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ODESSA NATIONAL MEDICAL UNIVERSITY

Department of infectious diseases with a course of dermatovenereology



APPROVED

vice-rector for scientific and pedagogical work.

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METHODOLOGICAL RECOMMENDATIONS

FOR LECTURES ON THE ACADEMIC DISCIPLINE

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Lecture №01-Conception of infectious process, infectious diseases

Dear Colleagues!

I am welcoming you on behalf of all of the infectious diseases chair staff on the beginning of your studying the human infectious pathology and I wish you to become proficient in this branch of science. The chair staff will do their best to help you become proficient in this knowledge. The one who thinks that his future specialty is surgery, therapeutics, gynecology or another specialty and that he doesn't need to study the infectious pathology is mistaken.

Nowadays there are about 2500 well-known microorganisms that cause infectious diseases. About 300 nosological forms have been distinctly described ('nosos' means 'disease' in Greek). According to the international classification the infectious diseases relate to 13 classes and 975 rubrics. They constitute up to 60-70% of the total morbidity. In polyclinics 4-6 patients out of 10 suffer from infectious diseases. The responsibility for the exposure of the infectious morbidity is taken by the physicians of the "first line" - therapists, surgeons, gynecologists and other specialists. Now it is distinctly ascertained that the infectious agents are the basic or leading ethiological factor of the different branches of the medical science.

Such fields of the inner diseases as rheumatology, pulmonology or hepatology cannot be conceived without taking into consideration the infectious factor. The infectious factor often determines the outcome of the surgery. The gynecological, urological and eye diseases cannot be treated without considering it. [The association of the viral hepatitis B and C with the primary liver cancer is undoubted, there is a certain connection between the cancer of the cervix of the uterus and the virus of the herpes simplex, leucosis and Bercet's lymphosarcoma. The significance of the infectious agents in bronchial asthma, arthritis, meningoencephalitis is undoubted.

Besides these many new earlier unknown diseases have appeared. Only during the last two decades such infectious diseases as *Helicobacter pylori*, HIV, Legionnaires disease, ehrlichiosis, cryptosporidiosis, hemorrhagic fever caused by Marburg virus, Ebola virus, hantavirus and others have appeared, they are responsible for the development of the ulcer disease of the stomach, pneumonia, meningoencephalitis, cutaneous diseases, lymphadenopathy, heart and vessels diseases. Many researchers think that the world is standing on the verge of the T-cell leucosis epidemic, which is already widely spread in Japan and in some regions of Latin America. That is why a physician of any specialty will more or less often encounter with the infectious pathology.

The origin of the infectious diseases dates back from the ancient times. The old archives that contain the man's first descriptions of his thoughts with the help of signs tell us that he already suffered from such diseases as leprosy, hydrophobia, malaria, trachoma, fungous, helminthic and some other diseases.

Although the infectious diseases exist as long as life itself, their studying started comparatively not long ago. It is one of the youngest branches of science. The scientific history of the infectious diseases started at the end of the XIX century when the term "infectious diseases" was introduced, and it was determined that they were caused by the microorganisms i.e. the organisms that could be found only with the help of a microscope.

The common feature of the majority of the infectious diseases is the possibility of transmission from the affected organism to a healthy one, and the ability of massive (epidemic) spreading. During the study of the infectious diseases the terms "infection" and "infectious process" are usually used. They both originate from the Latin words - "infectio" - "pollution", "contamination" and "infectio" - "to pollute". At the modern level of the science development it is impossible to give an exhaustive definition of the terms "infection" and "infectious process" which would open all the sides of this conception. Nevertheless it has to be done at least relatively and approximately just to avoid the confusion.

The term 'infection' means the penetration of a microorganism into another organism and their following interaction under various conditions connected both with the microbe itself and the qualities of the organism which receives it at the various stages of the development of the organic world.

The term "infectious process" means the totality of the physiological, defensive and pathologic reactions, which appear under the certain conditions of the environment as an answer to the affection of the pathogenic microorganisms.

An infectious disease is the extreme stage of the infectious process development, which manifests in different signs and changes of the biological, chemical and epidemiological order.

According to all of these definitions it is obvious that the term "infection" cannot be identified with the "infectious process". The contents which we put into the term "infectious process" does not let us make a complete image of the infection as a general biological phenomenon. The concept "infection" is much wider as infection is common to all the beings. The infectious process includes the patterns common to the complicated organisms. The term "infectious process" is used to identify all the dynamics of the pathologic changes connected with the infection irrespective of the fact that they develop into a special qualitative condition called an infectious disease or not.

The origin of the infectious diseases and their nature were discovered owing to the brilliant success of bacteriology. That is why for a long period of time the infectious process was identified only with the activity of the microorganism without any consideration of the physiological aspects of the macroorganism.

Later when the scientists started to pay more attention to the study of pathogenesis i.e. the mechanism of the sickness processes development, they advanced a thesis of the domination of the macroorganism in the infectious process. It was a second mistake as it is impossible to separate something that is by the nature closely connected and can be understood only in correlation. Besides, the pathological process also has to be examined under the influence of the environment. So if the disease develops as a result of the violation of this certain form of the organism's adaptation to the environment at the change of its conditions, then the infectious disease develops as the result of the influence of the part of environment which belongs to the living organisms. In other words, all the participants of the pathologic process are noted for the biological activity, functional mobility and the ability to develop.

The penetration of a certain number of microorganisms into the macroorganism is needed for the infectious disease to develop. Besides, it has to be of a certain quality i.e. pathogenicity and virulence. However, the development of the pathological process depends on the general condition of the macroorganism and its immune status. In case of the weak immune status the pathologic process develops rapidly and the disease takes a severe course, in case of the comparatively strong immune status the disease takes a mild course or may not develop at all. Spreading of the disease and its severity depend on the environment - both on the geographical position (in the tropics - overheating, in cold countries - supercooling), and on the social sphere (a luxury villa and overcrowded facilities). All these processes can be expressed in the formula: the infectious disease is pro rata to the number and quality of the microbe (pathogenicity, virulence) and inversely to the immune status and the environment. Each of the mentioned factors is variable and they should be considered as dynamically developing with the changing of the cause and effect.

Comparing an infectious disease with a non-infectious one we can point out the signs that are common for both of them - intoxication and functional disorders of the organs and systems, morphological changes and others. However, with all the similarities we should mention the peculiarities of the infectious diseases. This is, first of all, the cyclical course with expressed periods (incubative, prodromal, high point, fading healing). The second peculiarity is that the pathogen that caused the disease as a living agent has its own "interests" - it lives, multiplies as it tries to preserve its kind - at the same time it adjusts, changes or remains in its constancy - the death of the macroorganism is not "profitable" for it as the pathogen can die with it as well. The third peculiarity is that the affected organism can become a source of infection for healthy people. The common feature of the majority of the infectious diseases is the possibility of transmission from the affected organism to healthy one and the ability of massive (epidemic) spreading. The fourth peculiarity consists of the immune processes which make the organism insensible to the later affections in case of the same etiologic factor.

Different interrelations occur when organisms contact with one another, it happens in nature all the time. To understand the infectious diseases we should mention the basic types of such interrelations.

1. The meeting and contact of the organisms do not have any consequences, any reaction. No symbiotic relations appear after it. In such cases we talk about species inherited immunity. For

example, a human immunity to the horned livestock's plague, to the hemorrhage septicemia of cats and others (in Greek "symbiosis" means "state of living together").

2. The meeting of the organisms results in the symbiotic commonwealth. There may be no reaction at all on the part of both partners, the condition called saprophytosis ("saprobe" means "microorganism that lives in the dead organic remains") appears. Some researchers consider symbiosis to be any form of living together between the representatives of different species. To this symbiosis they refer:

a) synoikia (Greek) - neutral living together during which one species uses the other one as a place to live without harming it;

b) mutualism - the symbiosis that is profitable for both organisms;

e) commensalism (Lat. "com" - with, "mensa" - table) also (French - "commensa" - dependent) interrelation when one organism gets a benefit from the other without harming it;

d) parasitism - a microorganism feeds with the saps or tissues of the master harming it. Most of the infectious diseases belong to this kind of symbiosis.

Analyzing the pathogenic processes scientists divide the infectious diseases into endogenous and exogenous ones. The endogenous diseases or autoinfections develop from their own microflora which is situated on the skin, respiratory and alimentary tracts, conjunctive, genital tracts. Because of the disorder of the regulatory processes which provide the physiologic symbiotic balance, there develop local, widely spread or even general infectious processes. Such microorganisms are called conditionally pathogenic or half-parasites.

The diseases caused by the penetration of the microorganisms from the environment and to which a macroorganism is not resistant are called exogenous infectious diseases.

Such division is pretty relevant and only relatively right. Sometimes the endogenous infectious disease becomes dangerous to the others because of itself and because the symbionit acquires new biological qualities.

If the infectious disease is caused by one species of microorganism it is called simple. If two or more microbe agents participate in the disease, then we talk about mixed-infection. Joining one infection to the other may affect the infectious process in different directions sometimes intensifying it, sometimes decreasing its activity and manifestations. So while studying the infectious pathology we should consider not only the pathogen itself but their associations. Salmonella infection especially bent to join other infectious diseases and start the secondary pathological process, this phenomena is called nosoparasitism (in Greek "nosos" - "disease").

The growing number of the diseases caused by the conditionally-pathogenic pathogens is mostly connected with the changed reactivity of the organism and especially immune answer which as a rule in such cases forms very slowly and is not valuable. The autoimmune processes activate and take a leading role in pathogenesis and clinical manifestations.

Many conditionally pathogenic as new discovered microorganisms are characterized with intracellular localization of the pathogens. Such infections can cause widely spread pathological disorders and they are more difficult with their diagnosis and treatment.

In the modern conception an immune system is one of the major targets of the affection of the environment negative factors. There are six basic factors:

Human demographics and behavior. The important factors in changing human demographics include increases in the number of susceptible persons, the use of day care and immigration. A number of factors cause a rise in the number of susceptible persons and the greater the percentage of the population that is susceptible to the infectious diseases, the greater the potential for the disease transmission. In many countries in the developed world the number of older individuals is growing. Since aging is associated with an increased susceptibility to the infectious diseases, the potential for the disease transmission is also increasing in these countries. In the USA, the percentage of the population over 65 years was about 4% in 1900 and will reach almost 25% in 2040. Certain underlying diseases also place more patients at risk for various infectious diseases, and these have also increased. For example, the reported incidence of diabetes mellitus in the USA increased from 0.5% of the nation's population in 1935 to over 3% in 1995. It is estimated that there are actually 16 million persons with diabetes in the USA, so the true incidence of this disease may

be greater than 5% of the population. The rates for many malignancies are also increasing, and these patients have increased susceptibility to infectious diseases from the disease process, during chemotherapy and, in some cases, lifelong even after the cure. Some of the most highly susceptible patients are those receiving immunosuppressive therapy following organ transplantation. Almost 20 000 organ transplants were performed in the USA in 1995. Worldwide the greatest factor increasing susceptibility may be the spread of HIV, which has led to millions of persons at increased risk for a variety of infectious diseases

Such societal changes as the increased use of day care also affect the emergence of infectious diseases. The increasing frequency of both parents working outside home or of single parent families led to a greater use of day care. The combination of susceptible children, inadequate hygiene, frequent infections, and frequent antimicrobial use is the perfect setting for the emergence of antimicrobial resistance. Thus, it is no surprise that day care attendance has been an important factor associated with the emergence of penicillin-resistant *Streptococcus pneumoniae*. A recent Kentucky study demonstrated a 4-fold greater relative risk for colonization with a high-level penicillin-resistant *Streptococcus pneumoniae* among children attending day care.

The increase of immigration and changing the patterns of immigration also contribute to the emergence of the infectious diseases. Between 1984 and 1992, 0.5-1.5 million immigrants and refugees were admitted to the USA each year. In contrast to the previous waves of immigration many of these individuals came from the parts of the world where certain infections such as tuberculosis are common. This is an important factor in the resurgence of tuberculosis in the USA as the percentage of patients who were foreign-born increased from 22% in 1986 to 37% in 1996.

A variety of human behaviors also influence the emergence of the infectious diseases. The impact of the sexual revolution on the frequency of gonorrhoea, syphilis, and HIV is evident. Perhaps less evident is the impact of other changes such as changes in eating habits. There are changes in the types of food that people eat, how this food is prepared, and where the food is prepared. This can result in the new exposures to unfamiliar food or the dependency upon others to handle and prepare food safely. All these factors have contributed to the emergence of some of the newer food borne diseases. Another important behavior influencing the emergence of resistance has been the unnecessary use of antimicrobial agents. In 1992 over 110 million courses of antimicrobial drugs were prescribed to outpatients in the USA. Since three-quarters of these drugs are prescribed for upper respiratory infections that are often caused by viruses, over half of these 110 million courses may be unnecessary.

Technology and industry. The impact of technology and industry falls into three general areas. These include new technologies and products, changes in food production processing and preservation, and changes in industrial demographics. New technologies and products may have unexpected disease implications such as the association of air conditioning and whirlpool space with Legionnaires' disease, or new tampons with toxic shock syndrome, or the fast-food hamburger with *E. coli* O157:H7.

The second area, the changes in how food is produced, processed, and preserved has also been important. For example, in the last 50 years many of the new agricultural production strategies involve intensive rearing of young animals under environmental conditions that are conducive to the transmission of the infectious diseases- These production strategies often depend upon increased antimicrobial use. Thus, only substituting young animals for children, the situation is similar to the day care setting and has resulted in an increase in antimicrobial resistance for organisms that are transmitted through the food chain from animals to humans. Between 1979 and 1989, the frequency of drug resistance in human *Salmonella* isolates almost doubled from 17% to 31%. Today the resistance in humans is the result of antimicrobial use in animals. The many changes in food processing and preservation are also influencing disease emergence. The recent emphasis on 'natural' foods has led to use of fewer preservatives or secondary barriers to prevent spoilage. Thus, some foods are protected only by refrigeration. This has resulted in increasing problems with organisms that grow in the cold, such as *Listeria* or *Yersinia*. The lack of secondary barriers also increases the risk of food handling errors leading to diseases such as botulism. In the last 10 years, several outbreaks of botulism have occurred when "keep refrigerated" foods were not kept refrigerated.

The third change, that of industrial demographics, is characterized by consolidations of industry, larger market size, and wider geographic distribution for a variety of food products. Although these changes have the potential for greater quality control and better safety, when something goes wrong, it can really go wrong. Thus, in 1994, an ice cream product produced by a single company in Minnesota led to thousands of cases of salmonellosis in over 41 states.

Economic development and land use. Changes in economic development and land use are often cited in discussions of emerging viral diseases. Encroachment on rain forests, for instance, may lead to exposure to new agents such as Ebola or Marburg viruses. However, such changes are also influencing the emergence of other infectious diseases. For example, population growth and spread lead to environmental change and pollution. The inadequacies of hygiene and sanitation that exist in many of the “mega cities” in the developing world are potential ticking time bombs for the emergence of infectious diseases. Other types of development and land use practices are contributing to specific problems. Conservation activities, such as those directed toward deer populations, have contributed to the emergence of Lyme disease. Coastal agriculture expansion is leading to blooms of toxic microorganisms, while coastal population growth is leading to human faecal contamination of shellfish beds and transmission of a variety of viral and bacterial pathogens. The variation in environmental conditions, whether natural or man-made, can lead to the emergence of infectious diseases. In 1992-1993, the rainfall in the southwestern US was well above normal; this led to increased vegetation, and consequentially, to larger rodent populations. The increase in rodent populations resulted in greater contact with humans and the eventual outbreak of the first recognized epidemic of hantavirus infections in the US.

International travel and commerce. Advances in technology have had a rapid impact on international travel and commerce. A person or a food can be almost anywhere in the world in 24-48 hours. This facility in travel and commerce has increased the potential for the introduction of emerging pathogens to new geographic areas by infected travellers, by contaminated food, or even by transporting vehicles. The latter case is demonstrated by the introduction of the epidemic strain of *V. cholerae* from Central and South America into the oyster beds of Mobile Bay in the US. This introduction was attributed to the discharge of contaminated bilge water by ships entering Mobile Bay.

Microbial adaptation and change. As humankind is instituting a number of changes, the microbes themselves are changing. This is leading to the evolution of new pathogens, the development of new virulence factors, the development of antimicrobial resistance, and tolerance to adverse environmental conditions. A good example of this microbial change has been the emergence of *E. coli* 0157:H7, which probably evolved from an enteropathogenic *E. coli* that acquired *Shigella* genes. As a food borne pathogen, it combines the worst of *Shigella* and *Salmonella*. Like *Shigella*, this organism has a low infectious dose, requiring only a few organisms to cause disease. This leads to subsequent person-to-person transmission once the organism is introduced into a community and also poses a high risk for cross-contamination in the kitchen. This organism is more similar to *Salmonella* in its tolerance to adverse environmental conditions. Thus, it has been associated with outbreaks that were caused by foods with pH 4.0, conditions that are usually inhibitory to most bacterial pathogens.

The breakdown of public health measures. The breakdown of public health measures has been the result of a series of often unrelated factors. Earlier successes in the war against infectious diseases led to complacency. This, coupled with limited resources and competing priorities in public health, often led to the transfer of resources from infectious diseases to other areas or to newly emerging infections. Thus, the emphasis on noninfectious diseases and the emergence of HIV has led, in some health departments, to resources being shifted away from diseases such as tuberculosis. When tuberculosis re-emerged, it was frequently caused by drug-resistant organisms, since much of the curtailed public health activities had been directed toward assuring infected individuals received complete courses of appropriate antituberculosis drugs. In many parts of the world, sanitation and hygiene are inadequate, and even in parts of the developed world, the systems are aging or inadequately designed, increasing vulnerability to outbreaks such as that which occurred in Milwaukee with over 400 000 cases of cryptosporidiosis. The impact of the breakdown of public health measures can easily be seen during wars, population movements, and natural

disasters. One such example has been the emergence of epidemic dysentery in Africa. Since 1979, massive epidemics of dysentery caused by *Shigella dysenteriae* type 1 have occurred in cities, rural areas, and refugee camps in Central and Southern Africa. The epidemics have affected all age groups, often with case-fatality ratios greater than 10%. In 1991 alone, the disease caused 60 000 deaths in Burundi and at least 200 000 deaths in the rest of Africa. In contrast to *Shigella* species, which are more common in parts of the developed world, this organism is essentially resistant to all available oral antimicrobial drugs. Some of the newer fluoroquinolones are the last remaining effective oral agents.

Now even in developed countries approximately for 40 % of adult population tap different immunopathologic states that explains atypical and lingering. How even of classic infectious diseases, more often development of mixed-infection, superinfection, continuous, microbe carrying.

One of the relevant causes, of conservation, homing and even growing of infectious diseases is the variability of microorganisms. Bacteria and viruses evolve as well as all alive nature, but only more fast paces. Therefore they undergo genetical transformation that influence the changes of pathogenicity. virulence, resistance to medications.

The appearance of microorganisms with changed properties results in diffusion or returning of infectious diseases. Such facts find unawares members of public health services and there are handicapping with diagnostic, treatment and prophylactics, that is inevitable results in increasing of a sickness rate and lethality.

The diagnostic of the infectious disease should be as early as possible. Such haste is connected not only with the necessity of assigning the conforming treatment but also with the demand of carrying out urgent preventive actions, especially, if the disease has arisen in the collective. The diagnosis is grounded on the combination of symptoms characteristic for this or that infectious process. As in case with other diseases, the symptoms should be collected beginning with the complains of a sick person, anamnestic information of the development of illness symptoms, the nature of the epidemiological situation and the objective data, which are collected during the outer examination of the patient, and then at auscultation, percussion and laboratory investigations.

At the identification of the infectious diseases as well as other diseases, anamnesis is of great importance. It is necessary to point out one of the most important peculiarities of the anamnestic data in infectious diseases, it is epidemiological anamnesis. The epidemiological anamnesis should be extremely careful and full. When the patient himself cannot give the necessary data (a serious state, age), the information should be collected from relatives or the people around him.

Gathering the epidemiological anamnesis is as difficult as gathering the disease anamnesis, and the skill of collecting it needs to be developed just as the skill of objective examining, the more so as gathering the correct anamnesis is considered to be more difficult to learn than the procedure of the objective examination. At the inept approach to the patient and frivolous attitude to gathering the epidemiological anamnesis, the doctor cannot get the necessary information. Sometimes it is difficult to gather the correct anamnesis because in case of the disease with a long incubative period the patient and his relatives can forget some data, which are of the diagnostical and epidemiological value.

The following points are the most important for the epidemiological anamnesis:

1. A way of living and living conditions of the patient. It is necessary to explicitly find out whether the ambient situation could have promoted the intrusion of an infectious agent. If during the last three weeks before the onset of the disease the patient lived at the place where there were cases of the infectious diseases, the patient can have developed a similar disease. The information about the cases of this or that infection in the patient's house confirms this idea even more. The use of unboiled water, milk, dirty fruit, potherb, meat and fish products of poor quality can be a source of intestinal infection. The wounds, bruises, splinters, shabies are characteristic features of erysipelas, tetanus, septic diseases.

2. The patient's occupation. Thus the workers of cattle-breeding farms can more often get sick with brucellosis, the agricultural workers - with leptospirosis, hemorrhagic fever, tick epidemic typhus, the workers of rice fields are subject to the infection of ankylostomidosis and strongyloidosis.

3. The previous diseases and preventive vaccinations. This information is necessary as the previous diseases in a number of cases speak against the disease which is suspected at a given moment. However, it is always necessary to take into consideration that there is not a single infectious disease, which would not repeat, though in rare cases. Such diseases as flu, malaria, dysentery, diphtheria, erysipelas are the most recurring. And vice versa measles, epidemic typhus result in a firm and continuous immunity which guarantees from the recurrence of the diseases. The indications available in the anamnesis on the vaccination do not eliminate a possibility of the disease caused by the same infection, but in case of vaccination there are often distorted, atypical forms of the disease, the so called deleted forms. Having collected the data of an epidemiological anamnesis one starts to inquire about the main complaints and symptoms, paying attention to every detail in the sequence of their development.

One of the earliest symptoms which gives ground to think of an infection when there are still no other clinical manifestations of the illness is the temperature rise. The temperature which rises in the morning or in the evening up to 37°C usually is not considered normal. However, it is necessary to take into consideration the individual peculiarities of the patient, as for some patients the normal temperature limits are $37,0 - 37,3^{\circ}\text{C}$, and on the contrary for a number of patients the normal temperature does not rise above $36,2 - 36,3^{\circ}\text{C}$ and a slightest rise even on some tenths of a degree already speaks about an abnormal temperature.

The temperature rise can be fast (acute), when the patient clearly marks even the hour of the onset of the disease (ornithosis, leptospirosis, etc.). In case of the fast temperature rise, as a rule, the patient marks the chills of different expressness — from slight chills up to strong chills (in malaria, etc.). In other diseases the temperature rises gradually (typhoid, paratyphoids).

By the expressiveness of the fever there are distinguished the following conditions: a subfebrile condition ($37,0 - 37,9^{\circ}\text{C}$), a moderate fever ($38,0 - 39,9^{\circ}\text{C}$), a high fever ($40,0 - 40,9^{\circ}\text{C}$) and hyperpyrexia (41°C and higher). Taking into consideration the pathogenesis of the fever, the subfebrile condition should also be considered as a fever.

The nature of the temperature curve. The observation the dynamics of the fever increases its differential - diagnostic value. In some infectious diseases the temperature curve is so characteristic that it determines the diagnosis (malaria, typhinia). It is accepted to mark out several types of a temperature curve, which are of a diagnostic value.

The constant fever (febris continua) is characterized by the permanently high body temperature often up to 39°C and higher, the daily temperature fluctuations which are less than 1°C are observed in typhoid-paratyphoid diseases, Q fever, epidemic typhus, etc.

The remittent fever (f. remittens) is distinguished by daily fluctuations of the body temperature from more than 1°C but not more than 2°C (ornithosis, etc.).

The intermittent fever (f. intermittens) is manifested by the correct change of the high or very high and normal temperature with daily fluctuations of $3 - 4^{\circ}\text{C}$ (malaria, etc.).

The relapsing fever (f. recurrens) is characterized by the correct change of the high-fever and fever-free periods that last several days (typhinia, etc.).

The undulating or undulant, fever (f. undulans) is distinguished by a gradual increase of the temperature up to the high points and then its gradual decrease to the subfebrile and sometimes normal temperature; in 2 — 3 weeks the cycle is repeated (visceral leishmaniasis, brucellosis, lymphogranulomatosis).

The hectic (exhausting) fever (f. hectica) — a prolonged fever with considerable daily fluctuations ($3 - 5^{\circ}\text{C}$) with the decrease to the normal or subnormal temperature (sepsis, generalized virus infection, etc.).

The irregular (atypical) fever (f. irregularis) is characterized by large daily amplitude, a various degree of a temperature increase, an indeterminate duration. It stands closer to the hectic fever, but does not have a correct nature (sepsis, etc.).

The distorted (inverted) fever (f. inversa) is distinguished by a higher morning temperature than the evening one.

Besides these generally accepted types we consider expedient to name two more: an acute undulating fever and a relapsing one.

The acute undulating fever (*f. undulans acuta*) in contrast to the undulate one is characterized by relatively short waves (3 — 5 days) and by the absence of remissions between the waves; the usual temperature curve represents a series of damped waves, i.e. each subsequent wave is less expressed (in the altitude and duration) than the previous one (typhoid, ornithosis, mononucleosis, etc.): when the subsequent wave is caused by adding of a complication, the reverive interrelations are observed, i.e. the second wave is more expressed, than the first one (epidemic paratititis, flu, etc.).

The relapsing fever (*f. recidiva*) in contrast to the recurrent fever (the correct alternating of the fever waves and apyrexia) is characterized by a relapse (usually one) of the fever which develops in different terms (from 2 days to one month and more) after the termination of the first temperature wave (typhoid, ornithosis, canicola fever, etc.). The relapses develop in some of the patients (10 — 20 %). In this connection if the relapse has an important diagnostic value, the absence of it does not eliminate a possibility of the mentioned above diseases at all.

Each infectious disease can have different variants of a temperature curve, among which some are more frequent, they are typical for this or that nosological form. Sometimes they even allow to diagnose the disease quite accurately (tetran fever, etc.).

The duration of a fever is of an important value for the differential diagnostics. A number of diseases are characterized by a short-term fever (herpangina, small illness, acute dysentery, etc.). And if, for example, the fever lasts more than 5 days, it already allows to eliminate such frequently encountered diseases, as flu and other acute respiratory virus diseases, angina (certainly, if there are no complications).

On the contrary, the long-term fever (more than a month) is observed rather seldom and only in some infectious diseases which lead to the lingering or chronic flow (brucellosis, toxoplasmosis, visceral leishmaniasis, tuberculosis, etc.). Thus the expressiveness of a fever, the nature of a temperature curve and the duration of a fever allow to differentiate certain groups of infectious diseases, among which the differential diagnostics is based on other parameters.

For the differential diagnostics the interval between the onset of a fever and the appearance of organic lesions is particularly important. In some infectious diseases this period is less than 24 hours (herpetic infection, scarlatina, rubella, meningococemia, etc.), in others it lasts from 1 up to 3 days (measles, water-pox, etc.), and, at last, in a number of diseases it lasts more than 3 days (typhoid, virus hepatitis, etc.).

The nature and level of the infectious sickness rate also matters. For example, any feverishness during the epidemic of flu suggests a possibility of flu. The indication to the contact with the people sick with measles, scarlatina, water-pox, rubella and other droplet infections is important. These data are compared to the terms of an incubation period. Other epidemiological data (the stay on the territory which is endemic on malaria, and other diseases) also matters.

For the differential diagnostics the change of a temperature curve under the influence of etiotropic medications is important (Delagium stops malarial attacks, in endemic typhus the temperature quickly becomes normal after the reception of tetracyclines and others. Thus notwithstanding that the fever develops almost in all infectious diseases, there are a number of peculiarities of this syndrome, which one can use for the differential diagnostics. The differential diagnosis of a fever needs to be done to distinguish it from the body temperature rising of another nature (thermal shock, hyperthyroidism).

The second component which is not less important for the diagnostics and differential diagnostics of the infectious diseases is a rash on the skin - exanthema. It is because the rashes are a symptom of many infectious diseases, besides, they are well visible, quite often catch one's eye even at the first examination of the patient.

There are exanthemas, characteristic of this or that infectious disease and they are an obligatory component of a clinical symptomatology of this or that infectious disease.

The expressiveness and nature of exanthemas can be miscellaneous and are not always observed in other infectious diseases. In this connection their presence or absence in different infectious diseases essentially differs.

The exanthemas in infectious diseases are rather diverse. They differ in nature of different elements of an eruption, localization, terms of appearance, stages of a rash, the dynamics of

development of separate elements, etc. All these features are taken into consideration while making a differential diagnosis. In the diagnostics process the legible definition of separate elements of an eruption and unified comprehension of the terms are very important. The dermatologists and the infectionists do not always define some elements of an eruption in the same way. The following nomenclature is generally accepted in infectious diseases.

Roseola (roseola) — a small spot (diameter 2 — 5 mm) of pink, red or purple-red color, more often with a spherical form. It is formed as a result of a local vasodilatation of a papillary layer of a skin. The main distinctive feature of it is that the roseola disappears when pressing the eruption area with a transparent glass-spreading rod or when stretching a skin and comes up again after the stopping of pressure (stretching).

The so-called punctate rash is close to roseola. It consists of a set of shallow (in a diameter of about 1 mm) elements of the red color. At stretching the skin these elements, as well as roseolas, disappear. Each element rises a little above the level of the skin that stipulates a special "velvety" of the skin at the eruption area.

The macule (macula) represents an element of the eruption similar to the roseola, but larger (5 — 20 mm), it does not stick above the level of the skin, its color is the same as roseola's. The development of the spot, as well as in case of roseola, is based on vasodilatation. The form of maculae can be oval, spherical or more often improper with festoon edges. Unlike the dermatologists the infectionists distinguish "small-spot eruption", in which the elements of an eruption vary in diameter from 5 up to 10 mm, and "large-spot eruption" with the elements' diameter of 11 — 20 mm. This distinction has a differential - diagnostic value. For example, in a patient with rubella there is a small-spot eruption, and in a patients with measles — a large-spot one.

Papule (papula) — a superficial formation without a cavity, rising above the level of the skin. It has a mild or dense consistence, the reverse development ends without the formation of a scar. There are inflammatory and noninflammatory papules. In the infectious diseases only inflammatory ones occur. They are caused by the proliferation of epidermis and infiltrate development in the papillary layer of derma with vasodilatation and limited edema. Papulas have the same color as roseola and macula. There are papulas of a different size (1-20 mm). Small papulas (1- 1,5 mm) are called milliar ones, the larger (2 — 3 mm) papulars — lenticularis ones. The confluence of separate papules results in the formation of the eruptions elements called plaque.

Erythema (erythema) — is vast fields of the bloodshot skin which are red, purple-red or magenta. The erythema is formed as a result of large maculae joining. Therefore the erythema has festoon blurry edges. inside arithmetic fields there can be separate fields of the skin with normal coloring. There is no expressed inflammatory process.

Unlike the infectionists the dermatologists consider that the term "erythema" means inflammatory fields with a diameter from 2 cm up to several dozen centimeters (active erythema), and also cyanosis conditioned by the venous congestion (passive erythema).

Tubercle (tuberculum) — a formation without cavities which arise as a result of the development of an inflammatory infiltrate of granulematous constitution in derma. The hillock differs from a papule, it lies deep in the derma and the infiltrate is determined at the palpation. The hillocks have legible borders and a tendency to grouping. As against papules at further development the hillock can necrotize, forming ulcers and leaving a scar. The hillocks develop in dermal and visceral leishmaniasis, deep mycosis.

Node (nodus) — a limited dense formation with a diameter from 1 up to 5 cm and more that has a spherical or oval form and is situated in the deep layers of derma and hypodermic fat. More often they develop as a result of the inflammatory process.

In some cases they disappear without any traces (nodal erythema), in chronic illnesses they ulcerate and heal leaving a scar.

Wheal (urtica) - an element of an acute inflammatory nature that has no cavity. There develops an acute restricted edema of the skin papillary layer. It develops owing to the trichangiectasia of the papillary layer of derma, the increase of their penetrability and the outcome of protein-free exudation through a vascular wall, which then compresses the vessels. As a result dense formations of different size and form suddenly develop on the surface of the skin and rise above its level. The cyanotic porcelain-white coloring in the center and the pink-red one on the

peripherals are typical. An itch and a burning sensation of the skin appear with the development of a blister. The blisters develop in a serum disease, medicinal allergy and sometimes in some infectious diseases (leptospirosis, virus hepatitis, etc).

Vesicle (vesicula) — a small cavity formation containing serouse, less often serouse-hemorrhagic fluid. The blister develops directly in the false skin, under the corneous layer, in middle or on border with derma. It rises above the level of the skin as a half-round element with a diameter from 1,5 up to 5 mm. Hereinafter a blister can dry out, forming a semidiaphanous yellowish or brown crust. If a blister is opened (damaged), soaking superficial pink or red erosion develops on its place.

Herpetic eruption (herpes) — a bunch of small closely set bubbles on the erythematic inflammatory base (herpetic infection, surrounding deprive, etc).

Pustule (pustula) is also a blister but its contents is cloudy (purulent) because of a clump of a big amount of leucocytes.

Blister (bulla) — a cavity formation with a dimension of more than 5 mm (up to 10 cm and more). The borders of a vesica are legible, the outline is round or oval. The vesica rises above the level of the skin. It is usually unicameral and rolls off after a puncture. The cover of a vesica can be tight and flabby. The contents is serouse or serouse-hemorrhagic.

The vesicles can be situated on the background of the inflamed skin (a violent form of erysipelas, anthrax, multiform exudative erythema, Stivens — Johnson syndrome, etc.).

Hemorrhages (hemorrhage) — an extravasation into the skin of different kinds and dimensions. They develop as a result of the erythrocytes yield from veins to the ambient connecting tissue of derma or hypodermic fatty tissue. It can be a result of the damage (breakage) of the vessel or heightened permeability and fragility of a vascular wall.

According to the value and form hemorrhages are divided into the following elements: petechias (petechiae) — dotted hemorrhages on the background of the normal skin (primary petechias) or on the background of roseolas (secondary petechias); purpura (purpura), in which the dimensions of the elements oscillate from 2 up to 5 mm (the dermatologists consider purpura to be hemorrhages with a diameter up to 2 cm); ecchymomas (ecchymosis) — hemorrhages of the irregular-shaped form with a diameter of more than 5 mm.

Ecchymoses (sugillationes) — hemorrhages on places of injections that are not the sort of an exanthema but have a diagnostic value as a parameter of a heightened fragility of vessels, that is often observed in the development of a hemorrhagic syndrome.

The hemorrhagic elements of the eruption are observed in many infectious diseases and have a great value both for the differential diagnostics and for the evaluation of the illness severity.

All the reviewed above exanthemas belong to the primary morphological elements of the eruption. However, the secondary morphological elements of the eruption also have a diagnostic value. The dyschromias of the skin, flake, peel, anabrosis. ulcers, seams belong to them.

Erosion (erosio) — a defect of the epidermis which develops after opening of the cavity primary elements (vesicles, pustules, vesica). The bottom of the erosion is covered with epidermis or partially with the papillar layer of the derma. By the size and form the erosion corresponds to the primary element. After healing the erosion do not leave any stable changes of the skin.

Ulcer (ulcus) — a deep defect of the skin which affects the epidermis, derma, and sometimes underlying tissues. The ulcers develop as a result of the disintegration of the primary infiltrating elements in the deep parts of the derma — pimples, clusters, and the opening of the deep pustules. The form and the edges of the ulcer are of great importance for the differential diagnostics. The edges of the ulcer can be undermined, vertical saucer-shaped, callous, mild, etc. The ulcer always heals leaving a cicatrix. The ulcers develop both in the infectious diseases (dermal leishmaniasis, anthrax, tularemia, etc), and in the illnesses related with the competence of other specialists (lues, tuberculosis, trophic ulcers, neoplasm).

Skin dischromia (dyschromia cutis) — a disorder of the pigmentation, which develops on the place of the resolved morphological elements of the dermal eruption. The expressiveness and duration of the hyperpigmentation are various. As a rule, pigmentary spots are brown. Sometimes they are sharply distinguished, for example, after measles maculepapulas eruption, especially in

case of its hemorrhagic impregnation. Sometimes it is only a hardly noticeable brown blot (for example, on the place of typhoid roseola), which disappears fast and does not leave any traces.

Scale (squama) is a loosened tearing away peel of the corneous layer, which lost its connection with the underlying epidermis. Depending on the size of the flakes there is micro- and macrolaminar pityriasis.

Small-laminar, branny pityriasis (desquamatio pityriasiformis) is observed in measles, branny lichen. The smallest flakes get detached and the skin looks as though it is powdered with flour.

Macrolaminar pityriasis (desquamatio lamellosa) is characterized with a larger dimension of the flakes, and they can get detached from the skin by the whole layers. The similar pityriasis is characteristic of scarlatina, pseudotuberculosis, toxidermias, etc. The pityriasis develops in the period of convalescence from the infectious diseases and what is important for differential diagnostic - in the late period of illnesses or during reconvalescence.

Crust (crusta) a product of thickening and desiccation of different kinds of other elements exudates of the eruption (pustules, vesicles, anabroses, ulcers). There are serous crusts (semidiaphanous or grayish), purulent (yellow or green-yellow) and hemorrhagic (brown or dark red). The size of the crusts corresponds to the size of the preceding element.

Cicatrix (cicatrix) - coarse-fibroid growth of the connecting tissue, which substitutes deep defects of the skin.

The listed above elements of exanthema are basic and can be observed in infectious diseases, the differential diagnostics is based on their exposure. In case of the eruption it is necessary to identify the type of separate elements and, besides, to specify other peculiarities of exanthema.

The very important signs are the terms of the eruption development.

The localization of the eruption elements and the place of the greatest concentration of exanthema are of a diagnostic value. In some cases the sequence of the rash development is of the diagnostic value. The duration of the eruption elements existence is also important. Repeated rashes and the inclination for joining the elements of the eruption can be of a diagnostics value.

Enanthema - the rashes on the mucous - can be observed less often in infectious diseases and is less important for the differential - diagnostic value. However, in a number of illnesses the changes of the mucous are rather informative at their identification at the initial stage. The lesions of the oral cavity and eyes mucous are of the greatest practical value.

The most essential symptoms characteristic of the infectious diseases are the hyperadenoses, icterus, catarrh of respiratory paths, diarrhea, meningeal symptoms.

Hyperadenosis is the result of the frequent involvement of the lymphatic system in the infectious process. The degree of their affection can essentially differ - from a moderate enlargement to the development of a bubo with a diameter of 3-5 cm. The ability to detect the changes of the lymph nodes is of great importance in the differential diagnostics. This symptom is especially important now when HIV-infection is widely spreading in all the areas. At the same time the practical doctors quite often do not pay proper attention to the state of the lymph nodes and do not always correctly carry out the examination for the differential diagnostics.

The improvement of the infectious diseases diagnostics is closely connected with the development of microbiologic, gene-diagnostic, immunological methods of investigation. The latest methodological achievements allow not only to essentially raise the level of etiological confirmation of the diagnosis, but also to present the detailed characteristic of the microbe behavior in the organism. In particular, it is not possible to judge about the quantity of microbial bodies in different substrates of the organism, to determine the availability and concentration of antigens, toxins and even separate molecules of the microorganism. The gene-diagnostics opens especially wide possibilities, however, the biosensory (including immunosensory) methods of investigation, which are already being worked out in a number of the countries, are next in turn.

But a great number of the laboratory investigations that are available for a doctor are not always important for the diagnosis and are sometimes overestimated and distracts the attention from the clinical diagnostics that is also very important. The clinical examination of the patient is of primary importance and the laboratory and instrumental methods are supplementary. Every

laboratory test should be evaluated according to its specific features, sensibility and informativity, it is necessary to determine the indications and terms of the investigations in different nosologic forms and to state their comparative diagnostic value.

The treatment of infectious diseases is a more complicated task in comparison with therapy of other pathologic conditions as besides the correction of the disorders in the function of the organs and systems, it has a complicated task - to eliminate and suppress the infectious agent.

In the historical aspect only from the 17th century when the improvement of the agricultural production resulted in a better nutrition, it had an immediate effect on the outcome of some infectious diseases. At the beginning of the 19th century the improvement of the sanitary-hygienic control over food and water resulted in the decrease of many infectious diseases transmission. Later the knowledge of the specific etiology of the infectious diseases promoted the creation of the scientific base for their prevention and treatment. In the 20th century when the methods of immunization were widely used and especially when the antibiotics appeared the morbidity and mortality from infectious diseases were considerably reduced. The children's mortality was sharply reduced. The lifetime in the developed countries increased from 47 years on the average till 70 years.

Despite the increasing role of the microbial factor under different pathologic conditions, the practice of treating patients in polyclinics and somatic hospitals has not changed essentially. The treatment of the patients is mainly based on trial-and-error assigning the coolest or the most available antibiotic, as there are no real possibilities and the doctors striving to study the development of the infectious process in dynamics. At its best a single-pass serological or microbiologic research revealing the infectious agent is used as a sufficient argument for the statement of the clinical diagnosis and assigning the therapy. Therefore it is not surprising that there is no noticeable progress in outcomes of treatment, and there is an increase of negative consequences such as the medical disease, immunodefence disorders, development of dysbacteriosis, appearance of polyrefractory microorganisms.

Due to the technological achievements a large number of antibacterial and antiviral drugs have been made. The availability of drugs considerably dilates therapeutic capabilities, but also demands a scientifically reasonable differentiated approach.

The semi-centennial experience of the antibiotic therapy in the infectious disease treatment has not justified the initial hopes. After a considerable increase of the treatment efficiency of bacterial infections in the 50-60s, despite the appearance of a broad spectrum of new antibiotics. the multiple increase of uptaken doses, there have been no adequate progress in the results of treatment, but the number of cases of the drugs intolerance and therapy complications have increased.

The indispensable condition of the therapy efficiency is the differentiated approach to drugs in dependence on the way they act, capability to the intracellular infiltration, bacteriostatic or bactericidal influence.

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Lecture №02-The general characteristics of infectious diseases with air-borne mechanism of transmission. Influenza. Acute respiratory viral infections.

INFLUENZA.

Influenza is acute infectious disease which occurs in epidemics and is caused by a virus, it is characterized by an abrupt onset and such manifestations as general intoxication and affection of the respiratory tract mucosa.

Together with the diseases of the cardiovascular system and tumors, influenza takes the leading position in the human pathology. Influenza and other acute respiratory diseases constitute about 75% of all infectious diseases, and 85 - 90% in epidemics, thus resulting in great social and economic damage. Thus, in Ukraine in 1968 - 1972 in the epidemic period the economic damage equaled 112 millions roubles (about \$120 million according to the exchange rate in those years). During the epidemic outbreak it equaled 420 million roubles. The main thing is that besides relatively mild cases of the disease, there are severe cases resulting in disability and sometimes death when children or old people contract a disease. According to the USA statistics influenza takes the tenth position concerning fatal outcomes.

History.

The information concerning influenza epidemics is extremely contradictory. Thus, taking into consideration the clinical descriptions and data about the rapid spread of the disease, it is possible to think that an influenza outbreak in Europe occurred even in the 12th century (1175). There is no information about its earlier existence. The doctors of ancient Greece and Rome did not describe any influenza epidemics, there are no such descriptions in the ancient cultures of Middle East, Egypt, India and China. It is quite possible that the so called "English heat rash", a very severe disease resulting in a great number of deaths which occurred in the middle ages and disappeared in the 18th century was actually influenza.

Some authors consider French Etien Paskie to have given the first description of influenza in 1403 during the epidemic in Europe.

The first pandemic which spread from Asia to Europe and America was registered in 1580. There have been 23 great epidemics and pandemics since that time. During the pandemic of 1780 - 1782 the modern term "flu" or "influenza" appeared (from the French word "Gripper" meaning catch, envelope, Latin "influre", Italian "influenza" meaning penetrate, invade, instill).

In the manuscripts of the 14 - 15th centuries eight epidemics are mentioned, their names are "mass epidemic", "fatal infection", "catarrhal fever", "infectious fever", "quick catarrh", etc. Even the names show the essence of the disease. In spite of it, the authenticity of the information is not absolute.

It is impossible to determine the regularity of epidemics in the past. In some cases they were of local character affecting the population of few countries. In other cases influenza spread pandemically and affected the population of several continents.

However the first authentically documented pandemic of influenza (retrospectively - influenza type A virus) occurred in 1889. It is supposed to have begun in China and then spread to all the countries of the world in the nearest 1,5 - 2 years. From that time there gradually began to appear notions about influenza which fit the modern ones (the transmission of infection through air, the ability to cause a mass disease in a very short period of time, various clinical forms and typical complications are described very accurately, etc.)

In 1890 M.I. Afanasiev and in 1892 German doctor R. Pfeiffer isolated small bacilli from the sputum of sick people, most specialists considered them to be influenza pathogens for 20 -25 years.

Etiology.

During the influenza pandemic of 1918 - 1919 (filter-passing virus)) was more often considered to be influenza pathogen. This notion was confirmed by the classical experiments carried out by P. Zeiter who infected himself with washing off taken from the nasopharynx of an influenza patient and bacteriologically filtered.

In 1933 English scientists W. Smith, K. Andrews, P. Loudlow isolated influenza virus from a sick person, starting a new stage in the scientific study of the influenza etiological structure. In 1940 T. Frensis and T. Magil isolated a virus which was quite different from the ones isolated

earlier. It was suggested to name the first virus - influenza type A virus, and the virus isolated by T. Frensis - type B. In 1947 R. Taylor isolated and described a new type of influenza virus which was later named type C.

The influenza pathogen belongs to the group of orthomyxoviruses. Virions have a ball form and a diameter of 100 - 120 nm, they have a core of a tightly turned spiral of ribonucleic acid in the case of protein molecules.

On the external capsule there are glycoproteids in the form of a fence of pins: hemagglutinins (HA) and neuraminidase (NA) causing the development of a specific immunity after the disease.

The influenza virus quickly dies at drying, high temperature, it is resistant to low temperatures, extremely sensitive to ultraviolet rays and many disinfectants.

A characteristic feature of influenza type A virus is the changeability of its antigenic structure, changing under the influence of the population immunology. Thus, since 1933 four serologic subtypes have changed. Before 1947 there were AO viruses, from 1947 to 1957 - A1, from 1957 to 1968 - A2, and since 1968 - A3. The structure of hemagglutinin has changed comparatively quickly and considerably. There have been isolated its 4 independent subtypes HO, HI, H2 and H3 according to AO, A1, A2 and A3 viruses. Neuraminidase changes its qualities irrespective of hemagglutinin. Since the discovery of the virus there have appeared only 2 subtypes №1 for AO and A1 viruses and №2 for A2 and A3 viruses.

Influenza B virus has a more stable antigenic structure and doesn't change so often. It has one neuraminidase but different hemagglutinins.

The most stable in relation to antigens is virus C. It causes only sporadic diseases and small outbreaks. It is spread mostly in Ukraine, Moldova and other southern regions.

Epidemiology.

Influenza remains the most spread mass disease nowadays, which does not recognize any borders and affects great masses of the population (up to 50% and more) at short periods of time. The influenza contagious character was noticed even in 1735 by Gexgame during the epidemic in Scotland, he called the disease "epidemicus".

A sick person is the only source of the disease. The epidemiological role of virus carriers has not been studied well. The virus quickly multiplies in the epithelial tissue of the respiratory tract mucous membrane of a sick person and in 24 - 48 hours there is an aerosol cloud with a great concentration of influenza virus around a patient at sneezing and coughing. As the immunity of a specific type forms very quickly, the virus disappears from the organism of a sick person on the fifth day of the disease.

Influenza infection is spread with the help of small particle aerosol dispersion. The mechanism of virus spreading is based on the condition that the virus is in the air for a long time, it has an ability to keep its infectious force under unfavorable conditions of the environment and the ability of virus particles to move with air at long distances and penetrate different parts of respiratory tracts infecting a person.

The influenza virus of full value can live and be infectious in the air for 2 -3 hours. It can live for 1 -2 days on the furniture and other surfaces. The ultraviolet rays, humidity decrease and temperature increase and other factors shorten the virus life time. The virus lives within the limits of 1 -3 meters. The speed of influenza spreading depends on the speed of people moving on the territory. The considerable increase of transportation, the movement of great numbers of people within separate countries, between countries and continents ensures a constant possibility of the virus spreading at considerable distances and the ability to infect people in any part of the globe.

There are small local epidemics and pandemics. The epidemics last 10-14 weeks.

The majority of people are naturally susceptible to influenza. The sick rate depends on many factors. First of all, on the level of the population specific immunity and on the circulation of the influenza virus serotypes.

The number of the influenza cases among adults has considerably decreased during the last years, as for the children aged 7 -14 the number of influenza cases is growing slowly but steadily.

The influenza B sick rate tends to grow in all the age groups.

Pathogenesis.

After penetrating the respiratory tracts, the virus sticks to the epithelial cells which have receptors - things of the lipid and carbohydrate nature. When the virus fixes on the cell surface receptors some complex enzymatic processes begin to occur, they ensure its penetration a cell in which it reproduces. This complex multistage process results in the cell death, and new virions born in the cells occupy new areas of the mucous membranes. The virus multiplication cycle lasts 7-10 hours. Every virion which penetrated a cell gives birth to 1000 virions and there will be 10^{27} of them in a day. That's why the influenza incubation period is so short.

If there were no obstacles for reproduction, the entire tissue of the respiratory tract would be affected in 1-2 days and it would result in a lethal outcome. It happens in rare cases - "quick influenza" develops and a patient dies in 2 days. But it doesn't usually happen so, because a cell, in which virus reproduces, produces and secretes interferon. This interferon gets into the neighboring cells and after that they are not defenseless against the virus invasion. Interferon prevents virus protein from synthesis. The further development of virus infection depends on the struggle of these two forces -virus genome and cell interferon: either it stops at the very beginning or the disease lasts a short time and a patient gets well or the infection spreads in the lungs and fatal pneumonia develops.

The cells affected by a virus are rejected and the products of their decomposition are absorbed, causing a general feverish disease. At the same time in the submucous membrane there develop inflammatory processes with distinctive circulatory disorders, that clinically manifests by hemorrhage syndrome.

When the process spreads in the lung tissue, in severe cases with the development of influenza pneumonia, there are signs of general edema with scattered or confluent foci of hemorrhage.

Under these conditions the influenza virus easily penetrates the blood and viremia develops. However, viremia at influenza doesn't last long, as the virus quickly dies under the influence of nonspecific immunity factors -interferon, complement, properdin, β -lysines, β -inhibitors, histones, leukins, etc.

It is quite possible that the affection of the internals at influenza is connected with viremia. However, the great majority of authors doubt the specificity of such affections, as there are no specific receptors in all the other organs, and they think that in the pathogenesis of affections the leading role doesn't belong to the cytopathogenic phenomena, it belongs to the organism reaction to toxic products or other substances, which appear at the influenza virus reproduction process.

Besides, it is a fact that even in the mild cases of the disease there are signs of the organism hemopoietic and immune system considerable depression. The number leukocytes in blood decreases and their functions are suppressed. Macrophages become less active. Due to it bacteria and viruses become more active and the accompanying diseases take an acute form. Influenza "opens" the gate for the enemy, that's why it is called after Tarpeya, a legendary traitor, who opened the gate of Rome for the enemies. So influenza infection is mostly a combined virus-bacterial or virus-virus infection.

In conclusion it is necessary' to note that interferon production is very important for the disease outcome in the struggle between viruses and the organism protective forces. Antibodies of class IgM appear only at the end of the first week of the disease when the organism wins the first main battle, and antibodies of class IgG in two weeks.

Pathologic Anatomy.

There are three main groups of pathoanatomic changes at influenza: the first one - primary changes, caused by the virus itself; the second ones - secondary changes, caused by influenza virus in combination with cocci and bacterial flora; the third ones - late changes in patients who had influenza and died of complications or worsening of other diseases.

The most important morphological signs of the first group are dystrophic changes of the respiratory epithelium and lungs with distinctive disorders of microcirculation; sharp plethora, edema and pericellular infiltration of submucous membrane and thickening of basal membrane.

The interalveolar septum of lung tissue are considerably thickened due to plethora and edema with leukocytic-lymphoid infiltration. The walls of small vessels and capillaries are

thickened, in some vessels there are fibrous and leukocyte thromboses. The cells of alveolar epithelium became partially hyperplastic, in some places - died, there is a small microphagic exudate in the alveoli lumens.

In the second group there remain signs of pure influenza infection, but more or less they are prevailed by the purulent affections of the respiratory system and serious blood circulation disorders in the lungs. Pyo-hemorrhagic and pyo-necrotic tracheitis with a destruction of epithelium is developed in trachea. The lung tissue is low-pneumatic, the surface of the incision is motley, with alternation of large dark-red and gray foci. During microscopy massive foci of pyo-hemorrhagic pneumonia are found.

In the third group there are different kinds of pneumonia with various inflammatory exudate: purulent, pyo-hemorrhagic and abscess, plethora, edema and in some places hemorrhages into parenchymal organs, and also changes, which are characteristic of the accompanying chronic diseases.

Clinical manifestations.

The incubation period at influenza is short - from several hours to 2 -3 days. Its duration depends on the dose and toxic characteristics of the virus. The incubation period is short if the dose is big and the virulence is considerable. Thus, its duration has a prognostic meaning for a doctor.

There have been different opinions about the preliminary symptoms of the disease. It should be admitted that there is a prodromal period, which is characterized by an elevated temperature for a short period of time (2-3 hours), slight malaise, chilliness, myalgias. These symptoms don't last long and are usually ignored by both a patient and a doctor. The disease begins to develop on the next day. In some patients the disease develops so fast that a practically healthy person becomes seriously ill in several minutes or hours.

The first symptoms are chilliness (always more or less manifested), high temperature, headaches, dizziness, a syncope condition, fever, malaise, pains in different parts of the body i.e. the symptoms of general intoxication. The headache is located in the forehead, temples and over the brows, it can be of different intensity. There is an early distinctive symptom - pain in the eye pupils especially intense at the eye movement or pressing, hyperemia of conjunctivas and sometimes scleras. Dizziness and syncope conditions are characteristic of teenagers and old people. The fever which is one of the main symptoms of influenza does not last long - 1-4 days (in 86% patients). The 'two-humped' character of the temperature is connected with the condition when the chronic infection takes an acute form or a secondary flora joins. Such symptoms as unconsciousness, delirium, convulsions and meningeal manifestations are characteristic of children at intense toxicosis.

Such symptoms as malaise, pains in the limbs and muscles, bones or in the whole body appear during the first hours of the disease and disappear when fever and other signs of toxicosis decrease. Adynamia, malaise can be considerable and are manifested from the first day of the disease. The skin on the face is hyperemic during the first 2-3 days, in severe cases they become pale with cyanotic shade. It is often a bad prognostic sign. Sweating is a characteristic feature. Intoxication is a characteristic feature of influenza, its degree and frequency vary in case of different microbes. In different epidemics there is hemorrhage syndrome, in 10 -20% cases, its symptoms are nasal bleeding, sometimes reciprocal, hemorrhage in the fauces, metrorrhagia, short hemoptysis and gum bleeding sickness. Cough appears during the first days of the disease, dry, excruciating, heart-rending which is accompanied by the feeling of tickling, scratching behind the breast bone. Almost all the patients have a catarrhal syndrome which has such symptoms as rhinitis, pharyngitis, tracheitis. There are often such combined affections of the mucous membrane as rhinopharyngitis, laryngotracheitis, tracheobronchitis, etc. They usually appear in the first days of the disease. Such symptoms as herpetic rash is quite frequent, but appears; on the 3rd-4th day. Photophobia and lacrimation are finite rare.

There are no specific changes on the skin. Different kinds of rash which were described result from other reasons (taking drugs, accompanying diseases). As it has been mentioned before, quite often there is herpetic rash, theoretically there is a possibility of petechiae, hemorrhages, if we take into consideration the affection of vessels and their hyperpermeability. There can be random rash.

A natural manifestation of the influenza infection is the affection of the respiratory organs, as different pathological processes take place in them, they are located on a certain level, but sometimes affect the entire area. The affection of the upper respiratory tracks is accompanied with hyperemia and swelling of mucous membrane, sometimes with slight hemorrhages. There is nasal obstruction, rough breathing, and discharge of different nature and consistence: mucous, mucopurulent and staguinolent - in severe cases. During rhinoscopy swelling and hyperemia of mucous membrane can be seen, especially at the middle turbinated bone. At the same time accessory nasal sinus can be affected (maxillary sinusitis, frontal sinusitis, eustachitis with the development of otitis) with different nature of affection - from catarrhal to purulent.

During fauces examination the hyperemia of tonsils, uvula palatina and posterior wall of the throat could be found. Sometimes there are granules with vascular injection and hemorrhages on the soft palate. The development of influenza laryngitis and false croup is extremely dangerous, especially in children. Patients become pale, cyanosis develops, they often breathe with the help of additional musculature, the voice remains. Lethal outcomes are not rare, because not only larynx is affected, but trachea and bronchi as well, they are full with croupous superposition. The swelling of the mucous membrane of trachea and bronchi results in their permeability and leads to the deterioration of lung ventilation. Depending on the severity of the disease the degree of manifestations is different - from the hidden forms, which can be found with the help of pharmacological tests (aerosolic injection of eusporinum) to the severe forms accompanied with dyspnea and cyanosis. The most common and dangerous complication of influenza is pneumonia. It is necessary to mention, that even during the first days of the disease there are roentgenologic strengthening of the vessel picture in the inferiomedial parts, that looks like indistinct infiltrate, and hurried breathing, shortening of the percussion sound and appearance of so called "conductive" rhonchi, resemble pneumonia. But they often disappear without any traces in 2 - 3 days. It may not be pneumonia, but some circulatory disorders. Not everything is clear in the problem of pneumonia origin. After the detection of pathogen it was considered that during the first three days pneumonia is of virus etiology, on the 3 -5 day - virus-bacterial, later - bacterial etiology. There is a picture of the so called "big motley lung" on the section. Hemorrhage pneumonia foci of different sizes can be seen along the whole length, they are small and large and separated by some parts of unaffected tissue. The foci of festering appear quite early. The rough beginning with severe toxicosis, catarrhal syndrome, significant and diverse changes in the lungs, are characteristic of influenza infection, which is complicated with pneumonia.

Diverse changes in the cardiovascular system have been described. The vascular system is usually affected, and sometimes considerably, it is probably connected with a toxic action of influenza virus on capillary vessels. Dilation of capillaries, turbid background, sometimes formation of the arterial aneurysms, are seen at the capillaroscopy. Arterial and venous pressure decreases, especially in case of pneumonia, the speed of blood flow slows down. The pulse is very often corresponds the fever, there is sometimes tachycardia, especially at the beginning of the disease, in some cases there is bradycardia. The heart sounds are muffled, heart borders are widened, slight systolic murmur and sometimes extrasystoles appear. All these manifestations disappear when the general condition of the patient becomes better. There is elongation of the PQ interval, decreasing and notching, and sometimes inversion of the wave T at different abductions on the ECG. These disorders are interpreted as toxic and dystrophic. They are unstable and disappear in 1 - 2 weeks. The myocarditis described at influenza is disputed by other authors. More severe and diverse disorders are found in patients with chronic affections of the cardiovascular system (coronary atherosclerosis, rheumatic heart diseases, etc.). These disorders are not pathognomonic for influenza, and arise because of the aggravation of the main disease under the influence of influenza infection.

There are various affections of the nervous system during the influenzal infection. The functional disorders of the vegetative nervous system are distinctively manifested. We have already got acquainted with such symptoms as sweating, changes of the pulse rate, dizziness, etc. However, all these changes quickly disappear. At the same time serious affections of the central and peripheral nervous systems are observed, they are manifested as meningitis, meningoencephalitis, radiculitis, neuritis, etc. The rate of these complications is different in different epidemic outbreak.

The pathogenesis of these diseases is still a difficult question. Side by side with the theories of the toxic and parainfectious factors in their development, it is possible, that the virus invasion plays a significant role.

The complications in the digestive system are less often, and there are evidently no specific disorders, although fur, dryness in the mouth, decreased appetite, and heaviness in the epigastrium are observed. These symptoms are characteristic not only of influenza, but of any disease with fever. And now such forms of influenza as gastrointestinal, intestinal and abdominal which were the results of diagnostic mistakes are mentioned in conversations but not in literature.

The changes in the urinary tracts are manifested as pyelitis, pyelocystitis and sometimes nephritis, which result from metabolic-dystrophic manifestations of fever and bacterial superinfection.

The described affections of the endocrine system (adrenal gland, thyroid and pancreas glands) are very rare and it is not possible to completely exclude the influence of influenza virus in these cases.

The changes in the hemogram are manifested as leukopenia or normocytosis. If there are no complications and accompanying diseases, there is absence or decrease of the eosinophils, neutropenia and relative lymphocytosis in the hemogram at influenza (the percentage of lymphocytes increases whereas their absolute number is the same). ESR is normal or insignificantly increased. The connection of the bacterial complications is accompanied with leukocytosis and neutrophilia. It is important to take into account the absolute number of elements of white blood in the dynamic of the disease.

Diagnosis.

Besides careful clinical and epidemiological findings, modern methods of laboratory diagnostics are used for influenza diagnosis and differential diagnosis of other diseases.

Diagnosis does not seem to be difficult during epidemic outbreaks. However, at the same time besides influenza there 30-60% patients with the respiratory tracts affection syndrome are registered, they are not of the influenzal etiology, and clinical diagnosis is even more difficult during a non-epidemic period. As we see, influenza doesn't have specific symptoms which are characteristic of it only, but there are 3 strongly pronounced symptoms: abrupt onset with chilliness, general intoxication and the affection of the upper respiratory tracts. But they also accompany other acute respiratory diseases, and that is why there are many cases when patients with the diagnosis "influenza" are taken to hospital, but they have different other infectious and non-infectious diseases. That is why it is always important first of all to take into account the epidemic situation in the region.

A short incubation period is characteristic of influenza that is why the contacts with sick people, especially in the foci 1-3 days before the disease should be taken into account. If it is possible it is advisable to make up a general conception of the disease clinical picture in the people the patient contacted.

A careful and detailed physical examination of the patients, analysis and a comparative evaluation of the revealed changes with the consideration of the time past from the disease onset is also of great importance. It is important to remember that the preceding therapy can have a considerable influence on the natural disease course, sometimes changing or allaying some symptoms, and in other cases, on the contrary, resulting in the development of the new symptoms which are not typical of influenza. These can be various manifestations of the medication disease: skin rash, lymphadenopathy, the toxic affection of the liver, hemogenic system, development of asthmatic syndrome, etc. Only a careful analysis of all the clinical symptoms can reveal the main syndromes, the peculiar mosaic of which is characteristic of one or another nosological form.

There is not any typical temperature curve. A relatively short febrile temperature reaction (5-6) days with a quick rise and maximum values during the first 2-3 days and shortened lysis should be considered to be more or less typical if the fever lasts longer than this period, it is always necessary to think of a possibility of another disease or joining of a complication. The usage of antibiotics, analgetics, sulfanilamides and glucocorticoides can considerably change a natural course of the temperature curve.

An intoxication syndrome is the main in influenza, and various symptoms of the syndrome can be expressed in different ways and occur in different combinations. A headache and general malaise are the most frequent. But they are typical of many other diseases, mainly the infectious ones, and do not have a diagnostic value. In influenza there is no skin rash except a herpetic one. In acute meningitis of different etiology there is a complete or incomplete meningeal syndrome and typical changes of the spinal liquor. It is not meningitis but meningism that is typical of the severe hypertoxic form of influenza, meningism is characterized with incomplete meningeal syndrome, liquor hypertension without any inflammatory changes in the spinal liquor, the spinal puncture solves the diagnostic problem in these cases.

The development of edema swelling of brain - is accompanied by sopor, coma, convulsions, oligopnoe and bradycardia. These condition should be distinguished from coma and convulsion syndrome of another nature. A general malaise, dizziness, fainting, asthenisation, do not have a diagnostic value, but in combination with a headache and retroorbital pains as well as with catarrhal symptoms might help diagnose influenza. Nasal bleeding is the most frequent manifestation of the hemorrhagic syndrome in influenza, but they also occur in other diseases and can help in diagnostics only in combination with other characteristic symptoms. The appearance of the blood admixture in sputum is almost always a bad symptom. Acute hemorrhagic toxic edema of the lungs is one of the variants of hypertoxic influenza, its clinical symptoms are asphyxia, cyanosis, bubbling breathing and liquid pink foamy sputum. It must be distinguished from poisoning connected with breathing in vapors of poisonous substances, acute left ventricular heart insufficiency. Taking into account the epidemic situation, high temperature, intoxication and tracheitis can help diagnose influenza.

The appearance of sputum containing blood (pus and blood) in influenza, which is complicated by pneumonia, often testifies about the latter's staphylococcus nature. The pleura is often involved in the pathological process, severe respiratory and cardiovascular insufficiency develops. Hemorrhagic pneumonia and influenza should be distinguished from the croup pneumonia. In croup pneumonia there are no symptoms of the upper respiratory tract affection which are characteristic of influenza, the disease has a sudden onset with pains in the side and sudden temperature rise, there is "liver" dullness over the affected lobe and bronchial breathing with the following development of moist rale, the sputum is rusty though there can be admixture of crimson blood in it.

The fever and vomiting, which are observed in influenza may be diagnosed as alimentary toxic infection of salmonellosis or another etiology. But in influenza there are other symptoms of intoxication which are considerably expressed, they are combined with the nose stuffing, tickle in the throat, pain behind the sternum and dry cough. Sometimes even in influenza there are pains in the upper part of abdomen stipulated by mialgia. Diarrhea often occurs in this disease. That is why in case of moderate toxicosis, vomiting, pains in the abdomen and frequent watery stool with an admixture of slime and blood it is necessary to think of some acute alimentary disease, but not influenza.

The development of symptoms of the upper respiratory tract in influenza makes one distinguish this disease from other acute respiratory diseases caused by adenoviruses respiratory-syncytial viruses, paragrappal viruses, rhinoviruses, reoviruses, coronaviruses, ECHO-viruses, Koksaky viruses, mycoplasma pneumonia.

The catarrhal syndrome in influenza develops later and is less expressed than intoxication. Tracheitis, to be more exact laryngotracheitis is the main syndrome in influenza. Scattered dry rale together with hard breathing develop when the inflammatory process spreads along the bronchial tree. The symptoms of laryngotracheitis stay even in case of the development of pneumonia or other complications, this helps to suspect influenza as the main disease. Rhinitis and pharyngitis in influenza do not always occur and have peculiarities in the form of dryness and stagnant hyperemia of the nose and throat mucous membranes, absence of scanty discharge from the nose, spontaneous nasal bleeding.

Adenoviral infection is characterized by a more prolonged incubation period (7-14) days. The fact that there are simultaneous cases with various clinical picture in the foci of adenoviral infection is a characteristic feature; the clinical picture: acute rhinitis, rhinopharyngitis,

pharyngoconjunctivitis, covering conjunctivitis, exanthema, hepatolienal syndrome, etc. A less acute than in influenza onset, moderate intoxication in spite of the high and sometimes prolonged temperature reaction is typical of the adenoviral infection. However the syndrome of intoxication is less important as compared with the expressed catarrhal changes on the part of upper respiratory tract and conjunctiva, which are of exudative character. The pathological process sort of "crawls over" from one zone to another, and the involvement of each new are of the respiratory tract is accompanied with a temperature rise which results in the two or three top character of the temperature curve. Together with this or some time later peculiar tonsillitis may develop together with exudative pharyngitis which manifests itself with edema and bright hyperemia of the back wall of the throat, on which one can see hypertrophic lymph follicles. If the disease starts with rhinitis (it can be limited by it), the discharge from the nose can be abundant, serouse. Laryngitis and tracheitis in contrast to influenza are not characteristic of adenoviral infection.

If the adenoviral infection is complicated by pneumonia, in adults it has approximately the same course as a moderate severe affection of the lungs in influenza and can be cured by usual antibacterial therapy. The adenoviral infection itself preserves its main clinical features, which allow to distinguish it from influenza. In case of the combination of influenza and adenoviral infection the disease has the symptoms characteristic of both nosological forms.

The respiratory-syncytial infection (RS) in adults is usually a sporadic disease, which equally effects all the age groups. In contrast to influenza the disease does not often have acute onset. The intoxication syndrome is expressed moderately or slightly. The temperature is subfebrile or moderately febrile. The changes of the upper parts of the respiratory tract are slightly expressed. The symptoms of acute bronchitis which are often accompanied with bronchial spastic component (continuous cough that is dry or has some scanty sputum, scattered dry rale and rare medium bubbling moist rale, prolonged inhaling, difficult exhalation, swelling of the lungs and others) dominate. The liver gets involved more often in the respiratory-syncytial viral infection in adults than in other acute respiratory diseases. At the high point of the disease it is enlarged and sensitive at palpation, the Orthner symptom becomes positive (pain at beating on the costal arc).

Paragrippal diseases in adults like RS-infection have a more gradual onset the intoxication is slight or moderate as well as the temperature reaction, which in fact lasts longer than in influenza. Rhinitis and pharyngitis are moderately expressed, laryngitis is considered to be typical. There is no syndrome of false croup in adults as compared with children.

The rhinoviral infection occurs only in adults. The disease is characterized with subfebrile or normal temperature, slight intoxication symptoms or their complete absence and expressed exudative inflammation of the nose mucous membrane with abundant rhinorea, which is the main clinical symptom.

The coronaviral infection is also not severe disease, which is difficult to distinguish from a rhinoviral one and which affects not only adults but also children, and besides rhinitis the patients may have slight pharyngitis and even bronchitis.

ECHO- and Koksaky viruses can cause the diseases with affection of the upper respiratory tract. But the involvement of the brain meninx and spinal radices in the pathological process is more characteristic of the enteroviral infection.

Mycoplasma pneumonia can cause a respiratory disease in adults. It has a gradual onset and has a course with both low and febrile temperature, relatively slight symptoms of intoxication, slight affection of the upper parts of the respiratory tract, prolonged and persistent bronchitis.

The disease named "*legionaries*" disease is given to a new disease, which appeared in 1976 in the USA, its bacteriological nature was proved later. Now it is determined that this disease is widely spread in all the countries. The most cases are registered in the warm season. The elderly man suffering from different chronic diseases or alcoholics who use immunedepressors and smoke a lot fall ill more frequently. The disease takes a course of severe progressive abscedic pneumonia with parapneumonic pleuritis and affection of the parenchimal organs.

Ornitosis and Q-fever are diseases which must be no often differentiated from influenza complicated with pneumonia. Both diseases are not accompanied with affection of the upper respiratory tract but have an expressed intoxication and prolonged fever hepatolienal syndrome and atypical affection of the lungs. Well gathered epidemiological anamnesis (contact with birds or their

discharge in ornitosis, contact with different animals usage of raw milk and other dairy products, usage of cotton brought from endemic regions, etc. in Q-fever) helps to diagnose the disease.

It is necessary to say in conclusion that the differential diagnostics of influenza and its complications in spite of the seeming simplicity is actually quite difficult. The basis of diagnostics and differential diagnostics should be a careful analysis of clinical epidemiological data which can allow either to suspect influenza or doubt this diagnosis. The most simple clinical investigation of blood, urine and spinal liquor help in the diagnostics. The serological, bacteriological and immunofluorescent methods of investigation are of primary importance.

The virusological methods of diagnostics are used to isolate and identify the influenza virus. As a rule these methods are used to find out the nature of the outbreaks but not the sporadic cases of the disease because they are very laborious and less sensitive as compared with the serologic methods.

The infection of the chicken embryos is universal method of the primary isolation and cultivation of influenza virus. This method is more accessible and sensitive than the infection of the laboratory animals. It is performed by insertion of the virus containing material in the amniotic or allantoic cavities and causes the infection of organs and tissues of the chicken embryo with the following accumulation of the influenza viruses in the embryos liquid. The presence of the influenza virus in the allantoic or amniotic liquid is stated by the hemagglutination reaction (GAR). The simultaneous erythrocytes of the chicken and guinea pig testifies in favor of the viruses A and B presence, various the agglutination of only chicken erythrocytes suggests the presence of virus type C. In case of the erythrocyte agglutination absence it is necessary to make 2-3 additional passages by the way of embryos infection with the mixture of allantoic and amniotic liquid from the previous passage. In case of the negative results of GAR after the passages the investigation of the material is finished.

The methods of the influenza virus isolation in the tissue culture are preliminary and demand the following pathogen cultivation on the chicken embryo. The trypsinized cultures from the kidneys of monkeys and human foetus are the most suitable for the influenza virus isolation.

The serological diagnostics of influenza ensures an accurate determination of etiology by the way of revealing the quantitative growth of specific antibodies in the disease dynamics in blood. The serological diagnostics is especially important in case of the atypical or symptomless course of the influenza infection. In such cases the discovery of antiinfluenza antibodies in the blood of the examined people in the dynamics of the increasing concentration independently of virusological investigation is the only truthful of the influenza virus participation in the development of the disease and its cooperation with the human organism. Among the methods of influenza serological diagnostic the reaction of hemagglutination inhibition (RHAI) and the reaction of complement banding (CB) is the most widely spread.

The immunofluorescent method is recommended by WHO as one of the reliable means of quick deciphering of the etiology of acute respiratory diseases. The sorting of patients with acute respiratory diseases is done on the bases of the immunofluorescent method data, it is especially important for the prevention of the cross infection of children of an early age. Being widely used this method is an important and reliable means of control of the etiological structure of the acute respiratory diseases in different periods according to the epidemic situation. The essence of the immunofluorescent method is in specific reaction of antigen-antibody which reveal the presence of viral antigens in the cells by the way of joining antibodies to them, the antibodies are connected with the fluorescent mark, which lights in the ultraviolet rays.

Treatment.

During the epidemics 10-25% of the adult population fall ill with influenza, 1-2% of them need to be hospitalized. The most patients are treated in polyclinics.

During the out-patient reception or home visiting it is always necessary to find out if one or another patient needs to be hospitalized or can be treated at home. The severity of the patients condition determined by the intoxication degree complications and the presence or acute conditions of the preceding diseases must be taken into account. A patient with such symptoms as high temperature, consciousness disorders, convulsion syndrome, repeated vomiting, meningeal symptoms, hemorrhagic syndrome, respiratory and cardiovascular insufficiency should be

hospitalized. Even in case of a moderate severe influenza form together with an unfavorable premorbid condition in the form of ischemic heart disease, chronic, nonspecific lung diseases, nervous system diseases and others the patients need to be treated in hospital.

In most cases influenza is a relatively short disease, especially in case of mild forms. But the disease itself causes a lot of unpleasant feelings that is why it is understandable that a doctor is willing to alleviate a patient's suffering, to decrease the severity and length of the disease, to prevent complications.

It is necessary to be confined to bed even in case of influenza without any complications. Nutrition should not differ from the usual one but the usage of the substances that irritate the mucous membrane such as pepper, onion, mustard, nuts and others are not recommended. The abundant drink is very useful if the condition of the cardiovascular system allows it - tea, fruit and vegetable juices, kissel, compote. Such folk remedies as "linden tea", tea with dry raspberries, strawberries and honey are very popular. The catarrhal symptom cause a lot of unpleasant things for the patients. Naphthyzinum, halazolinum and 1% menthol oil are dropped into nose in case of expressed rhinitis. The symptoms of pharyngitis become less expressed when the throat is gargled with a 2% solution of soda, extract of camomile, sage and thyme. The cough and pain in the chest reduced when using hot milk with soda (1/2 tea spoon per glass), honey, extract of thermopsis, coltsfoot leaves, marshmallow root, althaea, preparation of libexin, bromnhexinum and others.

Taking into consideration the fact that the temperature reaction in influenza has a certain compensation-adaptation meaning - the suppression of virus replication, stimulation of endogenic interferon formation and mobilization of other defensive mechanisms of the organism, it is necessary to reduce it to normal values only in the patients who have problems with high temperature. The medicamentose mixture called antigrippin is successfully used to influence different pathogenic areas, it consists of acetylsalicylic acid - 0,5, ascorbic acid 0,3, rutin - 0,3, diphenylhydramine - 0.02, calcium lactate - 0.1. It is advisable 1 dose three times a day.

If a member of a family falls ill both he and all the rest are prescribed menthol-oxolinum ointment 0.25-0.5% as well as unguentum tebropheni 0.25-0.5% to be applied on the mucous membrane at the nose entrance as a preventive measure during the first days of the disease.

The usage of remantadinum is quite effective especially during the first days of the disease at a dose of 0.2 g (four tablets of 0.05) a day. The antiviral action of remantadinum is the most effective at the early stages of the infection development. The preparation usage from the first day of the disease resulted in the decreases of the expressiveness and duration of fever and other intoxication symptoms, there were almost no complications, these results were even more effective when remantadinum was combined with antigrippin; disability term shortened up to two days.

There is fast elimination of intoxication and noticeable improvement of the patients general condition were observed when during the first days of the disease lymphocytic interferon and fresh solution of ribonuclease enzyme were inserted in the nasal paths both by simple dropping and with a help of an individual inhaler.

The prescription of such chemical preparations as bonaphtonum, alpisarinum, adenoarabinosidum (vidarabin) which simultaneously decrease the edema of the respiratory tract mucous membrane as well as trasyolol, contrykal-acid ϵ -aminocaproic etc. inhibit the proteolytic cutting of viral polypeptides, which increase the inflammatory process. The distinct homogeneous results concerning the prescription of interferon and anti-influenza immunoglobulin have not been received so far. Interferon is protective polypeptide which is produced by the cells when the virus penetrates them and has inhibiting influence on the viral replication by interfering in the translation of viral i-RNA on the ribosome preventing the synthesis of viral specific protein. Interferons are divided into groups depending on the time of the preparation production:

- a) natural - the first generation – α , β , γ ;
- b) recombinative - the second generation;
- c) hybrid, synthetic or mutant - the third generation.

Taking into account the controversial data concerning the objectivity of interferon, nevertheless it is necessary to note that it is therapeutically effective in influenza only in case of its usage at the very beginning of the disease.

There are even more controversial data concerning the usage of anti-influenza human immunoglobulin in influenza with the treating purpose. Even without a detailed analysis one can come to the conclusion that it is advisable to administer high doses (9 and more ml) of polyvalent anti-influenza immunoglobulin only to the patients with severe hypertoxic form of influenza including the ones with complications trying to do it earlier because it can have not only viral neutralizing effect but also a slightly general stimulating one.

The patients with severe forms of influenza, expressed intoxication or complications are sent to hospital. While determining a plan of treatment of such a patient with severe influenza it is important to distinguish and eliminate the main syndrome, which has a decisive meaning for the patient. It is also necessary to remember that both high intoxication and acute edema-swelling of the brain, and acute respiratory and cardiac insufficiency are closely connected with one another and the elimination of one of them influences the others.

The most frequent clinical form which demands a complex of actions which are part of the intensive treatment is influenza complicated with acute pneumonia is more often of staphylococcus nature. Such symptoms as dyspnea, cyanosis, tachycardia, chills, purulent sputum with admixture of blood are typical of it.

One of the most important components of complex therapy is the administration of corticosteroids which are prescribed together with massive anti-staphylococcus antibiotic therapy to avoid the progress of the pulmonary destruction and the generalization of the process.

Such preparations as 5-20% albumin solution, native or dried plasma 150-200 ml, haemodesum 200 ml, rheopolyglucinum up to 500 ml, physiologic salt solution are used for detoxification. The liquid must be administered with a strict control to prevent an acute edema of the brain and lungs. The administration of lasix, anti-histamine preparations, rutinum, vitamin C, correlation of the acid-base and water-electrolyte balance are advisable. Antibiotics, sulfanilamides and nitrofurans are the preparations of the choice depending on the pathogen, patient's endurance and their availability in the hospital.

The treatment of the acute respiratory deficiency start with oxygen inhalation and glucocorticoids. The solution of euphyllinum (2,4%) or the solution of no-spa (2%) are also administered intravenously. The usage of fragrant herbs extracts such as mint, thyme, sage, inhalation of hot steam or mist dilute the sputum. In case of acidosis the correction is achieved with 4% of sodium solution. With the development of the lung edema the patient should be placed in the semi-sitting position, lasix (but not mannitum) is administered intravenously, the administration of venosis tourniquet, blood-letting.

In case of the acute cardiovascular insufficiency, first of all it is necessary to restore the amount of the circulation blood by the injection of plasma, blood substitutes, simultaneously use corticosteroids, and cardiac glycosides, cordiaminum, camphor, panangin, cocarboxylasum.

In case of the symptoms of the acute brain edema-swelling it is necessary to administer large doses of glucocorticoids and diuretic (lasix, acidum etacrynicum). To decrease the intracranial pressure (if there is no lungs edema) mannitum with physiological solution 1 g/kg or 20% glucose solution is injected intravenously. It is also advisable to intravenously inject 5-10 ml of the 2,4% euphyllinum solution.

Prevention. Living and dead influenza vaccines have been used to prevent influenza for a long time. However, the observations made in the last years have shown that the effectiveness of the vaccine prevention does not always satisfy the public health practice. At present the influenza preventive measures are taken at the time of epidemic with the help of chemical means (oxolinum, tebropheum, remantadinum) and interferon preparations.

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Lecture №03-Viral hepatitis

The problem of the viral hepatitis remains most actual, as these diseases according to spread step down only to acute respiratory and acute intestinal infections. Viral hepatitis is most frequent reasons of chronic hepatitis and liver cirrhosis and in some patients it may end by lethal consequences'.

The problem of the viral hepatitis is present under fixed attention of many scientist of the whole world. At present time definite successes in study of etiology, epidemiology, clinics, diagnosis of this polyetiologiical viral disease have been possessed.

ETIOLOGY.

At present time further viruses, causing viral hepatitis are known: virus of hepatitis A (VHA); virus of hepatitis B (VHB); virus of hepatitis E (VHE); virus of hepatitis D (VHD); associated with VHB, virus of hepatitis C (VHC). Search of new viruses, causing viral hepatitis continues. In literature one may come across different names of disease, caused by these viruses: infection hepatitis, epidemic hepatitis, serum hepatitis, syringe hepatitis. Uniting all these termini's - Botkins disease. Indicated diseases caused by above indicated viruses, possess many in general, however highly essential clinical, epidemiological, biochemical and immunological peculiarities have, been revealed. These peculiarities demand conduction of differential diagnosis between them. As a result of the above said, group of experts of WHO recommend to differentiate further variants of viral hepatitis: viral hepatitis A (VHA); viral hepatitis B (VHB); viral hepatitis E (VHE); viral hepatitis C (VHC); viral hepatitis D (VHD).

VIRUS OF HEPATITIS A (VHA).

Agent was first discovered in 1973 by Feinstone. This is RNA - containing virus. Under electron microscope complete as well as is empty parts with size of 27 - 30 nm are observed. On their surfaces capsomeres are seen. Nucleopeptide of VHA does not possess surface projections and covering. Core structure is not revealed in the virion. Virus contains 4 peptides (VP1-4), participating in reactions of immune precipitation. It is assumed that VP1 and VP3 are located partly on the surface and VP2 and VP4 are present inside the virion. However, up till date, there is not authentic information's about their importance in relation to antigenicity and immunogenicity.

VHA is stable during pH 3,0 - 9,0, sensitive to formaldehyde, may remain preserved for a period of few month's or even year's during temperature + 4 C, for weeks - during room temperature. Complete inactivation of virus takes place during 85 C in a period of 5 minutes. VHA is resistant to chlorine, in comparison with other viruses of this group and may enter through barriers of water cleaning stations. Complete inactivation of virus steps on during concentration of chlorine 2,0 - 2,5 mg/l with exposition for a period of 15 minutes, of lime chloride - 10 mg/l arthin 15 minutes.

Virus of hepatitis A may reproduce in number of human and monkey cellular cultures, from where viral antigen is obtained. It is necessary to remark, that successful adaptation of VHA towards culture of cells is very much necessary for study of biological properties, for obtaining of source of reagents for diagnostics (antigen, antiserum), as well as for construction of vaccines, (live, killed).

VIRAL HEPATITIS B (VHB).

VHB in natural condition is revealed in sick people and carriers, in forest marmots, in carth squirrels, in Peiking ducks. This DHA-containing virus is pathogenic for human and few types of primates - chimpanzee, garillas. VHB causes acute and persistent infection, damages primarily liver.

Virus consists of nucleus and covering. Further antigenic structure of VHB is differentiated: HBsAg - surface, HBcAg - internal (core), HBeAg - reflects infectiouness of virus.

Towards these antigens in organism of patients antibodies are produced: anti-HBs; anti-HBc; anti-HBe.

Presence of HBsAg in human organism testifies the presence of acute and latent proceeding infection. It is assumed, that prolonged conservation HbsAg in serum of the blood in sick man may testify about transfer of the process into chronic form. HBsAg is revealed in majority of patients in incubation stage. HBcAg is practically not determined in blood and fixed in directly by DNA-polymerize reactions, falling positive in acute period of disease, as well as after many months and years in carriers. Soon after discovery of HBsAg in blood of patients appear anti-HBc. Most often they are observed in carriers of infection. In early stages of disease HBeAg is revealed, which is then changed by anti-HBe. Very important diagnostic information may be obtained by using methods of determination of DNA HB. For this purpose molecular hybridization of nucleic acids and polymerize chain reaction (PCR) is used. Genospecific viral DHA is observed in serum of blood, in bioplates of liver, in lymphocytes of peripheral blood. Mentioned method enables to discover very small quantities of viral DNA in investigated samples, which moderately increases reliability of diagnosis.

VIRUS OF HEPATITIS C (VHC).

Virion of virus of hepatitis C consists of nucleus and lipid external membrane. Genome is represented by single chain RNA. VHC is favily resistant in external medium, particularly in biological fluids such as preparations of blood, sperm and others. Sensitive to chloroform, to other desinfective solutions and high temperatures (100 C and more).

Antigenic structure of VHC is less studied. It is established, that to the virus in organism of patient antibodies are produced (class Ig M). Their discovery in blood serum of patient sparks about presence of acute or chronic disease. Antibodies may stick to definite level for a period of 6 - 9 months, and thereafter their fitters in serum decrease right upto complete disappearance.

VIRUS OF HEPATITIS D (VHD).

VHD represents itself defective virus particle of size 30 - 35 nm, contains internal antigen (HDAg), made up of small circular RNA and surface covering, which is HBsAg VHB. It is considered that reproduction of virus is possible only during presence of HBsAg in organism of patient, therefore hepatitis D proceeds always as a coinfection or superinfection, joining to VHB.

On internal VHO, an organism replies by production of antibodies of class IGM, which used in diagnosis of disease.

VIRUS OF HEPATITIS E (VHE).

Virus of hepatitis E has been emanated from feces of patients with jaundice. Spherical particles similar to virus were able to discover due to the method of immune electronic microscopy. Material for investigation was collected from volunteers, infected by material from patients with jaundice with assumed diagnosis of viral hepatitis E. It is supposed, that VHE may be caused by few strains of virus of different antigens.

At present time a test-system, giving the possibility of discovering antigens of virus in fecal matter has been elaborated, serums of reconvalescenes are used for that.

EPIDEMIOLOGY.

Viral hepatitis A - antroponosis. The source of disease is sick person in prejadice period and in 15 - 20 days of climax period of disease, virus carrier. Primary localization of virus is gastrointestinal tract. Mechanism of transfer is fecal-oral. Virus is excreted from the organism of sick person with fecal matter. Specific final factors of transfer of hepatic A virus are water and blood. Character of infection of water depends upon conditions of water supply and its relation with fecal contamination. Intermediate factors of transfer are flies, transferring virus together with fecal matter on products of nutrition, dishes. In food products and on dishes virus may be brought in also with the help of sick people, hands of those are contaminated by virus.

Susceptibility to the disease is high. Mainly children and adults upto 30 year fall sick. Ratio of these, who underwent clinical forms of disease to those, possessing anti-VHA composes 1:22 - 1:125 in different cities.

Increase in the indices of morbidity of VHA is observed in autumn-winter period of the year,

Prophylaxis of VHA consists first of all in isolation of the patient, conduction of current and conclusive (final) disinfecting, observation of all rules of personal hygiene. Along with this specific prophylaxis also exists. This is passive immunization, realized by serum immunoglobulin. Active immunization is planned to realize by vaccines against hepatitis A. Elaboration of vaccines at present is realized on further directions: obtaining of preparations from liver of infected animals, obtaining of cultural vaccines, elaboration of genoengineering preparations.

Source of hepatitis B virus in nature is sick person with acute or chronic form, healthy carrier. Natural path of transfer is sexual. Infection may be transferred even during. Kisses through traumatized mucous, through milk of mother, through placenta from the patient to fetus (vertical path of transfer). Essential importance possesses even parenteral path of transfer: blood transfusion and its preparations, infections, manipulation, operative intervention.

Susceptibility to the disease is high. Most often drug addicts, homosexuals, prostitutes, medical works (surgeons, obstetrician - gynecologists, workers of hemodialysis departments, manipulative nurses, doctors-infectionists, often fall sick with hepatitis B.

Prophylaxis of VHB consists first of all in use of single use instruments in medial establishments, single use system for blood transfusion, its preparations, infuse solutions, in strict control during choosing of donors. Instruments of multiple use should be subjected to thermal processing with temperature not less than 100 C for a period of 45 minutes.

At present time for conduction of active prophylaxis against viral hepatitis B many vaccines have been elaborated and proposed (vaccine Havac-B - France, Heptavax B - USA and other.). It is considered that contingents of high risk should be subjected first of all to vaccination (individuals suffering from hemophilia, diabetics, workers of hemodialysis departments, medical workers and other contingents).

Epidemiology of viral hepatitis D has been studied insufficiently. It is assumed, that source of infection is sick person, basic path of transfer is parenteral.

Susceptible to hepatitis D are individuals, suffering from VHB or HBsAg - carriers.

Epidemiology of viral hepatitis E is identical with epidemiological laws of VHA, and hepatitis C - with hepatitis B. Specific prophylaxis upto present time has not been elaborated.

PATHOLOGICAL MORPHOLOGY.

Morphological changes in liver take place in all tissual components - parenchyma, connective tissue, reticuloendothelium, in lesser degree in bile pathway, i. e. diffuse damage of the organ is possessed. Degree of damage fluctuates from insignificant dystrophic and single necrotic changes of epithelial tissue of lobules of liver during high forms vast massive and submassive necroses of liver parenchyma. 3 variants of acute forms of the disease are differentiated: acute cycle, cholestatic and massive necroses of liver.

During acute cycle form diffuse damage of epithelial and mesenchymial elements are observed. Discompensation of beam structure with orderlies placement of hepatocytes with their considerable polymorphism is noted.

Along with the dystrophic changes, expressed processes of regeneration with figures of mitosis and abundance of double nuclear cells are determined. Characteristics are presence of scattered necrosis hepatocytes in all lobules. Changes of mesenchymial elements inside the lobules are expressed in proliferation of Kupfer cells with their change into macrophages, cytoplasm of these cells are basophilic, contains bile pigment and lipofascins. Capillaries in the center of lobules are dilated. In the portal tract proliferation of lymphohistocytary elements with admixtures of plasmatic cells eosinophils and neutrophils. Along with this, reticular hyperplasia of spleen and portal lymphatic vessels is observed.

Clinical manifestations of the disease correspond to the seriousness of destructive changes in parenchyma of liver.

During cholestatic variant of viral hepatitis majority of morphological changes are observed in intrahepatic bile passages with picture of cholangitis and pericholangitis.

PATHOGENESIS.

Pathogenesis of viral hepatitis is still not studied till the end due to big difficulties, caused by absence of accessible experimental model of the disease. At the base of existing notions about pathogenesis of acute viral hepatitis lay clinical observations, life time investigations of liver tissue and comparative study of viral hepatitis in animals.

G. P. Rundev (1966) has elaborated general scheme without detalization of definite branches. However, at present time many new information's have been located, considerably deepening modern knowledge of pathogenesis of acute viral hepatitis. Entrance of the agent of disease into the organism of patient takes place perorally (VHA, VHE), sexually (VHB, VHC), parenteral (VHB, VHC, VHD and not excluded for VHA - VHE), vertically (not excluded for all viral hepatitis).

Entering into the human organism, agent approaches regional lymphatic glands, where takes place its massive reproduction - second phase of pathogenetic chain. By reproducing in lymph glands, agent causes damage of cells and their death. Organism replies on this negative influence by immunological reaction of reticular tissue of the lymphatic gland, executing " barrier" function. This corresponds to period of incubation. On this level infections process may stop or during insufficiency of "barrier" function begins the phase of generalization of infection (primary viremia).

Virus from lymphatic glands continues to enter into blood in big quantities. Clinically this phase is displayed by signs of intoxication and beginning of liver damage. In this phase viruses of hepatitis combined with thrombocytes due to which composition of their phospholipid membrane is disturbed, metabolism of arachidonic acid is intensified, which leads to increase in their adhesive and aggregate activeness, viruses of hepatitis also render destroying action on cells of endothelium of small vessels, destroying the structure of their biomembrane. As a result of such influence, highly active endoperoxides are formed from arachidonic acid (compulsory component of phospholipids of membrane), rendering powerful influence on adhesion and aggregation of thrombocytes, erythrocytes. According B. K. Bezprozvanny, viruses of hepatitis in viremia combine also with erythrocytes. This according to our information, decreases their osmotic stability, increases their adhesive and aggregate functions. Such influence of viruses of hepatitis on the cells of blood - cells of endothelium of vessels already in the phase of viremia renders essential influence on T-cells on agent, damage of cells of liver does not take place totally.

However, given theory does not explain many sides of pathogenesis of viral hepatitis. It remains unclear why during autoaggression (presence of antibodies, T-lymphocytes, virus) their realization steps on only in single cases. It is also unclear why in the dead ones lymphocytes infiltration is not observed in the liver. Answer on this question was formulated by A. F. Bluger, saying that for realization of autoaggression it is necessary to have defects in the system of immunological hemostasis by genetic type. This argument, from our point of view, is highly non-convincing. By analyzing the information received by us, we came to the conclusion, that mechanisms of cytolysis of hepatocytes and other cells during viral hepatitis are completed in the following way. Virus enters into hepatocyte, where its reproduction is realized with the use of substance of cellular components, particularly those, as substrate of nuclear substance, mitochondria, microcosms. As a result of such nonpeculiar process for the cells, activeness of free radical oxidation (FRO) raises by many times in the cell this stimulated excessive accumulation of active forms of oxygen. Active forms of oxygen lead to oxidation of different biologically active substances and structural formations of biological membranes - phospholipids. In the lipids unsaturated fatty acids are primarily subjected to peroxide oxidation, which leads to their change in spatial placement, configuration, their inclusion into intensive metabolic processes. In the measure of adaptive capacity intensification of peroxide oxidation of lipids (POL) by first of all fermentative and non-fermentative antioxidant systems (AOS). In not high activeness of POL and sufficient capacity AOS course and result of disease is favorable. In case of extremely high activeness of POL exhaustion of AOS takes place, and overall this leads to disorders of activeness of cellular ferments, particularly of glycolysis, glycohemolysis, to rupture of phosphorilation, as a result of which the cell loses energetic potential, which itself leads to loss of cell, in particularity, of hepatocyte. Along with this permeability of hepatocytes as well as of its internal structural components is disturbed. Corrosion of hepatocytes takes place, it's synthetic, disintoxicative other functions is last.

Disturbance of permeability of lysosomal membrane enables exit proteolytic ferments into cytoplasm, which complete the death of hepatocyte. Fragments of destroyed cell become foreign for macroorganism and are made harmless by components of non-specific immune system.

Many of thesis's of given theory are proved by our works, as well as by works of N. I. Nisevich and V. F. Uchaikin. Correctness of such view on pathogenesis of cytolysis of hepatocytes during viral hepatitis is confirmed by positive results of therapy with the use of antioxidants.

During serious course of VH further phase of pathogenesis is possible - secondary viremia, which may lead to chronisation of the disease. Last in the pathogenetic chain of VH is residual phase, which clinically corresponds to period of early convalescence.

CLINICS.

Clinical picture of all viral hepatitis is very much similar and differs in percent relation by seriousness of course of disease and its results. For viral hepatitis A + E cyclic benign course with complete convalescence is primarily characteristic, and during hepatitis B, C and D not infrequently is observed medium serious and serious course, lingering and chronic forms of disease and lethal consequences.

Depending upon the expressiveness of clinical manifestations of disease and degree of functional disorders of liver, established by biochemical tests, differentiated are light, medium serious, serious and malignant (fulminate) forms (course) of viral hepatitis. All atypical cases of disease (non-jaundice, affected, subclinical) belong to light forms, such as clinical manifestations and functional changes in such patients are weakly expressed.

To evaluate correctly and time the seriousness of viral hepatitis is not always easy, as clinical manifestations sometimes even in cases, finishing by death in the beginning happened to be weakly expressed and only in the period of complete decompensation of function of liver symptoms indicating on particular seriousness of course of disease are revealed. Clinical criteria's of seriousness during viral hepatitis often carry subjective character and indices of functional tests are exact always and do not always reflect the degree of damage of liver parenchyma.

During evaluation of seriousness disease expressiveness of intoxication and jaundice is taken into attention along with enlargement of sizes of liver and spleen, loss in weight, level of bilirubin in blood serum, elaborated by us index of retraction of blood clot (IRBC). It is able to authentically evaluate the seriousness of disease in the climax of disease.

During this it follows to taken into account the duration of incubation period. Lesser is it, more seriously proceeds the disease. Attention is paid on the character and duration of prejaundice period. High intoxication, polyarthralgia, expressed dyspeptic symptomocomplex are characteristic for fulminate and serious forms of viral hepatitis. Prolonged intensive jaundice, hypotonia, bradycardia, changing into tachycardia, slackness, subfebrile temperature, decrease in diuresis, testifies about serious or even malignant course of viral hepatitis with indefinite prognosis.

Out of the laboratory tests, so as to evaluate seriousness of disease indices of concentration of overall bilirubin in blood serum of patients, IRBC and prothrombin index are used. In adults IRBC composes $348 \pm 43 \times 2$ conditional units.

During light course concentration of overall bilirubin is equal to 80-120 $\mu\text{mole/l}$. According to Endrashich method, prothrombin index is maintained on normal figures, IRBC - $261 \pm 22 \times 6$ conditions units. During medium serious course overall bilirubin composes 120 - 160 $\mu\text{mole/l}$, prothrombin index essentially does not change, IRBC equals $92 \pm 16 \times 4$ conditions units. During serious caused of VH concentration of bilirubin is not more than 160 $\mu\text{mole/l}$. Prothrombin index 100 - 80 units, IRBC - $39 \pm 3 \times 1$ conditions units, reduces the level of overall protein, fibrin, indices of coagulate system of blood.

Viral hepatitis proceed primarily cyclically. Differentiated are incubation period, which during hepatitis A composes on an average 15 - 30 days, during viral hepatitis B 30 - 180 days. Disease begins with signs of prevail intoxication - so called pre-jaundice period. Differentiated are few variants of pre-jaundice period:

1) Dyspeptic - patients complain of absence of appetite, nausea, sometimes vomiting. Temperature is subfebrile. Duration of period is composed of 3 - 7 days.

2) Astenovegetative - patients complain of weakness, headaches, indisposition, lowering of appetite. Body temperature is subfebrile or 37 - 38 C;

3) Influenza identical - patients complain of headaches, weakness; muscular pains, lowering of appetite. Body temperature is 37,5 - 39 C, and in separate cases 39 - 40 C. Duration of 2nd and 3rd variant of pre- jaundice period is composed of 5 - 7 days;

4) Polyarthralgic - observed basically during hepatitis B as well as C. Patients complain of pains in joints, sometimes muscular pain is observed, wetness, lowering of appetite. During this subfebrile period is present in majority of patients. Duration of this period is composed of 7 - 14 days;

5) Mixed type - all above indicated signs of intoxication are present in one or the other degree.

In some patients, disease may begin without any of the signs of intoxication.

With the appearance of oedematous signs of liver damage - climax period of disease - majority of patients feel better. Temperature is normalized, urine darkens, subictericness of sclera's develops, jaundice grows gradually, faces is discolored. Further course of the disease develops on the degree of liver damage by the virus, which determines the seriousness of the disease. During light course of VH jaundice grows in a period of 3 - 5 days, for a period of 1 week is held on one level, thereafter towards 15th - 16th days totally disappears, already the end of 1 - 2 weeks of jaundice period urine becomes light, faces is of yellow or orange color.

During medium serious and serious course of disease yellowish coloring of sclera's, skin is more intensive, jaundice period is more prolonged (20 - 45 day). From the side of cardio-vascular system hypotonia, in majority of patients - bradycardia, feeble cardiac tones is observed. In 80 - 90 % of patients' liver enlarges, its surface is smooth, borders are curved, moderately painful. In 30 - 40% of patients spleen is palpated. During serious course of VH in some patients meteorism of abdomen, caused by disorders of digestion (signs of damage of pancreas, secretory glands of stomach and disorders of biocenosis of gastro-intestinal tract) is observed. In some patients with serious course of VH moderate ascites may be observed. In some patients skin rash is observed - so called cholestatic variant of the course of disease.

From the side of central nervous system some or the other changes are observed in some patients. Already during light course of VH changes like change in mood, anemias, slackness, disorders of sleep may be present. With the growth of seriousness of disease these phenomena are frequently met, their expressiveness is more clear.

In serious cases clear cerebral disorders caused by considerable dystrophic changes in the liver, endogenous intoxication and increase in the activity of processes of POL, as well as by their intermediate products.

In the period of convalescence reverse development of symptomatic of disease, normalization of biochemical indices is observed.

Preliminary diagnosis of VH put on the basis of epidemiological anamnesis, finding of development of disease, clinical picture with account of peculiarities of pathways of transfer, duration of incubation period, presence of pre - jaundice period, presence of typical subjective and objective signs with account of patients age.

Diagnosis is confirmed by routine and specific laboratory tests.

In routine blood test of patients with viral hepatitis lymphocytosis is observed during moderately expressed course and during serious course of disease - anemia and leucopenia. ESR is slightly decreased. In urine urobilin and bile pigments is observed, in feces - during climax period particularly during medium serious and serious forms, stercobilin cannot be observed.

In blood serum on the stretch of whole jaundice period increased content of overall bilirubin, primarily on account of its direct fraction is observed. Interrelation between direct and indirect fraction composes 3: 1. In all patients already in pre- jaundice period of disease, on the stretch of whole jaundice period and in the period of early convalescence raised activity of ALT, AST - forms is observed, testifying about the presence of cytolytic processes in the liver. In patients of VH raised indices of thymol test, decreased indices of overall protein are observed, which testifies about decreased protein synthetic function of liver. During viral hepatitis disorders of indices of coagulate and anticoagulative system of blood, depending upon the period and seriousness of disease are observed. With the help of these indices (electrocardiogram,

thrombocytoqramm, biochemical indices of this system) it is possible to judge the seriousness of disease, phase and degree of DIC-syndrome.

In the diagnosis and differential diagnosis of VH instrumental methods of investigation are widely used - cholangiography, computer tomography.

With the purpose of specific diagnosis reaction of IFA, radioimmune method and their different combinations. With the help of these methods specific antigens (HBsAg) and antibodies to the antigens all known at present viruses of hepatitis are observed in the blood of patients. Discovery of antibodies in class of Ig M testifies about acute disease. Discovered antibodies in other classes of immunoglobulins testifies about long-drawn or chronic course of VH or about earlier infections process or about suffering of the disease in the past.

Differential diagnosis of VH followers to be conducted with diseases like leptospirosis, yersinioses, mononucleosis, malaria, mechanical and hemolytic jaundice, toxic hepatoses. During this it follows to take into account peculiarities of clinical picture of these diseases, possibility of modern specific and instrumental diagnosis.

During establishment of clinical diagnosis it followings to note the type of virus, causing disease, seriousness and course of viral hepatitis.

For leptospirosis characteristics are acute beginning of disease, often with shiver, continuation of fever course of climax of disease and jaundice, pains in muscles, particularly in gastrochemic muscles, hemorrhagic syndrome. In blood leucocytosis with neutrophills and change in the formula to the left of accelerated ESR is observed. Activeness of ALT and AST is moderately reused relation of direct and indirect bilirubin 1: 1. In blood serum concentration of urea and residual nitrogen in crease. In feace constantly bilirubin is observed, reaction of hidden blood is often positive, faces is not discolored. In the urine erythrocytes, leucocytar, like wax cylinders, are observed in large quantities along with decrease in diuresis right upto anuria. Nitrogenic coma is possible. Final recognition of diseases is affirmed by observation of leptospiras in the residue of urine or blood serum and growth of antibodies in blood serum of patients in the reaction of agglutination - leases with specific leptospiric antigen.

During generalized forms of yersinioses one may also observed jaundice, however it is accompanied by fever, metastatic centers in other organs and tissues, leucocytosis with nuetrophilosis, accelerated ESR, exacerbation's and relapses. Diagnosis is confirmed by serological methods with specific yersiniosic antigen.

During malaria clear altneration of attacks of apyrexia with shiver, replaced by seance of heat and sweatiness in observed, often painful, increased in size spleen is observed. In blood hemolytic anemia, in fat drop blood and smear different forms of malarial plasmodia are observed. In blood serum indirect fraction of bilirubin predominates.

During mechanical jaundice one may observe stones in gall bladder and bile passages, urdening of bile passages, enlargement of head of pancreas and other signs with the help of ultrabound investigation. In majority of patients moderate increase in the activeness of ALT, AST, leucocytosis, accelerated ESR is also scene.

For hemolytic jaundice characteristics are anemia, accelerated ESR, raised acrall bilirubin on account of indirect fraction. In feaces stercobilin is always present.

Different diagnosis of VH with hepatoses is complicated and demands from doctor thoughtful and painstaking work. During this essential significance possesses correctly collected anamnesis.

Chronic Hepatitis

There are near 40 disease with syndrome of jaundice (infection and non infection) Chronic hepatitis with an acute exacerbation can mimic acute viral hepatitis and can represent a significant problem in the differential diagnosis. This is best demonstrated for HBsAg-positive chronic hepatitis. These patients occasionally can be asymptomatic, except for recurrent bouts of jaundice and symptoms of hepatitis that can occur with almost seasonal regularity. Several features should suggest the presence of chronic hepatitis. These include previous bouts of hepatitis or jaundice, a prolonged and indolent preicteric phase of disease, protracted and only mild-to-moderate elevations in aminotransferase and serum bilirubin levels, and increased globulin and decreased

serum albumin levels. In most instances the presence of HBsAg with absence of IgM anti-HBc confirms the diagnosis of chronic infection. In the final analysis, however, differentiation requires the test of time. The persistence of symptoms or abnormal serum enzyme levels for more than 6 months indicates chronic hepatitis.

Acute Hepatitis Due to Other Viruses

Several other common viral infections can secondarily affect the liver and can cause an acute hepatitis-like picture. The liver disease associated with these infections usually is mild, self-limited, subclinical, and overshadowed by the other symptoms in these diseases.

Of prime importance as a secondary cause of viral hepatitis is the Epstein-Barr virus (EBV), the agent of infectious mononucleosis. When sought, mild elevations in serum aminotransferase levels are very common in acute mononucleosis. This syndrome should offer no diagnostic confusion with acute viral hepatitis; the liver disease is mild and subclinical. However, on rare occasions, EBV infection can be manifested as acute icteric hepatitis without the usual symptoms of mononucleosis. Physical examination may reveal little or no evidence of pharyngitis or lymphadenopathy. Several features of the hepatitis should suggest that it is due to EBV infection. First, fever (which usually is not prominent in acute viral hepatitis) is prominent and persistent in mononucleosis. High fever lasting into the icteric phase should suggest infectious mononucleosis. Most suggestive, however, is the presence of a significant lymphocytosis (more 50%) with atypical lymphocytes (more 20%). Without this hepatitis cannot be readily ascribed to EBV infection.

Much of what is said about EBV-related hepatitis can be repeated for the cytomegalovirus (CMV). However, the role of CMV infection in causing a hepatitis in adults still is subject to debate, especially as it relates to post-transfusion hepatitis. There is no doubt that primary CMV infection can cause mononucleosis syndrome that frequently is accompanied by hepatosplenomegaly and minor elevations of serum aminotransferase levels.

Several other common human viruses (including rubella virus, and mumps viruses; and Coxsackie B virus) can induce mild abnormalities in liver enzymes. These changes are not common and rarely are accompanied by jaundice. In the immunosuppressed host, however, several usually benign viruses can cause a disseminated infection, part of which may be hepatic involvement. Chief among these are the herpes simplex virus, CMV, and the varicella-zoster virus. These are all herpesviruses that are ubiquitous and common benign infections in humans. In the patient with poor host defenses, dissemination with these viruses can occur; Hepatic necrosis, marked elevations in the serum aminotransferase levels, icterus, and even death from hepatic failure have been described. In the immunosuppressed or the immunoincompetent host with fulminate hepatic failure, a search for these viruses should be made. These viruses, however, are not common causes of sporadic acute hepatitis in the otherwise, healthy host.

One more virus that is responsible for severe hepatic failure should be mentioned as a rare cause of acute viral hepatitis—yellow fever virus. It still occurs enzootic in Central America, South America, and central Africa. Clinically, it is marked by a short incubation period (3-7 days), severe hepatitis with high aminotransferase level elevations, and a high mortality (approximately 20%). It need be considered only in the recent traveler to enzootic areas who has not received adequate immunization.

Hepatitis Due to Nonviral Infectious Diseases

Elevations in serum enzyme levels and liver dysfunction can occur with many nonviral infectious diseases due to bacteria, mycobacteria, rickettsia, and fungi. Thus jaundice with mild elevations in aminotransferase can be seen with several types of sepsis as well as with pneumococcal pneumonia. Furthermore, minor elevations of liver enzyme levels with or jaundice often are seen with many severe infections that usually do not primarily involve the liver—pulmonary and miliary tuberculosis, brucellosis, tularemia, plague, gram-negative sepsis, legionnaires disease, and so on.

Three nonviral infectious agents that can produce an acute hepatitis-like syndrome deserve special note: syphilis, leptospirosis, and, Q-fever. Early syphilis, either primary or early secondary, can be accompanied by significant serum amino transferase level elevations. Jaundice, however, is rare, and the chancre of primary syphilis or the rash of secondary syphilis should be present.

Q-fever is the third nonviral infectious disease that may be mistaken for acute viral hepatitis.

This disease is caused by the rickettsial agent *Coxiella burnetii*. In this disease, as in leptospirosis, constitutional symptoms are prominent with fever, chills, and pneumonitis. Overt jaundice occurs in only about 5 percent of the cases, although subclinical hepatic involvement is quite common. In rare cases, hepatitis without pneumonitis occurs, and a differentiation from acute viral hepatitis may be difficult. Epidemiologic features should reveal exposure to farm or wild animals (cows, goats, sheep). Clinically, persistent fever, pneumonitis, and prostration are more prominent than in viral hepatitis. Liver function tests reveal jaundice with only mild elevations in aminotransferase levels. The diagnosis is made by demonstration of agglutination titers against *C. burnetii* in paired sera.

Drug-Related Acute Hepatitis.

The major differential diagnosis in acute hepatitis is between viral and drug-related hepatitis. Every patient with hepatitis should be questioned carefully about all medications that he uses. Drug-related acute liver injury is not nearly as common as acute viral hepatitis, but it often is much more serious and is a prominent cause of fulminate hepatic failure. Many drugs and toxins have been shown to induce hepatic injury, but few have actually been repeatedly implicated as causing an acute hepatitis-like syndrome.

Some of the most commonly encountered causes of drug related acute hepatitis are aspirin, acetaminophen, isoniazid, rifampicin, phenytoin and the anesthetic halothane.

Aspirin (acetylsalicylic acid) can cause dramatic elevations in serum enzyme levels (two- to five times normal); but it rarely causes jaundice. Aspirin hepatotoxicity seems to occur only with a high maintenance dosage, usually with serum salicylate levels of 20 mg/dl or greater. Characteristically, the biochemical abnormalities subside rapidly on withdrawing the drug. Paracetamol regularly causes severe hepatic necrosis similar to acute viral hepatitis.

Both isoniazid and rifampicin have been implicated in causing an acute hepatitis-like syndrome; both have been associated with fulminate hepatic failure. Rifampicin hepatic injury usually has its onset within the first weeks of therapy, whereas isoniazid hepatotoxicity is most common after 1-2 months of therapy. The incidence of isoniazid hepatotoxicity is approximately 1%, but it is definitely higher; in older age groups and approaches 10% in patients over the age of 40. Treatment with these drugs should be discontinued if symptoms of hepatitis or jaundice appear or if aminotransferase levels are persistently elevated more than five times normal. Phenytoin can cause an acute hepatitis, usually within 1-6 weeks of starting the medication and associated with other manifestations of hypersensitivity such as fever, rash, lymphadenopathy, and eosinophilia. It has a mortality of approximately 10%. Therapy with this drug should be stopped in any patient showing evidence of acute hepatitis.

Anoxic Liver Injury.

A syndrome resembling acute viral hepatitis can occur after anoxic injury to the liver due to a period of hypotension, severe left- or right-sided heart failure, or cardiopulmonary arrest. The clinical and historical features usually can distinguish this nonspecific type of liver injury from acute viral hepatitis. However, in some cases, no clear history of an anoxic episode is obtained, or the patient is brought to the hospital comatose and unable to give an adequate history. In these situations, a diagnosis usually can be made on the basis of serum enzymes. Within hours of an anoxic episode, there are marked elevations of aminotransferase level into the range seen with acute viral hepatitis. Most typical of anoxic liver injury, however, is the rapid resolution of these enzyme abnormalities. Jaundice is uncommon and mild; it generally occurs several days after injury. In some cases, aminotransferase levels remain elevated to two to five times normal for 5-14 days after the injury, in which case differentiation from acute viral hepatitis may be difficult.

Alcoholic Liver Disease

Alcohol abuse is the most common cause of serious liver disease. Alcoholic liver disease (i.e., fatty liver, alcoholic hepatitis, and cirrhosis) usually can be readily differentiated from acute viral hepatitis by history and biochemical tests. Acute alcoholic hepatitis is the syndrome that, perhaps, is most easily confused with viral hepatitis. These patients have the gradual and imprecisely dated onset of malaise, anorexia, weight loss, nausea and vomiting, fever, chills, abdominal swelling, and jaundice or dark urine. The history of alcohol intake should suggest the diagnosis, but many patients conceal or underestimate the amount of alcohol they consume.

Clinically, the patient usually appears chronically ill and typically is older than the average patient with viral hepatitis. Fever and tachycardia are common. Examination may reveal evidence of chronic liver disease and alcohol abuse that is not seen with acute viral hepatitis—wasting, palmar erythema, vascular spiders, gynecomastia, significant hepatomegaly, and signs of portal hypertension (ascites, edema, splenomegaly, and prominent abdominal veins). The laboratory data are most helpful. The white blood cell count is usually elevated with a left shift. The hematocrit may be slightly decreased, and the red blood cell indices reveal macrocytosis. Liver function tests reveal hyperbilirubinemia and typically a low albumin level and a prolonged prothrombin time. The aminotransferase values are most characteristic in that the AST levels almost always are elevated. Furthermore, the AST level is elevated out of proportion to the ALT level (which can be slightly elevated, normal, or even low). Thus, the aminotransferase levels in alcoholic hepatitis differ greatly from those in viral hepatitis—not only in the degree of elevation but also by the relative elevation of the AST to the ALT level.

RESULT OF DISEASE.

Viral hepatitis most often ends with complete convalescence. In some patients after undergoing of acute hepatitis may develop cholestasis, cholangitis, pancreatitis, dyskinesia of bile excreting pathways, in 5 - 10 % of patients protracted course with periodical exacerbations, caused by prolonged persistence of virus is observed. In such cases develops persistent hepatitis (CPH) or chronic active hepatitis (CAP). Both these variants of course of disease are characteristics of viral hepatitis B and C and often end up with liver cirrhosis.

Most threatening result of viral hepatitis - acute or subacute massive necrosis of liver, during which develops picture of acute or subacute hepatic encephalopathy. For acute viral hepatitis acute hepatic encephalopathy (AHE) is characteristic.

Mechanism of development of acute or subacute massive or submassive necrosis of liver is extremely complicated and less studied. As a result of intensive reproduction of virus in hepatocytes excessive accumulation of active forms of oxygen takes place, which in its turn leads to exhaustion of functional capacity of antioxidant system (AOS). This leads to growth of processes of POL, to destruction of structure of cellular membranes of hepatocyte and its intracellular structures, to accumulation of toxic peroxides, to inactivation of many ferment system of cells. In the cellular membranes additional channels appear natural channels are destroyed along with receptors formations which leads to irreversible disorders of fermentative reactions, to exit of lysosomal proteases, leading to complete destruction of hepatocytes.

During such destruction of hepatocytes all functions of liver are oppressed. At pigment metabolism is disturbed. Intensive growth of bilirubin up to extremes of high figures is observed in the blood of patients. In peripheral blood concentration of malonaldehyde and diene conjugates increases by many times, testifying about high intensities of formation of fatty acid radicals. Activeness of all components of AOS is exhausted. Synthetic function of liver sharply suffers. In blood appear proteins of incomplete value, products of degradation of fibrin, level of overall protein of blood decreases, its fraction suffers. Synthesis of components of coagulate system of blood is disturbed, which leads to deep coagulation (3rd phase of DIC-syndrome) and hemorrhages, sometimes massive leading to death of patients. Cycle of synthesis of urea and utilization of ammonia is disturbed, which leads to accumulation of these products in blood, to decrease in diuresis.

As a result of oppression of function of gastro-intestinal tract and disbiosis in the intestine, processes of fermentation are activated, highly toxic products such as indole, scatol, ammonia and others are accumulated and absorbed into blood.

By passing along with the flow of blood through the liver they are not inactivated and brought in to the central nervous system, causing signs of encephalopathy. Active forms of oxygen, circulating in high concentrations in blood, intercellular fluid and tissues of cerebral substance promote destruction of myelin and other products of POL, increase combination of poisons flowing in blood with cells of nervous tissue, intensifying manifestations of encephalopathy. Water -

electrolyte, carbohydrate, protein, fat vitamins metabolisms are disturbed. Complete "unbalancing" of metabolism develops, metabolic acidosis, which in 2/3 cases is a direct reason of lethal consequence. 1/3 of patients dies from massive hemorrhages.

Clinics and methods of prognosing of acute hepatic encephalopathy (AHE). Termini "acute hepatic encephalopathy" denotes unconscious condition of the with disorder of reflector activity, convulsions, upset of life vital functions as a result of deep brake action of cerebral cortex with its spread on to subcortex and belowlying parts of central nervous system. This sharp brake action of nervous-psychic activity, characterized by disorder of movements, of sensibility of reflexes and by absence of reactions on different irritators.

Hepatic coma - this is an endogenic coma, caused by endogenic intoxication as a result of loss of function and breakdown of liver.

At present many different classifications of acute hepatic encephalopathy exist characterizing one or the other stage of complication. Y. M. Tareev, A. F. Bluger proposed to differentiate three stages of AHE - precoma 1, precoma 2 and 3 - coma.

Precoma 1 characteristics are non constant disorder of consciousness, unsuitability of mood, depression, lowered capability towards orientation, tremors, inversion of sleep. Patients are irritated, sometimes - euphoric. They are troubled by paroxysms of depression, doom, presence of death. Fainting, short time unconsciousness, giddiness, hiccup, nausea, vomiting may be observed. Jaundice grows. Bradycardia is changed by tachycardia. Tendon reflexes are raised. Such condition prolongs from few hours to 1 - 2 day with moving into 2nd stage.

In the 2nd stage of precoma consciousness is more hampered, losses in memory is a characteristic feature, alternated with attacks of tachymotor and sensory excitation right upto delirium. During awakening orientation od time, space and action is last. Tendon reflexes are high. Jaundice raises sharply body temperature is subfebrile. Feebleness of cardiac tones is observed along with tachycardia and hypotonia.

Rhythm of respiration is disturbed. Liver begins to decrease size. In 1/3 of patients nasal hemorrhages, gastro-intestinal hemorrhages, uteric hemorrhages and hemorrhages of the localization are observed. Diuresis is decreased. Abdomen inflated; peristaltic of intestine decreased. Such condition prolongs for 12 hours - 2 days.

During the 3rd stage – proper coma - complete loss of consciousness and disappearance of reflexes is roted, first of tendon, thereafter of corneal and finally of papillary reflex. Pathological reflexes may appear. (Babinsky, clones of feet, rigidity of muscles of extremities, hyperkineses, convulsive syndrome, and thereafter complete areflexia). Expressed tachycardia, hypotonia, disorder of rhythm of respiration is observed. Abdomen inflated, peristaltic of intestine decreased, in part of patients free liquid is observed in abdominal cavity. Liver decreases in size. Considerably decreases diuresis right upto anuria. Soon (6 hours - 1 day) patients die of massive hemorrhages or during phenomenon's of deep disorder of metabolism with phenomenon of serious metabolic acidosis.

Some clinical hold to another classification of hepatic coma, which foresees further stages of its development: precoma - 1, precoma - 2, coma - 1, coma - 2. Precoma - 1 is the period of precursors. Precoma - 2 - in the clinics of disease clear clinical signs of encephalopathy are possessed - coma - 1 - period of excitation with the loss of consciousness. Coma - 2 - deep loss of consciousness, areflexia, disorder of rhythm of respiration, decrease in size of liver, hemorrhages anuria.

Prognosing of acute hepatic encephalopathy is possible in few days before appearance of precursors of this threatening complication. With the purpose of prognosing of AHE it following to daily examine the condition of coagulate and anticoagulative system of blood with the help of electrocoagulograph in serious patients, which enables us to obtain graphic record of whole of coagulation of blood and fibrinolysis in just 20 minutes.

New method elaborated by us for evaluation of indices of different phases of coagulation, enabling to evaluate indirectly the condition of liver according to the degree of retraction of blood clot and time of maximal retraction. Simple formulary for calculation of index of retraction of blood clot (IRBC) has been proposed.

$$\text{IRBC} = \frac{t}{h}$$

Where t - duration of maximal retraction of blood clot second;

h - height of oscillate movements of oneself writing;

For serious course of viral hepatitis decrease in IRBC is a characteristic feature. In patients in which it is equal to 32 cond units, coagulogram should be examined daily, and their conditions is evaluated as a threat to coma. During IRBC 9 cond units in patients precursors of coma appear. With its further development significance of IRBC decreases up to 0. In case improvement of overall condition of the patient IRBC rises.

This method may be used also for evaluation of effectiveness of conducted therapy. Used every where prothrombin index is not and early prognostic ten. With help it is possible only to documentate already developing and clinically diagnosed coma. Results of AHE are often favorable. In cases of reconvaescence, but of incorrect competence of patients in period of early reconvaescence in early liver cirrhosis develops.

During prognosing of AHE on preclinical stages and correct competence of patient complete reconvaescence steps on.

TREATMENT.

All patients with acute viral hepatitis in period of acute clinical manifestations should follow bed regime.

In the whole period of acute clinical manifestations and early reconvaescence patients are prescribed table № 5 according to Pevzner. It is prohibited to use all fried, fatty and piquant in food. Alcoholic drinks are strictly contraindicated. Out of the meat products white boiled chicken meat, veal, rabbits boiled meat is recommended. Patients are prescribed with fresh boiled fish. Out the first dishes it follows to recommend vegetable soups, pea, buck what cereal soups. Out the second dishes indicated are mashed potatoes, rise, buckwheat, out flake porridges, enriched with butter (20 -30 gm). In dietic nutrition it follows to include milk, cottage cheese, curds, non-piquant cheeses. Patients are prescribed with salads of fresh vegetables without onion, improved with refereed sunflower oil (olive, maize), beet root salads. It follows to widely recommend compote, kisses of fresh and tinned fruits and pulps, table mineral waters, broth of dog - rose, lemon tea. Patients may consume fresh apples, pears, plum, cherries, granates watermelons, encumbers, tomatoes in their food.

During presence of intoxication patients are prescribed with disintoxicative intravenous therapy for a period of 3 - 5 days. With this purpose 5 % solutions of glucose 200 - 400 ml is injected droply intravenous along with hemodesis 200 - 400 ml, 5 % solution of ascorbic acid 10 - 15 ml; acesolt or chlosolt 200 - 400 ml.

On the whold stretch of jaundice period enterosorbents (fibrolact and others) are prescribed internally. Beginning from the first day of disease and upto complete normalization of actives of transaminase patients should receive internally natural antioxidants, such as "Immortal", infusion of astragal of and other.

During threat of acute hepatic encephalopathy it follows to prescribe drop intravenous injection of salt and colloid solutions in overall volume of 1200 - 2400 ml in a day. Introduction of solutions is ralised 2 times a day (morning and evening) into subclavicular vein through the catheter. Hemodesis 200 ml; 5% solution of glucose solution - 400 ml; donors albumin - 400 - 500

ml; cocarboxylase, ATP, trasilol or hordox 100 000 - 200 000 units or contrical, eparmefolin, aminocapronic acid is pressurized.

During appearance of hemorrhages hemostatic therapy, adequate to the losses is prescribed. With this purpose one may use aminocapronic acid, vicasol, blood plasma, whole blood, erythrocytes or fibrinogen.

Patients are indicated with enema. During psychomotor excitation patients are fixed to the bed, seduxen or sodium oxibutirate is injected.

During decreased diuresis it follows to inject intravenously mannitol, manit, eyphyllin.

During organization and conduction of complex of therapeutic measures it follows to remember, that effectiveness of treatment very much depends on quality of nursing of patients, therefore in the ward of intensive therapy specially prepared personal should work, possessing methods of intensive therapy and resuscitation, as well as methods of nursing and service of patients with hepatic coma.

It follows also to remember, that recognized acute hepatic encephalopathy on preclinical stages and correctly conducted treatment may save patients life.

Dispensary observation after reconvaescent is realized by doctor in regional polyclinics during hepatitis A + E in a period of 3 months, during hepatitis B + C - in a period of 6 month.

In case, when restoration of hepatocyte is protracted (indices of activeness of transaminase are raised) observation is extend upto complete reconvaescence.

Prophylaxis.

If the patient is hospitalized, he should be placed in a private room with separate toilet facilities. The major reason for such isolation is to prevent the spread of type A hepatitis. Even with lax precautions, such spread is very rare; most patients with type A hepatitis are no longer excreting virus once they have become symptomatic. Nevertheless, there are exceptions, and isolation is prudent. Secretions and blood products should be handled with care bowris, masks, and gloves are not necessary, but a prominent sign reading "needle and blood precautions is appropriate. Labeling of blood specimens, as from a patient with hepatitis, is a common practice. If should be stressed, however, triat all blood from any patient should be handled as if potentially infectious.

If the patient with viral hepatitis is at home, the patient should be advised about care in personal hygiene of a private and careful hand washing. Attention also should be paid to blood and blood products and the handling of cuts and lacerations.

Recommendations regarding the prevention of acute hepatitis are governed by the type of viral hepatitis that is being considered. In the case of acute type A, hepatitis, all family members, and close personal contacts should receive immune serum globulin (ISG) at a dosage of 2-5 ml in as soon as possible after exposure. Office, factory, and school contacts do not need to be treated. Immune serum globulin can be given for up to 4 weeks after exposure, but it probably is only effective if given within 7-14 days. In the case of acute type B hepatitis, prophylaxis only needs to be provided for "regular" sexual contacts. The best form of protection is argued. Hepatitis B immune globulin (HBIG) at a dosage of 5 ml in as soon as possible and again 1 month later has been the conventional recommendation in this situation. However, the efficacy of HBIG in preventing the sexual spread of acute type B hepatitis has not been well proved. In addition, there is now evidence that postexposure immunization with HBV vaccine, can attenuate or prevent acute type B hepatitis. Vaccine should be given in 20 g amounts (0.5-1.0 cc) in as soon as possible and then 1 month and 6 months later.

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