, nausea, vomiting, loss of consciousness, muscular cramping, symptoms of meningitis; haemorrhages in the skin can develop. Severe forms of influenza usually occur during the first two weeks of an epidemic.

Influenza is characterized by specific leucopenia with relative lymphocytosis and a neutrophilic shift to the left, and aneosinophilia.

Complications. The chief complications are pneumonias due to the virus or secondary bacterial infection (pneumococci, staphylococci, haemolytic streptococci, etc.). Acute cardiovascular failure, laryngitis, tracheobronchitis, bronchitis, bronchiolitis, frontal sinusitis, maxillary sinusitis, otitis and various haemorrhages, from epistaxis to haemorrhagic oedema of the lungs, are also complications of influenza.

Diagnosis. It is not difficult to establish the diagnosis of influenza during an epidemic outbreak. During the interepidemic period, when the course of influenza is mild, it should be differentiated from other acute respiratory viral infections.

Influenza is characterized by an acute onset, marked toxaemia, mild catarrhal phenomena, and leucopenia.

A final and accurate diagnosis of influenza and other acute viral respiratory infections can be established in the laboratory by serologic, virologic and immunofluorescent methods. The first specimen of serum is taken not later than on the third day of the disease, the second not earlier than in three weeks. A four-fold increase in the titre is considered as a decisive diagnostic evidence. Serologic reactions are used to confirm the clinical diagnosis. The influenza virus can be isolated from the pharyngeal washings obtained during the first days of the disease or when the disease is in its full swing. The filtrate of the washings is mixed in the laboratory with a 2 per cent suspension of hen or guinea pig erythrocytes. The mixture is kept on ice for 20-30 minutes and the erythrocytes are precipitated by centrifuging. An isotonic sodium chloride solution and antibiotics are added to the precipitated erythrocytes with the

virus adsorbed on them. The obtained material is used to inoculate chick embryos, cell cultures, and experimental animals. The isolated pure virus culture is used for serologic identification of the virus type. The result is ready only in 72-96 hours.

The immunofluorescent method can confirm the diagnosis of influenza or differentiate it from other acute viral respiratory diseases. To that end, a smear is taken from the mucosa of the inferior concha (after preliminary cleaning of the nose from mucus and crusts). The cotton tampon with a smear is placed in a test tube containing 2-3 ml of physiological saline solution and delivered immediately to the laboratory. Fluorescent antibodies help detect the virus in 3-4 hours in the cells of columnar epithelium of the patient's nose. The disadvantage of this method is that it is impossible to identify the serotype of the circulating virus.

Treatment. Regardless of severity of the disease, the patient must keep bed until his body temperature normalizes and symptoms of toxaemia subside. Drinking of great amount of hot liquid (tea with lemon, jam or honey; warm milk) is recommended. Polyvitamins should be taken 3 times a day. If the nose is stuffy, a 2 per cent ephedrine (naphthyzine, or sanorine) solution should be instilled into the nose. Codeine, libexin preparations and steam inhalations are useful for cough. Analgin, amidopyrin, ascophen should be given to lessen headache and myalgia.

Anti-influenza donor immunoglobulin is an effective specific preparation. It is given in severe forms of influenza, preferably during the first days of the disease. Immunoglobulin should be given to children intramuscularly, 0.15-0.2 ml/kg body weight. Adults should be given 6 ml.

Influenza due to virus A should be treated with remantadine, which is effective only during the first 2 days. Remantadine is given as follows: 2 tablets (100 mg) three times after meals during the first day, 2 tablets 2 times a day during the 2nd and 3rd day, and 2 tablets (by one intake) on the 4th day.

Severe forms of influenza should be treated by repeated administrations of anti-influenza immunoglobulin, detoxicating fluids (isotonic sodium chloride solution, haemodez, polyglucin, rheopolyglucin), 800-1000 ml a day, with an obligatory administration of lasix, brinaldix (saluretics), or urea and mannitol.

Development of complications is an indication for antibiotic therapy.

Prevention and control. Live and inactivated vaccines are used for specific prophylaxis of influenza. Live anti-influenza vaccines are

produced for intranasal immunization of adult population (over 16 years of age) and for oral immunization of children aged over 1 year. Live vaccine is given by two doses at a three-week interval.

Prophylactic vaccination should be completed 1-2 months before the expected rise of the morbidity.

During an outbreak of influenza, endogenic interferon should be stimulated by various live vaccines (influenza, measles, poliomyelitis vaccine).

Human leucocytic interferon is indicated in the presence of a direct danger of infection with influenza virus. Interferon is given by insufflation (0.25 ml) or instillation (5 drops) of the preparation into each nostril twice a day.

Remantadine is also given to prevent influenza A. A tablet is given before night sleep for 5-30 days depending on the epidemic situation.

Anti-influenza immunoglobulin is used only for emergency prophylaxis in the focus of the disease (in paediatric hospitals, nurseries, sanatoria).

General hygiene is important for control of influenza spread. Adequate airing and intensive insolation of enclosures, using ultraviolet radiation (especially in children's and medical institutions), adequate washing of dishes in hot water, proper individual hygiene (washing hands, using separate dishes, towels, linen, etc.) are important prophylactic measures.

Patients with non-complicated influenza in the focus of infection should be isolated in home conditions. Patients with severe forms of the disease and complications, and also first patients with acute respiratory infections at closed children's institutions (sanatoria, children's homes, etc.) and in big families, should be hospitalized. The patients should be isolated until complete recovery.

Rooms where influenza patients are kept should be regularly aired and cleaned. Patients are given their individual towels and dishes. Persons who take care of influenza patients must wear masks (respirators). Contacts of patients with the rest of the family must be restricted. Asthenic infants (aged under 1 year) should be given anti-influenza immunoglobulin intramuscularly in a dose of 0.2 ml/kg body weight. Passive immunity lasts for 18-20 days.

After recovery of the patient, the room should be aired thoroughly and cleaned with soap-soda solution.

Especially strict sanitary and hygienic regimen must be ensured during epidemic in children's institutions, policlinics, hospitals, maternity houses, etc. Personnel of lying-in hospitals, children's medical and prophylactic institutions should wear respirators in

order to prevent infection and its spread. Rooms for isolation of influenza patients must be provided at hostels and other places where people live in close communities.

Children attending schools or preschool institutions should be isolated at home. If the disease is severe or home conditions are suboptimal, the patient should be hospitalized. After isolation of the patient from the rest of the group, the room should be aired properly and cleaned with a 0.5 per cent chloramine solution. The personnel must wear respirators. All healthy children must be examined every day in order to reveal timely new patients. The rooms must be treated with ultraviolet radiation when the children are out-of-doors.

Parainfluenza

Aetiology. The disease is caused by the virus belonging to the family of *Paramyxoviridae.* The parainfluenza virus contains RNA. Four serotypes are known that afflict humans. In laboratory conditions they are cultivated in cells of human embryo kidney. The viruses are unstable in the environment.

Epidemiology. The source of infection is a diseased human. Infection is transmitted by air-borne route. Infants are mostly affected, although adults can also develop the disease. A sufficiently stable immunity to a specific virus is produced in those who sustained the disease. Parainfluenza occurs during the whole year as sporadic infection, but seasonal rise in the morbidity (during the spring and the cold season) is also observed.

Pathogenesis. This is the same as in influenza.

Clinical picture. The incubation period lasts from 3 to 4 days with variations from 2 to 7 days. As a rule, the disease develops gradually and runs a sluggish course of 3-5 days. Catarrhal phenomena are not pronounced: cough, mild rhinorrhoea, less frequently subfebrile temperature. The patient complains of chilliness, headache, and slight fatigue. Hoarseness and chest pain are due to laryngitis (the most common symptom of parainfluenza) and laryngotracheitis. Nasal breathing is impeded. Serous nasal discharge gradually thickens and becomes mucous or mucopurulent due to secondary infection.

Children, and especially infants, develop severe laryngitis, which is often attended by the clinical symptoms of laryngeal stenosis and croup. The entire respiratory tract can be involved in parainfluenza. Bronchitis runs a severer course and is attended by lesion of small bronchi (bronchiolitis) and lung parenchyma (pneumonia).

Complications. Croup, pneumonia, acute tonsillitis, sinusitis, otitis and some other diseases develop; these usually occur in infants with rickets, anaemia and other disease due to secondary infection.

Diagnosis. As distinct from influenza, toxaemia is not manifest in parainfluenzal infection. Cardiovascular and nervous lesions are absent; involvement of the larynx and the lower airways is more pronounced. The diagnosis is verified in the laboratory by virologic tests (isolation of the parainfluenza virus from nasopharyngeal washings), serologic (blood serum tests) and immunofluorescence.

Treatment. Treatment is symptomatic. Anti-influenza immunoglobulin can be administered intramuscularly for therapeutic and prophylactic purposes. Antibiotics, sulpha drugs and inhalations should be given for complications.

Prophylaxis is the same as in influenza.

Adenovirus Infections

Aetiology. The causative agent belongs to the family of *Adenoviridae.* Among the 32 types of adenovirus isolated from man, types 3, 4, 7, 14, and 21 cause severe diseases. Type 8 causes keratoconjunctivitis in susceptible persons. Adenoviruses contain DNA. They are more stable in the environment than the influenza virus.

Epidemiology. The source of infection is a diseased person, who liberates adenoviruses with nasal, nasopharyngeal mucus, sputum, and conjunctival discharge during the first 5-6 days of the disease. Virus carriers are another source of infection. At later terms of the disease adenoviruses are shed with faeces. The infection is mainly transmitted by the air-borne route. Since the virus is stable in the environment, infection can spread by contact, food or water (bathing in swimming pools, ponds, lakes, etc.).

Infants aged from 6 months to 3 years are usually afflicted. Type-specific immunity is produced in convalescents.

Adenovirus infections occur as sporadic cases and epidemic outbreaks in children's institutions. The morbidity rises in the autumn and winter. Since the incubation period lasts from 3 to 12 days, outbreaks of adenoviral infection last longer than those of influenza.

Pathogenesis. Adenoviruses mostly affect respiratory mucosa, and less frequently conjunctiva. They can multiply in the intestinal mucosa as well. The lymphoid tissue of the regional lymph nodes is damaged, the vegetative nervous and endocrine systems are also

upset with subsequent vascular disorders (pallor, tachycardia).

Clinical picture. The incubation period lasts from 3 to 12 days, most frequently from 5 to 6 days. Acute adenoviral infection is characterized by the following clinical symptoms: rhinopharyngitis, rhinopharyngotonsillitis, rhinopharyngobronchitis, pharyngoconjunctival fever, membranous or follicular conjunctivitis, and pneumonia.

Rhinopharyngotonsillitis and rhinopharyngoconjunctivitis are more common. The incubation period lasts 5-6 days. The disease onset is usually gradual (2-3 days). The general symptoms are marked: malaise, chilliness, fever, headache. Local symptoms develop early: stuffy nose, hyperaemia of the fauces and the posterior wall of the pharynx, difficult swallowing, cough (dry or with expectoration of sputum) and chest pain. Some patients complain of abdominal pain, intestinal disorders, sometimes hepatic enlargement. Fever lasts from 2 to 7 days. Malaise and other general symptoms abate with normalization of body temperature, but catarrh can persist for 1-2 days more.

Acute rhinopharyngoconjunctivitis is characterized by a moderate impairment of the general condition, inflammation of the respiratory mucosa, the fauces, and the eyes (rhinitis, tonsillitis, pharyngitis, nasopharyngitis, laryngitis, tracheitis, bronchitis, conjunctivitis). The internal organs can be involved separately or in various combinations. Respiratory mucosa and the mucosa of the eyes can be involved simultaneously, but sometimes only pharyngitis or only conjunctivitis can develop.

Conjunctivitis lasts from several days to 2 weeks and longer. The eyelid mucosa and the eyeballs are injected, the conjunctiva can be affected with oedema and gentle granularity (catarrhal or follicular conjunctivitis). Membranous conjunctivitis is also possible. The eye secretion is meagre and serous in character. The cornea and the iris remain usually uninvolved. Among rare symptoms are nosebleed, nausea, vomiting and diarrhoea.

In addition to the mentioned symptoms, small round foci of corneal opacity develop in several days (to 2 weeks) after the onset of keratoconjunctivitis. The foci sometimes fuse together. The disease lasts 2-4 weeks and usually ends in complete recovery.

Pneumonia is the most severe form of adenoviral infection. It usually afflicts infants under 1 year of age. Pneumonia can occur with other forms of adenoviral infection. Pneumonia is usually focal (bronchopneumonia). The body temperature can remain high for 1-2 weeks and longer. Dyspnoea, cyanosis, and symptoms of toxaemia develop.

Complications. The condition can be complicated by otitis, sinusitis, pneumonia, pleuritis, arthritis, which are due to secondary infections. Adenoviral infection can be the cause of exacerbation of chronic diseases.

Diagnosis. Adenoviral infection is characterized by pronounced exudation; toxaemia is absent; conjunctivitis, especially membranous, is typical of the infection. An accurate diagnosis can be established only in the laboratory: virologically (isolation of the adenovirus in tissue culture), serologically, and by the immunofluorescent method.

Treatment. Symptomatic treatment is used: analgesics, cardiacs, antitussives. Severe cases should be treated with immunoglobulin, interferon, desoxyribonuclease. To prevent complications, the patient must remain in bed. Food must be adequate and rich in vitamins.

Prevention and control. Cases with severe course of the disease should only be hospitalized. The other patients should be isolated in home conditions till complete recovery. Chlorination of water in swimming pools is used to prevent outbreaks of the infection. For other preventive measures see "Influenza".

Smallpox (Variola)

Aetiology. The disease is due to DNA-containing virus belonging to the family of *Poxviridae*. The virus is highly stable in the environment. In dry pustules and exudates, that contaminate cloths and fomites, it can survive for days and weeks. Moreover, it can remain viable for years in dry pustular crusts.

The virus is stable to disinfectants. It can only be killed by an 8 per cent lysol, 3 per cent chloramine, or 2 per cent clarified lime chloride solutions.

Epidemiology. The source of infection is a diseased human. The patient becomes contagious from the very onset of the disease and remains so till the time when crusts fall off (6 weeks). The most dangerous period in this respect is from the 3rd to the 9th day of the disease. Patients with atypical clinical course of the disease (varioloid) are especially dangerous for the surrounding. The virus is dissipated with the respiratory secretions and skin elements. Dead people remain highly contagious for a long time.

The main route of infection transmission is air-borne. During sneezing, coughing, energetic talking, the virus is dissipated to a distance of more than 1 metre. Since the virus withstands the absence of moisture, it can be transmitted with dust as well. A person can be infected by direct contact with the diseased and by ingesting the

agent with food. The infection can be transmitted through contaminated fomites (bedding, clothing, toys, and the like).

People are highly vulnerable to smallpox. A stable immunity is produced in those who sustained the disease.

Since there are no non-human reservoirs of the smallpox virus, the World Health Organization undertook a program of worldwide eradication of this disease. Since 1980, smallpox has been completely eradicated thoughout the world.

Cases were reported of infection transmitted from monkeys, but this form of the disease is not transmitted from man to man, except in rare cases.

Pathogenesis. Respiratory mucosa of the upper airways and damaged skin are the portal of infection. During the incubation period the virus is accumulated in the lymph nodes and in lung tissues and is carried with blood to the skin, mucosa and other tissues. Multiplication of the virus in tissues gives rise to another wave of virusaemia which promotes diffuse specific affection of the skin and the mucosa.

Clinical picture. Smallpox can be mild, moderate and severe. The course of the disease can be divided into the incubation, initial period, rash, drying and falling off of the crusts and scabs. Moderately severe smallpox has an incubation period of 9-12 days, with extremes of 5-22 days.

The initial period is 3-4 days. The disease begins with a shaking chill. The body temperature abruptly rises to 40 and even 41 °C by the second day. Pulse and respiration rates are high. The patient develops weakness, nausea, vomiting, pain in the legs and in the lumbar region; sacral pain is also characteristic. Insomnia occurs. Delirium, loss of consciousness and cramping are possible. The face, conjunctiva and mucosa are hyperaemic. In 2-3 days of the disease, 30-40 per cent of patients develop prodromal or toxic rash. Polymorphous rash (like that in measles or scarlet fever) can be seen mainly on the face and limbs, the lower abdomen and the inner surfaces of the thighs, and also in the region of the chest muscles and the inner surface of the upper shoulder. Rash persists from several hours to 2 days, and then subsides. On the 3rd or 4th day, the body temperature drops substantially, and the patient feels relieved.

During the early eruption period the temperature normalizes. Small pink spots develop on the face, especially on the forehead, the haired part of the head, and the hands. The spots turn copper-red and form papules. During next 2-3 (less frequently 4-5) days, firm papules (nodules the size of a pea) develop on the whole trunk and

the mucosa of the soft palate and nasopharynx. Less frequently eruptions develop on the mucosa of the bronchi, conjunctiva, urethra, vagina and the rectum, which causes'severe pain.

In 2-3 days the nodules turn into vesicles in the same sequence: face, haired part of the head, the upper extremities, the trunk, and the lower extremities. The vesicles are pale pink, surrounded by red rim; they contain clear fluid. In 4-5 days the fluid turns cloudy, and by the 6th day (8-9th day of the disease) the vesicles turn into pustules (Plate III). The hyperaemic rim, oedema and infiltration around the pustules increase. Like vesicles, the pustules are multichamber, with a navel-like retraction in the centre. Formation of the pustules also begins with the face.

The body temperature rises with purulation to attain 39-40 °C and above, and at this level it is maintained for 3-5 days. The general condition of the patient worsens, consciousness is dimmed, pulse accelerates, dysrhythmia develops, arterial pressure drops. Pus and "* saliva issue from the mouth; odour is offensive. The face changes beyond recognition: the eyelids are oedematous, the eyes are closed, the nose and the lips are swollen. The patient fails to find a posture in which the tension in the skin can be released. Swallowing is painful, skin is itching. Eruptions in the mouth interfere with chewing and swallowing. If the nose and the airways are involved, the patient experiences difficulties in breathing. The leucocyte and neutrophil counts are high.

Crusts dry and fall off beginning with the 11-12th day. Itching intensifies and becomes tormenting. The body temperature normalizes within few days. Appetite appears, sleep normalizes and the recovery phase begins, which lasts 2-4 weeks and longer, depending on the severity of a particular case. Crusts and scabs fall off to leave red-brown spots, small scars and deep pits that remain for the rest of life.

In addition to this classic course of smallpox, the disease can run severer forms.

Confluent smallpox is characterized by confluence of the pustules to large bullae filled with pus. The body temperature rises to 41-42 °C. The patient's consciousness is dimmed, arterial pressure drops, tachycardia develops. Respiratory failure can cause asphyxia.

Haemorrhagic smallpox. This is a fulminating ("sledgehammer") form of smallpox. It can run two courses: haemorrhagic-pustulous, characterized by the symptoms of haemorrhagic diathesis during purulation (black smallpox), or purpura variolosa, a malignant smallpox, characterized by hyperaemia or large red spots. The

patient can die without the evidence of the typical skin lesions.

Smallpox can also run a modified and mild course, known as varioloid which is characterized by the absence of skin rash or fever. Toxaemia is mild, rash is meagre and it does not purulate (its evolution is terminated at the stage of vesicles). Rash develops on the 3rd or 4th day of the disease. After crusts have fallen off, no. pits remain on the skin (except hardly visible small scars). Fever persists only during the first 3-4 days and the second wave is absent. If rash is absent the patient feels a slight fever at the beginning of the disease, he complains of headache and sacral pain; rash can be only prodromal (typical smallpox rash is absent). If the disease runs a course without fever, scant papular or nodular rash develops that quickly subsides.

Complications. Encephalitis, meningoencephalitis and encephalomyelitis, iritis, keratitis, pneumonia with an outcome into lung abscess or gangrene of the lung and pleurisy.

Diagnosis. The diagnosis is based on clinical, epidemiologic findings, and the results of laboratory studies. Cases suspected for smallpox should be tested in the laboratory because the vaccinated can develop an atypical modified smallpox.

The contents of the vesicles, pustules, and also blood, crusts and scabs, can be examined in the laboratory.

Treatment. Treatment should be complex and depend on severity and the period of the disease. Specific therapy of smallpox is unknown. Early injections of immunoglobulin (1 ml/kg) are sometimes effective. Methisazone and other chemical preparations are used for therapeutic and prophylactic purposes. Antibiotics should be given parenterally for suppurative complications. Toxaemia can be decreased by intravenous infusions of haemodez, rheopolyglucin and polyglucin, a 5 per cent glucose solution, etc. Strophanthine, corglicon, adrenaline, cocarboxylase, and other preparations should be given for cardiovascular insufficiency.

Care of the smallpox patient is important. Mattresses should be convenient, inflatable cushions are recommended. Linen and cloths should be renewed frequently.

A 5-10 per cent potassium permanganate solution should be used to treat vesicles and pustules. Pruritus can be relieved by applying zinc oxide or menthol ointment; warm baths are recommended.

During the stage of pustular lesions of the alimentary mucosa, liquid or semiliquid food should be given. Pain during swallowing can be relieved by external application of a 0.5 per cent cocaine solution. The mouth should be rinsed with a 2 per cent sodium

hydrocarbonate solution or boric acid. The lips and the nasal mucosa should be lubricated with vaseline, persica or other oil. If the patient is critical, his mouth should be cleaned with a cotton tampon wetted with a solution of glycerol and boric acid. The eyes should be rinsed with a 1 per cent boric acid solution; a 20 per cent sulphacetamide solution should be instilled into the eyes.

In order to prevent secondary infection, it is necessary to cut patient's nails short to prevent scratching. The hands must be clean. It is recommended to bandage hands in children.

Prevention and control. Specific vaccination is decisive. At the present time, since smallpox has been eradicated globally, vaccination has been abolished from 1980. Although unlikely, cases of smallpox are possible, and prophylactic vaccination will then be important.

Dry smallpox vaccine is used for vaccination. It is dissolved in a 50 per cent glycerol solution immediately before administration. Vaccination is epicutaneous (on the lateral surface of the arm).

The vaccine can be administered by jet injection or by pricking. The immunity persists on an average for 5 years.

Diphtheria

Aetiology. This disease is produced by *Corynebacterium diphtheriae,* non-motile, gram-positive rod with a characteristic swelling at one end. Neisser-stained bacilli viewed microscopically by the fluorescent method demonstrate the presence of volutin grains (Babes-Erns granules) in their ends.

The genus *Corynebacterium diphtheriae* includes toxicogenic (causative agent of diphtheria) and non-toxicogenic corynebacteriae which do not cause diseases with clinical symptoms of diphtheria.

By their cultural biochemical and other properties *Corynebacteria diphtheriae* are classed into *mitis, gravis,* and *intermedins* groups. There is no correlation between the type of the causative agent and severity of the clinical symptoms of the disease. As the bacteria multiply they produce exotoxin which evokes the main clinical manifestations of the disease. *Corynebacteria diphtheriae* are stable in the environment. In the dry state they can survive on various objects, such as toys, dishes, linen, for many days; in milk and other foods they remain viable for 10-15 days. The bacteria are stable to low temperatures but are sensitive to high temperature. All disinfectants in common concentrations (3-5 per cent) kill the bacteria in 20-30 minutes.

Epidemiology. The source of infection is a diphtheria patient with clinically manifest symptoms or with an asymptomatic course of the disease, convalescents, and carriers of toxicogenic strains of the bacteria.

The infected person can be the source of infection during the last days of the incubation period and remain contagious for the entire duration of the disease. From the epidemiologic standpoint, the greatest danger are patients with mild and obliterated forms of the disease that now prevail and can be mistaken for lacunar or catarrhal tonsillitis, rhinitis, and the like.

Eradication of the agent from convalescents usually ends in 15-20 days, less frequently in 1-2 months.

Healthy carriers of toxicogenic strains of the bacteria are dangerous because their number is much greater than of diphtheria patients and convalescents.

The number of toxicogenic carriers depends on the morbidity; their number is much greater in the foci of diphtheria. Overcrowding and duration of contacts are important for the rate of carrier state. In closed collective bodies the number of carriers is 2-3 times greater than in other communities.

The main transmission mechanism is air-borne, because patients and carriers dissipate the bacteria with droplets of mucus during coughing, sneezing, crying, or talking. The infection can be transmitted through the fomites (dishes, toys), food (milk, cold dishes) that may be infected from a patient or a carrier.

Not all infected develop the disease; some become healthy carriers. The percentage of carriers in the focus of infection can be as high as 10. The presence of antitoxic immunity in vaccinated children does not exclude toxigenic carrier state, while disease does not develop.

Diphtheria occurs as sporadic infections with rises during the cold season.

Stable immunity is induced in those who sustained the disease.

Pathogenesis. The portal of entry is the mucosa of the upper airways. Less frequently the bacteria enter through the mucosa of the eyes, external genitalia or injured skin.

The bacteria multiply at the site of their entry and produce toxin. Local changes and general manifestations of the disease are associated with toxaemia of the patient.

Local changes in diphtheria are manifested by necrosis of the mucosa and formation of a fibrinous membrane that tightly adheres to the underlying tissue. Grey or yellow membrane consisting of fibrin, leucocytes, desquamated epithelium of the mucosa and

bacteria can be seen on the surface of inflamed mucosa. As the disease progresses, not only the multilayered epithelium of the faucial or pharyngeal mucosa is necrotized, but also the basement membrane. The thick fibrous membrane is detached from the underlying tissue with difficulty (diphtheritis inflammation). After the membrane is removed with a cotton tampon or a spatula, the tonsillar surface bleeds.

When the tracheal and bronchial mucosa (which is lined with a single layer of columnar epithelium) is involved, only the epithelial layer is usually necrotized and the formed membrane is therefore loosely adherent to the underlying tissue and is easily detachable (croupous inflammation). Regional lymph nodes are also involved.

The toxic form of diphtheria is attended by oedema of the facial and pharyngeal mucosa and by oedema of the neck connective tissue.

The diphtheria toxin affects first of all the nervous and cardiovascular system, the adrenal glands and the kidneys.

Clinical picture. The incubation period is from 2 to 10 days (usually 3-5 days). According to location of the primary lesion, the following clinical forms are distinguished: faucial diphtheria, laryngeal diphtheria, nasal diphtheria, and diphtheria of rare location (in the eye, ear, genitalia, skin, wound). Each of these forms is divided according to severity into mild and toxic forms. The toxic form is, in turn, subdivided into subtoxic, toxic (degrees I, II, III), hypertoxic and haemorrhagic.

Faucial diphtheria. The region of the tonsils is only involved (local form). If the membrane extends from the tonsils onto the mucosa of the palatine arches, uvula, fauces, the disease is diffuse. In the toxic form of the disease, in addition to the vast process in the fauces (Plate IV), involved also are the regional lymph nodes with toxic oedema of the neck cellular tissue; the condition is characterized by toxaemia. The localized form of diphtheria is most common. The catarrhal (without membrane) and insular (separate islands of membrane can be seen on the tonsils) subtypes are distinguished.

The onset of the disease is gradual, with moderate elevation of temperature to 38 °C, malaise, poor appetite, headache and slight pain during swallowing. The fauces become hyperaemic by the end of the first or second day. Greyish-white membrane of moderate thickness appears on one or, most frequently, both tonsils. When removed by a cotton tampon or a spatula, bleeding surface is exposed. Submandibular and anterior neck lymph nodes are slightly enlarged. Signs of toxaemia are absent. Timely treatment eliminates

the membrane in 2-5 days; the temperature normalizes.

The diffuse form of the disease usually begins acutely, the body temperature rises to 38.5-39 °C, the patient complains of chill, weakness, headache, and deranged sleep. The tonsils are oedematous and enlarged, with a thick grey membrane on both sides of the tonsils. It extends to the palatine arches, the soft palate and the nasopharynx. The regional lymph nodes are tender and enlarged to a slightly greater extent than in the localized form. The diffuse form of diphtheria is often the result of untreated local form. Timely specific treatment leads to recovery of the patient in 7-10 days.

Toxic form of faucial diphtheria. The onset of the toxic faucial diphtheria is usually fulminant: the body temperature rises to 39-40 °C, weakness is severe, the face is pallid and slightly oedematous. The heart sounds are dull; tachycardia is seen (140-160 beats per minute). The membrane is thick, greyish-white or brownish-grey; it covers the tonsils and extends to the soft and even hard palate. The nasopharynx and the nasal cavity can also be involved. Nasal discharge is serosanguineous. The breath is foul and sweetish. Oedema of the faucial mucosa and the membrane can mechanically impede respiration which becomes noisy and hoarse.

Changes in the upper neck lymph nodes and oedema of the neck are a specific symptom of toxic diphtheria. The extent of oedema of the subcutaneous fat corresponds to the degree of toxaemia; the following three degrees of toxic diphtheria are distinguished in this connection: degree I-oedema extends to the middle of the neck, degree II - oedema extends to the clavicle, and degree III - below the clavicle.

After specific treatment with antidiphtheria serum, the oedema and membrane disappear only in 5-10 days. Local symptoms of the disease subside.

Hypertoxic form is characterized by severe fulminant local process in the fauces, toxaemia attended by quickly developing cardiovascular failure. The patients often die in the first 4-5 days.

Laryngeal diphtheria (diphtheritic or true croup). The disease can be independent, or it can be superimposed upon faucial or nasal diphtheria (secondary croup). Three stages are distinguished in the course of laryngeal diphtheria.

The dysphonic stage of the disease begins with elevation of body temperature, malaise, and hoarseness. The patient complains of barking cough, which becomes' voiceless with progression of dysphonia to aphonia.

In 1-3 days, the disease transforms into the stenotic phase. Its early

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symptom is noisy respiration that resembles the sound of a saw cutting a wet wood. Another symptom of stenosis of the upper airways is retraction of the yielding parts of the chest during inspiration (due to rarefaction in the chest). Accessory muscles are involved in the respiration act. Duration of the stenotic stage varies from several hours to 2-3 days. If the patient is not given operative treatment (intubation, tracheostomy), asphyxia develops.

Asphyxia is characterized by marked anxiety of the child which is then followed by drowsiness, and cyanosis of the lips, the nose and the nails. Respiration is fast and shallow, pulse is weak and arrhythmic, arterial pressure decreases, the forehead is covered with cold sweat; convulsions develop and the patient dies of suffocation.

Nasal diphtheria. This disease is usually seen in infants. The body temperature is subfebrile or normal, nasal breathing is impeded, the nasal discharge is serosanguineous. Excoriation and fissures appear at the nostrils. Membranes and ulcers covered with crusts develop on the nasal mucosa. Toxaemia is mild.

Diphtheria of rare location occurs mostly in infants due to secondary faucial and nasal diphtheria.

The clinical picture of diphtheria has substantially changed in connection with vaccination of children. Faucial diphtheria often runs the same course as catarrhal or lacunar tonsillitis.

Complications. The common complications of diphtheria are insufficiency of the hypothalamic-pituitary system with collapse, myocarditis, peripheral paralysis and paresis. Complications usually develop after the toxic form of diphtheria.

Early and late myocardites are distinguished. Early myocarditis develops in 2-5 days after the onset of the disease and is characterized by tachycardia, dysrhythmia, transient elevation and then fall of arterial pressure (diastolic pressure is especially low). The pulse is small and thready; the skin is pallid; adynamia develops. The patient can die of collapse. Late circulatory disorders develop in the end of the first or on the second or third week of the disease.

Peripheral paralysis of the soft palate, accommodation, **and** polyneuritis can develop in 2-4 weeks after the onset of the disease. Muscles of the larynx and pharynx, and of the trunk and extremities are paralyzed less frequently.

Nephrosis is also among the complications. It is characterized by albuminuria, cylindruria, and the presence of single erythrocytes.

Diagnosis. The diagnosis is based on clinical, epidemiologic and laboratory findings.

The bacteriologic method is very important in identification of diphtheria. Sterile cotton tampons are used to take materials from the tonsils and the nasal mucosa (separate tampon for each smear). The material is taken in the morning before meals or at least 2 hours after meals.

When taking material for a tonsillar smear, it is necessary that the tampon should not touch the tongue, the buccal mucosa or the teeth. A spatula should therefore be used. In the presence of membranes, the material is taken at the border between the affected and healthy tissues. A nasal specimen is taken by one tampon which is first passed into one and then the other nostril. The tampons should be delivered to the laboratory not later than in three hours. If it takes longer time to deliver the material to the laboratory, tampons soaked in glycerol (5 per cent solution) should be used. The material should be protected from cooling. The label must indicate the name of the patient, the place from which the material is taken (fauces, nose, skin), and other necessary information.

The material taken from the fauces, tonsils, nose and other involved sites should be used to inoculate solid nutrient media (Clauberg's II, tellurite agar with blood) in Petri dishes. A preliminary result is ready in 1-2 days (colonies are studied in a binocular stereomicroscope; tests for toxicity and other rapid tests are performed). The final result can be obtained in three days.

Treatment. The main treatment is early administration of antidiphtheritic serum (diphtheria antitoxin). Before administering the serum, the patient should obligatory be tested for sensitivity to foreign protein (intracutaneous test). The dose of the serum depends on the clinical form of the disease, its severity, and duration. The severer the disease and the longer its duration, the greater the dose.

The first single dose for faucial diphtheria is 10 000-30 000 U; if the disease is diffuse, 30 000-40 000 U; and if its form is toxic, the dose should be 50000-120000 U. Injections should be repeated at 8-12 hour intervals, and then given every day, until signs of toxaemia disappear and the fauces are cleared of the membranes. Depending on severity of the disease, the daily dose for laryngeal diphtheria during the first day of the therapy should be from 15 000 to 30 000 U.

Administration of the diphtheria antitoxin should be combined with antibiotics: the tetracyclines and erythromycin, in common doses depending on the age of the patient (for seven days).

Detoxicating therapy of faucial diphtheria of the first and second degree includes haemodez and rheopolyglucin with a 10 per cent glucose solution (intravenous drip), the injection dose is 20-30 ml/kg.

Ascorbic acid, cocarboxylase, and insulin should be added to the solution. Diuretics should also be given.

Operative treatment (intubation and tracheostomy) is necessary in croup patients with severe stenosis, if conservative treatment fails (thermal procedures, steam inhalations, oxygen therapy, etc.), and if the second stage transforms into the third stage (asphyxia). Intubation consists in passing a tube into the lumen of the constricted larynx. In this time, diphtheritic croup is rare.

After abatement of acute symptoms, patients with mild diphtheria are allowed to leave their beds. Patients with toxic diphtheria should **be kept** in hospital regardless of the absence or presence of complications. Patients with subtoxic forms and toxaemia of the first degree should remain in bed for at least a month, with toxic diphtheria of the second degree, 40-45 days, and of the third degree, 50-60 days.

Prevention and control. Active immunization is the main prophylactic measure against diphtheria. Epidemiologic efficacy of immunization depends on timely vaccination of the entire children's population. Primary immunization in infants (in the absence of contraindications) should be conducted at the age of 3 months, using adsorbed vaccine (combined vaccine against pertussis, diphtheria, and tetanus).

The vaccination includes three intramuscular injections of 0.5 ml doses given at 45-day intervals.

The first revaccination should be done in 18-24 months after the vaccination (0.5 ml dose). The second and third revaccinations are given at the age of 9 and 16 years: 0.5 ml doses of the adsorbed diphtheria-tetanus anatoxin with decreased content of antigens (ADS-M toxoid). Subsequent revaccinations (0.5 ml) are given each decade, i. e., at the age of 26, 36, 46 and 56 years.

If a child develops a complication in response to the first vaccination with adsorbed diphtheria and tetanus toxoids and pertussis vaccine, next vaccination should be done with the ADS-M toxoid.

In order to prevent diphtheria spread, a constant epidemiologic supervision is necessary. It includes: control of the immunologic structure of population, control of circulating diphtheria agent among population; early detection of diphtheria cases, epidemiologic analysis and evaluation of efficacy of antidiphtheria measures.

The obtaining data are used as the basis for planning and carrying out of prophylactic and anti-epidemic measures. Control of the epidemiologic structure of population includes comparison of the

vaccination reports with the condition of immunity against diphtheria in children and adolescents. This condition is determined by the direct haemagglutination reaction with diphtheria diagnosticum.

In order to prevent formation of diphtheria foci, and for timely detection of patients and carriers, children should be inspected by a otorhinolaryngologist before formation of collective bodies (schools and the like). The screened patients should be treated.

Routes of infection spread should be disrupted by proper sanitary and hygienic measures, especially in children's institutions and food industry and catering.

Measures in the focus. Before the patient is taken to hospital, current disinfection should be done. A final disinfection with obligatory decontamination of the fomites and the bedding is necessary after hospitalization.

The main object of the anti-epidemic measures in the focus is timely detection of diphtheria patients, persons suspected for diphtheria, carriers of toxigenic bacteria, and persons with otorhinolaryngologic diseases that were not immunized against diphtheria.

The source of infection is revealed by questioning the patient and his contacts about the presence of diphtheria patients or persons suspected for diphtheria in their surroundings.

If a person who contacted a diphtheria patient or a carrier is revealed in the infection focus, he or she must be examined bacteriologically and observed for 7 days from the moment of isolation of the patient or the carrier, and after final disinfection.

If toxigenic bacteria of diphtheria are revealed after the first bacteriologic examination, the contacts should be given repeated examinations until no carriers are revealed any longer. Taking material from the fauces and the nose should be combined with examination of the contacts by otorhinolaryngologist.

Persons with various skin lesions (furuncles, pyoderma, excoriations, crusts, and the like) should also undergo bacteriologic examination.

In order to prevent diphtheria among contacts, preventive immunization should be performed in the focus of infection. Children in whom the term of vaccination has expired, adolescents under 16 years of age, and older persons, who were not immunized during the past decade and to whom vaccination is not contraindicated, should be immunized. The AD-M or ADS-M toxoids are used. They are given in a single 0.5 ml dose. All other contacts aged from 3 to 16 years should be examined (direct haemagglutination reaction). Per-

sons with titres lower than 0.03 U/ml (non-immune) should be immunized.

Children in schools and preschool institutions, and also workers of food industry and food catering establishments, should be admitted to their jobs only after obtaining a negative result of the test for the carrier state. Health education of population is also helpful.

Groups of children in which diphtheria cases or carriers were revealed, should be dismissed. All contacts (children and the personnel) should be tested for the carrier state by examining their smears (specimens taken from the fauces and the nose). The group can be re-collected after final disinfection if the results of testing are negative and if acute inflammatory processes in the fauces or the nasopharynx are absent. If laboratory examinations are infeasible, the children can gather in groups again in 7 days after isolation of the patient and in the absence of inflammation in the fauces or the nasopharynx. The children and the personnel should be observed for 7 days: two medical examinations during a day with obligatory thermometry. Taking material for bacteriologic studies should be combined with examination of all contacts by a otorhinolaryngologist.

Scarlet Fever

Aetiology. Scarlet fever is caused by beta-haemolytic streptococcus of group A.

In 1923-1925, George and Rowena Dick suggested an intracutaneous test with erythrogenic toxin to determine susceptibility of people to scarlet fever (the Dick test). If a person sustains scarlet fever, immunity is produced and the test is negative. Otherwise it is positive.

Streptococcus is stable in the environment. In can persist for a long time in foods, especially in foods containing milk and sugar. Dehydrated streptococci remain viable for six months. Disinfectants in common concentrations kill them in 15 minutes.

Epidemiology. The main source of infection is a scarlet fever patient, regardless of the severity of the disease. Patients are especially dangerous during the first days of the disease. The patient remains contagious during the entire course of the disease, and during the recovery phase in the presence of complications. Among the complications that are substantial for contagiosity of patients especially important are rhinitis, sinusitis, catarrh of the upper airways, otitis, etc. Abortive forms of the disease are especially important for the epidemiology of scarlet fever because they remain

unidentified. Patients with streptococcal tonsillitis and nasopharyngitis, and also healthy carriers can be the source of infection as well.

Penicillin rapidly eliminates streptococci from the patients.

The main route by which the infection is transmitted is air-borne. Direct contact with the patient or the fomites (dishes, toys, linen) or infected foods (milk, ice-cream, sweets) can also transmit the infection.

Infants from 2 to 7 years are especially susceptible to scarlet fever. Like in other air-borne infections, the morbidity rate varies with season. During the cold season the incidence of the disease increases. Scarlet fever is more common in countries with cold or temperate climate.

Pathogenesis. The portal of entry is the nasopharyngeal mucosa. Infection can also invade through wounds or burns. The cyclic course of the disease is due to the toxic, septic and allergic effect of the causative agent on the patient. When the agent multiplies at the site of entry and the regional lymph nodes, it evokes inflammatory and necrotic changes. The toxins and the products of tissue and microbial decay are absorbed in the blood of patients and dissipated in the entire body to cause toxaemia and allergic response. The body temperature is high, skin eruption develops. The cardiovascular and the central and vegetative nervous systems are also involved. Toxaemia lessens in 5 days due to development of immunity. Early septic complications develop in 3-5 days from the beginning of the disease. The complications can develop during later stages as well (in 15-25 days) due to the allergic condition of the patient and in the case of reinfection.

Clinical picture. The incubation period is 2-7 days; less frequently it can be as long as 12 days. The onset is fulminant: the body temperature rises to 38.5-39 °C; the patient vomits. Headache, lassitude, and painful swallowing are among other symptoms.

Examination of the fauces reveals scarlet hyperaemia of the soft palate, uvula and the tonsils; the tongue is coated.

The submandibular lymph nodes are tender to palpation. Typical punctate rash appears by the end of the first or on the second day of the disease. The elements of the rash are so close to one another (Plate V) that fuse into hyperaemic fields. The rash first involves the neck and the chest, then it extends over the entire body. The face is markedly hyperaemic. A pallid triangle of the skin around the mouth stands out (Filatov's symptom). The inner surface of the thighs, arms and the abdomen are severely affected with the rash which is intense and bright, especially in the skin folds. The skin blanches on pres-

sure and remains so for a considerable period of time in severe cases.

Catarrhal tonsillitis can in 3-4 days transform into lacunar, follicular or necrotic. The tongue clears and turns scarlet in 3-4 days of the disease. Its appearance is granular (raspberry tongue).

Haematologic changes: neutrophilic leucocytosis (from 10 to 30 x 10^9/1 and more, depending on the clinical form); eosinophilia beginning from the 3-4th day; accelerated ESR (20-50 mm/h). If the course of the disease is beneficial and complications are absent, the blood picture normalizes in 7-10 days. Leucocytosis persists in the presence of purulent complications.

The acute period lasts 5-7 days. As the rash resolves and body temperature decreases, tonsillitis gradually subsides too. By the end of the first or early in the second week, extensive desquamation begins (scaling off on the fingers and toes, and furfuraceous desquamation of the trunk).

The acute period is followed by apparent improvement of the subjective condition and normalization of temperature but the changes in the cardiovascular system become apparent. They manifest by slow pulse (bradycardia), a sudden fall of arterial pressure, enlargement of the heart, systolic murmur. The cardiovascular symptoms subside gradually within several weeks (sometimes in 6 months).

Severity of scarlet fever varies. The classic forms of the disease are differentiated into typical and atypical. The latter includes abortive or mild form of scarlet fever in which all its symptoms are non-pronounced while some of them (e.g. rash) can be absent altogether. A fulminant course is also atypical for scarlet fever. Toxaemia can be severe and the patient can die before development of typical symptoms of the disease.

Typical forms can be mild, moderate and severe. At the present time, severe forms of scarlet fever are rare but their possibility should be considered by the physician because they require intensive therapy. Severe forms of the disease can be attended by prevalent symptoms of toxaemia (toxic form) or local lesions (septic). The disease can be of the mixed form (toxicoseptic).

Signs of toxaemia develop rapidly in the toxic form of the disease: the body temperature is high, vomiting is recurrent, consciousness is dimmed; delirium, convulsions and meningeal symptoms develop; the heart sounds are dull, the pulse is fast, arterial pressure is low; catarrhal or necrotic tonsillitis develops; rash is late. The septic form of scarlet fever is characterized by vast and deep necrotic processes in

the fauces, necrosis of the lymph nodes and the adjacent cellular tissue (adenophlegmon).

Complications. By their pathogenesis, complications are classed as suppurative-septic and allergic. Suppurative-septic complications usually develop in the acute period of the disease and less frequently during the second period (in the septic form). These include suppurative lymphadenitis, catarrhal and purulent otitis, mastoiditis, necrotic tonsillitis, etc. Allergic complications include nephritis, lymphadenitis, arthritis, and some others.

Diagnosis. The diagnosis is based on clinical and epidemiologic findings. The bacteriologic method is not used in identification of scarlet fever.

Treatment. Treatment is aimed at elimination of the causative agent and control of toxaemia. Penicillin is effective. It is given intramuscularly 6 times a day for 5-7 day. The daily doses are 15 000-20000 U/kg body weight for children and 50 000 U/kg for adults. Bicillin can also be given (one injection per course). Bicillin is given intramuscularly, 20 000 U/kg.

Septic scarlet fever is treated with penicillin, 50000 U/kg a day. The daily dose is divided for 5-6 injections. Severe toxic and toxicoseptic forms require detoxicating and glucocorticosteroid therapy.

The patient must remain in bed until his temperature falls. As the temperature decreases and subjective condition improves, current disinfection should be performed and children can play in the room or out-of-doors.

During the acute period of the disease, the children are given great amount of liquid to drink (tea with lemon, 5 per cent glucose solution with ascorbic acid, fruit juice). Food should be liquid or semiliquid; proteins should be somewhat restricted. Adequate nutrition should be given after reduction of body temperature and lessening of inflammation in the fauces. If symptoms of nephritis develop, the patient must be given appropriate diet (vegetables, dairy products).

Prevention and control. Preventive measures are aimed at elimination of the source of infection and disruption of the transmission routes. The main aim is to prevent formation of infection foci which is especially important in children's institutions. The patient should be isolated at home. Children with severe forms of the disease should be hospitalized if there are other children under 8 years of age in the same home (or if adults working at preschool children's institutions, junior schools, surgical and maternity departments, or in milk industry reside in the same house).

After recovery the convalescent may be discharged from hospital not earlier than in 10 days after the onset of the disease. Convalescents working in above mentioned institutions, children attending preschool institutions, and also junior schoolchildren can be allowed to visit classes, kindergartens, and the like only in 12 days after expiration of the isolation term, provided inflammatory processes in the fauces or nasopharynx are absent.

Prevention of scarlet fever spread consists in observation of hygiene in residential houses, children's institutions, and prevention of overcrowding.

Methods for active immunization against scarlet fever are not known.

Measures in the focus. The patient should be isolated. If a child attends a kindergarten, school or the like institution, the authorities of such institutions should be informed. If a diseased child is isolated at home, the rooms should be treated with hot soap solution. Dishes and linen should be boiled. Persons who contacted the patient should be observed for seven days after hospitalization of the patient. Children under 9 years of age, who have not sustained scarlet fever should be isolated in home conditions for the entire term of observation. If cases of scarlet fever or acute tonsillitis are revealed, they should be isolated. The terms for isolation of tonsillitis patients in the focus of scarlet fever are the same as in scarlet fever, i.e., 22 days.

If a patient is treated at home, children under 9, who had contacts with the diseased, may be admitted to children's institutions only in seven days after recovery of the patient on the condition that inflammatory processes in the fauces or the nasopharynx are absent in the recovered child. The term of isolation is thus 17 days on average.

Measures should be taken to prevent infection spread in children's institutions. To that end, it is necessary to examine children every day (inspection of the fauces and the skin) and to take their temperature. Health education of parents is also important.

If a case of scarlet fever is revealed in a kindergarten or other children's institution, the patient should be isolated and the rooms disinfected. The rest of the children in the group should be isolated for seven days. The children and the personnel of this institution should be examined medically twice a day and their body temperature taken. If new cases of scarlet fever are revealed, the other children should be tested for susceptibility to scarlet fever (the Dick test). To that end, 0.1 ml of the toxin is administered into the volar

surface of the forearm. Children in whom the Dick test is positive, should be given 3 ml of gamma-globulin.

Measles (Rubeola)

Aetiology. The disease is due to RNA-containing virus *Paramyxoviridae.* The virus is pathogenic to humans and monkeys. In laboratory the virus is cultivated on human and monkey kidney cells. Attenuated strains of the virus are used as live antimeasles vaccine. The virus is rapidly killed when exposed to high temperature, ultra-violet radiation, or disinfectants. In the environment it is destroyed in 30 minutes.

Epidemiology. The only source of infection is a measles patient, who becomes contagious during the last one or two days of the incubation period, during the catarrhal period, and during 3-5 days following development of rash. In the presence of complications, the period of contagiosity elongates to 10 days from the day when rash develops. The infection is transmitted by air-borne route. The virus can be carried by air to adjacent rooms and flats within a house. All persons who have not sustained measles or were not vaccinated against measles are susceptible to this disease.

Vaccination with live measles vaccine considerably decreases the morbidity. Stable (life-long) immunity develops in those who sustained the disease. Repeated infections are rare. Before active immunization has become common practice, measles epidemic occurred at 2-3 year intervals. Morbidity usually increases in the cold season.

Pathogenesis. The portal of entry is the mucosa of the upper airways, where the virus multiplies in epithelial cells to evoke inflammatory process. The virus then enters the blood to cause toxaemia and to affect various organs and tissues. The virus is contained in droplets of mucus that are dissipated from the upper airways and the nasopharynx during coughing or sneezing. As the titre of antiviral antibodies increases, the virus is eliminated from the patient. Complications are due to weakness of the patient and superimposition of secondary infection.

Clinical picture. The incubation period is usually 9-10 days but can last to 17 days; in the immunized with immunoglobulin, it can be as long as 21 day.

The onset of the disease is usually gradual. Symptoms of initial catarrhal or prodromal period develop with elevation of body temperature to 38-39 °C; these are headache, rhinorrhoea, dry

barking cough, conjunctivitis, and photophobia. Whitish small papules surrounded by narrow hyperaemic rims (Koplik's spots) appear on the buccal mucosa on the 2nd or 3rd day of the catarrhal period; the spots persist for 2-3 days.

The appearance of the patient is quite specific: the face is oedematous, the eyelids are swollen and slightly hyperaemic; lacrimation and nasal discharge are seen. The catarrhal period usually lasts 2-3 days, and is followed by the rash and fever.

On the 3rd or 4th day of the disease, a new wave of fever is noted; the body temperature rises to 39.5-40.5 °C in 2 or 3 days after rash appears. Large spots of rash develop on the face and behind the ears (Plate VI). Within a 24-hour period, the maculopapular rash involves the whole face and the upper chest. On the next day the eruption extends over to the trunk and partly the limbs; in three days all skin of the extremities is involved. The rash consists of spots that are elevated above the skin surface. In 4 days after the rash appears, the body temperature drops to subfebrile and normalizes in 5-7 days. The rash begins blanching in 4 days in the same order as it appeared, leaving pale brown spots on the skin that disappear in 1-2 weeks. Resolution of the rash is often attended by furfuraceous desquamation.

In the absence of complications, the patient's condition improves with normalization of body temperature and fading out of the rash; the catarrhal changes decrease and disappear, and the patient recovers. The end of the incubation period is marked by mild leucocytosis and neutrophilosis; the catarrhal period is characterized by leucopenia and neutropenia, and the period of skin eruption is characterized by leucopenia with a relative neutrophilosis, eosinophilia and thrombocytopenia.

Depending on severity of the disease, mild, moderate and severe forms are distinguished. The disease runs an especially severe course in infants under 2 years.

Besides, measles can run an atypical course: it can be malignant or abortive (rudimentary). Malignant forms are characterized by a severe course and usually end by death of the patient. This form is exceptionally rare now. The abortive or rudimentary measles is usually seen in the vaccinated. The symptoms are mild; many of them are absent.

Mitigated forms of the disease occur in children immunized prophylactically with immunoglobulin. They are characterized by a prolonged incubation period (14-21 day) and a short clinical course. The catarrhal period is either mild or absent; the body temperature is subfebrile, the skin rash is typical of measles but is very scarce.

Mitigated measles looks very much like the response to vaccination with live measles vaccine, but the patients can be the source of infection, while the vaccinated children cannot.

Complications. Bronchitis, bronchiolitis, pneumonia, laryngitis, and tracheitis are among possible complications. If measles is aggravated by stenosis of the larynx, the condition can be complicated by croup, dyspepsia, otitis, or encephalitis.

Diagnosis. The diagnosis is based on clinical and epidemiologic findings.

Treatment. In uncomplicated cases, treatment includes preventive and hygienic measures. The room of the patient should be well aired. The patient requires thorough care: he should be given warm baths every other or third day; visible mucosa should be given regular sanitary treatment.

The diet should be adequate, easy to assimilate and rich in vitamins; much liquid should be given to drink. Amidopyrin should be given for headache; codeine is helpful in dry cough.

If measles is complicated with pneumonia, the patient should be given antibiotics, intravenous infusions of plasma, 20 per cent glucose solution, 10 per cent solution of calcium gluconate, cocarboxylase, corglucon, and ascorbic acid.

Prevention and control. Since susceptibility to measles is very high, the disease can be prevented by active immunization with live measles vaccine.

Infants of 1 year should be vaccinated in the absence of contraindications. The vaccine is given in a single 0.5 ml dose, subcutaneously, or 0.2 ml intracutaneously. Efficiency of the vaccine depends on observation of the requirements for its handling, storage, and use.

Only children with negative serologic reaction should be revaccinated.

In order to control the condition of immunity among population, random examinations are carried out. All persons with negative serologic reaction (except the pregnant) should be vaccinated. Infants borne from mother with negative serologic reaction are vaccinated at the age of 8 (not 12) months, in two months after the third vaccination against diphtheria, tetanus and pertussis (the infants are revaccinated in 6-10 months).

Measures in the focus. Measles patients should be isolated at home. Only severely ill patients (also complicated cases) should be taken to hospital. Measles patients should also be hospitalized for epidemiologic indications.

Isolation is unnecessary in 5 days (in the presence of complications, in 10 days) after appearance of rash. Since the pathogenic agent is unstable in the environment, adequate airing and general cleaning of rooms in the focus of infection can be sufficient.

Children who had no measles and who were not immunized or were not given immunoglobulin are not admitted to kindergartens, schools and the like institutions for 17 days, and those who were given immunoglobulin, for 21 day. Children vaccinated with live vaccine can remain in groups provided at least a month has passed after vaccination.

People in the focus of infection should be observed medically (inspection of the mucosa of the mouth and fauces, conjunctiva and skin at 3-4 day intervals) before quarantine terminates. If new cases of measles are revealed, the term of medical observation begins from the day when rash appeared in the last patient.

Emergency prophylaxis and eradication of outbreaks of measles in organized communities (kindergartens, schools, and the like) should be carried out by active immunization of all children with negative serologic tests.

Immunoglobulin is given only to those contacts, to whom vaccination is contraindicated or to infants under 12 months of age. The doses: 3 ml to infants from 3 to 12 months (infants under three months are not susceptible to measles); and 1.5 ml to infants from 1 to 6 years.

Quarantine should be established in children's groups only if there are children who had no measles or who were not immunized against it.

Rubella (German Measles)

Aetiology. The disease is due to the virus belonging to the family *Togaviridae.* This RNA-containing virus is cultivated on tissue cultures. It is sensitive to chemicals and is unstable to environmental changes.

Epidemiology. The source of infection is a rubella patient and a virus carrier. The patient is a danger to the surrounding people beginning with the last 1-2 days of the incubation period and remains so till the second week after the onset of the disease. Patients with latent or asymptomatic rubella, and also children with congenital rubella, in whom the virus can live for 18 months and longer, can also be the source of infection. The infection is transmitted by air-borne route.

Infants aged from 1 to 7 years are mostly affected. The disease also occurs in adults, especially in the pregnant, in whom it is particularly dangerous because the infection can be transmitted to the foetus and become the cause of stillbirth, congenital deafness, microcephaly and other malformations. Stable immunity is produced in those who sustained the disease.

Rubella occurs as small epidemics, with the rise in morbidity during the winter and spring. Epidemics occur at 5-7 year intervals.

Pathogenesis. The virus enters a human with droplets of mucus and multiplies in the epithelium of the upper airways mucosa. Later it is carried with blood to involve selectively the lymph nodes.

Clinical picture. The incubation period is from 12 to 21 days. The onset is gradual: the body temperature rises to 38.5 °C, the patient complains of weakness, moderate headache, myalgia and arthralgia. The symptoms of upper airway catarrh are mild, hyperaemia of the fauces is insignificant, conjunctivitis is moderate, the lymph nodes (suboccipital, postauricular, and the nodes of the posterior neck) are enlarged.

Small maculopapular lesions appear on the face and neck during the first or second day of the disease. In few hours the whole body is involved and dense rash covers the volar surfaces of the limbs, the back, and the buttocks. The rash persists for 2-3 days and then fades out without scaling or leaving any pigmentation.

Haematologic changes: leucopenia (3-4 x 10^9/1), relative lymphocytosis, increased quantity of plasma cells.

Complications. Complications are rare: arthritis, encephalitis, myelitis, nephritis.

Diagnosis. The diagnosis is based on clinical, epidemiologic and laboratory findings (blood tests).

Treatment. Treatment is symptomatic. The patient must remain in bed for 2-3 days. If complicated with encephalitis, the disease should be treated with glucocorticosteroids.

Prevention and control. The patient should be isolated for 5 days after rash develops. Children who contacted the patient may remain in groups. Pregnant women, who had no rubella, should be protected from contacts with the diseased. If a pregnant had rubella in her past history, or had contacts with the diseased, she should be given immunoglobulin (10-30 ml) to prevent infection of the foetus. Live attenuated vaccine has been elaborated and tested, but it is not yet used on a mass scale.

Whooping Cough (Pertussis)

Aetiology. Whooping cough is due to *Bordetella pertussis* that belongs to haemophilic bacteria. The bacilli are highly pathogenic to humans and unstable in the environment.

Epidemiology. The main source of infection is a pertussis patient which is especially contagious during the initial period of the disease. As the disease progresses, contagiosity decreases, and by the end of the sixth week the patient presents no danger to the surrounding people even in the presence of cough. Antibiotics accelerate elimination of the microbes from the patient.

Patients with mild atypical form of whooping cough are an active source of infection spread. Carriers can also be the source of infection. The pathogenic agent is transmitted by air-borne route.

Susceptibility to pertussis is high from the very first day of life. Preschool children are usually affected by the disease; only rare cases occur among adult population. Stable life-long immunity is produced in those who sustained the disease.

The whooping cough morbidity has substantially decreased since active immunization has been elaborated. Seasonal variations in the infection rate are not typical of this disease.

Pathogenesis. The portal of entry are the upper airways. The pathogenic agent multiplies on the laryngeal, tracheal and bronchial mucosa. The endotoxin irritates the respiratory mucosa thus evoking cough. Besides, it acts directly on the central nervous system, irritates the nerve receptors of the respiratory mucosa and stimulates the cough reflex to provoke paroxysm of cough.

Clinical picture. The incubation period is from 2 to 15 days (mostly 5-7 days). Three periods are distinguished: catarrhal, paroxysmal and the recovery period.

The catarrhal period lasts 1-2 weeks. It is shorter in infants during their first months of life, while in the vaccinated it can be longer. The disease begins with cough, mild rhinorrhoea, and malaise. The body temperature is normal or slightly elevated.

The paroxysmal period begins gradually. Paroxysms of cough occur at progressively shorter periods, especially at night. A typical paroxysm of whooping cough comprises a series of quick short coughs. A short pause is followed by a deep inspiration and a new series of coughs, etc. The prolonged and distressing inspiratory gasp is known as the whoop (hence the name, whooping cough). At the end of paroxysm a small amount of clear viscid mucus is liberated. Paroxysms of cough can terminate by vomiting.

During a paroxysm, the patient's face reddens, and turns cyanotic, the neck veins are engorged, the eyes are injected; involuntary defaecation and urination are possible. An ulcer can be seen on the frenulum of the tongue which is due to its mechanical damage caused by friction against the sharp edges of the lower teeth. From 8 to 10 attacks of cough can develop during a day (to 40 attacks in severe cases). Depending on the severity of the disease, an attack can last from 1-2 to 15 minutes, the number of cough series varying from 1 to 10-20. The condition of the child with a mild whooping cough during the interparoxysmal period is satisfactory and the child can be quite animated.

The paroxysmal period lasts 3-4 weeks, then the paroxysms become shorter and the interparoxysmal periods, longer. The recovery period begins. After paroxysms, the patient liberates thick sputum with a greenish hue. The frequency of paroxysms decreases, they become milder and lose their specific character.

Examination of blood reveals leucocytosis and lymphocytosis. The quantity of leucocytes increases to 12-50 x 10^9/L ESR is low or normal. The specific gravity of the urine is high. The overall duration of the disease varies from 5 to 8 weeks.

The following three main clinical forms of pertussis are distinguished: mild, moderate, and severe. The severity of the disease depends on immunization of children's population. The disease is mild in the vaccinated; no complications develop in them. The disease runs a severe course in infants under 1 year.

Complications. Nosebleeds, laryngitis, bronchitis, bronchopneumonia, pneumonia, emphysema of the lungs, haemorrhage in the eye conjunctiva occur. Encephalopathies are possible in infants under 2 years of age.

Diagnosis. The diagnosis is based on clinical, epidemiologic, anamnestic, and laboratory findings. It is difficult to differentiate between pertussis and parapertussis only by clinical signs; bacteriologic and serologic studies are therefore diagnostically decisive. Bacteriologic studies are based on isolation of the causative agent from the patient and its identification in the culture. A specimen is taken from the posterior wall of the pharynx by a sterile cotton tampon in patients or suspected persons, and the material is used for immediate inoculation of the culture medium (carbon-caseine). If the material is sent to the laboratory, it should be kept protected from cold. A preliminary answer is ready in 3 days, and the final, in 5 days.

Agglutination reaction can be informative during the second or third week of the disease. The test is considered positive with titres of

1:20 and higher. In view of mass-scale vaccination against whooping cough, the diagnosis is considered trustworthy with progressively increasing antibody titres in repeated examinations.

Complement fixation test can be conducted on the second week of the disease. It is positive with titres of 1:10 and higher. The diagnosis of whooping cough can be confirmed by an accelerated luminescent serologic method that has advantages over isolation of cultures. It is highly sensitive and the result is ready in short time.

Treatment. Bedrest is prescribed only in the presence of severe complications and fever. Fresh air is curative, and the room must therefore be well aired. In the warm season, the child must remain out-of-doors as much as possible; in winter, at least for several hours. It is necessary to organize children's leisure time in order to distract them from coughing.

Highly caloric adequate diet rich in vitamins should be given. The child must eat by small portions, better soon after an attack of cough.

During the catarrhal period and in the early paroxysmal period, the tetracyclines should be given to infants with a severe disease and in the presence of complications. The doses are 0.025 g/kg a day for 8-10 days. Erythromycin should be given in a dose of 0.005-0.01 g/kg to infants under five, 3-4 times a day for 10 days. Antipertussis immunoglobulin is also given: 3 ml during 3 days in succession, and then every other day several times depending on the patient's condition. Oxygen therapy, vitamins, and neuroplegics (aminazine, propazine, etc.) are widely used since they remove anxiety in children, improve sleep and appetite, and decrease the frequency and severity of paroxysms.

Prevention and control. Early diagnosis, isolation of the diseased, and active immunization are effective. Since it is difficult to establish a correct diagnosis during the first 2 weeks of the disease, specific prophylaxis is the main method to control the infection. Vaccination against whooping cough is done with adsorbed diphtheria and tetanus toxoids and pertussis vaccine (see "Diphtheria").

The patient should be isolated at home. Only children with severe and complicated forms of whooping cough, especially infants under 2, and children from families where the other children are susceptible to the disease, should be isolated (for 25 days from the onset of the disease if two bacteriologic tests are negative or for 30 days in the absence of tests).

Bacteriologic tests are performed in children with persistent cough for several days in the absence of changes in the respiratory system.

Measures in the focus. Rooms where the patients are present should be well aired. Exposed susceptibles under 7 should be observed for 14 days after separation from the patient, if they were not separated from the patient they should be observed for 25 days. Development of catarrh and cough should be considered as possible pertussis. Such children should be isolated from the healthy until the diagnosis is established.

All exposed susceptibles should be examined for the carrier state. Carriers of the pertussis agent who do not cough can be admitted to kindergartens, schools and the like institutions only after three successive negative tests (tests are performed at 3-day intervals).

Immunoglobulin should be injected intramuscularly to exposed infants under 1 year of age. A dose of 6 ml should be given by two injections with an interval of one day.

Prevention and control. Groups where pertussis cases were revealed, should be isolated for 14 days. New children are not admitted to such groups for the entire term of isolation. Infants aged under 1 ye'ar who had no pertussis and who were not vaccinated against pertussis should be given immunoglobulin intramuscularly.

All children and the personnel who had contacts with the diseased should be examined for the carrier state during two succesive days or at a 1-2 day interval.

If many children develop whooping cough, a special "pertussis" group can be formed on permission of medical authorities. A group of healthy children and a group with mild cough can be organized until the diagnosis is established.

Parapertussis

Epidemiology. The causative agent belongs to the genus *Bordetella parapertussis,* which resembles the pertussis agent. Its stability in the environment is low.

Epidemiology. The infection is transmitted by air-borne route from patients and carriers. The disease occurs as sporadic cases and epidemic outbreaks at kindergartens, schools and the like institutions.

Clinical picture. The incubation period lasts from 4 to 14 days. The onset is characterized by mild catarrhal symptoms; mild rhinitis, moderate hyperaemia of the fauces; the body temperature is usually normal. The main symptom is cough. Depending on its character, three forms of parapertussis are distinguished: pertussis-like, oblitera-ted, and asymptomatic form.

Complications. Complications are rare.

Diagnosis. Bacteriologic examinations are the only method of differential diagnosis of pertussis and parapertussis.

Prevention and control. Infants under 1 year of age should be isolated for 25 days. Infants over 1 year should be isolated for clinical indications. If cough terminates at earlier terms, the children can be admitted to kindergartens and schools after two negative bacteriologic tests.

Specific prophylactic measures are taken for epidemiologic indications. Children who sustained parapertussis should be vaccinated against pertussis.

Chickenpox (Varicella)

Aetiology. The viral agent causing this disease belongs to the genus *Herpesvirus* that also causes herpes zoster. The virus is unstable in the environment.

Epidemiology. The source of infection is the diseased person who becomes contagious 1-2 days before skin eruption develops and remains so 3-4 days after appearance of the last rash element. Patients with herpes zoster can also be the source of infection.

Infection is transmitted by air-borne route even during a short exposure in a room where the chickenpox patient is present. Besides, the disease can spread over a significant distance (to a neighbouring room, flat, through corridors). Infants aged from 6 months to 7 years are especially susceptible to chickenpox. Susceptibility is quite high. Life-long immunity is produced in those who sustained the disease.

Chickenpox is highly contagious. It occurs in epidemics, especially in large cities and in the cold season.

Pathogenesis. The portal of entry is the mucosa of the upper airways. From the mucosa, the virus enters the blood. In the epidermis the virus evokes a pathologic process with formation of spots, papules, and vesicles.

Clinical picture. The incubation period is 11-21 day, more commonly 14-17 days.

The prodromal symptoms are mild, but scarlatina-like rash can develop. The body temperature rises to 38 °C and higher (less frequently the temperature is normal); then circumscribed rose spots develop on various parts of the body. In few hours, the spots turn into papules and then into vesicles filled with clear fluid. The fluid then turns cloudy. A red rim is formed around the vesicles. In 1-2

days after their appearance, the vesicles dry, rupture (or are destroyed by the child), and crusts are formed.

New eruption develops within few days, and rash elements in all their stages can therefore be seen simultaneously on the skin of the patient. These eruptions are roseoles, papules, vesicles, and crusts. Pruritus is annoying. In some patients eruptions can be seen on the mucosa of the mouth, nasopharynx, larynx, and genitalia. Eruptions on mucosa soon convert to surface erosions with a yellowish grey bottom.

Fever lasts from 2 to 5 days. If eruption is intensive, fever lasts 8-10 days. Temperature rise can be due to new eruptions; the patient's condition worsens: sleep deranges, appetite is lost, the child becomes anxious and irritable.

Mild, atypical forms of chickenpox are known. The body temperature is normal, eruptions on the skin are insignificant. Asthenic children may develop severe forms of the disease: pustular, bullous, haemorrhagic. Severe cases are often complicated by laryngitis, false croup, pyoderma, erysipelas, stomatitis, otitis, lymphadenitis, bronchopneumonia, or nephritis.

Diagnosis. The diagnosis is based on clinical and epidemiologic findings. Whenever necessary, viroscopy, and complement fixation test can be conducted.

Treatment. The patient must keep bed. His skin should be treated with a week potassium permanganate solution after eruption subsides. Baths are also recommended. Patient's nails should be cut and his hands kept clean. Rash elements should be treated with a 5 >per cent potassium permanganate solution or a 1 per cent brilliant green solution. Antibiotics should be given for suppurative complications.

Prevention and control. Prevention of chickenpox includes control of its transmission to kindergartens, schools, paediatric hospitals, and observation of individual and social hygiene.

If chickenpox is revealed in a kindergarten or other children's institution, the patient should be isolated from the rest for 9 days. If new cases are revealed, children who sustained chickenpox can be admitted to the group after abatement of acute symptoms (normal body temperature). If chickenpox occurs in a group of a kindergarten, the group should be isolated (quarantine) for 21 day from the last day of exposure.

Measures in the focus. The patient should be isolated at home for 9 days from the onset of the disease. The room should be well aired.

Susceptible nurslings and infants under 7 years of age who were

exposed to the danger of contamination should be separated from the healthy for the period of time lasting from the 11th till the 21st day after the exposure. The focus of infection should be controlled medically (examinations, thermometry, and questioning of the exposed at 5-6 day intervals).

Mumps (Epidemic Parotitis)

Aetiology. The causative agent of mumps belongs to the family of *Paramyxoviridae.* Paramyxoviruses are characterized by high contagiosity and low stability in the environment.

Epidemiology. Human beings are the source of infection. The patient is contagious from the last days of the incubation period and remains so for 7-9 days. Patients with an obliterated form of the disease are a special danger. The infection is transmitted mainly by air-borne route. Susceptibility to mumps is high, but lower than in measles, influenza, or chickenpox. Children aged from 5 to 15 are especially susceptible. Outbreaks of the disease among adults are also possible.

Stable immunity is produced in those who sustained the disease. Seasonal variations in the infection rate are characteristic: the morbidity rises in the cold season. Epidemics of mumps occur at 4-5 year intervals.

Pathogenesis. The portal of entry is mucosa of the mouth, nose or pharynx through which the virus enters the blood that carries it to the parotid, submandibular, sublingual and other glands. Besides, it can afflict the sex glands, the pancreas and the central nervous system. The virus is excreted from the body with saliva.

Clinical picture. The incubation period lasts from 15 to 19 days, with variations from 11 to 23 days. The disease begins with a prodromal period that lasts 12-36 hours. The body temperature then rapidly rises to 38-40 °C and signs of involvement of the salivary glands become apparent: the gland is swollen and stands out before the ear, then it extends posteriorly and inferiorly; it is tender; pain intensifies during chewing, swallowing and talking.

Salivation discontinues on the involved side. The parotid gland of the other side becomes involved in 1-2 days of the disease. The submandibular and, less frequently, sublingual glands can also be involved. Salivary adenitis begins subsiding in 3-5 days of the disease and the swelling disappears completely by the 8-10th day.

The fever period lasts from 3 to 4 days, and in severe cases 6-7 days. Blood changes are characterized by leucopenia or normocyto-

sis, relative lymphocytosis and monocytosis. Signs of involvement of the other glandular organs can develop on the 5-10th day of the disease. Orchitis usually occurs in adolescents and adults. This condition is characterized by elevated body temperature, severe pain in the scrotum and the testis, and testicular enlargement. If the pancreas is involved, the patient complains of severe abdominal pain, nausea and recurrent vomiting; the diastase of the urine is high. Serous meningitis, and less frequently meningoencephalitis often supervene.

Diagnosis. Typical cases are easy to diagnose. Atypical disease should be differentiated by consideration of epidemiologic anamnestic findings. Serologic tests (complement fixation test, direct haemagglutination reaction) can be used.

Treatment. Treatment is symptomatic. The patient is given liquid or semiliquid food. Dry warmth (cotton wool pad) should be applied over the involved gland. Mouth care is necessary (frequent rinsing with sodium hydrocarbonate solution). Analgin, amidopyrin and other analgesics are useful. Cold is necessary during the first 2-4 days of orchitis; immunoglobulin (9-12 ml) should be prescribed on the 4-5th day. Cerebrospinal puncture and dehydration therapy are indicated for developing symptoms of meningitis or meningoencephalitis.

Prevention and control. Revealing and isolation of mumps patients is necessary. Individual and social hygiene, especially at children's institutions is also decisive. Children should be immunized at the age of 15-18 months. Live vaccine is given intracutaneously in a dose of 0.1 ml or subcutaneously in a dose of 0.5 ml (diluted 1:5).

If cases of mumps are revealed in a group of children, the exposed susceptibles should be isolated for 21 day from the day of contact with the diseased. During the entire quarantine the children should be given medical observation. If new cases of mumps are revealed at the children's institution, the diseased can be admitted to the group after the acute symptoms of the disease subside.

The rooms should be washed and well aired.

Measures in the focus. The patient is isolated for 9 days in home conditions. Hospitalization is only indicated in severe cases. Rooms where the patient is isolated should be well aired and cleaned.

All exposed susceptibles under the age of 10 should be observed (questioned, examined visually once in 5-6 days, with thermometry) and are not admitted to children's institutions during 21 day from the day of exposure. If the time of contact is known exactly, susceptible children can continue attending their groups in kin-

dergartens or schools, but beginning with the 11th day till the 21st day they should be dismissed from their groups.

Meningococcal Infection

Aetiology. The causative organism is *Neisseria meningitidis.* Several serogroups of meningococci are distinguished by their antigen structure: A, B, C, D, N, X, Y, Z. Particular groups of meningococcus prevail in certain areas.

Meningococci are rapidly destroyed in the environment, especially at low temperatures and in the absence of moisture.

Epidemiology. Human beings are the only source of infection. These may be patients with apparent or obliterated forms of meningitis or carriers of the cocci.

Patients with meningococcal nasopharyngitis, who dissipate the microbes into the air during sneezing and coughing are a special epidemiologic danger. Patients with meningococcal meningitis and meningococcaemia liberate the pathogenic microbes into the environment during the prodromal period, but the acute symptoms of the disease help early diagnosis and isolation of patients. The duration of the contagious period depends on the duration of the presence of meningococcus in the nasopharynx. The carrier state in convalescents persists for three weeks.

Carriers are less dangerous for the surrounding people than patients, but the number of carriers is much greater, and it is more difficult to reveal them. The carrier state can be sooner terminated by treating with antibiotics and sulpha drugs.

Healthy carrier state continues for 2-3 weeks. Longer carrier state (to 6 weeks) occurs in chronic inflammation in the nasopharynx.

Meningococcal infections afflict a comparatively small percentage of population even in intensive epidemic periods (actually not more than 10-15 per cent). The main part of the infected are carriers and patients with acute nasopharyngitis. Generalized forms are rare.

In the years of sporadic incidence the microbes live in the carriers whose number is around 1 per cent (from 8 to 12 per cent in the focus). During epidemics, the number of carriers in the focus of infection can exceed 40 per cent.

The infection is transmitted by air-borne route during talking, sneezing and coughing. Since the agent is unstable in the environment, the infection is transmitted only during intimate and prolonged contacts of susceptibles with the source of infection.

Susceptibility to meningococcus can be considered universal, but

the pronounced clinical picture of the disease can be seen only in few of the exposed. Specific immunity develops in the infected regardless of the presence or absence of the clinical manifestations of the disease.

Meningococcal infection is characterized by periodicity, seasonal variations, and age susceptibility. Periodic rise in the incidence occurs every 10-15 years. The infection rate can increase by 6-10 times during the cold season in epidemic outbreaks (compared with the summer incidence). On an average, the infection rate during epidemics increases 50-60 times compared with the interepidemic periods. Infants under 5 years are most susceptible to the disease. Infants prevail among the diseased in the interepidemic periods, while the age of patients increases during epidemics. Group incidence of meningitis and meningococcaemia can be seen during epidemic outbreaks. This is especially vivid in kindergartens, schools, children's homes, hostels, and in the army. The disease persists for a long time in close populated places.

Overcrowding, poor hygiene and socio-economic conditions promote distribution of meningitis. Meningitis incidence increases with the number of carriers. Meningococcal infection occurs in all countries of the world.

Pathogenesis. The portal of entry is the mucosa of the fauces and the nasopharynx where inflammation develops (catarrh of the upper respiratory tract, rhinitis, nasopharyngitis). Only in a small portion of the patients, meningococci overcome the local barrier (lymphatic throat ring) and enter the blood that carries them to various organs and tissues to cause bacteraemia. If the disease is mild, bacteraemia is manifested by polymorphous rash which subsides in few hours.

In persons sensitive to meningococci, the disease runs the course of meningococcaemia that can be attended by arthritis, endocarditis, lesions of the renal vessels, etc. In some patients, the microbes reach the pia mater to provoke suppurative inflammation. If the grey substance is involved, meningoencephalitis develops.

Toxic and allergic components play an important role in the pathogenesis of meningococcal infection. Toxaemia is more pronounced in severe septic forms of the disease. In view of massive decay of meningococci, endotoxin is produced which affects small blood vessels and impairs circulation of blood, causes haemorrhage into the skin, mucosa, serous membranes, and into the parenchyma of the internal organs. Purulent meningitis is due to transportation of the microbes by the blood into the pia mater encephali and spinalis.

Profuse purulent exudate on the surface of the frontal and temporal lobes of the brain looks like a pus cap.

Clinical picture. The incubation period lasts 4-6 days with extremes of 2 and 10 days.

The following clinical forms are distinguished:

(1) local forms (meningococcus carrier state, acute nasopharyngitis, pneumonia);

(2) generalized forms due to meningococcus dissemination via the blood stream (meningococcaemia, meningitis, meningoencephalitis, mixed meningococcal infection);

(3) rare forms (endocarditis, polyarthritis, arthritis, pneumonia, iridocyclitis).

Acute nasopharyngitis is diagnosed mostly during epidemic outbreaks, it can be an independent manifestation of the disease or a prodromal stage of meningitis or meningococcaemia.

The main symptoms are headache, vertigo, lassitude, pallor, dry cough, sore throat, oedema and hyperaemia of the posterior pharyngeal wall, hyperplasia of the lymphoid follicles, herpes, and stuffy nose. The body temperature is elevated during 1-3 days, mucosal inflammation persists for 5-7 days, and follicular hyperplasia to 2 weeks.

Pneumonia of meningococcal aetiology usually runs a severe course with liberation of great amounts of sputum; pleurisy is common.

Meningococcaemia begins suddenly with a chill, headache, and elevation of temperature to 40 °C and higher (intermittent or continuous fever). Haemorrhagic rash is a specific symptom. Rash is usually petechial with irregular firm eruptions of various size, which are slightly raised over the skin of the buttocks, dorsal surface of the thighs and shins. Haemorrhage into the sclera and faucial mucosa, micro- and macrohaemafuria, lesions of the joints, pneumonia and endocarditis are possible. The symptoms of toxaemia are pronounced: tachycardia, low arterial pressure, cyanosis, dyspnoea, dry skin, and thirst. The symptoms of meningitis are absent. Leucocytosis is marked (with the shift to the left).

Fulminating meningococcal sepsis with shock and adrenal haemorrhage (the Waterhouse-Friderichsen syndrome), meningococcaemia with acute adrenal failure develops suddenly, in full health. Within few hours the body temperature rises, the patient experiences chill, vertigo, weakness, confusion, myalgia, vomiting, and convulsions. Cyanosis and dyspnoea then develop, the body temperature drops to normal and the arterial pressure becomes low.

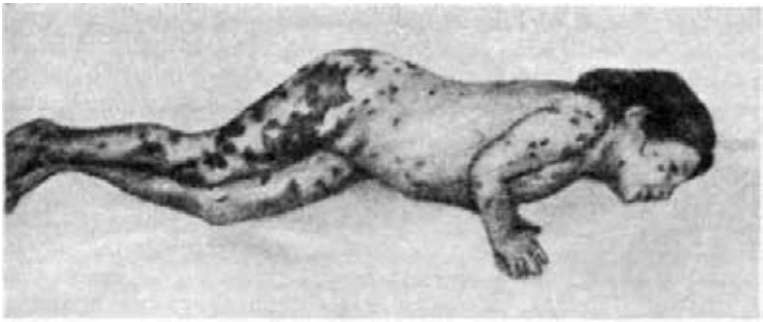

Fig. 11. Meningococcaemia. Haemorrhagic rash and vast haemorrhages into the thigh skin (after Kipnis)

The pulse is thready, fast, and soon becomes indeterminable. Petechial lesions and intensive haemorrhages develop in the skin (Fig. 11). Nosebleed, gastric and uterine haemorrhage are also possible. The symptoms of meningitis are marked (mixed form). Neutrophilic leucocytosis is seen. The cerebrospinal fluid is usually serosanguinous.

Meningitis usually begins suddenly with a shaking chill. The body temperature rapidly rises to 39-40 °C; severe headache, vertigo and vomiting develop. Nurslings can develop convulsions, comatous state and the fontanelle triad (protrusion of the frontal fontanelle, its tension, and the absence of normal pulsation).

Skin hyperaesthesia, hypersensitivity to light and sound stimuli, stable dermographism, herpes on the lips and the face can also develop. By the end of the first day, or early on the second day, signs of meningeal involvement become apparent: stiff neck (the patient cannot bend his head to touch the chest with the chin), the Kernig symptom (the patient is unable to extend the leg when the thigh is flexed on the abdomen), and the Brudzinski sign (an attempted flexion of the neck usually results in flexion of the thigh and leg). The abdomen is sunken. The patient assumes the specific posture with his head tilted back and the thighs raised to the abdomen (Fig. 12).

The cranial nerves can be involved to cause strabismus, anisocoria, paresis of the facial nerve, and lesion of the acoustic and abducent nerves. The psychic activity can also be upset: the patient can be drowsy, his consciousness can be confused or lost, delirium can develop.

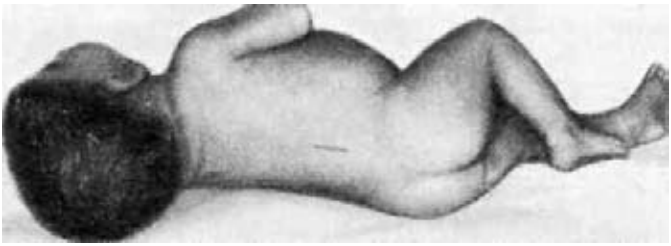

Fig. 12. Meningococcal meningitis. Typical posture.

Tachycardia is followed by bradycardia due to swelling and oedema of the brain. Leucocytosis is marked (20-40 x 10^9/1) with a neutrophilic shift; ESR is high and aneosinophilia is seen.

During puncture, the cerebrospinal fluid issues under pressure. On the first day of the disease it is clear, but later it turns cloudy and purulent. The examination of the cerebrospinal fluid reveals neutrophilic cytosis (12-30 x 10^9/1) and high protein content (to 1-3 g/1). The cerebrospinal fluid can ooze by slow drops due to its high viscosity, high cytosis and protein content, and also due to partial blockage of liquor ducts.

If treatment begins timely, the disease usually ends by complete recovery in 12-14 days.

The clinical forms of meningitis are varied. The meningeal symptoms are mild in meningoencephalitis, while the symptoms of encephalitis are more pronounced. These are deranged consciousness, muscular cramping, early paralysis and paresis. The hypertoxic fulminating form of meningitis, the main meningeal symptoms are quite pronounced. Symptoms of severe toxaemia are manifested: incoercible vomiting, muscular cramping, confusion, cardiovascular failure; swelling of the brain and wedging of the cerebellar tonsils into the great foramen, which is manifested by severe headache, drowsiness, stupor, motor anxiety, hyperaemic face and neck, and confusion. Arterial pressure increases.

Cardiac and/or respiratory failure develops and the patient can die during the first day of the disease.

Complications. Complications are rare, provided specific treatment begins in due time. In the times when sulpha drugs and antibiotics

were not known, the disease was complicated by otitis media and otitis interna with subsequent hearing loss, paresis and paralysis of the cerebrocranial nerves, and hydrocephalus. Modern therapy has considerably decreased the incidence of complications iind their severity. Staphylococcal pneumonia is possible.

Diagnosis. Meningitis is diagnosed on the basis of clinical and epidemiologic findings. Isolation of meningococcus is diagnostically decisive. The cerebrospinal fluid, blood and mucus (from the nasopharynx) should therefore be examined. The cerebrospinal fluid is taken into two sterile test tubes. The first specimen (1 ml) is sent to the laboratory for liquor test, while the second (2-5 ml) is immediately examined microbiologically. Two or three drops of the cerebrospinal fluid are used to inoculate serum agar (direct inoculation) and for preparing two smears (for bacterioscopy). The remaining fluid is kept under a layer of semiliquid agar (for enrichment).

The blood (5-10 ml) is immediately used to inoculate 50 ml of broth containing 0.1 per cent of glucose. The vial is kept in a thermostat for seven days: serum agar in Petri dishes is inoculated every day.

The nasopharyngeal mucus is taken on fast stomach or at least in 3-4 hours after meal from the posterior wall of the nasopharynx using a sterile cotton tampon on a soft wire (2-3 mm in diameter). The root of the tongue is retracted using a spatula. The mucus is immediately seeded on solid nutrient medium (serum agar or lincomycin medium that inhibits the growth of gram-positive cocci). During transportation to the laboratory, the materials should be protected from cold. Direct haemagglutination reaction, latex test, counter electrophoresis and radioimmune methods are important, since antibodies and the specific antigens can be detected in the blood serum and the cerebrospinal fluid of the patient during the very first days of the disease.

Treatment. Acute nasopharyngitis of moderate severity should be treated with sulpha drugs in a dose of 4-6 g a day for adults and 0.3 g/kg for children in the course of 3-5 days. Prolonged action sulpha drugs (sulphapyridazine or sulphadimethoxin) can be given to adults in a dose of 2 g during the first day and 1 g during subsequent 4 days.

Meningitis and meningococcaemia patients are treated with antibiotics. Penicillin should be given in daily doses of 300 000 U/kg for 5-8 days for adults and 300000-400000 U/kg for infants under 3 months of age. The daily dose is given intramuscularly at a 4-hour

interval maximum, and to infants under 2 months, at 3-hour intervals. Treatment should be continued for 5-8 days (until the cerebrospinal fluid normalizes). Chloramphenicol sodium succinate given in a dose of 0.05-0.1 g/kg for 6-8 days is highly effective. Ampicillin (0.15-0.2 g/kg a day) and other antibiotics can also be prescribed. Aetiotropic therapy is given simultaneously with pathogenetic treatment which depends on severity of the disease and the presence of complications. Toxaemia can be controlled by administering a sufficient amount of fluid containing the necessary amounts of salts to maintain the electrolyte balance. The liquid can be given per os or intravenously (polyion solutions, glucose, haemodez, plasma). Dehydration is attained by diuretics. Septic shock should be managed by infusion of polyion solutions (Locke-Ringer solution, etc.), a 5 per cent glucose and colloid solutions (polyglucin, plasma, albumin, protein) that should be injected until pulse reappears, and then the solution should be given by drip. Glucocorticosteroids (hydrocortisone, prednisolone) should also be given. In order to improve the cardiovascular function, strophanthin, corglucon, cocarboxylase, and ascorbic acid should be administered. Acidosis is corrected by a 4 per cent sodium hydrocarbonate or lactate solution. Symptomatic treatment and adequate nutrition are also necessary. Adequate patient care is important too.

Prevention and control. All patients and suspected persons should be immediately hospitalized in isolated rooms or special wards. Patients with acute nasopharyngitis should be hospitalized for special indications from closed collectives (kindergartens, children's homes, boarding schools, the army), and also in the presence of unfavourable sanitary and epidemiologic situation.

A patient can be discharged from hospital only after two negative bacteriologic tests of the nasopharyngeal mucus. The tests should be performed in 3 days after termination of the antibiotic therapy (at 1-2 day interval).

Convalescents can attend school and preschool institutions after one negative test performed in 10 days after discharge from the hospital.

Carriers should be screened out for epidemiologic indications in the focus of infection. The carriers should be treated with chloramphenicol in a dose of 0.5 g 4 times a day during 4 days. In three days after termination of chloramphenicol therapy, three tests should be performed every other day.

Measures in the focus. Current disinfection should be performed in the focus before hospitalization of the patient, and a final disinfection

is necessary after hospitalization. Persons who contacted the patient for 10 days should be observed medically with thermometry twice a day. All exposed should also be examined for the carrier state two times at a 3-day interval and inspected by an otolaryngologist. Persons with nasopharyngeal inflammation should be treated with sulpha preparations for 4 days.

After hospitalization of a patient, final disinfection should be done in children's institutions; quarantine should be established for ten days. Persons who had contacts with the patient should be examined for the carrier state two times and inspected by an otolaryngologist; children with nasopharyngeal inflammation should be isolated and treated; medical examination with thermometry twice a day should be conducted. Immunoglobulin (3 ml) is effective in persons who were exposed to infection. The preventive effect of immunoglobulin lasts a month. The rooms should be washed with a 0.5 per cent chloramine solution, irradiated with ultraviolet rays and well aired during the entire quarantine period.

Specific vaccine against meningococcal infection is not yet available.

Psittacosis (Ornithosis)

Aetiology. The causative agent of psittacosis belongs to the genus *Chlamydiales,* the family of *Chlamydiaceae.* The bacteria are quite large, with an average diameter of 400-1200 nm. The bacteria synthesize both DNA and RNA; they are sensitive to antibiotics, especially to the tetracyclines. They are stable in the environment and against the chemical and physical factors such as low temperatures. At a temperature of — 20 °C, they persist for 10 months and at — 7 °C can survive for over two years; they withstand drying, and are killed by a 2 per cent chloramine solution only in 24-72 hours. The bacteria are sensitive to high temperature: they are killed at 70 °C.

Epidemiology. The natural harbour of the psittacosis agent are birds (wild and domesticated). *Chlamyda psittaci* has been isolated from more than 140 species of birds. Humans are usually infected by poultry (ducks, turkeys, less frequently hens). Pigeons are the most dangerous psittacine birds. Besides natural and secondary foci of psittacosis, epizootics occur at poultry-raising farms the origin of which is difficult to relate to any natural nidus or to transmission of the disease by wild birds or pigeons. The source of infection can in such cases be birds in which the infection is latent. The infection

generalizes due to decreasing resistance during laying eggs, overcrowding, cold, or other adverse factors.

It is believed that a psittacosis patient is not contagious; nevertheless, hospital-acquired infections have been reported.

The main routes of infection transmission are dust- and air-borne; hence the lungs are usually involved.

Infection is transmitted through infected down and feather, during inhalation of dust containing the bacteria, by contamination of the mouth or eye mucosa with soiled hands. This happens in poultry raisers, during slaughtering and processing of poultry, or eating unboiled eggs.

Outbreaks of occupational disease among poultry raisers and slaughterhouse workers usually occur during the spring or autumn which is connected with care of the young birds and mass-scale slaughter of poultry. The susceptibility to psittacosis is high. Women are usually affected occupationally. The immunity produced in those who sustained the disease is unstable.

Pathogenesis. The main portal of entry is the mucosa of the upper airways. Multiplication and accumulation of the agent occurs in the lungs where it is brought with the blood. From the lungs, the pathogenic microbe is brought back to the blood that carries it to the liver, spleen, adrenal glands, nervous system, or myocardium where it multiplies to cause fine foci of degenerative and proliferative changes and haemorrhages. The agent circulates for 7-10 days. *Chlamydia* produce a toxic effect that accounts for the main clinical symptoms.

Depending on the organs and tissues involved, the following clinical forms of the disease are distinguished: influenza-like, pneumonic, typhoid, and meningeal. The pathogenic agent is retained in the cells of macrophage systems which causes relapses of the disease and its conversion into chronic forms.

Clinical picture. The incubation period usually lasts from 7 to 10 days with extremes of 6 and 25 days. The onset is usually acute: the patient develops chills, headache, myalgia and pyrexia (remittent fever). Hyperhidrosis, nausea, vomiting and poor appetite are also among the symptoms.

The influenza-like form is manifested by dry cough and the symptoms of laryngitis and tracheobronchitis that develop in 2-3 days.

In pneumonia-like form, cough intensifies on the 5-7th day and the patient expectorates mucoid or mucopurulent sputum; moist rales can be heard in the lower portions of the lungs; respiration is weak.

X-ray examinations reveal fine focal, confluent, segmental and

interstitial changes in the lungs that persist for a long time after body temperature normalizes. Depending on involvement of the conventionally pathogenic bacteria in the inflammatory process, the disease can run the course of a macrofocal or lobar pneumonia.

The blood changes are characterized by leucopenia with the shift to the left, aneosinophilia, and high ESR.

The fever period lasts from 2 to 4 weeks. The body temperature decreases lytically and the recovery phase begins slowly. Exacerbations and relapses of the disease are possible. In severe psittacosis, coma develops in 4-5 days and the patient dies of cardiac and/or respiratory failure. The patient can die in 2-3 weeks due to lung oedema.

The typhoid form is characterized by signs of toxaemia. The patient complains of poor appetite, constipation, aching pain in the entire body. Hepatic and splenic enlargement becomes obvious in 5-7 days. Examination fails to reveal any symptoms of lung involvement.

The meningeal form is rare. The disease begins acutely; the symptoms of meningitis supervene in 2-4 days. Fever persists for 3-4 weeks.

The disease can run mild, moderate and severe course.

In severe cases, the nervous and the cardiovascular systems are involved; the patient complains of severe headache, insomnia, irritability and delirium. The skin is pallid, the arterial pressure is low; bradycardia can be superseded by tachycardia. Renal involvement is manifested by decreased diuresis, albuminuria, and by the presence of single red cells and hyaline casts in the urine. In about 20 per cent of patients, early relapses develop (in 2-4 weeks); later relapses (in 3-6 months) are also possible in them. The chronic form of psittacosis can persist from 2 to 10 years.

Complications. Thrombophlebitis, hepatitis, pneumosclerosis, pleurisy, paralysis of the vocal cords, polyneuritis, and meningitis are possible.

Diagnosis. The diagnosis is based on epidemiologic anamnesis (contact with birds), clinical picture of the disease, and the results of x-ray and laboratory examinations.

Laboratory examinations include direct and indirect complement fixation tests and haemagglutination. A 5-ml specimen of blood is taken from the cubital vein into a dry sterile test tube in 4-7 days after the onset of the disease. At least two portions of the blood are tested at 7-10 day interval. Antibiotic therapy slows down accumulation of antibodies; therefore, the third portion of blood should be tested in 20-30 days from the onset of the disease. Titres lower than

1:8 to 1:16 can be considered positive. The diagnosis of psittacosis is confirmed if at least two-fold increase in the antibody titre is noted.

Haemagglutination reaction, inhibition of haemagglutination and indirect haemagglutination reactions are also used.

In order to detect the pathogenic agent, material taken during the first days of the disease (before the antibiotic therapy is started) should be sent to the laboratory. It is recommended that blood and sputum be taken simultaneously. The blood specimen (5 ml) is taken from the cubital vein into a sterile test tube, and the sputum is taken in the morning, before meal. Specimens of the lung tissue, spleen and pleural effusion are taken from the dead patients.

The materials are placed in sterile containers provided with ground-in stoppers, or into wide-mouth bacteriologic test tubes, which are then sealed tightly (either by soldering or by tight rubber plugs) and placed into metal containers. The sealed container should be placed into solid carbon dioxide or in a vaccum flask containing ice.

The material is administered to albino mice (intramuscularly, through the nose, or into the brain). After the mice dies, smears are prepared from their lungs and other organs, and stained after Romanovsky, Giemsa, or Castaneda to reveal the agent. Psittacosis agents can also be cultivated on chick embryos. The most rapid method is the intracutaneous test with the psittacosis antigen that can be performed on the second or third day of the disease (till the second or third month). The result is ready in 24-48 hours. The test is positive if the size of the hyperaemic area is 0.5 x 0.5 cm (+), 1 x **1** cm (+ +), or 2 x 2 cm (+ + +).

Treatment. The tetracyclines (tetracycline, oxytetracycline, terramycin, etc.) are most effective. They are given in doses from 1.2 g to 2 g a day, depending on severity of the disease and the body weight of the patient. Duration of the therapy is from 3-5 to 9-10 days after normalization of body temperature.

Oxygen therapy, vitamins and cardiacs are given for special indications. Plasma or blood (autohaemotherapy included) should be given during the recovery phase. In the presence of contraindications, vaccinotherapy should be given for chronic psittacosis.

Prevention and control. It is necessary to control psittacosis in domestic birds. If the disease is detected at poultry farms, 6-month quarantine should be established. All birds with the disease should be treated (for 14-21 days, tetracycline is added to the fodder in the amount of 200 g per ton), or the diseased poultry can be killed and processed at the same poultry farm. Their meat should be processed

thermally before using as food. Feather and down should be burned or disinfected with live steam at a temperature of 105 °C for 30 minutes. Eggs collected at poultry farms with quarantine should also be treated thermally before using as food.

Infected farms should be disinfected with a 5 per cent clarified lime chloride or 10 per cent lysol solution.

The personnel should wear overalls, goggles and masks.

If diseased poultry is processed at plants, rooms should be washed with a 2 per cent chloramine solution at 3-hour intervals. Excrements and feather should be treated with a 10 per cent lysol solution.

The most effective method to prevent psittacosis is aerosol immunization.

Measures in the focus. Psittacosis patients should be treated in infectious hospitals. Persons exposed to the danger of infection should be observed for 16 days.

Legionellosis

Aetiology. The causative agent belongs to the family of *Legionellaceae,* the genus *Legionella.* At the present time, 9 species of *Legionella* are known: *L. pneumophila, L. bozemani, L. micdadei, L. gormanii,* etc.

Legionellas are typical sapronoses that can survive and multiply in natural conditions of the environment. Open water bodies, especially those rich in blue-green algae, are suitable sites for multiplication of legionellae. They can also be accumulated in air-conditioning units, in showers, water tanks, or in soil of endemic areas (mostly in the United States). Legionellas are stable in the environment: they can survive in tap water for about a year, and in distilled water for 2-4 months.

Epidemiology. The fact of liberation of legionellas by humans or animals has not been confirmed. The only known route of infection transmission is by inhalation of minutest droplets of infected water in showers, water sprayers of air conditioning units. Alcohol abuse, smoking, diabetes mellitus, and immunodepressant promote susceptibility of legionellosis.

The disease occurs as epidemic outbreaks, usually in the warm season, or as sporadic cases during the whole year.

An epidemic of 1976 that broke out among the delegates of an American Legion Convention in Philadelphia was assessed as an epidemic of a new disease which was given the name of Legionnaires' disease. At the present time cases of this disease have been reported

from USA, Great Britain, Spain, Italy, France, Germany, USSR and some other countries.

Pathogenesis. The legionellosis agent gains entry to the human body by inhalation of infected water droplets. The agent affects bronchioles, where it dies to release the endotoxin that is detrimental to various organs and systems. Septic shock is possible in severe cases. The kidneys (acute renal failure due to upset microcirculation), the gastrointestinal tract, and the central nervous system are involved. Haemorrhagic syndrome can occur.

Clinical picture. The incubation period lasts from 2 to 10 days (usually 5-7 days). The disease can proceed with symptoms of pneumonia (Legionnaires' disease proper), acute respiratory disease or meningitis in infants of the first year of life. The disease begins acutely with elevation of body temperature to 38.5-40 °C, chills, malaise, myalgia and headache.

The pneumonia-like form of the disease is characterized by severe cough and piercing chest pain. Cough is first dry, then it becomes productive. Dyspnoea supervenes; vast zones of lung involvement are revealed by x-ray: pneumonia is often attended by pleural effusion. Some patients develop vomiting, diarrhoea, abdominal pain and gastrointestinal bleeding. Hypotension is seen. Bradycardia of the first days of the disease is superseded by tachycardia. In connection with involvement of the central nervous system the patients complain of vertigo and insomnia. Delirium, confusion, and discoordination are possible. The renal function is upset. Excretion of the urine decreases to anuria. Neutrophilic leucocytosis (10-15 x x 10^9/1), thrombocytopenia and lymphopenia are observed; the ESR increases to 70 mm/h and higher.

If the disease runs the course of an acute respiratory disease, the body temperature remains high during 2-5 days; bronchitis and pleurisy are possible. Intoxication is less pronounced than in pneumonia.

In moderate cases, the body temperature decreases by the end of the first week, and slow recovery begins.

If the disease is severe and is not treated in due time, the patient can die by the end of the first week from a rapidly developing cardiac and/or respiratory failure, septic shock, and acute renal failure.

Diagnosis. The diagnosis is based on clinical, epidemiologic and laboratory findings.

Laboratory studies include bacteriologic and serologic tests. The causative agent can be isolated from pleural effusion or specimens of lung tissue; less frequently from sputum or blood. The material is

seeded on Mueller-Hinton agar containing iron salts and cysteine, and 5 per cent carbon dioxide. The optimum cultivation temperature is 35 °C. The obtained culture is used to inoculate guinea pigs with subsequent cultivation in chick embryo. Direct immunofluorescent method reveals legionellae in specimens of lungs, bronchi (obtained during bronchoscopy) and sputum. The immunofluorescent method is performed with sera to 7 serogroups of *L. pneumophila.* Serologic tests (microagglutination and indirect immunofluorescence tests) are often used in legionellosis. Antibodies can be seen on the 6-7th day of the disease, with their maximum occurrence in 5 weeks. Paired serum specimens are taken at 10-15 day intervals. The four-fold increase in the titre of antibodies is considered diagnostically trustworthy; if a single serum specimen is tested, the titre of 1:128 and higher is regarded as diagnostically important. Antigens of 7 known serogroups of *L. pneumophila* are used as the antigen. Indirect haemagglutination and radioimmune methods are now being elaborated.

Treatment. Erythromycin is most effective; it is given in doses of 0.4-0.5 g 4-6 times a day until normal temperature stabilizes. Severe forms of legionellosis are treated with 0.2 g doses of erythromycin phosphate 2-3 times a day; the preparation is given in an isotonic sodium chloride solution: 5 mg per 1 ml of the solution. Efficacy of treatment increases with combinations of erythromycin and rifomycin which are given in doses of 0.15-0.3 g at 6-hour intervals. Oxygen therapy (at least 40 per cent oxygen concentration in the inhaled mixture) is also used. Acute renal failure should be treated with diuretics; haemodialysis should be conducted if necessary. If respiration function is severely upset and drug therapy fails, artificial ventilation is necessary. If septic shock or haemorrhage develop, appropriate treatment should be conducted.

Prevention and control. The specific prophylaxis of the disease is unknown. Protection of water sources is important. Decontamination of water, water-supply system, baths and showers, etc., should be done with calcium hypochloride in the concentration of 3.3 mg of nascent chlorine per litre. Heating water to 60 °C kills the pathogenic agent in the water-supply system.

Legionnela is rapidly killed by a 1 per cent formaldehyde solution. Air-conditioners should be maintained properly. If there are signs of water contamination with the agent, production of aqueous aerosols should be discontinued.

If an epidemic of legionellosis arises at a medical institution, water should be decontaminated and immunodepressants should be re-

stricted; operative interventions, in which immunodepressants are used, should be suspended.

Legionellosis patients should be taken to hospital for rendering adequate medical aid in cases of complications (septic shock, acute renal failure, lung oedema, and the like).

Reveiw Problems

1. An 11-month-old infant was isolated after dinner from the other infants in a day nursery and taken home by his parents. The diagnosis was influenza.

Plan the measures by which the source of infection can be detected and the influenza focus eradicated in the day nursery and at home.

2. Establish a differential diagnosis of influenza, parainfluenza, and adenoviral infection. What main sign confirms the diagnosis? Name the laboratory methods used to differentiate between influenza, parainfluenza and adenoviral infection.

3. A child was hospitalized on Feb. 12 from a kindergarten with a diagnosis of meningitis. On Feb. 15, another child was taken home from the same group. He had rhinorrhoea with a mucopurulent discharge, dry cough, hyperaemic fauces, granular posterior pharyngeal wall, and pallid skin. The body temperature, 37.2 °C.

What is the presumptive diagnosis in the second child? What laboratory tests should be performed to verify the diagnosis? What are the requirements for taking the necessary material and its delivery to the laboratory? Indicate the route by which the infection was transmitted and the measures that should be taken in the kindergarten and at home in order to localize and eradicate the focus of infection.

4. Three children from various school groups developed diphtheria during March. Still another child who attended a kindergarten fell ill on the sixth of April. All the diseased children were residents of the same overcrowded apartment. Repeated bacteriologic tests of the residents of this flat for the carrier state were negative.

A 6-year-old child had gone to visit his grandmother 4 days before the mentioned cases occurred and returned home on April 2. The child who developed the disease in April had contacts with him on April 2 and 3. Examination of the child after his return from his grandmother revealed the presence of crusts in the nose, sanguinous nasal discharge, fissures under the nose, and postauricular crusts. As reported by his mother, the crusts and fissures under the nose had developed long ago and resisted treatment. The child was not examined by physician.

What presumptive diagnosis can be established in the child that can be suspected as the source of infection? What laboratory tests can be conducted to verify the diagnosis? Specify the method of taking specimens and conditions for their delivery to the laboratory. How soon will the results of the test be ready? Explain the cause of formation of the infection focus, specify

the route of infection transmission and the measures that should be taken to localize and eradicate the focus.

5. A 3-year-old infant attending a kindergarten developed scarlet fever. The mother of the infant works at a day nursery, the father works at a plant. The sister is the first-form schoolgirl. The family lives in a separate flat.

Indicate the main symptoms characteristic of scarlet fever. What anti-epidemic measures should be taken to prevent infection spread in the focus and in the kindergarten.

6. A 5-year-old child attending a kindergarten developed catarrh of the upper airways and cough that intensified at night. Six days later paroxysms of cough became progressively longer. The body temperature was normal. The child received all necessary vaccinations in due time and continued attending the kindergarten.

What diagnosis can be suggested? What laboratory studies are necessary to verify the diagnosis? Specify the conditions for taking specimens, their delivery to the laboratory, and the terms for obtaining the results of the tests. What anti-epidemic measures should be conducted at the child's home and in the kindergarten if the suggested diagnosis proves correct?

7. A 27-month old infant was isolated from the group in a day nursery for catarrh of the upper airways, barking cough and temperature of 37.9 °C. Two days later the mother reported (by telephone) development of macular rash on the face and the upper extremities of the child; the body temperature was 38.9 °C. The infant had been vaccinated only against diphtheria, tetanus and pertussis.

What diagnosis can be suggested? What anti-epidemic measures should be taken in the day nursery and the child's home if the diagnosis is correct?

8. A child with the diagnosis of poliomyelitis was hospitalized from the junior group of a day nursery. Indicate the anti-epidemic measures that should be taken at the infant's home and the group of the day nursery.

Blood Infections

Rickettsioses

Rickettsial infections are caused by the microorganisms of the family *Rickettsiaceae.* They owe their name to Howard Taylor Ricketts, American pathologist who discovered them in 1910. Rickettsia parasitize on the arthropods (lice, fleas, ticks) and the mammalians (they invade the cells of endothelium and mesothelium). All rickettsial infections, except typhoid fever, are zoonoses. They are mainly transmitted through living objects, such as lice, fleas, ticks, or mites which dissipate the microorganisms with their saliva and excrements. The only exceptions are endemic rat-borne typhus (the infection is transmitted by ingestion of food contaminated with the urine of rats)

and Q fever (infection is transmitted through milk and urine of cattle, and also through dust containing the microorganisms).

Natural nidality is characteristic of the rickettsioses (except epidemic typhus): their causative agent circulates between susceptible animals and the blood-sucking arthropods.

Epidemic Typhus and Brill's Disease

Aetiology. The causative agent of epidemic typhus is *Rickettsia prowazeki.* The microorganisms are unstable in the environment but in dry lice faeces they can live from one to several months. **The** rickettsia can be found in the body of epidemic typhus patient, inside cells of intestinal epithelium of lice and in their faeces.

The causative agent of Brill's disease (recrudescent typhus) is the same *R. prowazeki* which persists in humans as latent infection for long periods of time and causes relapses of the disease at various intervals.

Epidemiology. The only source of infection is a human patient with epidemic typhus who becomes contagious during the last days **of the** incubation period (2-3 days), during the entire fever period, and till the 7-8th day of the disease after normalization of body temperature. The overall length of the contagious period is 20-21 day.

The infection is transmitted by body lice, less frequently by head lice (Fig. 13). Body lice deposit their eggs on hair, in pleats and folds of underwear and clothes, while head lice lay them only on hair. Eggs yield larvae which undergo triple sloughing before they grow to mature insects. This period lasts 7-10 days and should be taken into consideration when observing the focus and prescribing repeated sanitary treatment. When a louse sucks the blood of a typhus patient it becomes contagious in 4-5 days during which rickettsia multiply in the louse intestinal epithelium. After destruction of the epithelial cells the rickettsia gain entrance to the intestinal lumen and are excreted in great amount with faeces. When a louse sucks blood, it excretes a substance that causes itching. As a person scratches the site of a louse bite he rubs the faecal mass with rickettsia into the puncture wound and the scratch site. Contamination can occur when a crushed louse is rubbed into the skin. An **infected** louse lives 20-40 days instead of 45-60 days and dies of the ruptured intestine.

The incidence of epidemic typhus is characterized by seasonal variations, the highest incidence being during winter and spring. Seasonal variations are absent in Brill's disease; neither can any connection be established between sporadic cases. Brill's disease

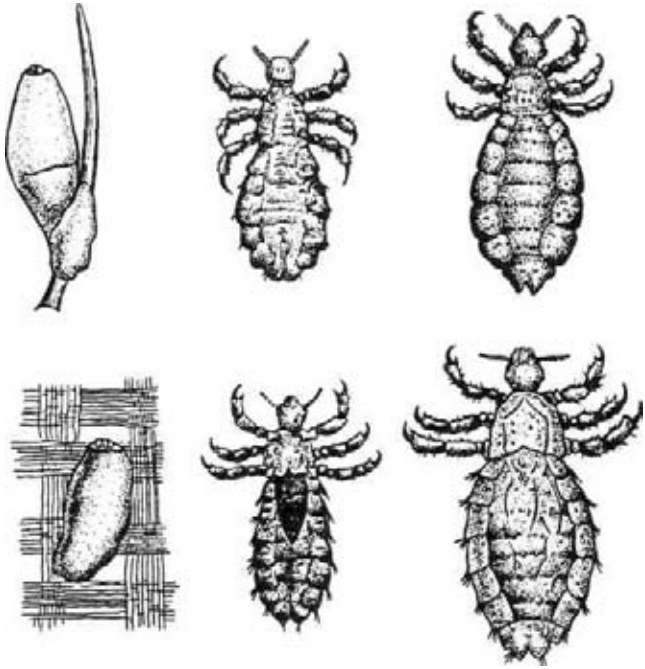

Fig. 13. Lice: head louse (top) and body louse (bottom)

occurs usually in the aged, who often report epidemic typhus in their early history or their stay in the focus of typhus in past life. The quantity of rickettsia is not great in the blood of a Brill's disease patient with the disease in its full swing. But such patients can become the source of infection if they are affected with pediculosis. Susceptibility to epidemic typhus is high; persons aged from 15 to 40 usually develop the disease. This can be explained by the intensive activity of people at this age. A sufficiently stable immunity develops in those who sustained the disease.

The social factor is decisive in epidemiology of this disease. Famine, inadequate housing and sanitary conditions, absence of baths and disinsectants, poor sanitation of population, its intensive migration in connection with war, famine or other disasters promote dissemination of the infection.

Epidemic typhus is now common in Algeria, Tunis, Marocco, South Africa, Iran, Bolivia, Guatemala, Colombia, Mexico and Chile.

Only sporadic cases of Brill's disease are reported from Europe and North America.

Pathogenesis. The pathogenic microorganisms enter the body through scratched or bitten skin. Rickettsia invade the cells of vascular endothelium where they multiply and are carried by the blood stream to cause rickettsaemia. Part of the microorganisms die to release toxin which causes toxaemia. In fine vessels, rickettsia cause thrombi with subsequent proliferation of the vascular wall and around the vessel; thrombophlebitis and specific granuloma thus develop.

Vascular changes become manifest in 4-8 days of the disease in all organs and tissues, especially in the brain, skin, conjunctiva, adrenal glands, myocardium, spleen and the kidneys. These lesions are manifested by specific symptoms on the part of the nervous, psychic, and cardiovascular systems, skin and other organs and tissues. Organic changes develop in 18-20 days and their development terminates by the end of the 4th week and later. Rickettsia are not completely eliminated from some patients, and the process becomes latent with persistence of the microorganisms in the reticuloendothelial cells. Relapses (Brill's disease) can be provoked by overstrain, either physical or psychic, poisoning, variations of temperature, etc.

Clinical picture. The incubation period lasts from 6 to 25 days (usually 12-14 days).

The onset of the disease is acute. The body temperature increases; headache, chills, malaise, and thirst develop; the patient loses appetite. Headache intensifies and becomes debilitating; insomnia develops. Irritability and anxiety of the first days are then followed by excitation. Increasing symptoms, especially weakness and fever, force the patient into bed on the 2-3rd day of the disease.

Hyperaemic and swollen face, hyperaemic conjunctiva, injected and dilated scleral vessels (rabbit eyes) are seen during the first days of the disease. The skin of the neck and the upper trunk is also hyperaemic. The tongue is dry and is difficult to protrude (Godelier's sign). The skin is dry and hot to feel. Dyspnoea (central), moderate tachycardia and hypotension are seen. Petechial haemorrhages can develop in 3 days on the conjunctival fold; the haemorrhages also appear on the shoulder or the thigh, below the point where a tourniquet is applied. Specific rash (Plate VII) appears on the 4-5th day of the disease by which the initial period of the disease ends. During the period of the disease in full swing the rash is first represented by roseoles which later change to petechia. Rash develops on the flanks, chest, and the back, covers the whole body. It

is intensive and its elements are different in size: from the size of a pin-head to that of a lentil. In moderate cases rash persists till the 12-14th day. As rash develops, fever intensifies and becomes continuous or remitting, and remains so for 6-8 days.

The height of the fever period is characterized by moderate neutrophilic leucocytosis (to 9-11 x 10^9/1), thrombocytopenia and aneosinophilia; ESR is high (18-25 mm/h).

The initial symptoms intensify with appearance of skin eruption, and new symptoms supervene. Involvement of the nervous system increases. Consciousness is dimmed, hallucination and delirium develop, the patient is restless, tries to raise in his bed or run. This condition, in the presence of high fever, is known as *status typhosus*. Symptoms of meningoencephalitis develop: stiff neck, Kernig and Brudzinski's symptoms, increased tendon reflex, tremor of the extremities, inarticulate speech, throat itching, and difficult swallowing. The heart sounds are dull, heart rate is fast, arterial pressure is low, collapse is possible. The liver and the spleen are enlarged. Constipation develops. Severely ill patients can defaecate and urinate involuntarily, or the urine can be passed in small portions while the bladder is overfilled.

In 12-14 days of the disease, body temperature drops and the recovery phase begins. The fever resolves by an accelerated lysis within 2-3 days; less frequently the fall of temperature is critical. Toxaemia decreases and all its symptoms (status typhosus in the first instance) subside gradually. Rash resolves, consciousness clears, the patient shows interest in the surrounding, sleep and appetite improve, urination normalizes, pulse and arterial pressure normalize as well. But despite the considerable improvement of the patient's general condition, weakness and pain in the legs and by the course of the nerve trunks persist for a long time. The central nervous system remains easily excitable.

Mild, moderate and severe forms of epidemic typhus are distinguished. The clinical picture of the disease has considerably changed in recent years (compared with the described classic symptoms).

Mild forms of the disease are of greater epidemiologic importance because the specific fever, rash, toxaemia, and nervous and vascular lesions are less pronounced. The body temperature of 38-39 °C persists for 7-9 days. The prevalent elements of the rash are roseoles. Headache and insomnia are pronounced, but other nervous symptoms are either absent or only mild. The status typhosus is usually absent.

Brill's disease runs a milder course, the status typhosus is less

pronounced and shorter than in epidemic typhus. Other symptoms are not so marked either. The fever period lasts 8-11 days. The onset of the disease is usually acute, the body temperature decreases critically.

Complications. Complications are now rare. They can be divided into 4 groups:

(1) lesion of the vessels and the heart-collapse, thromboses, thromboembolism, rupture of the cerebral vessels with hemiparesis or even paralysis, myocarditis, etc.;

(2) complications due to involvement of the central and peripheral nervous systems-psychosis, polyradiculitis, neuritis;

(3) complications due to secondary infection - pneumonia, otitis, parotitis, furuncles, abscesses;

(4) mixed complications - lesion of the vessels and the central nervous system with secondary infection; bedsores, gangrene of the ear lobules, fingers, toes, and nose tip; thrombophlebitis, nephritis, nephrosonephritis, etc.

Diagnosis. The diagnosis is based on clinical, epidemiologic and laboratory findings. Serologic methods of examination are most important diagnostically. Blood specimens (3-5 ml) are tested in the laboratory beginning with the 5-7th day of the disease. Rickettsia agglutination reaction, complement fixation test, indirect haemagglutination and immunofluorescent and allergic tests are among the most sensitive methods. The reaction of rickettsia agglutination with corpuscular rickettsia antigen is considered positive with titres of 1:160 and higher. But the use of these reactions is limited because their results are not always trustworthy and cannot be used for retrospective diagnosis. Complement fixation test is conducted with corpuscular or soluble rickettsial antigen. The diagnostic titre is 1:160 and higher. The maximum quantity of antibodies is found in 12-20 days of the disease (1:640-1:1280). Indirect haemagglutination tests are most valuable diagnostically. They are performed on the 3rd-5th day of the disease and the result is considered positive with the titres of 1:250 and higher. The maximum antibody level is seen in 14-20 days of the disease (1:1000 and higher).

Treatment. Modern treatment quickly decreases body temperature, eliminates toxaemia, promotes resolution of rash. But antibacterial therapy fails to restore the upset functions of the vascular and nervous systems or eliminate the causative agent from the patient.

The following tetracyclines are used during the full swing of the disease, in accordance with the severity of the patient's condition: tetracycline hydrochloride, terramycin, dioxycycline hydrochloride

per os, 0.3 g four times a day until normal temperature persists for three days. Chloramphenicol is inferior to the tetracyclines with respect to its efficacy but whenever necessary it can be given per os in doses of 0.5 g 4 times a day until normal temperature persists for 3 days.

In order to decrease toxaemia, a 5 per cent glucose solution or an isotonic sodium chloride solution (800-900 ml each) should be given intravenously. Upset circulation of blood is managed by administration of a 10 per cent glucose solution, Ringer solution, mesaton (1 ml of a 1 per cent solution), strophanthin (0.3-0.5 ml of a 0.5 per cent solution with glucose). The solutions are given intravenously at a low infusion rate. Barbiturates, bromides, aminazine are given to control excitation. In order to prevent thrombosis, anticoagulants (heparin, phenylin) are given.

Patient care is important. Bedsores are likely to develop, and the patient should therefore be helped to change his position in bed; the linen should be stretched to prevent formation of folds. Critical patients should be placed in bed over an inflatable rubber cushion. The sacral region, the buttocks and the shoulder blades should be wiped with camphor alcohol. Rubbing with warm water (37-38 °C) and taking warm baths (35-37 °C) are sedative.

Evacuation of the bowels and urination must be regular. The patient must rinse his mouth with a 0.5-2 per cent sodium hydrocarbonate solution. If the patient is debilitated by the disease and is unable to do it himself, his mouth should be treated with a cotton tampon wetted with a 2 per cent solution of boric acid and glycerol.

The diet must be sparing, sufficiently caloric and rich in vitamins. Meals must be given frequently in small portions. Since the patient is tortured by thirst, drinks should be given without any restriction. The patient is allowed to walk about after 7-8 afebrile days.

Prevention and control. The main measures are aimed at elimination of the source of infection and eradication of pediculosis among population.

Patients suspected for epidemic typhus should be hospitalized immediately. Patients with fever in whom the disease is not diagnosed by the 5th day should be hospitalized provisionally.

It is very important that patients with epidemic typhus, and also those suspected for this disease be hospitalized during the first 5 days because the infected louse is yet unable to transmit the typhus agent to the surrounding people. Isolation can be discontinued not earlier than in 12 days after normalization of body temperature.

Pediculosis among population shall be controlled by providing all

necessary facilities (baths, laundries), by improving sanitary standards, especially among migrating people, such as seasonal workers, builders, etc. Pediculosis can be detected by selective examination of workers at industrial plants, schools, bordering schools, hostels, etc. The screened persons with pediculosis must be given appropriate treatment. Their families and co-workers should be given prophylactic examination and, if necessary, appropriate treatment. Control of pediculosis includes baths at least once in 7-10 days with renewal of the linen and underwear.

Specific prophylaxis should be conducted for special indications. Dry live vaccine should be given. A new vaccine has been developed; it is a chemical vaccine against epidemic typhus consisting of soluble rickettsial antigen. The vaccine is given subcutaneously by a single 0.5 ml dose.

Measures in the focus. They include immediate hospitalization of the patient, epidemiologic examination, observation of persons who had contacts with the diseased, their laboratory examinations, disinfection of the focus, and examination and, if necessary, appropriate treatment of population in the vicinity of the focus.

After hospitalization of the patient, disinsection in the focus should be performed not later than in 3 hours in cities and towns, and 6 hours in rural areas. The patient should not change his underwear before hospitalization.

All exposed should be given appropriate treatment in special disinfection units or in common baths transformed into such Units. All garments, linen and underwear, and also the fomites should be disinsected in steam-formaldehyde or hot air chambers. The rooms and other enclosures should be treated with a 0.5 per cent chlorophos, 0.5 per cent methylacetophos, 5 per cent lysol solution, or 10 per cent dilor (10-15 g per square metre).

If special disinsection chambers are not available, soft fomites, linen, underwear should be boiled in a soda-soap solution or soaked in a 0.15 per cent aqueous emulsion of carbophos for 20 minutes, 0.25 per cent aqueous emulsion of dicresyl (20 minutes), 0.5 per cent aqueous emulsion of methylacetophos (30 minutes), the rate of liquid consumption is 4 litres per kg of linen (with subsequent laundry).

Garments and clothes can be treated by dusting with a 5 per cent methylacetophos, 1 per cent neopin, or 10 per cent dilor dust, or by spraying with aqueous emulsions used for soaking the linen. After disinfection, the articles should be wrapped tight in bedcloths for 2-3 hours and then well aired.

If head lice are detected (from 1 to 10 species, nits included), they

should be eliminated mechanically by combing, or by cutting and shaving the hair on the head. The hair should be collected and burned. If it is necessary to remove nits from hairs, rinsing with a 5-10 per cent acetic acid solution is recommended with subsequent combing (cotton wool or threads must be passed between comb teeth and wetted well with acetic acid solution).

If pediculosis is moderate or severe (from 10 lice and more), insecticides should be used. This procedure is however contraindicated to infants under 5 years, pregnant and nursing women, persons with injured skin, etc.

The following insecticides are recommended: a 0.15 per cent aqueous emulsion of carbophos (10-50 ml of the emulsion for a person), a 20 per cent soap suspension of benzyl benzoate.

The persons who were exposed to the danger of infection should be observed for 25 days with obligatory daily thermometry. In order to reveal the source of infection, all persons who had contacts with the diseased, and also persons who sustained a disease with fever within the past three months, should be examined by complement fixation and indirect haemagglutination tests. If the tests are positive, special medical observation must be ensured with repeated serologic testing. If body temperature rises in those who had contacts with the diseased, they should be hospitalized and diagnosis established.

Endemic (Murine) Typhus

Aetiology. The disease is caused by *Rickettsia mooseri* (the family *Rickettsiaceae,* the genus *Rickettsia).*

Epidemiology. The reservoir of infection in nature are rodents (rats, mice) and transmitters of infection among them, fleas and gamasoidea ticks. Infected rodents excrete. *R. mooseri* with urine. Food contaminated with the urine of infected mice is the main source of infection of humans. Stability of rickettsia to drying provides conditions for air-borne infection. Infection occurs during rubbing of faeces of fleas and ticks into injured skin and mucosa. Rickettsia are not transmitted by bites of infected fleas, while ticks can thus transmit the infection. Infection is not transmitted from man to man.

Murine typhus usually occurs in sea ports and mostly in countries with hot climate. Endemic foci have been reported from the Atlantic, Pacific and Indian coastal areas, and also from the countries around the Mediterranean, Black, Caspian, Baltic and the North seas.

Pathogenesis. The pathogenesis of murine typhus is the same as of epidemic (louse-borne) typhus.

Clinical picture. The incubation period lasts 5-12 days. The body temperature rapidly rises to 38-40 °C. Fever persists for about 2 weeks. Characteristic symptoms are pain in the extremities, joints, and in the lumbar region. Headache is another symptom. In 6-7 days of the disease rash develops; roseoles turn into roseole-papular rash in few days. Rash is seen on the face, abdomen, back, and even on the palms and soles. Bradycardia is noted. The clinical picture is similar to that of epidemic (louse-borne) typhus, but the course of the disease is more benign.

Complications. Complications are rare.

Diagnosis. The diagnosis is based on clinical and epidemiologic findings. Blood specimens (5 ml) should be tested in the laboratory. The blood is administered to male guinea pigs into the abdominal cavity (3 ml): the testicular tunicae become inflamed. Rickettsial agglutination and complement fixation tests are also conducted.

Treatment. Treatment of murine typhus is the same as of louse-borne typhus.

Prevention and control. Planned deratization and disinsection, and also protection of food against contamination with rodents are decisive measures. Vaccination should be performed for epidemiologic indication.

Q Fever

Aetiology. The disease is caused by *Coxiella burnetii*. The microorganisms are characterized by high stability to drying and ultraviolet radiation. In tap water they can survive for 160 days, in milk for 125 days, in oil and meat (at low temperature) for 30-40 days.

Epidemiology. The source of infection in natural foci are many animals and birds. The reservoirs and transmitters of the infection are ixodes and other ticks. Infected ticks attack domestic animals; secondary foci of infection thus arise in which the animals are infected due to intimate contacts. The disease in animals is often latent.

Domestic animals excreting rickettsia with milk (17-40 days), faeces, urine, placenta, amniotic fluid are the most important source of infection. Q fever is characterized by a variety of routes by which the infection can be transmitted, e.g. with dust and air, by direct contact with the diseased animal, with food (ingestion of diary products and other infected foods), water (bathing in infected water, drinking it), etc.

If pneumonia develops, the patient can excrete the pathogenic

agent with sputum, and he can therefore be regarded as a potential source of infection disseminating it by air-borne route and by direct contact.

There is no seasonal variations in the incidence of the disease, but in rural areas the morbidity rises in spring when the young animals are delivered.

Q fever is reported from all countries.

Pathogenesis. The portal of entry of the infection is the respiratory and eye mucosa, the skin and the alimentary tract. The lymph carries the rickettsia to the blood (primary rickettsaemia) and then to the internal organs (liver, spleen, kidneys), where the rickettsia propagates to cause secondary rickettsaemia and toxaemia.

Clinical picture. The incubation period lasts 12-19 days with extremes of 3 and 32 days. The onset is usually acute: chills and elevation of temperature to 39-40 °C.

The clinical symptoms are quite varied. The patient complains of weakness, lassitude, hyperhidrosis, severe headache, myalgia, arthralgia, lumbar pain and insomnia. Some patients develop nausea, vomiting, dry cough; the appetite is impaired, nosebleeds are possible. The fever period lasts from 3 to 15 days, most commonly from 7 to 9 days. Considerable variations in the body temperature are attended by repeated chills and hyperhidrosis. The pulse disagrees with the fever, bradycardia and hypotension develop. The body temperature normalizes by accelerated lysis. Some patients develop the symptoms of involvement of the respiratory organs (tracheitis, bronchitis, pneumonia), which are manifested by dry cough, and chest pain during cough and respiration. X-ray reveals changes in the lungs.

When ingested, rickettsia produces dyspepsia and abdominal pain. Arthralgia, roseoles, petechial rash and other eruptions are associated with allergic manifestations of the disease. Leucopenia, the shift to the left, relative lymphocytosis and monocytosis are seen in the blood; ESR is accelerated. Some patients can develop a severe disease with prolonged fever, inhibition of the nervous and cardiovascular system, and splenic enlargement. The recovery phase lasts 2-4 weeks. Relapses are possible; the disease can also transform into the chronic form.

Diagnosis. The diagnosis is based on clinical, epidemiologic and laboratory findings. Laboratory tests include complement fixation and micro-agglutination tests with specific soluble rickettsial antigen. Blood specimens (5 ml) should be taken beginning with the 7-10th day of the disease. The titres of complement fixation and micro-

agglutination tests of 1:8-1:16 are positive, but repeated tests are necessary to confirm the diagnosis (by progressively increasing titres). The immunofluorescent test is a reliable diagnostic method. Intracutaneous tests with purified allergen of the rickettsia are used for direct and retrospective diagnosis.

About 5 to 6 ml of blood are taken on the first day of the disease to inoculate two guinea pigs weighing 200-250 g. The temperature of the animals is measured daily; one guinea pig is sacrificed at the height of fever, while the other is left for serologic studies.

Treatment. Treatment is the same as in epidemic (louse-borne) typhus. Since relapses are possible, tetracycline therapy continues for 8-10 days, regardless of the presence or absence of fever, and regardless of the patient's general condition.

Prevention and control. The measures should be directed at eradication of ticks and protection of domestic animals against them. To this end, systematic disinsection should be carried out using carbophos, pyrethrum and other disinsectants during the period of tick activity. The infected animals should be isolated. At farms where Q rickettiosis is reported, quarantine should be established. Animal breeders must observe rules of individual hygiene. Only persons who sustained Q fever in the past, or vaccinated persons are admitted to take care of infected animals. The personnel should wear special overalls and observe the rules of personal hygiene at animal farms, slaughterhouses, etc. Health education among population is necessary.

Milk should be boiled while the diary product prepared only from boiled milk. Wool should be decontaminated.

Groups of people or animals should not be admitted to areas endemic for Q fever until these areas are not freed from ticks and rodents (disinsection and deratization measures). People should be protected from tick bites by wearing protective overalls impregnated with repellants. Patients should be hospitalized for clinical indications. Patient's excrements, garments, dishes and other belongings should be disinfected. The personnel must observe the rules of personal hygiene when taking care of patients.

Specific prophylaxis should be carried out among animal breeders, workers of slaughterhouses and meat processing plants in areas dangerous for Q fever. People should be vaccinated with M-44 vaccine. It is diluted with an isotonic sodium chloride solution and rubbed into the skin or given per os. Revaccination is necessary in two years.

Borrelioses

Relapsing Fever

Aetiology. Relapsing fever is caused by *Borrelia recurrentis* which belongs to the family of *Treponemataceae,* the genus *Borrelia.* The agents can live only in human beings and in lice. They are pathogenic for humans and monkeys. The microorganisms are motile and look like spirals. They are stainable with aniline dyes.

Epidemiology. The source of infection is a diseased human during the fever period, but the infection can probably be transmitted during apyrexia as well.

The infection transmitters are body lice, less frequently head lice. When a louse sucks blood of the patient, it becomes contagious in 5-7 days and remains so for 28 days. Humans are infected by rubbing a crushed louse or its fragments into injured skin or the eye mucosa.

Humans are highly susceptible to relapsing fever. The immunity is unstable and repeated infections are common.

Since the transmission mechanism is rather complicated, epidemics of relapsing fever occur only under very poor sanitary conditions, mass-scale pediculosis, intensive migration of population during war or famine.

Like epidemic (louse-borne) typhus, relapsing fever can occur in any country. At the present time, it is reported from the countries of the Middle East, North Africa, South-East Asia and South America.

Pathogenesis. Borreliae gain entry through damaged skin and eye mucosa, propagate in the blood, in the internal organs and the central nervous system. Part of the microorganisms are destroyed to release endotoxin. Accumulation of borreliae and the toxins in the blood causes fever, headache and myalgia. The endotoxin causes lesion of the vessels and upsets their permeability; haemorrhagic infarcts and necrosis develop in the liver and spleen, and the symptoms of involvement of the central nervous system develop. By the end of the attack, antibodies are formed that destroy borreliae. Subsequent relapses of the fever are caused by borreliae that survive in the bone marrow, the internal organs, and the central nervous system to give a new race of the microorganisms that differ in their antigen structure.

Clinical picture. The incubation period is usually 7-8 days, but it can vary from 3 to 15 days. The disease is characterized by alternation of fever and apyrexia periods. The disease begins suddenly and acutely, with a shaking chill, which is followed by fever,

strong headache and vomiting. The body temperature rises to 39 °C and higher within 1-2 hours. The maximum body temperature (40-41 °C) is seen during the second and third days of the disease. Severe headache is supervened by severe muscular pain, mainly in the calves. Pain can be sensed by the course of the nerves and in the joints. The patient is forced to bed on the very first day of the disease. The skin is dry, the tongue is coated and moist. Appetite is lost, dyspepsia is frequent. The spleen is enlarged on the second day of fever and pain develops in the left hypochondrium. In 3-4 days, the sclera and the skin become icteric, the hepatic enlargement becomes more pronounced. Cardiovascular failure is possible. Some patients develop fine roseolous, petechial and macular rash on the 4th or 5th day of the disease. The rash disappears in few hours. Nosebleeds are possible because of increased permeability of the capillaries and mucosa and decreased quantity of thrombocytes.

Leucocytosis with a neutrophilic shift to the left and moderate hypochromic anaemia develop from the first days of the disease.

During the periods of apyrexia, leucocytosis is followed by leucopenia, while neutrophilosis by lymphocytosis and increased number of plasma cells. Eosinophilia develops by the end of the disease. The first paroxysm lasts 5-7 days and ends critically. Normalization of body temperature is attended by profuse sweating. The patient's condition improves rapidly. In 6-9 afebrile days, another attack of the disease begins. All symptoms of the first attack are repeated. The second attack lasts 3-5 days. Each next relapse is shorter than the previous one, while the apyrexia period, on the contrary, becomes successively longer. In most cases, the course of the disease comprises several such relapses.

Complications. Nosebleeds are possible: pregnant women often abort with profuse uterine bleeding. The most severe complication of relapsing fever is splinic infarction which sometimes ends in purulation and rupture of the spleen with fatal haemorrhage and peritonitis. Diffuse nephritis is possible.

Diagnosis. The diagnosis of relapsing fever is simple during the fever period. It is established on the basis of clinical, laboratory and epidemiologic findings. A fingertip blood specimen is sent to the laboratory in the form of two thin and two thick smears on glass slides. The smears are stained with fuchsine or according to Romanovsky-Giemsa. Blood specimens should be taken at the height of the relapse.

During the afebrile period, when borreliae are scanty in the blood of the patient, the specimen is centrifuged and smears are prepared

from a concentrated sediment. The complement fixation test is also used.

Treatment. Antibiotics are used: penicillin, 3 000000 U a day for 5-6 days, tetracycline 0.3-0.4 g four times a day for 5-7 days, or chloramphenicol 0.5 g 4 times a day for 5-7 days. Camphor and cordiamin are given for circulatory disorders, and 1 ml of a 5 per cent ephedrine (subcutaneously) for collapse. Vitamins and plasma are also recommended.

Prevention and control. Patients with relapsing fever should be taken to an infectious hospital for isolation during the entire fever period and for 20 days after termination of an attack.

Measures against pediculosis should be taken (see "Epidemic Typhus and Brill's Disease").

Measures in the focus. After hospitalization of the patients, sanation of the focus should be performed. Patient's rooms should be disinsected. Persons who were in contact with the diseased should be treated in a bath or shower, while their clothes treated in a disinfection chamber. These persons should then be observed for 25 days after sanation of the focus. If persons with fever are detected, they should immediately be isolated and their blood studied microscopically.

Endemic Relapsing Fever

Aetiology. The disease is caused by various species of *Borrelia* (which are more than 20). The borrelia causing endemic relapsing fever can be found in great quantity in the blood of patients both during the fever and apyrexia periods.

Epidemiology. The source of infection are rodents and other animals, and also diseased humans. Natural nidi of tick-borne borreliosis are also known.

The reservoir and the transmitters of infection are ticks *Ornithodorus* which inhabit the cracks of clay-lined houses, in sheds, and rodent holes. After a tick bites an infected animal or human, it remains contagious for its entire life and transmits infection to its posterity. In natural nidi, the infection circulates between ticks and wild mammalians (rats, voles, hedgehogs, badgers, etc.) and birds. In populated places, domestic animals and humans become incorporated into the circulation of infection.

Humans are infected by tick bites through its saliva. Immunity is maintained in endemic foci due to repeated tick bites. The disease is characterized by natural nidality. Nidi of the infection are reported from Asia, America, Africa and South Europe.

The morbidity increase in spring and autumn due to increased activity of the transmitters (ticks).

Pathogenesis. Pathogenesis is the same as in epidemic relapsing fever.

Clinical picture. The incubation period is 11-12 days with extremes of 5 and 20 days. The onset of the disease is usually acute. The patient develops chill, the body temperature rises rapidly to 39-40 °C and higher.

The patient complains of headache and pain in the calves. The patient is excited. Delirium and confusion are not uncommon. Pulse is fast. The skin is slightly icteric. The spleen is enlarged insignificantly. A cherry coloured papule is formed at the site of tick bite. The attack lasts 2-6 days and ends in crisis, but another relapse begins after several afebrile days. Each next attack is shorter, while periods of apyrexia become, on the contrary, longer. From 6 to 12 relapses usually occur during the disease, but their number can be 15-16 and even greater. The overall length to the disease is thus 1-2 months. Signs of hypochromic anaemia, leucocytosis, monocytosis, and eosinopenia can be seen; ESR is accelerated.

Complications. Iridocyclitis, neuritis, meningitis, jaundice, and pneumonia are possible.

Diagnosis. The diagnosis is based on the specific clinical, laboratory and epidemiologic findings. Laboratory studies include examination of thin and thick smears. If borrelia cannot be found in the blood, its 0.5-1 ml specimen is given subcutaneously or intraperitoneally to guinea pigs: borrelia can be seen in great quantity in the blood of the animal in 1-5 days.

Treatment. Tetracycline, 0.2-0.3 g 4 times a day, and chlorotetracycline 0.25 g 6 times a day should be given until apyrexia is stable. Relapses of the fever are usually absent after antibiotic therapy.

Prevention and control. Control of rodents and transmitters of infection is the main preventive measure. Carbophos, chlorophos and other preparations are used to fight ticks in houses, sheds, and other enclosures. Cracks should periodically be closed in houses, walls should be white-washed frequently, entrance to the interior should be closed with screens impregnated with repellents. Repellents should be used to protect travellers to endemic regions. The skin should be inspected and ticks removed.

Measures in the focus. Patients should be isolated and treated. Disinsection in the focus is necessary. It includes treatment of housing, sheds and other buildings, control of ticks, treatment of animals, etc.

Tick-Borne Encephalitis
(Encephalitis acarinarum)

Aetiology. The causative agent is an RNA-containing arbovirus of antigen group B. The virus of tick-borne encephalitis withstands low temperature and freezing but is sensitive to high temperature and is killed by boiling for 2-3 minutes; the virus is rapidly destroyed in environment. In the laboratory, the virus readily propagates in chick embryo and various tissue cultures. Albino mice, hamsters, monkeys, sheep, goats, horses, cows and other animals are sensitive to the virus.

Epidemiology. The main reservoir and transmitter of infection are ixodes and gamasoidea ticks, in which the virus survives during their entire lives (2-4 years). Infected ticks transmit the pathogenic agent to several subsequent generations. In natural nidi, the virus circulates among mammalians (moles, hedgehogs, hares, squirrels), birds, and ticks. The character of human activity causes gradual changes in biocenosis in the natural nidi. Domestic animals are also involved in the circulation of the virus. Rodents, birds, ticks, cattle and small wild and domesticated animals are hosts for larvae. Humans can be infected through the tick bites and also when crushing ticks on their skin, especially if the skin has erosions or other injuries; the virus can gain entrance through the eye mucosa as well.

Cows and goats can disseminate the virus with their milk. Ingestion of such milk causes a special form of encephalitis-milk fever or two-wave meningoencephalitis.

The morbidity increases in spring and autumn when ticks are more active.

Newcomers develop the disease more frequently than native population in whom latent immunity is produced due to infection with minute doses of the virus. Stable immunity is produced in those who sustained the disease. Persons working in conditions of intensive exposure to ticks (railroad builders, wood cutters, shephards, hunters, geologists, and the like professions) are usually afflicted by the disease. Males aged from 20 to 40 dominate among the diseased.

Tick-borne encephalitis occurs in the USSR, China, Czechoslovakia, Poland, Hungary, Bulgaria, Yugoslavia, Austria, Finland, and Sweden.

Pathogenesis. After entering a human body, the virus multiplies in subcutaneous cellular tissue, lymph nodes, spleen, and are carried with blood stream to the central nervous system where it affects the grey substance of the brain and the spinal cord. The nuclei of the medulla oblongata and the neurons of the anterior horns of the

spinal cord are especially afflicted. When ingested, the virus multiplies in the intestine from where it is carried with blood to the central nervous system and the meninges. Patients with milk fever look like severely ill, but the disease is milder than in cases where the virus enters a human through a tick bite.

Clinical picture. The incubation period lasts from 8 to 23 days (10-14 days on an average). The onset is acute: the body temperature rises to 39-40 °C within 1-2 days, where it remains for 3-5 (to 12) days and then decreases critically in the end of the fever period. The patient complains of severe headache, general hyperaesthesia, lassitude, and weakness. The face, sclera, conjunctiva, fauces and the soft palate are hyperaemic. Leucocyte count increases to 12-18 x 10^9/1, and ESR is high. Further progress of the disease depends on its clinical form.

If the patient develops *fever* form, the body temperature decreases in 3-5 days and the patient recovers. The fever period lasts 7-14 days.

The *meningeal* form is characterized by stupor, drowsiness, flaccidity, and symptoms of meningitis: stiff neck, Kernig's and Brudzinski's signs. The cerebrospinal fluid contains moderately high quantity of leucocytes and protein.

The *meningoencephalitic* form of tick-borne encephalitis runs a severe course. In addition to the mentioned symptoms, delirium, hallucinations and epileptiform seizures are common. Speech can be inarticulate, swallowing is difficult. These are due to lesion of the nuclei of the 9th, 10th and 12th pairs of the cranial nerves; the 3rd, 4th, 5th, 6th and 7th pairs can also be involved. The cerebrospinal fluid issues under pressure, its protein content and cytosis are high.

The *poliomyelitic* form is characterized by flaccid paresis and paralysis of muscles of the upper extremities, neck, and shoulders which develop in 2-3 days of the disease. In 2-3 weeks the involved muscles undergo atrophy.

Milk fever begins acutely with elevation of body temperature to 38-40 °C on the first day of the disease, chill, severe headache, nausea, vomiting, muscular and back pain, hyperaemia of the face, injection of the scleral vessels. In 5-8 days the temperature decreases by accelerated lysis. In 75-85 per cent of cases the temperature rises again in 7-14 days, the patient develops headache, myalgia, and the symptoms of meningitis; sleep is deranged. Gait becomes disordered in some patients; neuritis of the acoustic and facial nerves, inadequate convergence and diplopia develop. The second attack of fever lasts 7-10 days and is severer than the first attack. Cytosis in the

cerebrospinal fluid is moderate (100-400 x 10^b/l and higher); the protein and sugar content is high; during the first attack of fever, leucopenia with lymphocytosis can be registered.

Diagnosis. The diagnosis is based on clinical, epidemiologic and laboratory findings. Blood (10-15 ml) is used for the complement fixation test, the passive haemagglutination and haemagglutination inhibition tests. The tests are repeated with the paired serum samples taken during the first days of the disease, in 3-4 weeks, and 2-3 months from the onset of the disease. Besides, during the first 7 days of the disease, the urine, the cerebrospinal fluid and mucus taken from the upper airways should be used for intracerebral administration to newborn albino mice. The material is taken in sterile test tubes and kept in a refrigerator or on ice.

Treatment. The patient must remain in bed during the acute period and subsequent afebrile 2-3 weeks. Specific donor immunoglobulin is especially effective in the first days of the disease. The preparation is given intramuscularly, 6-9 ml daily for 3-4 days. During the second wave of fever, immunoglobulin therapy should be repeated.

Symptomatic treatment includes a 25 per cent magnesium sulphate (10 ml intramuscularly), 10 per cent sodium chloride solution, glucose, haemodez, vitamins, and cardiacs. When paralysis develops, it is necessary to see that the patient remains in bed. The neck should be fixed in plaster, the involved extremity should be adjusted in a physiologically convenient position, etc. Physiotherapy, massage, and medical exercises are indicated during the recovery phase.

Prevention and control. Eradication of ticks, protection against their bites and active immunization are important.

Nidi of infection in the vicinity of populated places, sanatoria, rest homes, childrens' camps, etc., should be regularly treated with disinsectants and deratization preparations.

Measures of individual protection are very important in forests. Overalls protect from tick bites. Repellents and nettings are effective. It is recommended that persons working in the forest should inspect each other at regular intervals (2-5 hours). Ticks should be removed by gentle but steady traction rather than by crushing. This is necessary to prevent leaving embedded remnants of the ticks inside the skin.

Population in endemic foci and groups of people exposed occupationally should be given specific immunization.

Inactivated vaccine and then a preparation of attenuated live virus of tick-borne encephalitis are administered. If a tick bite is revealed,

the victim should be given 6 ml of specific immunoglobulin as a preventive measure.

Measures in the focus. An encephalitis patient is not dangerous for the surrounding but, whenever necessary, he or she should be hospitalized. Thorough epidemiologic examination of the focus helps reveal the cause of infection and plan prophylactic measures.

Prophylaxis of milk fever is aimed at eradication of infection transmitters-ticks, and protection of animals by treating them with a 1 per cent carbophos emulsion; milk should obligatory be boiled before use; vaccination of people and animals is indicated.

Japanese Encephalitis

Japanese encephalitis was identified as an independent nosologic entity in 1924 after an outbreak of the disease in Japan. The mortality rate was high.

Aetiology. The disease is caused by arbovirus of the antigen group B; the virus is unstable outside the macroorganism. It can be detected in the hosts-warm-blooded animals, and infection transmitters - mosquitoes. The virus grows in tissue cultures and chick embryos.

Epidemiology. The source of infection are animals, birds (sparrows) and humans during viraemia.

Mosquitoes *Culex* and *Aedes* are the transmitters. They usually inhabit wild nature where there are many lakes, swamps and sufficient sunlight. In this connection the disease is mostly endemic. At ambient temperatures below 20 °C, the virus inside the mosquito propagates slowly.

Natural nidi of Japanese encephalitis are reported from Japan, China, India, Korea, Vietnam, USSR, and African countries. In addition to the natural nidi, there are nidi of infection in populated places where the mosquitoes miltiply in small ponds and feed on domestic animals.

Humans get infected during work in field conditions, during hunting, fishing, road construction, etc. Men working in areas with natural nidi of Japanese encephalitis are mostly afflicted by the disease.

The disease occurs in the end of summer and in early autumn. In Japan the disease occurs already in June. Stable immunity develops in persons who sustained the disease.

Pathogenesis. The virus circulates with blood and afflicts, in the first instance, capillary endothelium of the brain and internal organs. Haemorrhages, oedema of the meninges, adrenal glands, kidneys,

liver, lungs and the intestine occur. Propagation of the virus in the brain tissue causes death of the neurons. The greatest changes occur in the grey and white substance of the brain, subcortical ganglia, in the hypothalamus and the mesencephalon.

Clinical picture. The incubation period is 5-14 days. The disease begins acutely with a chill, rapid rise of temperature to 40 °C and higher, headache, especially frontal pain, pain in the lumbar region, the abdomen and in the extremities, nausea and vomiting. The meningeal symptoms, high muscular tone, confusion of consciousness, cramping and tachycardia are observed. Oedema of the brain is a severe complication of this period. On the 3rd or 4th day of the disease the face becomes hyperaemic; sclera and the upper chest are also hyperaemic; hyperhidrosis develops. The symptoms of meningitis increase. Increasing muscular tone forces the patient into the position on his back or side with the head tilted back and with flexed arms and legs. The temperature gradually falls on the 6-7th day of the disease, consciousness clears, pulse slows down and the muscles relax. If the medulla oblongata is involved, the swallowing act and the cardiovascular and respiratory functions become upset.

By the 8-1 lth day, the temperature normalizes or remains subfebrile. The muscles are feeble, the memory is poor; psychic and coordination disorders are seen; complications develop. Leucocytosis, neutrophilosis, lymphopenia, and eosinopenia are seen; ESR accelerates to 20-30 mm/h. The cerebrospinal fluid is clear and oozes under pressure. The number of cells and the protein content in the fluid slightly increase. Lethality is from 20 to 80 per cent.

Complications. Pneumonia, thrombophlebitis, pyelocystitis, bedsores, impairment of memory, psychosis, spastic paralysis and paresis can develop.

Diagnosis. The diagnosis is based on clinical, epidemiologic and laboratory findings. During the first 7 days of the disease, blood, cerebrospinal fluid, urine and mucus from the upper airways are examined in the laboratory. The material is administered to albino mice intracerebrally. Complement fixation test, haemagglutination inhibition and neutralization tests are performed during the 1st and 3rd weeks of the disease. Intracutaneous test with the antigen prepared from the brain suspension of infected mice can also be performed.

Treatment. Specific immunoglobulin (3-6 ml) is given intramuscularly 3 times a day for 3-4 first days. In order to decrease oedema and brain swelling, dehydration therapy is indicated: 20 per cent solution of placental albumin, 15 per cent mannitol solution, and diuretics.

Cardiac preparations and vitamins are indicated. During the recovery phase, a 0.05 per cent proserin solution and caloric diet are prescribed.

Prevention and control. Control of encephalitis includes systematic destruction of mosquitoes in populated places by disinsectants, prevention of diseases in the animals, eradication of mosquitoes propagation, protection of enclosures from the insects by screens and netting impregnated with repellents, and destruction of larvae in open water bodies.

Active immunity can be produced in domestic animals and population in epidemic foci by vernal vaccination with inactivated vaccine. The vaccine is given subcutaneously by two doses. The first dose is 2 ml, and the second (in 10-15 days) is 3 ml. Specific immunoglobulin (6 ml) is given for passive immunization of persons attacked by mosquitoes.

Measures in the focus. These include isolation of patients, their protection from mosquitoes, and disinsection measures.

Malaria

The disease is caused by protozoa of the genus *Plasmodium* (class *Sporozoa).*

More than 100 types of malarial plasmodia are known. Four of them are parasitic in man: *P. vivax,* the causative organism of tertian malaria (the Plasmodium has two variants: the Northern and Southern strains with long and short incubation periods respectively); *P. malariae,* the causative agent of quartan malaria; *P. falciparum,* the agent of falciparum malaria; and *P. ovale,* the causative agent of ovale malaria, a mild variant of tertian malaria. There are several variants of *P. falciparum:* Indian, Italian, Nigerian, etc. The Italian strain causes the most severe malaria. Humans are susceptible to some types of agents that cause malaria of monkeys.

The life cycle of malarial plasmodia includes two hosts: the final host - srtsmale mosquito of the genus *Anopheles,* in which the sexual phase of growth occurs (known as sporogony); and the intermediate host, which is a human or a vertebrate (in which the asexual multiplication occurs, known as schizogony) (Fig. 14).

Sporogony. While feeding upon an infected human, a mosquito ingests male (microgametocytes) and female (macrogametocytes) sexual cells with the infected human blood. After maturation, gametocytes are transformed into gametes. Microgametes are motile due to flagellae (from 4 to 8); as they encounter macrogametes, they

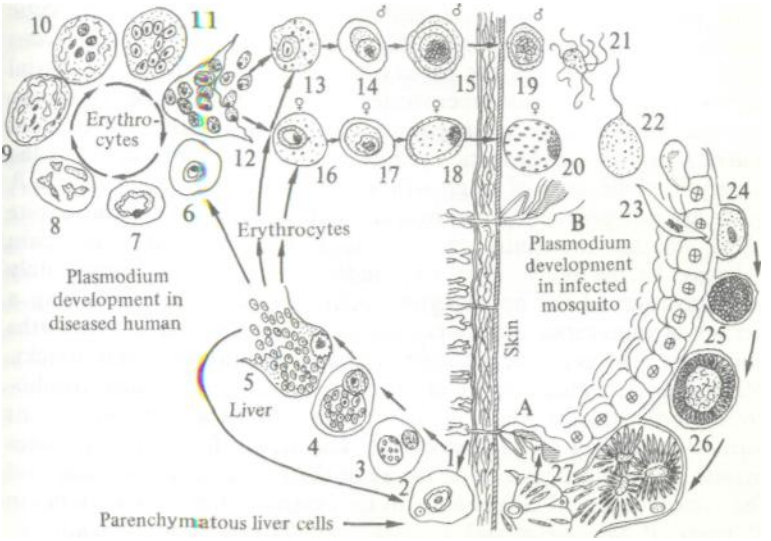

Fig. 14. Development of tertian malaria Plasmodium:
1-12-asexual cycle (7-J-extraerythrocytic stages; *6-12*-erythrocytic stages) in a diseased human. Sexual cycle of Plasmodium development male gametocyte (73-/5-microgametocytes) and female gametocyte (/6-K-macrogametocytes). Characteristic form of Plasmodium of tertian malaria-ring (6), adult schiz*>nt-(70); *19-27*- development of Plasmodium in an infected mosquito (sexual cycle)

fertilize them. The formed zygote converts into an ookinete that is embedded into the submucous layer of the mosquito stomach where it divides with subsequent formation of oocysts and sporocysts. After rupture of the sporocyst into the haemolymph, the salivary glands of the mosquito release 10 000-15 000 and more sporozoites which are inoculated into a human subject at the next feeding. .Sporogony continues from 7 to 14 days. The process discontinues at temperatures below 16 °C. The sporozoites remain viable in the salivary glands of a female anopheline from 40 to 60 days.

Schizogony. Inside a human body, plasmodia pass through two stages of asexual multiplication: the exoerythrocytic and erythrocytic stage of schizogony. Sporozoites are carried by the blood stream to the hepatocytes where they develop into schizoites and merozoites, which develop and multiply only in red blood cells. The exoerythrocytic stage lasts 8-10 days in *P. vivax* and *P. ovale*, 6-8 days in *P. falciparum*, and 15-20 days in *P. malariae.*

In the causative agent of malaria falciparum, exoerythrocytic schizogony occurs only during the incubation period that precedes infection of the red cells (the pre-erythrocytic cycle). In other malarial agents *(P. vivax, P. ovale),* merozoites invade not only the erythrocytes, where erythrocytic schizogony begins, but also other hepatocytes where a new exoerythrocytic cycle begins. *P. vivax* can undergo the exoerythrocytic stage of its growth for years. Besides, *P. vivax* and *P. ovale* are not genetically homogeneous. As a result, following a bite of an infected mosquito, sporozoites of various phenotypes gain entrance to the body. They can undergo schizogony immediately after invasion of the hepatocytes (tachysporozoites) or following a period of quiescence (bradysporozoites) that can last 2-14 months and more. The erythrocytic stage accounts for the malarial attacks. Merozoite parasitizes in the erythrocyte and develops into trophozoites and schizonts which divide to give a morula with subsequent formation from 4 to 48 merozoites. The newly formed merozoites invade new erythrocytes (after decay of the former erythrocytes), and the cycle is repeated. Schizogony in the erythrocytes lasts 48 hours in *P. vivax, P. falciparum* and *P. ovale,* and 72 hours in *P. malariae.*

Part of merozoites invading the red cells, after passing several asexual cycles of growth, give rise to the sexual forms.

Epidemiology. The source of infection are infected humans, whose blood contains gametocytes, patients with primary or relapsing form of malaria, and carriers. Humans can infect mosquitoes during the very first days of malaria induced by *P. vivax, P. ovale,* and *P. malariae,* and remain so until the parasites are contained in the blood.

Malaria falciparum patients become contagious only in 10-12 days after development of the first malarial attacks, because gametocytes are formed in the capillaries of the internal organs during 9-11 days. The life of plasmodia in a human body varies depending on the type of the parasite: *P. falciparum* survives for 18 months, some African species can live to 3 years; *P. vivax* can live to 3 years, *P. ovale* to $4^1/_2$ yearsf while *P. malariae* can survive for decades without inducing apparent clinical symptoms and the disease is only revealed occasionally after transfusion of blood from such infected donors. Only erythrocytic schizogony occurs in such persons.

The transmitters of plasmodia are about 80 types of mosquitoes of the genus *Anopheles.* In Africa the parasites are transmitted by *A. gambiae* and *A. funestus,* in Asia by *A. minimus, A. culicifacies, A. fluviatilis, A. sundaicus, A. superpictus,* etc., in Europe and North America by *A. maculipennis, A. superpictus,* in Central and South

America by *A. aquasalis, A. pseudopunctipennis, A. darlingi* and *A. albimanus,* in New Guinea and Australia by *A. punctulatus.*

The mosquitoes of various geographic zones have different susceptibility to plasmodia.

After sucking blood, a mosquito female deposits 100-500 mature eggs on the surface of well insolated water surface (ponds and the like). The larvae undergo their development from 2 to 7 days, depending on the ambient temperature (15-30 °C). If the temperature of water is below 10 °C the larvae do not grow. In temperate climate, the larvae give imagoes during 2-5 months, while in subtropic countries this period is as long as 5-8 months. In tropic countries mosquitoes appear during the whole year (except during the season of rainfalls). The time of malaria transmission is therefore only 2-5 months in temperate climate, 5-8 months in subtropic countries, and 8-10 months in the torrid zone.

Malarial plasmodia can be transmitted from an infected mother to the foetus through the placenta, during labour or blood transfusion, through syringes and needles, etc.

Susceptibility to malaria is high, especially in children, who make the prevalent incidence in endemic areas. Strictly specific immunity to a given species and strain is induced in persons who sustained malaria. The immunity persists only on the condition of repeated infections. Immunity can be lost if a person leaves the endemic area.

Depending on the intensity of plasmodia transmission and the infection rate of population, four types of malaria are distinguished (according to WHO classification).

1. Hypoendemic malaria-the spleen index (the percentage of population having enlarged spleens) in children aged from 2 to 9 years is about 10 per cent.

2. Mesoendemic malaria-the spleen index in children aged from 2 to 9 is from 11 to 50 per cent.

3. Hyperendemic malaria-the spleen index in children aged from 2 to 9 is constantly above 50 per cent; the index is also high in adults.

4. Holoendemic malaria-the parasite index (the percentage of population with parasitaemia) in nurslings is permanently higher than 75 per cent, and the spleen index in adults is high (New Guinea) or low (Africa).

In the holoendemic areas, natives sustain an acute form of malaria during early childhood, the death rate being high. Adults acquire immunity and do not develop acute malaria during their later lives. In meso- and hypoendemic areas, acute malaria occurs in children and adults but the overall morbidity is not high.

Malaria is common in almost all countries of Africa, Asia and Oceania.

The most common form is tertian malaria. Its causative agent *(P. vivax)* is well adapted to both temperate and torrid climate. Tropic malaria caused by *P. falciparum* occurs in the torrid zone on both sides of the equator (45° N. lat.-20° S. lat). Quartan malaria occurs in about the same areas. Ovale malaria occurs in West and East equatorial Africa.

Pathogenesis. Paroxysms of malaria are associated with the response of the thermoregulating centres to the release into blood of a great number of merozoites and other proteins that are formed during division of schizonts and decay of red blood cells. Foreign proteins cause a toxic allergic response in the patient. This response is characterized by oedema of tissues and proliferation of immunocompetent cells (lymphocytes, monocytes, stellar reticuloendotheliocytes, etc.). Destruction of erythrocytes by the parasites and autoantibodies, inhibition of physiologic regeneration of red blood cells in the bone marrow due to splenic hyperfunction cause progressive anaemia, leucopenia, and thrombocytopenia. Anaemia evokes dystrophic changes in the myocardium, central nervous system, liver and other parenchymatous organs.

Malarial plasmodia and their metabolites, the malarial pigment, and the products of protein degradation evoke anaphylaxis: hyperadrenalinaemia, hyperglycaemia, hypercholesterolaemia, hyperkalemia, and relative hyponatraemia. Hyperadrenalinaemia provokes hypertension, tachycardia, spasm of the peripheral vessels and upsets microcirculation in the internal organs.

Increased immunoglobulins (IgM, IgG), activated phagocytosis of invaded erythrocytes, and decay of the parasites in macrophages stop the first series of paroxysms after the second or third attack. The disease passes into its next phase, secondary occult period, or early (short) interparoxysmal period. Due to imperfect initial immune reactions, the blood fails to be completely freed from the parasites. Decreased immune reactions promote an increase in the number of malarial plasmodia and development of a new wave of attacks-early relapses. They follow in 2 weeks to 3 months after termination of the first series of paroxysms.

During early relapses, the developed immunity becomes sufficiently strong to suppress schizogony and to promote clinical recovery.

In quartan malaria, an equilibrium between the immune system of the macroorganism and the parasites is attained; it can persist for

decades. When this equilibrium is upset, the parasites retained in the erythrocytes begin propagating and attain a certain level (paroxysm) at which erythrocytic relapses become possible.

Late relapses also develop in tertian malaria, but they are due to exoerythrocytic forms of the parasites that develop from the persisting forms. Thus, unlike in other forms of malaria, true relapses of the disease and parasitaemia occur in tertian malaria.

The malarial agent of vivax (tertian) malaria persists in the macroorganism for 2-4 years, of ovale malaria for 3-6 years, of falciparum malaria for 1-1 $^{i}/_{2}$ years and of quartan malaria from 2-3 years to decades. Unstable type-specific (non-sterile) immunity develops after the sustained disease.

Clinical picture. The clinical symptoms depend on the specific causative agent of the disease that invades the patient. Four forms of malaria are thus distinguished: tertian or vivax malaria, quartan malaria, falciparum malaria, and ovale malaria. Each form can be mild, moderate or severe. The following periods are distinguished in the course of the disease: incubation period, primary (acute) manifestations, occult period, relapses, and the recovery period.

The incubation period of tertian (vivax) malaria is from 10-21 days to 6-14 months; of quartan malaria, 3-6 weeks; of falciparum malaria, 8-16 days; and of ovale malaria, 7-20 days.

Paroxysms are characteristic of the disease. A typical paroxysm includes the "cold stage", the "hot stage" and the "wet stage".

The malarial paroxysm begins with the cold stage: the patient is attacked by shaking chill that cannot be managed by warm cover. The lips, nose tip and the fingers become cyanotic. The body temperature rapidly rises to 40-41 °C within 90-120 minutes. The chill lasts 1-3 hours and is followed by the hot stage (fever). The face reddens, the skin becomes dry. The patient removes all covers and his underwear, he becomes restless, complains of thirst, headache, and lumbar pain. Respiration rate increases, tachycardia and convulsions develop, consciousness is confused. Nausea, vomiting, and pain in the spleen occur. In 5-8 hours, the body temperature falls critically to subnormal with profuse sweating. The patient is exhausted and drowsy. A paroxysm lasts 8-12 hours. It usually begins in the morning. The subjective condition of patients improves in the interparoxysmal periods.

Paroxysms recur at regular intervals: every other day in tertian malaria, and every third day in quartan malaria. During the first week of the disease, this regularity can be absent in non-immune persons; fever can be irregular. Despite a prolonged schizogony in

falciparum malaria (48 hours), paroxysms can occur daily or even twice a day. This is due to the onset of erythrocytic schizogony at various terms.

After 1-2 paroxysms, the skin and the visible mucosa of many patients turns pale yellow. Herpes labialis and nosalis occur. The spleen and the liver are enlarged. Palpation reveals their tenderness and firm consistency. The changes in the blood are the following: the haemoglobin and erythrocyte count decrease; leucopenia, often with relative lymphocytosis, thrombocytopenia, and aniso- and poikilocytosis are seen; ESR accelerates. Plasmodia can be found in blood smears.

In the interparoxysmal periods (apyrexia), the patient preserves his working capacity. As the number of paroxysms increases, the patient develops weakness during the afebrile periods; he complains of headache, myalgia, and arthralgia. The skin acquires a greyish hue; jaundice and hepatosplenomegaly intensify. The number of paroxysms in primary malaria varies from 10 to 12. The body temperature is maximum on the second week of the disease, but during later paroxysms it gradually decreases, the number of parasites in the blood decreases too, and paroxysms cease. In untreated or inadequately treated cases, a short afebrile period is followed by a reinvasion of the blood stream with the parasites to cause early relapses, during which the temperature reaction acquires the intermitting character, specific for each particular type of malaria.

Early relapses in vivax and ovale malaria are followed by an occult period lasting 8-10 months (and longer), which ends in late exoerythrocytic relapses due to multiplication of new generations of exoerythrocytic merozoites and reinvasion of the blood stream (true relapses). Late relapses in quartan malaria are due to multiplication of persistent erythrocytic forms of Plasmodia. The clinical course of late relapses is milder than attacks of the early period. The latent period or relapses are absent in falciparum malaria.

The severest course is characteristic of falciparum malaria. Its fever is irregular and the paroxysms are long (lasting 24-36 hours and longer). The afebrile periods are less pronounced. Chills and sweating are not characteristic because the temperature variations are not very marked. Parasitaemia increases rapidly to attain a high level in few hours.

If diagnosed untimely and not treated, falciparum malaria runs a malignant course with cerebral complications (malarial coma, psychosis), algid malaria with severe vascular failure (septic shock), and acute renal failure.

Tertian malaria (vivax and ovale) runs a benign course. Attacks of vivax malaria usually develop in the morning; while in ovale malaria they are more common in the evening.

Quartan malaria is usually benign. It is characterized by a prolonged course and a great number of relapses over many years. The patient can remain the source of infection that can be transmitted parenterally (schizont malaria).

Malaria in pregnant women is the cause of frequent abortion, eclampsia, premature labour, and stillbirth. Due to marked vegetative endocrine shifts and decreased immune defense in the pregnant, malaria runs a severe course with marked anaemia, jaundice, and oedema. Early diagnosis and timely treatment are therefore very important. Antimalarial preparations such as delagil or amodiaquine do not produce adverse effect on pregnancy or foetal growth.

Diagnosis. Diagnosis is established on the basis of clinical, epidemiologic and laboratory findings.

The laboratory methods include microscopy of thin and thick blood smears in which plasmodia are detected. The number of malarial plasmodia is not great during the first attacks. Blood should therefore be studied up to 3 times a day during 2-3 days. Blood specimens should be taken at the height of fever as well as during apyrexia.

Specific diagnosis of malaria is possible with serologic studies: indirect immunofluorescent test, indirect haemagglutination and enzyme-labelled antibody tests. These methods are used to examine blood donors (to reveal carriers of *P. malariae),* to reveal malaria in persons who took antimalarial preparations before attendance for medical aid, and to establish the absence of disease transmission in endemic areas.

Treatment. Treatment of malaria patients is aimed at termination of acute paroxysms, prevention of relapses and elimination of gamonts.

All antimalarial preparations are divided into four groups:

1. Gametoschizotropic drugs, preventing development of erythrocytic schizoites: quinine, mepacrine, proguanil, derivatives of 4-aminoquinoline: chloroquine (chloroquine diphosphate), nivaquine (chloroquine sulphate), plaquenil, amodiaquine, pyrimethamine.

2. Histoschizotropic preparations preventing development of trophozoites: proguanil, 8-aminoquinoline derivatives (primaquine, quinocide), pyrimethamine.

3. Gametocides destroying gamonts: pyrimethamine, 8-aminoquinoline derivatives.

4. Sporontocides preventing maturation and growth of gamonts in the mosquito stomach: proguanil, pyrimethamine, and 8-aminoquinoline derivatives.

In order to abate acute symptoms of all types of malaria, 4-aminoquinoline derivatives are given to adults (after meals) in the following doses: chloroquine or nivaquine, 2-2.5 g per course. The dose for the first intake is 1 g (4 tablets of 0.25 g), 0.5 g in 6-8 hours; on the second and third day, 0.5 g given for one intake.

Falciparum malaria is treated during five days (in the absence of immunity in the patient), a dose of 0.5 g is given for one intake on the 4th and 5th day.

Plaquenil's effect is similar to that of chloroquine. It is given per os, 2 g for adults for a course. The first intake is 0.8 g (4 tablets of 0.2 g); in 6-8 hours, the dose is 0.4 g; and 0.4 g is given for one intake on the second and third day.

Falciparum malaria is treated for 5 days: a dose of 0.4 g is given for one intake on the 4th and 5th day.

Population of endemic regions has immunity against malaria and only one third of the mentioned doses should be given. The duration of the therapy is also shorter.

Therapy with chloroquine and plaquenil terminates malarial paroxysms in 24-48 hours, and the plasmodia disappear from the blood in 48-72 hours after the beginning of the therapy, if malaria is due to the strain sensitive to 4-aminoquinolines. Radical treatment of patients (eradication of sexual and asexual parasites) is attained with gametocides and histoschizotropic drugs. Falciparum malaria patients are given pyrimethamine, simultaneously with or after the above mentioned drugs. The doses for adults are 0.03 g (6 tablets of 0.01 g can be given on the first day), or primaquine, 0.045 g during three days. The drugs are given per os. In order to prevent late relapses in tertian malaria, primaquine or quinocide should be given after mentioned therapy in a dose of 0.27%"a day (3 tablets of 0.09 g) for 14 days, and 0.03 g (3 tablets of 0.01 g) for 10 days, respectively.

The sexual forms of *P. vivax, P. ovale,* and *P. malariae* are destroyed after termination of the erythrocytic schizogony. Gametotropic preparations are therefore not used to treat malaria.

Malaria due to the chloroquine-resistant strains *P. falciparum* and *P. vivax* should be treated with quinine hydrochloride. The dose of 0.65 g ($3V_4$ tablets of 0.2 g) should be given 3 times a day for 10-14 days; or a combination of pyrimethamine (0.25 g) and sulphadoxine

(0.5 g), 2-3 times a day for 2-3 days, or a combination of sulphalene (0.2 g) and sulphadoxine (0.5 g), or a combination of pyrimethamine (0.025 g) and sulphalene (0.5 g) should be prescribed.

Radical cure is attained with a combination of quinine and tetracycline (0.5 g 4 times a day for 7 days).

In pyrimethamine-resistant cases, in order to attain a sporontocide effect, primaquine is given in a single dose of 0.045 g (5 tablets of 0.009 g).

Malignant forms of falciparum malaria should be treated with quinine or chloroquine base preparations given in a dose of 5-10 mg/kg 2 times a day (900 mg of chloroquine base maximum).

Pathogenetic therapy is aimed at decreasing vascular permeability, eliminating brain oedema and hyperazotaemia, and at maintaining diuresis. To that end, along with the aetiotropic therapy, it is necessary to give glucocorticosteroids, antihistaminics (dimedrol, suprastin), rheopolyglucin, haemodez, salt solutions and a 5 per cent glucose, diuretics (lasix, mannitol) and cardiovascular preparations.

Prophylaxis. The complex of antimalarial measures acts on all three factors of the epidemic process: the source of infection, routes of infection transmission and susceptibility of population. The choice of the leading measure depends on the malaria infection rate. Control of the source of infection is decisive.

This can be attained during the first visit to malaria patients and by active screening of population. Parasitoscopy of population is an important factor in this respect. All screened patients and parasite carriers should be given obligatory treatment.

Malaria patients with acute clinical symptoms should be placed in hospitals or treated at home. Patients with severe clinical forms of malaria, children and pregnant women should be hospitalized. Convalescents may be discharged from hospital not sooner than in 1-2 days after disappearance of the plasmodia from the blood. Convalescents and parasite carriers should be observed in outpatient conditions for $2^1/_2$ years in tertian malaria and $1^1/_2$ year in falciparum malaria.

Measures aimed at reduction of the number of infection transmitters include elimination of sites of mosquito multiplication, elimination of their larvae and imagoes. Water bodies that have no economic importance should be dried on the area with the radius of 3 km around populated places; swamps should be irrigated; all open water basins or watering systems should be given proper sanitary control.

Zooprophylaxis must be ensured in newly inhabited areas.

In foci of malaria and in places where such foci reappeared, or where anophelogenic danger increased, it is necessary to control the malaria vector (mosquito populations). Foci of infection should be regularly revealed. If mosquito populations increase, they should be controlled by destroying the larvae and the imagoes.

Open water bodies should be treated with chemicals. Irrigation of fields should be intermittent so that the larvae of mosquitoes could be destroyed before they turn into imagoes. Waterfowl and fishes feeding on the larvae should be raised in open water bodies.

Chemical preparations should be used to control mosquitoes in populated places. Buildings should be treated before the larvae turn into the winged insects. Depending on residual effect of the chemical poison, treatment can be given on one or two occasions.

If malaria incidence in a populated place is high, all residential and other buildings, and also cattle sheds should be treated. In large towns, all residential and other buildings, as well as cattle sheds should be treated in the vicinity of the anophelogenic water body. Treatment of the focus can be sufficient if the infection rate is low. Only those houses where malaria patients or parasite carriers reside, and also the neighbouring houses, should be treated. Mechanical protection of housing (especially of bedrooms) is attained with screens, mosquito netting on the windows and doors. Means of individual protection and repellents should be used. In order to kill mosquitoes within enclosures, it is recommended to use aerosols of pyrethrum or pyrethrin.

Chemotherapy is important in control of malaria and its prevention among population. Chemoprophylaxis of population in endemic areas begins 1-2 weeks before appearance of the first generation of mosquitoes and is conducted during the entire epidemic period, and also 6 weeks after its termination. Travellers to the endemic areas should receive chemoprophylaxis too. The following preparations can be used for chemoprophylaxis: chloroquine or novaquine in a dose of 0.5 g or pyrimethamine 0.025-0.05 g once a week. Ready-made combined preparations (pyrimethamine plus chloroquine) ^ire given in areas where drug-resistant strains of plasmodia are spread. The preparation is given twice a week. An obligatory condition for effective prophylaxis is regular administration of chemical preparations. The selection of a particular prophylactic preparation depends on the dominating parasite, its sensitivity to a given preparation, individual tolerance of the given preparation and the presence of contraindications. The preparations are given after meals with at least half-glass of water.

In order to prevent infection spread, donors should be selected **from** people with negative indirect immunofluorescence test with malarial Plasmodium antigen, and also those who did not visit endemic areas for more than 3 years.

Leishmaniasis

Leishmaniasis is a transmissive disease of humans and some animals. The disease occurs in countries of the torrid zone. Visceral and cutaneous leishmaniases are distinguished.

Leishmaniasis is produced by protozoa of the genus *Leishmania*. When invading human beings or animals, leishmania assume the form of spindle-shaped non-flagellate amastigotes, while in the body of a transmitter (sandfly) they are flagellated forms (promastigotes).

Visceral Leishmaniasis

The following variants are distinguished: Mediterranean (infantile) kala azar, Indian kala azar, East African, Chinese and American leishmaniasis.

Aetiology. Visceral leishmaniasis is caused by various species of *Leishmania donovani.* For example, Mediterranean littoral leishmaniasis is due to L. *donovani infantum,* the Indian kala azar is caused by L. *donovani donovani.* Leishmania readily grow on various media containing animal protein. Various rodents, dogs, cats, monkeys and human beings are susceptible to leishmania.

Epidemiology. The source of infection in the Mediterranean littoral leishmaniasis are dogs, jackals, foxes, possibly rodents; the source of Indian kala azar is a human patient, while the source of East African variant are humans, dogs, jackals, foxes, and rodents. Sandflies of the genus *Phlebotomus* are the vector of the infection. After sucking blood from an infected human or animal, female sandflies can transmit the infection in 6-8 days.

Mediterranean littoral leishmaniasis afflicts mainly infants aged from 1 to 5 years. Indian and East African visceral leishmaniases affect humans of all ages but young patients dominate. Stable immunity develops after the disease. The disease is reported as sporadic cases and epidemic outbreaks from the Mediterranean littoral, China, Middle East, India, Pakistan, Nepal.

Pathogenesis. The portal of entry of leishmania is the site of sandfly bite. The blood stream carries the microorganisms to the cells of mononuclear phagocytic system of the spleen, liver, bone marrow, and lymph nodes to cause their dysfunction and damage. Some cells

die, it is attended by the proliferation of the mononuclear phagocytic system which causes degeneration of the spleen, liver and the lymph nodes. These organs become enlarged and firm, their function is upset. The gastrointestinal tract and the kidneys are also involved. Destroyed leishmania and their metabolites cause toxaemia and upset metabolism in the macroorganism. Some patients develop a papule at the portal of infection.

Clinical picture. The incubation period of Mediterranean leishmaniasis is from 20 days to 3-5 months and longer, of Indian kala azar 6-8 months on average. Three periods are distinguished in the course of the disease: initial, clinically manifest, and terminal. The onset of the disease is gradual. The patient develops fatigue, malaise, and subfebrile temperature. His appetite is impaired, the skin and visible mucosa are pallid. When the disease is in its full swing, the temperature curve is irregular and undulant. Rises of temperature to 39-40 °C are followed by afebrile periods. Body temperature fluctuates not only within few days but also within 24-hour periods. Temperature variations are attended by chills and sweating.

The spleen is firm and enlarged from the first days of the disease. Splenomegaly becomes striking with time. Its lower edges descend to the navel and even lower (Fig. 15). The liver and the peripheral lymph nodes are also enlarged. The skin is pallid. Anaemia develops in 2-3 months. It progresses as the bone marrow is involved. Granulocytopenia and agranulocytosis are characteristic. Haemorrhages into the skin and mucosa are possible, epistaxis and gastrointestinal bleeding occur. Splenohepatomegaly causes portal hypertension, ascites, and oedema.

In most patients the red blood cell count is low: 1×10^{12}-2×10^{12}/1. Leucopenia (2×10^{9}/1 or lower), neutrophilopenia and eosinophilopenia with relative lymphocytosis, and monocytosis, and also thrombocytopenia are characteristic blood changes. The serum albumin is low while the globulin content is high at the expense of alpha- and beta-globulins; ESR is high (50-90 mm/h).

In the absence of timely specific treatment, acute forms of visceral leishmaniasis transform into subacute and protracted forms of the disease. The skin becomes pale grey. In Indian kala azar the skin is dark, almost black (kala azar in Hindi means black fever); oedema increases, diarrhoea supervenes (often with admixture of mucus and blood). The terminal period is marked by cachexia, marasmus, low muscular tone (frog belly syndrome). In the absence of adequate treatment, the disease lasts from 1 to 2 years.

Kala azar and East African visceral leishmaniasis are characterized

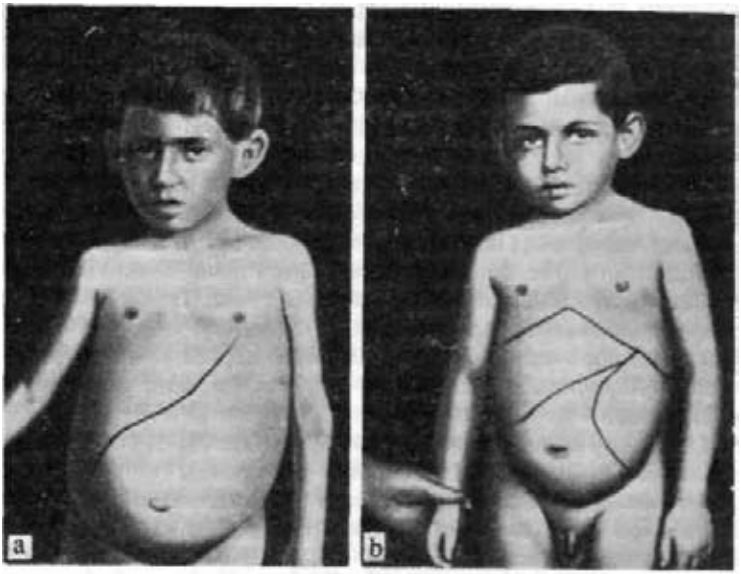

Fig. 15. Visceral leishmaniasis (kala azar):
a-before treatment (spleen lower edges descend below the navel); *b* -three months after treatment (the spleen has diminished in size)

by nodular and macular rash (cutaneous leishmanoid) which develops in 1-2 years after the onset of the disease (kala azar) and after clinical recovery (East African leishmaniasis). Patients are persistent sources of infection (for years and even decades).

Complications. Untimely treatment can cause death due to secondary infections. Frequent complications of visceral leishmaniasis are pneumonia, otitis, mastoiditis, furunculosis, epistaxis, ulcerative gingivitis and stomatitis, and rupture of the spleen.

Diagnosis. The diagnosis is based on clinical, epidemiologic and laboratory findings. Isolation of leishmania in Romanowsky-Giemsa stained smears of sternal marrow, lymph node bioptate and, less frequently, blood is decisive. The material is also inoculated into NNN medium for growing leishmania cultures. Serologic tests are also used: fluorescent antibody test, complement fixation test, latex agglutination with leishmania antigents tests. Inoculation of hamsters is also used in biologic studies.

Visceral leishmaniasis can be identified by the formol-gel test (2

drops of a 40 per cent formaldehyde solution are added to 1 ml of the patient's blood serum: the serum becomes cloudy and turns into a gel in the presence of leishmania).

Treatment. The specific remedy against visceral leishmaniasis is solusurmin (solustilosan, stibanol, pentostam). It is produced in powder form in sealed vials. Before use, it should be diluted in double-distilled water. The preparation is given once a day intramuscularly or intravenously in the form of 5, 10 or 20 per cent freshly prepared solutions. The course of treatment includes from 7 to 16 such injections. The dose of the preparation (from 0.04 to 0.1 g per kg body weight) should be gradually increased. Treatment can be repeated in a certain lapse of time.

Solusurmin is contraindicated in acute nephritis. Other preparations of pentavalent antimony can also be used: neostibosan, glucantime.

If antimony preparations fail, pentamidine should be given daily in a dose of 0.004 g/kg (10-15 injections per course).

If secondary infection supervenes, antibiotics should be given. Transfusion of blood and erythrocytes, and also vitamins are indicated for anaemia.

Prevention and control. Leishmaniasis control measures should in the first instance be aimed at elimination of the source of infection. These include extermination of jackals, foxes, stray (especially diseased) dogs; veterinary supervision of dogs in endemic areas is necessary. Timely treatment of visceral leishmaniasis patients with specific preparations is necessary; protection against flying insects is important too. Improvement of populated places helps eradication of insects and sites of their propagation. Enclosures should be treated with insecticides. Population should be protected from insect bites by repellents and other means.

Measures in the focus. In addition to treatment of patients and elimination of sandflies, the people surrounding the diseased should be given medical supervision. Veterinary supervision of dogs should be conducted. Persons who sustained the disease should be observed for 4-6 months.

Cutaneous Leishmaniasis

New World and Old World cutaneous leishmaniases are distinguished.

The Old World form. This form is, in turn, divided into two distinct types: an urban (anthroponotic) form (dry leishmaniasis

having an incubation period of many months to over a year, and lasting for many months and acute rapidly evolving (zoonotic) form, known also as rural, humid, moist, or wet cutaneous leishmaniasis.

Aetiology. The causative agent of anthroponotic cutaneous leishmaniasis is *Leishmania tropica minor*, and of the zoonotic form-*Leishmania tropica major.*

Epidemiology. The source of anthroponotic leishmaniasis is a human being, while in zoonotic forms these are wild rodents. In nature, the causative agent circulates in the system: diseased rodent-sandfly-healthy rodent.

The transmitters of leishmania are female sandflies of the genus *Phlebotomus: P. papatasii, P. caucasicus, P. sergenti,* and others.

Anthroponotic leishmaniasis occurs as sporadic cases in towns and cities during the whole year which is due to various incubation periods. In the zoonotic form, the incidence of the disease increases during the warm season. It occurs only in rural areas.

Susceptibility to cutaneous leishmaniasis is universal. The greater portion of population sustains the disease in childhood. Stable immunity is produced only to a specific causative agent.

Anthroponotic leishmaniasis occurs in the Middle East, South Europe, India, and Africa, while the zoonotic form in Asia, Africa and South Europe.

Pathogenesis. Leishmania enters a human through a bite of an infected sandfly. After inoculation into the skin, leishmania propagates at the portal of entry to form infiltration. In the anthroponotic form, the papules ulcerate in 3-6 months; in the zoonotic form in 15-16 days.

Clinical picture. The incubation period of the anthroponotic (dry) form is 2-8 months to $1^1/_2$-2 years and more. In the zoonotic (moist) form it is from 1 week to 2 months.

Cutaneous leishmaniasis affects the face, the neck, the upper and lower extremities, less frequently the trunk. The quantity of ulcers corresponds to the number of bites by infected sandflies.

The dry form is characterized by development of a pink papule at the site of a sandfly bite; in 5-6 months the diameter of the papule is 1-2 cm. The papule is later covered with scale and then crust, and in six months it is affected by necrosis with ulceration (ulcers have a granular bottom). The ulcer diameter increases and can be 4-6 cm. In few months, the ulcer begins healing and a scar is formed in a year.

The papule in the wet form is scarlet, looking like a furuncle. In 1 -2 weeks, the centre is necrotized and an ulcer is formed with a diameter of 2-5 cm. It is 1-3 mm deep, and has irregular shape. New nodules

are formed around the ulcer which later are necrotized too. The ulcers fuse into a large ulcer with a diameter of 10-15 cm (Plate VIII). The bottom of the ulcer is granulated. Copious seropurulent exudate dries into a dirty grey crust. In 2-3, sometimes 4-6 months, the ulcer undergoes epithelization and cicatrization (during 3-6 weeks). Scars remain after healing.

Diagnosis. Cutaneous leishmaniasis is diagnosed on the basis of clinical and epidemiologic findings. The laboratory method is also important diagnostically. Smears for laboratory studies are prepared from the exudate which is expressed from a punctured nodule (Romanowsky-Giemsa staining is used). In the presence of ulcers, granulated matter is taken from the bottom of an ulcer after cleaning it with cotton wool. Marginal infiltrate is also used for laboratory examinations.

Treatment. The cutaneous form is treated by local application of solusurmin. The preparation is given under the nodule or in the vicinity of the ulcer. Intracutaneous injection of monomycin and a 4 per cent quinacrine around the ulcer is also helpful. Severe cases should be treated with solusurmin like in visceral leishmaniasis.

Ulcerations with lymphangitis and lymphadenitis should be treated with monomycin: 250000 U 3 times a day for 10-12 days. Aminoquinol can be given in a dose of 0.2 g 2-3 times a day for 18-20 days.

Prevention and control. It is necessary to reveal timely patients with cutaneous leishmaniasis. Patients with ulcers on the exposed parts of the body should wear dry bandages. Deratization is obligatory in a given locality and the surrounding areas with a diameter of 1500 m. If a new populated settlement is constructed in a desert, deratization is necessary over an area with a diameter of 3 km. Population should also be protected from sandfly bites. Whenever necessary, all enclosures should be treated with insecticides.

Means of individual protection should be used: repellents, netting and gauzes against flying insects.

Specific prophylaxis is performed with a live culture of leishmania which is given intracutaneously in a dose of 0.1-0.2 ml 3 months before activization of sandflies.

The New **World form.** The disease is known by different names in various countries. Among more common names are American, Brazilian, or mucocutaneous leishmaniasis.

The disease is caused by *Leishmania braziliensis.* The reservoirs of the infection are rodents and domestic animals. The transmitting vector are sandflies of the genus *Phlebotomus.* Unlike in other forms

of cutaneous leishmaniasis, in American leishmaniasis the mucosa is involved in 1-2 years. This causes deformities of the nose, nasopharynx, airways, genitalia and the ears. The disease lasts from 2-3 years to decades.

The following complications are possible: infectious sepsis, gangrene, cachexia, and amyloidosis.

Haemorrhagic Fevers

This is a group of disorders of viral aetiology associated with natural nidality. The virus damages the endothelium of capillaries, arterioles and venules.

The most important clinical sign of a haemorrhagic fever is the haemorrhagic syndrome manifested by rash and haemorrhages in the skin and mucosa, bleedings of various location (nasal, gastrointestinal, uterine, renal, etc.). All haemorrhagic fevers are acute diseases characterized by fever and marked toxaemia. Renal involvement is characteristic. It is more marked in haemorrhagic fever associated with the renal syndrome. In most haemorrhagic fevers, blood changes are characterized by thrombocytopenia and leucopenia. The haemorrhagic fever with the renal syndrome is manifested by leucopenia during the first days of the disease, with development of the renal syndrome (leucocytosis, neutrophilosis with the shift to the left).

At the present time, 12 nosologic forms of haemorrhagic fever are known. They are differentiated by the names of areas where they are first revealed. According to Chumakov (1974, 1977) and Simpson (1978), the following fevers are distinguished. Tick-borne haemorrhagic fevers: Crimean-Congo haemorrhagic fever, Omsk haemorrhagic fever, Kyasanur forest disease; mosquito-borne haemorrhagic fevers: yellow fever, dengue haemorrhagic fever, Chikungunya haemorrhagic fever, and Rift Valley fever; contagious zoonotic haemorrhagic fevers: haemorrhagic fever with renal syndrome, Argentinian haemorrhagic fever, Bolivian haemorrhagic fever, Lassa fever, Marburg and Ebola haemorrhagic fevers.

Crimean-Congo Haemorrhagic Fever

Aetiology. The disease is caused by the virus of the family *Bunyaviridae.*

Epidemiology. The natural reservoir of the virus are wild animals, such as hares, African hedgehogs, and domesticated animals, e.g.

sheep, goats, cattle, and also ticks of 20 species that transmit the infection by transovarian route. The vector are ticks *Hyalomma plumbeum* (in the Crimea), *Hyalomma anatolicum* (in Central Asia and Africa), and biting midges *Culicoides* (Africa and America).

A human patient with Crimean-Congo fever is contagious during the first 5 days of the disease. Infection can be transmitted by contact with infected blood of a human being or an animal, and also during blood transfusion or by the air-borne route in the laboratory.

The natural nidus of the disease was revealed in the USSR (Crimea) in 1944. Later similar nidi were revealed in other Soviet republics (south regions), as well as in Bulgaria, Romania, Yugoslavia, in Africa and Asia. Rural population is mostly afflicted by the disease. First cases of the disease occur in March and April; the maximum rise of the morbidity occurs in July and August.

Pathogenesis. Capillarotoxicosis attended by marked haemorrhage underlies the pathology.

Clinical picture. The incubation period lasts from 3 to 5 days with variations to 14 days. The onset is acute: chills, elevated temperature to 38.5-40 °C, headache, myalgia, arthralgia, weakness, lassitude, rapid fatigue. Fever persists from 7 to 9 days. Face is hyperaemic, the conjunctival and scleral vessels are injected, the fauces are scarlet. The haemorrhagic signs become evident on the 3rd or 4th day; they are manifested by punctate eruptions on the sides of the chest, abdomen and the lumbar region. Development of skin eruptions is often attended by a transient fall of body temperature. The saliva and sputum, and also the vomitus can contain streaks of blood. Epistaxis, uterine and gingival bleeding are seen. Haemoptysis occurs in some cases. Consciousness is not dimmed but the patient is flaccid, inhibited and adynamic. Meningeal signs can be seen in severe cases.

During the first days of the disease, the haemoglobin content and red cell count are high. Hypochromic anaemia develops by the end of the fever. The leucocyte count is low ($3\text{-}1.5 \times 10^9/1$), with the shift to the left (to rod neutrophils); thrombocytopenia and eosinopenia are seen; ESR is high. Urine changes are transient. Insignificant albuminuria, haematuria, oliguria and azotaemia are possible. If the disease runs a malignant course the patient dies during the first days from septic shock; death at later terms is due to oedema of the lungs and brain, haemorrhage into the adrenal glands, or brain.

Death rate is high.

Complications. Complications are associated with secondary purulent infections.

Diagnosis. The blood of patients should be examined in the

laboratory during the first week of the disease. Blood specimens are inoculated into the brain of suckling mice. The material taken from the dead should be used to infect newborn albino mice. Serologic tests are performed with 2-ml blood specimens (agglutination tests; see "Haemorrhagic Fever with Renal Syndrome").

Treatment. Treatment is the same as in haemorrhagic fever with renal syndrome.

Prevention and control. Prophylactic measures are aimed at destruction of ticks in populated places from which the disease is reported. They also include protection of people from tick bites, inspection of bodies, using repellents, wearing special overalls, timely isolation of patients, observation of rules for taking blood specimens and other manipulations associated with patient care. Adequate shedding for cattle and their protective treatment are also necessary at 10-day intervals during the period of time from March till November.

Omsk Haemorrhagic Fever

Aetiology. The disease is caused by the virus which is similar immunologically to the virus of tick-borne encephalitis. The virus is pathogenic for many animals (guinea pigs, albino mice, monkeys, etc.). It can be cultivated in chick embryos.

Epidemiology. The source of infection are muskrats, voles and other rodents, and also birds. Humans can be infected by the bite of infected ticks which are the main reservoir of the virus. Infection can also be transmitted by contacts with the diseased animals in the laboratory. Mostly rural population, especially field workers are infected. Occurrence of the disease has two peaks, in the spring and summer, which is associated with increased activity of ticks. Cases occurring in winter or autumn are mostly associated with muskrat hunting.

Pathogenesis. Like in other haemorrhagic fevers, small blood vessels are involved in Omsk fever. Numerous haemorrhages develop. The involvement of the kidneys is insignificant.

Clinical picture. The incubation period lasts 2-3 days. The onset is acute: chill, headache, pain in the back and the whole body. The body temperature rises to 38-40 °C on the very first day of the disease and remains at this level for 3-7 days. Inspection of the patient reveals hyperaemic face and fauces, injected sclera and veins. On the 3rd or 4th day, by the moment when the haemorrhagic symptoms develop, the body temperature drops but then rises again. Roseoles

or petechiae can develop on the 3rd or 4th day in 20-25 per cent of patients. Epistaxis, gingival bleeding and, in severe cases, uterine haemorrhage can be seen. Intestinal or pulmonary haemorrhages are rare.

The haemoglobin content and the red cell count are high during the first days of the disease, but by the end of the fever period, hypochromic anaemia develops which subsides by the third week of the disease. The leucocyte count is low (to 4 x 10^9/1) with the shift to the left (to rod neutrophils).

Diagnosis. The diagnosis is based on clinical, epidemiologic and laboratory findings (see "Haemorrhagic Fever with Renal Syndrome").

Treatment. Treatment is the same as in haemorrhagic fever with renal syndrome.

Prevention and control. Measures are aimed at extermination of rodents, that are the source of infection, and ticks (the vector). Measures should be taken to protect people from tick bites. Observation of personal hygiene during muskrat hunting or pelt processing is necessary. Population in the areas dangerous for the fever should be vaccinated.

Measures in the focus. Patients should be hospitalized. Persons in the focus of infection should be observed for 20 days. Patients are not contagious.

Kyasanur Forest Disease

Aetiology. The disease is caused by the virus which is similar to that causing spring-summer tick-borne encephalitis.

Epidemiology. The source of infection are monkeys and possibly other animals and birds. The virus is transmitted by the bite of ticks *Haemophysalis spinigera, H. turanicus,* gamasoidea ticks, and fleas. The reservoir of virus are birds migrating from Omsk and Novosibirsk regions to India and back.

Kyasanur forest disease occurs in India.

Clinical picture. The incubation period lasts from 3 to 8 days. The onset is acute: the body temperature rises to 39-39.4 °C during the first day of the disease. The patient complains of headache and myalgia. On the 3rd or 4th day the condition worsens; the patient develops vomiting, diarrhoea, delirium, nasal, gastrointestinal, and gingival bleeding.

Generalized maculopapulous rash, bradycardia and hypotension are characteristic. Fever lasts 7-14 days. Haematologic changes: leucopenia, thrombocytopenia, aneosinophilia, then neutrophilic

leucocytosis. The urine is characterized by moderate albuminuria and haematuria. The recovery period lasts 1-2 months.

Complications. Encephalitis and pneumonia are the complications.

Diagnosis. Diagnosis is established on the basis of clinical, epidemiologic and laboratory findings. The virus is isolated from the blood by agglutination reaction. Blood should be tested from the first to the fifth day. Suckling mice, chick embryos and cell cultures are inoculated with the patient's blood. Complement fixation test, haemagglutination inhibition test and diffuse precipitation in agar are used for the purpose.

Treatment. Treatment is the same as in other haemorrhagic fevers.

Prevention and control. Measures include extermination of the transmitting vector and protection of people from ticks.

Yellow Fever

Aetiology. The disease is caused by *Flavivirus febris* of the genus *Flavivirus*, the family *Togaviridae*. The virus is unstable in the environment. It resists drying and can survive in the frozen state for a year; in a sealed vial with nitrogen, the virus remains viable for 12 years.

Epidemiology. Two epidemiologically different types of foci are distinguished: sylvan (rain forest) and urban. The reservoir of the virus in the sylvan form are monkeys, possibly rodents, hedgehogs and other animals. The vector of transmission in South America are mosquitoes *Haemagogus, Sperazzini* and other insects; in tropic Africa these are mosquitoes *Aedes simpsoni, A. africanus, A. aegypti* and other species of *Aedes.* Sylvan yellow fever is also called endemic because it usually occurs in the form of endemic foci and less frequently as epidemics.

Transmission of the virus from epidemic foci to towns and villages, where mosquitoes *Aedes aegypti* occur, can cause an epidemic outbreak. The source of infection in urban foci of yellow fever are human patients; the vector is mosquito *Aedes aegypti.* The mosquito becomes contagious in 6-18 days after sucking blood of a human patient, this period depending on the ambient temperature: 18 days for ambient temperatures under 21 °C, and 6 days at 31 °C. Once infected the vector remains infectious for its entire life (1-2 months).

Susceptibility to yellow fever is universal, but part of the indigenous population in endemic areas sustains the disease in the mild or asymptomatic form. Life-long immunity is produced in people who sustained the disease.

Sporadic cases and local group incidences are reported from subtropic and tropic zones of Africa, South and Central America. During summer, the disease can occur in other subtropic regions where the transmitters of the virus are available. According to the international rules, yellow fever is the infection that requires establishment of quarantine and should be reported to **WHO.**

Pathogenesis. As the virus is inoculated into a human by the bite of an infected mosquito, it multiplies during 3-6 days in the regional lymph nodes, in the cells of mononuclear phagocytic system, and enters the blood to cause viraemia. The blood carries the virus to the liver, bone marrow, kidneys, spleen, and brain to involve the vascular apparatus and to cause dystrophy and necrosis of their cells.

Clinical picture. The incubation period lasts 3-6 days. Three periods (phases) are distinguished. The *initial* (hyperaemic) phase lasts 3-4 days. The onset is acute: the patient develops severe headache, chill, vertigo, lumbar pain, pain in the extremities. The body temperature rapidly rises to 39-40 °C and higher. Thirst, nausea and recurrent vomiting with mucus are characteristic. The face, the neck and the upper chest are markedly hyperaemic and swollen from the first days of the disease. The scleral and conjunctival vessels are injected (rabbit eyes). The patient complains of insomnia. The pulse rate is 100-130. On the second or third day, the patient's condition worsens, he develops cyanosis and then slight jaundice of the skin and visible mucosa. Blood studies reveal hyperbilirubinaemia and high transaminase (mostly AsAT) activity. The liver and the spleen are slightly enlarged and tender to palpation. Tachycardia is followed by bradycardia. Epistaxis and gingival bleeding are frequent. Blood is seen in the vomitus ("black vomit").

Remission begins in 4-5 days. It lasts from several hours to one day. The body temperature drops to normal or subfebrile. The patient's condition improves, vomiting ceases, pain abates. If the disease runs a mild course, recovery begins with the fall of temperature.

In moderately severe and severe cases, the phase of remission is followed by the phase of *reaction* or *venous stasis* (toxaemia) that lasts 3-4 days. Remission can be absent and the initial period can be followed immediately by the reaction phase. The patient's condition rapidly worsens. The' temperature rises again, and jaundice intensifies. The skin is pallid; haemorrhagic rash (petechiae, purpura, ecchymoses) develops on the trunk and the extremities. Gingival bleeding, haematemesis, nasal and uterine bleeding leading to miscarriage, develop. Arterial pressure falls. Oliguria or anuria

attended by azotaemia develops. Haematologic changes: leucopenia, neutropenia, lymphocytopenia, high globulin and colour index, and accelerated ESR; blood coagulation is delayed.

The fever period lasts 8-9 days, and then the phase of recovery begins with a slow restoration of the upset functions of the organs and tissues.

A fulminating form of the disease leads to death in 3-4 days.

Complications. Pneumonia, myocarditis, parotitis, abscess of the kidneys, sometimes gangrene of soft tissues and extremities are the complications.

Diagnosis. Yellow fever is diagnosed on the basis of clinical and laboratory findings. Virus is isolated in the laboratory from a blood specimen taken during the first 4 days of the disease. Discovery of antibodies to the virus, using the complement fixation test and inhibition of indirect haemagglutination, is diagnostically important too: four-fold increase in the antibody titres in paired serums is diagnostically trustworthy. The virus neutralization reaction is also used. Serologic studies can confirm the diagnosis retrospectively because the antibodies to the virus can be revealed only on the second week of the disease.

Treatment. Specific therapy is unknown. Moderately severe forms are treated symptomatically: vitamin C, vicasol, vitamin P, cardiovascular preparations. Severe and fulminant forms should be treated by intensive therapy; resuscitation measures may be necessary: correction of haemostasis, complex antishock and detoxicating treatment.

Prevention and control. Prophylactic measures include thorough epidemiologic supervision of the territory where cases of yellow fever were registered in the past or are present in this time; vaccination of population in epidemic foci against yellow fever; individual and group protection against mosquitoes (repellents, netting, screening, etc.); and destruction of mosquitoes.

Yellow fever patients should be taken to hospitals protected from penetration of mosquitoes. Measures should be taken to prevent parenteral infection. Non-vaccinated people arriving from endemic regions should be isolated for 9 days. Aircraft arriving from areas dangerous for yellow fever should be disinsected.

Specific prophylaxis of yellow fever in the focus of infection should be done with live attenuated vaccine 17-D prepared from the virus by long passage in tissue culture and from the French neutrotropic Dakar strain. The 17-D vaccine diluted 1:10 is given subcutaneously (0.5 ml). Immunity develops in 8-10 days and persists for 6 years.

Vaccination should be registered in international certificates. Persons who travel to endemic regions should be vaccinated not later than 10 days before the departure.

Dengue Haemorrhagic Fever

The disease is also known as Philippine haemorrhagic fever, Southeast haemorrhagic fever, and Thai haemorrhagic fever.

Aetiology. The causative agent is the dengue virus of the genus *Flavivirus*, the family *Togaviridae*, which is similar to the other group B arboviruses causing yellow fever and tick-borne encephalitis. At least four serotypes of the dengue virus are known (dengue types 1, 2, 3, 4). The virus survives for several years in the dry state in the blood serum at 5°C and in the frozen (— 70 °C) state.

Epidemiology. The source of infection in the urban foci are human patients and in the sylvan foci, monkeys. The source of infection is dangerous during the first 5 days of the disease (viraemia). The infection is transmitted by female mosquitoes of the genus *Aedes (A. aegypti, A. albopictus*, and others) that become contagious in 8-12 days after sucking blood of an infected subject. Contagiosity persists for the entire life (3-4 months). Children and travellers are mostly affected by the disease in endemic foci. The disease occurs in the zone between 42 °N. lat. and 40 °S. lat. Foci of infection occur in the countries of Southeast Asia, Oceania, and in West Africa.

Pathogenesis. The virus is inoculated into the human being by the bite of an infected mosquito. The virus multiplies in the cells of mononuclear phagocytic system for 5-16 days and is then carried by the bloodstream to the central nervous system, kidneys, liver, muscles, and other organs and tissues, where the virus propagates and is again carried by the blood to cause secondary wave of fever. Since the vessels are involved, the haemorrhagic syndrome develops. Hypovolaemia develops (up to hypovolaemic shock).

Clinical picture. The incubation period lasts from 5-8 to 15 days. The onset of the disease is usually acute. It begins with a shaking chill and rapid elevation of temperature to 39-41 °C, high temperature persists for 3-4 days. Headache, myalgia, and arthralgia develop. The patient feels pain when pressure is applied to the eyeballs. Photophobia, perverted taste, nausea, vomiting, and diffuse abdominal pain are characteristic. The patient is stretched in his bed because of severe muscular and joint pains. Gait becomes slow and tense because of restricted movement of the joints (especially in the knees).

The patient's face is oedematous, the forehead and cheeks are hyperaemic (flushing face), the gaze is glossy, scleral injection is marked, punctate rash appears on the 2nd or 3rd day on the trunk, chest and abdomen, then on the face and extremities. On the 4th or 5th day it looks like in scarlet fever or measles, less frequently it is petechial. The first two days are characterized by tachycardia which is then followed by bradycardia; arterial pressure is low. On the 3rd or 4th day of the disease oliguria and even anuria develop; azotaemia is present. The temperature curve has usually one wave.

If the disease has two waves, the temperature falls by crisis on the 3rd or 4th day; profuse sweating follows. After 1-4 afebrile days the body temperature rises again and persists for 2-3 days. The second phase of fever is milder. The overal duration of the fever period is 5-9 days. The recovery phase is prolonged: up to two months. It is marked by asthenovegetative symptoms, arthralgia and decreased working capacity.

Haematologic shifts in the early stage of the disease are normocytosis with a relative neutrophilosis; during later period-leucopenia and relative lymphocytosis.

Complications. Complications are rare; these may be psychosis, polyneuritis, encephalomyelitis, orchitis, and pneumonia. Septic shock develops in severe cases on the 3rd to 7th day of the disease.

Diagnosis. The diagnosis is established on the basis of clinical, epidemiologic and laboratory findings. The virus can be detected during the first 2-3 days of the disease. To this end, suckling albino mice are infected into the brain. Serologic tests (inhibition of haemagglutination, complement fixation test, neutralization test) with paired serums are used on the 5-6th day and later.

Treatment. Treatment is symptomatic and pathogenetic.

Prevention and control. The main measures are aimed at disruption of the transmission routes in the endemic foci. They include destruction of the mosquito vector and the larvae, individual protection of people from mosquito bites using repellents, screening and netting. Special care should be taken to protect patients from mosquito bites, since they are the source of infection.

Chikungunya Haemorrhagic Fever

Aetiology. The causative agent of the disease is chikungunya virus of the genus *Alphavirus,* the family *Togaviridae.* The disease got its name "from the native word of the Newala district of Tanzania that means "fold in two" (huddle up with pain).

Epidemiology. The source of the chikungunya virus is a human patient. The disease is transmitted by female mosquitoes of the genus *Aedes (A. aegypti, A. africanus,* in Africa; *A. aegypti* in India and Southeast Asia).

Clinical picture. The incubation period lasts from 3 to 12 days (following the bite of an infected mosquito). The onset of the disease is acute. It begins with elevation of body temperature, severe pain in the joints, the extremities, and the spinal column. Pain is so severe that the patient doubles up. In 3-6 days the temperature falls, but after 2-3 afebrile days it rises again and persists for several days more. Pain in the joints and spine develops again. Papulous pruritic rash on the trunk and limbs is common.

The disease lasts 6-10 days, but arthralgia persists for longer periods.

Diagnosis. Diagnosis is confirmed by isolating the virus in the laboratory (complement fixation test, haemagglutination inhibition and neutralization tests).

Treatment. Treatment is symptomatic and pathogenetic.

Prevention and control. The main measures include control of the virus transmitters and protection of patients from mosquito bites.

Haemorrhagic Fever with Renal Syndrome

Aetiology. The disease is caused by the arbovirus. The virus is unstable in the environment; it circulates with the blood, and is excreted with the urine of patients during the entire fever period. In the laboratory, the virus propagates in trypsinized cultures of human embryo kidney cells. It can be detected by the immunofluorescent test.

Epidemiology. The source of infection are voles, field and wood mice, rats and other rodents. They excrete the virus with their faeces, urine and saliva. Humans are infected by contact with the rodents or their excrements, by ingesting food contaminated with infected rodent excrements, or by inhaling dust containing such excrements.

Primary and secondary foci of haemorrhagic fever with renal syndrome are distinguished. In primary (sylvatic) foci, the disease occurs the whole year round with a peak during the warm season due to intensified activity of people in forests (picking up of berries, mushrooms, or nuts, fishing, hunting, etc.). In secondary foci the disease occurs during the warm season and the first cold months,

which is associated with migration of rodents to human dwellings. Infection can also be due to occupational exposure of agricultural workers.

Haemorrhagic fever with renal syndrome occurs usually as sporadic cases but epidemic outbreaks among newcomers are possible. Natural nidi of haemorrhagic fever with renal syndrome occur in the USSR, Japan, Korea, China, Yugoslavia, Hungary, Bulgaria, Romania, Finland, Sweden, Norway, and Denmark. Human susceptibility to the disease is high. Stable immunity is produced in those who sustained the disease.

Pathogenesis. The portal of entry are damaged skin and mucosa of the eyes, lips, and the mouth. The virus multiplies inside the cells and is released into the blood (viraemia phase). The pathogenesis is based on toxaemia and capillary damage, which are manifested by haemorrhagic rash, multiple haemorrhages, oedema and lesion of tissues of the internal organs, and the central nervous system. The advanced stage of the disease is characterized by hypothalamo-pituitary-adrenal insufficiency and severe septic shock. Damaged vessels and changes in the blood coagulation system cause haemorrhage. Renal lesion is manifested by changes in the urine and upset excretory function, which is due to the direct action on the renal vessels. Involvement of the renal vessels causes sero-haemorrhagic oedema, compression of the tubules, destruction of the tubular and glomerular epithelium, and oliguria. Desquamation of the tubular epithelium can lead to tubular obstruction and anuria.

Clinical picture. The incubation period lasts from 7 to 45 days, usually 13-15 days. Four periods are distinguished in a typical course of the disease: fever, oliguria, polyuria, and recovery. The onset of the disease is acute. It begins with a shaking chill and elevation of temperature to 39-40 °C where it remains for 5-6 days.

The patient is first excited, he complains of insomnia, headache, pain in the eyes, muscles and abdomen, thirst, vomiting, and lassitude. Excitation is then followed by flaccidity, apathy, and sometimes delirium. Examination reveals hyperaemic face, fauces, neck, conjunctiva and the sclera. On the 3rd or 4th day (the beginning of the oliguria period), punctate roseoles and petechiae appear. Epistaxis and gingival bleeding develop; in severe cases, uterine, pulmonary and intestinal bleedings are possible. Leucopenia, thrombocytopenia develop; ESR is low.

The renal syndrome is pronounced: severe abdominal and lumbar pain, highly positive Pasternatsky's symptom. Oliguria develops (from 30 to 900 ml a day). Anuria is less common. The urine contains

protein, red and white blood cells, and hyaline casts. Oedema is absent. By the moment when the renal syndrome develops, the temperature falls but the patient's condition worsens: vomiting and thirst increase, arterial pressure falls, in severe cases residual nitrogen in the blood increases to 2 g/1 and more. The protein of the urine varies from 0.003 to 40 g/1.

With development of the renal syndrome, the blood composition changes: leucocyte count increases to 10-30 x 10^9/1, neutrophilosis develops with the shift to the left, ESR accelerates. On the 9th-13th day (the onset of the polyuria period) the daily diuresis increases to 3-5 litres. The specific gravity of the urine decreases to 1.001-1.003. The amount of protein in the urine decreases too. The patient's condition improves: vomiting ceases, appetite appears, but the patient remains weak and thirsty. Dry mouth, dyspnoea and palpitation remain.

During the recovery period, polyuria decreases, and the patient's condition gradually improves.

The disease can run mild, moderately severe and severe course. The most severe forms of the disease occur in the Far East.

Complications. The specific complications are massive bleedings, haemorrhages into the brain, adrenal glands, pancreas, and myocardium. Septic shock, acute cardiovascular failure with lung oedema, azotaemic uraemia, rupture of the kidney and other complications are possible. Secondary infection can develop.

Diagnosis. The diagnosis is based on clinical and epidemiologic findings. Blood counts and urinalysis, as related to the periods of the disease, are important. Urine changes are specific and more demonstrative in the oliguria period: proteinuria to 40 g/1 and higher, haematuria, cylindruria.

Laboratory diagnosis includes isolation of the virus (during the viraemia period) from the patient's blood and urine or tissues (inoculation into the cell culture, newborn albino mice, electron microscopy). Serologic tests are also important. Indirect immunofluorescent test, complement fixation test, passive haemagglutination inhibition test, diffuse precipitation in agar, and other reactions are used. Blood specimens, 2-5 ml, are taken for the purpose. Serologic tests can reveal the antibodies in the end of the first or early in the second week of the disease and later.

Treatment. Specific therapy is unknown. Severe cases should be hospitalized in departments equipped with an artificial-kidney apparatus. The patient must remain in bed for 3-4 weeks and more in severe cases, and for 2-3 weeks in diseases of moderate severity. Milk

and vegetable diet is recommended. Salt is not restricted. Drinking much liquid is desirable.

During the fever period, the patient must be given vitamins B_{12}, PP (nicotinamide), P (rutin), K (vikasol), ascorbic acid in large doses.

In order to decrease sensitization of the patient, pipolphen (0.025 g once a day) and dimedrol (0.03-0.05 g 2-3 times a day) should be given. Heparin (500 U per kg body weight) should be given to improve renal haemodynamics.

Detoxication of the patient and correction of acid-base balance are attained by isotonic sodium chloride solution, glucose, and haemodez. Vascular insufficiency should be treated by infusions of plasma (200-300 ml), 5 per cent of albumin, and rheopolyglucin. In the presence of recurrent vomiting and anuria or in threatened septic shock, prednisolone and hydrocortisone should be given.

If heart failure develops, strophanthin or corglycon are given intravenously in divided doses. Analgin, pantopon, and dimedrol should be given for pain. Antibiotics should be given for secondary infections. Convalescents should be observed in outpatient conditions for a year.

Prevention and control. Preventive measures include elimination of the infectious source and disruption of transmission routes. Specific therapy is not known.

Reduction of rodent population is attained by deratization and agrotechnical measures. Residential buildings, stores, and industrial buildings should be protected from penetration of rodents. Food and water should be protected with special care. Hay and straw should be removed from fields to prevent formation of rodent populations in them. Workers are recommended to wear cotton gauze masks and observe measures of individual hygiene when drying hay and straw, and during their handling and transportation in the foci of the disease.

Lassa Fever

Aetiology. The disease is due to *Lassa* virus of the genus *Arenavirus,* the family *Arenaviridae.*

Epidemiology. Haemorrhagic Lassa fever is the disease with natural nidality in Africa. The source and reservoir of infection is the African multimammate rat *Mastomys natalensis.* Infection is transmitted by person-to-person contacts, during pelt processing, or hunting in endemic areas, through fomites infected with rodent

excretions. Foodstuffs and water infected with rat excrements are an important factor of infection spread.

Another source of infection is an infected person who remains contagious during the entire length of the disease. Human-to-human transmission is effected through air-borne route, direct contacts, and parenterally. Cases have been reported of the disease among medical personnel because of nosocomial contamination with the blood of the diseased, or blood-stained medical tools and instruments.

Pathogenesis. This has been insufficiently studied. Through the portal of entry, the virus passes to tissues or regional lymph nodes where it multiplies and is then released into the blood that carries it to the liver, kidneys and myocardium, where, in turn, it multiplies and causes damage to these organs. Permeability of the vessels is also upset. The virus is released into the environment with droplets of mucus, urine and faeces.

Clinical picture. The incubation period is from 3 to 17 days (usually 7-8 days). The onset of the disease is mostly insidious. The disease begins with chills, elevation of body temperature, increasing muscular pain, weakness, vertigo, chest and abdominal pain, nausea, vomiting, and diarrhoea. The face and neck are oedematous; the mouth mucosa is hyperaemic and oedematous. Tremor of the eyelids and exudative pharyngitis develop. Body temperature of 39-40 °C can persist for 2-4 weeks and fall by lysis. The temperature curve may have two waves.

During the advanced stage of the disease, conjunctivitis develops. Ulceration of the lips, cheeks and fauces is possible. Roseole-petechial eruptions on the face, the trunk and the extremities can be seen; epistaxis can develop. Lymphadenopathy, leucopenia and thrombocytopenia are characteristic; ESR is high. Petechiae can turn into vast haemorrhages on the skin and mucosa; subcutaneous haemorrhages on the arms, abdomen, and legs can develop. Blood spitting, haematemesis, menorrhoea, intestinal and other bleedings, jaundice and signs of encephalitis (impaired vision, pathologic reflexes) can occur. Renal involvement can be manifested by oliguria, albuminuria arid microhaematuria.

The course of the disease is usually severe. The temperature fall is usually attended by septic shock. Following recovery, the patient remains weak for a long time; increased fatigue, headache and dyspnoea can persist.

Complications. Pneumonia is possible.

Diagnosis. The diagnosis is based on clinical, epidemiologic and laboratory findings. On the 7th to 10th day, antibodies can be

revealed in the patient's blood by the indirect immunofluorescent method. The complement fixation test is positive only in 10-14 days from the onset of the disease. Serum, blood plasma, faucial washings, saliva, and urine, and also specimens of the liver, kidney and other organs of the dead should be examined in the laboratory for the presence of the virus.

Treatment. Immune serum (plasma) of convalescents is a specific vaccine which is prepared not earlier than 5 weeks after the onset of the disease (the titre of the complement fixation test is not less than 1:16, 1:32).

Pathogenetic therapy can also be conducted.

Prevention and control. These measures include destruction of rats, the main source and reservoir of infection in human dwelling, protection of the houses from penetration of rodents. Rodents should be destroyed in the vicinity of the populated places in endemic areas. Predacious rats *(Rattus rattus)* that kill *Mastomys natalensis* rats can be specially raised. Foodstuffs and fomites should be protected from contamination with rodent excrements. Potable water should be boiled. Care should be taken when carrying out medical manipulations, taking materials for laboratory studies, and taking care of patients.

Current disinfection before and final disinfection after hospitalization of patients or after their death should be conducted in the focus of Lassa fever. Deratization measures are necessary as well.

Argentinian and Bolivian Haemorrhagic Fevers

Argentinian and Bolivian haemorrhagic fever belong to the groups of infectious diseases.

Aetiology. The causative agent of Argentinian haemorrhagic fever is *Junin virus.* It can be cultivated in Hela Vero tissue media. Guinea pigs are sensitive to the virus. Bolivian haemorrhagic fever is caused by *Machupo virus Johnson.* The viruses of the Argentinian and Bolivian fevers belong to the *Tacaribe* group, the genus *Arenavirus.*

Epidemiology. Argentinian and Bolivian haemorrhagic fevers have natural nidality. The natural reservoir of the virus are hamster-like rodents: *Calomys musculinus, C. laucha* for the Argentinian, and *C. callosus* for the Bolivian haemorrhagic fever. Both clinical and latent forms of the infection occur, and this facilitates circulation of the virus in natural nidi. The virus is transmitted through infected foodstuffs, direct contacts, and by inhalation of dust contaminated with rodent excrements; the infection is also transmitted through

bites of infected mites. A diseased human can also be the source of infection.

Pathogenesis. Pathogenesis of the disease is not studied.

Clinical picture. The incubation period is 6-8 to 12-16 days. The onset is gradual: the body temperature rises to 39-39.5 °C within 3-4 days. Headache, malaise, lumbar pain and pain in the extremities develop on the first day of the disease. Catarrh of the upper airways is possible. During the swing of the disease, that lasts 8-12 days, the body temperature is high. Examination reveals hyperaemic and oedematous face and neck. The mucosa is affected by haemorrhagic rash. Severe cases are marked by gingival and nasal bleeding. Dyspepsia develops: vomiting and diarrhoea. Leucopenia, eosinopenia and thrombocytopenia are seen; ESR is low. Severe forms are complicated by haemorrhages, encephalitis, coma, and acute renal failure. The patient can die on the 3rd or 5th day.

Diagnosis. The diagnosis is based on epidemiologic clinical and laboratory findings. Blood specimens for virus cultures are taken during the first 3-12 days of the disease. Complement fixation and virus neutralization tests can be conducted in the end of the 3rd week.

Treatment. Specific therapy is unknown. Plasma of convalescents is given intravenously. Pathogenetic therapy includes detoxication, blood transfusion, and symptomatic therapies. Shock should be abated.

Prevention and control. Deratization, protection of foodstuffs from contamination with rodent excrements, and individual protection against insect bites are necessary. Patients should be isolated. People attending them must observe precautions when taking blood specimens or performing other manipulations.

Live attenuated vaccine prepared from XY strain can be given against Argentinian haemorrhagic fever.

Ebola and Marburg Virus Haemorrhagic Fevers

Aetiology. The causative agent of Ebola haemorrhagic fever is Ebola virus (named after the river in Zaire) and of Marburg fever, Marburg virus which was isolated in Federal Republic of Germany. The viruses are morphologically similar but antigenically distinct.

Epidemiology. The source of Ebola virus fever are humans. The role of animals as the source of infection has not been established. Humans are infected by human-to-human contacts. Hands soiled with blood or excrements containing blood are an important

transmitting factor. Ebola virus can also be transmitted through infected syringes and needles.

The source of Marburg haemorrhagic fever are also humans (in the period of the disease when the virus circulates in blood and during recovery period). The reservoir of Marburg virus has not been discovered. Complement fixing antibodies were isolated in 10-36 per cent of cases in the blood of green monkeys in Uganda during serologic studies. The antibodies were also detected in other species (macaco, chimpanzee, orangoutang, baboon). Experimentally infected monkeys develop severe illness; they excrete the virus with the saliva and faeces.

The virus is dissipated with the patient's discharges containing blood (nasopharyngeal mucus, vomitus, faeces, semen). The disease can thus be transmitted by the air-borne, contact, alimentary and sexual routes.

The first simultaneous cases of Marburg virus fever were reported from the Federal Republic of Germany (Marburg and Frankfort on the Main) and Yugoslavia. The disease occurred among laboratory workers who were exposed to green monkeys imported from Uganda. Outbreaks were also reported from Sudan and Zaire.

Pathogenesis. Pathogenesis is not well studied. It is presumed that the virus acts directly on the cells of vascular endothelium to upset microcirculation. As a result, necrosis and haemorrhage in the liver, kidneys, testes, ovaries and lymphoid tissue occur. Viraemia persists for 14-19 days.

Clinical picture. The incubation period in Ebola virus fever is 2-15 days and in Marburg fever, from 1 to 9 days. The disease begins acutely with fever, headache, spine and lumbar pain. From the first days the patient complains of dry mouth, tickling throat, and pain in the fauces. Abdominal pain, diarrhoea and vomiting develop on the 2nd or 3rd day. On the 5th or 6th day, most patients develop maculopapular rash that persists till the 10th-14th day of the disease. The haemorrhagic syndrome occurs on the 3rd or 5th day. Petechiae and ecchymoses develop; epistaxis, haematemesis, bleeding erosions in the mucosa of the mouth and gums are seen; conjunctival injections and haematuria occur; severe cases are marked by gastrointestinal bleeding. The central nervous system can also be involved (paresthesia, crapms, stupor, the meningeal syndrome). Leucopenia is followed by leucocytosis with a neutrophilic shift. The recovery period lasts 1-3 weeks. In fatal cases the patient dies on the 7th-9th day of the disease (septic shock).

Diagnosis. The diagnosis is established on the basis of clinical,

epidemiologic and virologic findings (see "Lassa Haemorrhagic Fever").

Treatment. The patient is given serum of convalescents, pathogenetic preparations promoting restoration of the water balance, normalizing the volume of circulating plasma, abating haemorrhages, and improving the hepatic and renal function. Infusion of fluids (blood, plasma, albumin, dextran) is indicated in septic shock.

Prevention and control. Patients with Ebola and Marburg virus fevers should immediately be hospitalized (in special cubicles) and quarantine established to prevent nosocomial infection. Convalescents are discharged from hospital in 21 days after the onset of the disease in complete clinical recovery and three negative serologic tests. All fomites should be disinfected in a cubicle where the patient was present. The medical personnel must wear protective overalls and their mouths and noses should be protected with masks (cotton gauze). The hands must be washed with soap and disinfectants. On termination of work, sanitary measures should be taken. When performing parenteral manipulations, it is necessary to prevent damage to the skin so that infected material does not contaminate the worker. Syringes and needles should be disinfected and sterilized.

Pappataci Fever

Aetiology. The causative agent of pappataci *(Phlebotomus)* fever is the virus of the genus *Ukuniemvirus,* the family *Bunyaviridae.* The disease is highly contagious. The virus is found in the blood of patients by the end of the incubation period and during the first two days of fever. The virus dies outside the living microorganism.

Epidemiology. The source of infection is a diseased human being. The virus can be found in cats and dogs. It is transmitted by the sandfly *Phlebotomus papatasii* and *P. sergenti.* The sandfly acquires the capacity to infect in about 5-8 days after sucking blood of an infected individual. The sandfly remains the reservoir of infection for its entire life and transmits the virus to its posterity by the transovarial route.

Seasonal variations in the incidence of the disease in subtropic areas are due to the special character of the sandfly life cycles. The incidence increases in May or early June and also at the end of July and August. Seasonal variations are absent in the tropic regions.

The immunity after the disease is unstable and repeated infections are therefore possible.

Pappataci fever occurs in countries of the Mediterranean Basin, on

the Balkans, and also in Iran, Afghanistan, India, China, Burma, Indonesia, the Philippines, in the Central, North and East Africa and South America, in the USSR (Middle Asia, the Caucasus, south Ukraine, and Moldavia).

Pathogenesis. The virus circulates with the blood stream and damages the vascular wall. The vessels of the central nervous system and skeletal muscles are involved in the first instance.

Clinical picture. The incubation period lasts from 3 to 9 days, usually 4-5 days. The disease begins suddenly with a chill and elevation of temperature to 39-40 °C. The patient complains of severe headache (in the frontal and occipital regions), painful movement of the eyes, pain in the calves, sacrum and the spine. The main symptom is pain felt by the patient when his eyelid is lifted by the fingers (Taussig's first symptom), the patient also feels pain when pressure is applied to the eyeballs or when the eyes are moved (Taussig's second symptom).

Conjunctival injection of the sclera at the outer canthus is pronounced (Pick's symptom). The neck, face and chest are hyperaemic, the conjunctival vessels of the eyelids are injected, the faucial mucosa is hyperaemic, the palatine arches and the uvula are oedematous, the lips are attacked by herpes. Bradycardia and hypotension occur. Dyspepsia is possible.

Severe forms of the disease are manifested by signs of involvement of the central nervous system: unpleasant sensation by the course of the nerve trunks, hyperaesthesia, the meningeal syndrome.

Fever persists for 3 days; relapses are possible. The recovery phase lasts from 2 to 4 weeks. This period is marked by weakness and headache.

Leucopenia, neutropenia, and then lymphocytosis, monocytosis and aneosinophilia are seen. The cerebrospinal fluid issues under excessive pressure during lumbar puncture. Nonne-Apelt and Pandy tests are positive.

Diagnosis. It is established on the basis of clinical and epidemiologic findings. Complement fixation test with the specific antigen is used.

Prevention and control. Control of transmitters of the infection is the main measure. Sandflies are killed by treating residential and other buildings with a 2-3 per cent chlorophos or carbophos solution. This should be done once a season, during the period of larval development into the imagoes. Treatment can be repeated for indications. Sites of deposition of the larvae should be eliminated by timely disposal of wastes and refuse. Rodents and their holes should

be destroyed to prevent appearance of new generations of the sandfly. People should be protected from fly bites (gauzes, screens, nets, repellents). Patients should be isolated at home or in hospital, where conditions must be provided to preclude sandfly bites.

The specific prophylaxis includes percutaneous vaccination with a live formalinized vaccine (for epidemiologic indications).

Measures in the focus. These include isolation of the patient and his protection from fly bites. Elimination of the sandfly and its larvae is necessary.

Plague

Aetiology. The disease is due to *Yersinia pestis*, the bacillus of the genus *Yersinia*, the family *Enterobacteriaceae.* It is a barrel-shaped gram-negative nonmotile bacillus. Its pathogenicity toward humans and animals is very high. The bacillus remains viable outside the macroorganism for a long time. In dead rodents, *Yersinia pestis* can live 5 months (at 0°C); in dead (frozen) humans the bacillus can survive from 7 to 12 months. In the sputum the bacillus remains viable from several days to 5 months, in pus, to 40 days, and in water, to 3 months. Its stability toward disinfectants is low. At 100 °C the plague agent is killed in few seconds.

Epidemiology. Plague is a typical disease of rodents which are the primary source of the disease among humans. Rodents such as marmots, sousliks, hamsters, field mice and voles, brown and grey rats, house mice, etc. are highly susceptible to plague. The primary reservoir of plague infection are sousliks, voles, marmots and rats. Rodents usually develop an acute form of plague and die. But some of them (hibernating sousliks, marmots) develop the latent disease which remains in them till next year. Other animals are also involved in the epizootics. Spontaneous infection with plague has been observed in 300 species of rodents and 29 species of other animals (camels, monkeys, jackals, hedgehogs, etc.). Ectoparasites, such as fleas are involved in the spread of plague and its maintenance in nature. Fleas are the main vector of infection. They leave dead animals and attack another host. Fleas can survive in burrows of the dead for a year until the hole is occupied by a new animal.

Epizootics in natural nidi are explained by circulation of plague microbes in the system rodent-flea-rodent.

Natural nidi of sylvatic (steppe) and murine plague are distinguished. Natural nidi of sylvatic plague have been formed independently of the humans and their activities. The main nidus is

found in the vast deserts of Middle Asia. Lybian and southern jirds are the main reservoir of the infection. Siberian marmots maintain the infection in the steppes of East Asia. Natural nidi are known in Africa, North and South America, and on other continents, from which plague cases among people are reported annually.

Grey, Alexandrian and black rats, and house mice are the main sources and reservoirs of infection. In these animals plague can proceed as a long-standing condition or as asymptomatic carrier state. The main sources of murine plague are found in South and East Asia.

Humans are a great danger to the surrounding as a source of infection. These are patients with primary and secondary pneumonic types of the disease and the septicaemic form. Patients with uncomplicated bubonic forms are practically not dangerous.

The main route of infection transmission from an infected rodent to a human being is through a bite of an infected flea. The flea is infected through ingestion of blood of a bacteraemic animal. As the bacillus multiplies in the intestinal tract of the flea, a jel is formed at the entrance to the stomach that prevents the passage of subsequent meals. As a result the bacilli are regurgitated when the infected flea attempts to ingest another blood meal. The flea remains hungry and its activity increases. In the absence of rats, the flea attacks humans to infect them.

If a human being hunts in the focus of plague he may get contaminated by direct contacts with marmots, hares or other infected animals, either dead or captured. If an individual damages the skin when removing the pelt, or touches the mucosa with the contaminated hands, he gets infected. People also get infected during funeral ceremonies because the fluid issuing from the mouth or nose of the dead contains the plague agent.

Ingestion of contaminated food also leads to penetration of the plague bacillus into the gastrointestinal mucosa.

Susceptibility of humans to plague is extremely high. When infected from an animal, the patient usually develops the bubonic form. Bubonic plague is characterized by slowly increasing incidence.

In primary or secondary pneumonic plague the infection is transmitted from person to person by air-borne route which is a great epidemiologic danger because the disease can spread widely within a short period of time. Pulmonic plague usually follows the bubonic form and very soon it becomes the main clinical form. The immunity developed in the plague patient is rather stable and repeated infections are rare.

Pathogenesis. The pathogenesis depends on the route by which the plague agent penetrates the body. If the infection gains entrance through the skin, the bacillus is carried to the regional lymph nodes where the microbes propagate to cause various inflammations with haemorrhagic infiltration. The whole group of the lymph nodes and the adjacent subcutaneous fat are involved in the inflammation. A primary bubo is thus formed. From the bubo, the microbes enter the blood stream to cause bacteraemia. The microbes enter the internal organs and lymph nodes that are remote from the portal of entry; secondary buboes are thus formed. Secondary plague pneumonia is especially dangerous. Less frequently, a papule or vesicle (that transforms later into a pustule, filled with sanguinopurulent exudate) is formed at the portal of entry of the infection. The pustule turns into an ulcer with raised margins. The regional lymph nodes are also involved in the process.

If a person is infected by the air-borne route, haemorrhagic pneumonia and sepsis occur (primary pulmonic and secondary septicaemic forms). In alimentary infection, the disease is manifested by haemorrhagic enteritis and sepsis (intestinal and secondary septicaemic forms). In primary septicaemia, the lymphatic barrier is weak (usually due to incomplete phagocytosis of the plague agent, and due to the massive dose of infection and low body reactivity). Carried by the blood stream, the plague agent therefore generalizes the process.

The plague microbe forms exo- and endotoxins which cause toxaemia. The cardiovascular and the nervous systems are first of all involved: the pulse changes, arterial pressure falls, the patient is excited and delirious. Vascular changes are manifested by necrosis, infiltration and serous impregnation of the vascular walls.

Clinical picture. The incubation period lasts from 2 to 6 days. It is shorter in the pulmonic form while in the vaccinated it can be as long as 8-10 days. Plague begins suddenly with a severe chill and rapid elevation of temperature to 39 °C and higher. Toxaemia rapidly develops in all clinical forms. It is manifested by severe headache and vertigo, insomnia, myalgia, weakness, nausea and vomiting. The patient is first excited. His face and conjunctiva are hyperaemic, the tongue is white and swollen, speech becomes inarticulate. All these symptoms (unsteady gait included) resemble those of alcoholic intoxication. Circulatory disorder is marked; tachycardia develops (120-160 beats per minute); arterial pressure falls; arrhythmia occurs in severe cases. Severe cases are also characterized by cyanosis, pointedness of the features (expression of fright on the face of some

patients), delirium and hallucinations. Neutrophilic leucocytosis with a shift to the left and accelerated ESR are seen in the blood. The diuresis decreases; the urine contains protein, granular and hyaline casts and red blood cells. In addition to the symptoms that are common for all forms of plague, each particular form is also characterized by its specific symptoms.

Depending on the route of infection transmission, the patient may develop either a localized form of plague, such as cutaneous, bubonic, cutaneous-bubonic, or tonsillar (pharyngeal), or a generalized form, such as primary septicaemic, secondary septicaemic, primary pulmonic, secondary pulmonic or intestinal plague.

In the cutaneous-bubonic form, a spot is first seen at the portal of entry, which is then converted into a papule, a vesicle, a pustule, and an ulcer. The ulcer is surrounded by a zone of red, later it becomes covered with a dark crust and does not heal for a long time. As distinct from anthrax, a plague carbuncle is painful. The regional lymph nodes are almost always involved.

Lymphadenitis (plague bubo) develops on the first or second day of the bubonic form. The bubo is tender not only during movement but also at rest. The patient is therefore motionless. Pain makes him assume a forced position. If the bubo is m the inguinal area, the patient flexes his leg. In the presence of an axillary bubo, the patient lies on his back with the arm set apart from the trunk. The bubo fuses with the subcutaneous cellular tissue; the overlying skin is tense and cyanotic. The bubo either resolves spontaneously or purulates and scleroses.

Cutaneous-bubonic forms can be complicated by secondary buboes (Fig. 16), secondary pulmonic and secondary septicaemic plague.

The tonsillar (pharyngeal) plague lasts 2-3 days. The toxaemia is weak, the body temperature rises to 38 °C, the submandibular and neck lymph nodes are enlarged.

The primary septicaemic form is characterized by delirious hyperactivity or complete adynamia, dyspnoea, rapid and weak pulse, Haemorrhagic rash and haemorrhages into the skin and mucosa develop, haematemesis and bleeding can be seen. Untreated patient dies during first days of the disease.

The intestinal form is characterized by high body temperature, extreme weakness, loss of appetite, nausea, recurrent vomiting, ample liquid stools with streaks of blood and mucus, severe abdominal pain during the defaecation.

Primary pulmonic plague is characterized by a fulminating course

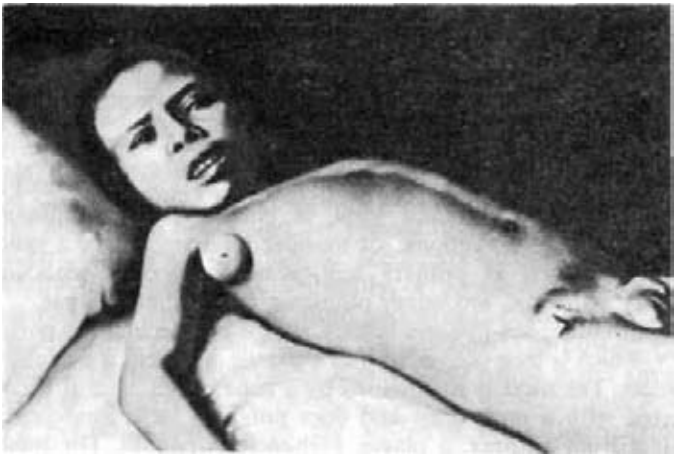

Fig. 16. Plague. Primary axillary bubo and secondary inguinal bubo (after Mohry)

with dyspnoea (40-60 breaths a minute), severe chest pain, cough with liberation of liquid blood-stained foaming sputum. Cardiovascular failure develops on the very first days of the disease.

In the pre-antibiotic era, pulmonic plague transformed into its secondary septicaemic form in 1-2 days and the patient died. The prognosis is more favourable today.

Diagnosis. The diagnosis is based on clinical, epidemiologic and laboratory findings. Special precautions must be observed when taking infected material, its transportation and further handling in the laboratory. The following specimens are taken: bubo contents, spontaneously draining exudate from ruptured buboes, vesicles, pustules, carbuncles and ulcers; sputum is taken from patients with the pulmonic form; if sputum is absent, faucial mucus is taken. Faeces should be taken from patients with intestinal lesions. Blood specimens of patients with all forms of the disease are studied. The dead should be autopsied and pieces of the buboes, cutaneous lesions, lymph nodes and the parenchymatous organs (spleen, liver, lung), as well as blood from the heart or large vessels should be examined in the laboratory.

Exudates from buboes, vesicles, or pustules should be taken by a sterile syringe. Since the amount of the material is small, about 0.5 ml of a sterile broth is taken in the same syringe and the contents are

transferred to a test tube. Sputum should be collected into wide-mouth bottles with ground-in stoppers. Blood (10 ml) is taken from the cubital vein. Several smears (4-5) are prepared at the patient's bedside. A 5-ml portion of blood is inoculated in a vial containing 50 ml of broth, while the remaining blood is placed in a sterile test tube. If the laboratory is remote, the blood is placed in two 5-ml test tubes and examined in the laboratory not later than 5-6 hours (in the absence of a refrigerator). In the laboratory, the smears are stained with Gram's stain and methylene blue (Loeffler). The serologic luminescence analysis should be conducted if a luminescent microscope is available. Hottinger's or Martin's culture media containing sodium sulphite and gentian violet are inoculated. The remaining material is used for infection of guinea pigs and albino mice. The serologic method is used for retrospective diagnosis in those who sustained a suspected plague, in patients to whom antibiotics were given, and in studies on the material taken from decaying corpses. Indirect haemagglutination and indirect agglutination inhibition tests are commonly used. The latter test with an antigen diagnosticum is used to control specificity of the positive indirect haemagglutination test. Serologic reactions should be conducted on the 5th day of the disease and then at 5-day intervals till the patient is discharged from hospital. The reaction of fluorescent antibodies can be used to detect the plague agent within 2 hours. Fleas and rodents, and also dead animals, especially camels, should be examined bacteriologically in the focus of infection.

Treatment. Treatment of the patient must be complex. Specific treatment includes the tetracyclines (tetracycline, doxycycline, oxycycline, methacycline) 0.2 g 6 times a day.

In order to prevent complications due to the antibiotics, dimedrol, 0.03 g 2-3 times a day, and vitamins (B_1, B_6, B_{12}, C, K) should be given. A 40 per cent glucose solution should be infused to patients with marked toxaemia. It should be given in the amount of 20-40 ml. A 5 per cent glucose should be given in the amount of 500-1000 ml. Isotonic sodium chloride solution or sodium hydrocarbonate should be given in marked acidosis. Haemodez, rheopolyglucin and plasma can also be given.

Lasix, furosemide and other diuretics should be given if liquid is retained in the patient. Cordiamine, camphor, caffeine, ephedrine, adrenaline and strophanthin should be used to correct cardiovascular disorders.

Prevention and control. Quarantine is necessary. The presence of natural nidi in various countries and reports of plague cases in them

indicate possible export of the disease to other countries.

The anti-plague measures should be taken in airports, sea ports, and railway border posts in accordance with the international requirements. Persons with plague should be detected and isolated. Those suspected for plague should also be isolated and observed. All persons who had contacts with plague patients should be observed. Objects suspected for contamination should be examined bacteriologically. Vaccination is necessary. Current and final disinfection, disinsection, deratization and quarantine measures are necessary. Special anti-plague institutions should be involved in prevention and anti-epidemic measures in natural nidi of plague.

The complex to antiplague preventive measures includes the following: (1) epidemiologic surveillance; (2) rodent control (deratization) and destruction of the flea vector (disinsection); (3) vaccination of population against plague; (4) health education of population.

Eradication of natural nidi located mostly in remote locations is an expensive measure. In this connection the species structure and populations of rodents and their ectoparasites should be systematically controlled in enzootic areas. Laboratory examinations are necessary for timely detection of epizootics, extermination of rodents and ectoparasites in populated places and the surrounding areas. Deratization and disinsection measures should be taken on the territories of the epizootic zone.

Dry live vaccine is used for specific immunization of people. Vaccination should be done for epidemiologic indications.

Dry live vaccine induces a 6-month long immunity in the vaccinated. The vaccine is given by cutireaction.

Measures in the focus. If plague is detected or suspected, measures should be taken to localize and eliminate the focus. These measures include: (1) revealing and hospitalization of patients, revealing and isolation of persons who had contacts with patients, the dead, or with infected materials; (2) revealing and burying the dead; (3) carrying out disinfection, disinsection and deratization in the focus, in populated places and in the field; (4) observation of population in the focus; provisional hospitalization of all patients with fever, lymphadenitis, tonsillitis, and pharyngitis; (5) establishing quarantines or restriction in migration of population; (6) epizootiologic examination of the focus and the adjacent areas; (7) vaccination of population for indications. The epidemiologic studies should be conducted by a special group into which personnel of the anti-plague institutions should be included.

Plague patients and people suspected for plague are placed in

special hospitals. Any room is suitable for preliminary isolation. All people must be removed from the room where the patient was present. The plague case should immediately be reported to higher medical authorities. Each hospitalized patient must be placed in a separate room or at least screened from the other patients in the room. The hospital must be guarded. The personnel must wear special anti-plague overalls.

Persons who had contacts with plague patients should be isolated for 6 days. Persons who had contacts with pulmonic plague patients should be isolated in individual rooms. All persons who had contacts with patients or the dead (with pediculosis) must have their body temperature measured at least twice a day and must be given .— preventive treatment for 5 days with doxycycline (0.2 g once a day\= intramuscularly) or tetracycline (0.5 g three times a day).

The dead must be buried in coffins (or without coffins) to a depth of 1.5-2 metres. Dry chlorinated lime should be placed on the bottom of the grave. The dead can be burned.

If hospitalization of all contacts is impossible in view of their multitude, observation is especially important. People should be observed at home with obligatory thermometry. Patients with fever should be examined by the physician (who must establish the preliminary diagnosis) and sent to the corresponding hospital. Whenever necessary, observation should be combined with vaccination and health education of population.

Current disinfection in the focus should be conducted when taking care of patients, during evacuation of patients and persons who had contacts with them. Final disinfection should be conducted in residential houses after evacuation of the patients and contacts, and also after burying the dead. Disinsection and deratization should also be conducted.

Tularaemia

Aetiology. Tularaemia is caused by *Francisella tularenis* of the genus *Francisella,* the family *Brucellaceae.* The disease is highly contagious for humans and some animals. The stability of the agent in the environment depends on ambient temperature and other factors. In water at 4 °C, the microbe survives for more than 4 months, in frozen foodstuffs for 3-4 months, in dried pelts to 2 months and in grains and straw (at 20-30 °C) for 20 days. When exposed to direct sunrays tularaemia agents are killed in 20-30 minutes. They are sensitive to disinfectants in normal concentrations and to high temperatures.

When boiled, they are killed instantaneously; at a temperature of 60 °C, they are destroyed in 10 minutes.

Epidemiology. The main reservoir and source of infection are rodents. The causative agent can survive in the ixodes for a long time. The reservoirs of infection in natural foci are water rats, small rodents (such as voles or house mice), hares, muskrats, and hamsters. The agent multiplies in the rodent. This process rapidly becomes generalized, and the bacillus is dissipated in the environment with the urine and faeces. More than 60 species of animals can be the source of the infection. Squirrels, foxes, cats, dogs, goats, cattle and sheep are of secondary importance, because the process proceeds in these animals with insignificant insemination of the internal organs, without bacteraemia, and hence without excretion of the bacillus into the environment. Human patients are not contagious.

The infection is spread among animals by blood sucking ectoparasites, and also through infected water and foods.

The infection is transmitted from animal to human by air-borne route, by direct contact (during skinning of infected rodents), by ingestion of contaminated foodstuffs or drinking infected water (bathing included), and by the bites of infected arthropods: ticks, lice, mosquitoes, etc.

Epizootics and outbreaks of tularaemia among people occur in localities where swamps, meadows, fields, steppes, forests, springs and desert rivers prevail.

Depending on location of the focus, the number of rodent populations, human activities and the quantity of immune population, the disease can occur as sporadic cases or epidemic outbreaks. Increased risk of epidemic tularaemia exists among agricultural workers, shepherds, farmers, hunters, laboratory workers and other occupations dealing with susceptible animals. Epidemic outbreaks of transmissible tularaemia occur in 72-85 per cent of tularaemia cases. Water- and food-borne infections come second.

Susceptibility of humans to tularaemia is high. Stable immunity develops in those who sustained the disease. In some persons this immunity persists for life.

Tularaemia occurs in many countries of America, Europe and Asia. The disease owes its name to the district of Tulare in California, where it was first discovered.

Pathogenesis. The tularaemia agent can gain entrance to the human body through the skin, mucosa of the mouth, nasopharynx, gastrointestinal tract, respiratory ducts and the eyes. Less frequently the agent causes inflammation of the skin at the portal of entry.

More frequently it rapidly reaches the regional lymph nodes and later the blood stream.

Primary buboes are formed at sites of accumulation of the organisms (in the regional lymph nodes). Specific granulomas contain leucocytes, fibrin, plasma and eosinophil cells. Tularaemia granulomas are necrotized, degraded, and look like tubercles. As the microbes propagate, they can cause secondary buboes. Circulation of the tularaemia agent with the blood stream causes toxaemia with involvement of various organs and formation of specific granulomas in them.

Clinical picture. The clinical picture of the disease depends on the route by which the agent gains entrance to the individual.

The incubation period lasts from 2 to 8 days. All clinical forms of tularaemia are characterized by some common symptoms. The disease begins suddenly: a short-lasting chill is followed by elevation of temperature to 38.5-40 °C. The patient complains of headache, muscular and lumbar pain, weakness, hyperhidrosis, and poor appetite. Examination reveals hyperaemic face and conjunctivitis.

The spleen and the liver are enlarged by the end of the first week. Leucopenia, moderate shift to the left, relative lympho- and monocytosis are seen; ESR is high. Fever can last from 5 to 30 days. Remittent and intermittent fevers are common. The temperature falls by lysis. The mentioned general symptoms are supplemented by specific signs of the disease that depend on the portal of entry of infection.

The following clinical forms of tularaemia are differentiated: bubonic, ulceroglandular, oculoglandular, angioglandular, gastrointestinal, pulmonic and primary septic (generalized) forms.

In bubonic form, infection penetrates through the skin and mucosa to the regional lymph nodes, where it causes lymphadenitis (bubo). The location of a bubo depends on the route of infection. Ulnar and axillary buboes usually occur in persons who were infected occupationally by direct contact with infected animals. Submandibular and neck lymph nodes are involved in water- and food-borne infections.

The size of a bubo varies from the size of a nut to that of an egg, and greater. A group of lymph nodes is often involved. The nodes do not fuse between themselves or with the surrounding cellular tissue. The nodes are only slightly tender. As the body temperature falls, the buboes slowly resolve. If treatment is untimely, an abscess can be formed that ruptures and drains spontaneously with liberation of thick cream-like pus.

In ulceroglandular tularaemia, a spot at the site of the agent

entrance during 6-8 days transforms consecutively to a papule, then to a vesicle, pustule, and finally to an ulcer with simultaneously developing processes in the nearest lymph node (bubo). Primary lesion of the skin is common for the transmissive form of tularaemia.

In oculoglandular tularaemia, the agent enters through the eye tunics with development of follicular proliferations over the conjunctiva and simultaneous enlargement of the lymph nodes (parotid, anterior neck, submandibular nodes, etc.). The eyelids become swollen, papules and ulcers can appear on the eye tunic.

The angioglandular form is characterized by hyperplasia of the tonsils with subsequent formation of a greyish white necrotic coat, and formation of deep slowly healing ulcers. Unilateral involvement is more common. Since the tularaemia agent invades the regional lymph nodes, submandibular, neck and other buboes develop (Fig. 17). The angioglandular form is common in water-borne outbreaks.

The gastrointestinal form of tularaemia develops on ingestion of the tularaemia agent with food. This form is characterized (in addition to the general symptoms) by severe abdominal pain (which is due to involvement of the mesenteric lymph nodes), nausea, vomiting and diarrhoea. The diagnosis of the gastrointestinal form is difficult.

Primary inflammation in pulmonic tularaemia occurs in the lungs. The disease is attended by development of focal pneumonia with a flaccid and long-standing course. X-ray studies and skin-allergic tests are decisive diagnostically.

The septic form of tularaemia is characterized by development of

Fig. 17. Tularaemia. Patient with bubonic plague (after Uglovoi)

general symptoms without primary local and regional reaction at the portal of entry of the infection. Clinically this form has a more pronounced picture of toxaemia. Polymorphous erythematous rash is more common in this from of the disease. During the recovery stage, specific complications can develop: secondary pneumonia, nervous and cardiovascular diseases (vegetative neuroses, degenerative changes in the myocardium, etc.).

Working capacity and appetite are restored very slowly in convalescents. Tularaemia relapses and conversion of the disease into the protracted form (lasting 2-3 months) are possible.

Diagnosis. Tularaemia is diagnosed on the basis of clinical, epidemiologic and (in the pulmonic form) X-ray findings. Laboratory studies (allergic, biologic and serologic tests) are important diagnostically. Skin-allergic tests can be conducted on the 3rd-5th day of the disease: 0.1 ml of tularin (diagnosticum) is injected intracutaneously in the upper third of the volar surface of the forearm. If a hyperaemic infiltration of at least 0.5 cm in diameter appears at the site of injection, the test is considered positive. The result can be assessed in 24, 36 and 48 hours.

Abrasion cutireaction can be used instead of the intracutaneous test.

The biologic tests are performed on albino mice and guinea pigs. The following inoculating material is necessary for subcutaneous or intra-abdominal infection of the laboratory animals: bubonic exudate taken before the 14th day of the disease; pustular contents; exudate from the ulcer bottom taken before the 8-12th day of the disease (this should be mixed with isotonic sodium chloride solution before inoculating the animals); conjunctival secretion taken before the 15-17th day of the disease; blood (5-6 ml) taken before the 6th day of the disease. The animals are observed for 15-20 days. Infected animals die in 3-4 days. The microbe is identified by the tularaemia agglutinating serum after death of the animal.

A 2-3 ml blood specimen taken on the 7-10th day of the disease is sent to the laboratory for the agglutination reaction. This reaction is repeated 2-3 times at 4-5 day intervals in order to follow the progress in the titre values. The agglutination reaction is considered positive with serum dilutions of 1:100 and higher. Indirect haemagglutination test is more sensitive and the result is ready earlier (red cells sensitized with tularaemia antigen are used as the diagnosticum).

Treatment. The tetracyclines produce the specific effect. They are given in a dose of 0.2 g 4 times a day. Chloramphenicol can also be given in a dose of 0.5 g 4 times a day for 7-10 days. Isotonic sodium

chloride solution or a 5-10 per cent glucose solution with ascorbic acid is given intravenously. Cardiacs are given whenever necessary. Vaccinotherapy should be used in long-standing cases. From 8 to 12 injections should be given at 5-6 day intervals. The dose for one injection is 50 000 (0.1 ml) to 250 000 (0.5 ml) microbes. The vaccine is given subcutaneously, intramuscularly and intravenously.

Prevention and control. Vaccination with a dry vaccine is the most effective means of prophylaxis. Population of enzootic areas, and also persons exposed to the risk of infection should be vaccinated and re-vaccinated. Vaccination can be given for epidemic indications as well. An area is considered enzootic if cases were reported or tularaemia agent was isolated in the past.

Vaccination is done by scarification or by intracutaneous injections. Various dilutions of the vaccine are used. The results are assessed in 5 and 7 days. If the local reaction is absent, another vaccination is done in 12-15 days.

Revaccination should be done in 5 years. All population in enzootic areas should be vaccinated except infants under 7 and persons to whom vaccination is contraindicated.

People can be vaccinated simultaneously against tularaemia and brucellosis, tularaemia and plague, or against all these infections simultaneously.

Complex preventive measures aimed at improvement of health in the enzootic area are important. These include flooding sites of rat habitation, drying of swamps over large areas, ploughing land and observation of all agricultural requirements such as timely harvesting, ploughing, weed control, timely withdrawal of straw and hay from fields, eradication of rodents and flying blood sucking insects, protection of foods and water from contamination with tularaemia agent, observation of safety rules when handling sources of infection and materials suspected for contamination, and also measures aimed to prevent export of contaminated materials from the infected areas.

Health education among population of enzootic areas is necessary.

Measures in the focus. Although tularaemia patients are not contagious, their detection and hospitalization helps timely control of the disease. Disinfection of the focus should be done as in intestinal infections. Deratization is necessary.

Water supply sources should be protected. Waterwells should be provided with covers, water boiled or chlorinated. Foodstaffs should be protected from contamination by rodents. Population should be vaccinated if no planned vaccinations were performed before the appearance of tularaemia in a given region.

Review Problems

1. Patient K., male, aged 56, was taken to hospital on the fifth day of a disease. Complaints: severe headache, insomnia, weakness, loss of appetite; body temperature 39 °C. Objectively: hyperaemic and oedematous face, hyperaemic skin of the neck and the upper third of the trunk, hyperaemic conjunctiva, ample roseolous rash on the sides and back, and on the flexor surfaces of the arms. In 1945 the patient had louse-borne typhus.

What diagnosis can be suggested? What examinations are necessary in order to verify the diagnosis? Plan the anti-epidemic measures to eliminate the focus of infection.

2. Q fever cases among animals were reported from town A. What measures should be taken to prevent infection spread among population?

3. A group of geologists is sent to work in the district which is endemic with respect to tick-borne encephalitis. What measures should be taken to prevent tick-borne encephalitis among the group?

4. Three cases of tularaemia were reported from town X. between October 15 and 23. Epidemiologic examination revealed increasing population of mice with lowering of ambient temperature. What measures can prevent the spread of infection?

Skin Infections

Anthrax

Aetiology. The disease is caused by *Bacillus anthracis.* It is an aerobic spore-forming bacillus that is rapidly destroyed in the absence of air, when heated to 75-80 °C, or when acted upon with disinfectants. In the presence of oxygen, the bacillus forms spores that are highly stable in the environment. Under beneficial conditions it can survive for years. These conditions include uncultivated soils in dry climates protected from direct sunlight and also underlying soil layers. In surface layers of soil, the spores pass into the prevegetative stage and are partly killed. Spores resist drying and high temperature (boiling kills them in 60 minutes); the spores also resist the action of disinfectants.

Epidemiology. The source of the anthrax bacillus are animals with acute disease (septicaemia type).

Domesticated animals, such as cattle, goats and sheep, horses, deer, pigs and camels, are of primary epidemiologic importance. A diseased human is not infectious. An individual is infected during slaughtering or skinning cattle, processing infected meat, and when attending diseased animals.

The transmission mechanism depends on the form of the anthrax agent. The vegetative form is transmitted by contact; the infection

can be transmitted by the bite of blood sucking insects, or by ingestion of infected meat. Spores can be inhaled by humans with dusty air.

Occupational (industrial and agricultural) and non-occupational anthrax are distinguished. Industrial anthrax occurs due to inhalation of the spores during processing of infected animal materials (hides, wool, hair, etc.).

In rural areas humans get infected during slaughtering, skinning, dissecting infected carcasses, preparing food from infected meat, and when attending the diseased animals.

Non-occupational anthrax develops due to accidental infection, usually with the spores.

The incidence of anthrax among people depends directly on the incidence of the disease in domestic animals and efficiency of preventive measures.

Sporadic cases are more common. Group incidence of the disease (usually infected from one source) are less frequent.

Humans are highly susceptible to anthrax. Adults are usually afflicted. Stable immunity is produced in those who sustained the disease. Seasonal variations in the morbidity are associated with increasing incidence of the disease among animals and increasing populations of blood-sucking insects.

Pathogenesis. The portal of entry are injured skin and mucosa. Two clinical forms of the disease occur in humans: cutaneous and septicaemic anthrax. The septicaemic form can be both primary and secondary (complicated cutaneous form of the disease). The cutaneous form is more common than septicaemic anthrax. The skin of the arms, head or other exposed parts of the body are involved.

A pustule develops at the portal of the anthrax agent entrance. It is a serous-haemorrhagic inflammation of the skin and subcutaneous fat with subsequent necrosis, oedema, and regional lymphadenitis. If the body resistance is low, the agent enters the blood and multiplies to cause primary septicaemia. Involvement of the regional lymphatics is attended by severe oedema and necrosis. General infection develops, which is manifested by increasing bacteraemia and toxaemia. Toxaemia is attended by sudden rises in the body temperature, cardiovascular disorders, and shock, which is the cause of death.

Clinical picture. The incubation period lasts from 2 to 14 days in the cutaneous form and from several hours to 6-8 days in septicaemic anthrax.

Cutaneous anthrax. The disease begins with development of a

pruritic spot at the portal of infection entrance. The erythematous spot rapidly develops to a copper-red papule and then a vesicle (pustule) containing cloudy sanguinous fluid. Because of severe itching, the patient scratches the pustule; sometimes the pustule ruptures spontaneously, and a black eschar forms and grows in size. The eschar looks like coal (hence the name, anthrax, which means in Greek coal or carbuncle). Secondary pustules develop around the eschar and undergo the same stages of development. Infiltration develops under the crust. It rises above the intact skin level in the form of a brown-red ridge. The carbuncle is surrounded by a massive oedema of the skin and subcutaneous fat (Fig. 18). The oedema is especially marked on the skin with underlying loose connective tissue. Except oedema and the carbuncle itself, the adjacent skin is specifically non-tender: even deep needle punctures

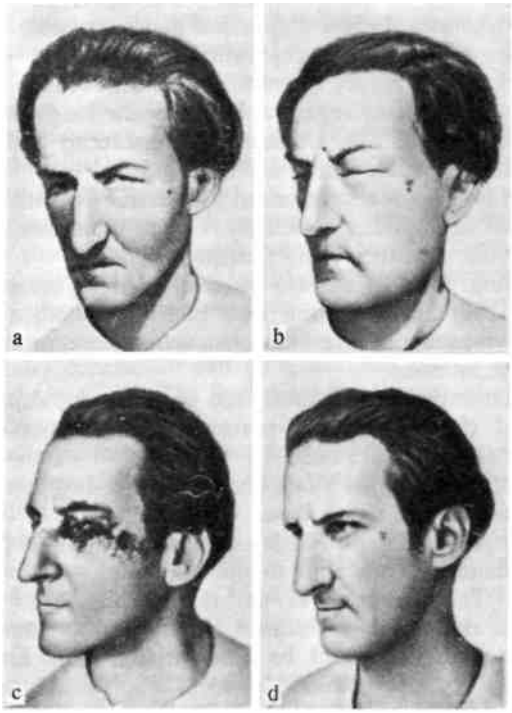

Fig. 18. Phases *(a-d)* of cutaneous anthrax

are painless. Lymphadenitis is common. Only one lymph node is usually enlarged. It becomes firm, mobile and painless.

During the first hours of the disease the patient complains of headache, lassitude and malaise. In 2-3 days, the body temperature rises to 39-40 °C. Signs of toxicosis develop: headache intensifies, weakness and lassitude become more pronounced, the cardiovascular system becomes involved (the pulse is fast, small and sometimes arrhythmic; arterial pressure is low). The liver and the spleen are enlarged. The general symptoms are less pronounced in cutaneous anthrax and the patient can continue performing his routine duties. The condition improves in 5-8 days. The body temperature decreases, oedema gradually subsides. By the end of the 2nd or 4th week, the crust falls off and the ulcer rapidly heals to leave a scar. Cutaneous anthrax can be complicated by septicaemia.

Septicaemic anthrax. The disease begins suddenly with elevation of temperature to 39 °C, chill, weakness, headache, non-productive cough, and dyspnoea. Diffuse abdominal pain is possible. Numerous haemorrhages develop. The temperature rises to 40-41 °C.

Severe toxaemia damages the vessels and thus evokes the haemorrhagic syndrome in many organs and tissues (the lungs and intestine included). In view of this, pulmonary (inhalation) and intestinal variants of septicaemic anthrax are distinguished.

Inhalation anthrax is characterized by pneumonia with oedema of the lungs and haemorrhagic pleurisy. Cough intensifies, sputum is first seromucous and then rusty (haemoptysis).

The intestinal form of anthrax is manifested by severe stabbing pain in the abdomen, vomiting with bile and blood, and bloody diarrhoea. Symptoms of intestinal obstruction develop later due to paresis of the intestine.

Septicaemic anthrax is characterized by euphoria, delirium, convulsions and the meningeal syndrome. Pulse is fast and weak (thready); arterial pressure falls.

The patient dies of septic shock during the first day (less frequently on the second day) of the disease.

Haematologic studies show high leucocyte count (to 20-25 x 10^9/1) and neutrophilia with the shift to the left.

Diagnosis. The diagnosis of anthrax in human is based on epizootologic, epidemiologic, clinical and laboratory findings.

Cutaneous anthrax should be differentiated from furunculosis, carbunculosis, erysipelas, insect bites, ulceroglandular tularaemia, bubonic plague, and glanders.

Excretions and blood should be examined in the laboratory

(preferably before treatment begins). Contents of vesicles, carbuncles and ulcers are taken with a syringe, pipette or a sterile tampon. The skin around the carbuncle should be carefully cleaned with alcohol.

Blood specimen (1 ml) should preferably be taken during the fever period. Venous blood (1-2 drops) are inoculated into a nutrient medium (agar or Hottinger's broth); two thin smears are also made on glass slides.

Samples of animal material, such as pieces of hide, wool, hairs (20-30 g) should be sent to the laboratory whenever necessary. Soil (200 g) and water (at least 1 litre) should also be examined.

Materials taken from the patient and animal specimens should be placed into sterile boxes, bottles, or other laboratory glassware. Dry smears are placed in Petri dishes and wrapped in dense paper. The pack must be labelled: "smear is not fixed". The lable must also contain information on the place and time of taking the sample, the name of the material, and the presumptive diagnosis. The name of the patient must be written on the label too.

The specimens should be placed in a special sealed box. The box should be handled with care and not overthrown. The luminescent method, thermoprecipitation, and detection of capsule formation are used in the laboratory. The tests are preliminary, and negative results do not exclude anthrax. Bacterioscopy and cultures help isolate and identify the anthrax agent.

Inoculation of albino mice, guinea pigs or rabbits (biologic tests) is performed simultaneously with inoculation of cultures. The experimental animals are observed for 10 days. Smears are prepared from blood and organs of the dead animals; corresponding cultures are also grown.

Preliminary conclusion can be formulated in 3-5 hours and the final is ready in 4 days. The final diagnosis is established only on the basis of the complex studies.

A skin allergic test with dilute immunoglobulin can be conducted on the first day of the disease. It is positive by the end of the first week in almost all patients.

Treatment. Patients with mild cutaneous anthrax should be given antibiotics alone, better penicillin: 500000-1000000 units intramuscularly 6-8 times a day for 5-7 days. Next come the tetracyclines (tetracycline, oxytetracycline). They are given per os, 0.3 g 4 times a day for 5-7 days.

In patients with moderate and severe diseases intravenous perfusion of fluids should be given in the volume sufficient to replenish the volume of circulating blood, to abate dyspnoea, cyanosis, and thirst

(2-5 litres daily). Polyglucin, rheopolyglucin or haemodez should be added (400 ml). From 90 to 120 mg of prednisolone, cardiac glycosides (0.25-0.5 ml of a 0.05 per cent strophanthin or 0.5-1.0 ml of a 0.06 per cent corglycon solution), and 1 000 000 units of penicillin should be included into the perfusion system. The remaining penicillin (from 7000000 to 12000000 U) should be given intramuscularly during a day.

Specific anti-anthrax immunoglobulin is given in the absence of increased sensitivity of the patient to immunoglobulin (40-50 ml, in a single intramuscular injection). If the skin test with dilute immunoglobulin is positive or if an anaphylactic reaction develops to subcutaneous administration of immunoglobulin, the anti-anthrax immunoglobulin should be administered only after premedication with 90-120 mg of prednisolone.

Prevention and control. Control of anthrax among domestic animals includes veterinary sanitation. It also includes timely revealing, isolation and treatment of diseased animals, their protection from insect bites, and decontamination of faeces. Diseased animals should be killed by a bloodless method in order to prevent formation of spores. Killed animals should be burned. Utilization of killed animals or their burying is prohibited.

Herds of animals where anthrax cases were registered should be observed. It is prohibited to pasture cattle on meadows suspected for infection with anthrax. Cattle may not be allowed to drink water from suspected ponds or other water bodies. Pastures should be given sanation treatment. Animals should be vaccinated with a live attenuated vaccines.

Prophylaxis of the disease among humans includes adherence to safety requirements when attending diseased cattle, slaughtering cattle, and when performing jobs such as skinning, processing of hides and wool, etc. Hides should be pickled (treated with a 2.5 per cent hydrochloric acid and a 15 per cent sodium chloride solution at a temperature of 30 °C for 40 hours). Wool should be treated with steam at 100-110 °C or with a steam-formaldehyde mixture at 62-65 °C for 2 $^{1}/_{2}$ hours. Furs should be given similar treatment.

Current and final disinfection are required. Preventive disinfection should be conducted at least twice a year at animal farms, slaughterhouses, at plants processing animal materials, in storehouses, and in vehicles used for transportation of cattle and animal products. Workers should wear protective overalls, they should be provided with disinfectant solutions and means of individual protection: goggles, masks, etc.

If a given batch of animal material is suspected for anthrax, its specimens should be sent to the laboratory for Ascoli's thermo-precipitation test. Specimens of wool, fur, hide, etc. (20-30 g) should be handled in sterile test tubes.

The specific prophylaxis of anthrax among population should be conducted with special live vaccine. Only people exposed to the danger of contamination should be vaccinated. Vaccine is given in a single dose, either subcutaneously or by scarification. Revaccinations should be repeated each year. For epidemic indications, the vaccine should preferably be given subcutaneously by jet injections. Contraindications are the same as for other vaccinations.

Measures in the focus. The patient should be hospitalized. Cutaneous anthrax convalescents should be discharged from hospital after cicatrization of the ulcer and falling off of the crust. Septicaemic anthrax patients can be discharged from hospital after abatement of clinical symptoms.

Final disinfection should be done in the focus of infection. Epizootologic and epidemiologic studies are necessary.

Contacts should be disjoined but they require medical observation during 8 days. The same measure is necessary in those who had contacts with diseased animals, pathologic materials, and in those who used infected meat as food.

Anti-anthrax immunoglobulin is recommended for prophylactic purpose. The immunoglobulin is given to persons attending the diseased animals, engaged in burying the dead, in processing meat of diseased animals, or to those who took this meat as food.

Rapid prophylaxis can be done with antibiotics and anti-anthrax immunoglobulin. Phenoxymethylpenicillin should be given in a dose of 1 g twice a day for 5 days, or tetracycline 0.5 g twice a day for 5 days. Other antibiotics can also be given: ampicillin (1 g twice a day) or oxacillin (1 g twice a day). Adults should be given 20-25 ml of immunoglobulin for prophylactic purposes. Adolescents should be given doses less than 12 ml; children should be given from 5 to 8 ml. Immunoglobulin should be warmed before intramuscular injections. Individual sensitivity to horse protein should first be tested by intracutaneous test. Immunoglobulin is useless if more than 10 days have passed since the day of contact or more than 5 days after ingestion of infected meat.

Rabies (Hydrophobia)

Aetiology. The disease is caused by the RNA containing virus of the family *Rhabdoviridae*. The virus parasitizes on the central nervous system of humans and animals. The brain of the dead contains specific cytoplasmic inclusions, the Negri bodies. The virus can be cultivated in rabbits, hamsters, albino mice and some other mammals.

Two types of the rabies virus are distinguished: *street* and *fixed {fixe)* viruses. As contrast to the street virus, the fixed virus cannot penetrate the central nervous system after its subcutaneous administration, nor is it present in the saliva of infected animals. Special strains of the fixed virus are used for the manufacture of rabies vaccine.

Epidemiology. The source of infection are animals. The main reservoir are foxes, wolves, jackals and polar foxes which infect domestic animals such as dogs or cats.

Cattle, goats and sheep, horses, swine, cats, mice, rats and some other animals develop rabies. The contagious period begins 7-10 days before the clinical signs of the disease develop, and persists till the death of the animal. The incubation period in dogs is 14-30 days.

Humans are usually infected by dogs, cats and foxes. The infection is transmitted with the saliva through the bite of an infected animal or when the saliva gets on an injured skin. Humans are highly susceptible to the virus.

The duration of the incubation period depends on the character of bite, the location of the wound, its area and depth, amount of saliva that contaminates the skin, etc. Entrance of the virus through the skin of the head, neck or fingers, is especially dangerous.

The disease occurs as sporadic cases among persons who did not attend for medical aid in due time (i.e., who were not given postexposure prophylactic treatment). Rabies occurs during the whole year but the incidence increases in the warm season. Dogs become infected more frequently during this period and hence the incidence among people increases too.

Pathogenesis. The virus contained in the saliva of a rabid animal enters a human being through an injured skin or mucosa and passes to the perineural space of the nervous trunks and finally to the brain and spinal cord. As the disease progresses, the virus moves from the central nervous system and the spinal cord to the periphery. It appears in the salivary glands and is excreted with the saliva. The disease is fatal.

Clinical picture. The incubation period lasts from 12 days to a year,

but more commonly it is 2-3 months. Its length in humans depends on the character of bite and the site of the wound. Three periods of the disease are distinguished: prodrome, excitation, and paralysis.

The prodrome is characterized by pain at the site of inoculation and along the course of the local nervous trunk. The general signs of the disease develop next: apprehension, fears, depression, deranged sleep, oppression in the chest, tachycardia and subfebrile temperature. The period lasts 2-3 days.

The excitation period is characterized by progressive respiratory distress and cardiovascular dysfunction. The inspiration is deep and noisy; all respiratory muscles are involved in the excursions. The expiration act consists of 2-3 spasmodic contractions of the diaphragm. The most pathognomonic sign soon develops: hydrophobia. As a cup of water is brought close to the patient's mouth, the glottal spasm occurs; although thirsty, the patient is unable to swallow water and throws away the cup. The patient is excited, his behaviour is maniacal. Aerophobia soon develops: even gentle breezes provoke convulsions. The pupils are irregular, pulse is fast, body temperature rises to 40 °C and higher. Hallucinations, delirium, aggressiveness and hyperexcitation can develop. The traditional picture of the "foaming at the mouth" can be seen. The patient cannot swallow the foam because of deranged deglutition.

In 2-3 days convulsions abate and paralysis develops. The lower extremities are first involved but paralysis rapidly extends over the whole body. In 12-20 hours the patient dies of apnoea and heart failure.

The disease may begin directly with the excitation period or paralysis. Hydrophobia and excitation can be absent in children.

Haematologic picture; high leucocyte count (to 30 x 10^9/1) combined with neutrophilia, monocytosis, and aneosinophilia.

Diagnosis. The diagnosis is not difficult if the history of exposure is known.

Laboratory tests confirm the diagnosis only after the death of the patient or animal by isolation of the Negri bodies and by inoculation of experimental animals. Specimens of brain (hippocampus) and medulla oblongata in alcohol or sterile glycerol or the whole dead animal should be delivered to the laboratory. Fluorescent antibody method is used for rapid identification of the rabies virus in the brain and salivary glands.

Treatment. Effective treatment is unknown. As a rule, treatment is aimed at decreasing the psychomotor excitement and at lessening the patient's sufferings. Salt solutions, glucose and vitamins should be

infused parenterally to supply the patient with the necessary nutrients and to replenish the liquid loss. Chloral hydrate (2 g in 100 g of starch solution), morphine, aminazine, dimedrol and cardiacs are indicated. Curare-like preparations and intensive respiratory support can prolong the life of the patient for 2-3 days. The patient should be placed in an isolated shaded room.

Prevention and control. Preventive measures include control of the source of infection and specific prophylaxis.

Destruction of animals that are the source of infection is important. Planned extermination of carnivorous predacious animals by hunters, permanent capturing of homeless cats and dogs and animals bitten by rabid animals are necessary. Pet animals should be supervised by veterinarians and immunized.

Dogs or other animals that bit humans or animals should be kept by their owners isolated from the surrounding for 10 days and observed by veterinarians. If signs of rabies develop, the animal should be killed and the local medical authorities informed. The killed animal (or its head) should be delivered to the laboratory.

First medical aid should be given to individuals who were bitten or otherwise contaminated with the saliva of a suspected animal, or who damaged their skin occasionally during section of dead humans or animals that died of rabies. The wound should be washed thoroughly with water and soap, treated with iodine tincture, and a sterile bandage should be applied. Urgent postexposure prophylaxis should be given (including vaccination against tetanus, passive and active immunization).

Active immunization includes administration of antirabies cultural inactivated lyophilized vaccine or antirabies brain vaccine inactivated by ultraviolet radiation. Passive immunization is done with gammaglobulin. The duration of the vaccination course and the doses depend on the character of bite and location of the wound. Persons with multiple bites or with wounded face, rural residents, repeatedly vaccinated persons and individuals with nervous disorders in their history should be hospitalized.

Medical personnel must conduct measures aimed at prevention of rabies: (1) examination of each bitten (or contaminated with saliva) person; it is necessary to see that all victims should regularly receive antirabic vaccination, the animals suspected for rabies should be delivered to the veterinary post for examination and observation for 10 days (the victim should be given prophylactic treatment during this period); it is necessary to see that antirabic preparations are stored and used properly; (2) constant exchange of information on

the epizootic condition of a given area between the veterinary posts; (3) reports to medicoprophylactic service on the epizootic situation in the area.

Measures in the focus. The patient must be hospitalized and disinfection conducted in the focus of infection. Higher medical authorities should be informed of each rabies case.

Epidemiologic examinations help reveal sources of infection and persons that might be infected by rabid animals and who must be given a course of prophylactic vaccination.

Tetanus

Aetiology. The disease is due to *Clostridium tetani* (the family *Bacillaceae,* the genus *Clostridium).* This is a motile anaerobic rod which readily forms spores in unfavourable conditions. Vegetative forms of Clostridia are unstable and are killed by boiling for 3 minutes. The spores, on the contrary, are highly resistant to high temperature, drying and disinfectants. They can be killed only by boiling for 30-50 minutes. The vegetative forms produce specific exotoxin that consists of tetanospasmin having the properties of neurotoxin and tetanohaemolysin that dissolves red blood cells. Tetanus toxin is a strong bacterial poison; by its toxicity it is only inferior to botulinus toxin.

Epidemiology. The tetanus agent and its spores are excreted from animals with their faeces and are accumulated in superficial layers of soil. Humans are infected when dust, soil, and animal faeces get on abraded or otherwise injured skin. Anaerobic conditions are favourable for multiplication of the agent. Women can be infected during labour or gynaecological manipulations outside hospital. Burns, animal and frost bites also provide beneficial conditions for tetanus infection.

Rural residents are mostly affected. The peak of the disease incidence is usually during the warm season. Occurrence increases during war.

Pathogenesis. Clostridia propagate in the human body to produce neurotropic toxin that is carried by the blood stream and the peripheral nerves to the spinal cord and medulla oblongata where it usually causes paralysis of interneurons of the polysynaptic reflex arcs that produce an inhibiting effect on motoneurons. Motoneuron impulses are not coordinated as they pass to the muscles and they cause permanent tonic contraction of the skeletal muscles. Periodic tetanic muscle spasms are due to intensified efferent and

afferent impulses in response to non-specific stimuli (sound, light, tactile, taste, and olfactory).

The convulsion syndrome promotes metabolic acidosis and hyperthermia. Heart and respiratory functions are upset. The patient can die of asphyxia, paralysis of the heart and respiratory muscles, and complications (pneumonia, sepsis).

Clinical picture. The incubation period lasts from 2 days to a month. The shorter the incubation period, the severer the course of the disease. During the prodromal period the patient sometimes complains of boring pain in the wound, muscular twitching around the wound, and restlessness. Mild, moderately severe and severe forms of the disease are distinguished.

The disease begins with specific contractions of musticatory muscles, known as trismus (lockjaw): the patient is unable to chew, open his mouth, or talk. Convulsive contractions of the facial muscles produce a characteristic face expression known as *risus sardonicus:* the mouth is stretched, the eyebrows are high lifted to form deep wrinkles on the forehead. Tonic muscular spasms spread over to the muscles of the neck, back, abdomen and the extremities. The patient assumes an arching posture (Fig. 19) resting only against the head and the heels (opisthotonus). The skin is moist with profuse perspiration. Tonic contractions of the respiratory muscles can cause respiratory distress. Dyspnoea and cyanosis develop. The patient can die of apnoea. The abdominal muscles are strained and stiff; they turn as firm as wood. Convulsions last from several seconds to several minutes. Their frequency depends on severity of the disease.

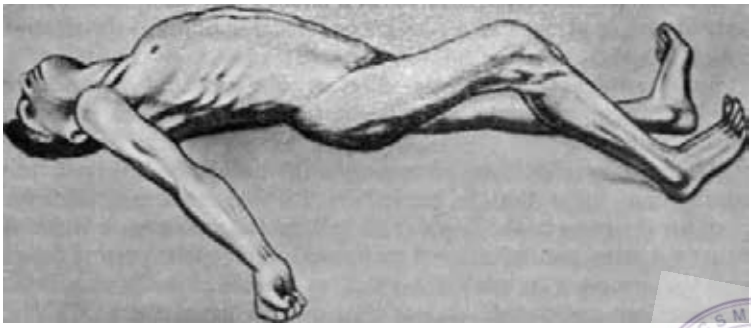

Fig. 19. Tetanus patient: characteristic arching posture (opisthotonus)

In mild cases they occur 1-2 times a day; in severe cases they are almost continuous.

Seizures are debilitating. The patient suffers from insomnia and apprehension. Consciousness is clear. Muscular spasms interfere with deglutition. This, combined with trismus, cause dehydration and wasting. Defaecation and urination are upset. Convulsions intensify due to increased reflex excitation in response to external stimuli (touch, breeze, noise, bright light).

Body temperature is either normal or subfebrile. Hyperpyrexia is characteristic of agony (41-42 °C). High leucocyte count and lactic acid of the blood are seen.

Tetanus is especially severe in women after extrahospital labour or abortion and in neonates (due to infection during umbilical manipulations). In addition to the described acute tetanus, the following forms are also differentiated: (1) fulminant tetanus that ends in death of the patient in 1-2 days of paralysis of the respiratory muscles; (2) subacute tetanus, characterized by short seizures of convulsion that follow at long intervals; (3) localized tetanus in which muscular spasms first develop around the wound.

The duration of the disease depends on its severity and varies between 2 and 4 weeks. In about 17-18 days, clonic convulsions abate and in 22-25 days tonic strain in the muscles lessens.

Complications. Bronchitis, bronchopneumonia and pneumonia are common complications of tetanus. Muscular rhexis, joint dislocation, and bone fractures are possible.

Diagnosis. The diagnosis is based on clinical findings. Laboratory diagnosis is difficult because the causative agent is hardly detectable in the wound exudate. Biologic tests can be conducted on mice by inoculating them with the material taken from the depth of the wound. The test is considered positive if the animal develops tetanus in 1-2 days.

Treatment. The specific treatment includes intramuscular injection of 100000-200000 U of antitoxic antitetanic serum to adults, 20000-40000 U to neonates, and 80000-100000 U to children. The injections should be given after desensitization. The serum should be warmed before use. The patient is given intramuscularly 1 ml of adsorbed tetanus toxoid 30 minutes before the serum is given. The toxoid should be given repeatedly at 3-5 day intervals (3-5 injections in the course).

In addition to horse antitetanic serum, the patient can be given the serum of donors immunized with adsorbed tetanus toxoid, or human antitetanic immunoglobulin in a dose of 900 U (6 ml). The wound

must obligatory be treated surgically; the wounds that might heal by the time when the disease develops, should be treated as well. Before treatment of the wound from 3000 to 10000 U of antitetanic serum should be injected in tissues surrounding the wound.

Aminazin (1-2 ml of a 2.5 per cent solution), promedol (1.5 ml of a 2 per cent solution), scopolamine (0.5-1 ml of a 0.05 per cent solution), and dimedrol (3 ml of 1 per cent solution) can be given as neuroplegics. A mixture can be prepared from the mentioned preparations. The following scheme should be followed: chloral hydrate-the lytic mixture-chloral hydrate, etc., at 3-3 $^{1}/_{2}$ hour intervals. Muscle relaxants (diplacin) are also given to treat severe cases.

Doses for children should be decreased according to their age.

Complications should be prevented with antibiotics. Artificial respiration should be used in severe cases. Isotonic sodium chloride solution (to 1500 ml), alkalifying solution (Locke-Ringer solution, to 1000 ml), blood plasma, polyglucin and other solutions should be used to correct liquid loss and acidosis.

Mesaton, strophanthin and corglycon should be given to normalize cardiovascular function. Respiratory function can be improved by inhalations of oxygen, or by cytiton (0.5-1 ml), intramuscularly or intravenously.

The patient is placed in an intensive care unit.

Food must be liquid and caloric. If the mouth would not open and deglutition is difficult, food should be given by a thin gastric tube passed through the nose (during drug-induced sleep).

Prevention and control. Effective prophylaxis of tetanus is attained with anatoxin. Children should be regularly vaccinated with combined vaccine (see "Diphtheria"). A complete course of active immunization includes primary vaccination and revaccination. Immunity is maintained by revaccinations at 10-year intervals.

Active immunization of susceptible individuals should be done with tetanus toxoid given subcutaneously in a dose of 0.5 ml, two times at a 30-40 day interval. Revaccinations are necessary at intervals from 6 months to 2 years (one subcutaneous injection of 0.5 ml). Subsequent revaccinations (with the same doses) should be conducted each decade.

Depending on previous active immunization, prompt prophylaxis includes thorough debridement of the wound and administration of tetanus toxoid alone or in combination with tetanus serum or antitetanic human immunoglobulin. For example, urgent prophylaxis against tetanus is contraindicated in children and adolescents

who received a complete course of vaccination in accordance with their age. Adults who were not vaccinated, should be given 1 ml of tetanus toxoid and 250 U (3 ml) of antitetanic human immunoglobulin or 3000 U of immune human serum immunoglobulin.

Urgent prophylaxis of tetanus is indicated in traumas associated with injuries to the skin and mucosa, in frostbites and burns of the second, third and fourth degree, in extrahospital abortions and labour, in gangrene or necrosis of any type, in abscesses, animal bites, operations on the gastrointestinal tract.

Besides, prevention of tetanus includes control of traumatism, surgical treatment of wounds, providing aseptic conditions of labour and abortions, immunization of pregnant against tetanus in areas dangerous for tetanus and health education of population.

Erysipelas

Aetiology. The disease is caused by *Streptococcus pyogenes* that belongs to group A streptococci.

Epidemiology. The source of infection is a human patient with streptococcal infection or a healthy carrier. Group A streptococci are constantly present in human beings (in the fauces, nasal cavity, on the skin). When favourable conditions for their propagation are provided (cooling, fatigue, some other disease), the streptococci evoke tonsillitis, pyoderma, rheumatic fever, glomerulonephritis, and some other diseases. In others they cause erysipelas, which is due to the specific predisposition of individuals to this disease. Exogenous and endogenous infections are distinguished. With the exogenous route of infection, the agent gains entrance into the skin through abrasions, intertrigo, scratches, or wounds. In the endogenous route, the causative agent enters the skin with the blood stream and lymph from the endogenous foci of streptococcal infection (rhinitis, otitis, tonsillitis, etc.). Susceptibility to infection increases after repeated invasion of the streptococcus.

Women are more frequently affected by the disease. The occurrence increases in the cold season. The disease is worldwide; it occurs as sporadic cases.

Pathogenesis. The allergic factor is important. As the agent gains entrance to the macroorganism it propagates intensively in the lymph space and capillaries to increase their permeability and brittleness. Congestive hyperaemia, oedema, infiltrations, and haemorrhages develop in the site of invasion. The general manifestations of the disease are due to toxaemia. Individual predisposition of

the patient, prolonged persistence of the L forms (which are reactivated under certain conditions and evoke relapses) are important in the pathogenesis of recurrent erysipelas. The allergic factor and invasion of a new serotypes of streptococci are also important.

Clinical picture. The incubation period lasts from several hours to 3-5 days. Mild, moderately severe and severe forms of the disease are distinguished. The disease can also be primary, repeated, and recurrent.

The disease begins abruptly with a shaking chill, rapid elevation of temperature to 39-40 °C and higher, headache, and vomiting. Delirium and excitation are possible. Pulse is rapid, arterial pressure lowered. In repeated attacks of the disease the temperature can be subfebrile or even normal.

Erythema, tenderness, oedema, and feverishness develop at the portal of infection entrance, usually on the face, the extremities, around the external auditory meatus, and on the haired part of the head. The margins of the erythema are distinct, the edges are elevated in the form of a ridge (erythematous erysipelas).

Sometimes, at the entrance of infection, in addition to oedema and erythema, the epidermis is detached and vesicles filled with serous, purulent or sanguinous fluid are formed (erysipelas bullosum or bullohaemorrhagic erysipelas). After opening of the bullae, crusts are formed. Compression of soft tissues by the fluid of oedema can cause necrosis. If the process is not confined to the primary focus, the condition is called wandering erysipelas; it does not extend beyond natural folds. Leucocytosis with a neutrophilic shift to the left and aneosinophilia are seen; ESR is high.

If the disease runs a beneficial course, the temperature falls in 2-5 days by crisis, the process is arrested, oedema subsides, the skin becomes pale and desquamating; the patient recovers. Less frequently the process spreads to other areas of the skin.

Damaged mucosa of the eyes, fauces, nose or genitalia can be the portal of entry of the infection. Neonates can be infected through the umbilicus.

Some patients may develop relapses of the disease. As a rule, the relapses appear on the same place and have the same clinical picture. Frequent relapses can cause development of fibrous tissue in the skin and subcutaneous fat.

Complications. Abscesses, phlegmona, phlebitis and thrombophlebitis, purulent otitis, diffuse nephritis and some other diseases can supervene.

Relapses of the disease can sometimes lead to stable disorder in lymph formation with possible elephantiasis and hyperkeratosis, especially on the lower extremities.

Diagnosis. The diagnosis is based on clinical findings.

Treatment. The specific treatment includes antibiotics: penicillin to 500000 U intramuscularly at 6-hour intervals for 8-10 days, or erythromycin, oleandomycin or oletetrin per os, 0.2-0.3 g 4-5 times a day. Treatment continues for 8-10 days. If relapses are frequent, another course should be prescribed in 8-12 days after termination of the first course. A new antibiotic should obligatory be used.

Desensitization can be attained with dimedrol or pipolphen in a dose of 0.05 g 3 times a day, diazoline or suprastin in a dose of 0.025 g 2 times a day. Vitamins are obligatory. Transfusion of blood of the same group is indicated. Immunoglobulin and vitamins are obligatory too, while hormones and physiotherapy should be given only for special indications.

During the acute period of the disease, the patient must stay in bed. If indicated, the patient may be hospitalized.

Erysipelas bullosum and phlegmonous erysipelas should be treated surgically with subsequent application of ethacridine lactate (1:1000) or furacin (1:5000).

Prevention and control. Preventive measures include improvement of labour hygiene and conditions for rest, control of traumatism, improvement of sanation, prevention of intertrigo, abrasion, or attrition, their treatment, debridement of wounds, treatment of pyoderma, observation of aseptic rules during medical manipulations and prevention of cooling.

Persistent recurrent forms of the disease should be treated with bicillin-5 the year round. The preparation is given in a dose of 1 500 000 U once a month for 2-3 years.

Acquired Immune Deficiency Syndrome

Aetiology. The causative agents of the disease are lymphadenopathy associated virus (LAV) isolated in France, and human T-cell lymphotropic virus type III (HTLV III) isolated in USA. According to WHO's recommendations, the AIDS virus is called LAV/HTLV-III virus. In 1986, at the International AIDS conference it was suggested that the causative agent of AIDS should be given the name of HIV (human immunodeficiency virus).

The virus belongs to the family *Retroviridae* named so because they contain reverse transcriptase, the enzyme that catalyzes the

transcription of RNA to DNA. Oncoviruses also belong to the family of retroviruses. The only oncovirus that has been isolated by the present time is T-cell lymphotropic virus type I (HTLV I) which is the causative agent of lymphosarcoma. The AIDS agent can be found in the blood, semen, urine, saliva and other body fluids of the patient or virus carrier. The infection can thus be transmitted with blood, by sexual intercourse and other contacts.

The virus is sensitive to high temperature. At 56 °C it is killed in 30 minutes. The virus is sensitive to ether, acetone, and chlorine preparations. It can artificially be grown only in human T-cell cultures.

Epidemiology. The source of infection are human beings. Both patients and virus carriers can be the source. The virus persists in patients for life, while the duration of the carrier state has not yet been established. Virus carriers are especially dangerous because they are not aware of their disease and dissipate the virus among the surrounding people.

The virus is transmitted by direct contact during sexual intercourse, through the fomites infected with the patient's or carrier's blood (the virus enters through minor defects on the skin or mucosa), through reuse of carelessly sterilized injection needles or lancets or other tools used in transfusion of blood, blood substitutes, coagulation factors, erythrocytes, leucocytes or, thrombocytes. The AIDS virus can be transmitted from diseased mothers (or virus carriers) to their foetus.

Persons belonging to the so-called risk groups are usually infected. These are homosexual men and bisexuals, drug abusers (intravenous infections by non-sterile syringes), haemophiliacs, persons who receive numerous blood transfusions, and children whose parents belong to the risk groups.

Haemophiliacs are often infected by injections of blood coagulating factors VIII and IX (the material is prepared from the blood obtained from at least 2000 donors).

AIDS is reported now from many countries of all continents. The endemic areas are believed to be the countries of Central Africa and USA.

Pathogenesis. The AIDS virus enters the blood of a human being and attacks selectively T helpers that include B cells and antibody products which support the function of the immune system.

The quantity of T helpers (relative to T suppressors) is reduced in AIDS patients. Besides, the immune control of atypical cell formation decreases and this results in higher occurrence of tumour

diseases in AIDS patients. Immune deficiency is the cause of cancer (Kaposi's sarcoma in persons aged under 60, lymphoma of the brain, angioblastic lymphadenopathy). Involvement of the central nervous system causes dementia, multiple sclerosis, etc. Reduced quantity of T helpers decreases bodily resistance to exogenous and endogenous microorganisms, which are otherwise not dangerous.

Clinical picture. It is believed that AIDS can run the following three main forms: (a) asymptomatic, (b) systemic lymphadenopathy, and (c) AIDS proper (with secondary infection superimposed upon the specific symptoms of AIDS).

Duration of the asymptomatic infection has not been determined. The signs of the disease are absent, but the specific serologic tests are positive; cases of transmission of the disease by such patients have been reported.

The incubation period of AIDS lasts from several months to 5 years. It is followed by the prodromal period (pre-AIDS). This period is usually called generalized (systemic) lymphadenopathy. The specific symptom of this period is enlargement of the lymph nodes on the neck, elbows, and in the armpits. The lymph nodes are moderately tender or painless. They do not fuse with the subcutaneous cellular tissue and are mobile. Their size varies from 1 to 3 cm in diameter.

The body temperature is 37-40 °C. Fever can be continuous or intermittent. Profuse sweating, especially during night, and weakness are characteristic. Stool disorders are persistent (at least **for** 2 months) and resemble those seen in enterocolitis. Unmotivated wasting is characteristic: the patient loses at least 10 per cent of his body weight. Candidal stomatitis and oesophagitis, suppurative and inflammatory lesions of the genitalia and skin, rash, and frontal alopecia often supervene. Lymphadenopathy can last from 3 months to several years.

During the period characterized as **AIDS** proper, all these symptoms increase. Weakness, fever and diarrhoea intensify; weight loss progresses; hepatomegaly, cough and leucopenia (with possible superimposition of erythroblastopenia) develop.

During the advanced stage of the disease, secondary infection supervenes. Several types of the disease are distinguished in this connection.

Pneumocystic pneumonia. The disease is characterized by hypoxaemia, chest pain, and diffuse infiltrations evidenced by x-ray. Pneumonia is often due to *Pneumocystis carinii,* less frequently due to *Legionella Pneumophila.* The lungs are involved in more than 50 per cent of AIDS patients.

The central nervous system is involved in about one third of patients. The following forms are differentiated: abscess (due to *Toxoplasma gondii),* leucoencephalopathy cryptococcal meningitis, subacute encephalitis; tumours (primary and secondary lymphoma of the brain); vascular lesions and lesions of the central nervous system with focal cerebral involvement. Lesions of the central nervous system are associated with the supervening secondary infections.

The gastrointestinal type is characterized by prevalence of diarrhoea, marked wasting, and fever. Secondary infection is usually due to *Cryptosporidia* and viruses.

Other diseases are also possible: ophthalmic lesions (conjunctivitis, keratitis, retinal haemorrhage, etc.), diseases of the kidneys, or skin diseases (usually Kaposi's sarcoma).

Secondary infections are usually due to: protozoa and helminths *(Pneumocystis carinii)* that cause pneumonia; *Toxoplasmodia* causing pneumonia or lesion of the central nervous system; *Cryptosporidia* causing intestinal lesions with long-standing diarrhoea; *Strongylidiae,* causing pneumonia and lesion of the central nervous system; fungi, causing candidiasis, involving the oesophagus and the mouth cavity; cryptococci, causing lesions of the lungs and central nervous system; bacteria *(Legionellae),* causing pneumonia; mycobacteria, causing disseminated infections; salmonellae, causing enteritis and sepsis; viruses, causing lesions of the lungs, gastrointestinal tract, and the central nervous system; herpesvirus, causing lesions of the lungs, mucosa, and gastrointestinal tract, etc.

Diagnosis. Difficulties in establishing the diagnosis of AIDS are associated with the polymorphous clinical picture of the disease. The diagnosis is based on epidemiologic, clinical, and laboratory findings. The disease usually afflicts homosexual men and bisexuals, prostitutes, drug addicts, and haemophiliacs. Serologic and immunologic tests are used to reveal antibodies to the AIDS virus in the blood of patients and carriers. Discovery of virus components (antigens, nucleic acid, reverse transcriptase) or virus cultures (blood cultures of human T-cells) are necessary for establishing an accurate diagnosis.

A blood specimen (5 ml) of a person suspected for AIDS is taken into 2 sterile test tubes containing 0.7 ml of heparin solution. All precautions should be taken when handling specimens of human material: the laboratory worker must wear gloves and special overalls; syringes, pipettes and laboratory wears must be discarded after a single use. Test tubes containing blood are placed in plastic bags that should be destroyed after use.

Serologic tests include reactions with enzyme-labelled antibodies

to whole virus, solid-phase radioimmunologic studies, immunofluorescent and immunoprecipitation tests.

The quantity of T helpers decreases relative to the quantity of T supressor cells in AIDS patients. But this index is also low in individuals of the risk groups. Leucopenia and lymphopenia are seen; the quantity of immunoglobulins, especially of IgA and IgG, is low. Skin allergic tests reveal anergia.

Treatment. Specific treatment is not effective. Acyclovir, riboverin and sumarin act on reverse transcriptase. Preparations acting on the virus, such as rifampidine, cyclosporin, and some other preparations are also used. Interferon is given in large doses.

Pathogenetic means include hormones of the thymus that act on immunogenesis. These preparations include thymosin, V fractions, T activin, thymostimulin and thymulin. Interleukin-2 is effectively used: it produces effect on maturation, proliferation and differentiation of T-cells. Treatment of secondary infection depends on the nature of the causative agent. The main difficulty of treating AIDS is that one secondary infection may be followed by others.

Prevention and control. Purely medical measures should be combined with measures taken by governmental institutions. The latter include improvement of work at medical and prophylactic institutions where aetiology, epidemiology, pathogenesis, clinic, diagnosis and prevention of AIDS are studied and AIDS patients and carriers are treated. Control of drug abuse, prostitution, homosexualism and other AIDS-promoting phenomena are also important measures.

Medical measures include detection, isolation and treatment of AIDS patients and virus carriers. Virus carriers should be detected and observed. Health education, especially among the young, is very important. Health education must give information on the main symptoms of the disease, measures that may prevent infection, information about the source and ways of infection transmission. Importance of mechanical contraceptive means (condoms) must be emphasized. Donors must undergo thorough serologic and clinical control.

AIDS patients and suspected individuals should be placed in separate rooms of infectious hospitals in order to protect them from nosocomial infection and to preclude dissipation of the AIDS virus. The number of healthy personnel should be minimized. Current disinfection is necessary. Medical personnel should take precautions while examining, treating and attending the patients. Laboratory personnel must be careful as well when handling blood and other materials of AIDS patients.

Higher medical authorities should immediately be informed of any new case of **AIDS.**

Carriers must be examined twice a year. If any symptoms are noted, the patient must attend his doctor immediately.

Elaboration of the vaccine is a difficult problem because of the high genetic variability of the virus.

Measures in the focus. Detection of the **AIDS** virus in the blood, saliva, **urine** or other body fluids is an indication for current disinfection in the focus of infection and observation of the following rules: it is prohibited to use articles that were used by the patient and through which the blood of AIDS patients or carriers might gain entrance through damaged skin or mucosa of the surrounding people.

Appendix I

Planned Preventive Vaccinations

Disease and vaccine	Vaccination	Revaccination	Notes
Tuberculosis. Live attenuated vaccine	A single dose on the 5th or 7th day of life, in the absence of contraindications. The vaccine is diluted with isotonic sodium chloride solution and injected intracutaneously (the lateral surface of the upper third of the shoulder). The dose is 0.05 mg	A single dose to children of 7 years, 11-12 years, adolescents of 16-17 years and also to adults at the age of 22-23 and 27-30. The dose of 0.05 mg is given intracutaneously	Revaccination should be given to healthy persons with negative Mantoux test (2 TU). In areas where tuberculosis practically does not occur in children, two vaccinations at the age of 7 and 14-15 will be sufficient. Subsequent revaccinations should be given at 5-7 year intervals, till the age of 30
Diphtheria. Pertussis. Tetanus. Adsorbed pertussis, diphtheria and tetanus vaccine	Three intramuscular injections of 0.5 ml each are given beginning with the age of 3 months at 45-day intervals	A single dose of 0.5 ml is given in $1^1/_2$-2 years after the first vaccination	This vaccine should be given together with the vaccine against poliomyelitis
Diphtheria. Tetanus. Adsorbed diphtheria and tetanus toxoid	Two intramuscular injections of 0.5 ml each are given beginning with the age of 3 months at 45-day intervals	A single dose of 0.5 ml is given in 9-12 months after the first vaccination	Adsorbed diphtheria and tetanus toxoid should be given to children under 6 years who sustained pertusis The vaccine should be given to children to whom immunization with pertussis, diphtheria and tetanus vaccine is contraindicated
Adsorbed diphtheria and tetanus toxoid with decreased antigen content	Ditto	First revaccination should be done in 6-8 months after the first vaccination; second and third revaccinations should be done at the age of 9 and 16	

Appendix I (concluded)

Disease and vaccine	Vaccination	Revaccination	Notes
		years. Subsequent revaccinations should be done each decade. The dose is 0.5 ml	
Poliomyelitis. Live polio-myelitis vaccine (Sabin's vaccine)	Three doses should be given beginning with the age of 3 months at 45-day intervals. The vaccine is given per os	The first two revaccinations are done at the age of 1-2 years and 2-3 years. Two doses are given at 45-day intervals. Subsequent revaccinations should be given at the age of 7-8 and 15-16 years (single dose)	The vaccine is produced in 2 and 5 ml ampoules. These are monovalent or trivalent liquid vaccines. The doses are specified on the label
Measles. Live measles vaccine	A single dose of 0.5 ml is given subcutaneously to infants aged over 12 months	The child should be given revaccination before entering school. Children with negative serologic reactions need no revaccination.	Children who were given only one dose should be given re-vaccination
Epidemic parotitis. Live mumps vaccine	One 0.5 ml dose should be given subcutaneously to infants aged over 15-18 months	Revaccination is unnecessary	

Appendix II

Measures to Be Taken in Some Infectious Diseases

Disease. Measures for patients and convalescents	Measures for contacts
Typhoid fever, paratyphoid fevers A and B. Patients should be hospitalized. Convalescents should be discharged in 21 afebrile days. Clinically healthy persons, who were not treated with antibiotics, can be discharged in 14 days. Faeces and urine should be tested 3 times for the presence of bacteria in 5 afebrile days at 5-day intervals; bile should be tested in 10 afebrile days	Observation for 21 days; thermometry and testing for carrier state (single bacteriologic study of faeces and urine, and of blood serum by indirect haemagglutination test with cysteine). Persons working at food catering and the like establishments should be dismissed until the tests are negative
Viral Hepatitis A and B. Patients should be hospitalized. Convalescents should be discharged after disappearance of jaundice, of pigment in the urine, and after normalization of blood bilirubin, but not sooner than in 3 weeks after development of jaundice or in 28 days after the onset of the disease	Observation during 35 days. Donors are not allowed to give their blood for 6 months. The presence of HBsAg and the transaminase level should be determined before they can be used as donors again
Dysentery (shigellosis). Hospitalization is necessary for epidemiologic and clinical indications. The time of discharge depends on clinical recovery and tests for carrier state	Observation for 7 days. Persons working at food catering and the like establishments, and also children attending schools and kindergartens are allowed to continue their routine duties but should be tested for carrier state

Appedix II (continued)

Disease. Measures for patients and convalescents	Measures for contacts
Diphtheria. Patients should be hospitalized until complete clinical recovery; discharged after two negative bacteriologic tests of faucial and nasal smears for carrier state (at 2-day intervals)	Observation for 7 days. One test for carrier state. Persons of food catering and the like establishments, and also children attending schools or kindergartens, and the personnel of these institutions should be dismissed until two successive results of the tests are negative
Pertussis. Hospitalization for clinical and epidemiologic indications. The patient should be isolated for 25 days from the onset of the disease and until two successive tests for carrier state are negative	Children under 7 years of age who had no pertussis should be separated for 14 days
Measles. Hospitalization for clinical indications. Isolation can be discontinued in 5 days after appearance of rash and not sooner than in 10 days in the presence of complications (pneumonia)	Children, who had no measles and were not immunized, should be separated. Gamma-globulin should be given to children to whom active immunization is contraindicated and to infants aged from 3 to 12 months (3 ml doses). Isolation term for children who were not given gamma-globulin is 17 days, and for the immunized-21 day. In order to arrest measles outbreaks at children's institutions, all children should be vaccinated immediately (except those who had the disease or who was vaccinated)
Meningococcal infection. Hospitalization until clinical recovery and two successive negative results of tests with nasopharyngeal mucus (performed not earlier than 3 days after termination of antibiotic therapy). Tests should be performed at 1-2 day intervals	Observation for 10 days. Children attending schools and kindergartens, and also the personnel of these institutions should be dismissed from their duties until the results of bacteriologic tests are negative

Chickenpox. Isolation at home can be discontinued in 5 days after appearance of the last rash element	Children under 7 years of age who had no chickenpox should be separated for 21 days from the first day of exposure. If the time of exposure is known exactly, the children should be separated from the 11th day till the 21st day of the suspected incubation period
Epidemic parotitis. Isolation at home can be discontinued in 9 days after the onset of the disease	Children under 10 years of age who had no epidemic parotitis should be separated for 21 days from the date of exposure. If the day of exposure is known exactly, the children should be separated from the 11th till 21st day
Scarlet fever. Hospitalization for clinical and epidemiologic indications. Isolation can be discontinued after complete clinical recovery but not earlier than in 10 days after the onset of the disease	Observation for 7 days. If exposure continues, observation should last 17 days from the onset of the disease. Children under 9, who had no scarlet fever, should not be admitted to the children's institutions for 7 days from the day of isolation of the patient