Ministry of Education and Science of Ukraine
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Microbiology, virology, epidemiology
with the course of infectious disease department

STUDY GUIDE

FOR THE PRACTICAL CLASSES OF EPIDEMIOLOGY WITH PRINCIPLES OF EVIDENCE BASED MEDICINE COURSE

For the students of medical faculty

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Contents

Chapter 1.
Epidemiology. Basic terms and definition. Epidemic process.

Epidemiology is the science of the epidemic process, the patterns of spread of infectious diseases among human populations and measures for the prevention and anti-epidemic control of infections.

The purpose of epidemiology is to reduce the prevalence of infectious diseases and finally eliminate infection, i.e. to achieve epidemic well-being of the population.

The task of epidemiology - the study of manifestations and factors of the epidemic process of infectious diseases and the development and implementation of preventive and anti-epidemic measures to combat them, including:

- determination of medical socio-economic significance of the disease and their place in the structure of the pathological population;
- identification of causal links of morbidity;
- development of recommendations for optimizing the prevention and control of infectious diseases.

The structure of epidemiology as a medical science contains two main parts:

- general epidemiology;
- special epidemiology.

A specific subject of study of epidemiology is the epidemic process, and the object - infectious conditions.
Research method - Integrated Epidemiological Method (IEM).

Epidemic process

Epidemiological process is a complex socio-biological phenomenon that occurs due to the interaction of micro-and macro-organisms at the population level, is manifested by specific infectious conditions of man (disease or carrier) and ensures the preservation of the pathogen in nature as a species.
"Epidemic process" is a continuous process of interaction of micro- and macroorganisms at the population level, which is manifested by the spread of specific infectious conditions among humans (disease or carrier) and ensures the preservation of the pathogen in nature as a species (according to LV Gromashevsky). In other words, an epidemic process is a process of occurrence and spread of infectious diseases among the population.
Links of the epidemic process: the source of the pathogen - the mechanism of transmission - the susceptible organism. These elements are closely linked and ensure the continuity of the epidemic process. If at least one of the links is eliminated, the epidemic process stops. This law has become the main methodological basis for the development of a modern system for the prevention of infectious diseases.
Theory of the epidemiological process (includes section 3):

- Section 1: examines the causes and conditions of the emergence and development of the epidemic process, its interaction with the population of the parasite and the host in certain social and natural conditions.
- Section 2: studies the mechanism of development of the epidemic process (theory of the transmission mechanism of Gromashevsky; Pavlovsky's theory of natural orientation; Belyakov's theory of self-regulation of parasitic systems; socio-economic concept of the Cherkasy epidemic process).
- Section 3: the doctrine of the epidemic process considers the manifestation of the epidemic process (distribution of infectious diseases, among the population and time) - studies the structure and dynamics of morbidity.

Epidemiological triad

An epidemiological process is a chain of related infectious conditions. This happens and is supported only in the presence and interaction of three links:

- sources of the pathogen;
- the mechanism of transmission of the pathogen;
- susceptible organism.

The source of the pathogen.

The source of the pathogen is a living infected organism (sometimes the natural environment), in which the pathogen has optimal conditions for its reproduction, accumulation and release into the environment. The optimal conditions for the existence of pathogenic microorganisms are an infected human or warm-blooded animal, due to the presence of a constant body temperature, pH and nutrient medium necessary for the existence of parasitic microorganisms. In recent years, a small group of saprophytic microorganisms has been isolated that live freely in water,

soil, and do not necessarily exist in a living being. However, getting into the body of a warm-blooded host, they acquire pathogenic properties and lead to diseases (listeriosis, legionellosis, gas gangrene, etc.).
Depending on the type of source of the pathogen, infectious diseases are divided into anthroponoses, zoonoses, anthropozoonoses and sapronoses.
In anthroponoses, the source of infectious agents is only an infected person (patient or carrier). Anthroponoses include most infections with an aspiration transmission mechanism (measles, chickenpox, meningococcal infection, etc.). In anthroponoses, there is a consistent transfer of pathogens from the body of the source of infection to the susceptible organism of another recipient, which in turn also becomes a source of infection for other people.
Only warm-blooded animals can be sources of infectious agents in zoonoses. The mode of existence of zoonotic agents in nature is an epizootic process, ie the process of spreading infectious diseases in animal populations. In most zoonoses, human diseases are random in the chain of the epizootic process, they are not related to each other. A sick person does not pose a danger to other people and is a "dead end" in the chain of the epizootic process (for example, in brucellosis, leptospirosis and tick-borne encephalitis, sick people are not contagious to the environment).
Many animal species are the source of zoonotic infections for humans. Thus, among domestic animals - cattle and small cattle (anthrax, brucellosis, leptospirosis, foot and mouth disease, etc.), pigs (leptospirosis, trichinosis, teniosis, brucellosis, yersiniosis), horses, donkeys (sap, scabies, leptospirosis). dogs and cats (rabies, toxoplasmosis, toxocariasis, filariasis), birds (ornithosis, salmonellosis). Wild animals can also be sources of these infections, but are less important for human infection due to liquid contact.
Of great epidemiological importance are rodents, which are sources of pathogens of more than 40 infectious diseases (plague, tularemia, yersiniosis, leptospirosis, rickettsiosis, hemorrhagic fever, tick-borne and Japanese encephalitis, etc.).
The causative agents of sapronoses are saprophytic microorganisms that live freely in the environment, for them epidemic and epizootic processes are not a way of life. Infection of humans with sapronoses is an example of "false parasitism" of saprophytes, which have acquired pathogenic properties only in the body of the host. Human sapronosis usually does not infect other people and is a "biological dead end" for microorganisms. Sapronoses include such diseases as legionellosis, yersiniosis, tetanus and others. The source of infection for such pathogens can be soil, water, ie those objects of the environment that are the place of their natural existence.

Mechanism, factors and ways of infection transmission.
The mechanism of transmission is the process of moving the pathogen from one organism to another, formed in the process of evolution and ensuring the existence of this species in nature. LV Gromashevsky in substantiating the theory of the transmission mechanism identified 3 of its successive stages:

- isolation of the pathogen from the infected organism;
- stay in the environment;
- penetration into the susceptible organism.

The implementation of the second phase involves various objects on which the pathogen can persist for some time, and sometimes multiply and accumulate. They are called transmission factors.
The main factors of transmission of infectious diseases are: water; food; air; household items; soil; live vectors.
The sequence and set of factors that are involved in the transmission of the pathogen in specific conditions, determine the route of transmission of the pathogen, ie the method of implementing

the transmission mechanism. Thus, the fecal-oral mechanism can be realized by water in the transmission of the pathogen through water, alimentary in the use of contaminated food, and contact-household - in the transmission of the pathogen through household items. Thus, in each specific situation, pathogens can be transmitted in one way or another, through different objects. LV Gromashevsky identified 4 types of transmission mechanisms: aspiration, fecal-oral, transmissible and contact. However, in modern conditions, new infectious diseases have appeared, which are transmitted by artificial means - through parenteral interventions, blood transfusions, injecting drugs. In recent decades, the possibility of transmitting certain infections from mother to child during pregnancy, childbirth and breastfeeding has been proven. Therefore, in recent years, many authors acknowledge the existence of two more mechanisms of transmission - parenteral and vertical.

Therefore, there are the following types of transmission mechanisms:

- Aspiration (sold by airborne and airborne dust).
- Fecal-oral (sold by water, food and household contact).
- Transmissible (with the participation of carriers).
- Contact (realized by sexual and contact-domestic ways).
- Parenteral (when the pathogen penetrates the skin with impaired integrity, with the use of contaminated medical instruments, injecting drug use).
- Vertical (infection of the child from the mother perinatally or intranatally).

There are clear patterns between which organs are mainly affected by this infection, and the way the pathogen is isolated from the source of infection, as well as the way it penetrates the susceptible organism. Such a pattern was discovered and substantiated for the first time by LV Gromashevsky as "The law of conformity of the mechanism of pathogen transmission to the primary (epidemiological) localization of the pathogen in the host organism". Based on this pattern, he developed an epidemiological classification of infectious diseases, which is widely used today.

Classification of infectious diseases (according to LV Gromashevsky)

1. Respiratory tract infections.
2. Intestinal infections.
3. Blood infections.
4. Infections of the outer coverings.

Mechanisms, ways and factors of transmission of infectious agents (according to Cherkasky BL, 2001)			
Primary localization of the pathogen	Transmission mechanism	Ways of transmission	Transmission factors
Respiratory tract	aspiration	air-drop, air-dust	aerosol, dust
Gastrointestinal tract	Fecal-oral	water, food, contact and household	water, food, hands, household items
Circulatory system	transmissible	inoculation, contamination	arthropod vectors

Outer covers	contact	sexual, contact and household	soil, dirty hands, household items, arthropods

Susceptible population - the third link in the epidemic process

Susceptibility is a species ability of an organism to react to the penetration and vital activity of a corresponding pathogen in it by the development of an infectious process (Cherkasky BL, 2001). Susceptibility is a prerequisite for the occurrence of an infectious process, and its manifestations always depend on the condition of macro- and microorganisms. The state of human susceptibility is influenced by such factors as age, physical and emotional state of the organism, the dose of the pathogen, its properties and specific conditions for the development of the epidemic process. Susceptibility to infectious diseases increases, in particular in early childhood, during emotional stress, physical exhaustion, and so on.

The human population is heterogeneous (heterogeneous) in the degree of susceptibility to each specific pathogen, which is manifested by the emergence of various forms of clinical manifestations of the disease - from erased, subclinical to severe. Thus, acute hepatitis B in almost 50% of infected people has a course of erased, non-jaundiced form, 1-2% - fulminant and only 40-50% develop a characteristic jaundiced form of the disease.

To assess susceptibility to infectious diseases use the contagiousness index - a quantitative indicator of the readiness of the human body to the disease at the initial infection with the pathogen. This indicator makes it possible to assess the likelihood of human disease after a guaranteed infection. The higher the index of contagiousness, the less important are the individual characteristics of man. The contagiousness index is expressed in decimal fractions or as a percentage. Thus, in measles, this figure reaches 1 (100%), ie almost 100% of people infected with the virus, there will be an infectious process with the subsequent development of the immune response. In mumps infection, the contagiousness index is 0.5 (50%), in diphtheria - 0.2 (20%), and in polio - 0.001 (0.03%). However, in practice, the most important indicator is the opposite of susceptibility, ie immunity (resistance, or immunity).

Driving forces of the epidemic process

The doctrine of the driving forces of the epidemic process was substantiated by LV Gromashevsky, who identified three primary driving forces (three parts of the epidemic process - the source of the pathogen, the mechanism of transmission and the susceptible organism), the interaction of which is a prerequisite for the emergence and development of the epidemic process. According to this theory, the elimination of at least one link in the epidemic process stops it. This postulate formed the basis for the formation of a system for the prevention and control of infectious diseases.

Thus, isolation and disinfection of the source of infection stop the further spread of the disease. For example, hospitalization and treatment of a patient with typhoid fever or the destruction of rodents with plague ensure that new cases of the disease among humans are prevented.

Disruption of the transmission mechanism is the most effective preventive measure for intestinal and blood infections with a transmissible transmission mechanism. Due to mass planned disinsection and drainage of swamps, the elimination of endemic regions of malaria in Ukraine has been achieved. Improvement of settlements, introduction of drinking water purification system, improvement of its quality, constant sanitary control and other measures have allowed to significantly reduce the incidence of intestinal infections in our country.

Increasing the population's immunity is carried out through the introduction of two areas of prevention - non-specific and specific (immunoprophylaxis). The use of mass vaccination has completely eliminated smallpox, got rid of polio in most countries, significantly reduced the

incidence of infections caused by immunoprophylaxis (measles, mumps, rubella, diphtheria, pertussis). Research and development of vaccines has shown that the effectiveness of vaccination depends on the stability of post-infectious immunity in this infection. Thus, the highest efficiency of immunization is proved in infections, after which sterile lifelong immunity is formed (polio, measles, rubella, etc.).

In addition to the primary, or main driving forces, there are "secondary" - natural and social factors that indirectly affect the epidemic process through each of its links.

The social factors that affect the development of the epidemic process include: economic factors; sanitary and communal improvement; the level of development of the health care system; nutrition features; working and living conditions; national and religious customs; wars; population migration; natural disasters. Social factors are important for the development of the epidemic process, they can cause the spread of infectious diseases or, conversely, reduce morbidity.

Natural factors are a set of environmental factors that affect the course of the epidemic process. Factors of inanimate nature (climate, temperature and humidity, level of insolation, water composition, terrain) can indirectly affect the state of parasitic systems, the relationship between micro-and macro-organisms. They determine the habitats of vectors, the ability of pathogens to exist in the environment. Climate change, fluctuations in temperature and humidity can increase or, conversely, reduce infectious morbidity. Forms of interaction of living beings (microbial competition, confrontation of microorganisms and protozoa, etc.) also have an impact on the course of the epidemic process.

Manifestations of the epidemic process

The manifestations of the epidemic process include its intensity, the distribution of diseases over time, by territory and among different groups of the population.

The intensity of the epidemic process is characterized by the incidence rate - absolute or intense. However, it should be noted that the calculated incidence rate does not always correspond to the true intensity of the epidemic process, due to the level of diagnosis, quality of registration and accounting of diseases, the level of medical treatment and so on. The level of morbidity is divided into 2 stages: sporadic and epidemic morbidity.

Sporadic morbidity is the level of morbidity common to a given area, or single diseases that occur in a particular area.

Epidemic morbidity is a group nature of diseases, it is divided into outbreaks, epidemics, pandemics.

Outbreaks appear to be exacerbated during human illness and are associated with a common source of infection, transmission, or transmission. Outbreaks appear to be exacerbated during family, community, or community use.

An epidemic is an intense and widespread spread of an infectious disease that affects the population of a region of a country or several countries. Epidemics are characterized by a high level of morbidity, which exceeds the sporadic level for this area.

A pandemic is an intense spread of an infectious disease that spans countries and continents.

Self-control Questions

1. Subject and object of epidemiology.
2. Epidemic process and its components.
3. Epidemiological triad.
4. The concept of anthroponoses, zoonoses, sapronoses.
5. Sections of epidemiology.
6. Determination of the transmission mechanism, its phase.
7. Ways and mechanisms of transmission of infectious diseases by LV Gromashevsky.
8. Factors and ways of transmission of infectious diseases.
9. Driving forces of the epidemic process.
10. Manifestations of the epidemic process.

Test tasks

1. The source of the pathogen is an object that is?
   A. The natural habitat of microorganisms.
   B. The place of reproduction of microorganisms.
   C. The place of conglomeration of microorganisms.
   D. The place from which the agent is released into the environment.
   E. All of the above.

2. All of the following statements illustrate the purpose of epidemiology in health care except
   A. Identification of population groups that are at risk of certain diseases.
   B. Evaluation of the effectiveness of interventions.
   C. Providing treatment for patients in a clinical setting.
   D. Determining the importance of the causes of the disease.
   E. None of the above.

3. Is there a reservoir of the pathogen in zoonosis?
   A. Man.
   B. Animal.
   C. Environment.
   D. Man and animal.
   E. Man, animal and environment.

4. The epidemic process is ...
   A. Spread of infectious diseases among animals.
   B. The spread of infectious diseases among blood vectors.
   C. The spread of infectious diseases among the population.
   D. The state of infection of a person or animal.

5. Epidemiology of infectious conditions as a branch of science studies ...
   A. Regularities of occurrence and spread of various types of mass health disorders.
   B. Principles and forms of anti-epidemic work.
   C. Patterns of occurrence and spread of infectious diseases among humans and the development of means to prevent, control and eliminate these diseases.

6. The first link of the epidemic process.
   A. Susceptible organism.
   B. The causative agent of an infectious disease.
   C. The source of the pathogen of an infectious disease.
   D. Transmission mechanism.
   E. Pathogen transfer rate.

7. Sources of infectious agents are ...
   A. Any objects on which pathogens are found.
   B. Live infected people or animals.
   C. Any environment in which the agent is stored for a long time.
   D. Vectors in which the agent undergoes a certain cycle of development.

8. The manifestation of the infectious process is...
   A. Disease or condition of the vector.
   B. The flu epidemic in the country.
   C. Outbreak of infectious disease in rodents.

9. The number of driving forces of the epidemic process
   A. 2.
   B. 3.
   C. 4.
   D. 5.

10. The secondary forces of the epidemiological process are
A. Natural and social phenomena.
B. Phenomena of nature.
C. Social phenomena.
D. Public policy.

Chapter 2.
Anti-epidemic measures in the center of infectious diseases.

The center of an infectious disease is the place of the source of the infectious agent together with the surrounding territory, within which the pathogens can spread among the susceptible population with the appropriate transmission mechanism.
Thus, the center of infectious disease in anthroponoses can be a place of permanent or temporary stay of people - an apartment, a room in a dormitory, a preschool, school, etc. In zoonotic infections, the focus is the area where the source of the pathogen is located - domestic or wild animals, birds, etc.
Territorial boundaries of the infectious disease center depend on the mechanism of infection transmission and the activity of leading transmission factors. Thus, in intestinal infections, the focus of infectious disease may be limited to an apartment or group of kindergarten in the transmission of the pathogen through household items, and may spread to the entire settlement or part of it by the implementation of the waterway. In the alimentary way of transmission, the cell is limited to the number of persons who are united by a common source of food (canteen, cafe, family center, dairy kitchen, etc.).
Outbreaks of respiratory infections are characterized by a relatively small area within which an aerosol transmission mechanism (1-3 m) can be implemented, which usually corresponds to the room or apartment where the patient is and his place of study or work. In blood infections, the area of the cell is due to the distance of flight or movement of arthropods (yes, a malaria mosquito can cover a distance of up to 3 km). In infections of the outer coverings (scabies, mycoses of the skin), the area of the cell is usually limited to the place of residence of the source of infection. In infections with parenteral and sexual transmission (HIV, hepatitis B, C, D, etc.), the focus of the infectious disease has no normal territorial boundaries and covers a range of sexual partners, recipients of blood or organs, a group of drug addicts, ie persons associated among themselves by sexual intercourse or parenteral interventions.
In addition to spatial boundaries, each focus of infectious disease has certain time constraints. Even after isolation of the source of the infectious agent, the cell remains epidemiologically dangerous, because the persons who communicated with the patient (contact persons) may be in the incubation period of the disease during the first visit to the center and become a source of new diseases soon. Therefore, most foci of infectious diseases require repeated visits to the epidemiologist, ie epidemiological surveillance. And the duration of the cell is limited by the maximum incubation period.

Epidemiological examination of the source of infectious disease
Comprehensive anti-epidemic measures are being taken to eliminate the outbreak and stop the spread of the infectious disease. However, these measures cannot be effective without a thorough epidemiological examination of the cell and identification of the causes and conditions of infectious disease.
Thus, the purpose of the epidemiological examination of the center is to establish the causes of infectious disease and the availability of conditions for its spread.
The following tasks are solved at the epidemiological examination of the center:

- determining the source of infectious agents;
- identification of factors and ways of its transmission;
- defining the boundaries of the cell;
- drawing up a plan of anti-epidemic measures aimed at eliminating the cell.

The following methods are used to conduct an epidemiological examination of the cell:

- Survey of the patient (collection of epidemiological history) and other persons who can

report or clarify the data on the causes of the outbreak;

- Inspection and sanitary inspection of the focus;
- Laboratory (bacteriological, biochemical, virological, serological) and instrumental studies (eg, rectoromanoscopy for shigellosis, radiography for tuberculosis);
- Study of medical documentation;
- Epidemiological surveillance of the cell, which ends with the analysis and generalization of data and the definition of a set of anti-epidemic measures aimed at eliminating the focus.

Survey of the patient and persons who have been in contact with him

The patient must be interviewed, regardless of his / her whereabouts (at the place of residence or in an infectious disease hospital). Surveys are conducted purposefully, taking into account the probable etiology of the disease and the mechanism of transmission. Thus, in intestinal infections, possible contact with the source of infection (communication with patients who have similar symptoms), possible factors and routes of transmission are clarified. Intestinal infections have a fecal-oral transmission mechanism, which can be realized by water, alimentary or contact-household routes of transmission. Therefore, the patient is interviewed about the conditions of water supply, accommodation, food (at home, in the dining room, cafe, etc.), collect food history, clarify the implementation of sanitary and hygienic skills, stay outside the place of residence during the incubation period. In addition, make lists of people who have communicated with the patient. It is often necessary to interview contact persons (family members, neighbors, co-workers and others who can provide additional information about the circumstances and causes of the disease).

Given the average duration of the incubation period, it is possible to determine approximately when and where the infection occurred. If the patient was on a business trip the day before, it is necessary to find out when he returned. If there is less than the minimum incubation period between his return and the onset of the disease, it is likely that the infection occurred on a business trip.

Inspection and sanitary inspection of the focus

Sanitary examination of the center of an infectious disease is performed at the place of residence and work of the patient, at illness of the child - in a children's institution. At intestinal infections pay attention to living conditions, degree of municipal improvement (a condition of toilets, system of clearing of garbage and water supply, at decentralized water supply specify a circle of the persons using one well). Evaluate the nature and location of food, food storage, sanitation of kitchens and dining rooms. Outbreaks of intestinal infections necessitate examination of food units (in children's institutions, schools, boarding schools, etc.), water supply sources, water mains, sewerage network, etc. When examining the foci of respiratory infections pay attention to the location of the premises in the apartment, overcrowding, the number of beds in the room (in kindergartens, barracks, boarding schools). Children's playgrounds inspect playgrounds, assess the isolation of different groups of children during walks and indoors. During the examination of the cell, increased attention is paid to persons who have been in contact with the patient, in order to identify possible sources of infection (patients with erased forms, carriers).

Laboratory examination

Laboratory tests are designed to confirm the data of the epidemiological survey. Research can be directed in the following areas:

- laboratory examination of the patient to clarify the diagnosis;
- examination of contact persons for detection of chronic carriers, patients with erased, atypical and subclinical forms of infectious diseases (bacteriological examination of

contacts in the centers of diphtheria, meningococcal infection, typhoid fever, etc.);
- examination of animals in foci of zoonotic infections (salmonellosis, bird flu, etc.);
- inspection of objects of the external environment (food products by food transmission, water - by water).

Study of medical records

Acquaintance with logs of registration of infectious diseases, case histories, ambulatory cards, vaccination cards allow to specify data on duration of an illness, a probable source of an infection, terms of immunization of the patient, etc.

Epidemiological surveillance of the focus

The main purpose of the epidemiological examination of the center is to identify the source of infectious agents and transmission factors. Epidemiological surveillance of an infectious disease center is carried out at least during the maximum incubation period.

All data obtained by the epidemiologist enters in the map of the epidemiological examination of the center (f357 / y), it is accompanied by the results of laboratory tests. Epidemiological surveillance ends with the analysis and generalization of the collected data, decision-making on a set of measures aimed at eliminating the cell. After the end of the observation period, the map is used as a statistical document for retrospective epidemiological analysis of population morbidity.

Accounting and registration of infectious diseases

The system of accounting for infectious and parasitic diseases is necessary to ensure measures to prevent their spread (including clarification of the diagnosis, ensuring the necessary isolation of patients, examination of foci and control of persons in contact with the patient, vaccinations, etc.), as well as to count statistical data on individual infectious diseases in the general system of information on public health. For each case of disease or suspicion of such a disease, detection of carriers, complications after vaccination, bite, salivation, scratching, fill in the "Emergency notification of an infectious disease, food, acute occupational disease" (f.058), which for 12 hours. is sent to the territorial SES at the place of registration of the disease (regardless of the place of residence of the patient). In addition, promptly in the SES reported by phone.

The emergency report should be filled in and sent by the doctor or paramedic who diagnosed the disease, regardless of the circumstances (when the patient goes to the outpatient clinic, when visiting home, at a preventive examination, etc.).

Data on the patient are entered in the "Journal of infectious diseases" (f.060).

Preventive and anti-epidemic work of the polyclinic

Sanitary and epidemiological well-being of the population is ensured by state and executive authorities at all levels - state, local, district. In the health care system, the fight against infectious diseases is performed by specialists in various specialties. Specialists of a medical profile take an active part in this work: carry out primary anti-epidemic measures in the center, carry out dispensary supervision of patients with chronic infections, carriers, etc.

Anti-epidemic measures are a set of measures aimed at preventing infectious diseases among certain groups of the population, reducing the incidence of the total population and eliminating certain infections.

Anti-epidemic measures are carried out directly at detection of an infectious disease, preventive - constantly, irrespective of presence or absence of the infectious patient. Preventive measures aimed at preventing infectious diseases among the population include: sanitary control over water supply, food quality, sanitary condition of catering, trade, children's institutions; carrying out planned disinfection, disinsection and deratization measures; planned specific prevention

among the population, etc.
The organizational structure of the system of anti-epidemic protection of the population includes medical and non-medical forces and means. A set of measures related to the cleaning of settlements from garbage, water supply, catering, is performed by state, municipal and other institutions. Among medical institutions, the main role in the organization of the anti-epidemic regime is performed by the sanitary-epidemiological service, whose activity consists of diagnostic, organizational, methodological and managerial functions. The activity of outpatient clinics in the organization of anti-epidemic work is aimed at the initial detection of an infectious patient, solving the issue of his isolation, dispensary supervision of convalescents and chronic patients. The leading role in the fight against and prevention of infectious diseases in outpatient settings is played by the Cabinet of Infectious Diseases (KIZ). The doctor-infectious disease specialist of KIZ actively manages preventive and anti-epidemic work of district doctors, using methods of epidemiological diagnostics.

Anti-epidemic measures in the center
Anti-epidemic measures in the center of infectious disease are complex and aimed at three areas: the patient (source of infection), the mechanism of transmission and persons who have been in contact with the patient.
Scheme of anti-epidemic measures in the epidemic center

1. Measures aimed at the source of the pathogen:

- timely detection of patients and carriers of pathogenic microorganisms;
- providing early diagnosis of diseases;
- registration of patients and carriers;
- isolation of sources of infection (hospitalization or isolation at home);
- treatment in outpatient settings;
- rehabilitation of carriers and patients with chronic forms of diseases;
- carrying out bacteriological control over the release of the patient from pathogens;
- sanitary and educational work, hygienic education of patients and carriers;
- dispensary supervision of the sick, patients with chronic forms, chronic carriers.

2. Measures aimed at breaking the transmission mechanisms:

- current and final disinfection in the cell;
- sampling of environmental objects for laboratory research;
- Prohibition of the use of food, water and other objects that may be factors of transmission in the cell.

3. Measures aimed at persons who have been in contact with the source of the pathogen:

- active identification of contact persons;
- solving the issue of contact insulation;
- medical observation;
- laboratory examination;
- sanitary and educational work;
- specific and nonspecific prevention.

Carriers and anti-epidemic measures against carriers
Carrier - is the preservation in the body and the release into the environment of pathogens of infectious diseases, which is due to the asymptomatic course of the infectious process (without clinical manifestations).
Carriers are accompanied by immunological shifts, functional and morphological changes

in the infected macroorganism, characteristic of this disease, but does not lead to clinical manifestations.
There are convalescent, transient and healthy carriers.
Convalescent carrier occurs after the disease (for example, diphtheria, typhoid fever, paratyphoid fever, polio, etc.), when a person continues to emit pathogens into the environment. This is due to the preservation of local foci of infection in the human body. Thus, in typhoid fever, the pathogen can persist for years in the macrophage system of the convalescent (in the liver, spleen, lymph nodes, bone marrow), and 3-5% of people form a lifelong carrier. According to the duration of isolation of the pathogen, convalescent carriers are divided into acute (up to 3 months) and chronic (more than 3 months).
Transient carrier is characterized by one or two isolation of the pathogen from a healthy person, in which there were no clinical symptoms of the disease in the last 3 months. The results of the next three bacteriological tests of feces and urine, as well as the results of serological tests are negative.
The so-called healthy carrier can occur against the background of the absence of any clinical manifestations of the disease and occurs in shigellosis, diphtheria, cholera, typhoid fever and others.

From an epidemiological point of view, the most dangerous source of infectious agents is a sick person. However, the number of carriers can be much larger than patients. The absence of clinical manifestations of the disease in carriers contributes to the formation of hidden sources of infection, as they do not seek medical help and remain active members of society. When comparing the epidemiological significance of carriers and patients, it should be emphasized that the main role belongs to carriers, given their predominance in number and latent nature of the pathogen, especially if the carrier of pathogenic microorganisms is observed in "food" and persons equated to them.
Measures to combat carriers are their detection and remediation, in some cases used isolation, removal from work, dispensary supervision. Carriers are detected by laboratory examination of certain contingents of the population in a planned manner and according to epidemic indications. Employees of prescribed groups are routinely examined for carriers of intestinal infections when recruited and periodically throughout the entire period of employment (periodicity is determined by regulations). Persons who have relapsed into intestinal infections, diphtheria, meningococcal infection before discharge from the hospital and during the period of dispensary observation are subject to mandatory examination for carriers of pathogens.

According to epidemic indications, healthy persons who have been in contact with a patient in the foci of intestinal infections, respiratory infections, etc. are subject to examination for carriers. Detected media are subject to mandatory remediation. Employees of the prescribed groups are rehabilitated in a hospital with mandatory quality control before discharge. If the pathogen is detected, such persons are suspended from work related to food, child care in children's institutions.

Measures against the patient as a source of infection are carried out in order to detect and isolate it early. The diagnosis of the disease is formulated by a doctor or paramedic on the basis of the clinical picture. Epidemiological data, results of laboratory and instrumental researches are used for its confirmation.
All cases of infectious diseases are subject to mandatory registration in treatment and prevention facilities. In case of influenza, sore throat, acute catarrh of the upper respiratory tract fill out a statistical coupon (form 25-u). In case of rash, recurrent, typhoid fever, paratyphoid A and B, dysentery, colitis, enterocolitis, toxic dyspepsia (in children under 1

year), measles, diphtheria, scarlet fever, cerebrospinal meningitis, epidemic encephalitis, poliomyelitis, poliomyelitis , viral hepatitis, anthrax, tick-borne encephalitis, malaria, brucellosis, tetanus, pertussis, whooping cough, foot and mouth disease and other infectious diseases fill the urgent message (f-58) and as soon as possible (no later than 12 hours) sent to the sanitary-epidemiological station. In case of detection of quarantine diseases (plague, cholera, smallpox, yellow fever) or for suspicion of them, urgent messages should be sent to the sanitary-epidemiological station immediately with a messenger and a telephone.

Isolation of an infectious patient in many diseases is necessary, especially in highly contagious. In case of detection of plague, cholera, smallpox, anthrax, typhoid fever, typhoid fever, diphtheria, acute viral hepatitis, hospitalization of patients is absolutely necessary. The hospitalization of patients with other infectious diseases should be guided by the severity of the disease and the conditions of the epidemic situation.

However, in most infectious diseases, hospitalization and isolation remain a radical measure, preventing the disease from spreading further. Sometimes temporary isolation of the patient can and should be carried out in a kindergarten, nursery, boarding school. In this case, the isolator must be deployed before sending the patient to the hospital in the children's institution.

According to the decision of the epidemiologist and clinician, the patient can be left at home, but it is necessary to protect the environment from infection and prevent the removal of the infectious agent from the source.

To do this, the patient is isolated in a separate room or part of it - in this case, the bed is separated from another room by a screen; the patient is provided with separate utensils and care items. Family members caring for the patient are instructed by an epidemiologist (or clinician) on the current disinfection of care items, utensils, secretions, etc. Employees of the treatment-and-prophylactic institution and the sanitary-epidemiological station exercise constant control over the patient's condition and over the implementation of the anti-epidemic regime.

Disinfection as an anti-epidemic measure is carried out in order to break the spread of infectious agents. If cases of plague, typhoid fever and some other diseases are detected, disinfection, disinsection and deratization are required. In case of cholera, typhoid fever, paratyphoid fever A and B, dysentery in the epidemic center in the summer, along with disinfection, disinsection is carried out. In such diseases as measles, mumps, rubella, influenza, whooping cough, the causative agents of which are unstable, disinfection is limited to ventilating the room and wet cleaning of surrounding objects.

Measures in relation to persons who have been in contact with the patient are determined by the epidemiological characteristics of a particular infectious disease. In cases of registration of quarantine diseases (plague, cholera, smallpox), all contact persons are isolated in specially deployed hospitals. In the settlement where the patient is found, strict quarantine is established. The content of measures during the observation of isolated individuals is determined by the epidemiological features of the disease.

In case of detection of typhus and typhoid fever, intestinal infections, diphtheria, scarlet fever, measles and other contagious infections, all contact persons are subject to special registration and medical supervision. The timing and content of medical supervision are determined by the epidemiological features of the disease. In cases of detection of infectious diseases in children's organized groups (nurseries, kindergartens, schools) measures are taken to limit children's contact, enhanced medical supervision of contact and their laboratory examination for early detection and isolation of sick children.

In order to prevent the emergence of new cases of diseases in the foci of infectious diseases, specific prevention measures are carried out, and in some infectious diseases - preventive chemoprophylaxis. Specific prevention in the center of an infectious disease is carried out by methods of active and passive immunization, use of bacteriophages, etc. In some cases,

preventive treatment with antibiotics and other chemotherapeutics.

Isolation of patients and carriers

Isolation of the patient is carried out by hospitalization in an infectious hospital or in house conditions. Hospitalization in an infectious hospital can take place in boxes, semi-boxes and wards (with low contagiousness of the infection).

Rules of hospitalization of infectious patients

1. Mandatory hospitalization
   A. In quarantine (conventional) infections - plague, cholera, yellow fever and highly contagious hemorrhagic fevers (Ebola, Marburg, Lhasa). These infections reach large sections of the population extremely quickly and lead to high mortality rates, and are therefore considered the most dangerous in all countries of the world. Measures to detect a disease suspected of plague or cholera are carried out according to special International Sanitary Rules. If a disease is detected, each country must notify the WHO regional office no later than 24 hours. In case of such infections, quarantine is organized, special hospitals are deployed to isolate patients, contact patients and people who leave the cell are observed (isolation for the incubation period).
   B. At especially dangerous infections (ONI). In Ukraine, the list of ONI is given in the Law on Sanitary and Anti-Epidemic Welfare of the Population. Patients with diphtheria, meningococcal infection, typhoid fever, paratyphoid fever, typhoid fever, malaria, tick-borne encephalitis, acute viral hepatitis, anthrax, tularemia, acute meningitis, rabies, tetanus, foot-and-mouth disease, leptospirosis are subject to mandatory hospitalization.
2. Hospitalization according to clinical indications:
   - in severe infectious disease;
   - in children under 3 years;
   - in the presence of concomitant diseases;
   - in the presence of complications.
3. Hospitalization according to epidemiological indications:
   - if the patient belongs to the prescribed groups of the population (employees of the food industry, children's preschool institutions, primary schools, surgical, maternity wards, operating rooms, etc.);
   - if the patient lives in conditions of high population density (dormitories, communal apartments, barracks, boarding schools, prisons, etc.);
   - in the case of illness of a person who lives with an employee of the prescribed group (for example, if a patient with an intestinal infection lives with his wife - a cook, he needs to be hospitalized);
   - in case of illness of a child attending a preschool institution;
   - in case of living of the patient in the conditions of lack of conveniences, for non-observance of sanitary norms and rules, for impossibility of isolation from other family members.

The responsibility for the correctness and timeliness of hospitalization of the patient rests with the doctor who identified him. The doctor decides on the evacuation transport, the procedure and time of hospitalization, coordinates it by phone with the relevant services and at the same time informs the regional SES.
Depending on the conditions, the patient can be hospitalized in cities by transport of disinfection stations, ambulance stations, in rural areas - by transport of CRH, outpatient clinics, individual vehicles, in some cases - by transport of other enterprises and institutions. It is strictly forbidden to hospitalize infectious patients by public transport. The order of hospitalization in each city and district is approved by order of the health department or CRH. Evacuation of patients should be performed within 3 hours in cities and 6 hours in rural areas after receiving notification of the need for hospitalization. After the hospitalization of the patient, the staff of the admission department of the infectious diseases hospital disinfects the transport at a special site. The medical staff of the hospital no later than 24 hours. from the moment of hospitalization of the patient is obliged to inform the SES, which in turn notifies the medical institution that referred the patient. A note on the date and time of hospitalization is made in the patient's outpatient card or in the outpatient journal.

Forms of isolation of the patient in an infectious hospital

1. General Chambers.
2. Boxed chambers:
    - open type - a ward for 1-2 people, divided by partitions that do not reach the ceiling;
    - closed type - the chamber is divided by solid partitions.
3. Semi-box - a ward for 1-2 people, which has a bathroom, a box and an exit to the corridor.
4. Meltzer's box is a ward for 1-2 people, which differs from the semi-box by the presence of a separate external exit, which allows the patient to be hospitalized, preventing his contact with other patients.

Indications for hospitalization of infectious patients in boxes:

- suspected quarantine infections (plague, cholera, yellow fever) and highly contagious viral hemorrhagic fevers;
- especially dangerous respiratory infections;
- especially dangerous infections with a high level of contagiousness (diphtheria, polio, etc.);
- the presence of mixed infections, if at least one of them has an aerosol transmission mechanism.

Indications for hospitalization of infectious patients in semi-boxes:

- severe clinical course of infectious disease;
- unspecified infectious disease;
- especially dangerous infections (except for respiratory infections).

Patients with homogeneous respiratory infections are hospitalized in boxed wards of closed type, and patients with other low-contagious infections are hospitalized in boxed wards of open type.
Providing the infectious hospital with boxes is one of the main factors in preventing outbreaks of nosocomial infections. Treatment of infectious patients is aimed primarily at removing the

pathogen from the body (etiotropic treatment) and restoring body functions (pathogenetic treatment). Before discharge of infectious patients from the hospital, control laboratory tests are performed to assess the quality of etiotropic treatment and release of pathogens from the pathogen. Particular attention is paid to quality control of treatment of patients belonging to prescribed groups.

Indications for outpatient treatment of infectious patients

- Clinical: mild, subclinical, sometimes moderate course in the absence of concomitant diseases that can complicate the course of the disease.
- Epidemiological: treatment of patients who do not belong to the category of catering workers and persons equated to them; patients living in separate apartments; persons who do not live with employees of food companies and children who attend preschool institutions.

In the treatment of an infectious patient at home, anti-epidemic measures are provided, conditions are created to stop the spread of infection. For patients with respiratory infections, separate rooms are allocated, which are ventilated and, if possible, irradiated with ultraviolet lamps. Patients are provided with individual utensils, household items. Current disinfection at home is carried out mainly by physical means: household items and patient care, utensils, linen are boiled for 30 minutes. or 15 minutes - in 2% soda solution. For HIV and tuberculosis, the boiling time is 1 hour. or 30 minutes in 2% soda solution. In some cases, for the current disinfection of the home, the use of disinfectants under the supervision of a physician or family doctor is allowed with mandatory prior instruction on their use.

Self-control Questions

1. The focus of infectious disease.
2. Stages of examination of the epidemic center.
3. Anti-epidemic measures in the center of an infectious disease.
4. Accounting and medical documentation
5. The work of a family doctor in cases of infectious diseases
6. Cabinet of infectious diseases and its functions.
7. Rules of hospitalization of infectious patients.
8. Forms of isolation of patients in an infectious hospital.
9. Measures aimed at the source of infection.
10. Measures are aimed at breaking the transmission mechanism.

Test task

1. “Emergency message” must be sent “

A. No later than 12 hours after detection of an infectious patient.
B. Only after bacteriological confirmation of the diagnosis.

C. After consultation with an infectious disease doctor.
D. After hospitalization of the patient.
E. No later than 24 hours after detection of an infectious patient.

2. Hospitalization of infectious patients is carried out:

A. Special transport of the disinfection service.
B. The patient's own transport.
C. By public transport.
D. All modes of transport.
E. Transport of an infectious disease hospital.

3. The set of measures performed in the hearth to interrupt the transmission of the pathogen includes:

A. Final disinfection.
B. Isolation of the patient.
C. Vaccination.
D. Hospitalization of patients in the hospital.
E. Observations during the maximum incubation period for contact.

4. The set of measures performed in the hearth in relation to the source of infection includes:

A. Isolation of patients.
B. Observations during the maximum incubation period.
C. Vaccination.
D. Final disinfection.
E. Disinsection.

5. Hospitalization of infectious patients should be performed:

A. For 3 hours in cities and 6 hours in rural areas.
B. For 12 hours.
C. Immediately after detection of an infectious patient.
D. The term of hospitalization of the patient after receipt of the message is not regulated.
E. All options are incorrect.

6. Hospitalization of infectious patients is carried out:

A. At especially dangerous infections, on clinical and epidemiological indications.
B. According to clinical and epidemiological indications.
C. Only for epidemiological indications.
D. Necessarily for particularly dangerous infections.
E. According to clinical indications.

7. When does the observation period in the epidemic center end?

A. After the maximum incubation period in contact persons.
B. Immediately after hospitalization of the patient.
C. Immediately after final disinfection.
D. After administration of immunoglobulins and vaccines to contact persons.
E. Immediately after hospitalization and final disinfection.

8. The boundaries of the epidemic center determines ...

A. Epidemiologist.
B. The doctor who first diagnosed an infectious disease.
C. District doctor.
D. Infectious disease doctor.
E. All answers are correct.

9. A patient living in a dormitory is subject to hospitalization:

A. With any infectious disease.
B. In quarantine infections.
C. At especially dangerous infections.
D. In infections with airborne transmission mechanism.
E. In intestinal infections.

10. Emergency notification of an infectious disease is sent to:

A. In the epidemiological department of SES not later than 12 hours from the moment of detection of the patient.
B. In the clinic at the place of residence.
C. To the infectious disease hospital not later than 12 hours from the moment of detection of the patient.
D. To the disinfection station no later than 12 hours from the moment of detection of the patient.
E. To the disinfection station not later than 24 hours from the moment of detection of the patient.

Chapter 3.
Desinfection. Deratization. Dezinsection. Sterilization.

Disinsection.

Disinsection is the study of methods and means of combating arthropods. This term, first used by MF Gamalia to define the means of insect control, has survived after it was established that ticks are also involved in the spread of infectious diseases.

The fight against arthropods is conducted in two directions: 1) preventive - the creation of conditions that inhibit their reproduction, and 2) extermination - the destruction of imaginal and pre-imaginal stages.

The main of these areas is preventive, ie a system of sanitary and hygienic measures, in particular, such as regular body washing and linen change, frequent cleaning, scheduled cleaning of settlements from garbage, reclamation works and more. The system of extermination measures includes the use of physical, biological and chemical agents.

Physical means include: a) mechanical (cleaning with brooms, brushes, catching arthropods with traps, crackers, sticky mass), which in isolation from other methods can not ensure the destruction of any species of arthropods and act as aids; b) physical (UHF currents, low temperature, high temperature in the form of open fire, hot water, steam and dry hot air). The biological method of controlling arthropods is based on the use of their natural enemies (pathogenic microbes, parasitic and predatory insects), as well as ionizing radiation in order to deprive them of the ability to reproduce full-fledged offspring.

Chemicals include substances that destroy arthropods — insecticides, mites — acaricides, larvae — larvicides, eggs — oocytes, repellents — repellents — attractants — attractants. Chemicals are used as follows: 1) dust - finely ground insecticide mixed with an inert filler (talc, kaolin, road dust, etc.); in most duets the insecticide makes 1-2% of all weight; 2) wettable powder is an insecticide, filler, surfactants, excipients; 3) granular powder containing particles of inert substance on which the insecticide is adsorbed; 4) microencapsulated preparation, in which the insecticide is covered with a thin polymer film, through which the preparation is slowly released into the environment, providing a long-lasting effect; 5) long-acting drug - an insecticide introduced into varnishes, paints, polymers; 6) emulsifying concentrate is a dispersed system of two immiscible liquids; 7) aerosol — a dispersed system consisting of solid (smoke) or liquid (fog) particles that are in a suspended state; 8) bait (dry or liquid).

Depending on the ways of penetration of insecticides into the body of arthropods they are divided into the following groups:

1) respiratory poisons or fumigants (hydrocyanic acid and substances based on it, methyl bromide, ethylene oxide, fir oil);
2) 2) intestinal poisons (talfton, borax, supromite, suprozole, boric acid, formalin, baygon);
3) 3) contact poisons (pyrethrophos, neopin, neopinate, nittifor, cresol, lysol, drug K, creolin, kerosene);
4) 4) poisons of combined action (insectolan, dibrophos, chlorac, chloropine, HL insorbicide, insect polymer, DDVF, chlorol, trolene, neocide, trichlophos, acetophos, carbophos, Prima-U, carbosol, neophos-2, perphos -2, phenosol-2, sulfidophos, sulfopine, pedisulf, etc.).

Repellents are used in cases where it is impossible to destroy arthropods with insecticides (open

area). With the help of repellents you can protect not only an individual, but also entire teams of loggers, geologists, land reclamation workers, builders and others. The protective effect of repellents is due to the fact that they neutralize the smell of human skin, act on the sense of smell of arthropods, scaring them away, as well as provide mechanical protection of the skin. To protect children, it is advisable to use cream "Eucalyptus" and emulsion "Til", to protect adults - dibutyl phthalate, dimethyl phthalate, rapudine, DET, rebepine, retofezol, REDET, as well as various lotions and creams.

Substances that attract insects (attractants) increase the effect of insecticides and reduce their costs. Most often used as attractants formalin in milk, ammonium carbonate, acetic acid, sugar, feed and sugar molasses, bread kvass, beer, chlorophos solution, esters of carboxylic acids, alcohols, essences.

Means of disinsection in the fight against individual arthropods are slightly different and depend on their type and place and time of these works.

Fly control is carried out by the Department of Public Utilities (scheduled collection and regular removal of household waste in cities), the veterinary service (collection and removal of manure from farms).

The comprehensive plan for the control of infectious diseases of the SES provides for a section of anti-mosquito measures, which all managers of enterprises and organizations are obliged to perform.

Measures for landscaping and sanitation of populated areas should prevent the reproduction of flies in organic waste. This can be achieved by constant cleanliness of the premises and areas, proper collection and disinfection.

The following agents are used to kill flies: 2% chlorophos fungi with ammonium carbonate, 24 times a month, 0.5% aqueous emulsion of dichlorvos, 2-3 times a month, 0.3-0.5% aqueous emulsion of dicresyl , 3-4 times a month, 0.2% aqueous emulsion of trolene, 2-3 times a month, alphacide - tablets, they are dissolved in fresh water, applied with a swab to the landing sites of flies (frames, tiles, window glass, etc.) .), kilzar - powder, used in the same way, primacidliquid, used in the same way, riapan-M - solution of the drug 1: 3, used in the same way, perfos- 1 - aerosol, pi-retrol-L - aerosol, muscanol - ready before drinking liquid.

Insecticide screen gives a good effect when used on food objects: 10-20% of sugar is mixed with 10% chlorophos solution. The paper treated with this liquid is dried. Before hanging, moisten with plain water.

To control flies, paper tapes are used, on which an adhesive mass of the following composition is applied: machine oil — 64.2%, polyisobutylene — 26.8%, rosin — 9%. This mass does not dry on paper for 30 days.

<u>The reasons for the spread of lice among the population are:</u>

a) weakening of attention to the fight against pediculosis in connection with the so-called elimination of typhus;
b) insufficient provision of the population with baths, means of lice control;
c) insufficient equipment of medical institutions, baths with dry heat and combined chambers;
d) incomplete and low-quality examination of pediculosis foci and untimely anti-pediculosis measures;
e) poorly organized health education, especially among children and adolescents.

Preventive measures are reduced to regular body washing and linen changes, proper organization of the network of baths and hairdressers, active detection of lice during medical examinations of patients at home or in hospitals (clinics), regular examinations in organized groups (preschools, schools, vocational schools, dormitories) , homes for the disabled, etc.). In children under 5 years, pregnant women, nursing mothers, people with damaged skin, it is

advisable to destroy lice mechanically.
The following insecticides are used to control the main pediculosis: 0.15% carbophos emulsion (10-50 ml per treatment), 20% benzyl benzoate suspension (10-30 ml per treatment), nittifor lotion (50-60 ml), 10% aqueous solution of soap and kerosene emulsion, pyrethrum, 0.06% aqueous solution of sulfidophos emulsion, soap "K".
After treatment of hair with insecticides and exposure for 40 minutes - 1 hour, it must be rinsed with acidified form.

Prevention of the spread of pediculosis is carried out constantly, which should be specified in the comprehensive annual plan of the family medicine clinic. In the outpatient clinic should be available laying:
- for examinations for pediculosis;
- for antipediculosis treatments.

Laying for examinations for pediculosis
Desk lamp.
Dandruff.
Thick crest.
Comb soaking solution. In the absence of a disinfectant solution, fill the comb with boiling water.
Laying for antipediculosis treatments.
Oilcloth or linen bag for the patient's belongings.
Galvanized bucket or tray for burning hair.
Oilcloth cape.
Rubber gloves.
Scissors.
Thick crest.
Hair clipper.
Etna.
Scarves (2-3).
Cotton.
Table vinegar or acetic acid (5-10%).
Insecticides for human treatment.
Insecticides for treatment of premises and linen.
List of antipediculosis drugs with instructions regarding their manufacture and use.

1. Carbophos - 0.15% water-emulsion solution. To make the first liter of 0.15% emulsion take 3 ml of 50% emulsifying concentrate of carbophos, dilute it in 1 liter of water at room temperature. The drug acts at all stages of development of lice. It is used exclusively by medical professionals. The rate of use for treatment is 10-50 ml, exposure - 30 minutes.
2. Benzyl benzoate - 20% water-soap emulsion or 20% emulsion (Pedicide). To make 100 ml of 20% suspension of benzyl benzoate take 2 g of soap (green or household crushed), diluted in 78 ml of warm water, add 20 ml of benzyl benzoate, mix thoroughly. The resulting suspension is applied to the hair 10-30 ml per 1 treatment, exposure 30 minutes
3. Lotion "Nittifor" (Hungary) - a factory-made drug, the rate of use per treatment is 5060 ml, exposure 40 minutes.
4. Lotion "Loncid" - a factory-made drug, the rate of use per treatment of 30-50 ml, exposure 30 minutes.

The method of application of drugs

Apply the required amount of the product on the hair (depending on the thickness and length of the hair), tie the head with a plastic scarf and towel, keep the appropriate time according to the instructions, rinse under running water with soap or shampoo. Then apply a warm 5-10% table vinegar, tie a plastic scarf and towel, leave for 30 minutes, rinse under running water, then comb with a thick comb. Children under 5 years, nursing mothers, pregnant women, patients with eczema, allergies are treated without the use of pediculocides. The mechanical method can also be used in the presence of single (1-10 pcs.) Lice at any stage of development. Disinsection of premises and linen is carried out with open windows with insecticidal cylinders Carbosol, Neofos-2 in the absence of people, birds and other animals. Food is hidden, the aerosol is not sprayed near the fire. It is forbidden to smoke, drink or eat while working with insecticides. After 2-3 hours, carry out wet cleaning and thoroughly ventilate the room.

To control lice that have settled in the folds of clothing, it is recommended: a) boiling linen in 2% soda solution, b) soaking linen in 0.06% sulfidophos solution, 0.15% carbophos emulsion, 20% soap and kerosene emulsion, 0.25% emulsion dikreznlu, c) sprinkled with 2% methylacetophos dust, 1% neopin dust, 2% sulfolane dust, 1% sulfopine dust, 10% dilor dust, d) spraying folds of clothes, hats with drugs "Neofos-2", "Carbozol", "Pedisulf". In extreme situations, when it is impossible to use other means of combating pediculosis, you can use butadione, taking it orally 0.15 g 4 times a day for 2 days (1.2 g). The dose for children 4-7 years is 0.05 g 3 times a day, 8-10 years-0.08 g 3 times a day, older than 10 years - 0.12 g 3 times a day for 2 days.

Prohibited to control lice: hellebore water, DDT and HCH (including soap). 5% boric ointment is not formally prohibited, but it is very poorly washed off the hair, so it is rarely used.

Cockroach control.

Preventive measures consist of daily thorough cleaning of the premises, removal of food waste and debris. maintenance of water taps in proper condition, timely repair of premises. Cockroaches can be killed indoors by the following means: RM insects, dibrofin insects, borax insects, D insects, sulfolane, riapan and riapan-A, kilzar, carbosol, suzol, perfos-P, pyrethrol- P and other insecticides, most recently appeared on sale. We should not forget about boric acid, the use of which is especially effective in the form of baits. Its content in the bait should be 3040% (at least 20%). It is better to dissolve the acid not in hot water, but in milk, bread kvass, sugar syrup and then add it to mashed potatoes, porridge, soaked bread, grease with oil (this also prevents the bait from drying out quickly). The death of cockroaches when using boric acid begins on the 7th day and ends on the 28th or 30th day. You can prepare a paste consisting of brewed potato starch (50 g), boric acid (100 g) and 850 ml of water. With a paintbrush or tampon apply the paste on furniture, walls, baseboards, inject into the cracks. If necessary, you can repeat the treatment in 2 weeks.

Pest control

Deratization is a set of measures aimed at destroying rodents - sources of infectious agents and protecting crops, food and property from them. Rodent control measures also consist of preventive and exterminating, forming a single complex. Preventive measures, in turn, can be divided into general sanitary (timely removal of debris, equipment impermeable to rodents, storage of food in geretically closed containers, etc.), sanitary (development of building structures that prevent rodents from entering the building, closing windows, ventilation ducts, special equipment for sewage, water supply, etc.), agricultural (careful harvesting, protection of hay or straw, compliance with veterinary and sanitary rules on farms, poultry farms, etc.). Extermination measures are aimed at destroying rodents in all their habitats and creating conditions in which it would be impossible to reproduce their numbers. The greatest effect is given by simultaneous use of mechanical destruction of rodents by means of various tools of catching and chemicals - raticides. Raticides are used in the form of food-based poisoned baits,

by pollination and water poisoning, by pollination of burrows, passages leading to objects that are often visited by rodents. In addition, poisonous substances can be used in the form of gases , holds of sea and river steamers, granaries, etc.). The following raticides are allowed for deratization measures: ratindan (difenacin dust), zoocoumarin, zinc phosphide, crisis, monofluorine, barium fluoroacetate, fluoroacetamide, glyphtor. Good results were obtained with the use of paste "Vazkum" (Vaseline-50%, talc-49.5%, zoocoumarin - 0.5%), which is applied to sheets of cardboard measuring 25x50 cm and laid out on the paths of rodents. The biological method of rodent control (the use of Salmonella by Merezhkovsky and Isachenko) is used to a small extent, because rodents that have suffered from the disease acquire long-term (3-4 months) immunity. To increase the effectiveness of this method, sublethal doses of raticides can be added to the bait.

Disinfection and sterilization.

Disinfection (disinfection) is a set of measures aimed at the destruction or removal of infectious diseases in the environment. The main purpose of disinfectants is to break the mechanism of transmission of the pathogen by disinfecting possible transmission factors. Disinfection is widely used in a set of preventive and anti-epidemic measures.

There are the following disinfection measures:

1. Actually disinfection - the destruction of pathogenic microorganisms in the environment.
2. Disinsection - destruction of arthropod vectors.
3. Deratization - extermination of rodents.
4. Sterilization - complete destruction of microorganisms and their spores on the environment.

The following types of disinfection are distinguished:

a) focal disinfection - is carried out in the center of an infectious disease, ie where the infectious patient is or was, for example, in the apartment or infectious department;

b) preventive disinfection is the disinfection of facilities where pathogens are suspected to be present without an identified source of infection (eg disinfection of drinking water, food, disinfection measures in public places - toilets, hairdressers, train stations, hotels, etc.)

Focal disinfection

Focal disinfection is divided into current and final.

1. Current disinfection is carried out in the presence of the source of infection (patient, carrier) and is aimed at destroying pathogens immediately after their removal from the body. Thus, in the patient's environment perform constant disinfection of feces, vomit, sputum, dressings and other objects that may contain microorganisms. Current disinfection is carried out throughout the period while the patient or carrier is the source of infection, ie until the end of the contagious period.

   Current disinfection is carried out by medical workers in infectious hospitals at hospitalization of patients. If the isolation of infectious patients is carried out at home, the current disinfection is performed by the patient's relatives. Disinfection is considered timely if it is started no later than 3 hours. from the moment of detection of the patient.

   The current disinfection is of the greatest importance in intestinal infections, because

their pathogens are periodically excreted from the body with excrement easily accessible to disinfection. Disinfect the patient's use, utensils, sanitary equipment, patient's underwear, etc. are also disinfected.

In respiratory infections, current disinfection is less important, but it makes it possible to reduce the number of pathogens in the air. Use ventilation, UV UFO, wet surface treatment with disinfectants, sputum disinfection, etc.

- The simplest methods of disinfection are used for current disinfection at home:
- - wet cleaning with detergents;
- - boiling dishes in 2% soda solution for 15 minutes;
- - boiling laundry in 2% detergent solution before washing;

-disinfection of excrement (for intestinal infections) for 1 hour. disinfectant solutions 2. Final disinfection is carried out in the epidemic center after removal of the source of infection (in the apartment - after hospitalization, in the infectious department - after discharge or death of the patient). The purpose of the final disinfection is to destroy the pathogens left in the room where the patient was. In contrast to the current disinfection is carried out once.

Premises, excrements, vomit, linen, household items and other objects that could be contaminated are subject to disinfection.

Final disinfection is most important in foci of infection in which pathogens are in the environment for a long time. The scope and timing of focal disinfection, the choice of objects to be disinfected, and the means for its implementation depend on the properties of the infectious agent, the sanitary condition of the foci and are regulated by regulations. High resistance of pathogens in the environment requires a high level of disinfection. Therefore, employees of the disinfection service (for example, plague, cholera, typhoid fever, Brill's disease, Ku-fever, salmonellosis, tuberculosis, ornithosis, diphtheria, fungal diseases of hair, nails, skin, etc.) are involved in its implementation. In the foci of viral hepatitis A, polio, dysentery, rotavirus infection, acute intestinal infections of unknown etiology, the final disinfection can be carried out by employees of medical and children's institutions, the population with the consent of epidemiologists.

Preventive disinfection

Carried out in the absence of an identified source of infection, but when its presence is assumed. Current disinfection is constantly performed at water supply, sewerage, catering, enterprises that process and sell food and raw materials of animal origin, in hospitals, including dental clinics. Current disinfection is also carried out in places of mass concentration of people (railway stations, shops, hairdressers, transport, toilets, swimming pools, etc.), where the probability of the presence of sources of infection among the population is assumed.

Disinfection methods

There are the following methods of disinfection: mechanical, physical and chemical.

The mechanical method of disinfection involves wet cleaning, washing, washing, shaking and beating. This also includes the filtration of air and water, which consists in the purification of foreign particles, including microbes. The mechanical method does not lead to complete release of microorganisms, so it is usually combined with physical and chemical.

The physical method of disinfection is the disinfection of objects by the action of physical

agents: ultraviolet radiation, dry hot air, water vapor, boiling, etc.
Boiling at 100 ° C for 15 - 45 minutes used for processing of linen and ware, the remains of food. The antimicrobial effect of boiling is enhanced by adding 2% sodium bicarbonate or soap to the water.
Radioactive radiation destroys all vegetative forms of microorganisms and their spores. It is widely used for sterilization of disposable medical instruments, sutures, etc.
Dry hot air (dry heat) has bactericidal, virucidal, insecticidal and sporocidal effects. At a temperature of 160-1800C dry air is used in air sterilizers for disinfection of laboratory utensils, instruments, sterilization of metal, glass and silicone rubber, in the chambers - for disinsection of clothing, mattresses, pillows, blankets. At dry-heat processing at a temperature above 100 ° C the structure of plant and animal fibers changes, at a temperature of 170 ° C they are charred.
Hot steam is used in special chambers - steam, steam and steam formalin. Saturated water vapor has bactericidal, virucidal and sporicidal action. Its properties are enhanced at elevated pressure, which is used in autoclaves for sterilization of medical instruments. The steam-air mixture is used in a steam-formalin disinfection chamber for processing of things of the patient and bed linen. The chamber method of disinfection is used for plague, cholera, typhoid fever, epidemic typhus, Brill's disease, Ku fever, anthrax, hemorrhagic fevers, typhoid fever and paratyphoid fever, tuberculosis, diphtheria, mycosis of the skin and nails.
For disinfection of fur and leather products and other unstable materials are designed steam-formalin chambers, which use formalin vapor at a temperature of 50-60 ° C.
UFO is widely used for disinfection of indoor air in hospitals, dental clinics and more. The chemical method of disinfection is the most common and generally accepted in hospitals. It involves the use of chemicals that have a detrimental effect on infectious agents.
Modern disinfectant, as a rule, is a composition of several active substances in proportions that allow to achieve maximum synergy with the most resistant microorganisms, and also contain functional additives that facilitate washing and disinfection.
Modern disinfectants must meet several basic requirements, without which no drug can be recommended for use:

- microbiological efficiency;
- high degree of resistance to organic impurities (for example, blood);
- aggressiveness towards construction materials intended for the manufacture of medical instruments;
- stability during storage and transportation;
- safety for medical staff and patients;
- convenient form of issue;
- efficiency.

Characteristics of the main groups of disinfectants
(according to the active substance)

I. Halogen-containing agents (chlorine-containing - chlorantoin, deactin; iodine-containing, bromine-containing, etc.). The active substances of this group are chlorine, iodine, bromine. Thus, iodine is one of the skin antiseptics allowed for the treatment of injection and surgical fields. Chlorine-containing products are widely used in hospitals, for disinfection of water in swimming pools, in catering establishments, etc. They have a wide range of antimicrobial action (bactericidal, tuberculocidal, virucidal, fungicidal, sporocidal properties). The advantages of chlorine-containing drugs include speed of action and relatively low cost. However, they are aggressive against structural metals, toxic, irritate the mucous membranes of the upper respiratory tract and eyes, can form environmentally hazardous compounds and cause corrosion of metals.

II. Peroxidants ("Dexoxon-O", "Dismozon-Pur", "Odoxon", etc.) contain active oxygen, hydrogen peroxide, peroxide compounds, ozone. Most products have a wide range of antimicrobial action. Peroxidants are environmentally friendly, easy to However, they can have a corrosive effect, low resistance, which limits the shelf life of drugs, high irritant effect on mucous membranes and respiratory organs.

III. Aldehyde-containing agents ("Lysoformin-3000", "Septodor Forte", "Descoton Forte", etc.). Contain such active substances as formaldehyde, glutaraldehyde, orthophthalic aldehyde, succinic aldehyde. They have a wide range of antimicrobial action: bactericidal, tuberculocidal, virucidal, fungicidal, sporocidal properties. Aldehyde-containing agents are multi-purpose in hospitals, almost do not cause corrosion of metals, are effective in the presence of organic compounds. The disadvantages of drugs in this group can be considered the ability to record organic contaminants (blood, mucus, pus, etc.), which requires prior washing of medical devices. Aldehyde-containing products also irritate the skin and mucous membranes.

IV. Surfactants. This group includes Quaternary ammonium compounds ("TIME - Defect", "Dekonex 51 DR", "Septodor", etc.), which have antimicrobial action, amines and ampholytic surfactants. A characteristic property of these compounds is that they have a washing effect, have no odor, do not cause corrosion of metals. However, surfactants show a narrow spectrum of antiviral activity, the absence of tuberculocidal and sporocidal. In the presence of organic substrates, their antimicrobial action is reduced. They change the permeability of the microbial cell membrane, so they are widely used in composite products together with other disinfectants.

V. Guanidine-containing agents (Vitasept, Gembar, etc.) This group of disinfectants includes drugs whose active ingredients are polyhexamethyleneguanidine phosphate, polyhexamethyleneguanidine hydrochloride, chlorhexidine bigluconate, etc. Guanidine-containing agents are able to form a film on the treated surfaces, which provides a long-lasting residual bactericidal effect. The disadvantages of the drugs are the narrow range of antimicrobial activity and the formation of a stable film on the treated surfaces.

VI. Alcohol-containing products ("Aerodesin 2000", "Bacilol AF", "Denex Solarcept", etc.). The group is represented by disinfectants containing alcohols: ethanol, propanol-1, propanol-2, 2-ethylenehexanol, n-propanol, phenoxypropanol, as well as composite agents based on them in combination with other active substances. Disinfectants of this group have a wide range of antimicrobial action: bactericidal, tuberculocidal, virucidal properties, but do not have sporocidal action. The drugs are environmentally friendly, do not leave stains and sediment after evaporation. However, alcohol-containing drugs evaporate quickly, which leads to a decrease in concentration, and can be inactivated by organic contaminants.

VII. Composite preparations. This is the most numerous group of drugs ("Dekonex 50 FF", "Korzolex plus", "Lysoformin special", "Septodor Forte", etc.). The combination of drugs from two or more groups allows to expand a spectrum of

antimicrobic action of means, provides at the same time washing properties. Therefore, composite drugs are widely used for combined treatment of medical instruments: simultaneous disinfection and pre-sterilization cleaning.

Modes of processing medical instruments

All medical devices, if they come into contact with blood, wound surface and mucous membranes during operation or can cause damage to them, must be carefully treated, which includes three stages: disinfection, pre-sterilization cleaning and sterilization.

Disinfection

After use, all medical devices are subject to immediate disinfection, which is carried out by physical or chemical methods.

Physical method. Boiling medical products in distilled water for 30 minutes is most often used to disinfect glass, rubber, metal, and heat-resistant polymeric materials. or in 2% soda solution - 15 minutes.

Among the physical methods for disinfection of products made of heat-resistant materials can also be used steam (in a steam sterilizer at t 110 ° C for 20 minutes) and air (in an air sterilizer at t 120 ° C for 45 minutes) methods.

The chemical method of disinfection is the most common and generally accepted in the hospital. This is a complete immersion of medical instruments in disassembled form in one of the disinfectant solutions in a closed glass (plastic, enameled) vessel for 60-120 minutes. depending on the disinfectant solution (concentration and exposure according to methodical recommendations).

All disinfectants must have a registration certificate and be accompanied by guidelines for their use.

In the case of using such disinfectants as "Ecotab-forte", "Septamine", "Septodor-forte", "Septodor", the two stages of treatment (disinfection and pre-sterilization cleaning) are combined into one.

After disinfection, the products are thoroughly washed under running water and subjected to pre-sterilization cleaning.

Disinfection, collection and storage of disposable instruments are carried out in accordance with the instructions of the Ministry of Health of Ukraine from 22.10.93 №223 ("Instructions for collection, disinfection and storage of used disposable medical devices from plastics"). All disposable medical devices are boiled for 30 minutes after use without rinsing and disassembly. or for 60 minutes immersed in a disinfectant solution. After disinfection, disposable products are collected in containers and stored until disposal.

Pre-sterilization cleaning involves the removal of protein, fat and other contaminants, drug residues.

For pre-sterilization cleaning of medical instruments use one of the following detergents: "Biolot", "Biodez", "Biomy", "Bodefen" or "Lotus", "Lotus-automatic" with the addition of hydrogen peroxide.

Pre-sterilization cleaning is carried out by manual or mechanized methods (using installations, machines). In the case of mechanized cleaning, the tools are immersed in the machine and the processing is carried out in accordance with the operating instructions.

The quality of pre-sterilization treatment should be constantly checked by objective methods of control by testing for the presence of blood residues and detergents. At least 1% of the cleaning instruments are tested by samples. The results of the inspection are recorded in a separate journal. Azopyramine and Fakel reagents are used to detect blood residues, and phenolphthalein detergents are used. In the case of positive samples, the entire batch is reprocessed and the reasons for unsatisfactory cleaning of medical instruments are determined. The control of pre-sterilization cleaning is carried out by the staff of SES and disinfection service once a

quarter, the self-control is carried out by the staff of the dental clinic daily, and the senior nurse - at least once a week.
Azopyramine test
Azopyram detects the presence of hemoglobin, peroxidases of plant origin (plant residues), chloramine, chlorinated lime, detergents with bleach, rust and acids.
Method of azopiram test. Azopiram is treated with a working solution of the examined object - wiped with a swab dipped in the reagent, or with a pipette apply a few drops of reagent. If there are traces of blood immediately or no later than 1 minute. after contact of the reagent with the contaminated area, a color appears, initially purple, which then quickly, within a few seconds, turns pinkish-purple or brownish. Coloring that appears less than 1 minute later after applying the reagent to the subject, is not taken into account.
Test with reagent "Torch"
1-2 drops of solution are applied to medical devices. In the presence of residual blood in 3-5 minutes pink or cherry color appears.
Phenolphthalein test
A 1% solution of phenolphthalein must be prepared for the phenolphthalein test. 1-2 drops of solution are applied to medical devices. If there is a residue of the washing solution, a pink color appears.
After the test, regardless of the results, remove the remnants of reagents from the examined items, rinse them with water, then again carry out pre-sterilization cleaning of these products.

Basics of sterilization. Methods and modes of sterilization
Sterilization ensures the death of vegetative and spore forms of pathogenic and non-pathogenic microorganisms. The following sterilization methods are used:
1. Thermal (steam, air, glasperlene sterilizers).
2. Chemical (gas sterilizers, disinfectant solutions).
3. Radiation (installations with a radioactive source of irradiation for industrial sterilization of disposable products).

Based on fundamentally new technologies, new types of sterilizers have been created - plasma and ozone.
Steam and air sterilization methods are most often used in the practice of LPZ operation. Steam method. Saturated water vapor under pressure is used for sterilization.
Processing modes:
a) t 132 ± 2 ° C - 20 min. at a pressure in the chamber of 2,0 kgf / cm2;
b) t 120 ± 2 ° C - 45 min. at a chamber pressure of 1.1 kgf / cm2.

Mode "a" is recommended for processing of products from corrosion-resistant metals, glass, textile materials.
Mode "b" - for products made of rubber, latex and certain polymeric materials (high density polyethylene, PVC - plastics).
Air method. For sterilization use dry hot air in drying cabinets.
Processing modes:
a) t 180 ° C (+2 -10) ° C - 60 (+5) min .;
b) t 160 ° C (+ 2-10) ° C - 150 min.

Used for metal, glass and silicone rubber products. The method is not suitable for sterilization of textile products.
Sterilization of products can also be carried out directly on the shelves of the oven, after which they are laid out on a sterile table and stored for no more than 12 hours.
Gas method. For sterilization use ethylene oxide, a mixture of ethylene oxide and methyl bromide in a ratio of 1:25, a vapor of aqueous or alcoholic solution of formaldehyde.
Gas sterilization as a "cold" sterilization method is used for thermolabile medical devices - ethylene oxide and a mixture of ethylene oxide and methyl bromide at temperatures of 18 °, 35

°, 42 ° and 55 ° C, aqueous formaldehyde solution at 70 ° and formaldehyde vapor in ethyl alcohol at temperatures of 42 ° ,, 45 °, 65 ° and 80 ° C.
Chemical method. For sterilization use one of the sterile disinfectants in accordance with the guidelines, for example:
a) hydrogen peroxide (6% solution) - complete immersion of products in closed vessels at t 18 ° C, exposure 360 min., t 50 ° C - 180 min .;
b) dexoxone-1 (1% solution) at t not less than 18 ° C, exposure - 45 minutes;
c) glutaraldehyde from Reanal (Hungary), pH 7.0-8.5 at a temperature not lower than 20 ° C, exposure 360 min.
The temperature of the solutions during sterilization is not maintained.
The chemical method of sterilization is used for products made of polymeric materials, rubber, glass, corrosion-resistant metals, other materials that do not withstand heat treatment.
After sterilization, the products are washed with sterile water, removed from the solution with sterile tweezers, alternately transferred to 3 sterile containers with sterile distilled water (in the case of 6% hydrogen peroxide solution - in two) and stored in sterile closed boxes for no more than 3 days in case of storage on the laid out sterile table - no more than 12 hours.
Maintaining the sterility of medical devices from the moment of their sterilization to the beginning of their intended use is one of the important moments of their processing.
In recent years, widely used chambers for storage of sterile products - special cabinets equipped with quartz emitters that provide a mode of maintaining the sterility of instruments.

Sterilization quality control

Physical, chemical and bacteriological methods are used to control sterilization equipment.
The physical method of control is carried out with the help of control and measuring equipment (manometers, timers), which allows to record the temperature and pressure in the sterilization chamber. This method is easy to use, but the temperature measured by the equipment does not reflect the temperature in the sterilized products. Therefore, this type of control is complemented by other methods that allow you to correct the shortcomings of instrumental methods.
For bacteriological control, biological indicators are used, which contain a number of viable microorganisms with high resistance to inactivation in the sterilization process. The disadvantages of this method of control are that the evaluation of the effectiveness of sterilization is carried out only after 48 hours, ie the evaluation of the results becomes known after the use of sterilized products.
In recent years, the chemical method of control has become increasingly important. Its advantages are accuracy, speed of sterilization evaluation and ease of use. To do this, during each sterilization cycle to air or steam sterilizers lay thermal indicators in the amount of at least 5. Unsatisfactory sterilization control results require re-sterilization of all medical instruments (material), technical inspection of the sterilizer and elimination of defects.

Self-control questions

1. Definition of "disinfection" and methods of its implementation.
2. Groups of chemical disinfectants.
3. Quality control of disinfection.
4. Definition of "deratization".
5. Types of rodent control works.
6. Definition of "disinsection".
7. Disinsection methods.
8. Definition of "sterilization" and its stages.
9. Sterilization quality control.

10. Types of rodent control works.

Test task

1. Focal disinfection is divided into:

A. final and preventive;
B. current and final;
C. preventive and chamber;
D. current and chamber.

2. Select the definition of disinfection:

A. a set of measures aimed at destroying pathogens of infectious diseases in the environment;
B. a set of measures aimed at the destruction of rodents;
C. a set of measures aimed at reducing the number of pathogens;
infectious diseases in the environment;
D. a set of measures aimed at the complete destruction of pathogens of infectious diseases, their spores and non-pathogenic microorganisms in the environment.

3. To assess the quality of pre-sterilization cleaning of medical instruments use:

A. bioassays;
B. indicator paper;
C. azopyramine and phenolphthalein samples;
D. microbiological method.

4. To control the quality of sterilization of medical instruments use:

A. chemical indicators, thermometry;
B. test with reagent "Torch";
C. azopyramine and phenolphthalein samples;
D. microbiological method.

5. Focal disinfection is carried out:

A. when identifying the source of an infectious disease;
B. in crowded places (railway stations, dormitories, children's preschools, etc.);
C. if it is possible to spread infectious diseases at an unknown source of infection;
D. at the enterprises of the food industry.

6. Choose environmentally friendly methods of rodent control:

A. physical, chemical;
B. chemical, biological;
C. mechanical, biological;
D. chemical, radioactive.

7. Deratization is:

A. destruction of rodents - sources of infectious agents and protection from them of crops, food

and property;
B. destruction of insects and rodents - sources of infectious agents;
C. destruction of rodents - sources of infectious agents;
D. protection against crops, food and property from rodents.

8. Repellents do not use:

A. for clothing;
B. for sawing in living quarters;
C. for impregnation (application on mosquito nets, nets, etc.);
D. for application to exposed skin.

9. The mechanism of action of insecticides:

A. destroy vectors;
B. attract carriers;
C. scare away vectors;
D. all options are correct.

10. Disinsection should be carried out in the centers of the following infectious diseases:

A. leptospirosis;
B. typhus;
C. anthrax;
D. yersiniosis.

Chapter 4.
Preventive vaccination against infection diseases.

Vaccine prophylaxis is the artificial creation of an immune response by introducing a vaccine into the human body in order to form a resistance to infection.
The beginning of a successful fight against infectious diseases is considered to be 1798, when the English doctor Jenner invented a method of vaccination with material from smallpox in cows to prevent infection with smallpox. He called the vaccination method vaccination, and the material taken from cowpox a vaccine (from the Latin "vacca" - cow). The smallpox vaccine has been used for over 150 years, and since 1958 work has begun to eradicate smallpox worldwide. In October 1977, the last case of smallpox was registered in Somalia, and on May 8, 1980. The WHO has declared the elimination of this disease on the planet. From now on, smallpox vaccination has been removed from the preventive vaccination calendar. The set of measures that led to the destruction of smallpox has become a model for the elimination of many diseases using the method of active immunization.
Since 1974, in accordance with the "Extended Program of Immunization" in all countries of the world provides mandatory vaccination against tuberculosis, diphtheria, tetanus, pertussis, polio, measles. The WHO has also recommended that hepatitis B vaccination be included in the vaccination calendar from 1997 onwards.

Mechanisms of formation of postvaccination immunity

There are two main forms of anti-infective immunity: nonspecific and specific.
Nonspecific immunity protects a person not only from pathogens of infectious diseases, but also from other substances, allows you to maintain homeostasis. Nonspecific adverse effects are caused by various factors: the barrier function of the skin and mucous membranes, the

bactericidal action of gastric acid, the complement system, interferons, lymphokines, etc.
Specific immunity, directed against specific pathogens, is divided into hereditary (species) and acquired.
Hereditary immunity was formed in the process of phylogeny and provides species immunity to specific microorganisms (for example, known human resistance to rinderpest, avian cholera, etc.).
Acquired immunity is divided into natural and artificial. Naturally acquired immunity occurs after an infectious disease, when a person is immunized with small doses of the pathogen (active immunity) or due to maternal antibodies that enter the body of the child through the placenta and breast milk (passive immunity). Artificially acquired immunity is formed after the introduction of artificial specific immunotropic drugs. After the introduction of vaccines (weakened or killed microorganisms, their toxins) in the human body antibodies to the pathogen are formed, but the disease does not develop. Thus active immunity is formed. Vaccines provide long-term protection against a specific infectious disease and are used to prevent it.
With the introduction of drugs containing antibodies (immune sera and immunoglobulins) creates a passive artificial immunity. It provides short-term protection, so such drugs are used for emergency prevention of some diseases (rabies, tetanus) and for the treatment of some infectious diseases (diphtheria, botulism, etc.).
Humoral immunity is the body's resistance to infection due to the presence of specific antibodies. Vaccine prophylaxis is aimed at creating an active artificial anti-infective immunity by introducing into the human body antigens of an infectious agent in the form of a vaccine. After the initial introduction (vaccination) into the non-immune organism of the vaccine strain of the pathogen in the blood appear antibodies of class JgM with subsequent switching to the synthesis of antibodies of class JgG, immune memory cells are formed. After repeated administration of the antigen (revaccination) due to the inclusion of memory cells in the blood quickly accumulate protective antibodies and there is a so-called "booster" effect. In this case, almost immediately begins the production of specific antibodies and their level may be higher than after the initial introduction of the antigen. The third dose of antigen usually further enhances the formation of antibodies, but subsequent additional doses of antigen may not lead to increased production, but on the contrary - to immunosuppression.
The main patterns of the immune response used in immunoprophylaxis:

- obtaining intense and long-lasting immunity is ensured by repeated administration of vaccines;
- the immune response to vaccination is specific and individual. Active immunization does not ensure the development of all vaccinated children with the same degree of immunity;
- the highest level of artificial immune response can be obtained against infections, after the transfer of which creates a fairly stable natural immunity (measles, rubella, mumps, etc.);
- active immunization causes the formation of immunity after a certain period of time, so it is advisable to use it mainly for prophylactic purposes.

Classification and characterization of basic vaccines
Classification of vaccines
1. Live vaccines.
2. Inactivated vaccines:
a) corpuscular;
b) chemical;
c) recombinant;
d) toxoids.

Characteristics of live vaccines

Live vaccines are immunoprophylactic drugs made on the basis of attenuated (weakened) strains of infectious diseases in the absence of virulence and preservation of antigenic and immunogenic properties of microorganisms. Due to the preservation of the ability of microorganisms to multiply in the body of a vaccinated person, a vaccine infection develops without pronounced clinical symptoms, which causes the formation of a stable immune response.

Advantages of live vaccines:

- stimulate the formation of long-lasting and stable immunity;
- a single injection of the vaccine (except for the polio vaccine) is sufficient to create a protective level of antibodies;
- live vaccines are administered in different ways: subcutaneously, intradermally, intranasally, per os.

Disadvantages of using live vaccines:

- the need to comply with the "cold chain" (from manufacture to use, the vaccine should be stored and transported at a temperature of +4 - + 8C);
- when administering live vaccines, it is not recommended to use disinfectant solutions, which can remain on the skin for a long time and lead to inactivation of the vaccine (for example, iodine tincture);
- during the use of the vaccine is not recommended to prescribe corticosteroids, antibiotics, because they can adversely affect the formation of the immune response;
- have higher reactogenicity compared to inactivated vaccines.

At present, live vaccines against polio, measles, mumps, rubella, tuberculosis, etc. are widely used in Ukraine.

Characteristics of inactivated vaccines

1. Corpuscular vaccines are bacteria and viruses that are inactivated by physical (high temperature, UV) or chemical factors (formalin, alcohol, phenol). Corpuscular vaccines contain whole cells of microorganisms. Virulent strains are used for their production, which die but retain their antigenic and immunogenic properties (pertussis vaccine as a component of AKDP; leptospirosis, encephalitis vaccines, etc.).

   Corpuscular vaccines have slightly lower reactogenicity compared to live vaccines, but their immunogenicity is also lower. To create a stable immunity is usually carried out 2- or 3-fold vaccination. Due to the fact that after vaccination with inactivated vaccines, short-term immunity is formed, there is a need for additional revaccinations.
2. Chemical vaccines are antigenic components that have been isolated from a microbial cell (for example, a typhoid chemical vaccine enriched with Vi antigen, a meningococcal polysaccharide vaccine, a vaccine against hemophilic type B polysaccharide infection). Bacterial polysaccharides are thymus-dependent antigens, so their conjugates with a carrier protein (diphtheria or tetanus toxoid in minimal amounts or a protein of the microorganism against which the vaccine is made) are used to form T-cell immune memory. An important feature of chemical vaccines is low reactogenicity.
3. Recombinant vaccines are made using genetic engineering methods. The production of

such vaccines is a complex process that schematically consists of the following stages: gene cloning; their introduction into producer cells (viruses, fungi, bacteria); cell culture; extraction of antigen and its purification. An example of such a widely used vaccine is the hepatitis B vaccine. To make it, the region of the hepatitis B virus gene that encodes the synthesis of surface antigen (HbsAg) is inserted into the DNA of yeast cells, which multiply rapidly and accumulate a significant amount of HbsAg. The antigen is isolated, purified from yeast residues and used as a vaccine against hepatitis B. Recombinant vaccines are safe and effective, and can be used to develop associated vaccines that create immunity against several infections simultaneously (eg, hepatitis B vaccine + DPT).

4. Anatoxins are bacterial exotoxins devoid of toxic properties (under the action of formalin and fever), but with preserved immunogenic and antigenic properties. In the process of production, toxoids are purified from ballast substances (nutrient medium, microbial cell residues) and concentrated. These procedures reduce the reactogenicity of toxoids and reduce the volume of drug to be administered. Anatoxins are produced as monopreparations (diphtheria, botulism, tetanus, staphylococcal, gangrenous) and associated (diphtheria-tetanus, botulinum trianatoxin). To achieve intense antitoxic immunity requires double administration of toxoid followed by revaccination. Preventive effectiveness of toxoids reaches 95-100% and persists for several years. An important feature of toxoids is the development of stable immune memory, so it is reasonable to prescribe toxoids to prevent diphtheria in the center of infection and emergency prevention of tetanus (administration of toxoids stimulates the rapid accumulation of antitoxic antibodies in serum in high titers, which prevents development). Anatoxins have low reactogenicity. However, their disadvantage is the impossibility of the formation of antibacterial immunity in the population (formed only antitoxic), which does not provide protection against infection and the development of the carrier.

Organization and carrying out of preventive inoculations

Preventive vaccinations are carried out in vaccination offices at medical and preventive institutions (hereinafter - PHC), in medical offices of preschool and secondary schools, in medical centers of enterprises and in vaccination rooms of business entities licensed for medical practice in accordance with subparagraph 26 of Article 9 of the Law of Ukraine "On licensing of certain types of economic activity" (as amended), as well as in the case of indications - in stationary conditions. Vaccination is allowed only with vaccines registered in Ukraine in accordance with the indications and contraindications for their implementation in accordance with the calendar of preventive vaccinations in Ukraine and instructions for use of vaccines approved by the Chief State Sanitary Doctor of Ukraine or his deputy. Transportation, storage and use of vaccines is carried out in compliance with the requirements of the "cold chain" in accordance with the "Procedure for ensuring proper storage, transportation, reception and accounting of medical immunobiological drugs in Ukraine", approved by this order. Preventive vaccinations are carried out by health professionals who have the rules of organization and technique of vaccinations, as well as emergency measures in case of postvaccination reactions and complications. Responsible for the organization and conduct of preventive vaccinations is the head of the medical institution and persons who carry out medical practice as business entities and have a license for medical practice in accordance with subparagraph 26 of Article 9

of the Law of Ukraine "On licensing certain economic activities" changes). The procedure for carrying out preventive vaccinations is determined by the order of the head of the medical and preventive institution with a clear definition of the responsible persons and functional responsibilities of the medical workers who take part in their carrying out. The volumes of preventive vaccinations are coordinated with the territorial sanitary- epidemiological stations (hereinafter - SES) in May and November of each year. To ensure timely preventive vaccinations, the nurse orally or in writing invites to the treatment and prevention facility persons to be vaccinated (when vaccinating minors - parents or persons replacing them) on the day designated for vaccination; in a children's institution - pre-informs parents or persons replacing them about the immunization of children who are subject to preventive vaccination.

On the day of appointment of preventive vaccination, immediately before its implementation, a medical examination with mandatory thermometry to exclude acute illness and inform persons to be vaccinated, parents and persons replacing them (when vaccinating minors) about possible side effects in post-vaccination period. In the medical documentation there is a corresponding record of informing about possible manifestations of side effects, which is signed by the citizen, and a record of the doctor about the permission for vaccination.

Preventive vaccinations should be carried out in compliance with sanitary and anti-epidemic rules and regulations. The equipment of the office where preventive vaccinations are carried out should be as follows: refrigerator or thermal container (if the vaccine is stored in another room, for temporary vaccination points), cabinet for tools and medicines, boxes with sterile material, changing table and medical couch, tables for preparation of drugs to use, a table (cabinet) for storing documentation, a vessel with a disinfectant solution.

If a needle cutter is used for used syringes, it should be placed next to the drug table and medical couch.

Prophylactic vaccinations in dressing and manipulation rooms are strictly forbidden.

Prophylactic vaccinations are performed only with disposable or self-locking syringes. Self-blocking syringes (dose accuracy, non-reusability) guarantee the safety of injections during immunization for the patient.

Used syringes are disinfected and disposed of. If a needle cutter is used, the disconnected needles and syringes are collected in separate airtight containers before disinfection.

During disinfection and disposal of used syringes in order to avoid the risk of infection of medical workers due to micro-injuries, manipulation to disassemble the prickly parts of the injection equipment is prohibited.

Vaccinations for tuberculosis prevention and tuberculin testing should be performed in separate rooms, and in their absence - on a specially designated table or another day. It is forbidden to use for other purposes the tools intended for carrying out vaccinations against tuberculosis.

The record of the vaccination is made in the forms of medical records approved by the Ministry of Health of Ukraine.

Adult patients receive a certificate. The following data are indicated: type of drug, dose, series, control number. In case of using the imported drug, the original name of the drug in Ukrainian is entered. The data entered in the immunization card are certified by the signature and seal of a doctor or a person engaged in private medical practice.

Following prophylactic vaccination, medical supervision should be provided for a period of time specified in the instructions for use of the relevant vaccine.

Medical documents must indicate the nature and timing of general and local reactions, if any, and register them in accordance with the “Guidelines for the Organization of Epidemic Surveillance for Side Effects of Immunobiological Drugs”.

If you develop an unusual post-vaccination reaction or suspicion of complications after the vaccine, you must immediately notify the head of the treatment facility or a person engaged in private medical practice, and send an emergency report of an unusual post-vaccine reaction or suspicion of complications after vaccination - according to medical forms. documentation

approved by the Ministry of Health of Ukraine to the territorial SES.
Medical contraindications to vaccinations for each specific child are established by the commission on vaccination issues, established by the order of the medical institution, in accordance with the "List of medical contraindications to preventive vaccinations", approved by this order. To resolve complex and controversial issues regarding contraindications to vaccinations, a commission on vaccinations is created at the regional children's hospital.
The fact of refusal of vaccinations with the indication that the medical worker provided explanations about the consequences of such refusal is made in the forms of medical records approved by the Ministry of Health of Ukraine and signed by both citizens and medical workers, which is reported to the territorial SES.
Each vaccination room should have instructions for the use of all drugs used for vaccinations (including those that are not included in the list of mandatory).

Immunization within the vaccination calendar can be carried out only with vaccines registered in Ukraine. Vaccines from different manufacturers for the prevention of the same diseases can be interchanged.

List of medical contraindications to preventive vaccinations

Vaccine	Contraindications
All vaccines and toxoids	Severe complications from the previous dose in the form of anaphylactic shock. Allergy to any component of the vaccine. Progressive nervous system diseases, hydrocephalus and hydrocephalus syndrome in the stage of decompensation, epilepsy, epileptic syndrome with convulsions 2 times a month and more often. Acute disease or exacerbation of chronic1.
All live vaccines	Congenital combined immunodeficiencies, primary hypogammaglobulinemia (vaccines are not contraindicated in selective immunodeficiency of Ig A and Ig M), transient hypogammaglobulinemia and malignancies, pregnancy, AIDS, immunosuppressive therapy2
BCG3	The child's weight is less than 2000 g: at a weight of 1500 - 1999 g vaccinations are not carried out for up to 1 month. life, by weight 1000 - 1499 g - up to 2 months. Complicated reactions to the previous injection of the vaccine (lymphadenitis, cold abscess, skin ulcer with a diameter of more than 10 mm, keloid scar, osteomyelitis, generalized BCG infection). Tubinfection. Defects of phagocytosis
OPV4	Children who are contraindicated in live vaccines, as well as members of their families, are recommended to be vaccinated with inactivated polio vaccine (IPV).
AKDP	Convulsions in the anamnesis (instead of AKDP enter ADP or a vaccine with an acellular pertussis component)
LCD (live measles vaccine), HPV (live mumps vaccine), rubella vaccine or trivaccine (measles, mumps, rubella)	Allergic reactions to aminoglycosides. Anaphylactic reactions to egg white. Administration of blood products5

Notes

1. Scheduled vaccination is postponed until the end of acute manifestations of the disease and exacerbation of chronic diseases and is carried out immediately after recovery or in remission. Acute respiratory disease, which has a mild course and without fever, is not a contraindication to routine vaccination. Contact with an infectious patient, quarantine are not contraindications to routine vaccination. Features of vaccination against

tuberculosis - see paragraph 3 of these notes.

2. Immunosuppressive therapy - therapy performed with cytostatic drugs, including monotherapy with cyclosporine A and others, corticosteroids in immunosuppressive doses, radiation therapy. Corticosteroid therapy is considered immunosuppressive if prednisolone is greater than 1 mg / kg / day and lasts more than 14 days under systemic use. Scheduled vaccinations with inactivated vaccines and toxoids are carried out after the end of therapy, vaccination with live vaccines - at least 1 month. after cessation of therapy. If the duration of corticosteroid therapy is less than 14 days regardless of the dose or more than 14 days at a dose of prednisolone less than 1 mg / kg / day, or used as a replacement therapy, or used topically, such therapy is not considered immunosuppressive and is not contraindicated. vaccination.
3. It is unacceptable to combine tuberculosis vaccination with other vaccinations and parenteral manipulations in one day. BCG vaccination and the Mantoux test should not be performed for 4 weeks after an infectious disease accompanied by fever and during quarantine.
4. After OPV vaccination, it is proposed to limit parenteral interventions for 40 days.
5. Vaccinations against measles, mumps and rubella after administration of blood products (whole blood, plasma, immunoglobulin preparations, erythrocyte mass), except for washed erythrocytes, are possible within the time specified in the instructions to the drug, but not earlier than 3 months. After emergency prophylaxis of tetanus with tetanus human immunoglobulin in newborns, BCG vaccination is carried out according to the generally accepted scheme. If the interval between vaccination against measles, mumps, rubella and the introduction of blood products for therapeutic and prophylactic purposes is less than 14 days, vaccination against these infections should be repeated.

Post-vaccination reactions and complications

A. Codes of clinical manifestations of post-vaccination reactions

1. Raising the temperature to 39 C.
2. Temperature increase more than 390 C (strong general).
3. Temperature that is not registered in the medical records.
4. Pain, soft tissue edema> 50 mm, injection site redness> 80 mm, infiltrate> 20 mm (severe local).
5. Lymphadenopathy.
6. Headache.
7. Irritability, sleep disturbances.
8. Rash of non-allergic origin.
9. Anorexia, nausea, abdominal pain, dyspepsia, diarrhea.
10. Catarrhal phenomena.
11. Myalgia, arthralgia.

B. Codes of clinical manifestations of post-vaccination complications

12. Abscesses.
13. Anaphylactic shock and anaphylactoid reactions.
14. Allergic reactions (Quincke's edema, urticaria, Stevens-Johnson syndrome, Lyell's syndrome).
15. Hypotensive-hyporesponsive syndrome (acute cardiovascular insufficiency, hypotension, decreased muscle tone, short-term disturbance or loss of consciousness, history of vascular disorders).

16. Arthritis.
17. Continuous shrill scream (lasting from 3 hours and more).
18. Febrile convulsions.
19. Afebrile convulsions.
20. Meningitis / encephalitis.
21. Anesthesia / paresthesia.
22. Acute flaccid paralysis.
23. Vaccine-associated paralytic polio.
24. Guillain-Barre syndrome (polyradiculoneuritis).
25. Subacute sclerosing panencephalitis.
26. Mumps, orchitis.
27. Thrombocytopenia.
28. Subcutaneous cold abscess.
29. Superficial ulcer more than 10 mm.
30. Regional lymphadenitis (s).
31. Keloid scar.
32. Generalized BCG infection, osteomyelitis, osteitis.

Form of submission of information on the case of side effects (complications) after the use of immunobiological drugs

Post-vaccine reactions and complications are health problems that occur after immunization. Regional health care institutions shall notify the Ministry of Health of Ukraine and the State Enterprise "Center for Immunobiological Drugs" for each case of complications after the use of a bacterial, viral or serum drug, shock, death after administration of the drug, unusual reaction or increased reactogenicity of the drug. 24 hours after receiving information from the place.

Every case of complication (or suspected complication) after vaccination is subject to registration and investigation. Based on the results of the investigation, an act of investigation of side effects (complications) after vaccination is drawn up, which must contain the following information:

1. Last name, first name, patronymic. Date, month, year of birth. Place of work (children's institution). Place of residence.
2. Institution that investigated (discovered) a case of side effects (complications after application) of an immunobiological drug
3. Information about the drug. Name of the drug. Series. Control number. Expiration date. Manufacturer. In what quantity the preparation is received. Date of receiving. Conditions and temperature of storage in area, area, place of application.Violation of the vaccination procedure (method of administration, dosage, storage conditions, from an open ampoule, etc.).The number of people vaccinated with this series in the area, region or the number of doses used.Vaccination has unusual reactions to vaccination.
4. Vaccine health information. Date of vaccination. Who was examined before vaccination (doctor, paramedic, nurse), temperature before vaccination. Individual features (prematurity, birth trauma, traumatic brain injury, corticosteroid therapy, which preceded vaccination, etc.). Transferred diseases (for children of the first 3 years of life with indication of date and duration of illness); indicate the date and duration of the last illness. Allergic diseases (including drugs and food). The presence of seizures in the history of the vaccinated, his parents, siblings, with or without fever, as long ago. Vaccinations with dates of administration of the drug:BCG vaccine; AKDP vaccine; ADP-toxoid; ADP-M-toxoid, polio, measles, mumps vaccines and the like.Have the

vaccinated person or his close relatives had unusual reactions to the vaccination (what are the nature of the reaction)? Additional data (contact with infectious patients in the family, children's institution, hypothermia, etc.).

5. Clinical course. Date of illness, complaints. Date of application. Objective: symptoms of local and general reaction, diagnosis. Date and place of hospitalization. The course of the disease (briefly). Final diagnosis: basic; complications, comorbidities. Date of discharge. Result. Residual phenomena. In case of death: date, pathological diagnosis.
6. 6. The conclusion of the commission on the causes of complications. Positions and signatures of commission members. Date of examination. An extraordinary message was sent by telephone, telegraph (underline). Date.

When sending an act of investigation to the Ministry of Health of Ukraine and the State Enterprise "Center for Immunobiological Drugs", the name of the institution that sent the information and its location must be indicated.

Immunological efficacy of vaccination.

The study of the immunological efficacy of vaccines is performed by comparing the titers of specific antibodies in the serum vaccinated before and at different times after immunization, as well as by comparing these results with antibody levels obtained at the same time in people who received placebo or comparison drug used serological reactions: ELISA, RPHA, RTTGA, as well as allergic tests, Mantoux test.

For each infection is determined by its own, protective antibody titer: for measles, mumps and influenza, it is equal to 1:10, tetanus 1:20, diphtheria 1:40 RPGA For whooping cough 0.03 MK-ml, hepatitis B 0.01 IU-ml by enzyme-linked immunosorbent assay, etc. At infections where the protective level of antibodies is not established it is necessary to carry out tests of preventive efficiency of vaccines on indicators of morbidity of this infection. To study the immunological activity of vaccines use limited groups of people, usually no more than 100 people in a group. For a single immunization, paired sera taken immediately before vaccination and for a clear period of time, of course, 30 days after vaccination, should be tested. At two-, three-fold administration of vaccines it is necessary to investigate 3-4 samples of serum, including the sample before vaccination. Serum samples should be stored frozen. The duration of serum samples should be kept to a minimum, and test systems for antibodies should be highly sensitive and standard.

The coefficient of immunological activity (effectiveness) is determined by the following formula, where:

KE = a * 100 / A - b * 100 / B%

KE - coefficient of immunological activity;

A - the number of vaccinated with the test drug, which examined the paired sera;

B - also in the control group of people;

a - the number of vaccinated, in which there was an immunological shift;

b - also in the control group.

Epidemiological effectiveness of immunization is generally assessed by reducing the incidence, the impact on such manifestations of the epidemic process as cyclicity, seasonality, foci, the prevalence of children's groups, changes in the age structure of the disease. With a high level of morbidity, the presence of a large sample in quantitative and qualitative terms of the studied groups (experimental and control), the epidemiological effectiveness of immunization is assessed using the index and the coefficient of effectiveness.

1. The index of effectiveness (K) of immunoprophylaxis shows how many times the incidence of vaccinated (a) is less than the incidence of unvaccinated (b) or vaccinated placebo:

K = *ab*

2. The coefficient of effectiveness (E) shows what percentage of vaccinated is protected from the disease by this infection:

E = *(b - a) b* x 100%

To determine these indicators, it is necessary to have accurate data on the number of vaccinated and unvaccinated persons and the number of diseases among them. Based on these data, intensive incidence rates among vaccinated and unvaccinated, which are used in the above formulas, are calculated.

Self-control questions

1. Types of immunity and their characteristics.
2. Immunoprophylaxis.
3. Types of vaccines and their characteristics.
4. Calendar of preventive vaccinations of Ukraine.
5. Post-vaccination reactions and complications.
6. Accounting and reporting documentation.
7. Epidemiological effectiveness of immunoprophylaxis.
8. Clinical effectiveness of immunoprophylaxis.
9. "Cold chain"
10. Indications for urgent immunoprophylaxis.

Test task

1. Anatoxins include:

A. diphtheria vaccine;
B. vaccine against tuberculosis;
C. hepatitis B vaccine;
D. pertussis vaccine;
E. measles vaccine.

2. Live vaccines include:

A. tuberculosis vaccine;
B. hepatitis B vaccine;
C. tetanus vaccine;
D. diphtheria vaccine;
E. pertussis vaccine.

3. Recombinant vaccines include:

A. hepatitis B vaccine;
B. vaccine against tuberculosis;
C. polio vaccine;

D. measles vaccine;
E. mumps vaccine.

4. Immunoprophylaxis is the creation of an immunological layer among the population using:

A. live, inactivated, chemical vaccines, toxoids and immunoglobulins;
B. toxoids;
C. live, inactivated and chemical vaccines;
D. only live and inactivated vaccines;
E. immunoglobulins.

5. Possible way of formation of active natural immunity:

A. after the disease;
B. administration of the vaccine;
C. introduction of immunoglobulin;
D. administration of toxoid;
E. all of the above is true.

6. Passive artificial immunity is formed after the introduction of:

A. sera;
B. toxoids;
C. live vaccines;
D. inactivated vaccines;
E. recombinant vaccines.

7. What fluctuations in temperature are allowed when storing vaccines in the refrigerator?

A. + 4- + 8 ° C;
B. temperature fluctuations are not particularly important for the storage of vaccines;
C. above + 8 ° C;
D. for storage of dry vaccines temperature fluctuations do not matter;
E. from -3 to + 10 ° C.

8. Antibodies are synthesized:

A. T-lymphocytes.
B. B-lymphocytes.
C. Macrophages.

9. The purpose of vaccination:

A. Creating a specific immunity to infectious agents.
B. All answers are correct.
C. Synthesis of high levels of antibodies.
D. Population formation of immunological memory cells.

10. Cold chain is ...

A. temperature control system during storage and transportation of vaccines;
B. temperature control during storage of vaccines;
C. cooling of vaccines before administration to provide an immunogenic effect;
D. control of temperature during transportation of vaccines;

E. cooling vaccines before administration to reduce allergic reactions.

Chapter 5.
Epidemiological method of research and its structure.

Epidemiological method is a set of methodological techniques used to study the causes, conditions (risk factors) and mechanisms of morbidity among the population (aggregate, by groups, territories and over time) in order to justify prevention measures and evaluate their effectiveness. By analogy with clinical medicine, where before prescribing treatment the patient is diagnosed with the help of clinical (physical, instrumental and laboratory) studies, during the study of population morbidity epidemiological study makes it possible to establish an epidemiological diagnosis and develop an adequate set of preventive and anti-epidemic measures. The main postulate of modern epidemiology is the obligatory interaction of the three main driving forces (sources of infection, transmission mechanism and susceptible organism), without which the emergence and spread of the epidemic process is impossible. However, the quantitative manifestations of the epidemic process (sporadic morbidity, epidemic outbreak, epidemic, pandemic) depend on the action of secondary driving forces - social and natural factors that directly affect the epidemic process.

Thus, the main object of study in epidemiology is the epidemic process and its manifestations. The study of the epidemic process is carried out using the epidemiological method, which uses methods of microbiology, immunology, medical statistics, medical geography and more. The epidemiological method allows to establish the causes and conditions of occurrence and spread of infectious diseases among the population, causal links.

Epidemiological research method is the main in modern epidemiology. Thanks to it the analysis of distribution of diseases in a certain territory, on time is carried out, and also the reasons and conditions (risk factors) of formation of morbidity for the purpose of a substantiation of preventive and anti-epidemic measures are defined.

The structure of the epidemiological method consists of the following techniques:

1. Descriptive (descriptive and evaluative) techniques. Allow to define priority problems of prevention on the basis of the analysis of structure of morbidity on groups of infections, and on separate nosologies - on territories, risk groups and time.
2. Analytical techniques are used to assess hypotheses about risk factors, to determine areas of prevention in accordance with risk factors.
3. Experimental studies allow to prove or disprove hypotheses about the risk factors of the disease, to quantify the effectiveness of means and methods of prevention.
4. Mathematical modeling is used to predict the manifestations of the epidemic process.

The structure of the epidemiological method of research Observation:

1. Descriptive (description of individual cases; description of a series of cases;

screening studies; environmental (correlation); epidemiological examination of the cell; operational epidemiological analysis; retrospective epidemiological analysis; expert opinion; statistical observation).

2. Analytical (cohort; case-control; transverse cross-sectional; investigation of outbreaks).

Experimental:

1. Controlled experiment (randomized controlled study; field study; study at the communal level).
2. Uncontrolled experiment ("natural experiment"; preventive and anti-epidemic activities of health facilities).
3. "Physical" modeling (modeling of the epidemic process; experimental epizootology).

Heuristics:

1. Generalizing (analysis of expert opinions; systematic reviews; meta-analysis).
2. Mathematical modeling (stochastic (formal-mathematical) modeling; quantitative modeling).

The epidemiological method was formed and successfully used initially to study infectious diseases. However, currently it is widely used to analyze the causes and mechanisms of non-infectious diseases, such as cardiovascular, cancer, endocrine pathology. In recent years, the concepts of "clinical epidemiology" and "evidence-based medicine" have gained widespread recognition.

Clinical epidemiology is research on the diagnosis, spread, treatment and prevention of diseases based on epidemiological methods. In turn, evidence-based medicine is a scientific substantiation of medical decisions using the epidemiological method of research.

Descriptive epidemiology

The purpose of the descriptive-epidemiological study is to determine the priority problems of prevention based on the analysis of the structure of morbidity by groups of infections and individual nosologies, and in relation to individual nosologies - by territories, risk groups and time of risk, as well as formulating primary hypotheses or risk factors for morbidity.

Risk areas are areas with high incidence rates. They are determined by the presence of action (or more pronounced action) in a certain area of the factors of formation of the epidemic variant of the pathogen and the factors of its spread.

Risk groups - social, age, occupational, household and other groups with a high incidence rate.

Risk time - the period of action of the factors that determine the formation of an epidemic variant of the pathogen and the subsequent period of increased morbidity.

<u>Risk factors:</u>

- Elements of the social and natural environment, features of human behavior and the state of the body's internal systems, which increase the risk of disease;

  Conditions that form an infectious disease (risk of formation and spread of an epidemic variant of the pathogen, the risk of infection).

The category of concepts that quantify the manifestations of the epidemic process include the following: endemic morbidity, exotic morbidity, sporadic morbidity and epidemic morbidity

(outbreak, epidemic, pandemic). (considered during the study of the topic "The doctrine of the epidemic process").
In addition to morbidity, quantitative manifestations of the epidemic process are indicators of prevalence, mortality, mortality. Quantitative manifestations of the epidemic process are studied in the long-term and annual dynamics of morbidity.
To analyze the level and structure of morbidity, mortality, mortality, disability use data from primary documentation of infectious diseases (statistical forms, reporting) and data from sample studies (eg microbiological and cherological monitoring in the system of epidemiological surveillance of individual infections).
Analysis of the level and structure of morbidity by groups of infections and individual nosologies is carried out to determine their epidemiological (prevalence in the population), social (negative impact on various forms of society) and economic (direct and indirect economic losses) significance, which allows to conclude priority problems of prevention of this or that disease at the moment.
The epidemiological significance of the diseases is assessed by the indicators of the average long-term morbidity. In the presence of a pronounced long-term trend or cyclicality in the assessment of epidemiological significance, it is necessary to use the predicted incidence rates, or trend line.
Epidemiological significance:

- Social: quality of life, life expectancy, disability, mortality, morbidity.
- Economic: 1-direct (costs of examination, treatment, rehabilitation); 2- indirect (disability) (economic costs due to partial or complete disability).

Social significance - is calculated on the basis of the total damage caused by diseases to human health, taking into account not only the frequency of diseases, but also their severity and duration. Criteria of social significance are: mortality, disability, indicator of lost full years of life (unlived), indicator of inefficient use of the working population (number of persons out of 100 able-bodied population who did not participate in the production process daily during the year).
Economic significance is determined by the damage caused to the national economy due to labor constraints. Direct losses are the costs of outpatient and inpatient examination and treatment of patients, payments for temporary disability, disability, etc. Indirect economic losses are calculated on the value of products that were not received due to disability due to illness, disability or mortality. Comprehensive assessment of the significance of infectious diseases is one of the main criteria for the priority of infections in the direction of preventive and anti-epidemic measures.

Analytical epidemiology.
The purpose of analytical epidemiological research in health care is to assess hypotheses about the conditions (risk factors) that are put forward in the descriptive and evaluative study, and to identify areas of prevention in accordance not only with areas, groups and times of risk, but also possible (hypothetical).) risk factors.
Hypotheses (scientific, practical) are formulated not only on the basis of descriptive epidemiology, but also in the process of theoretical and clinical research. The nature of hypotheses is determined by the level of knowledge and worldview of society as a whole and a particular researcher or research team. In the course of testing the initial hypotheses, new hypotheses are formulated, which are also subject to testing.
There are two main analytical epidemiological research methods:

- cohort study,
- case-control study.

Cohort study. In epidemiological studies, a cohort is a group of people with an epidemiological trait. The cohort study determines the intensive rates of morbidity in cohorts that are exposed and not exposed to the risk factor. An example of such a study is observation for 44 months. for persons aged 50-69 years, when it was found that the incidence of lung cancer (per 100 thousand population) was among the cohort of smokers 127.2 per 100 thousand population, and in the cohort of non-smokers - 12, 8 per 100 thousand population. When assessing the statistical significance, it was found that the difference in intensive indicators indicates that the differences in indicators are not accidental. However, in this version of the study it is necessary to prove the equality of conditions for comparison groups on all grounds except the estimated (in this case - smoking).

In epidemiological diagnosis, cohort studies based on collected morbidity data are called retrospective epidemiological studies. The study with the assessment of morbidity in the dynamics is carried out during a prospective epidemiological study. The results of a cohort study reveal an immediate and relative risk of the disease.

Immediate (additional) risk is the difference in morbidity rates in persons who were exposed and not exposed to the risk factor. In the example above, the immediate risk of developing lung cancer from smoking is:

127.2 - 12.8 = 114.4 per 100 thousand smokers aged 50-59 years.

Relative risk (risk ratio) is the ratio of morbidity in the group of persons exposed to the risk factor to the indicator in persons who are not exposed to this factor. In this example, it is: 127.2 / 12.8 = 9.94 times.

That is, the risk of lung cancer among smokers is 10 times higher than among non-smokers.

Case-control study. This type of study is based on the comparison of information about the presence of the studied factor among patients and non-patients with this disease.

Experimental epidemiology.

The experiment, in contrast to observation, involves the artificial reproduction of the phenomenon (its parts) or artificial interference in the natural course of the process. An experiment in epidemiology is understood as an artificial intervention in the process by eliminating the factors that are likely to cause disease or contribute to their occurrence. The researcher's task is to see the differences on the basis of impact and compare the result.

The experimental method is used for diagnostic purposes (infection of laboratory animals sensitive to various pathogens with pathological material from patients and corpses during outbreaks of particularly dangerous infectious diseases), as well as to assess the effectiveness of vaccines, disinfectants and rodenticides, to determine the virulence of various strains of infectious agents. diseases.

Experimental epidemiological methods are possible in the following variants:

1. controlled epidemiological experiment;
2. uncontrolled epidemiological experiment;
3. "natural experiment";
4. "physical" modeling of the epidemiological process;
5. experimental epizootology.

A controlled experiment is usually associated with a study of the effectiveness of a therapeutic or prophylactic drug. In this case, one group receives it, and the other, equivalent, does not receive. Then the incidence in both groups is compared. As a result, a quantitative assessment of the preventive effect of the drug (vaccine, chemotherapeutic agent, etc.) or measure (hardening, smoking cessation, etc.), ie its potential effectiveness. The generally accepted standard of experimental research is a randomized controlled trial. The result of an epidemiologically controlled experiment is not only a proof of the hypothesis of a risk factor, but also a quantitative assessment of the action of a preventive measure (measure), ie its potential effectiveness.

An uncontrolled experiment involves artificially interfering with the natural course of the onset and spread of disease through the prevention of health care. For example, diphtheria toxoid is injected into a contact diphtheria cell for prophylactic purposes, and emergency prophylaxis with antibacterial drugs is performed in a cholera center.
The scientific value of an uncontrolled experiment is limited, because no control groups are provided during the preventive measure. However, from a deontological point of view, it would be wrong to leave without help people who have been exposed to the infection and the risk of disease, if there are reliable means of prevention.
The proven result of reducing the incidence or prevention of diseases characterizes the actual effectiveness of the measure. When evaluating the results of an epidemiological experiment, two main approaches are used to evaluate the results: 1) analysis of the level, structure and dynamics of morbidity in different teams, differing in the use (non-use) of the drug or (non-conduct) of the event; 2) analysis of the same indicators in the same place (team) in different periods of time, which differ in the use (or non-use) of the drug, conducting (or not conducting) activities.
At epidemiological researches, especially the analysis of efficiency of the carried-out actions, "external control" (by means of a spray sample) - for example, the next enterprises of a similar profile, school where actions aren't carried out is necessarily formed. "Internal control" is also formed with the help of an individual sample(half of the workers of each shop receive a preventive drug, the other - no).
"Natural experiment" is an independent study of the impact on a relatively isolated group of people, the result of which is an unusually high incidence, such as a local outbreak of an infectious disease.
"Physical" modeling of the epidemic process is its imitation in natural conditions. Yes, instead of the causative agent of intestinal infection can be introduced into the human body. E. coli M - 17 (the basis of the drug "colibacterin") or bacteriophage and further analyze its spread.
Mathematical modeling is possible with sufficient study of the mechanism of development of the epidemic process. Mathematical modeling is used to predict the manifestations of the epidemic process on the basis of mathematical formulas. This method is used in retrospective epidemiological analysis, has a scientific purpose.

Statistical indicators used in the epidemiological method.
Intensive epidemiological indicators
Intensive epidemiological indicators determine the level, frequency, prevalence of the phenomenon in the environment where it occurs.
Level (frequency) number of diseases first detected x 1000 (10000, 100000) morbidity =
(primary) population

Total morbidity = (prevalence) = the number of diseases detected for the first time this year and in previous years x 1000 (10,000, 100,000) / population

Frequency of morbidity among different groups of population = the number of diseases in a given of the population group x 1000 (10,000, 100,000) / population

Mortality rate = number of dead x 1000

Population

Mortality number of deaths x 100
(with a certain = ----------
disease) the number of patients with this disease

Extensive epidemiological indicators

Extensive epidemiological indicators characterize part of the whole and are expressed as a percentage.

Specific weight (structure, distribution) the number of cases of certain individual infections of the disease x 100
diseases among all = ----------
infectious diseases the number of cases of all diseases

Case distribution The number of cases during a given month diseases for
months (months) x 100
year = ----------
number of cases per year

During the epidemiological analysis, the probability of the obtained indicators is evaluated, and during the comparison of indicators, the probability of the difference between them is evaluated, ie the average values are calculated, the probability of average and relative indicators is evaluated, and correlation analysis is performed.

Visual representation of the results of the epidemiological study.

Linear diagrams, plane diagrams, cartograms are used in epidemiological researches. The line diagram allows to display numerical values with curved lines and, thus, to analyze dynamics of the phenomenon in time or to reveal dependence of signs from each other. If the graph shows several curves, you can compare the changes in oscillations.

The plane diagram in the form of a rectangle or columns gives the chance to present the statistical data independent of each other (intensive indicators). To depict the ratio of homogeneous quantities using the plane of a rectangle or circle (for extensive indicators). A radial, linear, or linear-pie chart is used to display the distribution of morbidity by month. Cartograms are graphical maps of the area, which show the distribution (spread) of a disease in the territory.

Epidemiological diagnosis.

The application of the epidemiological method in health care practice is called "epidemiological diagnosis". Epidemiological diagnosis is a set of methods for recognizing specific manifestations of the epidemic process, the causes and conditions of its occurrence and development.

Epidemiological diagnosis can be compared with the clinical diagnosis of internal diseases, but they differ in the subject of study. If the clinical diagnosis is aimed at establishing a diagnosis in a particular patient, the epidemiological diagnosis assesses the epidemic situation in a particular area, among populations, at certain intervals, in order to streamline the planning and implementation of preventive and anti-epidemic measures. Thus, epidemiological diagnosis helps to increase the effectiveness of measures to prevent and combat infectious diseases.

Epidemiological diagnosis is divided into two areas - retrospective and operational epidemiological analysis.

Retrospective epidemiological analysis is a study of the level, structure and dynamics of infectious diseases over a period of time (at least a year), which provides solutions to epidemiological diagnostics to justify and plan preventive and anti-epidemic measures (VD Belyakov). Thus, the ultimate goal of retrospective epidemiological analysis is the current and future planning of preventive and anti-epidemic measures based on identified risk factors over time, among groups and groups and in the territories, ie, those natural and social conditions that cause this epidemic situation.

When conducting a retrospective epidemiological analysis, a descriptive method of the epidemiological method of research and analytical cohort research for the past years are used.

The scheme of retrospective epidemiological analysis includes:

1. Analysis of the long-term dynamics of morbidity of the total population.
2. Analysis of the annual dynamics of morbidity of the total population.
3. Morbidity analysis by population groups (social, age, occupational, etc.).
4. Analysis of long-term and annual dynamics of morbidity by population groups.
5. Analysis of morbidity by teams.
6. Morbidity analysis by territories.
7. Analysis of morbidity on certain grounds, which follow from the features of each nosological form of the disease and the ultimate goal of the study (etiological structure of diseases and analysis of pathogens in intestinal infections, morbidity of vaccinated and unvaccinated respiratory infections, etc.).

Analysis of long-term morbidity dynamics

The incidence of infectious diseases of the general population and individual socio-age groups is characterized by unevenness over time. The incidence for the previous few years, expressed in annual terms, is called the long-term dynamics of morbidity.

The nature of changes in the level of infectious disease in the long-term dynamics is determined by the combined action of three groups of causes. The first group of reasons consists of those of them that act constantly and determine the main direction of changes in the intensity of the epidemic process in the long-term dynamics, ie, the epidemic trend. It can characterize the stabilization, growth and reduction of morbidity. These three variants of the epidemic trend reflect the effect of conditions that affect the epidemic process in connection with preventive and anti-epidemic measures, as well as, probably, with changes in the biological properties of the pathogen (eg, increase and decrease in pathogenicity of the pathogen).

The second group of causes acts periodically and reaches a maximum and minimum impact on the epidemic process after a certain number of years. The changes in the intensity of the epidemic process caused by them are called periodic or cyclic fluctuations (cyclicity). A specific feature of this form of manifestation of the epidemic process is the relatively ordered wave-like fluctuations in the level of morbidity. Cyclicality is characterized by diversity in both the duration of periods and the magnitude of the amplitude. There are small cycles (period 2-5 years), medium (7-15 years) and large (20 years or more). Rises in incidence occur in all infectious diseases, but they are natural only in respiratory infections, in which the incidence is regulated by the immune system. Preventive and anti-epidemic measures reduce the manifestations of cyclicity (eg, immunoprophylaxis for respiratory infections).

The third group of reasons does not have a certain order of action in time. This is a large number of random factors that are constantly changing and cause irregular fluctuations in the epidemic process. They combine (under the influence of random factors), both rises and falls in morbidity, which have no pattern. Irregular fluctuations of the epidemic process in the longterm dynamics occur in connection with changes in social and (or) natural conditions that are not regular.

The analysis of long-term dynamics of morbidity provides definition of an epidemic tendency for what use a statistical method of alignment of a time series on a direct method by the least

squares method. To study long-term morbidity, morbidity indicators for a period of at least 10 years are analyzed, which allows, taking into account both rises and falls in morbidity, to determine the long-term trend and cyclical nature of the epidemic process. The number of rises and falls in morbidity, intervals between rises, how many times the incidence in the years of rises exceeded the incidence in the years of its decline, and so on. Based on the assessment of long-term trends in morbidity, we can identify the reasons why the number of cases decreases or increases.

Analysis of the annual dynamics of morbidity

The study of the annual dynamics of morbidity is based on the study of infectious morbidity per year, which is quantified in terms of morbidity by month. Year-round or off-season morbidity, which is characterized by the minimum intensity of the epidemic process, is calculated. However, the incidence of most infectious diseases during the year varies significantly, due to the influence of natural and social factors.

Seasonality is a periodic rise in incidence at certain times of the year, when 50% or more of the annual incidence is registered in a few months. Thus, respiratory infections are characterized by winter-spring, and intestinal infections - summer-autumn seasonality.

The result of accidental causes on the epidemic process are episodic outbreaks or, conversely, a decrease in morbidity.

When analyzing the annual dynamics of morbidity, it is necessary to give a quantitative description of the distribution of morbidity during the year, to determine the duration of the seasonal increase in morbidity and its share. Extensive indicators are used to analyze seasonality, determining the proportion of diseases in each month in relation to the amount of diseases per year. With a uniform distribution of morbidity by month during the year, the average monthly morbidity rate is 8.33% (100%: 12 months). Months in which the proportion of morbidity exceeds this number are considered months of seasonal rise.

To assess the significance of the incidence during the seasonal rise in the total incidence for the year, the coefficient and index of seasonality are calculated. Seasonality ratio is the ratio of the number of diseases registered during the period of increasing morbidity to the total number of diseases per year, expressed as a percentage. Conditionally, the months of seasonal rise include those in which the proportion of diseases exceeds 8.33%, ie the number of diseases exceeds the average monthly number.

$$\text{Seasonality ratio} = \frac{\text{Number of months of increase}}{\text{Total number}} \times 100\% = \%$$

Seasonality index - the ratio of the number of diseases in the month of seasonal rise to the number of diseases that are registered in other months; it shows how many times the seasonal increase in morbidity exceeds the off-season level.

$$\text{Seasonality index} = \frac{\text{Number cases on months of increases}}{\text{Number cases on other months}} = ..,..$$

Morbidity analysis by territories

The study of morbidity on a territorial basis is conducted to identify risk areas where there is a higher probability of disease. Risk areas are most often identified for natural focal zoonoses, in which the spread of infection is limited by the range of animals-sources of infection or vectors. Most anthroponoses are distributed throughout the globe, ie ubiquitous.

The area where infectious diseases are registered is called the nosoarea. Due to the peculiarities

of territorial distribution, all infectious diseases can be divided into 2 groups: with global and regional nosoareal.
Most anthroponotic infections and some zoonoses, the source of which is caused by domestic animals, are characterized by ubiquitous or global distribution throughout the globe. But the incidence of these infections in different areas differs, due to social and natural conditions. For example, the reasons for the uneven distribution of intestinal infectious diseases may be the sanitary condition of the settlement, the presence and condition of water supply and sewerage, the possibility of infection of food products during their production, storage and transportation, the state of food enterprises and more. Therefore, it is necessary to identify areas of risk, ie, areas where social and natural factors cause a relatively high level of morbidity. It should be noted that the unevenness of the epidemic process in the territory may depend on the volume and quality of preventive and anti-epidemic measures and the completeness of registration of infectious diseases. To determine the causes of this unevenness, it is advisable to analyze the long-term dynamics of morbidity in different areas. Regional morbidity is inherent in natural focal infections.
The analysis of morbidity by territory is determined by administrative (state, region, city, district) and geographical boundaries. In administrative territories (region, city, district) the incidence is analyzed by territorial medical associations, medical districts (in cities), district hospitals, medical and obstetric points (in rural areas), medical units at industrial enterprises. Calculations of intensive morbidity rates for administrative units, territorial medical associations and hospitals are carried out per 100,000 population, and at medical stations and medical and obstetric points - per 1,000 population. In order to visualize and analyze the uneven spread of infectious diseases in the territory use a cartogram, which is applied to the incidence or cases of disease in accordance with the places of registration of the disease. Intensive incidence rates in the area can be represented in the form of a bar chart.

Morbidity analysis among population groups
Infectious disease is characterized by uneven distribution not only by territory but also among different groups and groups. Different nosological forms are characterized by certain indicators of morbidity in different groups of the population (age, professional, social, etc.) and teams (children's preschools, schools, boarding schools, orphanages, etc.).
The following features are used to analyze the incidence by population groups:

1. Typical, on the basis of which the selection of epidemiologically significant socio-age groups (age, profession, gender, membership).

2. Group, which indicate the risk of infection - population density, congestion, population, the degree of public amenities, water supply, etc.
3. Individuals who indicate the risk of disease (general resistance and immunity).
4. The analysis of morbidity by groups of the population and collectives is carried out on intensive indicators on 1000, 10000 or 100000 persons of the given age, profession, etc.

The most significant feature of the population, which is associated with the possibility of the disease, is the age composition. Age groups are distinguished according to the research program, the purpose of which is to identify the causes of the predominant morbidity of persons of a certain age (risk groups). When analyzing the incidence by age, small age groups are used to identify possible causes that led to the incidence in these groups (for example, age groups - 0-1, 2-3, 4-6, 7-14, 15-19, etc.) . Within the social and household groups there are epidemiologically significant groups: children of preschool institutions, students of schools, boarding schools, vocational schools, students, workers, employees, medical workers,

employees of children's preschool institutions, catering, water supply and more. The choice for the analysis of certain age and social groups depends on the epidemiological features of the nosological form. Thus, when analyzing the incidence of intestinal infections, it is necessary to identify groups of children who attend and do not attend preschools, schoolchildren, employees of preschools, food companies. In the analysis of the incidence of hepatitis B, groups of medical workers, donors, surgical patients, etc. are distinguished.
As a result of the analysis of morbidity by population groups, risk groups are identified, ie, groups of the population with high morbidity rates.
In the analysis of morbidity, considerable attention is paid to the distribution of morbidity by teams, comparing it with morbidity among individuals who are not in teams. Favorable conditions for the growth of morbidity due to overcrowding and non-compliance with the anti-epidemic regime can be created in the teams. Kindergartens, schools, boarding schools, orphanages, etc. are considered to be epidemiologically significant groups.
When analyzing the incidence of teams calculate the following indicators:
1. Indicator of the number of affected groups - the proportion of teams in which there are cases of disease (cells), among the total number of teams of a certain profile and in total among all teams.
2. Indicators of cellity - the average number of cases in one cell (team).
3. The share of cells (teams) with different number of cases (from 1, 2, 3, etc.) among the total number of cells (teams).
The obtained data allow us to draw conclusions about risk groups - groups with a high level of morbidity and their share among all groups.
Identification of risk groups and groups provides grounds for establishing epidemiological causal links between morbidity in these groups and groups with risk factors, ie, with the action of those causes and conditions that lead to increased morbidity. The obtained results of such analysis are the basis for targeted preventive and anti-epidemic measures.

Operational epidemiological analysis is a continuous monitoring of the epidemic process, which allows to identify the causes of the epidemic process and to develop effective preventive and anti-epidemic measures. Operational analysis is designed to study the characteristics of the epidemic process among the population in a short period of time in order to identify changes in the causes and conditions that affect the intensity of the epidemic process.
In the operative epidemiological analysis it is possible to allocate two directions of the analysis of the information which is collected or arrives to the epidemiologist:

a) analysis of information, which includes indirect (indirect) signs, which can be used to draw conclusions about the probable trend of the epidemic process;
b) analysis of information on signs that directly reflect the state and trends of the epidemic process.
The first direction of operational epidemiological analysis -dynamic inspection and assessment of the implementation of planned activities in risk areas, in groups and groups of risk and in periods (time) of risk. But it is necessary to take into account the possible variability of the situation, which could not be foreseen when planning activities. Therefore, it is necessary to constantly monitor the social and natural factors that may intensify the epidemic process and the objects that have epidemiological significance. For example, the analysis of the incidence of intestinal infections requires operational data on the sanitary condition of food industry, catering, water treatment plants, food and water quality, equipment malfunctions at epidemiologically important facilities, violations of the technological process. These data may indicate specific opportunities for infection of the population through various routes of transmission (food, water, household) in connection with the peculiarities of social and natural living conditions. Make a layout of tables for the city (district), or for a separate territory, which

has a set of specific factors that are likely to implement water, food or household transmission. This direction of operative epidemiological analysis, which by indirect (indirect) signs may indicate possible trends in the epidemic process, is the main one. Preventive measures, which are carried out as the systematic receipt of this information, should prevent the activation of the mechanism of transmission of intestinal infections and the increase in the incidence of these infections.

The second direction of operational epidemiological analysis involves the assessment of information that directly reflects the state and trends of the epidemic process:

a) continuous monitoring of infectious diseases and assessment of its dynamics;
b) analysis and evaluation of laboratory test results;
c) epidemiological examination of foci with single and group diseases (epidemic outbreak, epidemic).
d) sanitary and epidemiological intelligence.

In the operational epidemiological analysis an important place is occupied by the observation of morbidity, which is the result of the causes that preceded the manifestations of the epidemic process. These causes acted much earlier than the incidence, so they cannot be prevented, but their effects can be reduced.

The tasks that are solved in the operational epidemiological analysis, set specific requirements for its information support. The information support system should ensure continuous and prompt receipt of comprehensive information about the registered disease and its possible causes, rapid processing of this information, its consistent clarification and addition, as well as ensuring the search for the necessary data for analysis.

Data on patients from treatment and prevention facilities to the sanitary-epidemiological station must be transmitted by telephone, fax, e-mail or messenger immediately after the identification of the patient. The information received during the day is summarized, patients are divided into groups and nosological forms of infections in the territory, age and occupational groups. Daily data, as they are received, are summarized in weekly and monthly reports. Data of daily registration of patients are presented in absolute figures, and data for a week and a month - in intensive indicators of morbidity which are calculated on 100000 population.

Observations of the level, structure and dynamics of infectious morbidity are carried out by comparing the frequency of registrations of individual infections with the normative level of morbidity for a given day, week, month, as well as data for similar periods in previous years, with indicators in other territories, groups and more. All indicators of the normative level of morbidity are calculated on the basis of data on morbidity for previous years after the exclusion of episodic outbreaks with reliably established causes of their occurrence.

Self-control questions

1. Epidemiological method of research.
2. The structure of the epidemiological method of research.
3. Operational epidemiological analysis.
4. Retrospective epidemiological analysis.
5. Manifestations and analysis of annual and long-term dynamics of morbidity.
6. The concept of "risk area", "risk time", "risk group", "risk factor".
7. Experimental methods of epidemiological research method.
8. Methods of mathematical modeling in epidemiology and their significance.
9. Basic principles of formation of control and research groups.
10. Preventive and anti-epidemic measures.

Test task

1. Name the techniques and methods of a comprehensive epidemiological method:

A. Descriptive-evaluation, analytical, experimental, mathematical modeling.
B. Descriptive, analytical, experimental, metrological.
C. Descriptive-estimative, metrological, experimental, mathematical modeling.

2. Hypotheses about risks (factors, time, territory, groups) are formulated at the stage

A. descriptive and evaluative;
B. experimental;
C. analytical;
D. mathematical modeling.

3. Test the working hypotheses at stage...

A. descriptive and evaluative;
B. analytical;
C. research planning;
D. descriptive.

4. Select the definition that corresponds to the term "risk factor" -

A. circumstance, the presence of which determines the likelihood of complication of the epidemic situation;
B. spatial unit (geographical or territorial-administrative), which is characterized by higher compared to other territories rates of morbidity of the population for a particular infectious

disease;
C. time interval (years, months), when the disease is most likely to occur compared to other time intervals;
D. the part of the population that has a higher risk of contracting the pathogen due to the action of natural and / or social factors.

5. Retrospective epidemiological analysis is.

A. epidemiological examination of foci in connection with the emergence of group diseases;
B. rapid establishment of the causes of the epidemic;
C. analysis of the results of laboratory tests of samples from the center of salmonellosis;
D. study of the epidemic situation over a period of time and prediction of morbidity.

6. The first stage of retrospective epidemiological analysis includes.

A. collection of data on infectious diseases;
B. collection of demographic data;
C. analysis of the annual dynamics of morbidity;
D. establishing a retrospective epidemiological diagnosis;
E. drawing up a survey program.

7. The purpose of operational epidemiological analysis is to obtain data on.

A. sanitary and hygienic condition of facilities in a certain area;
B. epidemic situation for several years;
C. socio-economic condition of the population.

8. Epidemiological diagnosis is...

A. analysis of the level, structure of infectious morbidity for a certain period of time in the past and forecasting morbidity for the future;
B. recognition of manifestations of morbidity and epidemiological situation on the basis of CEM and scientific data on the causes, conditions and mechanisms of occurrence and spread of infectious diseases;
C. analysis of a specific epidemic situation in a particular area at this time, which directly reflects the state and trends of the epidemic process.

9. The seasonality factor is.

A. the ratio of the number of diseases registered during the period of increasing morbidity to the total number of diseases per year, expressed as a percentage;
B. the ratio of the number of diseases in the month of increasing morbidity to similar in the off-season;
C. the ratio of the number of patients in the cells to the number of cells of the same type;
D. the ratio of the number of diseases in the period of increase to the average.

10. The experimental method allows.

A. to establish the causes of the outbreak of infectious disease in DDZ
B. to determine the territorial features of the distribution of cases of viral hepatitis A over 10 years
C. hypothesize the causes of an outbreak of measles at school
D. confirm hypotheses, determine the feasibility of using new approaches (tools, methods,

techniques) in disease prevention and their potential effectiveness

Chapter 6.
Evidence-based medicine. Basic principles and provisions.

It is known that even long-standing medical traditions and "generally accepted methods" have not yet been subjected to adequate scientific verification. Gradually, ideas emerged in medicine that increase its effectiveness - for example, the "Gold Standard of Therapy" and "Drug of Choice". The term evidence-based medicine was proposed by a group of Canadian scientists at McMaster University (1990). Evidencebased medicine spread in the late 80's of the twentieth century. as a concept of new clinical thinking in the process of forming a new field of medical knowledge - clinical epidemiology, which uses the methods of epidemiology in relation to the results of the application of various medical technologies. EBM can be defined as the latest technology of collection, analysis, synthesis and application of scientific medical information, which allows to make optimal clinical decisions both in terms of patient care and cost-effectiveness. Formation of EBM at the present stage of development of society is associated with the development of the health care system due to rapid scientific and technological progress, rising health care costs due to rising prices for medicines, high cost of new medical technologies for diagnosis and treatment of various diseases, expanding the range of medical services and for other reasons. The financial resources that society allocates for health care are limited even in the most highly developed countries, and the need for public spending on health care is constantly growing. Therefore, the problem of choosing a medical technology with proven effectiveness from a large number of alternatives in our time becomes especially relevant because it increases the effectiveness of treatment.

Evidence-based medicine (English evidence-based medicine; science-based medical practice) - an approach to medical practice in which decisions on the use of preventive, diagnostic and therapeutic measures are made based on available evidence of their effectiveness and safety, and such evidence is searchable, comparable, generalized, and widely disseminated for patient benefit (Evidence Based Medicine Working Group, 1993).

The globalization of information processes in all areas of knowledge and, in particular, in medicine, has posed qualitatively new problems of decision-making to the doctor, health care provider and patient. Even new handbooks often cite outdated information, and the recommendations of experts in textbooks and reviews are not supported by evidence. The flow of medical information is growing - about 40,000 medical and biological journals are published worldwide, in which about 2 million articles are published annually. Practitioners and health care managers are in dire need of critical evaluation of information.

Only evidence-based medicine or evidence-based medicine can solve these problems. It is now the focus of clinicians, healthcare professionals, lawyers, patients and the public. Evidence-based medicine involves the use of the best modern evidence to treat each patient in good faith, based on common sense and common sense. According to another definition, evidence-based medicine is a branch of medicine that is based on evidence

that seeks to compare, summarize, generalize, and disseminate evidence to be used for the benefit of patients.

The practice of evidence-based medicine involves combining individual clinical practice with the best available independent clinical evidence derived from systematic research. Individual clinical practical experience is understood as professionalism and judgments that were obtained by an individual clinician by means of his clinical practice. The best independent clinical evidence is the data of clinically relevant studies, often in fundamental areas of medicine, but mainly clinical studies with the accuracy and precision of diagnostic tests (including clinical examinations of patients), assessment of adequacy of prognostic markers, and efficacy and safety of therapeutic, rehabilitation and preventive measures. Physicians should use both individual clinical practice and the best available clinical evidence, and never just one thing. Without individual practical clinical experience, practical decisions are significantly influenced by evidence obtained even from flawlessly conducted studies, which may be inadequate for the individual patient. On the other hand, making practical decisions, without taking into account independent practical decisions, can also harm the patient.

Evidence-based medicine is a branch of evidence-based medicine that involves the search, comparison, analysis, and implementation of evidence for use in patients (Evidence Based Medicine Working Group, 1993).

Evidence-based medicine involves a thorough, sound study based on common sense, using the best current evidence to treat each patient (O. J. Sackett et al., 1996). It is used in daily medical practice (in diagnosis, treatment and prevention) of medical technologies and drugs, the effectiveness of which has been proven in pharmacoepidemiological studies using mathematical estimates of the probability of success and risk. Evidence-based medicine is based on testing the effectiveness and safety of methods of diagnosis, prevention and treatment in clinical trials. The practice of evidence-based medicine is understood as the use of data obtained from clinical trials in the daily work of a doctor.

In most countries, some of the rules for conducting clinical trials set out in the GCP (Good Clinical Practice) standard, as well as the rules for the production of medicines (GMP standard) and laboratory tests (GLP standard), have become generally accepted.

The main principle of EBM - each clinical decision should be based on scientific facts that are statistically proven on a large representative group of patients; no new medical technology (new method of treatment, diagnosis, prevention) can be recognized without mandatory testing in the context of randomized controlled trials. The mechanism of implementation of the principles of D.m. in wide clinical practice there is a standardization of medical care and the introduction of a formulary system.

The main method of EBM (gold standard) are randomized controlled trials in which patients are randomized to randomize. In practical terms, **EBM sets itself the following tasks:**

- improve the quality of medical care in terms of efficiency, safety and cost;
  optimize the activities of the national health care system.

To obtain evidence of the effectiveness of medical technology EBM operates with the following basic pharmacoepidemiological concepts:

- actual clinical outcome - a phenomenon that is important for changes in health (recovery, disability, mortality, life expectancy) and / or quality of life;
- indirect (indirect) criterion of effectiveness - a laboratory indicator or symptom, the dynamics of which directly characterizes the patient's condition and is reflected in the final clinical result;
- absolute risk - the absolute difference between the frequency of development of an adverse effect with the use of drugs and the frequency of development of the same effect without the use of drugs;
- relative risk - the ratio of the frequency of adverse effects among subjects exposed to the factor under study (used drugs) to the frequency of development of a similar effect in the group of persons not exposed to this factor (not used drugs).

International experience in the use of evidence-based medicine

In most economically developed countries of the world EBM today has become widespread. Symposiums on the problems of clinical epidemiology and EBM are constantly held, monographs, reference books and international journals are published, in particular "Clinical Evidence", "Evidence Based Medicine", "ACP Journal Club", etc., which inform the medical community of the world on these issues. According to the principles of EBM The International Regulations for Scientific Research in Medicine (GCP) have been established. It guarantees the reliability of the results of various methods of pharmacotherapy and protection of the rights of the subjects of clinical trials - patients.

In Ukraine recently EBM is rapidly evolving: modern principles of organization of the health care system are based on the most important provisions of EBM started in NUPh, medical universities of Kyiv, Ternopil, Dnipropetrovsk and others.

Areas of medical science formed in the process of development of evidence-based medicine technologies

Development of ideas of evidence-based medicine. The international system of evidence-based medicine is evolving exponentially: since its inception in the early 90's and until now, the number of centers, monographs and forums on the problem is estimated at dozens, the number of publications - hundreds. The U.S. Health and Science Policy Agency subsidized 12 such centers in 1997 for 5 years, established at leading universities and research organizations in various states; the number of centers on individual problems is growing (children's health, first aid, general practice, mental health, etc.) Common to the whole area is the use of the principle of evidence at any level of decision-making - from the state program to the appointment of individual therapy. The world's largest organization - The Cochrane Collaboration.

The role of evidence-based medicine in physician practice

The globalization of information processes in all areas of knowledge and, in particular, in medicine, has posed qualitatively new problems of decision-making to the doctor, health care provider and patient. Even new handbooks often cite outdated information, and the recommendations of experts in textbooks and reviews are not supported by evidence. The flow of medical information is growing - about 40,000 medical and biological journals are published

worldwide, in which about 2 million articles are published annually. Practitioners and health care managers are in dire need of critical evaluation of information.

Therefore, there is a problem - which medicine to choose: traditional or alternative, "university" or folk, domestic or Western. And when making any decision in medicine (medical, diagnostic,

management) there is a problem of choosing an approach based on practice, experience, intuition, the logic of scientific ideas or evidence of effectiveness and safety obtained in the process of bona fide experiments.
Only evidence-based medicine or evidence-based medicine can solve these problems. It is now the focus of clinicians, healthcare professionals, lawyers, patients and the public. Evidence-based medicine involves the use of the best modern evidence to treat each patient in good faith, based on common sense and common sense. According to another definition, evidence-based medicine is a branch of medicine that is based on evidence that seeks to compare, summarize, generalize, and disseminate evidence to be used for the benefit of patients.
The practice of evidence-based medicine involves combining individual clinical practice with the best available independent clinical evidence derived from systematic research. Individual clinical practical experience is understood as professionalism and judgments that were obtained by an individual clinician by means of his clinical practice. The best independent clinical evidence is the data of clinically relevant studies, often in fundamental areas of medicine, but mainly clinical studies with the accuracy and precision of diagnostic tests (including clinical examinations of patients), assessment of adequacy of prognostic markers, and efficacy and safety of therapeutic, rehabilitation and preventive measures. Physicians should use both individual clinical practice and the best available clinical evidence, and never just one thing. Without individual practical clinical experience, practical decisions are significantly influenced by evidence obtained even from flawlessly conducted studies, which may be inadequate for the individual patient. On the other hand, making practical decisions, without taking into account independent practical decisions, can also harm the patient.

Definition of evidence
A physician who uses the principles of evidence-based medicine in his practice always compares individual clinical knowledge and experience with evidence of the effectiveness of treatments and drugs obtained by other clinicians in systemic studies, and honestly, accurately and meaningfully uses the best results to choose treatment for a particular patient.
The methodological basis of evidence-based medicine is systematic research - scientifically sound, well-organized clinical trials with the definition of endpoints - the patient's recovery, the development of possible complications and more.
The standard of quality of research on the effectiveness of treatment is randomized controlled clinical trials.

All randomized clinical trials are based on the current level:

- clinical ideas for the diagnosis of diseases and basic research on their pathogenesis;
- experimental studies to study the pharmacological properties and mechanisms of action of drugs.

Clinical trials should be controlled, randomized, and often double-blind.
Controlled study involves strict selection of patients according to the inclusion / non-inclusion criteria according to the study protocol.
Randomized study - random, ie independent of the wishes of the investigator and the patient, the division of patients into experimental and control groups. The purpose of randomization is to avoid patient selection and to create conditions for comparing the effect of a drug with a placebo or other drug.

The double-blind method is a study in which neither the doctor nor the patient knows which drug the patient is taking. A simple (single) blind method - only the patient is not informed about the drug. The doctor knows what medication his patient is taking. Open study - both the doctor and the patient know what drug is used for treatment.

The most evidence-based studies of drug efficacy are randomized, double-blind, controlled trials. These large-scale, often international, studies are based on certain rigid principles, the sequence of which is traced throughout the study.

At the planning stage of the study:

1. clear scientific questions are formulated, for example:
    - Is the efficacy of the study method different from placebo (placebo-controlled studies)?
    - Is the effectiveness of the treatment being studied different from the previous one (comparative studies)?
    - How safe is the method of diagnosis or treatment?
    - How effective and accurate is the diagnostic method in determining the symptom being studied?
2. a plan for future research is clearly spelled out. The "gold standard" for the study of a new method of treatment, without which in developed countries (USA and Western Europe) no drug enters the market, is a double-blind placebo-controlled clinical trial. A good plan allows you to get results that can only be interpreted in one direction, without "differences", ie the interpretation of the results does not depend on the benefits (or benefits) of the study.
3. researchers obtain the consent of the ethics committee. The essence of this is that scientific research in no way violates the interests of the people who take part in it. Patients should not be left without the most effective of the known means. The test substance should not be toxic, carcinogenic, cause adverse reactions and effects that impair the patient's health, etc.

Once the study is planned and approved, its direct implementation begins. Such studies usually involve dozens of medical centers from different countries, whose activities are clearly monitored by independent commissions. Violation of the rules established at the planning stage can greatly discredit the medical institution, so the staff adheres to these rules. The number of patients participating in the study can range from a few dozen to a million.

The obtained results are subjected to careful statistical processing and analysis, which allows to identify and assess the reliability of the differences.

Conclusions and recommendations for doctors and patients, as well as implementation in the standards of medical care are based only on reliable and verified research results. Standards for the provision of medical care are established by conciliation commissions and committees of experts on the basis of these reliable studies.

Thus, modern research of the highest level of evidence is able to produce reliable facts that are embedded in the basis of clinical practice. They create the foundation of evidence-based medicine, which, unlike empirical medicine, allows for diagnosis and treatment with the highest efficiency and safety and lowest cost.

Aspects of evidence-based medicine

The positive impact of evidence-based medicine should be considered in terms of the following aspects.

- **Medical and ethical aspect.** Doctors prescribe only those diagnostic procedures that provide real information about the patient's condition, do not harm health and allow you to choose the most effective treatment. Doctors prescribe only those treatments that have previously proven effective in correct studies in thousands of such patients. The patient

is aware of what is happening to him, participates in decisions about his health and can always check the correctness of the appointments. Evidence-based medicine makes communication between doctor and patient honest, open and transparent.

- **Economic aspect.** Payment for medical services can be made from various sources: the state budget, funds for compulsory or voluntary health insurance, and, finally, personal funds of citizens. These four sources are combined, first of all, by the unwillingness to pay for excessive examination and unreasonable and ineffective treatment. On the other hand, it is desirable to get the maximum effect from the money spent. Evidence-based medicine prevents the use of extra funds and helps to use them effectively.
- **Legal aspect.** Citizens, insurance companies, the state, and public organizations have a single tool in the form of standards for providing the most adequate medical services. Evidence-based medicine allows you to control any activity in the field of medicine.
- **Educational aspect.**

1. The concept of continuing distance postgraduate education of doctors. Constant adherence to the standards of evidence-based medicine would allow to effectively and professionally train medical staff and improve their skills in a timely manner.
2. The concept of a single standard for postgraduate training of doctors. At the same time, there will not be such striking differences between diplomas and certificates obtained in different medical institutions and, accordingly, in the qualifications of doctors.
3. The concept of a unified approach to the treatment of patients. Evidence-based medicine allows patients to be treated according to the only most effective approaches, with the doctors themselves better understanding each other.

EBM solves the following problems:

1. Standardize the activities of scientists, doctors and health care organizers according to the principles of EBM.
2. To increase the effectiveness of pharmacotherapy of acute diseases and syndromes and to stabilize the long-term remission of chronic pathological conditions, reduce mortality and improve the quality of life of patients.
3. Increase the safety of treatment and reduce the risk of complications and worsening of the disease through the rational appointment of drugs and treatments.
4. Optimize the performance of national health systems.
5. Optimize the economic provision of treatment, giving preference to less expensive and at the same time sufficiently effective drugs, methods of diagnosis and treatment.

Guiding principles of EBM:

The principle of using scientific and medical information only the highest level of evidence. Such information is concentrated in the results of clinical trials conducted exclusively on humans, and summarized in clinical guidelines, systematic reviews, metaanalyzes, international consensus, and others.

The principle of constant updating of information on the achievements of medical science and clinical practice. It accelerates its use to optimize the diagnostic process, increase the efficiency and safety of any medical interventions, improve the performance of scientific institutions and national health authorities. This is facilitated by professional publications,

electronic databases accessed through the Internet, and frequent reprints of modern leading directories.

The principle of constant acquaintance of all participants in the medical field with the achievements of science and practice. Conditions are created for daily control of the professional activity by its comparison with world achievements. It helps to improve the results of scientific and clinical research, increase the professionalism of scientists, general practitioners, public health officials at all levels.

The principle of optimal diagnostic expediency. It provides for the maximum use of all currently accepted methods of examination of patients, including anamnestic, physical, instrumental and laboratory, and in a single diagnostic complex.

The principle of rational pharmacotherapy as a basis for individual programs of highly effective, safe and economically justified treatment of any disease. It is based on the optimal use of three groups of drugs and resuscitation measures (pharmacotherapy algorithm):

- basic drugs that can radically change the course of the disease, stabilize its development, eliminate dangerous manifestations, prevent disaster;
- drugs for special indications in the presence of patients with clinically threatening syndromes, complications, exacerbations of comorbidities, which also requires medical intervention. These are often encephalopathies or comas, respiratory disorders, or cardiovascular, renal or hepatic failure, etc .;
- additional drugs that are added to the treatment program in order to complete the pharmacotherapy of acute diseases, or to provide long-term remission - chronic pathological conditions.

The principle of scientifically sound prognosis of the disease. The doctor is not always able to cure the patient, but to alleviate his suffering and provide him and his relatives with reliable information about the inevitable adverse effects of the disease is obliged in any case. Therefore, the prognosis, ie the prediction of possible clinical outcomes of the disease and the probability of their occurrence in the future, should be based on the results of the same studies that are conducted on diagnosis and treatment.

The principle of continuous improvement of safety of medical interventions (diagnostic, medical, physiotherapeutic, surgical, organizational). It is achieved by conducting the same clinical trials as establishing their effectiveness (mostly randomized).

The principle of standardization of medical interventions in order to use only the most effective, safe and cost-effective methods of diagnosis, prevention and treatment, taking into account the type of treatment and prevention facilities. It is based on the results of clinical trials conducted to establish the effectiveness of drugs, certain methods of medical interventions, as well as on the results of research on the effectiveness of organizational technologies. Based on the results of such studies, appropriate clinical recommendations are created, ie standards of medical interventions, for example, for the treatment of heart failure, hypertension, stroke, epilepsy, infectious diseases, etc. Such standards include, in particular, the minimum amount of care required for patients, which is mandatory for all medical institutions in the country, as well as the optimal care provided as far as possible.

The principle of minimizing the economic costs of diagnosis and treatment of diseases. Treatment tactics should be based on pharmacoeconomic approaches.

The principle of collective responsibility for the high efficiency of diagnostic and therapeutic technologies. This primarily applies to such common diseases as stroke, myocardial infarction, acute poisoning by toxic substances and the like. From the standpoint of EBM now in the treatment process is leading to conscious action not only the doctor but also the patient, who has the right to complete information about their health, the nature of the disease, risk to life, real approaches to treatment, positive and negative consequences of each of existing

methods.
The principle of constant optimization of the activities of national health care systems in order to rationally use public resources and opportunities of patients, the organization of promising national projects and programs, special training and retraining, etc. It contributes to the improvement of the results of the work of direct executors (scientists, doctors, managers), the activities of treatment and prevention facilities and the medical industry in general, the formation of state policy on health care in general.

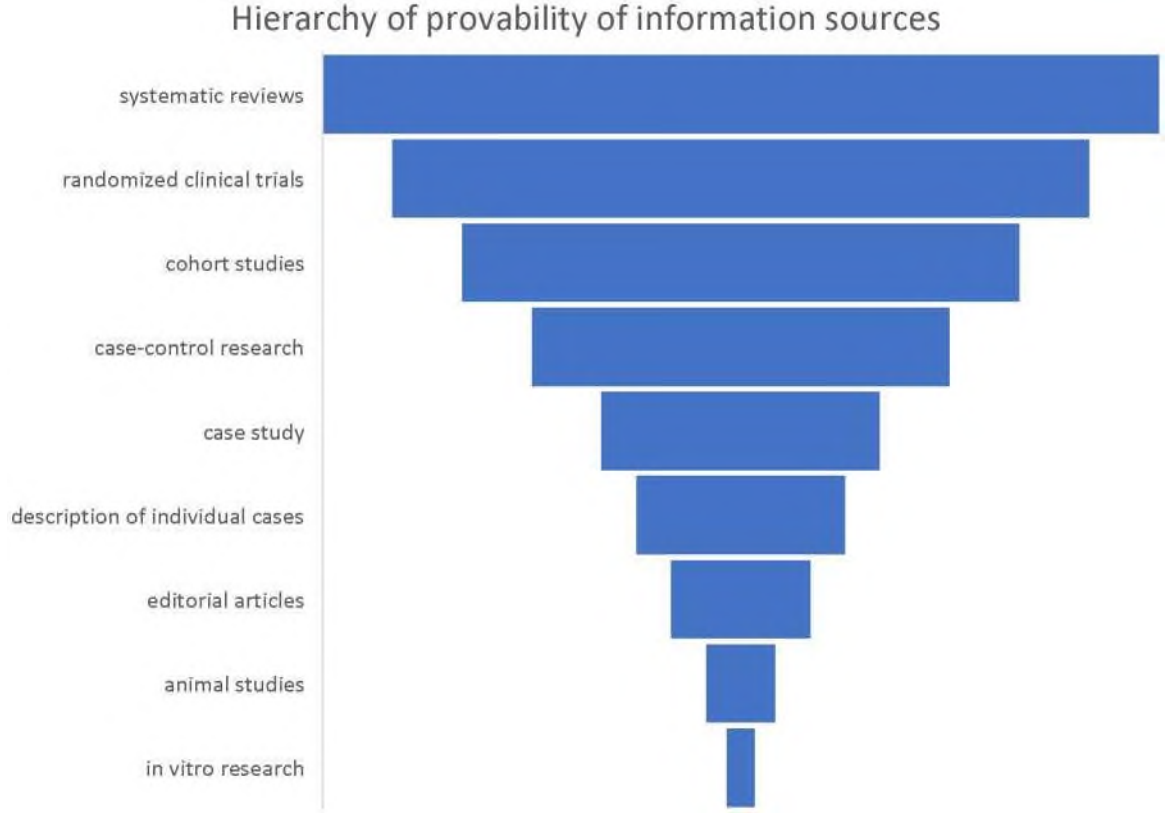
In 1948, British doctors published the results of the first clinical trial of the effectiveness of streptomycin in tuberculosis. One group of patients was treated with streptomycin, the other - according to the then standard pharmacotherapy regimens. The distribution of patients into groups was performed according to the table of random numbers. **The principle of randomization** - "randomly selected groups" - has become the gold standard of medicine. The most acceptable and reliable is a randomized study with the principle of double-blind control. During a **randomized study** of the effectiveness of a drug in a particular disease, groups of patients (at least two) are distributed randomly. This achieves the practical identity of groups of participants in quantitative and qualitative indicators. Analyze and evaluate the effectiveness of a particular type of medical intervention. **Non-randomized** studies suggest that patients be divided into groups at random, where random distribution is not possible for technical or ethical reasons.
Cohort studies involve the formation of two or more groups (cohorts) of patients, of which only one evaluates the relevant medical or therapeutic intervention, although the clinical outcome is recorded in all groups. Observations can last for years (for example, the effect of smoking on the development of lung cancer).
Transverse (or one-time) studies are conducted by questioning, examining, collecting answers to a specific question among doctors and patients. Examination and collection of information about the patient (or group of patients) is carried out once. This makes it possible to establish the picture of the disease in one patient (or group of patients), to clarify the symptoms, to determine the individual manifestations and severity of the disease. The end result is a description of the disease in an individual patient, and in a set of options - is a study of the relationship of some symptoms with the variant of the disease.
Case-control studies are performed in situations where the expected clinical effect is very rare or slow. Form a group of people from individual cases of the disease or clinical effect. Next, a control group is selected from persons without such a disease or condition, but similar in important prognostic characteristics - age, sex, comorbidities. The number of patients who have experienced certain adverse and undesirable effects is calculated in all groups. The results are correlated taking into account known and measurable prognostic factors.
A case description or series of cases is a brief report of successful treatment or manifestations of threatening complications of pharmacotherapy, which is essential for prompt medical information. The value of the method lies in obtaining prompt notification of the complexity of treatment, the occurrence of side effects, etc., because waiting for years for relevant more reliable information is often impractical.
Recommendations for the management of patients should be systematized according to the principle of reliability of the effectiveness and appropriateness of use.

Levels of evidence and degree of recommendations
In practice, health professionals can use many potential sources of information about medical interventions:

- materials of researches carried out by medical experts or experts from other areas;research

- materials and other information from pharmaceutical and other companies;
- research reviews and clinical guidelines;
- opinions of experienced specialists (experts);
- opinions of colleagues;
- their personal experience;
- Patient testimonials based on personal experience.

For a doctor, the most valuable are studies published in scientific medical journals. This is due to the fact that articles in journals are strictly selected and edited, which reduces the likelihood of receiving poor quality information, or incomprehensible, uninformative message.
In turn, scientific reports in journals do not always contain the results of original research. It can also be comments, discussions. Along with medical and biological studies, as well as studies performed on animals are published in journals.
The most convincing information is research, characterized by the fact that it is a systematic process conducted according to a clearly defined protocol, which seeks to exclude or explicitly indicate the researcher's own passions and allow to obtain results that are relevant to patients / clients and practitioners, working in this field.



Research data have different levels of evidence. Using the "pyramid of evidence", The doctor should always prefer the results of the most evidence-based research. In terms of the effectiveness of therapy and prevention, the most evidence-based studies are randomized clinical trials (RCT). In the case where there are many RCT, systematic reviews allow to take into account the differences between them and to get a generalized assessment based on the whole set of RCT. Therefore, it is considered that the conclusions of systematic reviews are more conclusive than the results of individual RCT.

Gradations (classes) and levels of evidence were developed at Oxford:
Class I - the presence of consensus and / or evidence of the effectiveness, appropriateness and

effectiveness of the procedure.
Class II - conflicting evidence and lack of consensus on the effectiveness and appropriateness of the procedure
IIA - "scales" of evidence / consensus tend to the effectiveness and appropriateness of the procedure;
IIB - "scales" of evidence / consensus tend to inefficiency and inexpediency of the procedure;
Class III - the presence of consensus and / or evidence of ineffectiveness and inexpediency of the procedure, and in some cases - even its harmfulness.

In turn, the degree of proof of the effectiveness and feasibility of the procedure is divided into three levels of reliability:
Level A - data obtained from at least two randomized trials;
Level B - data obtained in one randomized clinical trial and / or meta-analysis, or in several non-randomized trials;
Level C is a consensus of experts' beliefs based on research results and clinical practice.

EBM is a method of medical practice that differs in the use of the most reliable information for medical decisions. The main goal of EBM is to constantly increase the efficiency of medical services for the diagnosis, treatment and prevention of diseases, as well as the use of methods that lead to the rational use of limited resources.
EBM uses the achievements of a relatively young science - clinical epidemiology. Clinical Epidemiology (CE) develops the scientific foundations of medical practice. The main postulate of CE: every clinical decision should be based on strict scientific grounds. This is "evidence-based medicine", literally - "evidence-based medicine" or, more accurately, reflects the meaning of the term, "science-based medical practice" or "science-evidence medicine" **The concept of "evidence-based medicine" means the following:**

- guaranteeing the most effective and safe treatment based on the most reliable evidence available;
- collection, interpretation and integration of reliable clinical data obtained from the observations of specialists and during trials, patient reports;
- technology of search, analysis, generalization and application of medical information, which allows to make optimal clinical decisions;
- a process of lifelong learning that allows you to integrate the most reliable of the existing evidence with individual experience;
- a new paradigm of clinical medicine, which differs from the previous one with less influence of subjectivity on the choice of criteria for diagnosis and therapy and requires the doctor to critically evaluate the opinions of various experts and the results of clinical trials;
- information technology for choosing the best options for medical activities.

According to well-known experts, EBM is the conscious and consistent use of the best proven results of clinical trials in the treatment of a particular patient. The concepts used in this definition have the following meanings.

- Conscious: conscious application of test results to each patient.
- Consistent: taking into account in each clinical case the risk-benefit balance of the treatment used, taking into account the uniqueness of each patient, including his general condition, comorbidities and benefits.

- Best proven research results: based on a critical approach, the specialist chooses the best from the full range of research on the diagnosis or treatment of a particular disease.

An objective prerequisite for the emergence of EBM was the increase in scientific medical information, as well as the lack of financial resources associated with rising health care costs. Every year more and more new methods of diagnosis, treatment and prevention are introduced into medical practice. These methods are more or less actively studied in numerous clinical studies, the results of which are often dissimilar and even opposite. Therefore, from a large number of methods it is necessary to choose the one that has the highest efficiency and safety. Keep in mind that the novelty or high cost of a new intervention does not guarantee its superiority over others.

Conditions for the effective functioning of evidence-based medicine:

The introduction of the principles of evidence-based medicine in the practice of medicine requires:

- conducting research with a high level of evidence;
- availability of scientific journals of the so-called "high level of citation", in which works of only high scientific significance are published;
- the presence of doctors who know what, in which journals and how to read;
- opportunities to apply knowledge in practice;
- patients' interest in implementing the principles of evidence-based medicine;
- the state's interest in disseminating reliable scientific knowledge among doctors, pharmacologists and patients;
- doctors' interest in disseminating evidence-based medicine.

Clinical trials

Conducted in 4 phases:

The first phase is performed on 20-80 healthy volunteers in order to establish the dose range of the drug, its tolerability and safety.

The second phase of the clinical trial is the first experience of using the active substance in patients with the disease. The main goal is to prove the clinical effectiveness in the study of 200-600 patients, to determine the levels of therapeutic doses of the substance, dosing regimens.

The third phase of clinical trials is a rigorous controlled study that is conducted to determine the safety and efficacy of active substances in conditions close to their use in the treatment of patients. More than 2,000 patients are involved in such studies. Study the effect of the substance in combination with other drugs. Conduct controlled trials with placebo, the reference drug, or the standard of care. Uncontrolled clinical trials (blind and open) may also be performed.

The fourth phase of clinical trials is conducted after the registration (licensing) of the drug in order to obtain even more information in terms of safety and efficacy.

During the clinical study establish:

- improvement of schemes and terms of drug dosing;
- interaction with food or other drugs;
- the influence of certain factors of the drug on survival, etc.

In a clinical study, the goal of treatment of patients is determined by **surrogate endpoints** - the

parameters of the disease, which provide a direct or long-term result of the factor.

There are three types of endpoints:

- primary endpoints are the leading indicators that indicate a possible prolongation of the patient's life (reduction of overall mortality, mortality from the disease);
- secondary endpoints are characterized by improving the quality of life of the patient or by reducing the incidence of non-lethal complications, or by alleviating the clinical signs of the disease;
- Tertiary endpoints are indicators that are not relevant to improving the quality of life or prolonging it, but may indicate the ability to prevent disease by eliminating risk factors.

Clinical trials

Significant progress in elucidating the causes and spread of diseases has led to the development of new methods for their diagnosis, treatment and prevention, many of which have reduced the incidence, especially infectious. All this contributed to the strengthening of the empirical approach in medicine. The peculiarity of the approach is the focus on the direct study of phenomena. Real observation is used as a method. Only such an approach, according to most scientists, has largely guaranteed the effectiveness of applied methods of diagnosis, treatment and prevention of diseases. The predominance of the empirical approach in medicine has led to the fact that almost by the middle of the XX century. judgments about the effectiveness of diagnostic methods and methods of treatment of patients were based mainly on personal experience, the experience of this team and authoritative opinion.

However, in the XV-XVI centuries. some scientists have believed that the potential effectiveness of treatments and disease prevention, although consistent with empirical knowledge, must be evaluated experimentally. Experiment (experience) is a general scientific method of testing causal hypotheses by means of controlled intervention in the natural course of the studied phenomenon. The purpose of epidemiological experimental research is to assess the potential and actual effectiveness and safety of prophylactic and medicinal products, methods and schemes of treatment, diagnosis and prevention of diseases.

A **clinical trial (CT)** is a controlled experimental study in which subjects receive prophylactic, diagnostic, or therapeutic agents to evaluate their effectiveness and safety.

The general rules for involving human CT follow from the Nuremberg Code and the more detailed Helsinki Declaration of the World Medical Association. Later, in order to streamline preclinical and clinical studies, the WHO in 1974 developed "Guidelines for the evaluation of drugs for human use." Subsequently, on the basis of this document in the United States were developed national rules for CT, issued in 1977 under the name "Rules of Good Clinical Practice" (Good clinical practice, GCP). Then similar rules were adopted by other countries (EU, Japan, Canada, Australia). In order to harmonize them, international conferences were held (the first in 1991, www.ich.org), in which drug manufacturers played a significant role, so GCP does not fully meet the requirements of the Declaration of Helsinki. The language of these documents also differs. While researchers talk about medical intervention trials as research options that focus on evaluating the effectiveness and safety of the intervention, the ICH documents use the more general term "research." Since 1998, the WHO has been implementing the project "Implementation of International Standards in the Practice of Clinical Trials in Central and Eastern Europe". Thus, GCP rules have been developed to ensure that CT results are reliable and accurate and protect the rights, inviolability and confidentiality of subjects. They cover the entire chain of clinical trials - setting, conducting, performing, controlling, inspecting, registering, analyzing and reporting on CT.

The concept of three E in clinical trials should meet: Efficacy; Effectiveness; Efficiency

(Benefit for the individual patient / population / society as a whole).
The process of clinical trials of new drugs includes four interrelated phases.

Classification of experimental epidemiological studies.
Randomized clinical trial: evaluation of the potential efficacy and safety of immunobiological drugs and medicines.

Randomized field study: evaluation of the potential efficacy and safety of immunobiological drugs.
Continuous field study: assessment of the real efficacy and safety of immunobiological drugs and medicines.

The drug undergoes serious tests before it appears on pharmacy shelves. The following practice is accepted in the world: at first these tests are carried out within the framework of the preclinical phase (preclinical phase), which implies the development of the drug in research centers and laboratories. Usually, organizations that develop new drugs are called research and development organizations. In large pharmaceutical companies there are departments of research and development (Research and Development Departments). However, many small companies are developing 3-4 new drugs or even just one drug. Often the financing of such companies is provided by the issuance of shares, which mobilize funds for research. Upon completion of the preclinical phase, such Research and Development companies can sell their formula to large pharmaceutical companies or start conducting CT themselves. As a rule, they have neither the experience nor the ability to conduct CT, then they begin cooperation with contract research organizations (Contract Research Organizations).

Stages of drug development.
Development of a formula (Development of a Compound). Research laboratories are developing the concept of a new product. The characteristics of the product should be aimed at a positive effect on unwanted pathological conditions of the patient or to slow down / prevent their development.
Preclinical Testing. In order to prove the absence of any side effects in the product and its effectiveness in the claimed field of medicine, conduct tests on animals (mice, rats, dogs and monkeys). This is a preclinical phase of the study. The purpose of the stage is to prove that the product has no carcinogenic, mutagenic, teratogenic effects. Also preclinical research allows to understand interaction of a product with an organism. As soon as the pharmaceutical company proves the safety of the product and the possible effectiveness in animal testing, it transmits this information to the regulatory authorities of the state. The result of this application is an official permission to start the CT.
Clinical Trials / Studies in Humans. It is already carried out on people. CT of the drug - can last for several years. In each subsequent phase, more and more subjects are involved. There are three phases of the study. There is a fourth, post-marketing (post-registration) phase, when the effect of the product is observed after its entry into the market of drugs (prophylactics). To ensure the safety and effectiveness of the product, the manufacturer is obliged to analyze the results of each phase.

Test phases of immunobiological drugs:
I phase. Laboratory tests of vaccines - preclinical study in laboratory animals of toxicity and safety, physical properties, chemical composition of the drug. Study of immunogenicity in laboratory animals. Determination of antigen concentration.
Phase II. Limited studies on immunogenicity and safety. Determination of the correct antigen concentration, the number of components of the vaccine, manufacturing techniques, the effect of subsequent doses and the main side effects. The final choice of the type of vaccine for the

third phase of RCT. The research is conducted only after a positive opinion of the ethics committee, the national body for control of biomedical drugs on volunteers.
Phase III. Large-scale trials of vaccines in healthy patients (thousands of volunteers). Determination of vaccine efficacy and adverse reactions; duration of observation (usually 1 - 2 years, but not less than 6 months). Measuring efficacy, establishing the frequency and types of adverse reactions (randomized field study).
Phase VI. Post-license quality control of vaccines. Continuation of the study of the frequency and severity of adverse reactions, the actual effectiveness in the field experiment (continuous field study).

Phases of clinical trials of drugs.
Phase I. The new product is being tested on humans for the first time. The objectives of this phase of the study are related to product safety. Usually 20 to 100 healthy volunteers (volunteers) are encouraged and hospitalized in a special center. If testing on healthy volunteers is not possible (drugs for the treatment of cancer, AIDS, etc.) or meaningless, you can get permission to conduct the first phase of the study on patients with a certain pathological condition. As a rule, healthy volunteers receive a reward. Most often volunteers - men and women 25 - 30 years (women are not pregnant or breastfeeding); if the drug is intended for use in pediatrics, then at later stages may involve children (non-randomized CT).
Phase II. Evaluate the effectiveness and safety of the drug in patients with the disease for which it was developed. These are often placebo-controlled studies. Sometimes this phase of CT is divided into two more phases. The purpose of the first of them is to assess the short-term safety of drugs. The second is proof of the clinical effectiveness of the drug and determination of the therapeutic dosage level when tested on a group of patients. The number of patients at this stage varies from 40 to 300 and depends on the size of the expected effect. If the planned effect is significant, a small number of patients are enough to prove the statistical significance of the experiment. On the other hand, if the effect is insufficient, patients need much more (randomized or non-randomized CT).
Phase III. Drugs are tested on large groups of patients (hundreds of people) of different ages, with different comorbidities, in numerous research centers in different countries. Studies of this phase are often randomized controlled. They examine all aspects of treatment, including risk / benefit assessment. Based on the results of the CT, the State Pharmacological Center of Ukraine makes a decision on registration or refusal to register drugs.
Phase VI. Occurs after the drug has been approved for use. This phase is often called post-marketing (post-registration). The purpose of research is to identify differences between the new drug and other drugs in this pharmacological group, compare its effectiveness with analogues already on the market, demonstrate the benefits from the point of view of health economics, and identify and identify previously unknown or incorrectly identified side effects and risk factors. As a result, the safety and efficacy of the drug may be periodically reviewed according to new clinical data on its use (continuous / randomized clinical / field study).

Inclusion and exclusion criteria. Criteria for inclusion of patients (subjects). Needed to describe the population (general population) to which the patients included in the study correspond.
Exclusion criteria. Needed to create a homogeneous sample, ie less variability of variables in the initial state and in estimating the magnitude of the effect of the intervention. Persons with severe comorbidities, life-threatening conditions or interfering with experimental conditions (for example, with dementia) are excluded from the number of CT participants. Thus, the statistical sensitivity of the experiment increases.
Consent of participants. Ideally, all patients who meet the inclusion criteria should participate in the trial. In practice, not all patients agree. Some may prefer one of the proven treatments and do not want to give it to the tried and tested method. Others do not want to be studied or choose

another treatment. Such patients are not included in the study. It is necessary that the response rate, ie the share of people who responded to the request to participate in the study, was quite high, at least 80%. Patients will follow the recommendations depending on the acceptability of the study. The results of treatment of such patients are higher and do not depend on treatment. Subjects, actively choose a method of treatment, are treated more diligently, more correctly perform the appointment. This property of people is called accuracy or diligence, but more often - compliance.

Planning the number of participants. The number of patients included in the experiment (sample size) should be justified, based on:

- the expected level of efficiency;
- research structures;
- pre-established threshold of statistical significance of effect detection;
- prevalence of the disease.

When planning a study, expect the number of patients to be sufficient to detect the expected effect. Calculations are quite complex, they are performed using statistical programs.

Randomization - random distribution of patients into groups. Its purpose - minimal differences between groups, by all indications are random, not intentional. The methodology of statistical analysis of data proceeds from the principle of random staffing of groups: differences of groups by definition are casual.

Randomization is carried out in different ways: the use of tables of random numbers, computer programs. Sometimes randomization is replaced by pseudorandomization (division into groups by the first letter of the name, date of birth, medical card number, day of the week of admission to the clinic, etc.). Its application can affect the correctness of the sample and, accordingly, the evaluation of results. The most terrible adverse consequence of pseudorandomization - will be known to belong to each patient to a particular group (main or control). Thus, the main condition of randomization will not be fulfilled - hiding its results; its most important function - ensuring the blind nature of the study - will not be realized. In studies where no measures were taken to conceal the results of randomization or concealment was insufficient, the assessment of the effectiveness of the intervention was overestimated by approximately 25%. To ensure concealment, reliable technical measures are taken (for example, after the registration of the patient who agreed to the test, information about him is entered in the database of the organizer of the study).

Placebo. When evaluating the effectiveness of a new drug, the question arises about its effectiveness, ie the ability to reduce the likelihood of adverse outcomes compared to the absence of intervention. In the control group, the lack of intervention may be psychologically unacceptable for patients, leading to non-compliance with the test regimen. Patients left without treatment switch to self-medication. That is why patients in the control group are given a substance (procedures performed) that do not differ from active intervention. A placebo is usually a dosage form that lacks the active ingredient, such as a tablet form that is identical in color and shape to the active ingredient but contains only an indifferent substance, kaolin or starch, and for injectable forms, an isotonic sodium chloride solution. The use of placebo is not always possible, and sometimes unethical, for example, when it is unacceptable to deprive patients of effective treatment. Then the control group is prescribed standard treatment and placebo, and the main group - standard treatment and the study drug. The effectiveness of a new drug is easier to show in comparison with placebo, in comparison with an existing drug it is necessary to prove a greater or the same effect of a new drug.

It is believed that the use of placebo has a positive effect, the "placebo effect". The beneficial effect of placebo is related to its psychological effect on the patient. Placebo has little effect only on results that reflect the patient's subjective condition (sleep quality, pain intensity). Clinically

important results are not affected by placebo (life expectancy, remission duration, functional defect, etc.).
Difficulties in prescribing the drug. Regardless of the nature of the intervention (therapeutic, diagnostic, prophylactic), it should be clearly described and standardized.
At appointment of some interventions selection of a dose does not cause difficulties: parenteral administration of drug according to the scheme provides receipt in an organism of a certain amount of active substance. The use of oral forms of drugs already leads to difficulties in dosing. Depending on compliance, patients may not take the daily dose, and in the case of severe side effects - and reduce it altogether. There are interventions that are difficult to dose. These include surgery, chiropractic, acupuncture.
During CT, treatment previously prescribed to the patient is usually stopped. The period after cessation of previous treatment and before the beginning of CT is set so that the concentration of the active substance decreases. If patients in the main group are taking additional drugs (co-intervention), there may be a shift in results toward higher efficacy. If patients in the control group use the same drugs as in the main group (contamination, contamination), the result may be shifted towards the ineffectiveness of the drug.
The trial takes measures to prevent contamination and co-intervention and to increase patient and staff compliance with the protocol's proposed actions. One way is to conduct the introductory stage to the test. At this stage, patients who do not follow the regimen are detected, for example, by determining in the urine of substances introduced into the drug as a label. Then only executive patients are included in the trial. Co-intervention and contamination are almost inevitable, they must be taken into account when analyzing the data.

Outcomes ("target" signs) - events that will evaluate the effectiveness of treatment or other interventions. Types of results:

- clinically important results (mortality, life expectancy, frequency of exacerbations, maintenance);
- intermediate;
- indirect;
- surrogate results.

Quality of life. When assessing the effectiveness of the intervention should not forget to assess the quality of life. Sometimes a small increase in life expectancy can be achieved by unacceptable suffering during treatment, such as oncology. To assess the quality of life, complex scales are used, the final score of which is obtained as a result of summing up various information (about the intensity of pain, mood, breathing, ability to wash yourself, take care of yourself).

Termination of the trial.
The duration of CT is planned based on the number of participants, the expected frequency of cases and the difference between interventions (the size of the effect), the planned statistical significance of the result. It is incorrect to test until the result is statistically significant, because sooner or later statistically significant differences can be achieved. That is why the duration of the CT is set in advance.
In long-term trials, the rules for terminating CT are set due to the need to maintain the safety of participants and the possible receipt of convincing results in favor of one of the studied interventions.
Trial with data analysis depending on the prescribed or received treatment. The results of controlled randomized trials can be analyzed and presented in two ways: either on the basis of the appointment of a treatment in randomization, or on the basis of treatment actually received by the patient. The correct presentation of the results depends on the question.

- If the question is which treatment tactics are best for making a clinical decision, then the analysis based on the treatment prescribed at randomization should be used, regardless of whether all patients actually received this treatment. This approach is called intention to treat analysis. Advantages of this approach: the question asked corresponds to what is usually of interest to the clinician when prescribing treatment, and the compared patients are really divided into groups randomly. Disadvantage: if many patients do not receive the proposed treatment, the differences between the experimental and control groups disappear, the probability of a negative test result increases. In this case, the lack of differences between groups can be interpreted differently: either the experimental intervention is actually ineffective, or it was simply not applied.
- If we are interested in whether experimental treatment is really better than control. In this case, the analysis based on the received treatment is more suitable for the answer, ie an assessment of the effect of the treatment that each patient actually received and regardless of what treatment was prescribed to him at randomization. The mechanism of the studied effect is clarified. The disadvantage of this approach is that if most patients do not receive the proposed treatment, the trial ceases to be randomized and becomes a routine cohort study. This means that all differences between groups, excluding the method of treatment, must be leveled in some way (by imposing restrictions, selecting pairs, dividing into subgroups or standardization) to achieve full compatibility, as is the case in non-experimental studies.

International requirements.

The basis of the CT is a document of the international organization "International Conference on Harmonization" (ICH). This document is referred to as the "Guideline for Good Clinical Practice (GCP)".

The CT must be conducted in accordance with the basic ethical principles of the Helsinki Declaration, the GCP standard and current regulatory requirements. Prior to the start of the CT, it is necessary to assess the ratio of possible risk to the expected benefit to the subject and society. At the head of the corner is the principle of the priority of the rights, safety and health of the subject over the interests of science and society. The subject can be included in the study only on the basis of voluntary informed consent obtained after detailed study of the study materials. This consent is approved by the signature of the patient (authorized person).

CT should be scientifically substantiated, detailed and clearly described in the study protocol. The Independent Ethics Commission (NEC) is responsible for assessing the risk-benefit balance, as well as reviewing and approving the research protocol and other documentation related to the CT. After receiving approval from the NEC, you can start conducting CT.

Development of drugs and their CT - procedures are very expensive. Some firms seeking to reduce the cost of testing first conduct it in countries where the requirements and cost are much lower than in the country of the developer. Yes, many vaccines were first tested in India, China and other third world countries. Charitable deliveries of vaccines to the countries of Africa and Southeast Asia were used as the II-III stages of CT.

Principles of qualitative clinical trials.

In Ukraine, clinical trials are regulated by orders of the Ministry of Health of Ukraine №690 of September 23, 2009 "On approval of the Procedure for clinical trials of drugs and examination of clinical trial materials and model regulations on ethics commissions", №944 of December 14, 2009 "On approval of the Procedure preclinical study of drugs ", №1169 of September 26,

2017" Drugs. Good clinical practice 42-7.0: 2008 ». The standards set out in these orders are identical to the Consolidated GCP of the International Conference on the Harmonization of Technical Requirements for the Registration of Pharmaceuticals for Human Use (ICH), which prepared by the Association of International Pharmaceutical Manufacturers, the International Confederation of Consumer Societies. Good clinical practice: an international ethical and scientific standard for planning and conducting research involving humans as a subject, and for documenting and presenting the results of such research.

Adherence to this standard serves as a guarantee to society that the rights, safety and well-being of the subjects of research are protected, consistent with the principles established by the Helsinki Declaration of the World Medical Association, and that these CT are reliable.

The purpose of this national standard is to establish common rules with the countries of the European Union, the United States and Japan, which facilitate the mutual recognition of CT data by the authorized bodies of these countries.

Principles of quality CT (GCP).

- CT must be conducted in accordance with the basic ethical principles of the Declaration of Helsinki, GCP rules and applicable regulations.
- Prior to the start of the CT, an assessment of the relationship between the expected risk and the expected benefit to the patient and society should be made. CT can be started and continued only if the expected benefit outweighs the risk.
- The rights, safety and health of the subject are more important than the interests of science and society.
- The data of preclinical and clinical study of the studied drug should serve as a substantiation of the planned CT.
- CT should be scientifically sound, detailed and clearly described in the study protocol.
- CT are conducted in accordance with a protocol approved in advance / approved by the Independent Ethics Commission.
- Only a qualified physician can be responsible for providing medical care to a patient.
- All persons involved in the CT must have professional education and experience relevant to the task.
- The subject may be included in the trial only on the basis of voluntary informed consent obtained after detailed study of the study materials.
- The collection, processing and storage of information obtained during the CT must ensure accurate and correct presentation, explanation and confirmation of data.
- Documents that allow to establish the identity of the subject must be kept secret from unauthorized persons.
- The production and storage of the study drug, as well as its handling is carried out in accordance with the Rules of organization of production and quality control of drugs, or Good Manufacturing Practice (GMP). The drug is used in accordance with the study approved by the protocol.

Documents required for a randomized clinical trial:

- research protocol and amendments thereto;
- the form of written informed consent, its further editions;
- materials to involve the subjects in the study (for example, advertisements);
- researcher's brochure;
- information on the safety of the study drug;
- information on payments and compensations to the subjects;

- CV (curriculum vitae) of the researcher at the moment and / or other materials confirming his qualification;
- any other documents that may be required by the Independent Ethics Commission to perform its duties.

Regulations on the Independent Ethics Commission.
The main task of IEC is to protect the rights and health of the subjects, as well as to guarantee their safety. IEC receives for consideration the documents mentioned above (documents required for the RCT).
IEC considers the issue of conducting CT in a timely manner and gives a written opinion, indicating the name of the study, the documents considered and the date of one of the following possible decisions:

- permission to conduct research;
- requirements to amend the documentation provided to obtain a test permit;
- refusal of permission to conduct research;
- revocation / suspension of previously issued research permits.

IEC assesses the qualification of the researcher on the basis of his CV at the moment and / or other necessary documentation obtained at the request of IEC.
In the course of the research, the IEC reviews the documentation with a frequency that depends on the degree of risk of the subjects, but at least once a year.
If the protocol indicates the inability to obtain the consent of the subject or his or her legal representative prior to enrollment in the study (eg, in emergency therapy), the IEC should ensure that the protocol and / or other documentation fully reflects the ethical aspects of the study.
In order to avoid unreasonable interest or coercion of the subjects, IEC considers the procedure and amounts of payments to the subjects.
The IEC should include a sufficient number of persons with the necessary experience and qualifications to expertly assess the scientific, medical and ethical aspects of the planned study.
It is recommended to include in the IEC:

- at least five members; including:
- one member and no longer a scientist;
- one member and no longer an employee of the medical institution / research center in which the tests are conducted.

Only IEC members who are not employees of the researcher or sponsor may vote on the research permit / approval. IEC draws up a list of its members indicating their qualifications. IEC acts in accordance with the approved standard procedures, keeps the necessary documentation and keeps the minutes of the meeting. Its activities must comply with GCP Rules and applicable regulations. At official meetings, the IEC makes a decision if there is a quorum determined by the relevant regulations. Only IEC members directly involved in reviewing and discussing research documentation can vote and make recommendations for testing permission. The researcher provides information to the IEC on any aspect of the study, but does not participate in the debate or vote on the permission to conduct the trial.

Informed consent. The doctrine of informed consent means that the physician must provide the patient with the following information before asking the patient to consent to a course of treatment or a separate procedure that is associated with risk and has alternatives:

- the essence of the proposed treatment (procedure);
- risks and benefits of the recommended measures, the degree of danger of the most adverse consequences (death or severe disability);

- alternative methods of treatment (procedures), risks, danger of adverse consequences;
- consequences of delayed or not started treatment;
- the probability of a successful outcome, the manifestation of this success;
- possible problems and the duration of the rehabilitation period and the patient's return to normal activity;
- other related information in the form of answers to questions, presentation of similar cases from their experience, the experience of the team, etc.

The information must be provided in a form accessible to the patient in a language he understands. The question of the competence of the decision often arises when the patient is clearly incapacitated (children, persons declared incapable due to mental disorders, etc.). Here, decisions are made according to the same schemes, with the participation of guardians or trustees. As for the homeless, decisions are made by social workers, specially authorized to do so. If there is no consensus in the family or in the guardianship authorities, the issue of the guardian is decided by the court. Voluntariness - the absence of any external pressure (threat, bribery, enslaved financial conditions) on the patient when making a decision, especially when signing written consents or refusals.

Self-control questions

1. Evidence-based medicine basic terms and definitions.
2. Levels of evidence and degree of recommendations.
3. Principles of evidence-based medicine.
4. Aspect of evidence-based medicine.
5. Standards of good clinical practice.
6. Clinical studies.
7. Methods of formulating a clinical question / task.
8. Principles of analysis of economic efficiency of medical interventions.
9. Search and study of new drugs.
10. Patient rights in clinical trials.

Test task

1. The principle of minimizing the economic costs of DM is based on:

A. Pharmacoeconomic approaches.
B. Legal and economic approaches.
C. Material and personnel approaches.
D. Economic and educational approach.

2. What is characteristic of the "Ia" class of evidence - «

A. systematic review or meta-analysis of randomized controlled trials;
B. at least one randomized controlled trial;
C. at least one well-designed controlled study without randomization;
D. at least one well-planned quasi-experimental study, such as a cohort study.

3. The high level of assessment of evidence corresponds to:

A. The described effect is plausible, well-defined and not vulnerable to bias.
B. The effect described is plausible but not accurately estimated or may be vulnerable to bias.
C. Concerns about plausibility or vulnerability to bias significantly limit the significance of the effect being described and substantiated.

4. The concept of "gold standard" includes:

A. Double-blind placebo-controlled randomized trials.
B. Simple nonrandomized studies.
C. Triple blind studies.
D. Double-blind nonrandomized studies.

5. What is the PICO formula?

A. Abbreviations used to help formulate a clearly defined research question.
B. Abbreviation used to formulate a clearly defined problem.
C. Abbreviation used to determine the parameters of the study.
D. Abbreviations used to help optimize the performance of national health systems.

6. A method in which neither the patient nor the doctor supervising him knows which method of treatment was used:

A. double blind;
B. single blind;
C. triple blind;
D. placebo controlled.

7. A study in which only the patient does not know what treatment he is receiving is called...

A. placebo-controlled;
B. double blind;
C. triple blind;
D. single blind.

8. How to create the conditions so that in a randomized controlled trial, patients receiving placebo were not deceived:

A. the attending physician obtains the patient's oral consent to perform the test;
B. the patient signs the "Information Consent" (where his consent to the use of placebo is provided);
C. placebo does not have a harmful effect on the body, so its use does not require consent;
D. the patient signs a consent to the processing of personal data and hospitalization.

9. Conscious, clear and dispassionate use of the best of the available evidence in making decisions about care for specific patients - this is one of the definitions:

A. biometrics;
B. evidence-based medicine;
C. clinical epidemiology;
D. medical statistics.

10. One of the prerequisites for the emergence of evidence-based medicine is-.

A. limited financial resources allocated to health care;
B. the emergence of new medical specialties;
C. improvement of research methods;
D. development of mathematical statistics.

Chapter 7.
Meta-analysis, systematic review and search of scientific and medical information.

Establishment of strong medical associations that create standards of medical care and monitor their implementation.

Algorithm of actions

Work in evidence-based medicine consists of four main stages:

- Formulation of a clear clinical problem based on the specifics of the patient.
- Search for literature on the problem.
- Evaluation (critical approach) of research for their validity and usefulness.
- Application of useful findings in clinical practice.

The answer to this problem can be found in monographs, journals, collections of works, abstracts, general scientific and popular science publications, databases, electronic publications.

A monograph is one of the main sources of information that can be used to search for bibliographic references, but the information provided is rapidly becoming obsolete and does not contain full recommendations for clear, reasonable action.

Journals are the main source of primary scientific information, reflect current trends in science and practice, but often have highly specialized topics. There are not many interdisciplinary journals.

Medical journals must be read in order to be aware of their professional field; know how qualified specialists work with patients, how to use diagnostic methods, know the clinical features and course of the disease; understand the etiology and pathogenesis of diseases; distinguish useful treatment from useless and harmful intervention; navigate the reports on the need, benefits, benefits and cost-effectiveness of treatment and prevention.

Systematic reviews are traditional descriptive reviews, which often contain shifted estimates of the final results due to the lack of application of the scientific approach. An alternative approach, which is becoming increasingly popular, is to compile systematic reviews that include appropriate statistical generalization of facts (meta-analysis). Evidence-based clinical medicine depends on the availability of qualitative generalizations that can be obtained from carefully compiled systematic reviews.

Systematic reviews collect, critically evaluate, and summarize the results of primary research on a particular topic or problem. Approaches that reduce the possibility of systematic and

accidental errors are used in the preparation of systematic reviews. Systematic examinations help physicians stay up-to-date, despite the huge number of medical publications, and can help substantiate clinical decisions with research, although they do not in themselves allow decisions to be made and do not replace clinical experience.

The advantages of systematic reviews are:

- the presence of a total reliable result;
- the ability to identify problems of individual sensitivity;
- promoting the formation of integrated information networks and expanding professional communication;

  evaluation (critical approach) of research on the validity and benefits; - application of useful findings in clinical practice.

To select the material and the author, you can evaluate the work and its significance, and for this use:

- **Citation index** - a measure of the significance of the scientific work of any scientist or research team accepted in the scientific world. The value of the citation index is determined by the number of references to the publication, or to the author's name in other sources.
- **Hirsh index, or h-index** - a scientometric indicator that is a quantitative characteristic of the productivity of a scientist, group of scientists, scientific organization or the country as a whole. The mechanism for calculating the Hirsch index is quite simple: the Hirsch index is equal to N if a scientist (scientific institution) has published N scientific articles, each of which has been cited at least N times. All other articles were cited less than N times.
- **Impact factor** - an indicator of citation of scientific journals, which determines their informational significance. Today it is recognized that the impact factor of the journal is one of the formal criteria by which you can compare the level of research in related fields of knowledge.
- **I-10 index** is a citation index, which means that a scientist (journal, organization, country) has published at least 10 papers, each of which has been cited 10 or more times. The number of works cited less than once can be any.

Scientometric database - bibliographic and abstract database, a tool for tracking citations of scientific publications. The scientometric database is also a search engine that generates statistics that characterize the state and dynamics of demand, activity and impact indices of individual scientists and research organizations. The most relevant are such scientometric databases as:

- **SCOPUS** - the largest abstract interdisciplinary scientometric database and a tool for tracking citations of articles published in scientific journals. Indexes scientific journals, conference proceedings and serials.
- **WEB of SCIENCE** - the world's most authoritative analytical and citation database of journal articles of the Philadelphia Institute of Scientific Information. It contains a system for correcting the identification of scientists and takes into account all citations in scientific papers that are placed in it.
- **Index Copernicus** - an online scientometric database with information about the authors of publications, research institutions, publications and projects. It has several

performance assessment tools that allow you to track the impact of research papers and publications, individual scientists or research institutions.

- **Google Scholar** - a free access search engine that provides full-text search of scientific publications of all formats and disciplines. The service takes into account the total number of citations, the total number of cited publications and the Hirsch index.

Meta-analysis

Traditional descriptive analysis of medical information often leads to distortion of information. An alternative approach, which is becoming increasingly popular, is a systematic analysis with statistical generalization of data (meta-analysis). Meta-analysis includes determining the main purpose of the analysis, the choice of methods for evaluating the results, a systematic search for information, generalization of quantitative information, its analysis using statistical methods, interpretation of results.

What are the statistical methods and when they are used:

What does a statistical test do?

Statistical tests work by calculating test statistics, a number that describes how the relationship between the variables in your test differs from the null hypothesis of no relationship. It then calculates the p-value (probability value). The value of p estimates how likely it is that you will see the difference described by the test statistics if the null hypothesis of no connection were true. If the value of the test statistics is more extreme than the statistics calculated by the null hypothesis, then we can conclude that there is a statistically significant relationship between the variables of the forecast and the results. If the value of the test statistic is less extreme than the value calculated from the null hypothesis, then you cannot conclude that there is a statistically significant relationship between the forecast variables and the results.

Statistical assumptions

Statistical tests make some general assumptions about the data they verify:

- Independence of observations (ie without autocorrelation): The observations / variables you include in your test are unrelated (for example, multiple measurements of one subject are not independent, while measurements of several different subjects are independent).
- Homogeneity of variance: the variance in each group being compared is the same among all groups. If one group has much more variation than others, it will limit the effectiveness of the test.
- Data normality: data follow a normal distribution. This assumption applies only to quantitative data.

If your data do not match the assumptions about the normality or homogeneity of the variance, you may be able to perform a nonparametric statistical test that allows comparisons to be made without any assumptions about the distribution of the data.

If your data does not meet the assumption of independence of observations, you can use a test that takes into account the structure of your data (re-measurement tests or tests that include blocking variables).

Types of variables

The types of variables you have usually determine what type of statistical test you can use. Quantitative variables represent the number of things (for example, the number of trees in a forest). Types of quantitative variables include:

- Continuous (also known as variable ratios): represent measures and can usually be divided into units of less than one (for example, 0.55 grams)
- Discrete (also integer variables): represent the number and usually cannot be divided

into units less than one (for example, 1 human).

Categorical variables represent the grouping of things (for example, different species of trees in the forest). Types of categorical variables include:

- Sequential: submit data in order (ratings).

  Nominal: represent group names (for example, trademarks or species names).
  Binary: represents data with a result of yes / no or 1/0 (for example, win or lose).

Choice of parametric test: regression, comparison or correlation

Parametric tests usually require more stringent requirements than non-parametric ones and are able to draw stronger conclusions from the data. They can be performed only with data that meet the general assumptions of statistical tests. The most common types of parametric tests include regression tests, comparative tests, and correlation tests.

Regression tests

Regression tests are used to check causation. They look for the effect of one or more continuous variables on another variable.

Comparative tests

Comparative tests look for differences among groups. They can be used to test the effect of a categorical variable on the average of some other characteristic. T-tests are used when comparing the means of two groups (for example, the average height of men and women). The ANOVA and MANOVA tests are used when comparing the performance of more than two groups (for example, the average height of children, adolescents and adults).

Correlation tests

Correlation tests check whether two variables are related, without suggesting causal relationships. They can be used to check the automatic correlation of two variables that you want to use in (for example) a multiple regression test.

Choice of nonparametric test

Nonparametric tests do not make as many assumptions about the data and are useful when one or more general statistical assumptions are violated. However, the conclusions they draw are not as strong as in parametric tests.

There are several types of meta-analysis:

- cumulative meta-analysis - allows you to demonstrate the curve of accumulation of estimates in the process of new evidence;
- prospective meta-analysis - useful not only for summarizing previous clinical trials, but also for those trials that are planned to be performed in the future. This approach can be implemented where a network of information exchange and joint programs already exists. In practice, instead of prospective, hybrid prospective-retrospective metaanalysis is often used, which combines the obtained results with previously published ones. This allows the use of general evidence for individuals in each of the group trials, although they may differ in better planning;
- meta-analysis of individual data - which is based on the study of the results of treatment of individual patients, in contrast to the literature. This approach is only available to participants in a clinical trial network who have access to a medical history.

Finding information for meta-analysis requires some experience. In the absence of a systematic approach, many important studies may not be considered. Even a thorough computer search does not always reveal the required research due to poor indexing. For this reason, computer selection should be supplemented by "manual" search of research, study of bibliographies in

articles and inquiries of researchers and drug manufacturers working in the field.
The highest level of reliability is provided by randomized controlled trials, but under certain conditions, for example, in the analysis of adverse effects, retrospective (case-control) or prospective studies, ie observational studies, are more informative. However, many analysts believe that only the results of randomized controlled trials can be used as evidence.
When summarizing data, a critical evaluation of the studies being compared is mandatory. Sometimes the generalization of the results is impossible due to the small amount of research material, their incomparability with each other or a similar statement. In some cases, some fairly reliable tests may differ qualitatively from many others, which does not allow them to be combined for statistical analysis. In this case, an alternative to meta-analysis may be the "synthesis of the best evidence", which is used in the absence of reliable research.
In such cases, a thorough analysis of available research is conducted to determine whether the information obtained is sufficient for conclusions. Next, the findings should be verified in a randomized controlled trial.
If there are sufficiently homogeneous studies, their statistical combination is justified, which allows a more objective assessment of the effect. Statistical methods of data aggregation are numerous and varied, and their choice depends on the characteristics of the available indicators. There are methods to combine data on survival, dose-response, informativeness of diagnostic tests.
Meta-analysis is conducted in order to summarize existing information and disseminate it in a way understandable to readers.

Advantages of meta-analysis

Meta-analysis allows a scientifically sound and reproducible way to summarize information obtained from different sources, which gives a number of advantages. In particular, it can combine studies whose data are statistically inaccurate, which will provide a reliable total result. At generalization the heterogeneity of results which studying of the reasons allows to reveal other clinical problems can be shown. For example, the effectiveness of treatment depends on the individual characteristics of the organism. Accordingly, it is possible to predict the results of therapy in certain groups of patients in the presence of these features and test this hypothesis in future studies. During the meta-analysis, the authors constantly communicate with their research colleagues to clarify certain aspects of their published messages or to search for other research. As a result, information networks are formed, which in the future will facilitate individual and long-term meta-analysis.

Cochrane databases

In his program book, the famous English epidemiologist Archie Cochran pointed out that society is in the dark about the true effectiveness of medical interventions. Decisions based on reliable information are not possible due to the lack of generalized data on the effectiveness of medical interventions. Cochran wrote: "It is a shame that physicians have not yet created a system of analytical generalization of all current randomized clinical trials (RCTs) in all disciplines and specialties with periodic updates."
In 1987, Cochrane conducted the first systematic review of RCTs on pregnancy and perinatal issues, and invited physicians in other specialties to use this experience. He stressed that scientific medical examinations should be created on the basis of a systematic collection and analysis of facts, and then regularly updated with new ones. Without this, it is not possible to judge the advantages or disadvantages of an intervention, make decisions quickly and maintain the quality of care at a decent level. In addition, it is difficult to plan new ones without systematically updating research reviews. Researchers and the organizations that fund them often do not pay attention to promising topics.
Cochrane's dream of systematic updating reviews, which would cover all relevant tests of medical interventions, was embodied in the Cochrane Cooperation - an international

organization whose goal is to search for and summarize the most reliable information about the results of medical interventions. As suggested by Cochran, the methodology for compiling and updating reviews of controlled trials in obstetrics and perinatology has been taken into account by the UK National Health Service's Research and Development Program. Funds have been allocated for the organization of the Cochrane Center to coordinate its efforts, both in the UK and abroad, as well as to establish and update systematic reviews in all areas of medicine.

Principles of Cochrane Cooperation

In the years that have passed since its establishment, the Cochrane Cooperation has undergone significant changes, without deviating from the declared tasks and principles. The main task of this international organization is to create, update and disseminate systematic reviews of the results of medical interventions, which should facilitate stakeholders in decision-making in various fields of medicine.

Cochrane Cooperation is based on eight principles:

- the spirit of cooperation;
- enthusiasm of the participants;
- no duplication in the work;
- minimization of prejudices and systematic errors;
- constant updating of data;
- relevance of reviews;
- availability of reviews;
- constant improvement of quality of work.

Systematic reviews - the main result of the Cochrane Cooperation - are regularly published in electronic form under the name "Cochrane Database of Systematic Reviews" (Cochrane Database of Systematic Reviews). International problem groups are involved in compiling and updating the Cochrane Reviews. The group is attended by researchers, doctors, representatives of consumer organizations - all who are interested in obtaining reliable, up-to-date and relevant information in the field of prevention, treatment and rehabilitation of various diseases.

The Cochrane Electronic Library consists of four separate databases.

1) The Cochrane database of systematic reviews contains final reviews and review protocols that are being prepared.

2) The Cochrane Register of Controlled Tests is a bibliographic database of all identified controlled test publications.

3) The abstract database of reviews on the effectiveness of medical interventions contains structured abstracts of those systematic reviews that have been critically evaluated by the staff of the York Center for Compilation and Dissemination of Reviews (UK).

4) The Cochrane database on the methodology of examinations is a bibliography of articles on methods of synthesis and analysis of clinical trial results.

Cochrane Database of Systematic Reviews

No one owns the exclusive copyright to the systematic reviews contained in the Cochrane Electronic Library. This allows authors to ensure the widest possible dissemination of the results of their work.

Cochrane Register of Controlled Tests

The Cochrane Test Trials Register is a bibliographic database of controlled test publications identified by Cochrane Association members and other organizations. The database creation process reflects the efforts being made to systematically study journals and other medical journals around the world to create an internationally universal and unbiased source of data for systematic reviews. As none of the existing bibliographic databases can be considered complete, the project is carried out jointly with the US National Library of Medicine (PubMed) and Reed Elsevier Publishing House, Amsterdam, the Netherlands (published by Embase).

Randomized controlled trials as sources of evidence

Once a high-quality systematic review has been found, which answers the question, RQFs published after the date of the search information for the review are searched, or three years before the review is published, if it was not specified.

If systematic reviews are not found, search for RCTs on relevant topics, at any time published in the Cochrane Electronic Library and in the Best Evidence database, as well as in the last three years in the Medline and Embase databases.

Step 1. Cochrane Register of Controlled Tests It contains more links than the Medline database.

Step 2. Database on the Best Evidence CD

It contains abstracts of RWCs that have passed quality control, and comments to them.

Step 3. Search for the last three years in Medline and Embase databases.

This search allows you to identify RCTs that are not yet included in the Cochrane Electronic Library and the Best Evidence database.

Research reports on side effects and complications of interventions can be found in the Cochrane Electronic Library and in the Best Evidence database. After searching, they go to the Medline database, using the term "adverse effects" (/ ae) from the Medical Subject Headings (MeSH) of the National Medical Library of the United States.

When using the term MeSH ae.fs. (adverse effects - floating subheading) reveal all articles, one or more sections of which are devoted to side effects and complications of interventions. To narrow the search, these can be combined (the word AND) with other keywords (for example, systematic review on hypertension, cohort studies on asthma).

A concise guide to evidence-based medicine

Clinical Evidence concise is a regularly updated database of treatments that are widely used in common diseases. The guide is published twice a year in English by BMJ (Biomedical Journal) and once in Russian by Mediasphere. The guide briefly presents the current data on medical and preventive interventions obtained in the process of exhaustive search of medical literature. Based on these data, interventions are classified into those whose effectiveness or harm has been proven, expected, not established, or unlikely. The handbook is not a textbook or a clinical recommendation. It brings together the most reliable of the existing evidence, or states that there is none or not enough for definitive conclusions.

At the same time, according to the compilers, a number of features make it a unique publication:

- the content of the directory is determined primarily by the clinical issues under consideration, rather than the availability of data obtained in the process of research on a particular topic. The preparation of sections does not begin with the search, evaluation and generalization of existing evidence, but with the formulation of important clinical questions, which are then answered using reliable information available at the time of preparation of the next issue;
- The compilers of the handbook identify gaps in clinical data that are important for clinical practice, but do not try to fill them in on their own. The authors believe that it will be useful for doctors to know in which cases their uncertainty in their own actions is not due to gaps in knowledge, but the lack of evidence;
- the directory is updated every 6 months (it is published once a year in Russian); the electronic version is updated monthly. This allows the reader to regularly receive the latest information in various fields of medicine.

It should be noted that the compilers of the handbook seek to refrain from any recommendations. It is believed that a simple summary of existing evidence will ensure their widespread use. Experience in the development and implementation of clinical guidelines suggests that it is virtually impossible to provide advice that would be useful in any situation.

Therefore, the approach to the interpretation of existing evidence should not be standard, but individual, taking into account the specific clinical situation. Based on the materials in the guide, you can develop clinical guidelines that are used in a particular region (country), and doctors or patients can form their own opinion about the best interventions. The directory only contains the existing evidence, the final decision is made by the doctor or patient independently.

Principles of directory creation
The thematic sections of the handbook contain information obtained in the process of rigorous selection of reliable data relevant to medical practice.
Choice of main topics. In some sections of the handbook, diseases (conditions) are considered, which are either the most common in outpatient and inpatient care, or have important clinical and social significance. When deciding on the choice of topics for the first issues of the handbook, data on the frequency of referrals, morbidity and mortality in the UK were analyzed; the advice of general practitioners and relevant patient groups was also taken into account. The website www.clinicalevidence.com presents a list of sections that will be included in future issues of the guide.
Choice of clinical issues. The clinical issues addressed in the handbook relate to the advantages and disadvantages of preventive or medical interventions, with the greatest attention being paid to clinical outcomes that are crucial for patients.
The selection of issues taking into account the relevance for medical practice was carried out by consultants and compilers of the section with the active participation of general practitioners and relevant groups of patients. In each subsequent issue of the handbook, new clinical issues emerge and existing ones are updated. Readers can suggest new questions by filling out and submitting a comment and suggestion form on www.clinicalevidence.com, or by contacting the guide directly.
Search and evaluation of data. The authors find the answer to each question in the process of searching for relevant information in electronic databases Cochrane Library, Medline, EMBASE and some others.
Sources of information include: systematic surveys, randomized controlled trials (RCTs), if necessary, cohort studies, the Internet.

Evidence-based medicine resources

- ACP Journal Club. The Best New Evidence For Patient Care - Summarize the best new evidence for internal medicine
- American College of Physicians (ACP). Internal Medicine. Doctors for Adults - National organization of physicians specializing in the prevention, detection and treatment of diseases in adults
- Australian National Healthand Medical Research Council - Library of Clinical Recommendations of the Australian National Health Research Council
- Best Evidence - Abstract and full-text database on medicine
- BritishMedicalJournal
- CanadianMedicalAssociation - a database of clinical guidelines developed or approved by the Canadian Medical Association
- Center Health Evidence - Center for Evidence-Based Medicine, University of Alberta
- Center for Evidence-based Medicine at the University of Oxford
- Clinical Evidence - International database of systematic reviews

- Cochrane Collaboration open learning material for reviewers
- Cochrane Library
- Current Controlled Trials - An international database that combines registers of randomized controlled trials in various fields of medicine
- eGuidelines - a database of abstracts of clinical recommendations, protocols, standards and materials for their creation and implementation in medical practice, published in the journals Guidelines, Guidelinesin Practice, Medendium
- Embase - Bibliographic database
- Evidence Based Medicine. University Library at the University of Illinois at Chicago - Evidence-Based Medicine Resources at the University of Illinois Library
- Evidence-Based Medicine - a database of specialized information
- Health Canada - Population and Public Health - Database of clinical guidelines of Canada
- Health Services / Technology Assessment Texts - Science-Based Reviews from the Agency for Health and Research Quality (AHRQ)
- Informed Health Online. Institute for Quality and Efficiency in Health Care - Medical Information Network of the Institute for Quality and Efficiency in Health Care (IQWiG)
- Introduction to Evidence-Based Practice. Duke University Medical Center Library and the Health Sciences Library at the University of North Carolina - Introduction to Science-Based Practice
- JAMAevidence - Basic tools for understanding and applying the medical literature and making clinical diagnoses
- Lamar Soutter Library. University of Massachusetts Medical School - Center of Evidence-Based Medicine, University of Massachusetts Medical School
- Medscape - A web resource for doctors and other health professionals
- National Guadeline Clearinghouse - A public resource based on actual clinical guidelines
- National Institute for Clinical Excellence - A database of clinical guidelines developed by the UK National Health System
- New Zeland Guidelines Group - Clinical guidelines for various health issues
- PRODIGY (Clinical Guidance) - Draft up-to-date clinical guidelines to assist GPs in making informed decisions
- ScHARR-Lock's Guide to the Evidence - Search engine for retrieving bibliographic lists of identified reviews and recommendations
- Scottish Intercollegiate Guidelines Network - Compendium of clinical guidelines developed by the Scottish SIGN Group
- Section on Evidence Based Health Care, The New York Academy of Medicine - New York Medical Academy Resource Center
- Sheffield Evidence for Effectiveness and Knowledge - Links to various sources of evidence-based medicine: guides, tests, descriptions of clinical situations, access to full-text medical journals, etc.
- Suny Downstate Medical Center Evidence Based MedicineTutorial - Suny Downstate Medical Research Brooklyn Medical Research Library

- Supercourse Epidemiology, the Internet and Global Health - Online courses on epidemiology and evidence-based medicine
- The Cochrane Collaboration
- The Evidence for Policy and Practice Information and Coordination Center
- The Faculty of Medicine & Dentistry at the Universityof Alberta - Faculty of Medicine and Dentistry of the University of Alberta in Edmonton
- The KT Clearinghouse. The Canadian Institute of Health Research - Center for Evidence-Based Medicine, University of Toronto
- The Ministry of Health. New Zealand Guidelines Group - Promoting the Use of Evidence in Health Care and Disability
- The National Institute for Health and Care Excellence - National Institute for Health and Clinical Care
- The New England Journal of Medicine
- The University of Sheffield. Evidence Based Information Practice - Electronic database of resources for science-based medical practice
- TurningResearchIntoPractice - Medical search system with an emphasis on evidence-based medicine
- University of Alberta Evidence-based Practice Center - Evidence-Based Practice Center, University of Alberta
- University of Michigan. Department of Pediatrics. Evidence-Based Pediatrics Web Site - University of Michigan Pediatrics
- University of Southern California. Department of Family Medicine - Department of Family Medicine, University of Southern California
- UpToDate - Part of WoltersKluwerHelth, a leading provider of information and business intelligence for students, professionals and institutions in the fields of medicine, patient care, healthcare and pharmacy
- The School of Evidence-Based Medicine is a resource for Ukrainian doctors, which combines scientific and practical work, educational activities, creates a platform for the exchange of experience and professional development.

Self-control questions

1. Systematic review.
2. The best available clinical database.
3. Electronic databases of scientific and medical information.
4. Definitions and principles of meta-analysis.
5. Meta-analysis - advantages and disadvantages.
6. Search for scientific and medical information.
7. Cochrane databases.
8. Principles of Cochrane cooperation.
9. Sources of evidence-based medicine.
10. Clinical recommendations.

Test task

1. Types of meta-analysis:

A. cumulative;
B. prospective;
C. prospective-retrospective;
D. individual data;
E. all the answers are correct.

2. The possibility of demonstrating the curve of accumulation of estimates in the process of the emergence of new evidence is possible when using.... meta-analysis.

A. cumulative;
B. prospective;
C. prospective-retrospective;
D. individual data.

3. What kind of meta-analysis makes it possible to use the results with previously published?

A. prospective-retrospective;
B. cumulative;
C. prospective;
D. individual data.

4. What kind of meta-analysis makes it possible not only to summarize previously conducted clinical trials, but also for those who plan to perform in the future?

A. prospective;
B. prospective-retrospective;
C. cumulative;
D. individual data

5. What kind of meta-analysis is based on the study of the results of treatment of patients, not literary?

A. individual data;
B. prospective-retrospective;
C. cumulative;
D. prospective.

6. What does not apply to the benefits of a systematic review?

A. the ability to identify problems of individual sensitivity;
B. evaluation (critical approach) of research on the validity and benefits;
C. promoting the formation of integrated information networks and the expansion of professional communication;
D. reflect current trends in science and practice, but often have highly specialized topics.

7. When and by whom was the first systematic review?

A. 1987 A. Cochrane.

B. 1990 E. Wagner.
C. 1854 D. Snow.
D. 1998 R. Fletcher.

8. From the standpoint of evidence-based medicine, the doctor must decide on the choice of treatment on the basis of?

A. articles from a peer-reviewed journal with a high citation index;
B. articles from an unknown source;
C. experience of colleagues;
D. information from the Internet.

9. The indicator that characterizes the reliability of the information given in the scientific journal is...

A. citation index;
B. reliability index;
C. confidence index;
D. significance index.

10. Which of the following is not part of the Cochrane Electronic Library?

A. Cochrane database of systematic reviews;
B. Cochrane Register of Controlled Tests;
C. abstract database of reviews on the effectiveness of medical interventions;
D. Cochrane database on survey methodology;
E. All variants are part of the Cochrane Electronic Library.

Chapter 8.
Basics of Healthcare management.

Management is: the way, manner of communication with people; power and the art of management; special kind of skill and administrative skills; governing body and administrative skills. (The Oxford English Dictionary., London., 1983, Vol.VI, p. 106).
Management is the art of achieving results through leading people. (Mary Parker Follett).
The object of management as an activity is the production and economic organization and environmental factors.
The subject of management are employees of the organization, whose actions affect the object of management.

Types of management:

By resources:

- financial management;
- personnel Management;
- information management;
- management of material and technical resources.

By areas of activity:

- production;
- banking;
- trade;

- advertising;
- pharmaceutical;
- medical;
- construction;
- agricultural, etc.

By functions:
- strategic;
- operating;
- innovative;
- investment, etc.

By internal and external environment:
- international;
- in-house.

Management is implemented through laws, patterns, principles and categories.
In their activities, managers are guided by general social and economic laws and specific laws and patterns characteristic of the science of management and management.
The general social laws include: the law of cyclical social processes, the law of organization of social life on the basis of basic values, the law of social stratification, the law of conformity of organizational and national culture.
Economic laws include: the law of demand, the law of supply, the law of profitability, the law of diminishing returns.
Specific laws of management and management include: the law of proportionality of managed and control subsystems, the law of optimal ratio of centralization and decentralization of management, the law of unity of universal characteristics of the organization, the law of human resources management, the law of correlation of management levels with goals and personnel.
The general categories of management include the concepts:
- organizations;
- functions and methods of management;
- levels of management;
- leadership style;
- communications;
- management decisions.

Basic management tools:
- hierarchy;
- organizational culture;
- market.

Levels of management and groups of managers
According to the functions performed by managers, they are divided into the following levels of management:
- technical - provides daily operations and actions necessary for the effective operation of the organization;
- management - provides coordination of structural units of the organization;
- institutional - defines the mission and goals of the organization, provides long-term planning, relations of the organization with the external environment.

Managers of the **first level** - grassroots management (supervisors) - do not manage the work of other managers, mainly monitor the implementation of production tasks (provision of medical services), are responsible for the direct use of material resources (medicines, medical supplies). The typical job title at this level is administrator, senior nurse.
Middle-level managers direct the work of junior managers and have a wide range of powers. Middle managers are divided into:

- linear - manage individual units. They manage the personnel, finances and technological processes of the unit. An example of such a line manager can be the head of a clinic in a multidisciplinary hospital.
- functional - functional managers manage functional units. They hold the positions of chief accountant, head of the economic department, head of the department of therapy, surgery, clinical laboratory, etc.

In recent decades, there has been a noticeable trend towards restructuring and reduction of the management staff of large corporations. This applies primarily to middle managers.
Many foreign companies abandoned middle managers, which made it possible to make the pyramidal structure of the organization flatter and accelerated the transfer of information to lower hierarchical levels. In such organizations, the process of making and implementing management decisions is also faster.
Top managers are responsible for long-term planning, setting broad goals and strategies, directly managing the work of middle managers.
The highest organizational level is the smallest level of management. Even in the largest organizations, senior executives have only a few people.
Typical positions of senior executives in business are the Chairman of the Board of Directors, the President, and the Vice President of the Corporation. In the army, they can be compared with generals, among statesmen - with ministers, and in the treatment and prevention facility - with the chief physician.
Today in Ukraine, the heads of state treatment and prevention facilities are mostly doctors who have significant experience and high qualification in medical specialization, but do not have special training in health management and economics. The presence of special education is not a priority when appointing a chief physician.
Non-state-owned health care facilities can have two top managers: a chief physician who is responsible for the quality of care and a director. The director is responsible for the rational financial and economic activities of the treatment and prevention institution, as well as for the use of material, financial and labor resources. That is, such specialists, who are qualitatively new for Ukraine, must "release the chief physician from non-medical work."
International experience in countries with developed health care systems shows the expediency of managing many specialized medical institutions with specialists in Health Service Management or Health Care Management.
Top managers are responsible for making the most important decisions for the organization as a whole or for the main part of the organization.
If the company's top management decides to move the corporation to produce computers before the company can compete with IBM, then middle and lower-level executives can do little to prevent a major failure.
Senior executives imprint their identity on the entire company. For example, the atmosphere in which the government operates, and the whole country, usually undergoes significant changes under the new president.
Therefore, successful senior executives in large organizations are highly valued and paid well. Senior managers are responsible for large-scale goals.
Top managers are accountable to:

- board of directors (in the corporation);
- official bodies (in the government);
- proxies (non-profit organizations).

Karl Marx's saying is well-known: "A separate violinist manages himself, an orchestra needs a conductor." The identity of the manager is often identified with the conductor. He does not know how to play as professionally as a violinist or a cellist. He does not know how to write music as a composer. However, we can hear the genius of musicians and composers only through the work of a conductor.

We associate the success of the organization with the activities of managers. They form the goals of the organization, provide it with resources, plan and exercise control, make decisions and organize activities.

The personality of the manager is the main factor in ensuring the effective development of the firm.

The roles of the manager in the organization were specified by the American researcher Henry Mintzberg and classified into three categories:

- interpersonal;

  informational;

  roles related to management decisions.

The roles of the manager are interdependent, they interact to create a whole. Interpersonal roles derive from the authority and status of the leader in the organization and cover the scope of his interaction with people. They can make the manager a point of concentration of information, which gives him the opportunity and at the same time forces him to play informational roles and act as a center for information processing. Assuming interpersonal and informational roles, the leader is able to play roles related to decision-making: resource allocation, conflict resolution, finding opportunities for the organization, negotiating on behalf of the organization. All these 10 roles, taken together, determine the scope and content of the manager's work, regardless of the nature of a particular organization.

For example, the head of a medical institution directly interacts with the heads of departments. They come to him for advice on the organization of treatment and prevention. Nachmed receives a large amount of information about the course of the treatment and diagnostic process in the hospital departments. Some of this information cannot be obtained from informal sources. Informal information helps him make management decisions to resolve existing or potential problems. During conversations with the chief physician, the chief medical officer passes on some of the information he received from the heads of the hospital departments. The chief physician uses this information to make management decisions at the institution level. The ideal image of a modern manager implies that a person has the appropriate qualities and skills.

Qualities of the manager - a set of characteristics of the manager due to the following factors:

- human genotype;
- the influence of society;
- education;
- experience.

The human genotype is the basis for the formation of such qualities as the ability to take risks; leadership qualities; stress resistance.

The influence of social factors determines the formation of such qualities of the manager as responsibility, desire for professional growth, authority, internal control, tolerance. Society forms the following moral qualities of a manager: patriotism, national consciousness, state position, intelligence, humanity, decency, sense of duty, civic position, honesty, friendliness.

Education and experience give a person special knowledge, skills and abilities.
Qualitative characteristics of a person are a necessary condition for the formation of a future manager.
In addition to the manager, in a market economy, the fundamental role is played by the entrepreneur.
The term "entrepreneur" was introduced by the French economist Richard Cantillon, who lived in the early XVIII century. This word means a person who assumes the risk associated with the organization of a new enterprise or with the development of a new idea, new product or new type of service.
The words "entrepreneur" and "manager" are not synonymous.
The main difference between a manager and an entrepreneur is that the entrepreneur generates an idea (creates a private dental hospital), implements the idea at his own expense or at the investor's expense (founds a hospital, finances the process) and hires a chief physician and manager to manage the dental hospital. The manager manages the dental hospital created by the entrepreneur.
The roles of manager and entrepreneur overlap. An entrepreneur who started a dental hospital, if he has the appropriate education, can head it himself, ie become a manager. The hired manager of a dental hospital may himself initiate the activities of another dental hospital or other institution, such as a diagnostic center.
In order for a person to be fascinated by the idea of creating their own business, not only knowledge is needed. Entrepreneurs are people with certain psychological qualities:

- self-confidence, determination: the ability to quickly make individual management decisions;
- initiative, propensity to innovate;
- leadership qualities;
- perseverance and persistence;
- independence: seeks to be independent of the rules and control of others, has his own opinion and can defend it;
- risk appetite;
- purposefulness;
- the ability to persuade (he must convince others of the rationality of his idea and involve them in the implementation of the idea as partners or employees);
- energy, stress resistance: entrepreneurs can work up to 12-18 hours a day in a crazy rhythm;
- need for achievements; tolerance for uncertainty: the ability to make management decisions without sufficient information about the external environment.

The peculiarity of the health care industry is the need for two types of leaders: managers and managers. This is due to the fact that today there are two types of organizations in the field of health care.
The first type - public health care facilities (hospitals, clinics, clinics at medical research institutes, sanitary-epidemiological stations, health centers, etc.) operate as organizations that are not independent economic entities. Such health care facilities receive funding from the state budget, the state clearly defines and controls all items of expenditure. According to the Constitution, medical care in Ukraine is provided free of charge to the population, and state treatment and prevention facilities cannot charge for it. The list of medical services that can be paid for by patients is not significant. Therefore, the head of a state treatment and prevention institution can be called a manager, not a manager.
The second category of managers - civil servants, government officials, heads of health

authorities. They form the state policy and strategy in the field of health care, organize social management of public health care.
The second type - non-state health care facilities that function as independent economic entities in market conditions. The management of such institutions is provided by health managers.
The program stated: "Medical management is a completely new qualification. The health care manager manages the infrastructure in order to effectively organize the provision of medical services. Such a specialist should, on the one hand, subordinate the organizational structures of health care to the task, and on the other - to represent the interests of the field of professional medical activities to the customer from other areas, insisting on such restrictions on the parameters of the order, which are dictated by the laws of the organization of health care.
A healthcare management specialist is a specialist trained in various educational and qualification levels (bachelor, specialist, master) who is able to perform work in management and economic activities:

- in various linear and functional subdivisions of medical and preventive institutions of all forms of ownership;
- at the enterprises of medical and microbiological industry,
- in pharmaceutical companies,
- at pharmacy bases and warehouses,
- in stores "Optics" and "Medical Equipment",
- in diagnostic centers,
- in sanatoriums,
- at sanitary-epidemiological stations,
- in medical and social protection institutions
- in the structures of the Red Cross Society.

Healthcare management professionals can also be involved as managers of non-state-owned medical institutions and health insurance institutions.
The professional activity of a bachelor in management of enterprises and organizations in the field of health care in primary positions is:

- implementation of general management functions through the implementation of mainly administrative and operator and partly heuristic labor procedures;
- making operational decisions within its competence;
- functional and informational preparation of decisions;
- operational management of primary units - linear (main activity) or functional (preparatory and auxiliary activities), as well as independent organizations, which mostly do not have a management staff;
- management of subordinates whose competence is not higher than junior specialists and technical staff.

The main areas of professional activity of the bachelor:

- organizational and managerial,
- administrative and economic
- information-analytical.

Bachelor of Management with the acquisition of relevant experience can adapt to such areas of related professional activities as economic, marketing, accounting and control.
Specialists with a bachelor's degree in management of enterprises and organizations in the field of health care can continue their studies in the "specialist" or "master's" program.

The professional activity of a specialist in the management of enterprises and organizations in the field of health care in primary positions is:

- implementation of general management functions through the implementation of mainly heuristic and administrative and partly operator work procedures;
- making tactical and strategic decisions within its competence;
- tactical (with elements of strategy) management of primary units - linear (main activity) or functional (personnel, commercial, supply and marketing, transport, storage, economic and medical support), as well as independent organizations at all stages of their life cycle, mostly without or with a minimum of management staff (deputy, accounting);
- management of subordinates whose competence is not higher than junior specialists and bachelors.

The main areas of professional activity of the specialist:

- organizational and managerial;
- administrative and economic;
- information-analytical.

The specialist in the management of enterprises and organizations in the field of health care, provided they gain relevant experience, can adapt to the following areas of related professional activity:

- economic;
- marketing;
- accounting and control;
- foreign economic;
- educational;
- research.

The professional activity of the master of management in the field of health care in primary positions is:

- implementation of general management functions through the implementation of mainly heuristic and administrative and partly operator work procedures;
- making strategic and tactical decisions within its competence;
- management of subordinates whose competence is not higher than specialists and bachelors.

The main areas of professional activity of the master of management in the field of health care:

- information-analytical;
- organizational and managerial;
- administrative and economic.

Master of Management in Health Care with the appropriate experience can adapt to the following areas of related professional activities: financial and economic, marketing, accounting and control, foreign economic.
In accordance with the positions that may be held by a master of management in health care, suitable for the performance of production functions (implementation of certain types of activities) and typical for this function tasks. Each task corresponds to a system of skills to solve this typical task, taking into account the specifics of the health sector and the region.

Self-control questions

1. Qualification level of medical staff.
2. Management - basic terms and definitions.
3. Types of management.
4. Levels of management and groups of managers.
5. Characteristics and responsibilities of the top manager.
6. Characteristics and responsibilities of a middle manager.
7. Characteristics and responsibilities of the first level manager.
8. Standardization of medical practice.
9. Problems of standardization of medical practice.
10. Management quality and professional leadership skills.

Test task

1. Improving the quality of preventive and curative-diagnostic measures, solving problems of preserving and improving the health of the population - corresponds to the concept:...

A. the purpose of standardization;
B. standardization tasks;
C. subject of standardization;
D. null hypothesis of standardization.

2. What standards are distinguished by the hierarchy of application?

A. International.
B. National.
C. Regional.
D. Local.
E. All answers are correct.

3. Established by laws, other normative legal acts social norms and norms or their complex, on the basis of which the levels of basic state social guarantees are determined - is characteristic of...

A. state social standards;
B. standards-recommendations;

C. medical and economic standards;
D. comprehensive standards.

4. Standards issued in the form of guidelines, instruction letters, do not require strict adherence, ie methods of diagnosis or treatment can be improved and changed without special approval in the Ministry of Health - is typical for.

A. standards-recommendations;
B. state social standards;
C. medical and economic standards;
D. comprehensive standards.

5. The hierarchy of the system of application of standards does not include.

A. international standards;
B. national standards;
C. regional standards;
D. local standards;
E. sectoral standards.

6. A technical normative document that defines the requirements for the provision of medical care to a patient with a specific disease or syndrome or in a specific situation, it is -.

A. clinical protocol;
B. clinical recommendation;
C. form;
D. nosological manual.

7. The statements developed on the basis of the certain methodology for the help to the doctor and the patient in decision-making concerning rendering of rational medical care in various clinical cases, it -.

A. clinical protocol;
B. clinical recommendation;
C. form;
D. nosological manual.

8. The document, which lists the drugs, presents the optimal treatment regimens for the disease with drugs and provides brief information on drugs, it is -..

A. clinical protocol;
B. clinical recommendation;
C. form;
D. nosological manual.

9. Which of the following does not apply to personnel management components?

A. Planning.
B. Preparation.
C. Use of personnel.
D. Restructuring.

10. For effective management of the health care system, it is important to identify the main hierarchical levels of government. What are the levels of health care management in Ukraine?

A. Basic, regional, state.
B. Regional, regional, district.
C. Urban, regional, rural.
D. basic, state.
E. Basic, state, international.

Answers.

1-E. 2-C. 3-B. 4-C. 5-C. 6-C. 7-B. 8-A. 9-B. 10-A. 11-C. 12-A.	**Chapter 1.**
1-A. 2-A. 3-A. 4-A. 5-A. 6-A. 7-A. 8-A. 9-A. 10-A.	**Chapter 2.**
1-B. 2-A. 3-C. 4-A. 5-A. 6-C. 7-A. 8-B. 9-A. 10-B.	**Chapter 3.**
1-A. 2-A. 3-A. 4-A. 5-A. 6-A. 7-A. 8-B. 9-B. 10-A.	**Chapter 4.**
1-A. 2-A. 3-B. 4-A. 5-Г. 6-E. 7-A. 8-B. 9-A. 10-D.	**Chapter 5.**
1-A. 2-A. 3-A. 4-A. 5-A. 6-A. 7-D. 8-B. 9-B. 10-A.	**Chapter 6.**
1-E. 2-A. 3-A. 4-A. 5-A. 6-D. 7-A. 8-A. 9-A. 10-E.	**Chapter 7.**
1-A. 2-E. 3-A. 4-A. 5-E. 6-A. 7-B. 8-C. 9-D. 10-A.	**Chapter 8.**