

G. S. Matnazarova

O. M. Mirtazaev, N. S. Saidkasimova

EPIDEMIOLOGY

Tashkent 2023

Authors:

G. S. Matnazarova – Doctor of Medicine, Head of the department of Epidemiology of the Tashkent Medical Academy

O.M.Mirtazaev - Doctor of Medicine, Professor of the department of Epidemiology of the Tashkent Medical Academy

N. S. Saidkasimova – senior teacher of the department of Epidemiology of the Tashkent Medical Academy, PhD

Critics:

1. B. J. Kurbanov - Doctor of Medicine, the first Deputy of Head of Sanitary-Epidemiological Welfare and Public Health Committee by Ministry of Health of the Republic of Uzbekistan

2. Z.A.Nuruzova - Doctor of Medicine, Head of the Department of Microbiology, Virology and Immunology of the Tashkent Medical Academy

This textbook describes the emergence, history of development and recent achievements of preventive medicine - epidemiology, including a section on general epidemiology.

The textbook focuses on the history of science, the doctrine of the epidemic process, methods of epidemiological investigation, measures to fight against infectious diseases, and the epidemiological surveillance system. This textbook was written according to the epidemiology program approved by the Ministry of Higher, Science and Innovation and Health of the Republic of Uzbekistan and the program for training general practitioners in the process of reforming the healthcare system in our republic. In cooperation with the creation of a new generation of educational literature, current problems of the present time were also taken into account. The textbook is intended for students and general practitioners of the international faculty of higher medical educational institutions in the field of treatment, pediatrics and professional education.

INTRODUCTION

By the 21st century, positive changes have taken place in the science of epidemiology and, accordingly, in education. Nowadays, epidemiology is interpreted as the most important part of knowledge in all fields of medicine, not only as a teaching about the epidemic process. Population epidemiological investigation methods are used not only for infectious diseases, but also for determining the causes of the emergence and development of all human diseases and developing measures to prevent them. The further reduction of infectious and non-infectious diseases among people, and the complete elimination of some of them, directly depends on the level of knowledge of doctors serving in the field of medicine and their work. This process, in turn, requires future general practitioners to have a deep knowledge of the science of epidemiology, to fully apply theoretical knowledge of this science to practice. In the period after the independence of the Republic of Uzbekistan, a number of changes took place in the healthcare system, including the reform of the healthcare system, laws, orders and methodological instructions were issued on public health care, education, infectious and non-infectious diseases. The textbook was prepared based on the guidelines in the above-mentioned official documents. One of the urgent problems of the current period is the introduction of advanced international experiences into the system of higher education, the establishment of cooperation with leading foreign educational institutions, and the creation of new generation educational literature together with them.

Until now, a special textbook on epidemiology has not been created in English for the use of international faculty students and future general practitioners of medical universities in Uzbekistan in treatment, pediatrics and professional education.

In the preparation of this textbook, the latest achievements of epidemiology in our country and abroad were collected and summarized. Also, the results of the

analysis and discussion of the books published for the students of the Faculty of Medicine, the lectures read, and the practical trainings held in the departments of epidemiology of the Tashkent Medical Academy and Moscow State Medical University named after I.M. Sechenov of Russia over the last 20 years were also taken into account. We believe that this textbook will be of great help to pedagogues and students in teaching epidemiology in medical institutions and improving the educational process. The textbook may not be free of some errors and omissions. The authors are grateful in advance for the critical comments and suggestions of the readers.

List of abbreviated words

AKDS – Adsorbed pertussis, diphtheria, tetanus vaccine

USA- United States of America

VGA – Viral hepatitis A

VGW - viral hepatitis V

VGS - Viral hepatitis C

GAT - Geographic information system

DPM - Treatment and prevention institution

Committee of SEO and JSQ -sanitary-epidemiological tranquility and public health

WHO - World Health Organization

DAT – evidence-based medicine

IIGM- Infectious socio-hygienic monitoring

IO – Confidence Intervals

MSB – Central Sterilization Unit

OET – Operational epidemiological analysis

RNS – Randomized Controlled Trials

RNT – Randomized controlled trial

RET – Retrospective Epidemiological Analysis

SAG – Super Antigen

ShPM- Conditionally pathogenic microorganisms

Part I

GENERAL EPIDEMIOLOGY

Section 1

SUBJECT OF EPIDEMIOLOGY

Chapter 1

DEFINITION OF THE SCIENCE OF EPIDEMIOLOGY

Epidemiology is a science that studies the patterns of occurrence and spread of any pathological conditions among people and develops control and prevention measures.

The term "epidemiology" comes from the Greek words epi (on) + demos (people) + logos (science), thus denoting the science of what is common among the people, that is, what happens to them.

Hippocrates is considered the founder of the science of epidemiology. The writings of Hippocrates "Seven Books on Epidemics", "On Air, Waters and Localities" and others have survived to this day. V. A. Bashenin wrote in his textbook on general epidemiology: "For almost 2000 years, more original scientific views have not been expressed in epidemiology than the views of Hippocrates». Since the time of Hippocrates, that is, about 2400 years ago, the word "epidemic" was understood as mass diseases among people, which could include diseases of an infectious and non-infectious nature.

Of course, in the ancient and Middle Ages, epidemics were mainly the result of the spread of contagious diseases, although ideas about what an infection is and how it enters the body varied. Even in antiquity, two theories of the development of the epidemic arose. The first theory, put forward by Hippocrates, assumed that the cause of epidemics is the penetration into the human body of certain substances - miasms, located in space or in the soil, in particular, in marshy places. According to this view, the inhalation of miasma by a large number of people leads to the emergence of a mass disease. This point of view was substantiated on observations when the possibility of infection of victims from other patients could not be traced. Apparently, the mention of swampy places is not accidental: it is likely that it was about observations in the nidus of malaria, in which it is impossible to trace the contagiousness of the patient - he does not pose a direct threat to others (the patient is, as it were, "not contagious").

The second theory suggested that the cause of the development of epidemics is the spread of a living pathogen among people. This point of view was expressed

by the greatest philosopher of Greece Aristotle (4th century BC), later she found followers in Ancient Rome. Mark Terentius Varro (116-27 rr. BC) called this agent "Contagium vivum" In essence, as historical experience has shown, this brilliant conjecture predetermined the entire course of the development of epidemiology, it was based on the obvious contagiousness of patients with widespread spread of nosoforms such as plague, smallpox and some others. During the Renaissance, the contagionist hypothesis was developed in the writings of the Italian physician Fracastoro (1478-1553). He published the book "Siphilides Libris III" (hence the name of the disease - syphilis), in which he formulated the position on the contagiousness of the patient to others. Since it is not difficult to trace contacts with patients in venereal diseases, the book presented irrefutable evidence in favor of the confrontationist theory. It should be noted that this was a major milestone in understanding the essence of epidemics. A consistent supporter of this hypothesis was the founder of Russian epidemiology D.S. Samoylovich (1724-1810). Samoilovich's works on plague were recognized by all European scientists, and he was elected a member of various foreign Academies.



D.S. Samoylovich was the first in the world to try to use a microscope to detect the supposed causative agent of the plague. Unfortunately, the resolution of the existing microscope and the technique of microscopy did not allow us to obtain a positive result. There is no doubt that the constant discussion of contagionists and supporters of the miasmatic theory served as the basis for the further development of science.

D.S. Samoylovich



The next, and decisive stage in the knowledge of the inner essence of the epidemic was the great microbiological discoveries and achievements of the second half of the 19th century, which were preceded by the discovery of microbes (A Leeuwenhoek, 1632-1723). The studies of L. Pasteur (1822-1895), R. Koch (1843-1910) and their numerous students determined not only the triumph of contagionist theory, but also led to the development of many practical measures in the fight

L. Pasteur against infectious diagnosis of diseases, the use of disinfection, development and introduction into wide practice of specific prevention with the help of vaccines and sera, etc.)

A significant contribution to the study of epidemics and to the fight against them was made by domestic doctors. This was due to the historical features of the development of society in Russia: frequent wars in territories with natural focality, low economic level and even poverty of a significant part of the population - inevitably led to the emergence and spread of epidemics of many contagious diseases (parasitic typhus, smallpox, intestinal infections, including cholera, the so-called «children's infections», trachoma, etc.). A lot of efforts in the fight against epidemics were made by the zemstvo medicine that was formed in tsarist times, its well-known, as well as many figures now forgotten, who modestly performed their duty, and sometimes and even often with danger to their own lives.

World War I, followed by two revolutions, civil war, economic devastation, famine led to an unprecedented spread of various epidemics. So, according to far from complete data, the incidence (incident) of only typhus in 1919 r. amounted to 2743, in 1920 r. - 2550 per 100,000 population.



D. K. Zabolotny

It was under these conditions that in 1920 the world's first department of epidemiology was established in Odessa (Novorossiysk University). Its organizer is the outstanding scientist and active practical worker D.K. He owns the discovery of the presence of natural nidus of this disease. D. K. Zabolotny wrote the first textbook on epidemiology, created a school of domestic epidemiologists, to which L. V. Gromashevsky, M. N. Solovyov and others belonged, who subsequently made a huge contribution to the development of epidemiology. D. K. Zabolotny is rightfully considered the founder of Soviet epidemiology.



L. V. Gromashevsky

The current epidemic situation in the country needed a fundamental theoretical basis for both scientific research and practical work. One of its main creators was L. V. Gromashevsky (1887-1980), who formulated the doctrine of the epidemic process, in particular, the mechanism of transmission. Subsequently, many scientists and practitioners made a great contribution to the development of science and practice.



E. N. Pavlovsky

E. N. Pavlovsky (1884-1966) created the theory of natural nidus of a number of infectious diseases, according to which the persistent preservation of the pathogen is ensured.

V. A. Bashenin (1882-1977), co-author of the discovery of anicteric leptospirosis, considered epidemiology as a science designed to study all diseases, not just infectious ones. A. A. Smorodintsev discovered nidus of Japanese

encephalitis in the country, led the study of the etiology, clinic and epidemiology of hemorrhagic fever with renal syndrome in nidus first discovered in the country, established the viral nature of the disease, proved the role of mouse-like rodents as sources of infection. In addition, he created vaccines for the specific prevention of influenza, tick-borne and Japanese encephalitis, measles, mumps, and rubella. V. M. Zhdanov formulated a coherent system for understanding the evolution of infectious diseases, his successes in the epidemiology of viral infections are significant. V. D. Belyakov (1921-1997) created the theory of self-regulation of the epidemic process.

An anti-epidemic service was created in the country (territorial sanitary and epidemiological stations, and then a number of departmental institutions with a similar name, but with the same functions), which managed to change the situation for the better. Already before the Great Patriotic War, the morbidity (incidence) level for many nosoforms was significantly reduced, smallpox was eliminated, and, quite symptomatically, a discussion arose about the complete elimination of typhus (a very low incidence rate gave the right



V. A. Bashenin

to such projects). At present, a favorable situation has developed in Russia with respect to many nosological forms, although there are still enough problems relatively high incidence acute intestinal infections, influenza and acute respiratory infections, viral hepatitis B and C, individual natural focal nosoforms, HIV infection. The anti-epidemic service carries out preventive and anti-epidemic work in relation to all contagious diseases, regardless of the current situation, although, of course, the priorities in the activities of the anti-epidemic service are



V. D. Belyakov

determined by the prevailing specific circumstances. So,

epidemiology, which was originally formed as the science of epidemics, i.e., the mass spread of diseases, gradually transformed into the science of the epidemic process, i.e., it began to study not only epidemics, but also to find out the causes of a single or a small number of diseases.

If earlier the focus was on acute infectious diseases, in recent years it has increasingly shifted towards chronic diseases (chronic viral hepatitis, HIV infection, osteoporosis, etc.), which cause long-term suffering for people and place a heavy burden on health care.

Along with this, in recent decades, the population approach has been intensively developed in many private medical sciences. (Population - lat. populatio, from lat. populus - people, population). The population approach means the study of diseases (pathological conditions) among people. It is epidemiological population studies that have demonstrated the relationship between exposure to ionizing radiation and certain forms of cancer, between exposure to chemicals and the occurrence of certain types of malignant neoplasms, between drinking large doses of coffee and the development of coronary heart disease, between smoking and the development of lung cancer, etc.

The combination of these approaches came to be called non-infectious epidemiology. Numerous discussions about the appropriateness of using the term «epidemiology» in relation to any population studies have led to the realization of the need to use this science to solve any medical problems at the population level.

Questions for chapter 1

1. Definition of the science of epidemiology
2. Founders of the science of epidemiology
3. Theories of the development of the epidemic
4. Science of the epidemic process

Chapter 2

THE SUBJECT OF EPIDEMIOLOGY.

THE PLACE OF EPIDEMIOLOGY IN THE STRUCTURE

MEDICAL SCIENCES, MEDICAL

EDUCATION AND PRACTICAL

HEALTH CARE

The question of the subject of epidemiology is the most controversial. Initially, any mass diseases - epidemics - were considered the subject of epidemiology. In the original definition, due to lack of knowledge, it was very difficult to judge the nature

of the disease. But, of course, almost any mass diseases were implied, although, basically, epidemics of infectious diseases were observed. This understanding is not accidental, since the development of epidemiology truly began with this. The discovery of the causative agents of infectious diseases has reoriented epidemiology to the study of exclusively infectious pathology.

The subject of epidemiology has become an epidemic process, that is, the emergence and spread of any infectious diseases, regardless of the quantitative indicators of this spread.

Along with this, in accordance with the natural development of science, the idea began to form that the subject of epidemiology can be any nosological form, regardless of its internal essence (i.e., not only infectious), which is spreading among people. With such an assessment of science, it seemed to be transformed into a methodological basis for all medicine. It is no coincidence that J. Gordon (1954) called epidemiology a "diagnostic discipline in public health." Thus, the evolution of medical science has led to the realization that epidemiological studies are the crowning achievement of proving the causes of the development of any pathological processes among the population. It is no coincidence that now all hygienic research at the final stage is also based on the methods developed and accepted in epidemiology, although for some reason they were called «system analysis». Epidemiological departments have been created in leading scientific clinical centers (in the centers of cardiovascular pathology, oncology, etc.). The concept of «clinical epidemiology» appeared, and after that "evidence-based medicine". In the latter, a hierarchy of evidence of the cause of the development of pathology, the effectiveness of preventive or therapeutic measures, drugs, etc.

At the highest level (as if "proof of last resort") are epidemiological methods implemented according to strictly developed canons. Of course, if we talk about the modern understanding of the subject and the definition of the essence of epidemiology, then this is a science that studies the causes of the emergence and spread of any pathology (or an emerging state of health) in a population, and also develops the necessary adequate measures in accordance with the data obtained. Public health is the absence of pathology. Understanding the essence of the well-being of a population is possible only on the basis of knowledge of the patterns of development of pathology. Health is most often provided with the help of conscious (although not always) measures in relation to the emerging or in anticipation of the possibility of the occurrence of pathology in the population. That is why both pathology and the health of the population are known on the basis of the study of pathological conditions.

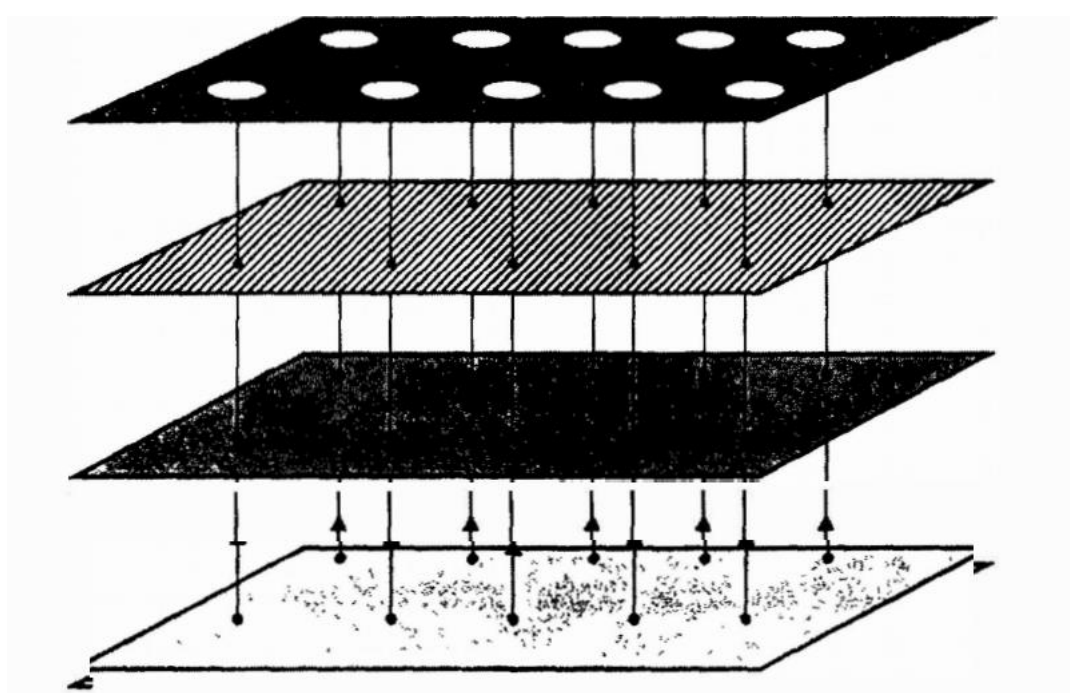
So, the subject of epidemiology are:

- the process of occurrence and spread of any pathological conditions among people (in the population),
- the state of health (the impossibility of the emergence and spread of pathological conditions).

The epidemiology of infectious diseases is the most important component of general science (note that, in fact, many processes that are not classified as infectious are). Therefore, it is necessary not only to study the biological essence of the interaction between parasite and host populations, but also to use population methods professionally at the modern level. It is with population studies that it is possible to establish the specific significance of biological, social and natural factors.

In anti-epidemic institutions, epidemiologists traditionally deal only with infectious diseases, but the epidemiological method, in particular population studies, is increasingly being introduced into the activities of hygiene departments (the aforementioned «system analysis»), especially in diseases caused by a violation of ecological well-being. Epidemiologists and specialized specialists of scientific laboratories most often study the epidemic process in detail: the nature of the formation of sources of infection, their contagiousness over time, the features of the methods of infection and the formation of immunity, etc.

Each medical science (therapy, surgery, oncology, etc.) strives for a holistic study of the diseases included in its circle at several hierarchical levels. V. D. Belyakov (1989) presented the structure of medical sciences schematically in a simplified form (Pic. 2.1).



Pic. 2.1 The structure of medical science

Vertical lines - medical sciences on the basis of the groups of pathologies they study, horizontal planes - medical sciences that study pathology at different levels of life organization: subcellular, cellular, organismal and population. At the junction of vertical lines and horizontal planes specific medical sciences are formed.

Epidemiology is studied by students of all medical schools. The system of medical education in our country includes educational institutions of three levels: secondary medical schools, higher medical schools and postgraduate educational institutions.

The training of doctors in epidemiology in these institutions is carried out at all faculties, but varies significantly in scope.

The study of epidemiology by clinicians is necessary for them to acquire the skills of population thinking and perform certain preventive functions. An important element is knowledge of the basics of hospital epidemiology.

Training of epidemiologists is carried out at medical and preventive faculties. In our country, a continuous multi-level system of postgraduate education of various specialists, including epidemiologists, has developed, which makes it possible to acquire modern professional knowledge. Epidemiologists can work in anti-epidemic institutions, research institutes of an epidemiological profile, in medical institutions (maternity hospitals, hospitals, clinics, etc.).

Questions for chapter 2

1. The subject of epidemiology
2. Place of epidemiology in the structure of medical sciences
3. The concept of "clinical epidemiology"
4. The concept of "evidence-based medicine"
5. Epidemiology of infectious diseases

Section 2

EPIDEMIOLOGICAL METHOD

Chapter 3

EVOLUTION OF EPIDEMIOLOGICAL RESEARCH TECHNIQUES. MODERN STRUCTURE OF THE EPIDEMIOLOGICAL METHOD

If we consider the method of epidemiology from historical positions, then for a long time it was intended mainly for the study of the epidemiology of infectious diseases. The study of the epidemiology of infectious diseases has been a good starting point for the development of epidemiology in general. Therefore, in modern conditions, this method is used to study the causes of the occurrence and spread of any diseases (not only infectious ones).

There are many natural, biological, social factors against which pathology develops and spreads. The task of the epidemiological method is to find the causes that ensure the emergence and spread of pathological conditions in a population of people.

Since the question of causality has arisen, it requires some discussion. According to the Philosophical Dictionary, ed. M. M. Rosenthal and P. F. Yudin (M., 1968, p. 289 - "Causality"), it is necessary to distinguish between complete and specific causality. A complete cause is a set of all circumstances under which an effect occurs. A specific cause is a set of circumstances, the appearance of which (in the presence of other circumstances that already existed in a given situation before the onset of the effect and form a favorable background for the action of the cause) leads to the appearance of the effect (in our case - morbidity, mortality, etc.). The most significant (essential) components (components) of the complete cause in a given situation are combined into a specific cause, and the remaining components act only as factors contributing to the action of a specific cause. It is the specific reason that is primarily the subject of study and identification for both science and practice. The Web Sphere Dictionary (quoted by R. Fletcher et al., Russian translation, M., 1998) indicates that a cause is "that which causes an effect or result."

It seems to us that the philosophical definition of a specific cause is of great help in epidemiological research and research. Speaking about the structure of the epidemiological method, its development and improvement, we should note that the method, like the method of other sciences, is a set of certain techniques and differs from techniques in the same way as the whole from the part. Reception is an integral part of the method.

If we leaf through the textbooks on epidemiology, we will see that the question of the methods included in the epidemiological method is covered in a very contradictory way. So, D.K. Zabolotny in a textbook on epidemiology (1927) indicates two methods used in the epidemiological method - bacteriological and statistical. L. V. Gromashevsky in 1949 distinguishes the method of single

observation, the method of mass observation, the observational-descriptive method and the experimental one. V. A. Bashenin in 1958 describes the historical, statistical, microbiological methods and the method of epidemiological examination. V. D. Belyakov in 1964 included in the epidemiological method the method of observation, the statistical method, the method of epidemiological examination, the historical method, and the experimental method of epidemiological analysis.

Such inconsistency reflects the evolution of views regarding the method, as well as contradictions in views regarding the subject of science. With the development of knowledge, the improvement of the method inevitably occurs, new techniques and methods of study appear.

In the process of evolution of epidemiology, the epidemiological method was improved. On the one hand, new techniques appeared, on the other hand, old techniques were improved.

Observation from antiquity to the present remains one of the main techniques used in epidemiology. Actually, everything that makes up the content of the main textbooks and fundamental books on epidemiology has been accumulated in the process of observing numerous epidemics over the centuries and millennia.

In antiquity and in the Middle Ages, the development of epidemics of contagious diseases, especially severe and rapidly spreading, was striking first of all. Even the miasmatic theory of the origin of epidemics seems to have taken as its starting point observations in the nidus of contagious diseases, in particular, perhaps, in malaria (inhalation of miasms in swampy places), although the conclusions - and this is quite understandable - turned out to be erroneous.

In justification, it must be said that the problem of methods of infection, even in later times, was far from being solved easily. Suffice it to recall the work of Walter Reed's commission in occupied Cuba, which tried to solve the problem of yellow fever infection (sick and healthy were placed in the same bed, healthy volunteers were dressed in the underwear of the sick, etc.). Only a verification of the statement of the Cuban doctor Finlay showed the true mechanism of transmission - the virus penetrated through the blood-sucking of pathogen carriers that attacked a person - *Aedes egypti* mosquitoes. For a long time, the ways of infection with hemorrhagic fever with renal syndrome (HFRS) remained unclear.

So, based on the concept of the contagiousness of infectious patients, the observation was reduced, first of all, to clarifying the specific circumstances under which infection of the surrounding people is possible (from what sources of infection, in what way, etc.).

And indeed, when society during the course of observation fixed attention on such diseases as plague, especially pulmonary, venereal diseases and others that were

severe and (or) the circumstances under which infection occurred were obvious, this technique made it possible to understand the causes of the spread of diseases.

However, in modern conditions, since in the field of view of science and practice there are nosoforms that clinically develop not always clearly and even asymptotically, registration cannot be complete. In other words, there may be no need for observation in the immediate vicinity of the source of infection. That is why it is inevitable to involve clinicians to identify patients in whom the disease is mild or atypical. Thus, clinical data allow us to expand the understanding of the actual spread of the disease.

The use of additional clinical techniques also provides the epidemiologist with data for judging the most likely routes of transmission of the pathogen. So, if patients with severe forms of intestinal infection predominate in the structure of patients during an epidemic outbreak, there are reasons with a high degree of probability to assume infection with a large dose of the pathogen, i.e., infection through food.

In a number of cases, to establish the actual number of infected people and evaluate the methods of infection, it is inevitable to use microbiological, immunological, biochemical and other laboratory methods, sometimes zoological, entomological and other studies.

Since data gradually accumulated on the impossibility of establishing all the regularities in the occurrence and spread of infectious diseases in nidus, observation began to be used also to study events associated with the development of morbidity among the population or some part of it. As they say now, there was a need for population studies. But even in this case, clinical data, materials from various laboratory studies, data from zoological, entomological and other research methods are used to assess the situation. Of great importance is the connection of methods for studying many social, biological and natural factors, including astrobiological ones (A. L. Chizhevsky, 1929).

It is difficult to find a science in which statistical methods would not be widely used. In modern epidemiology, the use of statistical techniques is of particular importance. Among scientists engaged in biomedical research, the language of statistics is becoming international.

Statistical (biometric) methods are so widely used in epidemiology that the uninitiated are often unable to differentiate between epidemiological and statistical studies. The principal feature of epidemiological research is that epidemiology pays special attention to research planning; it is the ideologist of the selected study, provides a meaningful interpretation of the obtained indicators, and statistical methods are only a research tool.

Throughout the history of the development of epidemiology, one can trace the tendency for it to apply an increasing number of techniques from other sciences. Nature is less and less willing to reveal its secrets, and therefore the epidemiologist-researcher, like the epidemiologist-practitioner, has to apply more and more new techniques and improve the old ones.

In the process of the epidemiological method, various methods of research were accumulated and improved. To date, they have been systematized and two methods have been identified:

- epidemiological examination of outbreaks;
- epidemiological analysis.

Each of these methods consists of a combination of proper epidemiological techniques and techniques from other sciences. The specifics of their selection is determined by the subject of study. Hence:

The epidemiological method is a specific set of techniques that is designed to study the causes of the occurrence and spread of any pathological conditions in a population of people.

Questions for chapter 3

1. Evolution of epidemiological methods of research.
2. Modern structure of the epidemiological method
3. Techniques used in the epidemiological method
4. The epidemiological method is
5. Method of epidemiological examination of foci;
6. Method of epidemiological analysis.

Chapter 4

METHOD OF EPIDEMIOLOGICAL EXAMINATION OF NIDUS

The epidemic focus is the location of the source of infection with the territory surrounding it to the extent that the pathogen is able to be transmitted from the source of infection to people who are in contact with them.

There are two concepts that characterize the epidemic focus.

These are the boundaries of the focus and the duration of its existence.

The boundaries of the focus are determined by the characteristics of the mechanism of transmission of a particular infectious disease and the specific features of the environment in which the source of infection resides.

The duration of the focus is determined by the residence time of the source and the duration of the maximum incubation period of a particular infection. After the departure of the patient or his recovery, the focus retains its significance during the maximum incubation period, since new patients may appear.

The method of epidemiological examination of nidus is a specific set of techniques that is designed to study the causes of the occurrence and spread of infectious diseases in this nidus. This means that the purpose of the epidemiological examination of the focus is to identify the source of the infectious agent, the ways and factors of its transmission, and the contacts at risk of infection.

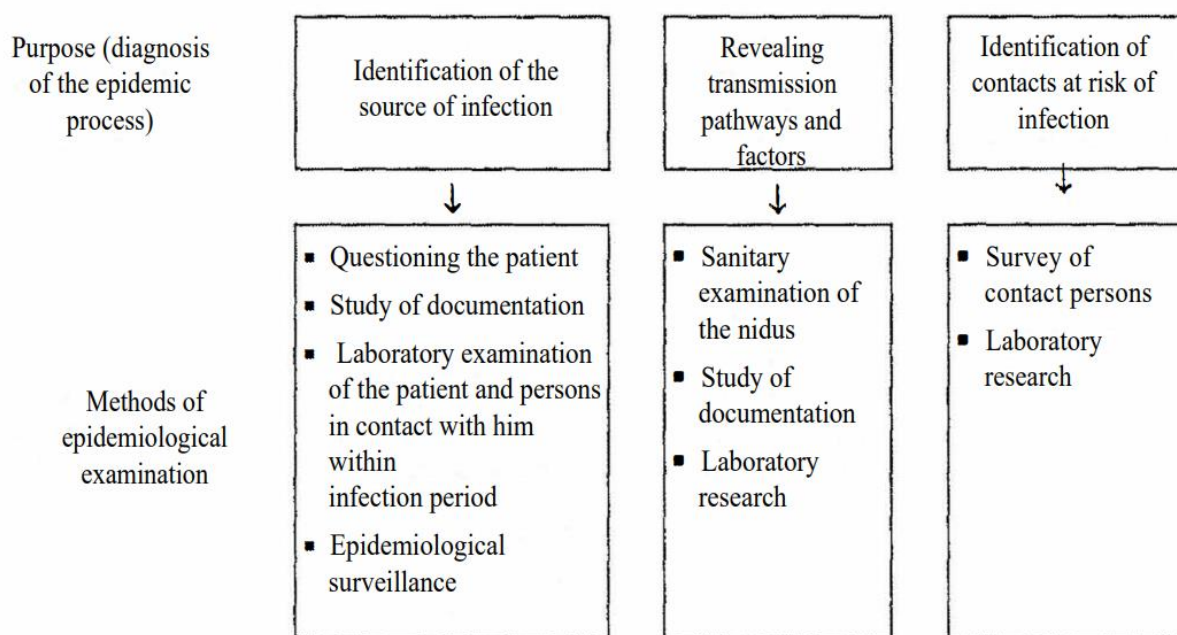
Epidemiological examination of nidus is one of the important sections of the activity of an epidemiologist and is promptly carried out immediately after the fact of the existence of an epidemic focus is established.

Nidus can occur in apartments, kindergartens, educational institutions, various industrial enterprises, in certain areas, etc.

The number of cases in a focus may be limited to one case or many cases (outbreaks). This work is carried out urgently, because without an epidemiological diagnosis it is impossible to develop targeted anti-epidemic measures to eliminate the focus (epidemiologist's recipe).

Techniques used by the epidemiologist when conducting an epidemiological survey of nidus:

- questioning of the patient and persons in contact with him;
- study of medical and other (veterinary, water supply, nutrition, housing and communal services, etc.) documentation;
- sanitary examination of the outbreak;
- laboratory and instrumental studies of the patient, contact and suspected transmission factors;
- epidemiological surveillance during the maximum incubation period.



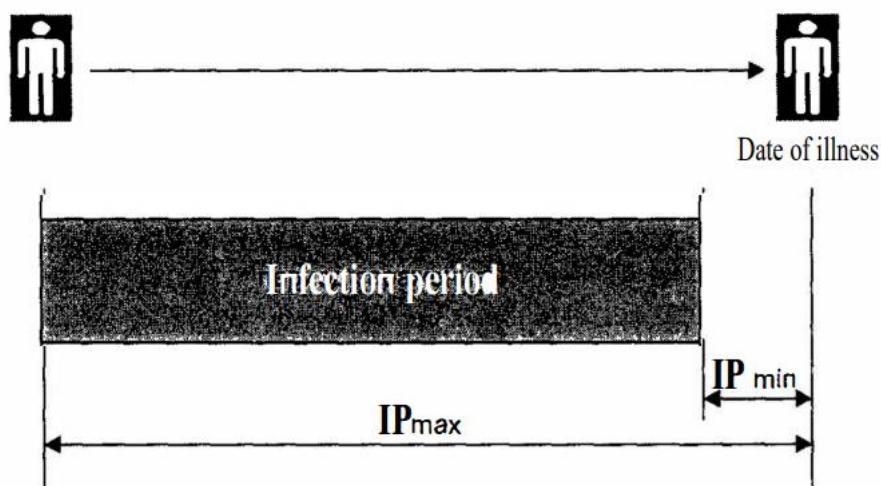
The scheme of the epidemiological examination of the nidus

The work of an epidemiologist begins even before entering the epidemic focus. It consists in the fact that the epidemiologist studies the documentation in the anti-epidemic institution, which characterizes the epidemic situation in the outbreak. In addition, the epidemiologist ensures that the laboratory is ready for the upcoming sampling from the patient, contact, suspected transmission factors.

Further, the work of the epidemiologist is carried out directly in the epidemic focus. An epidemiological examination begins with a questioning of the patient (if he is not hospitalized in an infectious diseases hospital) and those who came into contact with him.

The purpose of the survey is to collect such information that would allow the epidemiologist to formulate a hypothesis about the source of infection, the ways and factors of transmission, that is, the causes of the outbreak. To do this, the epidemiologist first of all determines the time frame (period) of possible infection.

To determine the period of infection, it is necessary to know the exact date of the disease of the person who formed this focus. The time between the maximum and minimum incubation periods (IP) will correspond to the time of infection (Fig. 4.1).



Pic.4.1 Determination of the period of infection

Then the place of stay of the sick person, his contacts, information about the food products used (in the event of an intestinal infection), the presence of diseases among animals (in the event of a zoonotic infection), etc.

The results, the specific content of the survey is determined by the characteristics of the infection.

The study of documentation is carried out in medical institutions (MPI), preschool institutions, industrial institutions, etc. (depending on the specific features of the epidemic focus). This technique involves the collection of information on the registration and registration of similar infectious diseases within the focus, obtaining information from case histories, outpatient cards, vaccination documentation, and in case of zoonoses, the documentation of the veterinary service is studied.

A sanitary examination of the focus is carried out in order to ascertain the conditions that could contribute to the occurrence of the disease or diseases. An assessment of the sanitary condition and sanitary maintenance, the places of stay of the sick is carried out, the specific content of the examination is determined by the nature of the infection.

Laboratory and instrumental studies in the focus are necessary to confirm and clarify the clinical diagnosis, identify sources and factors of infection transmission, evaluate the effectiveness of treatment, sanitation, etc.

Epidemiological observation in the outbreak is carried out during the lifetime of the outbreak. This technique is designed to identify new cases or carriers.

During this period, all the techniques that have already been discussed are used. The documents in which the results of the epidemiological examination of the nidus are drawn up are a map or an act of the epidemiological examination of the nidus.

The materials of the epidemiological survey are used in the system of epidemiological surveillance.

Evaluation of the diagnostic capabilities of the method of epidemiological examination of the nidus. In the modern period, epidemiologists use this method much less frequently than in past times. This is due to the fact that the practical experience of its application has shown that in many cases the diagnostic value of this method turned out to be rather low.

However, the method of epidemiological examination of nidus retains its value in a number of different situations:

- occurrence of at least one case of an exotic infection;
- the appearance of many sporadic cases, seemingly unrelated, but which raise the incidence rate above the prevailing ordinary, corresponding to this period;
- multiple focus;
- unusual (abnormal) situations;
- in conditions of a fairly isolated stable team, in which the actions of each member can be traced more or less reliably.

The last three situations, especially the last one, indicate the great importance of epidemiological examination in a hospital setting; to a lesser extent, they are useful in other organized groups.

Indeed, in hospitals, although there is a change of patients, it is strictly controlled, the nutrition system is under control (even products brought from outside can be taken into account and even examined), all medical manipulations are taken into account, especially injections, including the administration of drugs using vascular and other catheters, various invasive diagnostic and therapeutic procedures, the nature of anesthesia, surgical interventions, etc.

Thus, the method of epidemiological examination is quite well adapted to hospital conditions and therefore can be widely used. Its use is indicated in organized groups in the event of two or more cases of the disease. Speaking about the current state of the situation on the use of epidemiological surveys in nidus, I would like to emphasize that its use is based on extensive experience (positive and negative), i.e., it is the result of a generalization of observations in various populations. In this regard, I would also like to point out that modern clinical medicine necessarily uses the collection of anamnestic data, which makes it possible to establish, at least approximately, the possible causes of the development of the disease.

Apparently, initially the interest in taking an anamnesis was based on the desire to establish the possibility of infection (which corresponds to the epidemiological

survey currently accepted at the initial stage). But modern history taking (important not only for infectious diseases) has definitely broader tasks, which are undoubtedly based on the great previous experience of many generations of doctors and its generalization.

However, gradually, as others got into the field of view, and many different nosological forms, science and practice faced such a situation that finding out the specific circumstances of infection (epidemiological examination of nidus) often turned out to be ineffective. It became clear that this method can give positive results only under certain conditions that help clarify the causes of infection. As the evidence becomes clear that due to the impossibility in some cases of clearly limiting the outbreak, as well as due to the constant movement of people, including due to significant migration processes within the settlement, using public transport and visiting various public places and events, an understanding has come often futility of the epidemiological examination of the focus. Finally, the presence of a healthy carrier may completely negate the attempts of epidemiologists to find out the reasons for the formation of an epidemic focus. Therefore, this method should be used in practice, taking into account its advantages and disadvantages.

Epidemiological examination of nidus is ineffective (or may be ineffective) under the following circumstances:

- a single case of disease (excluding exotic infections);
- the presence of carriage in this nosoform, especially if it dominates in frequency in relation to the manifest forms of infection;
- the likelihood of communication in different places (transport, shops, etc.);
- the likelihood of infection at a considerable distance from the location of the source of infection (for example, contamination of the product at a food enterprise - infection at home).

It should be noted that when studying the causes of the emergence and spread of non-communicable diseases, the epidemiological survey method is also used by epidemiologists or doctors of other specialties. In this case, epidemiological data are collected using special questionnaires or questionnaires. The methodology for developing such questionnaires is described in the section “Collection of epidemiological data”.

Returning to the historical roots of the formation of the epidemiological method, I would like to note that the shortcomings of the epidemiological survey became apparent rather soon, as already mentioned, as the circle of infections that became widespread, which science and practice were forced to become interested in, expanded.

It required adequate mass character of the process of emergence and spread of diseases (epidemic process), the so-called population methods for studying this phenomenon, i.e., finding out the causes of the occurrence of not one or several diseases in some small group or family, but the incidence among the population or a significant part of it. It should be noted, however, that after population studies of communicable and noncommunicable diseases, the use of epidemiological surveys will often provide crucial additional information for assessing the causes leading to morbidity.

Questions for chapter 4

1. The concept of an epidemic focus
2. Hearth boundaries
3. The duration of the outbreak
4. Techniques used by an epidemiologist when conducting an epidemiological examination of foci
5. Scheme of the epidemiological examination of the focus
6. Assessment of the diagnostic capabilities of the method of epidemiological examination of foci

Chapter 5

EPIDEMIOLOGICAL ANALYSIS METHOD

The method of epidemiological analysis is a specific set of techniques designed to study the causes of the occurrence and spread of any pathological conditions in a population of people.

When searching for a cause in population studies, one must keep in mind that the action of a possible causal factor is subject to a certain law - the law is not of necessity, but of the probability of events. It should be noted that among the medical sciences, epidemiology was the first to use these probabilistic laws to understand the causes of developing events (the occurrence, spread of morbidity, etc.). According to these laws, the cause leads to the effect (say, the emergence of diseases) with a certain degree of probability, the more likely this causal factor is. From what has been said, it follows that the cause does not necessarily lead to the effect (in our case, the disease). This means that probabilistic laws determine the relationship not between individual phenomena (events), but between categories of phenomena. So, for example, one cannot think that someone drank poor-quality water - fell ill with typhoid fever (this is not at all necessary), but it is very likely that the consumption of poor-quality water (one category of phenomena) can lead to the appearance (growth) of the incidence of typhoid fever (another category of events). That is why, when assessing the probability of a possible cause, one has to operate not with single phenomena, but with a multitude of events. The probability of the action of a causal factor (and by no means its unconditional influence) was reflected in the now accepted very successful term risk factor. This term does not show the absolute strength of this cause, but only its possible effect, which, under certain conditions, can receive a quantitative characteristic. This quantitative characteristic is determined by the frequency of reproducible events, i.e. frequency indicators.

Epidemiological analysis is carried out in stages. There are three stages:

- collection of epidemiological data,
- descriptive stage,
- analytical stage.

The result of this work is the formulation of an epidemiological diagnosis of the **cause (risk factors) of the occurrence and spread of pathological conditions.**

5. 1. Collection of epidemiological data

Data collection is an extremely important step in epidemiological diagnosis. Data quality is the key to the success of any epidemiological study. Mistakes made at this stage are almost impossible to eliminate.

Based on the purpose of epidemiological diagnosis, the main data to be collected are:

- ◆ Outcomes resulting from favorable or unfavorable effects on a particular population of people. Examples of outcomes studied can be any diseases, pre-nosological conditions, changes in laboratory parameters, etc.
- ◆ Influencing factors, which include data on the state of the environment, social factors, bad habits, etc. Examples of influencing factors are materials of the state service for monitoring and controlling the level of environmental pollution, alcohol consumption, types of operations performed in hospitals , about the nature of manipulations in health facilities, etc.
- ◆ Data on the composition and size of the studied populations.

Collecting data takes a lot of time and effort. Data can be obtained from literary sources; already existing special databases; through a survey (questionnaire); medical examination; laboratory studies of material from humans, animals and sources in the environment; instrumental and laboratory studies of environmental factors, etc. In practical terms, state statistics are important sources of information. Outcomes are also typically measured by counting the incidence of diseases and other health-related conditions that occur.

An epidemiological case definition is a set of standard criteria for deciding whether or not a given individual has a specific disease/condition.

The standard epidemiological case definition provides a uniform diagnosis of each case, regardless of when or where it occurred and who identified it, allows you to compare the number of cases that occurred at a certain time / place with the number of cases that occurred at another time / place.

In other words, the use of a standard case definition makes it possible to make sure that the differences revealed when comparing the number of cases (indicators of the frequency of their occurrence) in different population groups (in different territories, in different periods of time) are associated not with differences in the methods of diagnosing diseases, but with the action of other causes that are really of interest to the epidemiologist.

The epidemiological definition does not always coincide with the clinical case definition, since it is intended not for clinical diagnosis and treatment selection, but in order to pass the entire spectrum of clinical and laboratory manifestations of a given disease through the prism of case definition, to separate cases from “non-cases”. The epidemiologist deals with populations of people, his task is to divide them into cases and “non-cases”, so that one can evaluate, first of all, the frequency of occurrence of diseases as a reflection of the action of causal factors and, using the same case definition, compare data, received in different situations. In epidemiological practice, the use of case definition allows for active case finding in epidemiological investigations even when no clinical diagnosis has been formulated.

The following is an example of a measles epidemiological case definition developed by WHO.

Clinical case definition. Any patient with the following symptoms:

fever and

maculopapular (i.e. non-vesicular) rash and

cough, rhinitis (i.e. runny nose) or conjunctivitis (i.e. red eyes).

Or any patient whose doctor suspects a measles infection.

Laboratory diagnostic criteria:

at least a four-fold increase in antibody titer or shedding of measles virus, or the presence of specific measles IgM antibodies.

Classification of cases.

Clinically Confirmed: A case that satisfies the clinical case definition.

Laboratory-confirmed: A case that meets the clinical case definition and is laboratory-confirmed or epidemiologically linked to a laboratory-confirmed case.

As can be seen from this example, an epidemiological case definition typically consists of a set of clinical and laboratory criteria, ideally combined in an algorithm that ensures that these criteria are applied unambiguously.

Epidemiological definitions may differ depending on the purposes for which they are applied, as well as on the actual possibilities of their application.

If we talk about the purposes of applying the case definition, then in a number of situations its sensitivity comes to the fore. In the event of, for example, an unfavorable epidemic situation for any quarantine infection, the most important is the earliest possible active detection of all cases of the disease.

It is clear that if you formulate the definition of a case of cholera as "the presence of diarrhea", you can be sure that the majority of cholera patients will come into view, but the specificity of such a broad definition will be minimal, since most cases of diarrhea can be caused by completely different causes than cholera disease.

In other words, to establish the causes of morbidity, the definition should be narrower, ensuring its sufficient specificity.

Sometimes several definitions may be required, if only because it is not always possible to apply certain laboratory and instrumental tests, the results of which appear in the case definition. Therefore, among such obvious requirements for a

standard case definition as simplicity, clarity, reliability, reproducibility, consistency, sensitivity, specificity, there should be accessibility for public health practice.

As already noted, in practical terms, the sources of information are the materials of state statistics. Unfortunately, standard (epidemiological) case definitions in our country are introduced only for some infectious diseases (measles, poliomyelitis, mumps, and some others).

Diagnosis of most diseases, which determines their further registration, depends on the qualifications of clinicians and their attitude to recording not only pronounced cases, but also mild and atypical forms.

In a number of cases, epidemiological data are important, and sometimes decisive (most often in the context of a developed or developing outbreak, especially a local one, as well as in mass morbidity, for example, during an influenza epidemic).

Laboratory, especially microbiological, studies help (the latter, as a rule, only with positive results, and also by no means always, since against the background of the development of a mild form of one disease, carriage of other pathogens is possible). Laboratory methods are often useful in dysentery, diphtheria (isolation of a toxigenic strain of diphtheria bacillus) and some other nosological forms. Unfortunately, such microbiological confirmation of the disease is not possible in all cases. In particular, in viral infections, laboratory studies are not always used for individual diagnosis due to the high cost, duration of the study, and the need to have an appropriate, well-equipped laboratory. However, virological studies are used to determine the nature of the emerging epidemic, especially in influenza epidemics.

Immunological methods, the use of which in some infections gives satisfactory results (tests of paired sera), unfortunately, are often belated, therefore, when solving operational problems, they are not always important.

So, the diagnosis of mild forms of infection largely depends on the qualifications of the doctor, who, in particular, must take into account laboratory data and the epidemic situation.

The completeness of registration and accounting of patients depends on the behavior of the patients themselves. In some cases, patients do not consider it necessary to seek medical help. This applies, of course, primarily to people suffering from mild forms of illness.

Non-working people often find themselves outside the scope of official registration and accounting, since social insurance issues become relevant for them only when hospitalization is necessary. Unfortunately, there is still a deliberate underestimation of incidence rates.

This deliberate underestimation of the registration and accounting of patients, especially those suffering from mild forms of illness, takes place not only in the practice of polyclinics and anti-epidemic institutions, but also in hospital conditions.

So, we must initially admit that there is no full registration and accounting yet, and it is unlikely that it will be in the near future.

Defects in registration and accounting are important in a general assessment of the current situation, but they are especially evident in assessing the structural distribution of diseases among the population. The point is that very often there are unequal approaches to registering diseases among the population of different groups, in particular, the reliability of registering and recording diseases among children, especially in the first years of life, is higher than that among adults. This, of course, can lead to erroneous conclusions. Especially often this phenomenon occurs in nosoforms, which by no means always manifest themselves in the form of pronounced clinical forms of the disease.

Such incomplete registration in each place, in each administrative unit has a certain, more or less constant value, i.e., an error in accounting carries a standard, systematic error to some extent. As a result, if it is required to evaluate events that develop over time, then it is sometimes possible to obtain a relatively reliable picture of the dynamics of the epidemic process in epidemiological diagnostics. However, all these shortcomings in registration and accounting can lead to a fatal error and conclusions when comparing the incidence in different administrative territories, therefore, when determining areas (places) of risk, great care is required and a thorough study of the existing registration and accounting system in each territory separately taken for comparison.

Thus, the first task of practical institutions in diagnostic work to establish the causes of the occurrence and spread of diseases is to streamline registration and accounting, their unification in different territories, i.e., the development of uniform criteria in the diagnosis of diseases and their strict implementation. This is best handled, as already noted, by applying the standard case definition. All this will make it possible to accurately state the facts, and then to identify (catch) emerging outbreaks in a timely manner, to ensure an effective epidemiological examination of nidus, and to conduct full-fledged population studies.

In addition to state statistics, epidemiologists and doctors of other specialties widely use other sources of information.

Publications of various morbidity registers and demographic data can be very useful. Registers are personal lists or file cabinets for the entire population or a specific group of people. Most often, registers are formed for patients with chronic pathology or those who died from a certain type of pathology. Patients are followed up

throughout their lives. Epidemiological data collected in registries allow for effective tracking of disease progression and identification of risk factors. There are registries of oncological, cardiovascular, occupational diseases, etc.

Often information can be obtained by extracting records from already existing databases created for other purposes. For example, to study the incidence of infections in the surgical site and the impact on the risk of their occurrence, the timing of the use of prophylactic antibiotics can be successfully used as the main source of data surgical patient records ("inpatient medical records"). Data is collected using specially designed forms or entered directly into a laptop computer. One way or another, for subsequent data processing, information collected using paper forms is usually entered into computer databases. Data entry is made either by entering from the keyboard, or by scanning forms and then recognizing the resulting images using special text recognition systems. Neither method allows avoiding errors in data entry, so one of the mandatory stages of primary data processing is the so-called "cleaning" of databases, which involves finding errors and eliminating them.

Epidemiological data often have to be collected using special questionnaires (questionnaires), which can be filled in by the respondents themselves or during the survey by the researchers themselves or their assistants. Experience shows that self-administered questionnaires provide a higher degree of standardization of data collection because they avoid possible systematic differences in interview technique. On the other hand, self-completion questionnaires are limited because all questions must be unambiguously understood by all interviewees. In difficult situations, the participation of a specially trained journalist is simply necessary. Therefore, before compiling the questionnaire, it is important to understand who will collect data through the questionnaire: the researchers themselves, specially trained support staff (preferably not interested in the results of the study), or the subjects themselves - the design of the questionnaire largely depends on this. In any case, the language of the questionnaire should be simple and understandable. For example, not everyone knows what mumps is, but you can be sure that this disease is familiar to everyone under the name "Mumps":

Failed Design	Recommended Design
Have you ever had epidemic parotitis? Yes/No	Have you ever had mumps (mumps)? Not really

It is essential, especially in self-administered questionnaires, to define the terms used:

Failed Design	Recommended Design
Do you have a regular menstrual cycle? Yes/No	Do you have a regular menstrual cycle (once a month, there are warning signs)

	for 4 days, each time lasting the same number of days)? Yes (if Yes, go to next question)/No
--	--

Failed Design	Recommended Design
Tachycardia Yes/No Fever Yes/No	Tachycardia (more than 150 bpm) Yes/No Fever (more than 37.5°C in the armpit) Yes/No

Even if the terms seem clear, the question should be carefully assessed for potential problems. A seemingly simple question, “How much alcohol did you drink last week?” actually creates a lot of problems:

What is considered alcohol?

What is the unit of measurement?

Is a week an adequate period if you are interviewing abusers?

The survey may be conducted at different times (including after the holidays). Not everyone can honestly answer this question.

When developing a questionnaire, you should decide which questions to give preference to solve the tasks: open or closed.

Open-ended questions do not have ready-made answers, for example:

What factors related to your professional activities affect your health?

Open-ended questions are good for assessing knowledge or attitudes towards a particular issue. They allow you to determine people's understanding of the problem and allow for a detailed response. However, answers to such questions take a lot of time and labor, are difficult to group (code), and difficult to analyze data.

Closed questions have a set of ready-made answers and corresponding instructions, for example:

What factors related to your professional activities affect your health?

Circle the numbers of all correct answers:

1. Round the clock work
2. Night work

3. Antibiotics

4. Disinfectants

5. Cytostatics

Mark in brackets the degree of their influence in points from 1 to 4:

Round the clock work

night work

Antibiotics

Disinfectants

Cytostatics

Question instructions should be short, simple, clear and unambiguous. In some cases, it may be necessary to provide response options such as “I don’t know”, “I’m not sure”, “I refuse to answer”.

Questions regarding quantitative variables should not be made closed (it is generally assumed that this means coding), it is enough to indicate the units of measurement. As noted above, information encoding can be performed later, at the stage of entering data into a computer database.

Failed Design		Recommended Design	
Age	1 (20-29 years old) 2 (30-39 years old) 3 (40-49 years old) 4 (50-59 years old) 5 (60 years and over)	Age _____ years	Or Date of Birth __/__/____

In this example, grouping by age certainly makes coding easier, but makes it virtually impossible for the researcher to analyze the data for other age groups, such as those aged 25 or older than 80, if required. Having data on the age of each subject of the study, it is subsequently easy to make a distribution for any age groups. Entering a date of birth is even more advantageous, as it provides information about the age of each research subject at any point in time.

The developed questionnaire should be pre-tested. If assistants are expected to be involved, it is useful to collect information yourself before entrusting it to someone, after that you need to train those who will be directly involved in the collection of information to make sure that the information is collected correctly. After the pilot test, it may be necessary to make changes to the study instrument.

Most epidemiological studies are selective. But in any case, even at the planning stage of data collection, care must be taken to ensure that the sample size ensures the achievement of the goals and objectives of the study. A situation is hardly acceptable when it turns out that significant funds and efforts spent on conducting a study did not allow obtaining statistically reliable results just because the planned sample size turned out to be less than what was actually required.

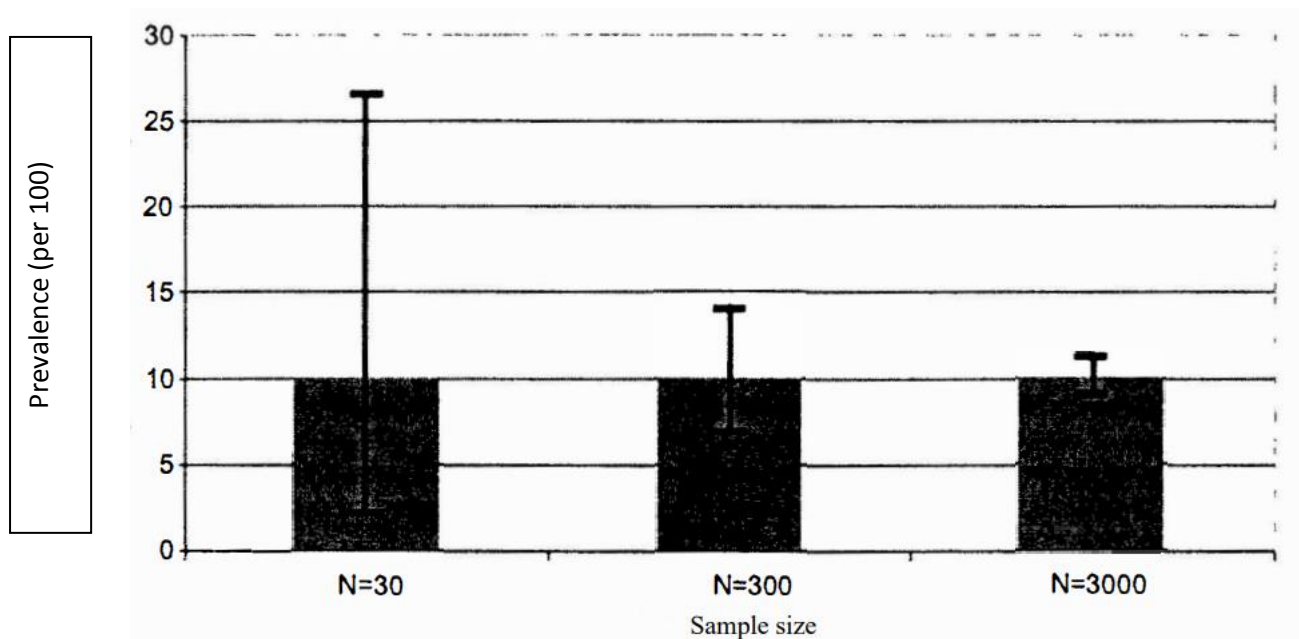
In order to estimate in advance the required sample size, it is necessary not only to formulate the main goal of the study, but also to try to formulate it in precise statistical terms. If the purpose of the study is, for example, to study the prevalence (for an explanation of the term, see the glossary, Appendix 1) of a disease in a population, the sample size will depend on what the required accuracy of the prevalence estimate is. The data given in table. 5.1 and illustrated in fig. 5.1, show how strongly the confidence intervals of the prevalence index (equal in the above example 10 to 100) depend on the sample size, narrowing with increasing sample size.

Table 5.1

95% confidence intervals for different sample sizes

Prevalence rate (per 100) = 10	Exact Fisher 95% confidence Intervals		
	N=30	N=300	N=3000
	2,11-26,53	6,85-13,97	8,95-11,13

There are special methods and appropriate computer programs that facilitate the task of preliminary estimation of the required sample size. In the above example, the Statcalc module from the Epi Info 6 software package was used to estimate the sample size required for an experimental epidemiological study.



Pic. 5.1 95% confidence intervals for different sample sizes

5. 2. Descriptive stage

Descriptive research methods include:

- receiving surveillance,
- clinical practices,
- methods of laboratory and instrumental research,
- techniques for studying the spatial distribution of the disease,
- reception of the distribution of cases by time,
- acceptance of the distribution of cases by different groups of the population,
- techniques of formal logic,
- statistical techniques (Student's t-test, Chi-square, Fisher's test, correlation coefficient, regression coefficient).

The purpose of descriptive methods of research is to determine the problems of medicine and prevention in general, and according to the nosological forms of diseases. Formation of hypotheses about risk factors.

The tasks of descriptive (descriptive) methods of epidemiological studies are to describe the intensity, dynamics, spatial characteristics and structure of morbidity (mortality, etc.) and, accordingly, to identify the time, groups and areas of increased risk of morbidity.

5. 2. 1. Intensity

The number of cases, expressed in absolute numbers, can give a first general idea of the significance of the problem (for example: in 1993, 12 cases of drug addiction were registered in N., and in 2003 - 1200 cases), as well as to determine short-term trends (primarily, when deciphering flashes).

Absolute figures can be used to describe outbreaks and manifestations of diseases that have arisen in those territories or in those communities where the population size remains unchanged over a certain period of time.

However, as a rule, to assess the incidence, it is necessary to use relative frequency indicators, which, as already mentioned, are a measure of the probability of an event. This unifies the characteristics of the spread of various diseases, i.e., allows you to compare, compare events that change in time and space, as well as in different population groups.

Among the frequency (intensive) indicators, the incidence should be considered the most important. In the domestic literature, the term “morbidity” is more often used, while this latter concept reflects not only the frequency indicator, but rather is used in a broader sense (“there is a incidence”, “high incidence”, “morbidity is expected”, etc.) .

It is in connection with the uncertainty of the term "morbidity" that it is advisable, when it comes to characterizing the frequency of an event, to use the term "incident" accepted in international practice. This term can be considered synonymous with "incidence" only in cases where the latter is really intended to demonstrate the frequency of the event. In addition, "incident" is a better term also because it is used to refer to the frequency of not only diseases, but also all other phenomena (outcomes) that epidemiology studies.

In general terms, the incidence rate is the result of measuring the frequency of occurrence of a disease in a population at risk, i.e. among those individuals who are likely to have a given disease. For this, two main indicators are used: cumulative incidence (CI) and incidence density (ID).

The most commonly used is the cumulative incidence indicator, which is calculated as the ratio of the number of cases of disease n that have arisen (“accumulated” - hence “cumulative”) for a certain period of time T , to the size of the risk population N in the same period of time (population size at the beginning or before end of observation, or half the sum of these values). It is this indicator that is often referred to by the term "morbidity". The formula for calculating the cumulative incidence (the word "cumulative" is usually omitted) is as follows:

$$CI = \frac{n}{N}(x10^n)$$

The 10ⁿ multiplier serves only to ensure that the resulting indicator does not have too many zeros after the decimal point, and simply makes it easier to perceive the information.

It is mentioned when the value of the indicator is reported as a unit of measurement (per 100, per 1000, per 100,000, etc.). For example, if there are 60 cases in a population at risk of 300,000 in a year, the n/N ratio would be 0.0002. If we use the appropriate multiplier (10⁵=100,000), the CI rate is 20 cases/100,000.

When calculating the indicators of cumulative incidence, it is imperative to take into account the duration of the time interval in which the counted cases occur. CI can be calculated for a year, for a month, for any other period of time, and, strictly speaking, in fact, the formula for calculating the cumulative incidence should look like this:

$$CI = \frac{n}{N \times T} (\times 10^n)$$

For example, given the example above, the cumulative incidence rate should be calculated (and presented) as follows:

$$CI = n / NT (X 10^n) = (60: 300\,000 \times 1 \text{ год}) \times 10^5 = 20 \text{ cases}/100\,000/\text{year}.$$

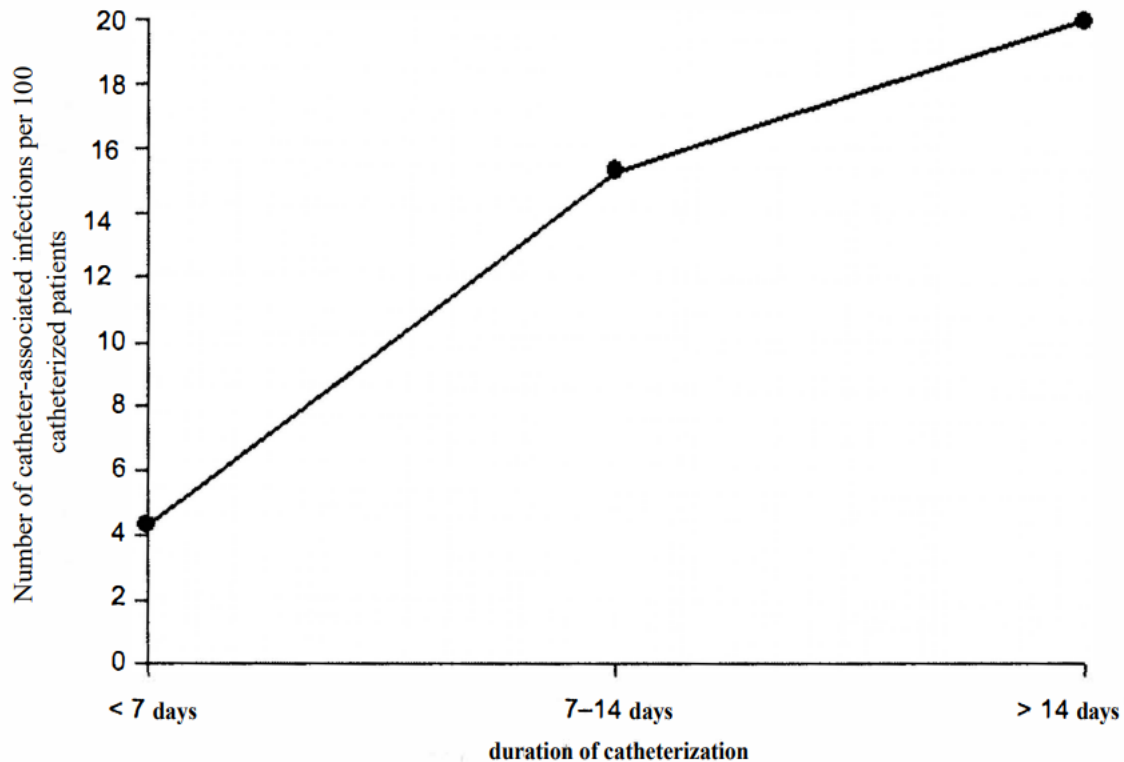
Since CI is usually calculated for one unit of time (one year, one month), it is customary to omit the value of T. The same is done if the CI indicators calculated for the same period (5 years, 10 years, etc.) are compared. However, when comparing indicators calculated for different periods of time (it is better not to do this at all), it should be borne in mind that different values of T do not allow comparing indicators without reducing them to a common denominator.

Only in the absence of any understanding of the nature of the risk does it make sense to use as the denominator the total number of people located (who were) in a given territory at a given period (moment) of time (“population”), as is often done in statistics. Sometimes the choice of the denominator is obvious: it would hardly occur to anyone to attribute the number of vaginitis to the size of the population represented by both sexes, or the number of postoperative complications to the total number of patients, including those treated with conservative methods. Therefore, it seems at least strange that indicators appearing in official reports, reflecting, for example, the incidence of neonatal sepsis, in the calculation of which the total population is used as a denominator. In other words, the denominator in the incidence rate, representing the size of the population at risk, should not include individuals who are not at risk of disease at all.

In cases of point (momentary) exposure to a risk factor (for example, a single consumption of a contaminated food product or a surgical operation), the cumulative incidence rate is a completely satisfactory measure of the incidence rate. However, when the likelihood of illness is related to the duration of stay at the site of risk of

infection, or when it is related to the duration of exposure to risk factors, differences in the duration of exposure to risk factors can be important when comparing indicators.

For example, in figure 5.2 shows that the risk of catheter-associated infections depends not only on the presence of a catheter, but also on the duration of catheterization.



Pic. 5.2. Dependence of the incidence of bloodstream infections on the duration of central venous catheterization

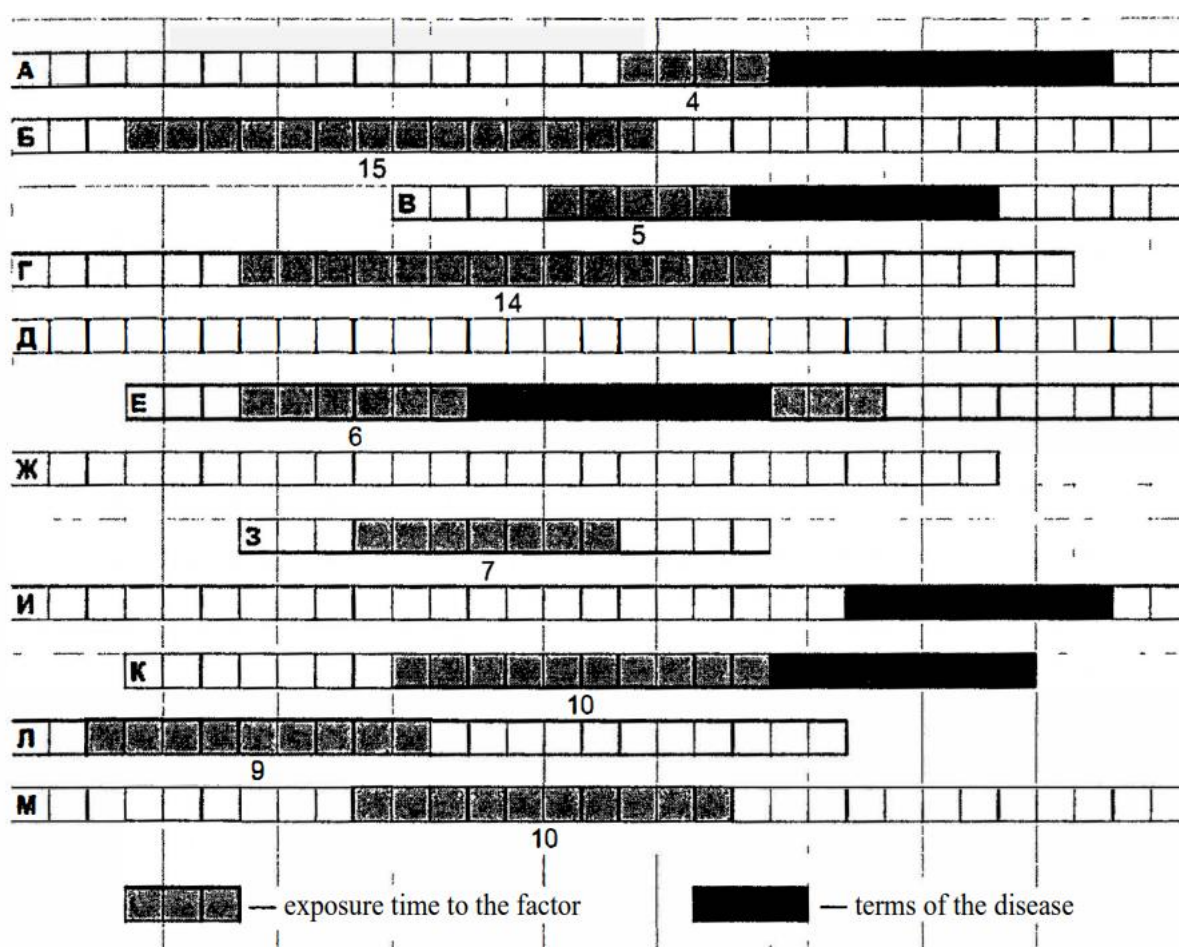
In such cases, the incidence density indicator is used. Incidence density (incidence rate, "incidence intensity") measures the frequency of new cases of a disease (n) occurring over a certain period of time (observation period), taking into account the total time of exposure to risk factors added by all members of the risk population (pT):

$$PI = n/pT(10^n).$$

Total $10^n = 10^3 = 1000$: The rate is calculated per 1000 "person-days", per 1000 days of hospitalization, per 1000 catheter days, per 1000 days of mechanical ventilation, etc.

Each member of the risk population who did not develop a disease adds to the denominator all the time (risk time) during which he was under the influence of a factor capable of causing this disease. For sick people, only the time spent under exposure to the risk factor before the onset of the disease is used to calculate the

denominator. The time of exposure to the factor after the onset of the disease is not taken into account, since the risk of the disease has already been realized.

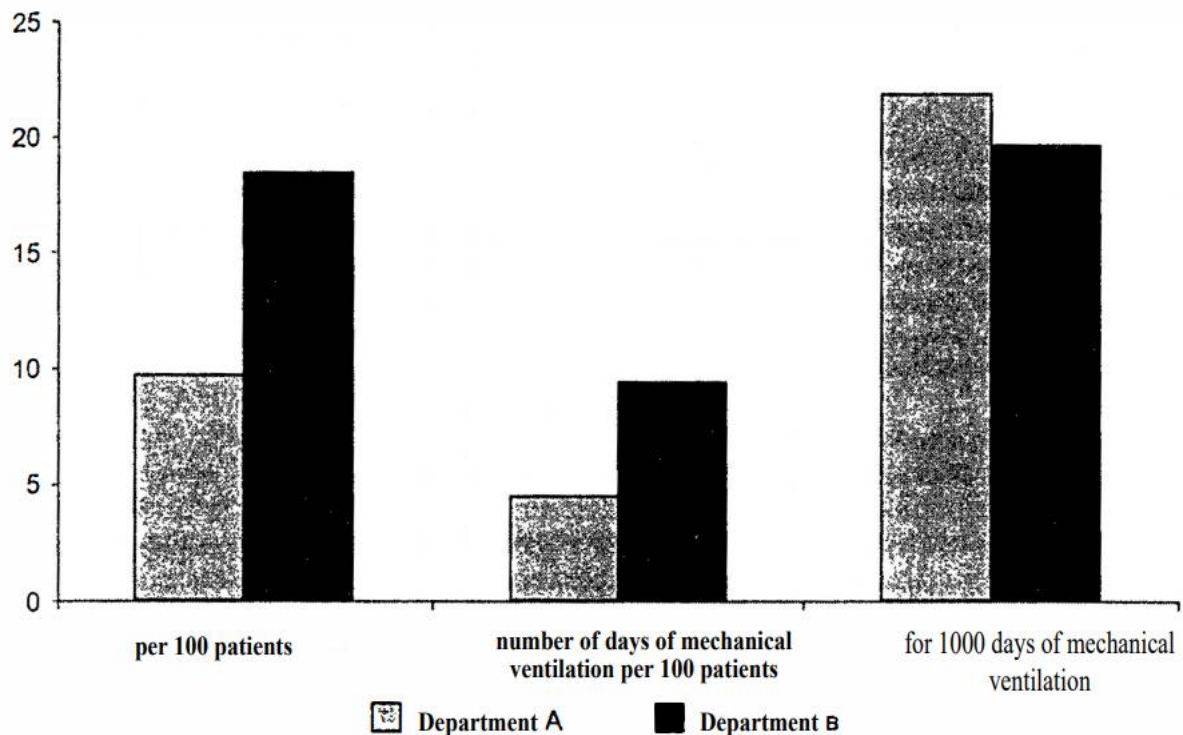


Pic. 5.3. Data for calculating the incidence density

On fig. 5.3 shows hypothetical data to illustrate the calculation of the incidence density. In total, judging by these data, 5 cases of the disease were registered, however, the case of disease and is not associated, apparently, with the action of the studied factor (there is no exposure to it), so the numerator value is 4. The denominator value should be equal to the sum of the entire risk time rT added by all members of the risk population, i.e. $pTA + rTB + rTB + rTT + pTE + rT3 + rTK + rTJI + rTM$ (Д, Ж and И are not exposed, so nothing is added to the denominator). The calculation of the indicator will look like this:

$$PI = \frac{n}{pT} (x 10^n) = \frac{4}{4+15+5+14+6+7+10+9+10} \times 1000 = \frac{4}{80} \times 1000 = 50$$

In cases where, in addition to the very fact of exposure to a factor, the duration of exposure to it is of great importance, the incidence density indicator provides a more correct comparison of disease incidence rates. Most often, this indicator is used in the study of the epidemiology of noncommunicable diseases and in hospital epidemiology. The diagnostic value of the incidence density indicator can be demonstrated, for example, using the data in Fig. 5 4.



Pic. 5.4. Frequency of nosocomial infections of the lower respiratory tract in two neonatal intensive care units

On fig. It can be clearly seen from Table 5.4 that when comparing the cumulative incidence of lower respiratory tract infection (LRTI) associated with artificial lung ventilation (ALV), calculated per 100 patients undergoing mechanical ventilation, it turned out that the frequency of nosocomial infections in department B is almost twice as high as the corresponding indicator in department A. However, LRTI is another example of a disease in which the likelihood of their occurrence is closely related to the duration of exposure to the main risk factor (in this case, mechanical ventilation). An assessment of the duration of mechanical ventilation in the two departments by comparing indicators that reflect the intensity of ventilation use (the number of days of mechanical ventilation per 100 patients with mechanical ventilation) showed that the duration of artificial ventilation in department B was also almost twice the corresponding indicator in department A.

If we calculate the corresponding incidence density indicators, it turns out that comparing the incidence, taking into account differences in the duration of mechanical ventilation, leads to the conclusion that the risk of LRTI in the two departments is actually approximately the same.

Another important advantage of the incidence density indicator is the fact that it allows you to solve the problems associated with estimating the frequency of diseases in populations that change in size.

Unlike incidence rates, which reflect the incidence of diseases, the prevalence rate is used to quantify the state of disease. Prevalence differs from incidence in that it takes into account not only those diseases that have arisen during the studied period of time, but all that are present in the observed period, i.e., it describes the level of prevalence of the disease.

In this case, we are talking about either a fairly short period of time (periodic prevalence), or (much more often) a specific point in time (momentary or point prevalence). In quantitative terms, the prevalence rate (Π) is defined as the ratio of the number of all cases of the disease existing at a certain point (short period) of time (P) to the size of the risk population at the same point in time (N):

$$\Pi = P/N(\times 10^n)$$

The term "prevalence" has several synonyms, among which the most widely used are "prevalence", "affection" and "morbidity". The use of the term "prevalence" (an almost literal translation of the English term) does not cause any particular problems, except for doubts about the appropriateness of using synonyms to refer to the same indicator in principle. "Infection" is most often used by parasitologists, while, unfortunately, when reporting specific data, the same indicators are sometimes referred to as "infection", and sometimes - "Incidence". In both cases, we are talking about prevalence, and this is another reason why one should be very careful in using the term "incidence" to refer to epidemiological indicators.

5.2.2. Dynamics

Dynamics is the distribution of absolute numbers or frequency indicators (intensity) over time.

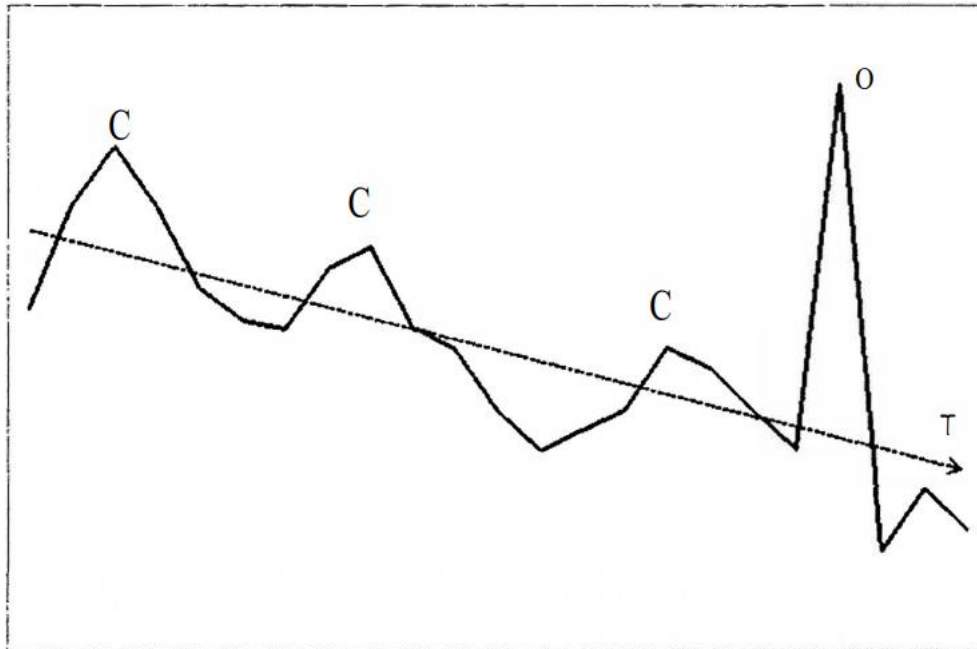
Description of the dynamics of morbidity (other outcomes) allows you to assess changes in the situation over a certain period of time, make assumptions about the possible causes of changes and predict the development of the situation in the future. At the same time, the dynamics is considered as a reflection of the impact of causal factors, the set and/or strength of influence of which changes over time.

When studying the dynamics of the development of morbidity (in relation to infectious morbidity - the epidemic process), as a rule, several main components can be distinguished (Fig. 5.5):

1. Unidirectional changes (trends, trends). In this case, we are talking about the assessment of the most general patterns of the dynamics of the process (growth, decline, stabilization).
2. Periodic rises in incidence that occur at a certain time (at certain time intervals). Periodic rises in incidence in certain years with a certain rhythm are often called

cyclicality. A stable (repeating from year to year) increase in the incidence in certain months of the year is called **seasonality**.

3. Random fluctuations, i.e., rises in incidence that occur at any time, outside of rhythmic fluctuations, appearing unexpectedly. This kind of rise is called **flare** (although not everyone accepts this term in this context).



Pic. 5.5. Schematic representation of the main components of the incidence dynamics: unidirectional changes/trends (T),

periodic climbs in incidence (C) and random fluctuations / outbreaks (O)

Traditionally, it is customary to single out, depending on the scale of time measurement, the so-called **long-term dynamics** (distribution of the frequency of the studied outcomes over years) and **monthly (intra-annual) dynamics**. However, the time scale can also be graduated in other units, depending on the tasks at hand: sometimes when investigating outbreaks, it is advisable to measure time in hours. The choice of how to measure time is dictated by the duration of the alleged causative factors and, accordingly, the frequency of occurrence of the corresponding outcomes. So, for example, the study of long-term dynamics makes it possible to identify the leading risk factors that act for a long time (permanently) and determine the main patterns of the development of the process.

There are many techniques for analyzing dynamics (or, to use the term adopted in biostatistics, time series analysis). A much more difficult task is the interpretation of the identified features of the process dynamics.

The periodicity of long-term dynamics is characteristic of many diseases, especially infectious ones. In modern conditions, with long-term observations of the epidemic process, several types of long-term fluctuations in the incidence rate have been

recorded: rises in incidence with an interval of approximately 3-5 years, 20-22 years and 30-40 years or more.

The rises with an interval of 3-5 years reflect, as a rule, the internal features of the population relationships of the pathogen and the host, and are most characteristic of airborne infections. With these nosoforms, infection occurs easily and uncontrollably: in the presence of a source of infection, others are quickly involved in the circulation of the pathogen (manifest and asymptomatic forms of infection). This leads to the formation of an immune layer among the population and, accordingly, the growth of population immunity. Eventually, the population of susceptible individuals becomes so rarefied that the epidemic process either ceases altogether (small populations) or is sustained by rare infections. It is impossible to exclude the influence on the reduction and termination of the incidence, according to V. D. Belyakov, also in parallel with the development of a decrease in virulence and reservation processes in the parasite population (typhus - Brill's disease, chicken pox - shingles, etc.). This is followed by a gradual accumulation of susceptible people, an increase in their proportion among the population (the birth of a new generation and mortality among older age groups), which leads to a new rise in morbidity. The interval between rises is the shorter (about 3 years), the larger the population. Large metropolitan areas are characterized by the shortest well-being intervals.

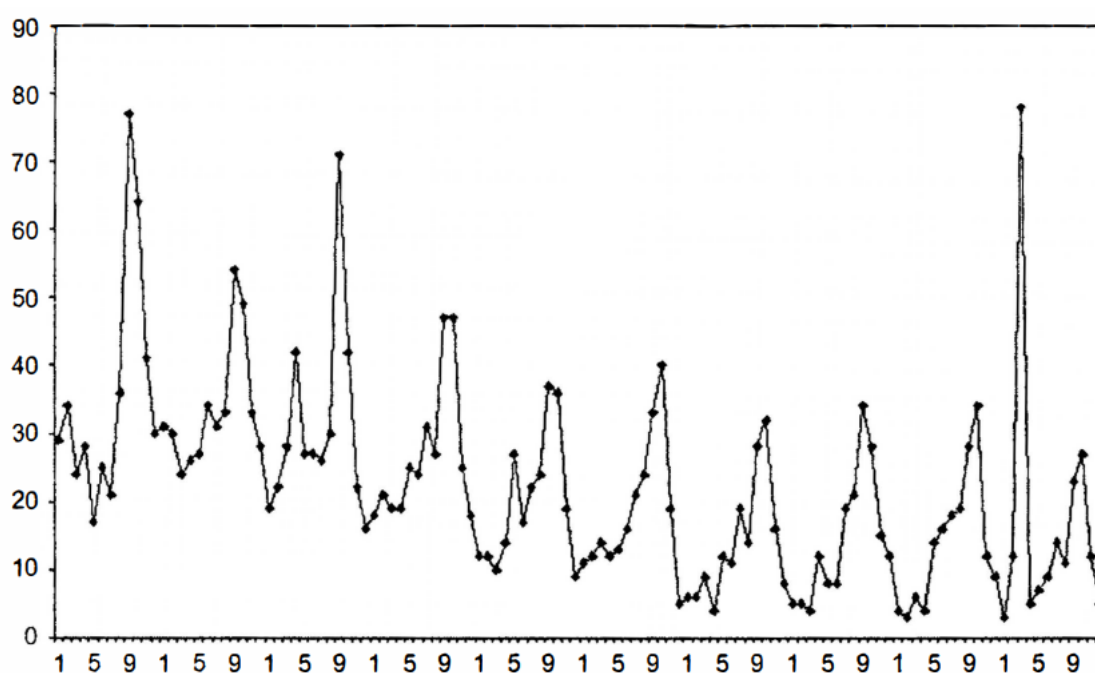
In acute intestinal infections, a similar long-term dynamics is also observed, and it is more obvious in places that are unfavorable in sanitary and hygienic terms.

Of particular interest to epidemiologists is seasonality analysis. The seasonal rise in incidence is most characteristic of most infectious diseases, although it is also observed in some non-communicable diseases (it is well known, for example, that in winter there is an increase in the incidence of cardiovascular, cerebrovascular, respiratory diseases and some other diseases).

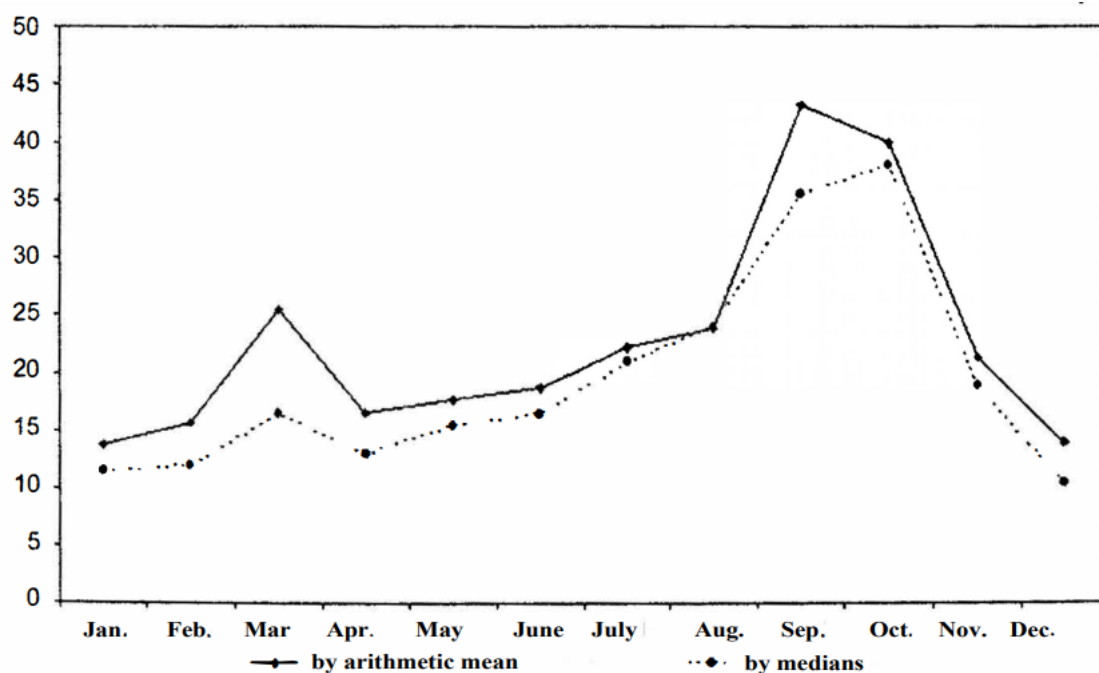
Traditionally, seasonality is usually described using the so-called typical seasonal curve. To construct a typical curve, the average values of the number of cases of diseases for each month over a number of years constituting the period of study of the incidence are usually used. At the same time, it should be borne in mind that the formal description of seasonality (as, indeed, in the study of other manifestations of dynamics) is strongly influenced by the presence of "pop-up" values ("outliers"), associated, as a rule, with outbreaks of morbidity, which are not a consequence of general patterns and determined by random, "momentary" (even if more powerful) factors. The ideal solution to this problem is to exclude cases that are known to be associated with outbreaks, but this is not always possible and, in turn, is determined by the quality of the outbreak investigation. There are also a number of formal ways

to identify and eliminate outliers, the simplest of which is to use the median instead of the arithmetic mean, which is more resistant to extreme values.

On pic. 5.6 as an example, a hypothetical monthly dynamic for 10 years is shown. The results of constructing typical seasonal curves in two ways (by arithmetic mean and by median) are shown in Fig.5.7. It is clearly seen that the median curve reflects seasonal fluctuations much better. The only drawback of using the median is the fact that the duration of the study period should not be less than 10-12 years.



Pic. 5.6. Sample image of monthly dynamics



Pic. 5.7. Two options for constructing a typical seasonal curve

There are several ways to quantitatively describe a typical seasonal curve, which make it possible to measure the duration and severity (amplitude) of the seasonal rise, to determine its beginning and end. To do this, it is necessary to determine the ordinary level of morbidity, which, in relation to the study of seasonality, is most often defined as the average monthly level of a favorable stage in the development of pathology among people. This allows, in particular, to establish the time of the upcoming seasonal rise, since when calculating well-being (relative well-being), months of the “off-season” are taken to determine the level of the ordinary. One of the methods for determining the ordinary level was proposed by V. D. Belyakov, calling it "year-round morbidity." This method is perhaps the most common in the practical work of epidemiologists (see p. 129).

5. 2. 3. Spatial characteristics

Spatial characteristic is the distribution of frequency indicators (intensity) over the territory.

Since the population is unevenly distributed over the territory, and these territories can differ significantly in natural and social characteristics, the manifestations of morbidity can also differ among residents of different places.

Onenka distribution of diseases in different territories (i.e., among their inhabitants) is one of the most important aspects of the professional study of diseases among people, since it not only identifies residents of places who suffer more than others from certain diseases, but allows you to analyze the processes of occurrence and the spread of morbidity, i.e., to establish the influence of various natural or social conditions on the incidence of the population, as well as to predict the future situation.

The first stage of a spatial study is a description of the spread of diseases across territories, including a quantitative characteristic. It is, therefore, primarily about stating the fact of the peculiarities of territorial distribution. This geographical direction in medicine has received recognition and has become of great importance both in our country and abroad.

The spatial characterization of the spread of diseases is necessary not only for special studies, but also in the daily work of an epidemiologist at any level, since it allows one to assess the specifics of the situation in different territories. We are talking about the constant differentiation of the territory, taking into account the dominant professional activity of the population, which makes it possible to plan and carry out activities of both a strategic and tactical nature, taking into account the specifics of the situation in various rural areas and in cities. The division of territories is primarily focused on differences in the levels of morbidity and its structure, but, in addition, it takes into account the peculiarities of natural (climate, landscape),

environmental and social factors (economy, nature of economic activity - in industry, in agriculture, features of industrial enterprises , detailed environmental profile, etc.).

At the same time, of course, spatial differentiation is necessarily built on the basis of established internal administrative boundaries, since the entire system for registering and recording diseases is built on an administrative principle. I would like to emphasize that a spatial assessment can and should be based, firstly, on reliable data, and secondly, on a unified system of registration and accounting.

Unfortunately, spatial characterization is often used to state facts, although its main purpose is to use materials for the analytical stage, that is, to identify risk factors present in certain places.

The spatial characteristic can be presented in the form of various tables or in the form of maps (cartographic method), on which the epidemic situation is applied. When maps are used, it may happen that the spatial characteristics of the nidus will not coincide with the established administrative boundaries, this is especially often the case with natural focal diseases, sometimes this has to be taken into account in diseases associated with adverse environmental impacts. Maps provide clarity for the perception of the material (characteristic of the incidence of residents of various cities, various rural areas or their individual parts).

There are two main ways of depicting spatial characteristics on maps: cartograms and cartograms. A cartogram is a schematic geographic map on which data is plotted with hatching of varying density, coloring with a certain degree of saturation (background cartogram) or dots (dot cartogram).

Background cartograms (picture 5.8) are used to analyze relative indicators, dot charts (picture 5.9) usually contain the absolute number of cases of diseases, other data expressed in absolute numbers.

Chart charts use various chart shapes as pictorial symbols, which makes it possible to display more complex data. However, the map should not be overloaded with bars, circles and other icons that scatter attention and do not allow focusing on the main essence of the problem.

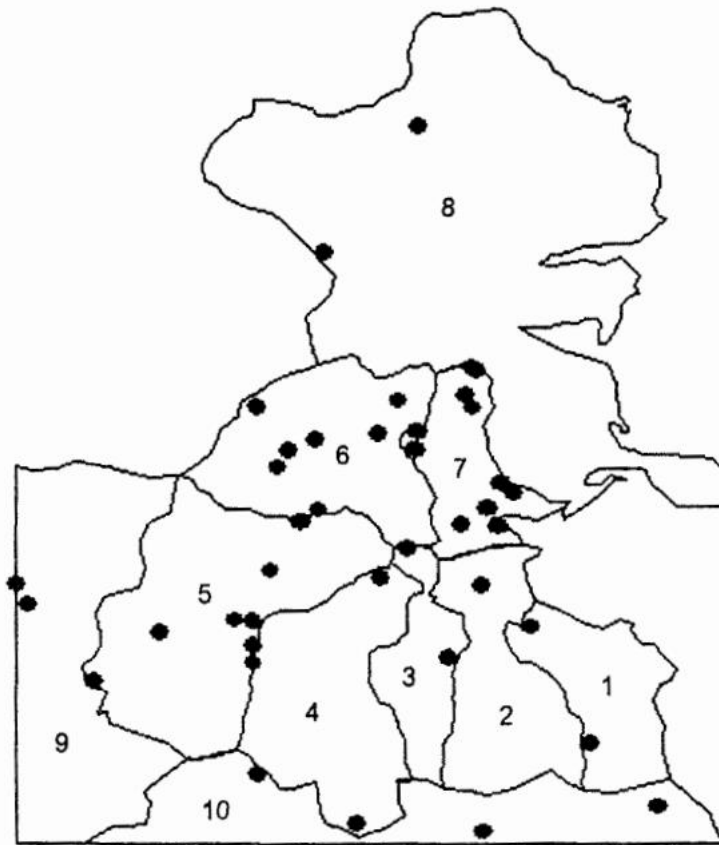
When the cartographic method of the spatial distribution of morbidity is used, the specific purpose of the study should be clearly formulated, in particular, territories or population groups (urban, rural) should be precisely defined. The cartographic method, as already mentioned, due to its clarity, allows you to quickly notice the differences in the incidence of different population groups.

The possibilities of computer technology allow a new approach to the study of epidemiological and geographical aspects. Modern geographic information systems (GIS) not only facilitate the technical side of this task, but also provide an

opportunity to study, for example, changes in the epidemic situation over time, quickly analyze epidemiological data, and even predict the development of the situation.



Pic. 5.8. Approximate view of the background cartogram



Pic. 5.9. Approximate view of a dot cartogram

5.2.4. Description of the structure of morbidity and identification of risk groups

Structure is the distribution of frequency indicators (intensities) among different population groups.

The heterogeneity of a population is characterized not only by the fact that each of its representatives has some features that distinguish it from others, but also by the fact that, for a number of reasons, it is possible to unite a certain number of people into groups. One group includes persons who have the same type or more or less similar indicators either in biological or social, or sometimes natural factors. For example, the population is divided into children and adults, since there is a fundamental difference between these groups in a number of indicators, while at the same time, a number of characteristics uniting them are noted within the groups. So, children, due to the lack of immunity or its insufficiency, suffer from so-called childhood infections (rubella, chicken pox, etc.), adults are more likely to suffer from malignant neoplasms and cardiovascular diseases. Livestock workers, unlike other populations, constitute a group of people for whom there is a high risk of suffering from zoonotic infections, etc. The assessment of the incidence, taking into account a well-thought-out structural distribution, is of great importance for selecting the most vulnerable population groups, the so-called risk groups, and the

implementation of generally accepted priority measures in the fight against morbidity in the most affected group; in addition, at the analytical stage, the assessment of the structural distribution of morbidity is of decisive diagnostic importance, since it becomes possible to conduct comparative studies.

It must be borne in mind that there is a standard scale of structural differentiation, based on the accumulated experience of anti-epidemic work, which is mandatory in all territories (administrative units), - without this, it is impossible to compare, compare different populations of the country (living in different regions, in cities and villages, in places with different social, ecological and natural characteristics). But along with this, taking into account the specific characteristics of the population, it is possible (necessary) to divide into some groups specific to this population that reflect their particular characteristics. So, for example, the founder of population analytical studies, J. Snow, in order to clarify and prove the role of water in the spread of cholera, divided the population of London according to the principle of providing water by two different water companies, which differed in the place where water was taken from the River Thames upstream of the city and downstream at the place of drains. After the accident at the Chernobyl nuclear power plant, the population that found itself in the area of the radioactive cloud was differentiated according to the radiation dose and the degree of radioactive contamination of their places of residence.

Epidemiologists studying cardiovascular pathology, phthisiatricians, obstetricians dealing with the problem of neonatal infant mortality, etc. have their own system of structural division of the population.

It should be noted that the grouping (selection of groups), which differs in each case from the standard one and ensures effective diagnostic work, requires good professional training and care.

In the system of work of anti-epidemic institutions, when the incidence of various infectious diseases is characterized, the following grouping is most often used:

- ◆ By age (0-2 years old, 3-6 years old, 7-14 years old, 15 years old and over).
- ◆ Separation of children according to the indicator of visits to children's health-improving institutions (yes/no).
- ◆ Separation of children brought up at home and children in orphanages, orphanages, boarding schools.
- ◆ Separation by place of residence (urban/rural).
- ◆ Separation by gender.
- ◆ Separation of victims by etiology (if the same disease is caused by different species or types of pathogen).

Recently, the differentiation of the population, especially children, according to the degree of observance of the vaccination calendar (according to registration data) has become of great importance. This takes into account the vaccination status, taking into account the age characteristics of the child population, since the entire vaccination system (vaccination, stages of revaccination) must be accurately characterized.

As a rule, the structure of those affected by certain diseases is given in intensive indicators (in terms of the frequency of diseases in the corresponding groups), which makes it possible to compare the incidence of different groups of the population - this is also necessary for stating a fact and directing efforts in the fight, primarily in relation to groups with an increased level of morbidity (risk groups), but this is also important for the subsequent analytical stage. However, the structure of the incidence of various population groups can sometimes be represented not only in intensive (frequency), but also in the form of extensive indicators. Extensive indicators indicate the proportion of different groups (in%) among all cases. Extensive indicators can be shown in tables, but are most often presented in the form of charts, usually pie charts, in which a sector with an angle corresponding to the share of this affected group among all cases is assigned to the diseased population of each population group. Of course, bar charts are also possible. Extensive indicators captivate with their clarity, but they are most often not suitable for the analytical stage. Only in some cases, extensive indicators are of great importance for the further analytical stage. So, for example, studying the characteristics of people affected by HIV infection, the WHO European Office stated that among those with AIDS in France, Germany and some other Western European countries, there was a high proportion (proportion) of homosexuals, and in Spain and Italy - drug addicts.

In none of these states is it possible to calculate exactly in intensive terms the significance of homosexuality and drug addiction, since their absolute number is not known. But if their proportion among the sick is very high, then, undoubtedly, these are risk groups for HIV infection, since it is quite obvious that the proportion of homosexuals and drug addicts among the entire population is significantly lower than among AIDS patients.

So, the descriptive stage of population epidemiological studies allows, on the basis of ascertaining the nature of the spread of a particular pathology among the population, to build some preventive and anti-epidemic measures based on the available scientific data and accumulated practical experience. At the same time, it is possible to choose priority areas of activity (in relation to the most vulnerable groups of the population, at the most dangerous time and in the most dangerous places).

In many cases, such a system dominates in practice. But it must be borne in mind that this system is associated with possible large economic losses, most often without the proper effect, since it does not reveal the true cause of the incidence that operates in this population. In other words, practitioners cannot and should not stop at the descriptive stage, which does not always make it possible to obtain an effect when carrying out activities.

5. 2. 5. Formation of hypotheses about possible risk factors

Due to the fact that the measures taken on the basis of the descriptive stage may be ineffective, it becomes necessary, taking into account the collected data characterizing the manifestations of morbidity, to make assumptions (make hypotheses) about the causes of the current situation, i.e. about causal relationships between the resulting morbidity (consequence) and the specific factor that led to such morbidity. A hypothesis, therefore, means an attempt to mentally penetrate into the essence of a still insufficiently understood phenomenon.

Given that in population studies, reliable data can only be obtained through comparative tests, logical techniques have been introduced into practice, with the help of which hypotheses are formed:

- reception differences;
- reception of similarity;
- acceptance of accompanying changes;
- reception of analogy,
- acceptance of leftovers

The formation of hypotheses is based on the initial professional assessment of the available material.

Reception of the difference schematically looks like this:

Circumstances A (probability of the presence of a possible causative factor)	Circumstances B (probability of a possible causal factor is not present or it is not high)
The incidence is significant or obvious and causes concern (+)	The incidence is absent or very small (-)

It can be seen from the above diagram that the incidence can be (or it is significant) under the influence of some factor that is absent (or its influence is extremely small) in well-being, i.e. this factor determines the difference between the two existing situations.

Examples.

1. Among the inhabitants of Kashmir, cancer of the skin of the lower abdomen and thighs occurred among those who warmed themselves in winter by wearing an earthen pot full of burning coals suspended from their necks. Among those residents who did not use this method of heating, skin cancer of the lower abdomen and thighs did not occur. The reception of the difference made it possible to hypothesize about the risk factor (cause).

2. In two children's institutions there were cases of pseudotuberculosis. In other children's institutions, such cases were not registered. During the investigation, it turned out that all children's institutions, except for these two, where diseases have arisen, receive vegetables from one vegetable warehouse. Two children's institutions where the disease occurred receive vegetables from another vegetable warehouse. Reception of the difference made it possible to hypothesize that the diseases arose as a result of eating raw vegetables infected with the causative agent of pseudotuberculosis.

3. In a children's combine (nursery-kindergarten), many diarrheal diseases arose among children in kindergarten groups, which were then diagnosed as dysentery caused by *Shigella Flexner 6*. There was not a single case of diseases among children in nursery groups. An epidemiological investigation showed that the children of kindergarten groups were served boiled cod with mashed potatoes for dinner the day before, while toddlers were served only mashed potatoes. It turned out that a woman was involved in the processing (cutting, dividing into portions) of boiled cod - a kitchen technician (not a cook), who, during the investigation, was diagnosed clinically, sigmoidoscopy, immunologically (high antibody titers) with a protracted infectious process - shigellosis *Flexner 6*. In this case, the acceptance of the difference - the incidence among kindergarten children and the absence of diseases in toddlers - made it possible to hypothesize about the source of infection and the transmission factor.

Unfortunately, multiple hypotheses can often be generated based on the difference, making diagnostic work difficult.

Reception of similarity schematically looks like this:

Circumstances (situation) A	Circumstances (situation) B that differ significantly from circumstances A (by some natural, social, demographic and other characteristics or by their combination)
The incident is significant or obvious and causes concern (+)	The incident is significant or obvious and causes concern (+)
Presence of some factor X	Presence of some factor X

The method of similarity indicates that under conditions of completely different circumstances there is a factor X common to both situations, which, obviously, acts as a causal one.

Example.

The role of rodents as sources of infection in hemorrhagic fever with renal syndrome (HFRS) was confirmed by observations of outbreaks that occurred in summer and winter, in field and stationary conditions of life of organized groups. These outbreaks occurred only in the case of intensive colonization of premises by rodents (voles). In this case, the method of similarity made it possible to hypothesize about the role of rodents as sources of infection, since they were found stably in the premises of groups affected by HFRS, although living conditions were significantly different in many respects.

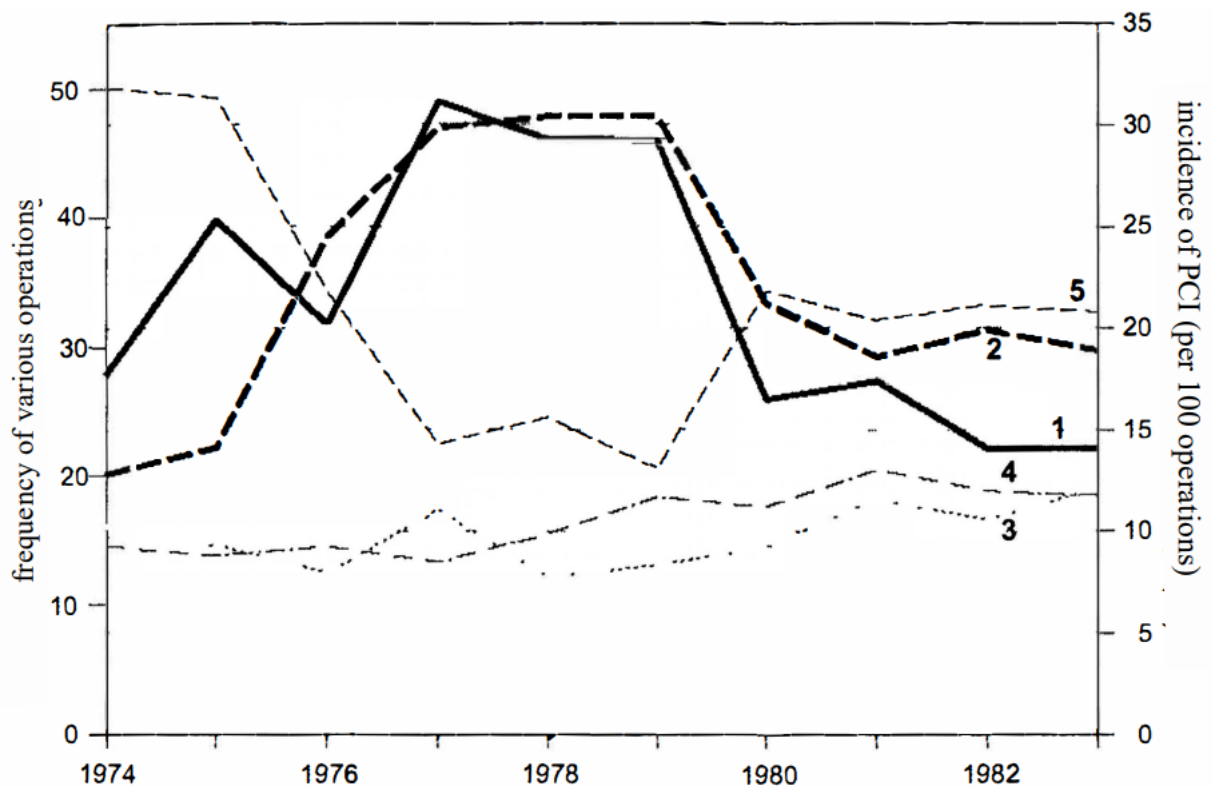
In some cases, it is advisable to apply techniques and similarities and differences. At the same time, differences are created by eliminating the alleged risk factor in a number of groups with the help of targeted measures.

The reception of concomitant changes is usually used when evaluating events in dynamics (identifying changes in time, space, etc.).

Examples.

1. British and American doctors noted that the dynamics of mortality from lung cancer and the dynamics of the number of cigarettes smoked per day are synchronous. This allowed them to formulate a hypothesis about the risk factor (cause) of death from cancer.
2. In fig. 5.10 presents data on the long-term dynamics of purulent-septic infections (GSI) in a trauma hospital and the dynamics of the frequency of various types of operations.

Visually, it can be concluded that the dynamics of the incidence of GSI correlates with the frequency of operations when metalosteosynthesis was used.



Pic. 5.10. Long-term dynamics of the frequency of various types of operations and PCI:

1 - PCI, 2 - metal osteosynthesis, 3 - plastic surgery, 4 - operations on ligaments, 5 - other

Reception of analogies is the extrapolation of materials related to well-studied diseases to observations related to poorly studied nosological forms. This technique is used quite widely and its success depends on the experience and professional knowledge of a specialist, since an experienced person always has more reasons for analogies.

For example: professional knowledge of the mechanism of development of the epidemic process of viral hepatitis B allows extrapolating them to observations regarding viral hepatitis C, G, F, i.e., to hypothesize that, for example, vertical transmission of the G and F virus is probably possible.

Residual intake is used in the study of several risk factors. At the same time, some of them are consistently excluded from this sum of factors, the assumptions about which are justified by other logical methods of forming hypotheses. Those risk factors that are easier to substantiate and study are excluded. As a result, a hypothesis is formed about the influence of the remaining risk factor.

Example.

It is well known that dysentery can be transmitted by water, food and household contact. When studying the ways of transmission of this infection in a particular

locality, the specialist was able to determine the proportion of contact-household and water transmission routes. It turned out to be small, which allowed him to hypothesize about the leading role of the food transmission route in this locality.

So, all of the above methods of logic are used to form hypotheses about possible risk factors (causes of the onset and spread of diseases).

It must be emphasized that the visual assessment of the data obtained from population epidemiological studies is completely insufficient. Therefore, it is mandatory to involve biostatistical techniques that allow statistical testing of hypotheses, i.e., to evaluate them. Techniques for evaluating hypotheses are analytical techniques, although it is difficult to draw a dividing line in this case.

All the data presented are designed for practitioners who are obliged to build a strategy and tactics for their actions after establishing local causal relationships (that is, based on epidemiological diagnostics). Annual reports drawn up in anti-epidemic institutions should, therefore, be based not only on descriptive data, but also on analytical ones, which make it possible to carry out epidemiological diagnostics, which is the basis for planning and implementing targeted measures. Analytical techniques underlie the investigation of the causes of outbreaks, since without identifying a specific causal factor, work cannot give positive results.

5. 3. Analytical stage

Analytical methods of research include:

- ◆ Receptions of formal logic.
- ◆ Statistical techniques (estimation of the correlation coefficient, regression coefficient, relative risk, prevalence ratio, etc.).
- ◆ Cohort studies.
- ◆ Case-control studies.

The **purpose** of the analytical techniques of the study is to evaluate hypotheses about the causes (risk factors) of the occurrence of diseases (other outcomes).

5. 3. 1. Techniques of formal logic

As already noted, the formulation of hypotheses begins at the descriptive stage. At the analytical stage, the use of formal logic techniques to formulate new hypotheses continues. It is almost impossible to draw a clear line between the descriptive and analytical stages in terms of formulating hypotheses.

5. 3. 2. Methods of biostatistics

The simplest and most accessible methods for evaluating hypotheses are the methods of biostatistics, with the help of which, as already mentioned in the previous section, statistical testing of hypotheses is carried out. So, if differences in incidence rates are found in two population groups and these differences are hypothetically associated with some factor, then within each group there should be statistically significant more often those who are exposed to this factor, compared with those who are affected by this factor. does not have an effect, or this effect is less pronounced.

When evaluating events in dynamics, correlation analysis is used.

At the same time, the frequency indicators of the pathology that has arisen and the frequency or quantitative characteristics of the mentioned factor are compared. Depending on the value of the correlation coefficient, the strength of the relationship between the alleged cause and its effect (morbidity) is judged. The stronger the relationship (for example, $r=0.9$), the more likely the significance of this cause.

It is important, however, to keep in mind the need to differentiate causal statistical relationships from ordinary non-causal, random ones. In the latter case, we are talking about the synchronization of events that are not related to each other. Most often, this is observed when one category of phenomena affects two others simultaneously, as a result, an apparent connection is visible between the latter. Here, professional skill is very important to eliminate errors.

In the process of evaluating hypotheses, some of them are confirmed, others are rejected, while forming new hypotheses.

So, all those hypothetical risk factors that have passed the statistical test become an epidemiological diagnosis (risk factors, causes of the onset and spread of diseases).

Example:

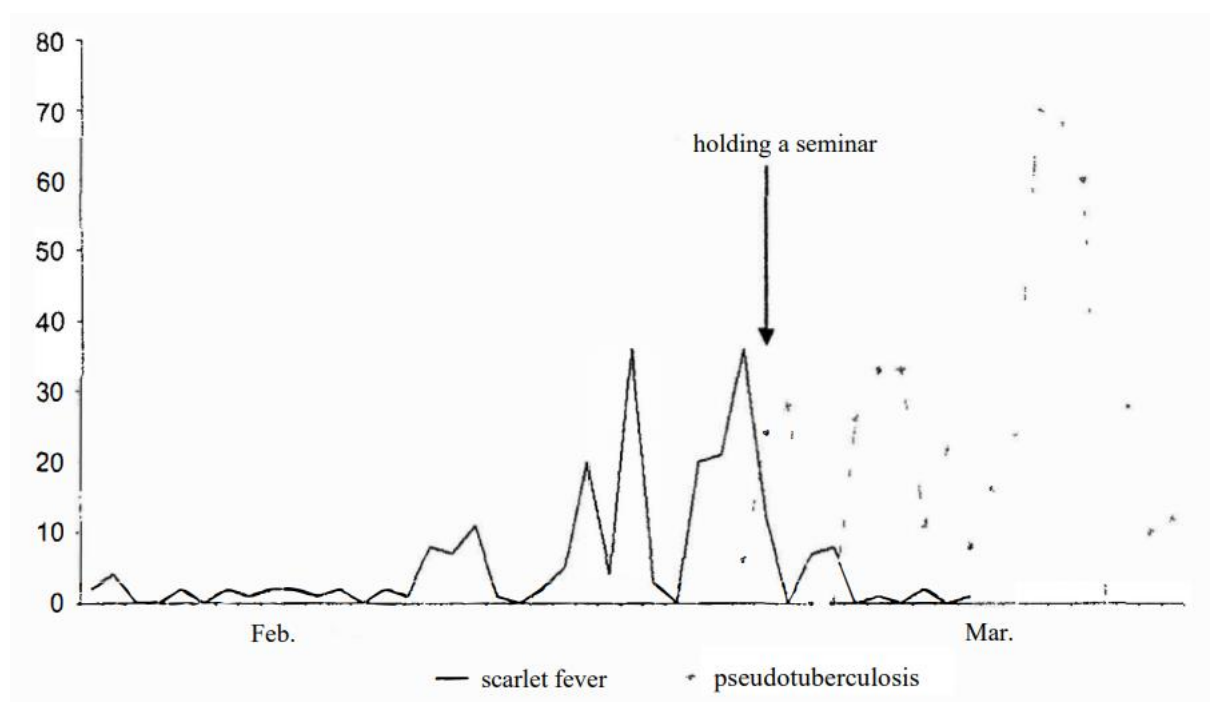
An outbreak of pseudotuberculosis occurred in one of the Siberian cities (M. L. Livshits). 562 people fell ill. Prior to this outbreak, the disease had never been reported in the city. The outbreak began against the backdrop of an increase in scarlet fever cases in the city, as evidenced by the presented data on the monthly incidence of scarlet fever (Fig. 5.11). In mid-February, local doctors noticed certain changes in the usual scarlet fever clinic. One of these doctors suggested the presence of pseudotuberculosis in these cases. A seminar on the clinic and diagnosis of pseudotuberculosis was organized with the doctors of the city. After that, the diagnosis and registration of pseudotuberculosis took on an unreasonably wide scope, as evidenced by the sudden almost complete cessation of registration of scarlet fever. Of course, such a situation distorted the real picture of the dynamics of the epidemic process and created difficulties for epidemiological analysis. It required a retrospective study of all case histories with diagnoses of scarlet fever and

pseudotuberculosis by qualified infectious disease doctors. Only after carrying out this work did it become possible to determine the number of cases and study the dynamics of pseudotuberculosis by the dates of the disease (Fig. 5.12).

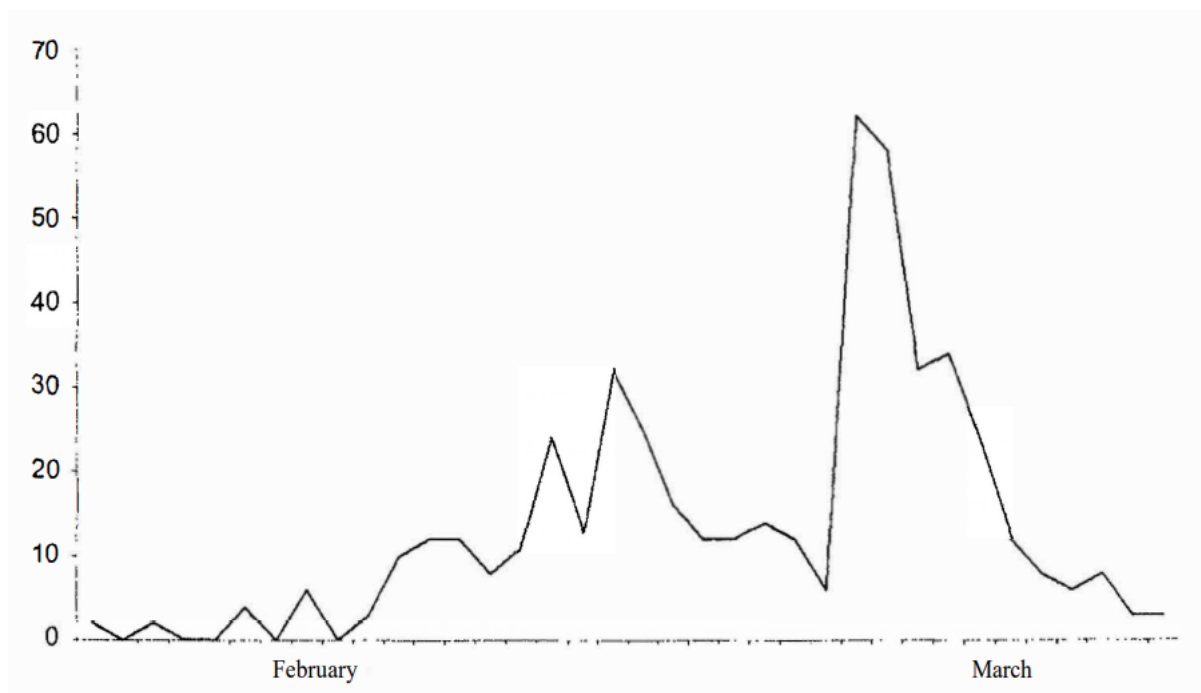
The presented data indicate a rather rapid development of the process, but by no means an explosive beginning of the outbreak.

Epidemiologists were faced with the task of identifying the causes of the emergence and spread of pseudotuberculosis diseases.

Extremely important, as has been emphasized repeatedly, is the availability of professional knowledge of the epidemiologist on this disease. It is well known that pseudotuberculosis is transmitted through vegetables, fruits, less often water. This knowledge directs the epidemiologist to search for a transmission factor.



Pic. 5.11. Incidence of scarlet fever and pseudotuberculosis by registration dates



Pic. 5.12. The dynamics of the incidence of pseudotuberculosis

But, before starting to search for the transmission factor, sources of infection, it was necessary to calculate the frequency indicators of the incidence of pseudotuberculosis in dynamics, by territory, in various population groups, i.e., to carry out the descriptive stage of the study.

This work showed that the territorial distribution of diseases is diffuse, covering all 4 districts of the city.

The morbidity rate of the adult population was 12 times lower than that of children. This circumstance allows us to speak about the possible predominant effect of the alleged transmission factor among children.

Attention was drawn to the fact that the total incidence rate of unorganized preschool children and schoolchildren was 5 times higher than the same indicator among children united in boarding schools. Thus, it could be assumed that the operation of the desired transmission factor in groups of round-the-clock stay of children encounters significant obstacles. The practical non-contagiousness of pseudotuberculosis itself ruled out the occurrence of focal diseases.

The data of the epidemiological examination of the sick people made it possible to assume that the infection of the victims occurred outside the collectives, only individual units of the desired factor, and not its totality, were contaminated with the contagious onset. The latter assumption is also confirmed by the nature of the dynamics of the epidemiological process (see Fig. 5.12), namely, the absence of an explosive beginning of the epidemic.

The noted epidemiological features of the pseudotuberculosis outbreak suggested the effect of a food factor.

In the process of studying the range of food supply within the city, special attention was paid to products that are not subjected to heat treatment before eating.

The epidemiological examination of the diseased people made it possible to focus special attention on fresh apples, the use of which 2-10 days before the disease was noted by 90% of the diseased.

Moreover, the established fact of a high proportion of non-standard apples (with skin defects) deserves special attention. To form a hypothesis about the causes of the epidemic, the method of concomitant changes was used. For this, a comparative dynamics of the weekly sale of non-standard apples in the city and the incidence of pseudotuberculosis was carried out.

The two curves presented in Figs. 5.13 are absolutely synchronous. The strength of the association between putative cause and incidence was determined using correlation analysis ($r=+0.9$).

In this case, the hypothesis about the cause of the epidemic has passed the statistical test and can be considered an epidemiological diagnosis. The withdrawal of apples from the market led to the end of the epidemic, which is a brilliant confirmation of the correctness of the epidemiological diagnosis.

However, the epidemiological diagnosis made only with the help of these methods is not always perfect and requires further verification. By analogy, the diagnosis made by the attending physician also quite often requires verification (with the help of additional laboratory and instrumental studies, according to the effect of the prescribed treatment, etc.).

The specialist epidemiologist is also forced to verify the epidemiological diagnosis, either by the effect of prescribed interventions or by other analytical techniques, such as cohort studies and case-control studies. These techniques are more often carried out by scientific teams, which are joined by institutions of practical health care.

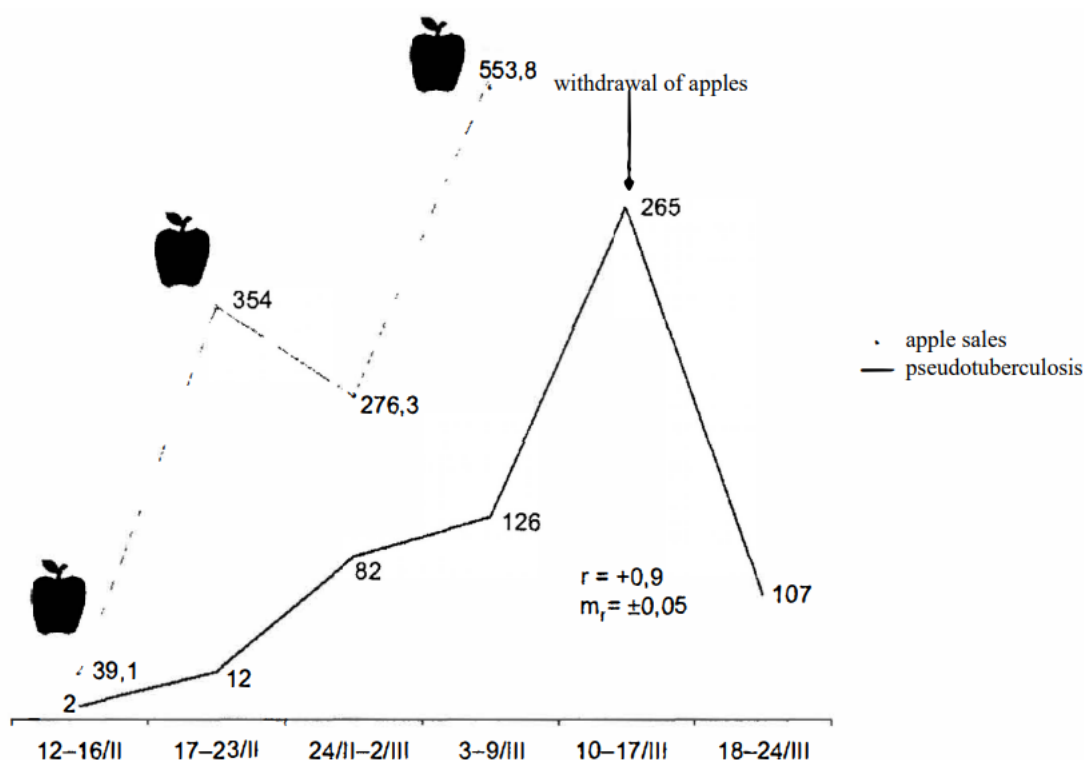


Fig. 5.13. Comparative dynamics of weekly sales of apples (kg/100 thousand population) and weekly incidence of pseudotuberculosis (by date of illness)

5. 3. 3. Cohort studies

In a cohort study, two or more groups (cohorts) of people are selected from a population who initially do not have the disease (outcome) under study. The groups differ from each other in that one group of people is affected by the studied risk factor, and the other is not. After that, they are compared with each other in terms of whether they have a given outcome. In this way, it is possible to understand how the studied risk factor is associated with subsequent outcomes (diseases).

A schematic diagram of a cohort study is shown in fig. 5.14.

It should be noted that the term “prospective study” found in the literature cannot be used as a synonym for a cohort study, although this is sometimes encountered. A prospective study is called when data collection is ongoing and ongoing until analysis is carried out. Indeed, the classical cohort study involves the prospective observation of cohorts formed in the original population of exposed (i.e., exposed to the factor under study) and unexposed for a certain time, sufficient for the subjects of the study to develop the disease under study (see diagram at the top). Fig. 5.14). In other words, exposed and unexposed subjects are included in the study (either randomly or depending on the presence or absence of exposure to a factor before an outcome occurs).

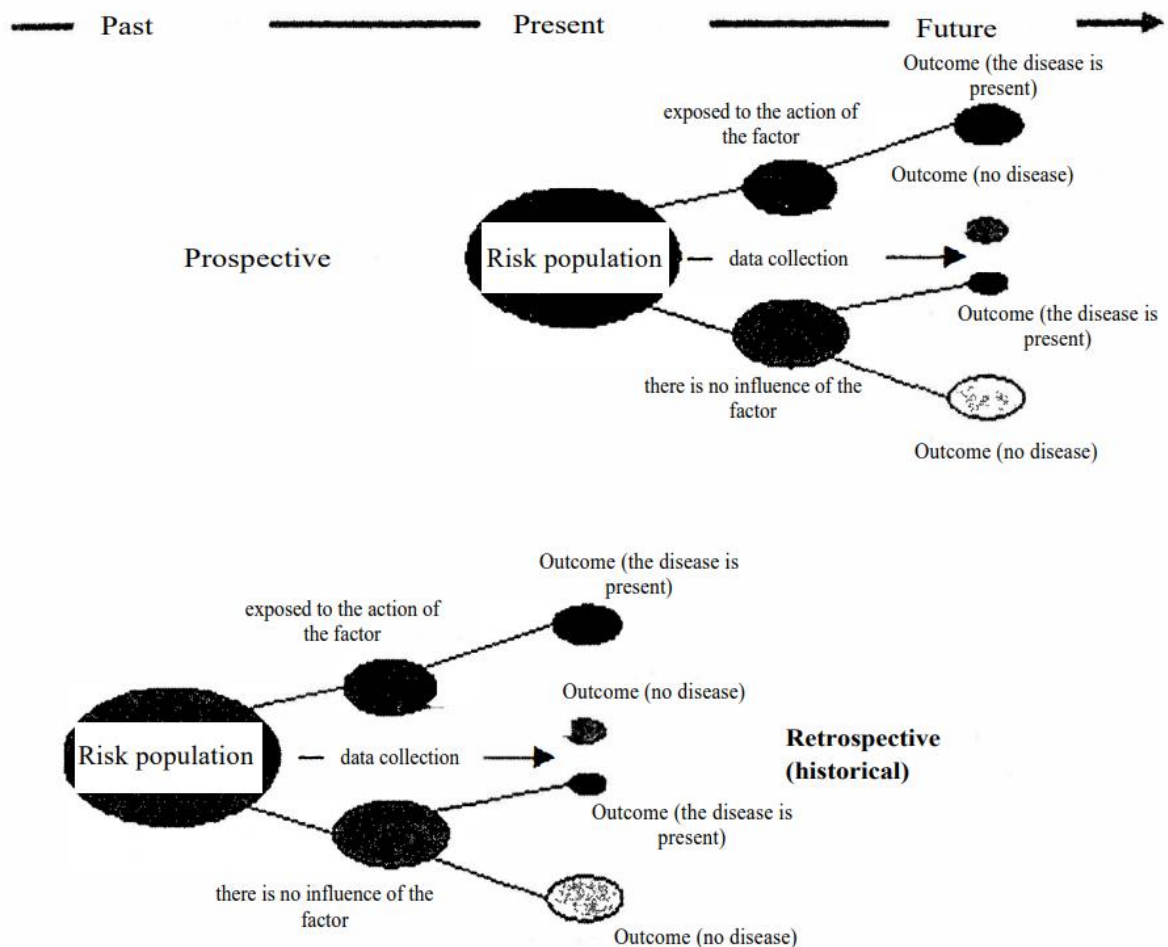


Fig. 5.14. Design of a cohort study

However, there is another possibility: the population where cases of the disease of interest have already occurred can be similarly divided into cohorts that differ in the presence or absence of exposure to the risk factor under study in the past, and the distribution of the studied outcomes in the cohorts can be compared (if appropriate information on the impact is available). In other words, study subjects are selected after the outcome occurs. Such a cohort study is called a retrospective (historical), i.e. a study is called retrospective when the analyzed data refers to the past.

Cohort research has a number of obvious advantages. First of all, the obvious simplicity of the question is attractive, which determines the purpose of the study: do people get sick if they are exposed to a certain factor? In doing so, you can determine in advance what data is needed, and collect this data accurately and completely. A cohort study also allows for the assessment of a wide range of single-factor outcomes, as well as a wide range of factors for a single outcome.

However, a cohort study can be inefficient and expensive if the outcome under study is rare and many subjects must be included in whom the outcome under study is never found.

In addition, the outcome may be far behind in time, so participants may be lost, and study results may not be available for a long period. The latter is less of a problem in historical cohort studies, but in this case, the quality of the data may be poor: a condition for a retrospective cohort study is the availability of reliable and sufficiently detailed information on the impact of risk factors.

5.3.4. Case-control study

When designing a case-control study, individuals are selected from the population based on whether or not they have the disease under study (any other outcome under study).

The structure of the study implies the presence of two observation groups (Fig. 5.15):

The experimental group (cases) includes individuals who have a given disease (or other studied outcome).

The control group (comparison group) includes individuals who do not have this disease (or any outcome).

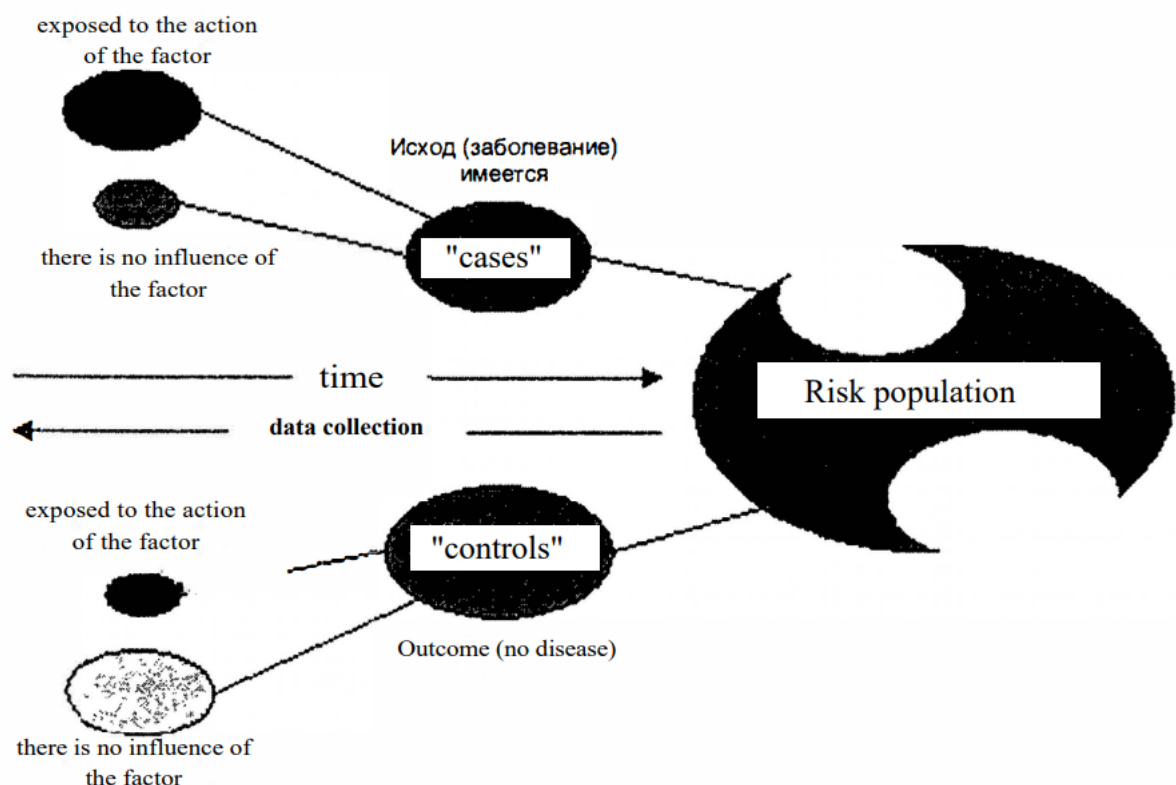


Fig. 5.15. Design of the study "case-control"

The experimental and control groups are then divided into two subgroups: "exposed" and "unexposed" to the studied risk factor.

When forming a case group, strict, objective criteria for outcome must be applied. Uniformity of the outcome should be assured, since similar diseases or outcomes

may have different risk factors, for example: not all diseases of intestinal infections, detected in the study population only by the presence of diarrheal syndrome, can be selected for study.

The aim should be to use "incident" (newly diagnosed) cases rather than "prevailing" (already existing at a given time) cases whenever possible. When using "prevalent" cases, the effect of the disease itself on potential risk factors can lead to difficulties in interpreting the data. For example, in a study evaluating the effect of coffee consumption on the risk of peptic ulcer disease, "prevailing" cases (long-standing ulcers and avoiding coffee drinking) will differ in relation to exposure from "incident" cases, whose onset of the disease is relatively recent and who still did not have time to change their attitude to the use of this drink.

The most important and responsible moment of this study is the selection of the control group. Ideally, individuals in the control group should differ from those in the experimental group only in that they do not have the disease under study, which is unlikely to be achievable. The selection of the control group in view of what has been said is the most difficult part of the planned study.

There are several general rules for the formation of a control group.

- ◆ It is advisable to form a control group from the same initial population as the cases. In other words, "controls" should represent a population of individuals who could be identified and included in the study as cases if they also developed the disease. Often the choice is obvious: when an outbreak occurs in a kindergarten, it is advisable to select children attending the same kindergarten as a control group. However, if, for example, all cases of a particular disease are selected in a hospital, the "controls" should represent those people who, if they had developed the disease under study, would have been admitted to the same hospital.
- ◆ The control group should be selected from the population at the same time as the test group is selected.
- ◆ Both cases and 'controls' should be selected independently of the exposure to be studied.
- ◆ The selection criteria for the control group should be the same as for the experimental group. Exceptions or limitations made in identifying cases should equally apply to "controls"
- ◆ In quantitative terms, 1-4 (preferably 2-4) "controls" per 1 case should be selected: a further increase in the control group has little effect on the statistical power of the study. If the entire population of those who are suitable for controls is known, and its number significantly exceeds the indicated ratio, a random sample should be taken. To improve the quality of the study, you can select several control groups, selected in different ways, and evaluate the comparability of the results.

It is generally accepted that case-control studies are less reliable than cohort studies. This is not entirely fair: a well-designed case-control study in some situations can give much more reliable results than a cohort study. Moreover, the case-control study has a number of clear advantages. First of all, this scoping design is excellent for rare diseases (in a cohort study, the population under study can be prohibitive in this situation). The case-control study provides a quick response and is therefore the method of choice in outbreak investigation. In a case-control study, many factors can be examined simultaneously (and quickly) to study a single outcome. However, only one outcome can be studied.

Problems that arise when conducting case-control studies are related to the fact that the data of interest on the impact of a factor may not be available or inaccurate. Sometimes it is simply not possible to select a sufficient number of controls that satisfy the requirements formulated above.

The choice of an analytical study scheme depends, first of all, on specific tasks, but is largely determined by the resources available for it and the timing. Knowledge of the possibilities of various approaches, their advantages and disadvantages allows the epidemiologist to optimally plan the study.

5. 3. 5. Basic statistical techniques for analyzing cohort and case-control studies

The data of analytical studies are usually summarized in four-field (2X2) tables (Table 5.2).

Table 5.2

Principal form of a four-field table

	Outcome available	Outcome missing	
Exhibited	a	B	a+b
Not exhibited	c	D	c+d
	a+c	b+d	N = a+b+c+d

The data of complex studies, which involve the study of many factors and their gradations, generate a lot of 2x2 and 2xN tables, but they all have a similar form.

Sometimes, in order to emphasize the differences in the way data are organized in cohort and case-control studies, the tables are rotated by 90° from each other.

Table 5.3

Options for building a four-field table

Case-control study

Cohort study

	Exposure (+)	Exposure (-)		Outcome (+)
Outcome (-)				
Outcome	a	b	(+)	a
Impact (+)	c	d		D
Outcome (-)				

Impact measurement

Epidemiology is a quantitative science. This, in particular, means that its task is not just to establish the factors influencing the occurrence of diseases (and other conditions related to human health), but to measure the effect of their impact. Without this, it is not only impossible to judge the significance of various factors, their contribution to morbidity, but it is also impossible to draw conclusions about the presence of a causal relationship between the studied factors and outcomes. In order to discover a causal relationship, it is necessary to compare the probability of developing diseases among those who are affected by a certain factor, and the probability of developing diseases among those who are not affected by the studied factor. And in order to compare these probabilities (i.e., the risk of a disease with and without a factor), you need to measure them.

In a certain sense, a direct reflection of the risk of diseases, i.e. "realized" risk, are considered in the previous chapter indicators of the incidence rate (incidence, to a lesser extent prevalence). In cases where the incidence is calculated not for the entire population in which diseases may occur (risk populations), but for subpopulations that differ in the presence (absence) of the effect of the factor under study (for example, vaccinated and unvaccinated, etc.), these indicators often referred to as indicators of absolute risk.

The absolute risk (R) associated with any potential risk factor (Re) measures the probability of the studied outcome (illness, death, etc.) in individuals exposed to this factor ("exposed" to it). The absolute risk in the absence of exposure to this risk factor (Rne) reflects the probability of the studied outcome (illness, death, etc.) in persons not exposed to this factor (not "exposed" to it).

If we use the data of the 2 x 2 table, then the formulas for calculating the absolute risk will look like this:

	Outcome (+)	Outcome (-)	
Impact (+)	a	b	$Re = \frac{a}{a+b}$
Impact (-)	c	d	$Rne = \frac{c}{c+d}$

By measuring the risk of disease among those who are affected by the factor and among those who are not exposed to it, one can think of a comparison procedure. A “qualitative” comparison (“more-less”) allows one to make a judgment about the nature of the studied factor, more precisely, about the nature of its impact. It is clear that if the risk of disease in the group exposed to the factor F under study is higher than the probability of disease among those who are not exposed to this factor ($Re > Rne$), it can be assumed that the occurrence of factor F increases the risk of the outcome under study. If $Re < Rne$, this means that the factor under study appears to lead to a decrease in the probability of occurrence of the outcome under study. In situations where $Re = Rne$, it is hardly possible to judge any impact of this factor.

In order to make a quantitative comparison of absolute risks, two options are available: use the division (Re/Rne) or subtraction ($Re - Rne$) procedure.

The indicator resulting from the division is most often called the relative risk (risk ratio). In other words, the relative risk (RR)* is the ratio of absolute risks in the presence (Re) and absence (Rne) of the impact of the factor under study:

$$RR = \frac{Re}{Rne}$$

Using the data of the 2x2 table, the formula for calculating the relative risk can be represented as follows:

	Outcome(+)	Outcome(-)
Impact (+)	a	b
Impact (-)	c	d

$$RR = \frac{\frac{a}{a+b}}{\frac{c}{c+d}}$$

RR is easy to interpret. If the relative risk is >1 (i.e., $Re > Rne$), then, as noted above, the onset of the disease may be associated with the action of the factor under study. The greater the RR value, the greater the effect of the factor, the more important may be its etiological role. If $RR=1$ ($Re=Rne$), then the factor has no effect, and $RR < 1$ ($Re < Rne$) means the preventive effect of this factor. In essence, RR shows how many times the risk of disease for the exposed is greater (less) compared to the unexposed.

In almost all epidemiological studies, we study a limited population and then try to extrapolate the results to the entire population. In cases where we considered each group as a sample and would like to apply the results to larger groups of the population, it is necessary to calculate confidence intervals.

- From English Relative Risk (Risk ratio)

The Confidence Interval (CI) is the range of all possible values of an exact estimate, which, if the study is repeated an unlimited number of times, will contain a true

estimate with a probability of at least 95% (the so-called 95% confidence interval). In essence, the calculation of confidence intervals for RR is an attempt to combine ideas about the size of the impact of a factor and an estimate of the probability of randomness of observed differences in the incidence of persons exposed to the factor under study and free from it.

The RR confidence interval does not have to include exactly one. If the factor under study is indeed a risk factor, the lower limit of the confidence interval should be greater than 1. If the factor has a preventive effect, then the upper limit of CI should be less than 1. The narrower the confidence interval, the more reason to trust the data obtained. For example, RR=2.12 (1.69-2.66) is more credible than RR=2.12 (1.03-4.36).

Calculating the boundaries of confidence intervals manually is quite difficult. This is where computer programs (eg Epi Info 2002) come to the rescue.

Risk difference (RD) - the difference in absolute risks in the presence and absence of exposure to the studied factor, shows the absolute increase in incidence due to the action of the factor:

$$RD = Re - Rne = \frac{a}{a + b} - \frac{c}{c + d}$$

By itself, this indicator (sometimes called attributable risk, AR) is difficult to interpret, but it can be used to calculate other, more informative indicators. One of these indicators is the attributive fraction (etiological fraction, etiological proportion) - the ratio of the risk difference to the absolute risk in exposed, expressed as a percentage. The attributable fraction (AF) is the proportion of all cases in those exposed that are due to this factor (of course, if the relationship found is actually causal).

5. 4. Sources of error in epidemiological studies and ways to eliminate them

There are two kinds of errors: systematic error and random error.

In addition, confounding factors can confound the results of epidemiological studies.

A systematic error (confusion) - occurs in epidemiological studies when results are obtained that systematically differ from the actual values.

Many types of bias have been described: selection bias, observation bias, and response bias.

To avoid bias, the population under study should be clearly defined. Case and control should be selected from the same population. Standardization of measurement tools

is needed. Useful is the use of multiple sources of information and multiple control groups, selected in different ways.

Random error is the discrepancy, due solely to chance, between the result of observing a sample and the actual value inherent in the entire population.

Interfering factors (confounders)

All diseases (like all biological phenomena) have multiple causality. An interfering factor (confounder) is a variable that distorts (“confuses”) the assessment of the impact on the disease due to the fact that it simultaneously has a causal relationship with the disease in question and a statistical relationship with the factor. This phenomenon is called confounding or mixing. Strictly speaking, confounding is not in itself an error in epidemiological research: it is a true phenomenon that can and should be described, understood and taken into account in the course and analysis of the study. The conclusions of a study in which “interfering” factors are not taken into account may be erroneous.

One way to control the available factors is stratification analysis. It is based on the principle of identifying strata (subgroups) that are homogeneous in terms of available variables. Comparison of exposed and unexposed (in a cohort study) or sick and healthy (in a case-control study) is performed within each stratum, after which data related to individual strata are combined and based on them an overall estimate of the effect of this factor is obtained.

Let us consider, as an example, the results of assessing the risk of death of patients in the neonatal intensive care unit due to the occurrence of nosocomial infections in them (according to Hemming V. G. et al.). Judging by the data in Table. 5.4, HBI infection significantly affects the risk of death of newborns in the intensive care unit.

Table 5.4

	Died	Survived	
contracted nosocomial infection a	46	92	RR=2.43 (1,80-3,26)

did not contract a nosocomial infection	104	653	
---	-----	-----	--

However, infection with nosocomial infections is far from the only factor that increases the risk of death in patients in the neonatal intensive care unit.

Another factor, for example, the immaturity of the fetus at birth, which obviously not only increases the risk of death of newborns, but also affects the risk of nosocomial infections. It cannot be ruled out that nosocomial infection is not really a significant risk factor, and data on its effect are associated with the immaturity of children (measured as birth weight), while nosocomial infection acts as a concomitant factor.

In order to understand whether nosocomial infection affects the risk of death of children in itself, and if so, to what extent, one can resort to the procedure of stratification analysis. To do this, the population of newborns should be divided into strata by body weight, within which the differences in this factor will be minimal and will not hinder the assessment of the significance of HAI infection for the death of newborns. The results of the analysis are given in table. 5.5.

Table 5.5

Body weight (g)	Nosocomial infection	Died	Survived	RR (95% CI)
Less than 1000	got infected	12	13	1,44(0,74-2,76)
	not infected	10	20	
1000-1499	got infected	12	30	1,27(0,70-2,31)
	not infected	24	83	
1500-1999	got infected	7	11	3,07(1,49-6,32)
	not infected	18	124	
2000 и более	got infected	15	38	2,60(1,58-4,29)
	not infected			
Overall risk score based on body weight				1,88(1,40-2,54)

It is clearly seen that within each stratum (i.e., practically regardless of body weight), HAI infection does affect the risk of neonatal death. At the same time, the total risk assessment* of death due to HI infection, taking into account differences in body weight (RR=1.88), turned out to be less than the "rough" risk assessment (RR=2.43). This means that the statement about the relationship between the risk of infection with nosocomial infections and the body weight of newborns is not without meaning.

As already noted, stratification analysis is a simple and reliable way to analyze confounding factors. Its only drawback is the reduction in the sample sizes corresponding to the selected strata. Therefore, to simultaneously analyze the impact of many factors, taking into account their interaction, various methods of statistical modeling are used, the most common of which is the method of multiple logistic regression.

Ways to control interfering factors

It is possible (and necessary) to control the interfering effect both at the stage of planning and organizing epidemiological studies (randomization, restriction, and selection are used for this) and at the stage of data analysis (stratification).

- The corresponding computational procedure is not discussed in this book.

Randomization - the distribution of the studied persons or phenomena into groups, carried out according to a random principle.

Restriction - limiting the composition of the studied groups only to individuals who have not been exposed to potential interfering factors.

Selection of controls - The idea is to select controls for each case so that they do not differ in any of the suspected confounding factors, thereby eliminating the need for stratification by multiple factors. There are many ways of selection - the simplest is pairwise selection (1:1). When fitting, differences are compared not between all cases and controls, but within each pair.

Questions for chapter 5

1. Method of epidemiological analysis
2. Stages of epidemiological analysis
3. Collection of epidemiological data
4. Descriptive stage,
5. Analytical stage.
6. IntensityДинамика
7. Spatial characteristic
8. Description of the structure of morbidity and identification of risk groups
9. Formation of hypotheses about possible risk factors
10. Logical techniques by which hypotheses are formed:
11. Acceptance of difference;
12. Reception of similarity;
13. Acceptance of accompanying changes;
14. Taking the analogy
15. Acceptance of residues
16. Analytical research techniques

- 17.Receptions of formal logic.
- 18.Statistical techniques (estimation of the correlation coefficient, coefficient
- 19.regression, relative risk, predominance ratio, etc.).
- 20.cohort studies.
- 21.Case-control studies

Chapter 6

EXPERIMENTAL RESEARCH TECHNIQUES

Experimental methods of research include controlled, uncontrolled, natural epidemiological experiment and modeling of the epidemic process.

The purpose of experimental methods of research is to prove hypotheses, to quantify the effectiveness of means and methods of prevention.

Experimental epidemiological studies imply, as a rule, artificial interference in the natural course of events (“manipulation” of events) related to human health and factors affecting it.

A controlled experiment is a prospective study in which the researcher actively introduces (or has the ability to control) one or more factors of immediate interest, while other factors remain unchanged or are controlled. Most often, the studied factors are measures aimed at the treatment and / or prevention of diseases, so another term for this type of epidemiological research is **epidemiological testing**.

Epidemiological testing is needed to study the effects of interventions to reduce the risk of disease. These activities are often referred to as interventions in this context. A wide variety of interventions can be evaluated: the use of new drugs/treatments, new medical technologies, new prevention methods, new screening/diagnosis programs, new methods of organizing care, etc.

At the same time, the studied outcomes (events / phenomena that are present / absent after the intervention) can be not only illness / recovery or death / survival, but also individual clinical (laboratory) tests, subjective signs (survey data). Sometimes outcomes such as “treatment/prevention failure” etc. may appear as dependent variables.

When evaluating the effectiveness of a set of measures (control programs), often not only the immediate result (reduction or prevention of morbidity) is studied, but also related events, for example: the introduction of an effective program for the control of nosocomial infections in a hospital leads not only to a decrease in the incidence of infections, but also changes the behavior of staff, leads to a reassessment of priorities, a change in the organization of the diagnostic and treatment process, the level of professional training, etc. These outcomes, although they are more difficult to measure, are also very important.

Subjects of epidemiological tests can be patients (patients), healthy volunteers, relatives of patients, large population groups, etc.

Epidemiological trials are sometimes classified according to the population being studied and the nature of the intervention. If the study population consists of patients, i.e. people who already have a certain disease, and the main goal is to evaluate the effectiveness of new drugs (treatments), such a **study is called a clinical trial**. When the subjects of the study are persons free from the disease and the intervention is aimed at its prevention, such **studies are called field trials**. This classification is not generally accepted, since there are no fundamental differences between these two types of research from a methodological point of view.

As already noted, epidemiological trials should be controlled, i.e. organized in such a way as to minimize the impact of errors, as well as take into account a possible

confounding factor. This can be achieved by using the already mentioned methods of forming comparison groups (selection, restriction, etc.), and the most effective of them is, of course, randomization. Epidemiological trials are usually organized as randomized cohort studies. The most common term for such a study is a **randomized controlled trial (RCT)**.

Randomization is the distribution of study participants into groups so that each of them has a known and equal chance of being in one of the groups. Randomization eliminates selection bias in prescribing an intervention, provides the possibility of masking ("blinding") participants and researchers, and makes it possible to use probability theory in the statistical evaluation of differences in outcomes between groups. The main elements of randomization are the generation of an unpredictable sequence of inclusion of trial participants and the concealment of this sequence, primarily from researchers involving participants in RCTs. The most effective way of randomization is the generation of random numbers using appropriate computer programs. There are various, often quite complex, methods of randomization: it is enough to list some of its types to understand that there is simply no room in the textbook for a detailed presentation of all aspects of conducting RCTs (simple randomization, block / restrictive randomization, stratified randomization, weighted randomization, cluster randomization, etc.).

RCTs also differ greatly in the way they are organized (parallel RCTs, cross-sectional RCTs, RCTs with factorial design, etc.). The possible number of RCT participants also varies: the number of participants can be variable or fixed. So-called multicenter RCTs have certain advantages (higher reliability of results), when studies using the same protocol are carried out at several medical centers at once.

An important element of the RCT protocol is the "blinding" of participants. It is possible to conduct "double-blind" (when neither patients nor the doctors studying their condition know who is receiving the intervention under test) and even "triple-blind" (data analysis is carried out "blindly") RCTs.

Randomized clinical trials are placebo controlled. However, this is not always technically possible (for example, when evaluating the effectiveness of new surgical interventions), and sometimes it is impossible for ethical reasons (in these cases, the comparison group receives a different intervention and different types of intervention are compared).

The following indicators are used to quantify the results of RCTs: absolute and relative risk, risk difference, attributive fraction, etc.

Data from individual RCTs are often conflicting. There can be many reasons, but along with possible methodological defects, very often this problem is associated with insufficient statistical power of each individual study. One way to solve this

problem is to create systematic reviews and their quantitative variety - meta-analysis.

An uncontrolled experiment is widely used in practice to evaluate the effectiveness of activities. These studies are based on the principle: "we will conduct an event and see what happens."

Undoubtedly, they have a certain diagnostic value, but are highly prone to errors. For example, a decrease in the incidence after the use of a new vaccine may be due not to the effect of immunization, but to a natural decrease, reflecting, for example, the nature of the long-term dynamics of the epidemic process.

A natural experiment is usually understood as a situation in which an increase (cessation) in the incidence occurs under the influence of natural factors or factors that are a side effect of human activity, i.e., do not depend on the will of the researcher (accident at a nuclear power plant, destructive earthquake, dumping of toxic waste into body of water, careless use of a new drug, etc.). Such a situation may provide unique data that is hardly possible to obtain in a specially designed study.

Of course, the study of the data of a natural "experiment" can lead to valuable conclusions.

Modeling of the epidemic process. The use of a model experiment opens up great cognitive opportunities for epidemiology. The modeling method is widely used by all sciences. In epidemiology, it has also become quite widespread.

Another Topley in 1942. pointed out that one of the ways to solve a big problem in epidemiology is the way: "to look at the facts as they are." For over 25 years in the field of experimental epidemiology, series of observations on mice have been performed that are classic. One of the most valuable contributions was the observation of the nature of the epizootic process among a mixed population of mice, consisting of sensitive and resistant animals. The experiment was accompanied by all sorts of changes (adding sensitive mice to the infected herd, adding genetically resistant mice, etc.).

Despite frequent warnings that the results of studies in mice cannot be transferred to humans, Topley pointed out that the situation in military collectives resembles some experiments on mouse populations.

The essence of modeling the epidemic process of any infection is to build a model of the process and study it, and then transfer the results obtained to the natural process.

In the modern period, a mathematical model is used, modeling the epidemic process of intestinal infections using the strain of *Escherichia coli* M-17, modeling the

epidemic process of intestinal and various hospital infections using bacteriophages. Mathematical modeling can be used only for those infections that are theoretically well studied and have a mass distribution. A mathematical model of influenza, HIV infection and some others has been developed.

In our country, a methodology for constructing an operating model of the epidemic process of bacillary dysentery has been developed in detail. The principle of modeling is that persons who take orally a completely harmless physiological drug - colibacterin, excrete a strain of *Escherichia coli* M-17 with intestinal contents. This strain was obtained under laboratory conditions and, therefore, is rarely found in the intestinal contents of the population and in a free form in the external environment. This circumstance makes the strain labeled. The drug colibacterin is a lyophilized suspension of *Escherichia coli* strain M-17. This strain has the ability to multiply rapidly and displace other microorganisms from the intestine, which is its preventive effect, contributing to the normalization of the intestinal microflora. The detection of this strain is easily possible on all elements of the external environment where this microbe-marker enters.

The advantage of the modeling method lies in the fact that it is possible to accurately trace the sources and routes of transmission of pathogens of intestinal infections operating under given conditions. Everything remains as in a natural epidemic process.

The use of such methods of experimental modeling creates favorable opportunities for further study of the epidemiology of various infections.

Questions for chapter 6

1. Experimental methods of research
2. Purpose of experimental methods of research
3. A controlled experiment is
4. Epidemiological tests.
5. Clinical trial
6. Field test
7. Randomized controlled trial (RCT).
8. Uncontrolled experiment
9. Natural experiment
10. Modeling the epidemic process

Chapter 7

USE OF TECHNIQUES

EPIDEMIOLOGICAL DIAGNOSIS

IN EVIDENCE-BASED MEDICINE

In the last decade, the role of such a **direction in healthcare** as evidence-based medicine (EBM) has significantly increased. Despite the fact that the need for EBM

was recognized many years ago, this direction has received real development only recently.

The term "evidence-based medicine" (evidence-based medicine; the English definition sounds like evidence-based medicine) was first proposed in 1990 by a group of Canadian scientists from McMaster University in Toronto.

Evidence-based medicine is based on clinical epidemiology, which is a branch of medicine that uses the epidemiological method to obtain medical information based only on strictly proven scientific facts, excluding the influence of systematic and random errors. The main postulate of **clinical epidemiology** - any decision in medical practice should be based on strictly proven scientific facts - formed the basis of evidence-based medicine.

The terms "evidence-based medicine" and "clinical epidemiology" quickly took root in the biomedical literature, but there was no clear definition of them. And at present there is no single definition of evidence-based medicine (clinical epidemiology), but several variants can be found in the literature. Here are some of them:

- ◆ EBM is the conscientious, accurate and meaningful use of the best results of clinical trials to guide treatment decisions for a particular patient.
- ◆ EBM is a branch of medicine that seeks, compares, summarizes, and widely disseminates the evidence obtained for use in the interests of patients.
- ◆ EBM is an approach to health care that collects, interprets, and integrates reliable, relevant, and applicable evidence from special studies that take into account clinicians' observations and patient complaints.
- ◆ EBM is a method (variant) of medical practice, when the doctor uses in the management of the patient only those methods, the usefulness of which has been proven in benign studies.

It soon became clear that the principles of evidence-based medicine are applicable not only to clinical practice, but also to any field of medical science, including the general problems of organizing an optimal healthcare system.

There are several reasons why evidence-based medicine is needed. One of them is the increase in the volume of available information (new drugs, methods of treatment, diagnostics, prevention, etc.), which, for practical use, must not only be analyzed, but also summarized and critically evaluated.

Another reason is economic. The soundness of financial spending depends on how convincing the scientific evidence is regarding medical and cost-effectiveness. It is quite natural that the most rational solution would be to direct these resources to the development of methods of prevention, diagnosis and treatment, the practical

benefits of which are confirmed by studies that meet the criteria of evidence-based medical practice.

The main principle of evidence-based medicine is that every decision in medicine must be based on strictly proven scientific facts.

The main goal of introducing DM principles into healthcare practice is to optimize the quality of medical care in terms of safety, efficiency, cost and other significant factors.

The principles of DM allow the development of the most effective, safe and economical modern therapeutic and preventive strategies that can be implemented at the state, regional, population and individual levels, contributing to the choice of the best option in each case.

The implementation of the principles of DM in medical practice involves the implementation of several stages:

- 1) the formulation of a clear question to which an answer must be found;
- 2) searching the literature for the best evidence to answer the question (for example, searching for relevant biomedical articles);
- 3) a critical assessment of the evidence found in terms of their validity, reliability and applicability;
- 4) implementation of the obtained results in medical practice;
- 5) assessment of the effectiveness of implementation.

Formulation of a question and search for an answer

The search for a solution to any medical problem begins with a question. The ability to break down a question into its component parts greatly helps in finding an answer and is one of the fundamental skills necessary to comply with the principles of DM. For the most part, each of the questions that doctors usually face can be divided into several components (Gordon Guyatt, 2002):

- ◆ The main characteristics of the patient population in relation to which it is necessary to solve a certain clinical (medical) problem.
- ◆ The type of intervention/exposure occurring in the patient population. These can be medical interventions (diagnostic procedure, use of medications, surgery, preventive measures, etc.), the effectiveness of which is evaluated in clinical trials; or exposure to certain harmful factors leading to adverse outcomes.
- ◆ An outcome that can be observed in a population as a result of the intervention/exposure.

♦ Type of clinical trials (method of their organization) conducted by various researchers, the materials of which will become the object of a search in the literature and provide the most complete and reliable answer to the question posed.

There are several types of questions that often arise in the course of medical practice and determine the way in which research is organized, the results of which will help to find an answer to them. These questions concern the following aspects:

- **Treatment.** In this case, the clinical question is devoted to assessing the effectiveness of therapeutic / preventive intervention, and the treatment outcomes of interest will be recovery, improvement in the condition of patients, reduction in the risk of complications, and prevention of the development of diseases. In other words, in this case, the doctor is faced with the question of whether this or that method of treatment, this or that medication is effective in relation to a particular disease, whether certain preventive measures really lead to the prevention of diseases or the development of complications.

- **Risk assessment.** The question is devoted to assessing the possible negative impact of factors (including medical interventions) on the condition of patients, morbidity and mortality. Similar questions concern such an aspect as the ability of certain factors, under the influence of which a certain population of people is, to influence the development of diseases.

- **Diagnostics.** In this case, the issue concerns assessing the quality of a diagnostic test in terms of the ability to accurately make a diagnosis with its help, i.e., to establish the presence or absence of the studied disease in patients.

In other words, we are talking about how accurate and informative this or that diagnostic method is for making or refuting a diagnosis.

- ♦ **Forecast.** The clinical question is devoted to assessing the further development of the disease in a patient (s) with this disease. Quite often, this question arises among doctors when they have to face a situation in which it is necessary to predict the further course of a disease or condition.

Depending on which of these questions needs to be answered, various scientific studies are conducted, the results of which are published in printed or electronic biomedical publications. A medical worker who strives to follow the principles of evidence-based medicine in the course of his work should be able to determine which of the studies conducted will solve the problem he is facing and, accordingly, be able to search and find evidence-based information in the literature that contains the answer to his question.

To answer the question regarding the effectiveness of a **curative/preventive intervention**, the literature is searched for experimental studies conducted in the form of randomized controlled trials (RCTs), in which the distribution of

participants into groups is carried out randomly. In RCTs, after the formation of the main (which is affected by the intervention under study) and control groups (without the intervention under study or with another intervention), patients are continuously monitored to identify predetermined clinical outcomes (recovery, improvement, prevention of the development of the disease, etc.).).

It should be noted that there are situations when there is no need to search for publications with the results of RCTs to answer some clinical questions related to the evaluation of the effectiveness of therapeutic measures. Moreover, to evaluate the effectiveness of medical interventions, such studies are not always required. For example, it would hardly occur to anyone to evaluate in RCTs whether appendectomy is effective or not in acute appendicitis.

Ideally, the question of potential risk factors leading to various adverse outcomes in the population of people exposed to them would have to be answered in the same RCTs. However, such studies to assess risk factors may not be possible or acceptable for ethical reasons. It is unlikely that anyone will voluntarily agree to participate in experimental studies, exposing themselves to prolonged exposure to a potentially unfavorable factor in order to assess the degree of its influence. In such cases, to answer the question of whether the studied risk factor can lead to adverse outcomes, it is necessary to look for data from analytical studies (case-control studies and cohort studies).

However, it should be noted that the results of such studies are less reliable than RCTs.

In analytic studies, participants exposed and not exposed to the risk factor under study are followed up over a period of time in order to identify specific clinical outcomes. An example of an analytical study would be to study the effect of a risk factor, such as smoking, on the likelihood of developing lung cancer.

The assessment of the accuracy and information content of a **particular diagnostic method** (diagnostic test) is carried out according to the type of cross-sectional (sectional) studies. First, a selection is made of patients suspected of suffering from the disease under study or having a certain condition. Examination of patients is first carried out using the diagnostic method under study, and then a generally accepted method for diagnosing a disease or condition (“Gold Standard” or reference method) is used to make a diagnosis. After that, the results of applying both methods are compared.

In the course of analytical studies devoted to the study of the **prognosis** - cohort studies, an assessment is made of the further course of the disease, as well as the identification of factors that may affect it. In such studies, at the first stage, participants belonging to a certain population are selected (for example, patients

with a certain disease or condition of a certain stage), then they are determined by the presence or absence of certain factors that can affect the further course of the process (for example, sex or age factor, bad habits, the presence of any concomitant diseases). These studies estimate the length of time that study participants are followed up to the clinical outcome under study.

Thus, one of the main tasks of a doctor who needs to solve a certain medical issue is to correctly determine the type of study, the materials of which may contain an answer to the question he is facing, as well as the ability to search the literature for relevant evidence-based (evidence-based) information.

Various printed publications (books, magazines and other periodicals), as well as electronic data sources, can serve as sources of information containing an answer to a question of interest to a doctor. In the modern period, it is the latter that are the most informative, since constantly updated computer databases make it possible to quickly search for the necessary evidentiary information. Main electronic databases:

- Medline
- Cochrane Library
- Ovid etc.

The number of medical publications is extremely large and continues to grow steadily. This indicates an increase in the number of clinical studies, which contributes to improving the quality of medical care, but at the same time makes it difficult to find the most reliable information. Compilation of **systematic reviews** (RS) provides a significant help in navigating the huge amount of biomedical information. When compiling the RS, the results of many similar studies devoted to one specific medical problem are searched, selected, critically evaluated and summarized. At the same time, in the preparation of RMs, in contrast to the preparation of conventional reviews, approaches are used that reduce the impact of systematic and random errors. Thus, the findings in CO are more reliable than those in disparate individual studies.

The highest quality RMs are produced by the international Cochrane Collaboration community. These reviews, collected in the Cochrane eLibrary, are now available on the Internet and on CD.

To combine and generalize the results of many studies on the same topic, special statistical methods are used to generate a quantitative systematic review, called a **meta-analysis**.

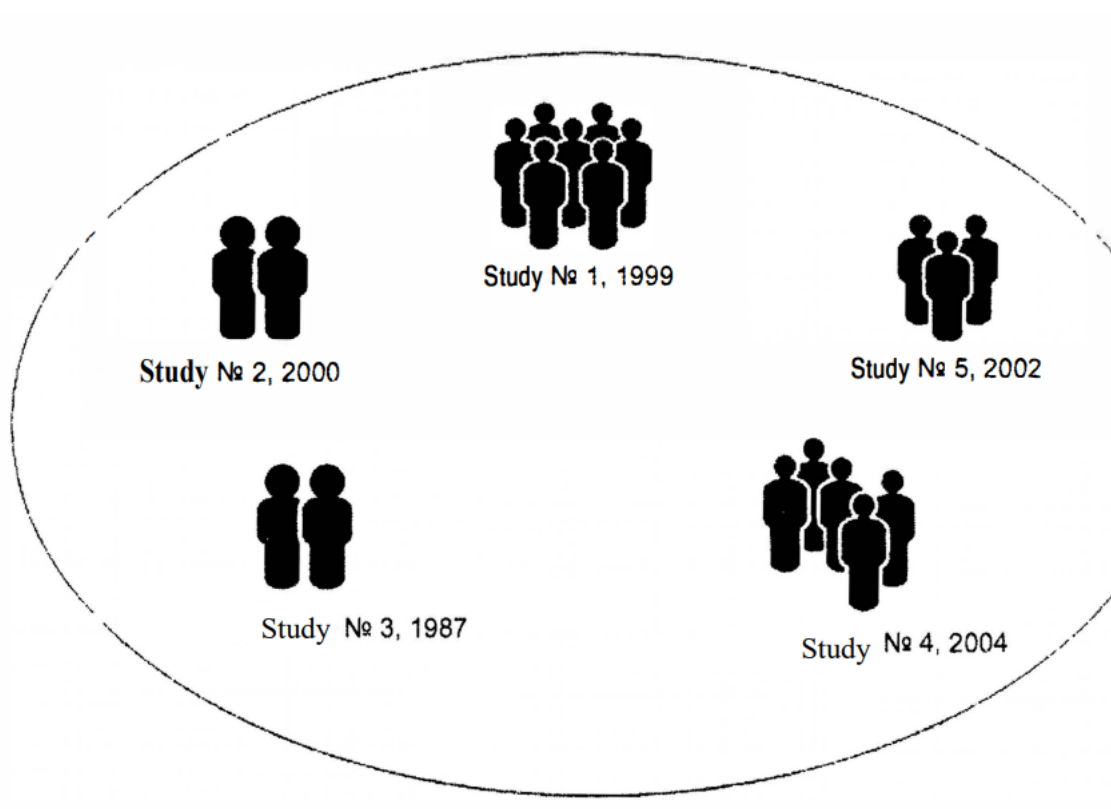
Meta-analysis (literally - analysis of analyzes, synthesis of information) - a review in which, using a quantitative method of evaluation, data from several studies

(mainly RCTs) on the same problem are summarized, and the final result is presented in the form of one generalized indicator.

Often there is a situation where the results of individual studies are uncertain, in particular due to small patient populations or infrequent outcomes. The way out of such situations (especially in the latter case, when it is necessary to overcome the “weakness” of small studies) is to combine data from several disparate but similar clinical studies on the same issue, and form, as it were, one large study (Pic. 7.1).

This meta-analysis approach provides more statistical power than any single study by increasing the sample size.

Meta-analysis is intended to improve the reliability of estimates of concurrent results. Combining data from multiple studies effectively creates one large study with higher statistical power. Increasing the amount of data reduces the likelihood of systematic and random errors, resulting in increased data reliability and greater reliability of decision making. However, it must be taken into account that it is unacceptable to use meta-analysis to combine the results of observational studies.



Pic. 7.1. Combining the results of several disparate studies in a meta-analysis

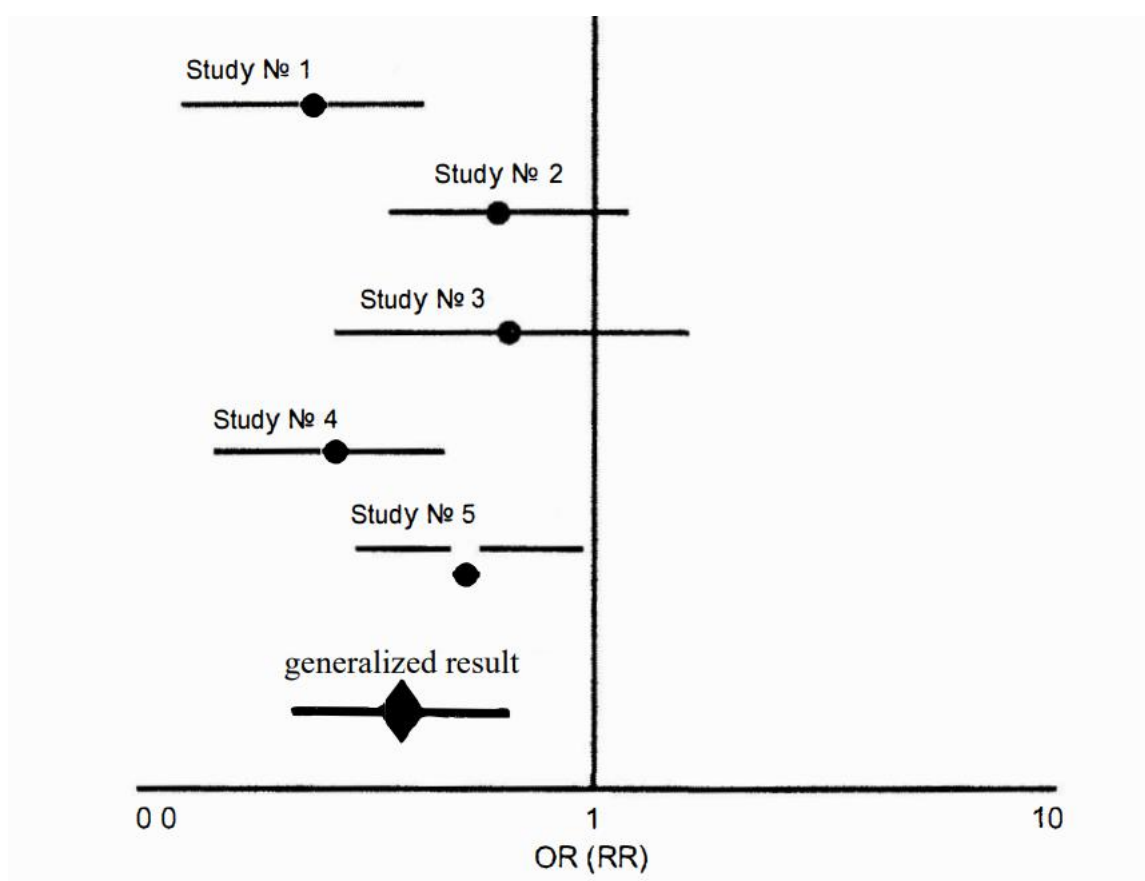
There are several basic steps in compiling a meta-analysis.

The first stage consists in identifying and selecting the most reliable studies from all available articles on this issue in terms of the quality of their conduct and the reliability of the results.

At the second stage, each article is assessed for compliance with predetermined criteria, indicating either a general quality indicator or individual qualitative characteristics of studies.

The third step is to combine the quantitative results of the selected studies. This forms, as it were, one large study with a higher statistical power than each individual study. Each of the studies included in this review is “weighted” by sample size, i.e. a study with a larger patient population receives a larger share than one with fewer patients. the quality of research should also be taken into account.

Subsequently, using statistical methods, a generalized result is determined, for example, a combined assessment regarding risk or odds ratio. The result of the meta-analysis is presented in the form of a graph, which shows both the results of individual studies and a generalized indicator - point indicators of odds ratios OR or relative risk RR with confidence intervals (CI) (Fig. 7.2).



Pic. 7.2. Meta-analysis results presentation (MetaView)

There is a specially developed MetaView program that allows you to visually demonstrate the results of a meta-analysis. The program, using a logarithmic scale of 0.0-1-10, is used to present the results in the form of one generalized graph, which indicates the point indicators OR or RR with CI for each individual study and the generalized indicator with CI.

The results of this hypothetical meta-analysis, presented in Figs. 7.2, testify in favor of the fact that the studied method of intervention has a pronounced positive effect: the generalized indicator OR (or RR), taking into account confidence intervals, is on the left side of the graph, i.e. <1 .

At the same time, if the CI of point indicators OR (or RR) of all disparate studies overlap each other (as in our case), the so-called homogeneity is noted, which is evidence of the homogeneity of the results of these studies. When the CIs of not all individual studies overlap, one speaks of heterogeneity, indicating a less reliable pooled estimate.

Proponents of combining data into a single meta-analysis argue that this method allows you to see the strengths and weaknesses of all included studies. On one graph, you can present the number of studies, point estimates of effectiveness with CI for each of them, as well as a generalized point estimate with CI.

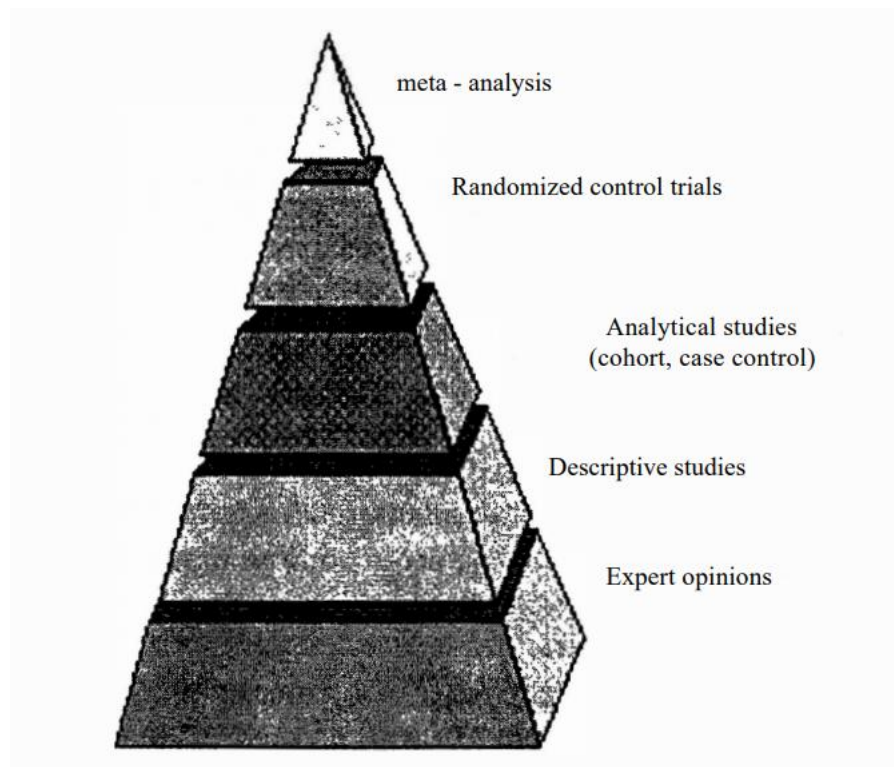
Literature on meta-analysis of clinical trials is available in print publications (biomedical journals, collections, etc.), as well as electronic sources of information: electronic databases on CD-ROM (for example, Cochrane Library), databases on the Internet (MedLine , Ovid, etc.).

Assessment of the validity of research results

An important aspect of evidence-based medicine is to determine the degree of validity of the information received.

The reliability of the data obtained in the course of different studies is different. As mentioned above, the results obtained from well-organized RCTs have the highest reliability, while analytical ones are less reliable.

On =Pic. 7.3 presents the so-called "pyramid of evidence" reflecting the hierarchy of the evidence of the results obtained in various studies.



Pic. 7.3. Pyramid of Evidence

The "gold standard" is considered to be randomized controlled trials, referring to experimental studies capable of showing what is true in science. And the more carefully they are set, the higher the likelihood that their results are due to a real-life connection between phenomena, and not an artifact or a random coincidence.

Other studies that provide evidence-based information are analytical (cohort and case-control studies). More reliable results can be obtained using cohort epidemiological studies. Case-control studies are much easier to perform, but often less reliable.

Descriptive studies rank even lower. A critical approach in assessing the reliability of the information received implies the answer to three main questions:

- Are the results of the study justified? (validity)
- What are these results? (reliability/validity)
- Will the local results help? (applicability)

The validity of the results (validity) means the following:

- Are the conclusions supported by the description of the methodology and the results obtained?
- How sound is the methodology, are the proposals made by the authors acceptable, are there any interfering factors that could not be taken into account?
- If a sample was used, was it selected to avoid bias/bias?

To answer the question of whether the results of the study are reliable / reliable, it is necessary to find out the following:

- What are the results described in the research article?
- How large is the demonstrated effect to be significant?
- How confident we are that the results are within reasonable expectations and are not purely coincidental!

And finally, it is necessary to establish whether the results of this study can be applied in medical practice (applicability). To do this, you need to define:

- Are the problems the clinician is dealing with similar enough to those described in the article to extrapolate the results?
- Can generalizations be made that allow the results to be used in the workplace of a particular clinician?

To establish the reliability of the results of various studies (analytical, experimental, meta-analysis), there are certain recommendations that can be found in the additional literature on evidence-based medicine.

Implementation of the obtained results into practice and evaluation of effectiveness

After formulating the question, searching for information and obtaining evidence, it is necessary to move on to its use in medical practice. Evidence obtained, i.e. the answer to a question posed by a doctor to solve a specific medical problem can be subsequently successfully introduced into practice. One of the most important elements of evidence-based medicine is the transformation of research results into high-quality and understandable clinical practice guidelines (CPR), developed taking into account all the requirements of evidence-based medicine, and which indicate the best ways to address medical issues.

Every day, doctors of both medical and preventive profiles make many decisions about the necessary diagnostic methods, methods and schemes for the treatment and prevention of diseases, and evaluate the prognosis for the development of diseases. Many of these decisions play a significant role and can change the course of diseases or affect the ability to prevent them. At the same time, the correctness of the decision, which is ensured by the possession of reliable, scientifically substantiated information, is extremely important. However, it must be emphasized that in order to make a decision in medical practice, evidence-based data alone on the effectiveness of a particular intervention method is not enough. In other words, evidence alone is not the only basis for a definitive decision on any medical issue. In addition to the available evidence. decision-making should always be based also

on an assessment of the benefits and risks of the intervention and, not least, the cost of the intervention.

Questions for chapter 7

1. Use of epidemiological diagnostic techniques in evidence-based medicine
2. Evidence-based medicine is
3. The main principle of evidence-based medicine
4. Implementation of the principles of evidence-based medicine in medical practice
5. Randomized controlled trials
6. Case-control studies
7. Cohort studies
8. Forecast - cohort studies
9. Compiling systematic reviews
10. Meta-analysis compilation steps

PART II

EPIDEMIOLOGY OF INFECTIOUS DISEASES.

Section 3

TEACHING ABOUT EPIDEMIC PRONESS.

Chapter 8

DEFINITION OF THE EPIDEMIC PROCESS.

The epidemic process, according to a very successful definition by L. V. Gorolshevsky, is a chain of interconnected infectious conditions

This external, often visible (with the development of pathology) event affects the circulation among people (in the population) of parasites, i.e., living agents whose evolutionary development has led to the fact that their life has become possible only at the expense of other species, including people count. These other living creatures

became for them a habitat in which the implementation, i.e., the possibility of using, genetically determined metabolic processes was ensured, providing nutrition, reproduction, and sometimes preservation (for example, encapsulation of *Trichinella* larvae in the host's muscles). Thus, parasites living inside or on the surfaces of other living beings are in an ecological relationship with the host organism. The peculiarity of these relationships lies in the fact that the host organ is a kind of autonomous system with sufficiently stable biological characteristics, fundamentally different from the surrounding external conditions.

The parasite in evolution turned out to be adapted to the host organism because, in comparison with the latter, it possessed (possesses) an incomparably faster process of reproduction. For example, in many species of bacteria, the doubling of the population occurs in a few tens of minutes. In the microworld, with such powerful rates of reproduction, the likelihood of formation of mutant forms is high, recombinant phenomena (exchange of genetic material) are possible, the ingress of genetic material from outside - all this with the selective influence of the host organism (the destruction of individuals insufficiently adapted to life in it led to the formation of parasitic species. As L. V. Gromashevsky rightly pointed out, the parasite turned out to be the winner in evolutionary development.

An ecological understanding of the phenomenon of parasitism was expressed as early as the 19th century, but it was gradually forgotten, the idea of a relationship that was called symbiosis triumphed, based not on the essence of the phenomenon of parasitism, but on its consequences (parasitism was identified only with an indispensable pathology). That is why parasitism was opposed to commensalism (lodging), in which the interacting parties (the agent living in the host organism and the host itself) do not have any detrimental effect on each other, and mutualism, when the parasitic agent brings some benefit to the host.

The ecological concept of parasitism began to revive again in the 1930s and 1940s. 20th century (E. N. Pavlovsky, A. A. Filippchenko, V. M. Zhdanov and others). However, it was most clearly formulated by V. A. Dogel (1947), who is rightfully considered the founder of ecological parasitology. According to his concept, the essence of parasitism is life in the host organism, which has been evolutionarily defined as a habitat. The specificity of the infectious process (influenza, dysentery, etc.) depends on the genetic characteristics of the parasite. However, the nature of the manifestation of parasitism (a disease of varying severity, carriage) is determined not only by the genetically determined characteristics of the parasite (the degree of pathogenicity or even harmlessness, or even some usefulness), but also by the state of the interacting parties (infective dose, virulence of the parasite, pronounced resistance, or, conversely, immunodeficiency in the host, etc.).

8.1. Characteristics of parasites

During the interaction of the parasite with the host organism, as already mentioned, both certain variable factors (for example, the infecting dose and virulence) and rather stable characteristics of the parasitic agent are important.

The value of the infectious dose can be judged from the data obtained in experiments on military volunteers who were infected with the causative agent of typhoid fever (Table 8.1)

Table 8.1

Dependence of the probability of occurrence of typhoid fever on the infectious dose of the virulent strain Quiaies (no R. B. Hornfck et al., 1970)

Infectious dose	Total number of volunteers	The number of sick abs. (%)
10^9	42	40 (95)
10^8	9	8 (89)
10^7	32	16 (50)
10^5	116	32 (28)
10^3	14	0

In the same experiments on volunteers, the significance of the virulence of the pathogen was shown (Table 8.2).

Table 8.2

Dependence of the nature of the infectious process of typhoid fever on the virulence of the pathogen (infectious dose 10^7 (according to R. B. Hornick et al., 1970)

Virulence pathogen	Total volunteers	got sick	rescheduled infection	Not infected
Strains with Vi antigen	47	24(51%)	19(40%)	4(9%)
Strains without Vi antigen	39	10(26%)	16(41%)	13(33%)

Notes: 1. In the group “Has had an infection”, there were volunteers who either experienced a slight, short-term fever, or immunological changes were detected, or

the pathogen was found in the blood, or the pathogen was excreted from the feces for more than 5 days. In all these cases, treatment is not required.

2. In the "Not infected" group, there were volunteers in whom no infectious process was registered clinically, serologically, or bacteriologically

3 In the groups "Sick" and "Not infected" after infection with virulent and without Vi-antigen strains, the indicators were significantly different ($p < 0.05$)

Parasites according to genetically determined pathogenicity can be simplified (roughly) divided into three groups:

■ ***pathogenic***

■ ***conditionally pathogenic***

■ ***non-pathogenic.***

Pathogenic should include those parasites that in the host organism, if this foreign agent turns on the metabolic processes leading to reproduction, necessarily cause disease.

The measles virus should be attributed to such parasites, it is not excluded that the variola virus. Apparently, this group is not very numerous. However, at present, many more different types of parasites are classified as pathogenic. This group includes those agents that, under normal conditions, not necessarily aggravated by any additional unfavorable circumstances, cause diseases, and with a fairly clear clinical characteristic (often laboratory confirmation is not necessary). Unfortunately, due to often stereotyped thinking, when infected with these parasites, the possibility of developing an infectious process without pathology is not allowed ("if you carefully examine, you can find signs of pathology"). Such parasites include, for example, pathogens of typhoid fever, cholera, rubella, etc.

Opportunistic pathogens include many microorganisms that are permanent inhabitants of the host organism or free-living, that is, in the latter case, those for which the host organism is not an obligatory habitat (see below). These agents can cause disease only under some aggravating circumstances, in particular under the following:

- infection with unusually large doses; the value of the dose for reproducing the infectious process, in particular the disease, has already been mentioned, but here we mean especially high infectious doses; for example, food poisoning (poisoning) occurs when the pathogen before infection had the opportunity to intensively multiply (accumulate) in the food product;
- increasing the virulence of the parasite; as a rule, this is observed with multiple passages and selection, which is most often realized under the influence of a macroorganism; an increase in virulence also occurs when additional genetic material enters from outside (for example, in bacteria - bacteriophage and plasmids);

- significant weakening of the protective functions of the host organism; this also applies to local protection (violation of the integrity of the skin and mucous membranes, as well as a decrease in the protective capabilities of the local lymphoid tissue), and general resistance (for example, after suffering a severe form of influenza that exhausts the patient, staphylococcal complications are often observed);
- unusual, i.e. not evolutionarily determined, methods of infection (unusual "entrance gates"), which lead to the penetration of the pathogen into tissues that do not have sufficient local protection resources (leading to the development of purulent pathology, the pathogen enters after injuries accompanied by damage skin, subcutaneous tissue, joints, bones, etc.).

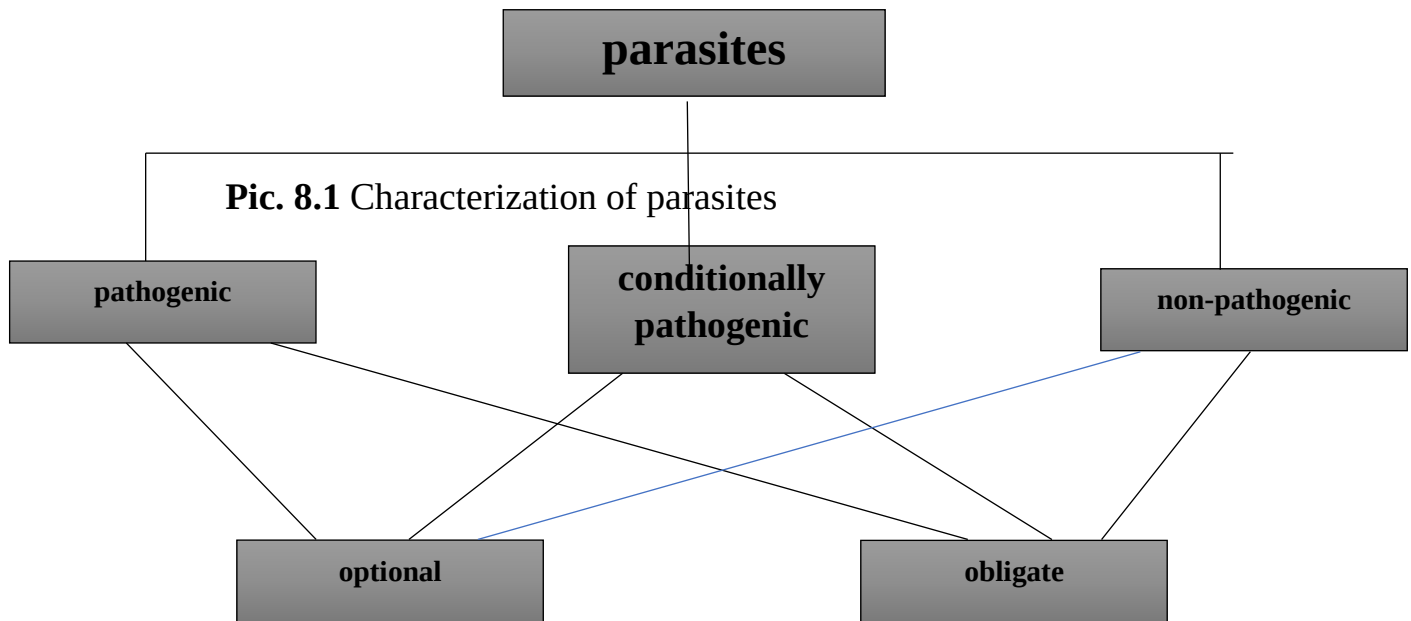
Non-pathogenic parasites include a large group of microorganisms, most often they are permanent inhabitants of the skin and mucous membranes, as well as the intestinal lumen. As a rule, they are characterized by a saprophytic mode of nutrition (utilization of inanimate organic substrates). These parasites can play a certain role in the metabolic processes of the host organism, often to the benefit of the latter. However, these parasites in some situations become very dangerous. For example, in some forms of radiation sickness, the death of the affected person most often occurs not directly from radiation, but from the activation of non-pathogenic microflora, which, under conditions of significant host immunodeficiency, exhibits pathogenic properties. The picture is similar with HIV infection: AIDS is the result of the defeat of an infected person by some non-pathogenic agent. It should also be noted that the transformation of non-pathogenic bacteria is possible not only with the loss or significant inhibition of the host's defense mechanisms, but also with the introduction of genetic material into the parasite population from outside (infection with plasmids or genetic material bacteriophages). This is seen in diphtheria (toxigenic strains are initially harmless corynebacteria affected by a moderate bacteriophage); the so-called pathogenic strains of intestinal worms are bacteria containing plasmids.

There are no clear boundaries between the three groups of parasites mentioned; on the contrary, a whole range of transitions is observed, which does not always make it possible to attribute one or another parasite to any group. So, for example, some authors refer to *Staphylococcus aureus* as pathogenic, others as conditionally pathogenic, etc. That is why the mentioned differentiation ("classification") is simplified, although often useful.

It is necessary to point out one more important circumstance: along with parasites, which in the evolutionary process have acquired the ability to exist only at the expense of the host - we call them obligate parasites, there is a certain group of free-living agents, i.e. not parasites, which, when they enter the human (or animal) organism can take root in it, and sometimes cause pathology. This is explained by

the fact that in the host organism there may be ready-made intermediate products of the multistage metabolic process of a free-living microorganism, with the assimilation of which the parasitic life activity of the latter begins. Such microorganisms are called facultative parasites. On the example of facultative parasites, we can see one of the options for the formation of obligate parasitism in the process of evolution.

This is schematically shown in **Pic. 8.1**.



8.2 Characteristics of the macroorganism (host)

An organism (macroorganism) becomes a host for that kind of extraneous living agent that finds conditions for nutrition and reproduction. In the event that the organism cannot become a habitat for the microorganism (due to the lack of necessary conditions, its metabolic processes are not included), the latter dies off and/or is mechanically removed as a foreign body.

Thus, we are talking about **species susceptibility** to a particular parasite or, conversely, immunity. In the past, this last phenomenon was called species immunity, although it has nothing to do with immunity. Thus, a person suffers from the measles virus, but does not suffer from canine distemper, which is caused by a virus similar to the measles virus; suffers from typhoid fever, but is indifferent to the introduction of *Salmonella pullorum*, which causes a severe fatal infection in chickens, although the causative agents of these diseases are very close to each other (according to modern ideas, they belong to the same species).

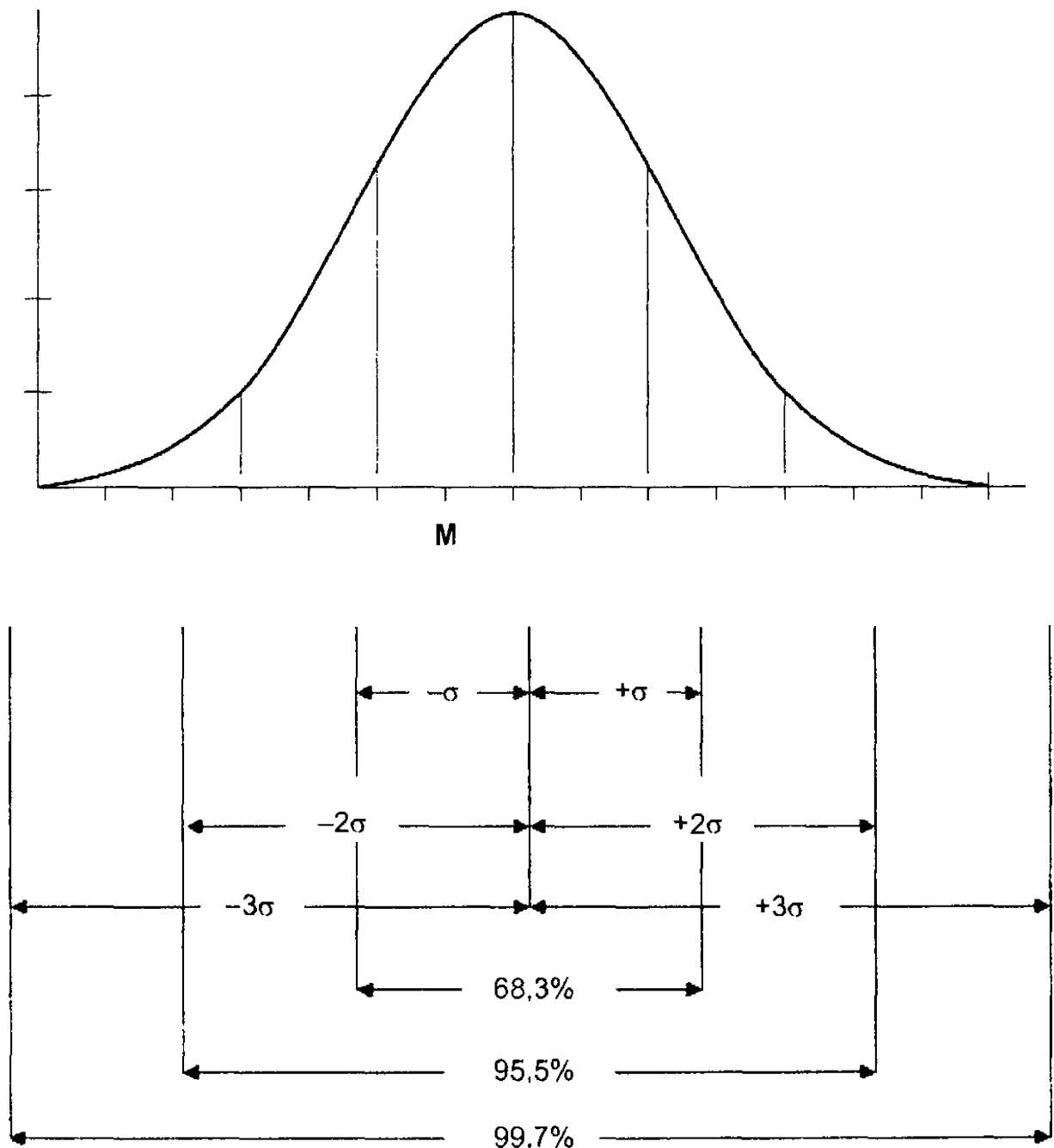
The host organism participating in the interaction with the parasite, which penetrated into its body or settled on the skin or mucous membranes, acquired only defensive means of protection in evolutionary development. This is a mechanical protection of the internal environment of the body, characteristic of the skin and mucous membranes (the protective function of the skin is especially effective), as

well as the lymph nodes; various non-specific humoral (complement, globulins, lysozyme, etc.) and cellular (micro- and macrophages) protection factors involved in the inflammatory reaction, as well as specific protection - immunity.

It should be noted that these factors (with the exception of mechanical barriers) under natural conditions are included in the defense practically only against those agents that can parasitize, i.e. actively exist, since the initial dose (before reproduction) is very insignificant (as if invisible to the body). Under artificial conditions, when it is possible to immediately introduce large doses of a microorganism, the picture may be different - defense mechanisms, including the immune system, are actively involved in the fight against a foreign agent. So, for example, to obtain diagnostic immune sera with high titers of antibodies against dysentery pathogens, intravenous immunization of rabbits with large doses of live or killed dysentery bacilli is used, although rabbits are not susceptible to these microorganisms. This example shows that it is the dosage that often determines the situation in everyday life.

In the presence of species susceptibility, individual differences are observed in this reaction to the introduction of the pathogen. As can be seen from Table. 8.2, at the same infecting doses, the consequences were different: some fell ill with typhoid fever, others suffered the infection asymptotically, and still others did not become infected at all. From Table. 8.1 and 8.2 it can be seen that susceptibility to the parasite or to its individual strains can be determined by the infecting dose, which leads to the development of an infectious process, including leading to pathology. If we take into account that in this experiment the group of volunteers was quite homogeneous (men of the same age, social conditions identical in all respects), then we can imagine the significance of certain subtle genetic differences that could not be identified. Apparently, a homogeneous group is characterized by a spread of susceptibility in accordance with the Gaussian normal distribution curve (Pic 8.2): the largest number of people become infected (or fall ill) from medium infectious doses, but there are

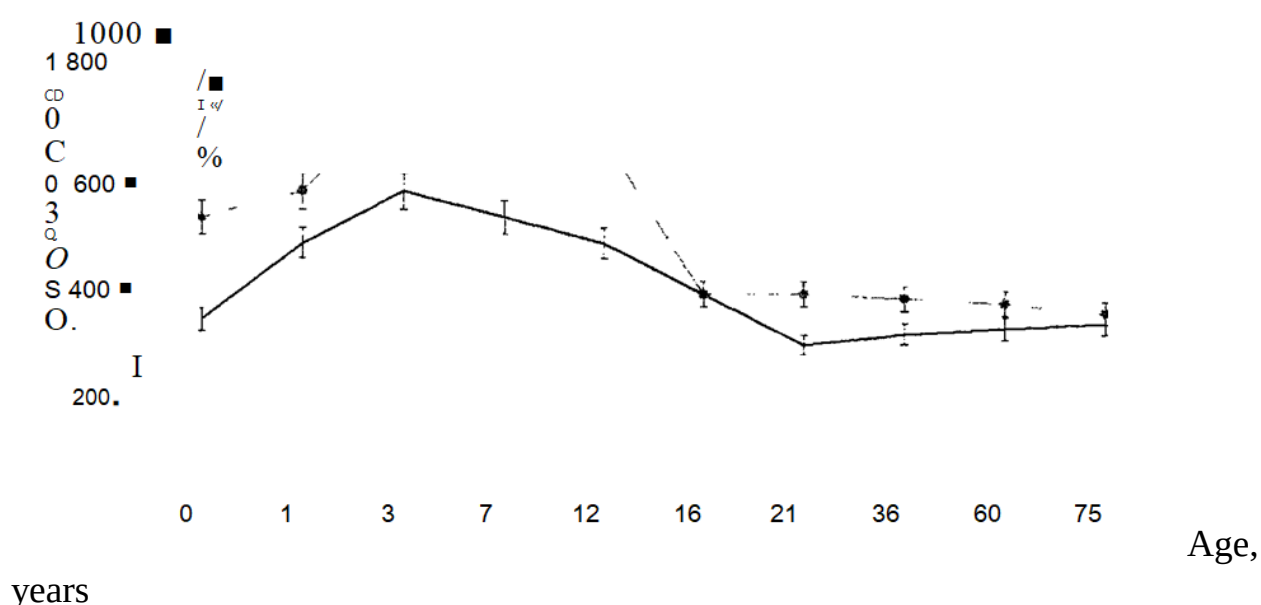
highly susceptible people who become infected (get sick) at low infectious doses (the higher the dose, the more they become). On the other hand, a certain number of individuals have increased resistance to varying degrees - the higher the resistance, the fewer such people in the population.



Pic. 8.2. Characteristics of the susceptibility of people of a homogeneous population

It is also necessary to pay attention to the fact that if the infectious process can proceed in two ways: asymptotically and in the form of pathology, then the infectious doses for the same person will be different: the dose that causes pathology will be higher.

Along with genetic characteristics, including gender, racial and, possibly, some others (for example, differences in blood groups), phenotypic characteristics are also important - age, diet, stress, concomitant diseases, etc. It should be noted that it is very often asserted without proper grounds that the susceptibility of children to many pathogens is higher than that of adults; susceptibility is expected to be high old people. Meanwhile, it is known that adults who for some reason avoided infection with measles and varicella viruses in childhood endure these infections very hard, incomparably harder than most children. Studies in the laboratory of M. R. Sapin showed that the power of the lymphoid system in the wall of the small and large intestines (the relative size and number of plaques) in children is higher than in adults (Fig. 8.3).



Pic. 8.3. Graphic image of medium-sized (height) lymphoid nodules that are part of the lymphoid plaques of the jejunum (solid line) and ileum (dashed line) of the human intestine in postnatal ontogenesis (M. R. Sapin)

Apparently, the idea of greater vulnerability of children is based on the high incidence of children in the first days and months of life (they are indeed very susceptible to many parasites) and the existence of so-called "children's" infections, although adults rarely get sick due to the presence immunity after childhood illness. In relation to the elderly, a more thorough epidemiological study using modern methods is also required. According to our relatively few observations (145 patients), it was found that the frequency of postoperative purulent complications after appendectomy in people of active age and in the elderly was the same - the differences were not statistically significant. Similar data were obtained when studying the likelihood of developing purulent-septic infections (PSI) in patients in a trauma hospital (Table 8-3).

Table 8.3

The incidence of GSI depending on age in patients trauma hospital

Age groups	Total patients	The frequency of development of GSI (in %)
16-25 age	40	10
26-40 age	112	16,1
41-60 age	108	12
60 years and older	29	6,9
Total	289	12,8

Note Differences are not significant everywhere ($p > 0.05$)

Nonspecific protection factors: mechanical (skin, mucous membranes, lymph nodes), cellular (macro- and microphages), humoral (complement, lysozyme, beta-lysine, interferon, etc.) - have limited capabilities (with the exception of the skin) . Therefore, in the evolutionary development, an additional, new system was gradually formed, which ensures the fight with the help of mechanisms directed strictly specifically against the invading parasite. We are talking about the already mentioned immune system. This system, apparently, turns on immediately (immediately) upon reaching, as a result of reproduction, such an amount of the parasite that is necessary to irritate the lymphocytes. However, the effect of its action is far from immediate, most often after a few days or even weeks. This is due to the need to accumulate an appropriate clone of lymphocytes responsible for combating a specific infectious agent. The capabilities of the immune system, as a rule, are incomparably higher than those of non-specific protective factors; Thus, recovery from acute infectious diseases is provided by the formed immunity.

Unfortunately, chronic infections indicate that sometimes the immune system is not able to provide reliable protection (for example, with syphilis, leprosy, etc.); the protective role of the immune system in helminthiasis is doubtful.

It should also be noted sometimes, as it were, a paradoxical reaction of the immune system. This refers to the allergization of the body, which develops quite distinctly in some nosological forms (tuberculosis, brucellosis, tularemia, glanders, etc.), while in others it is noticeably less pronounced (anthrax, dysentery, etc.). Obvious expediency - from the point of view of protecting the organism from the parasite - cannot be seen here.

Immunity can be general, which is formed most often when the pathogen enters the bloodstream (the formation of antibodies - IgM and IgG, the activation of lymphocytes specific against this parasite with different functional orientations that perform cellular protection).

In addition, in the mucous membranes, as well as in some secretory organs (salivary, mammary glands), there are accumulations of lymphoid tissues intended for local humoral (IgA, IgG) and cellular protection. Especially powerful lymphoid tissue is represented in the intestinal mucosa, much less of it in the mucous membrane of the respiratory tract.

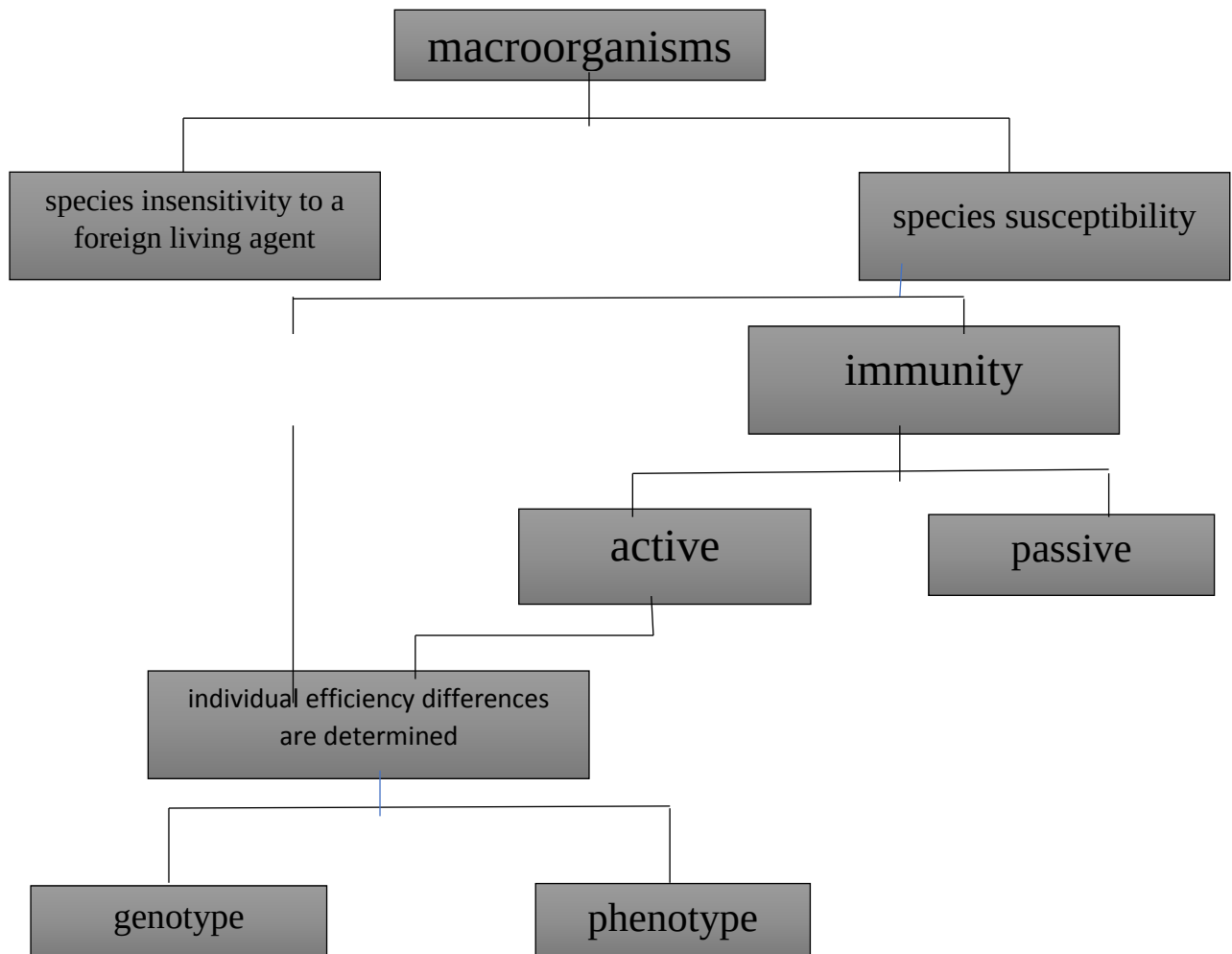
It should be noted that the intensity of immunity increases with repeated, especially multiple encounters with the parasite. During repeated encounters with the pathogen, in comparison with the primary immune response, both the intensity of immunity and the speed of the immune reaction (the so-called booster effect) increase. This is associated with the accumulation after the primary immune response of B- and T-memory lymphocytes specific for each parasite. The activity of the immune system, as well as nonspecific defense factors, varies in individuals depending on genotypic and phenotypic characteristics.

Along with the immunity that is produced by the host organism when it encounters a foreign agent, so-called passive immunity is also possible. Under natural conditions, it is observed in newborns who receive ready-made antibodies from an immune mother. Such immunity is kept in children for a relatively short period, since immunoglobulins introduced from the outside are short-lived. Meanwhile, it is known that children born from immune mothers do not fall ill with the corresponding diseases for 3-6 months. Such a phenomenon needs to be assessed after carefully planned epidemiological studies, since the likelihood of becoming ill for children of a few months of age is generally not high due to the protective isolation measures implemented by the parents. It is known that the probability of getting sick at a very early age depends, in particular, on the options in which people can generally develop an infectious process. So, meningococcal infection, in which the level of carriage among the population is high, most often affects young children (the possibility of meeting with the pathogen becomes real soon after birth). On the other hand, children over 6 months of age usually get sick with measles, since the probability of meeting with a measles patient (you can only get infected from a sick person) is much less. The protective role of mother's milk containing IgA against any causative agent of intestinal infections needs very serious verification and evaluation.

Schematically, the possibilities of a macroorganism in defense against a parasite are shown in pic. 8.4.

So, the interaction of a macroorganism and a parasite at the organismal level can lead to the development of an infectious process, which, depending on the infecting dose and the properties of the parasite (species genetic characteristics, virulence), as well as on the state of the host's protective capabilities (nonspecific defense, immunity) develops in different ways: in the form of a **healthy carriage or pathology** of varying degrees of severity. All forms of the infectious process are

important, although unequal, in the preservation and maintenance of the type of pathogenic agent.



Pic. 8.4. Characteristics of human susceptibility

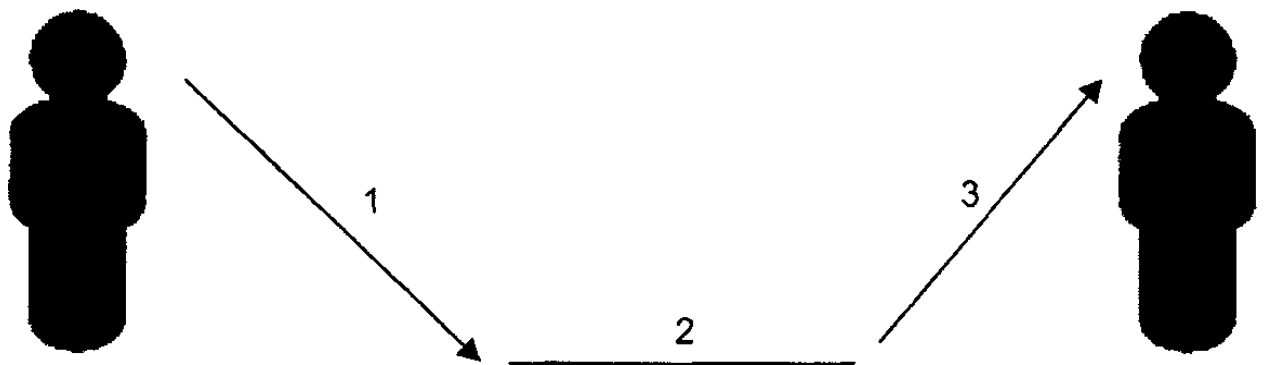
A person is susceptible to parasites that are strictly adapted to his body. Diseases caused by such parasites are called anthroponoses. But due to a certain biological similarity with animals, a person is susceptible to some parasites of the latter (these are the so-called zoonoses). Along with this, human diseases sometimes occur when infected with the mentioned facultative parasites. In other words, a person may be susceptible to some free-living microorganisms. In such cases, the diseases are referred to as *sapronoses*.

It should be noted, however, that interaction at the organismal level, no matter how favorable it may be for the parasite, is not able to ensure the preservation of the species. This is due to the fact that the host organism is mortal. He can die a natural death, he can die under various, often random circumstances, in particular as a result of an infectious process. Only when it becomes possible to move from one individual of the host to another, conditions are created for the preservation of the parasitic

species. In other words, in the evolutionary development of the parasite, not only the ability to live in the host organism, but also to change one individual of the host for another was formed. The appearance of such a possibility is based on the already mentioned rapidity of generational change in the parasite, which is incomparable with the slower rate in the host. **According to Gromashevsky's suggestion, the evolutionarily established ability to move a parasite from the organism of one host to another is called a transmission mechanism.**

Teaching JI. V. Gromashevsky about the mechanism of transmission revealed one of the most important evolutionary features of the formation of a parasitic species: adaptation of a living foreign agent was possible only to those tissues that could ensure the release of the parasite from the host organism. Moreover, the adaptive possibilities in evolutionary development were limited by the need for the parasite to get (penetrate) into similar tissues of another host individual (in the tissues to which it is adapted).

Thus, the mission of the transmission mechanism is not limited to ensuring the release of the parasite from the host organism, it performs another specific function, namely, it delivers the parasite to the same tissue from which it was isolated. For example, if the parasite vegetated in the intestinal mucosa, then due to the appropriate transmission mechanism, it should get into the intestinal mucosa of another host individual. In a generalized version, the transmission mechanism can be represented as a diagram (Fig. 8.5).



Pic.8.5. Transmission mechanism:

1 - the phase of removing the pathogen from the infected organism,

2 - the phase of the pathogen in the external environment,

3 - phase of the introduction of the pathogen into a susceptible organism

All three phases of the transmission mechanism have a clear specific character: the elimination phase depends on the localization of the pathogen in the body, the second phase is the entry and presence of the parasite only in those environmental objects that could be contaminated with the material of the first phase, and, finally, the third phase is determined the specifics of the objects of the external environment that ensure the penetration of the parasite into the tissues to which it is adapted.

The phase of removing the pathogen from the infected organism (1st phase) and the introduction phase (3rd phase) are short and correspond to the time of release of certain substrates from the body (droplets of mucus from the respiratory tract when coughing or sneezing, fecal matter during defecation, etc.). etc.) and the perception of these secretions (when inhaling, drinking contaminated water or eating contaminated food, etc.).

On the other hand, the second phase with different transmission mechanisms has a different duration. For example, when infected by direct contact, in particular with sexually transmitted diseases, it may be absent altogether; with other methods of infection, the pathogen must sometimes be in the external environment for a long time, since a quick combination of the 1st and 3rd phases is by no means always possible. In these cases, due to mutations (possibly, the exchange of genetic material) and selection, the parasite has developed the ability to persist (survive) in environmental objects for quite a long time, such that, with the appropriate mechanism of transmission, it ensures its successful movement from one individual of the host to another. another.

It should be noted that for obligate parasites the external environment, its various objects are not a habitat, so we are talking only about the preservation of viability. At the same time, of course, it must be borne in mind that due to various physical (ultraviolet part of the sun's rays, humidity anomalies, etc.), chemical (oxygen in the air, which has a strong oxidizing function, etc.)), and sometimes biological (antagonism of the permanent inhabitants of the external environment) factors with the lengthening of the exposure, part of the parasites die off, and, accordingly, the risk of infection of susceptible people decreases.

Only in rare cases in the external environment is it possible for obligate parasites to reproduce. So, sometimes, under an accidental confluence of circumstances favorable for the parasite, reproduction of various representatives of the family of intestinal bacteria in foods rich in proteins or sugars (meat, dairy products, confectionery products) is observed, which creates a threat of food outbreaks. However, such rare episodes have no practical significance for the preservation of the parasitic species.

True, there is some exception to the general rule about the significance of the external environment for obligate parasites, as an unfavorable environment in which only preservation, survival can take place: in geohelminths, maturation in eggs of larvae to the invasive stage occurs in the soil (this process is realized at more lower temperatures than the temperature of the human body, and other physical and chemical characteristics of the environment).

In the second phase, the pathogen, depending on the type of transmission mechanism, falls, as already mentioned, on (c) some environmental objects specific to this transmission mechanism (air with airborne droplets, soil, water, food products - with infections of the digestive tract). path, etc.), in which it can be stored and with

the help of which the implementation of the third phase is ensured. Such objects of the external environment are called **transfer factors**. In the second phase, the participation of one or a relay race of transfer factors is possible. In some cases, within the framework of the same transmission mechanism, not one, but several transmission factors may be involved, which act independently, as if in parallel. For example, dysentery can be contracted through water or food. In such cases, one speaks of a specific implementation of the transmission mechanism in **various ways**, and if there is a participation of a relay race of transmission factors, then the path is usually designated by the final factor (water route, food route, etc.). In epidemiological diagnostic work, the identification of specific factors and routes of transmission is of great importance, since it then allows effective targeted measures to be taken.

Thus, the localization of the parasite in the host organism and the mechanism of transmission form a specific system: **each localization has its own mechanism of transmission** (and vice versa).

Taking into account the need for the indispensable movement of the parasite from one individual of the host to another, only 4 such systems were formed (Table 8.4)

Table 8.4

Evolutionarily formed correspondence systems the main localization of the pathogen in the body and the mechanism of transmission

Localization in the body	Mechanism of transmission
Integuments (skin, some open mucous membranes, conjunctiva, external genitalia)	Contact (direct and indirect contact)
Дыхательные пути	Airways Airborne
Gastrointestinal tract	Fecal-oral
Circulatory system (blood, endothelium of blood vessels)	Transmissive (vector) - due to arthropod ectoparasites

In some cases, with the development of an infectious process, it is possible, after some time, that the parasite will penetrate into tissues that are outside the main (primary) localization. This happens under the following circumstances:

1. With a complicated pathogenesis, reflecting the peculiarities of the adaptation of the parasite in the process of evolution to life in the host organism. So, for example, in typhoid fever, after infection and primary reproduction of the pathogen in the

mucous membrane of the small intestine, it penetrates through the lymphatic system into the blood, in which it continues to multiply, then, fixing in the Kupffer cells of the liver, begins to be released through the bile ducts again into intestines

With ascariasis, invasive larvae released in the intestinal lumen from swallowed eggs undergo a complex migration process (intestinal wall, blood, alveoli, respiratory tract, pharynx, intestines, where, finally, sexually mature helminths mature).

In all cases of such a complicated pathogenesis, the parasite in the final phase must necessarily reach the primary (main) localization. Only in this case the transmission mechanism is implemented.

2 When the course of the infectious process is complicated If highly virulent races of the parasite enter the body, or the protective capabilities of the host are significantly weakened (decrease in overall resistance, immunodeficiency), or both of these factors are combined, it is possible, although in general not very often, the exit parasite beyond the primary (main) localization. Among the tissues into which the parasite accidentally enters, there may be those in which the pathogen finds very favorable conditions for vegetation. In this case, serious damage to tissues of secondary localization is possible. So, with meningococcal infection, the development of generalized forms is occasionally possible - cerebrospinal meningitis, encephalitis, meningococcemia (the main localization of the pathogen is the nasopharyngeal mucosa). With poliomyelitis, irreversible damage to the gray matter of the spinal cord is possible, although the main (primary), and, as a rule, harmless, localization is the cells of the mucous membrane of the small intestine. It is important to note that such secondary localization is of no importance for the preservation of the parasitic species, since it does not ensure the release of the parasite into the external environment (secondary localization is a dead end, and the pathogen that finds itself in it is a suicide bomber, "kamikaze"). But, unfortunately, this secondary localization often determines the severity of the disease, therefore, with such nosoforms, clinicians, as a rule, focus on not primary, but secondary localization.

So; due to the evolutionarily established system - the localization of the pathogen in the body and the corresponding transmission mechanism - which reflects the population relationship of the parasite and the host, the preservation (existence) of the parasitic species is ensured. These population relationships are realized (manifested) in the form of an epidemic process.

Currently, another method of infection has been registered due to, as they say, **vertical transmission**, i.e., infection of the fetus by the mother. At the same time, in some cases, they mean only intrauterine infection, in others - intrauterine infection and infection during childbirth during the passage of the birth canal.

Apparently, the second point of view is less justified, since infection of a child during childbirth occurs as a result of contact with the mucous membrane of the birth canal and can be attributed to infection with a contact transmission mechanism.

Intrauterine infection, unfortunately, is now fixed quite often (rubella, HIV infection, viral hepatitis B, etc.), but this can hardly be considered as a transmission mechanism that ensures the preservation of the pathogen as a species. Intrauterine infection is most likely of secondary (although, of course, by no means harmless) significance, which must always be taken into account and somehow prevented.

Apparently, it is legitimate to speak of a vertical transmission mechanism (namely, a mechanism, and not an accidental episodic infection) only in genetic (hereditary) diseases.

Questions for chapter 8

1. Definition of the epidemic process
2. Characteristics of parasites
3. Non-specific protective factors:
4. Types of immunity
5. Characteristics of human susceptibility
6. Mechanism of infection transmission.
7. Transmission factors

Chapter 9

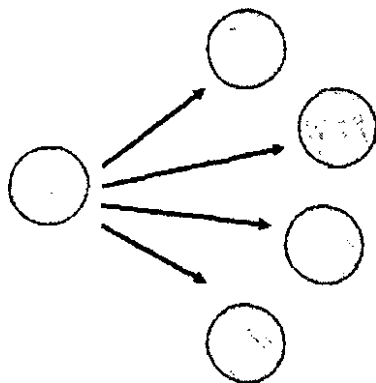
COMPONENTS (INTERNAL STRUCTURE) OF THE EPIDEMIC PROCESS.

As already mentioned, the epidemic process, which essentially reflects the population relationship of the parasite and the host, manifests itself in the form of a certain set of infectious conditions. This set can be represented in the form of several simple modifications:

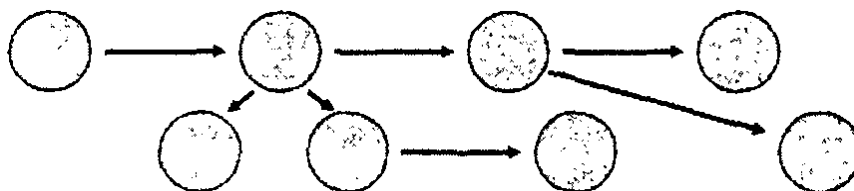
1. « Chain »



2. « Fan »

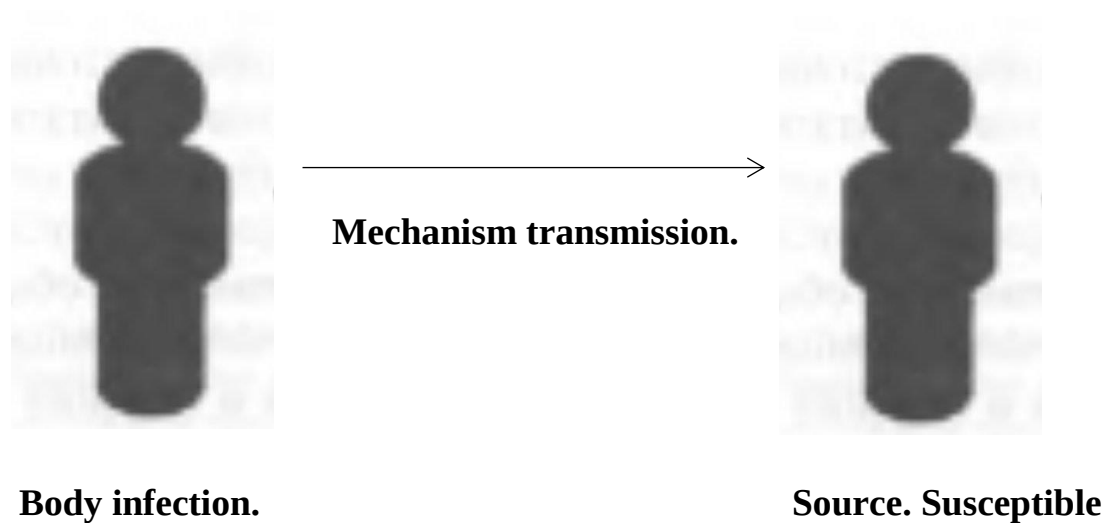


3. Combination of options 1 and 2



The presence of modifications shows the need to choose the minimum structure (elementary cell) that reflects any set of infections (infectious conditions) regardless of the variant of the development of the epidemic process. It can be seen from the

above diagrams that such an elementary cell (the minimum set) is two interconnected infectious states. The specified minimum structure consists of three parts that depend on each other: the first causes the formation of the second, the second - the third (pic. 9.1).



Pic. 9.1. Links of the epidemic process.

The first link is the source of infection, i.e., the parasite donor, which, using the transmission mechanism (second link), infects a susceptible person (parasite recipient).

A break within the elementary cell (switching off any of its links) inevitably leads to the cessation of the epidemic process. In other words, only the preserved elementary cell ensures the continuity of the epidemic process and reflects its qualitative features, regardless of modifications.

The sequence, the continuity of the development of the epidemic process is determined by the fact that the human body, which perceives the parasite, becomes a new source of infection when an infectious process occurs.

The functional features of the first and second link (parts) of the elementary cell are reduced to the need to ensure the development of the epidemic process as quickly and powerfully as possible. The third part of the elementary cell, on the contrary, performs, if possible, an inhibitory function. Unfortunately, this is not always possible under natural conditions (as evidenced by the existence of the parasite and the epidemic process). But in the fight against infectious diseases, in a number of cases, this feature is used, and often very successfully (specific prophylaxis through vaccination), for example, in smallpox (eliminated on a global scale), measles, poliomyelitis, etc.

9.1. Source of infection

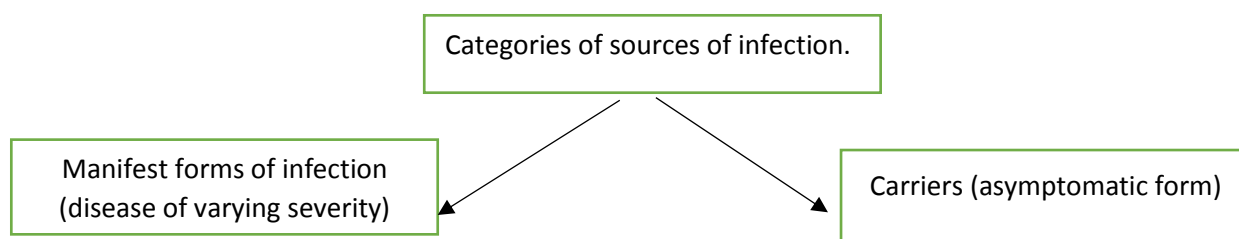
The source of infection (the first link of the elementary cell) is the natural habitat of the parasite, where it feeds (switching on metabolic processes), reproduces, and then exits, ejects beyond the source.

The source for infections that are peculiar only to humans, i.e., **anthroponoses**, can, of course, be only a person.

In infections caused by non-pathogenic parasites, the source is only a healthy person. At the same time, a person, as is often believed, having become infected after birth (or even during the passage of the birth canal, remains infected and, accordingly, a source for life. In such cases, we mean the permanent inhabitants of the skin and mucous membranes or lumen of the intestine, while it is assumed that such non-pathogenic parasites, once settled, remain there forever. To a certain extent, this is where the term “permanent inhabitants” comes from.

A more detailed study of the ecological and, accordingly, epidemiological aspects of the relationship between these parasites and the host (human) was rarely carried out, which, firstly, is explained by the not very great interest of researchers (the parasite does not cause pathology), and secondly, similar research is associated with great technical difficulties and significant financial costs. There are only a few publications. So, F. Kaufman (1959) describes the experience of two authors who conducted dynamic observations (apparently, on themselves) with the aim of microbiological evaluation of excreted *E. coli*. They studied strains of *Escherichia coli* isolated with fecal masses during the year using intraspecific identification techniques, in particular, using very laborious immunological studies. After a year of observations, the authors stated that most strains of *Escherichia coli* remain in the body for no more than one to two weeks, i.e., a rather intense epidemic process takes place, only very rarely they established the fact that the same strain during the year (observation period). The above studies have shown that a person can be a source of infection most often for a relatively short period of time, only in rare cases is the so-called resident carriage possible. Of course, such a conclusion applies only to *Escherichia coli*, but most likely we are observing some general patterns in this example. A similar conclusion was made, in particular, by V. K. Noble (1986), who, summarizing observations of the population of the skin, pointed to the existence of transit, temporary and resident flora. It should be noted that the resident carrier is a long-term, but most likely not lifelong, although it is hardly possible to completely exclude the latter. The source of infection in opportunistic parasites, if their vegetation is not accompanied by the development of the disease, should obviously be evaluated in the same way as the source for non-pathogenic parasites. In the event that pathology develops, some analogies (with a certain caution) with the situation that develops during the circulation of pathogenic parasites are acceptable.

The source of infection (Fig. 9.2) during the formation of an epidemic process caused by pathogenic parasites is a sick person (manifest form of infection of varying severity) or a carrier (with the exception of measles and some other nosoforms, which are caused, as it were, by absolutely pathogenic pathogens).



Pic.9.2.Categories of sources of infection.

Manifest forms indicate the rapid development of the infectious process and are potentially the most dangerous sources of infection, and the more dangerous the more severe the disease develops and proceeds. So, in experiments to assess the danger of patients with typhus, it was found that a single feeding of body lice on patients with severe forms led to infection of 60~80% of insects. When feeding lice on patients with mild forms, it was possible to infect, according to various authors, from 2-3 to 30% of insects that fed on blood. The large variation in infection rates is obviously due to differences in the severity of the course of the disease in patients who fed lice on themselves.

In the first post-war years, quantitative microbiological studies of the feces of patients with dysentery were carried out. According to these materials, the more difficult the infectious process develops, the higher the concentration of the pathogen in the fecal masses (up to 10^8 and even 10^9 bacteria per 1 g) and the excretion lasts longer (T. A. Avdeeva, 1963).

This danger of manifest forms is also due to the fact that the disease is often associated with infection and, accordingly, the isolation of the most virulent races of the parasite.

In most nosoforms, the patient is most infectious during the period of rapid development of clinical symptoms, most often from the first days of their manifestation (dysentery, cholera, influenza, etc.). So, with influenza, the absolute number of patients is contagious for the first 3-5 days of illness. But this is not a general rule, especially high contagiousness is possible even in the prodromal period (measles) and even in the last stages of the incubation period (viral hepatitis A). On the other hand, there are nosoforms in which the contagiousness manifests itself somewhat later: with natural smallpox, the patient becomes contagious approximately 5-6 days after the first signs of the disease appear, with typhoid fever at the second - the beginning of the third week of the disease.

As the signs of recovery increase, the patient's danger to others most often decreases and disappears with recovery. But even this position is not absolute, since in a

number of nosoforms it is possible to isolate the pathogen even at the stage of convalescence (diphtheria, abdominal hyphae, etc.).

In chronic infections, which are characterized by either a continuous course in a manifest form, or manifestation in the form of periodic relapses (phases), infection in the first case is possible at any time, in the second - most often in the primary acute phase and during the period of Striae or at certain stages (stages) of the disease, for example, with syphilis.

Along with the manifest forms, the danger may come from people carrying asymptomatic forms of infection.

These asymptomatic forms (healthy carriage or, as L. V. Gromashevsky suggested to call it, infection carrier) in acute diseases can be divided into primary and secondary (immune) carriage.

Primary carriage is the carriage of people who meet the parasite for the first time in their lives, i.e. asymptomatic infection cannot be associated with the protective function of the immune system. Apparently, such a phenomenon is observed in a variety of nosoforms. This is evidenced, in particular, by experiments on guaranteed non-immune volunteers when infected with the causative agent of typhoid fever (see Tables 8.1 and 8.2), observations in military teams in 1957 in the foci of influenza caused by a new type of A2 virus, or according to the modern nomenclature A (H2N2). But especially many observations that irrefutably testify to such a primary carriage were made in the foci of cholera in places where such a disease had not previously been recorded at all or was encountered with drifts that took place several decades ago. Such primary carriers, judging by many epidemiological observations, are usually not dangerous: they release the pathogen in extremely small quantities, and for a short time (single, not confirmed by many repeated microbiological studies).

Secondary (immune) carriage poses a great epidemic threat. In some nosoforms, immunity, protecting against disease, is not able to ensure the destruction of the pathogen. In such cases, the carriers secrete the pathogen for a sufficiently long time and in large quantities (its concentration in the secretions reaches significant numbers). The danger of such carriers is exacerbated by the impossibility of identifying them without leading epidemiological data or without special laboratory studies. Epidemiological data show that in some nosoforms, diseases occur almost exclusively as a result of infection from secondary (immune) carriers (diphtheria, meningococcal infection, typhoid fever, etc.). Immune carriage may be the result of the transmission of the disease, or the so-called pro-epidemic, or, finally, vaccination.

After the transfer of the disease, carriage may be limited to the stage of convalescence (a few weeks - no more), but sometimes it can last several months (diphtheria) or years (with typhoid fever, it can become, although not very often, lifelong).

Proepidemicization, i.e., the gradual acquisition by people of their nitet, is possible with nosological forms, which are characterized not only by manifest, but also by asymptomatic forms, and in conditions of a rather intensive circulation of the parasite in the population. Most of all, this happens when the parasite is still possible to meet in childhood (as already indicated, children aged 3-12 years have the greatest resistance), and - it is not excluded - with its small dose. Multiple encounters with the pathogen gradually lead to the formation of a sufficiently pronounced immunity, although not always ensuring the destruction of the parasite that has entered the body. In this case, we see the transformation of the primary carriage into the secondary.

Vaccination, as a factor leading to possible secondary infection, is observed with some inferiority in the formation and development of post-vaccination immunity. Thus, the introduction of diphtheria at toxin cannot protect against infection and subsequent vegetation of diphtheria bacillus, since immunity is antitoxic: rakter.

In chronic infections, characterized by periodic is nifestation of the infectious process, between relapses there is a less (maybe) condition, which is often called **persistence**, reflecting the conservation of the metabolic processes of the pathogen. With persistence, a person is not contagious. With the phase development of a chronic process, the latent stage is also usually not dangerous, except for artificial intervention (taking blood from them for transfusion, etc.). In some chronic infections, it is possible (along with the variant associated with periodic manifestations) to develop an infectious process. in the form of carriage (viral hepatitis B and C), in such cases, their i potential danger in natural ways of infection, apparently] is significantly inferior to the danger posed by patients.

9.2. Transfer mechanism

The second link, the evolutionarily established mechanism of transmission, ensures the spread of the parasite in the population the faster, the more adapted it is to the conditions of life of people in society. At present, in this regard, the airborne mechanism of transmission is the most significant, since during its operation, if there are no effective means of intervening in the epidemic process, the incidence of the individual is high (for more details on the mechanism of transmission, see above).

9.3. Susceptible organism

From the foregoing, we can conclude that the probability of inclusion in the parasite cycle of the **third link - the recipient or susceptible organism** - depends both on the state of the organism itself, and on the powerful source of infection and the effectiveness of the transmission mechanism. Otherwise, grief, the probability of the formation of the third link and, accordingly, the end!

The formation of the elementary cell of the epidemic process is an integral indicator of the participation of all three links.

The validity of this provision can be assessed, in particular, according to the above data on the danger of sources depending on the severity of the course of the disease: the longer the parasite is excreted and the higher its concentration in the secretions, the more likely it is to receive a sufficient dose for the occurrence of an infectious process in the susceptible out people.

The quite logical idea that the probability of the formation of the third link and, accordingly, the development of the epidemic process depends on the possibilities of transmission of the parasite, can be confirmed by many observations. So, most of all, the population suffers from the so-called uncontrollable (there are no means of specific prevention) airborne infections; the incidence of intestinal infections is high among the population, which is not provided with good-quality water, etc., etc. In particular, the significance of the 2nd link can be traced on the example of the occurrence and spread of respiratory tract infections, in which the infectious process can proceed both in the form of a disease and primary carriage. For nosoforms with an airborne transmission mechanism (it is believed that it is extremely effective, as if a high-power standard - almost 100% of people become infected in the foci), the manifestness index (the former name is the contagiousness index) is defined as a selective indicator of reproduction. susceptibility (everyone gets infected, and only the susceptible get sick). These indices were determined at a time when there were no vaccinations and there were no antibiotics. So, for measles, it is equal to 1 (all those infected who lack immunity carry the infection in a manifest form), and, accordingly, the conclusion is: susceptibility to the measles virus is universal (100%). For scarlet fever, the manifestation index is 0.4 (among those reliably infected with a toxigenic strain of hemolytic streptococcus, 40% fall ill, the rest may have a primary carriage of the pathogen) - susceptibility, therefore, is 40%. With diphtheria, this index is 0.2 (susceptibility - 20%), and so were determined, and sometimes calculated without proper objective assessment, indices for a number of nosoforms. For measles, scarlet fever and diphtheria, the indices were obtained on the basis of an assessment of the nature of the development of the epidemic process in fairly significant populations isolated from communication with the outside world (residents of Fiji and the Faroe Islands, who did not have immunity against the causative agents of these diseases) and can be considered reliable. mi. Meanwhile, long-standing observations testified to the doubtfulness of the assertion that the index characterizes only the degree of susceptibility (and nothing more). So, in pre-vaccination time in England it was found (Frost, 1928) that when communicating with patients with diphtheria at home, the ratio of carriers : patient was 6: 1 (1 patient as a result of 7 effective infections), in schools 47: 1 (1 patient with 48 effective infections), that is, in the first case, the probability of falling ill in susceptible children was approximately 8 times higher than in the second, when the tightness of

communication for the majority was less pronounced. In the second case, with all the activity of the transmission mechanism, he could not ensure the delivery of the pathogen in the dose that caused the disease, with the same probability as in the first case. In other words, the materials presented on reliably calculated manifestation indices for diphtheria and scarlet fever reflect the average statistical probability of meeting doses leading to the development of manifest forms of infection in a fairly large population of non-immune people. In individual centers, depending on the closeness of communication, the situation obviously had certain differences. Thus, even with airborne infections, we see the importance of the transmission mechanism for the formation of the third link.

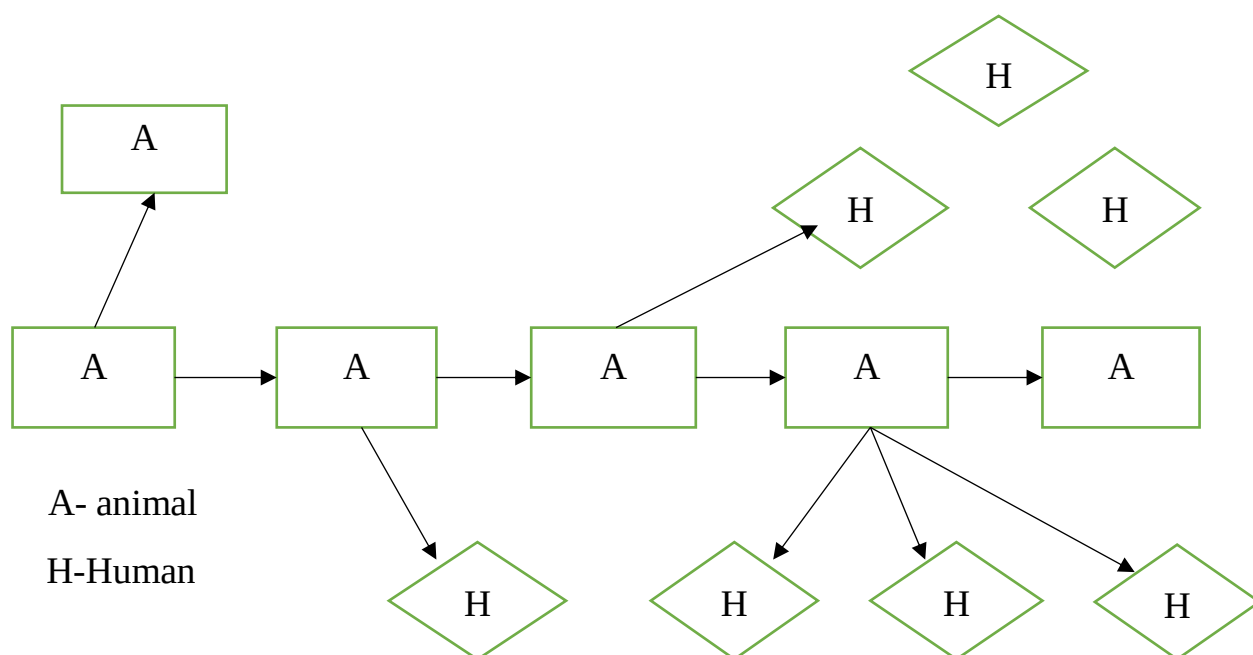
So, the possibility of forming the third link is determined primarily by the degree of species susceptibility to various parasites, which is characterized by a dose that causes disease or carriage. For example, with typhoid fever, the dose that causes disease in 50% of infected volunteers is 10^7 microbial cells of a virulent strain, with dysentery - 0.5×10^3 - 0.5×10^4 microbial cells, with tularemia, people get sick when they are injected with 25-50 microbial cells of virulent strain. roll strain Shu. However, against the background of species susceptibility, the following variables also matter:

- the total power of the source of infection and the mechanism of transmission, which ensures the delivery of the dose of the parasite necessary for infection;
- virulence of the pathogen (the higher the virulence, the lower the infectious dose) - see table. 8.2;
- individual characteristics of the susceptibility of people exposed to infection;
- possible phenotypic transformations of susceptibility associated with internal (eg comorbidities) or external (irradiation, etc.) factors.

After the transfer of the infection, as you know, immunity develops. If one elementary cell is formed, then only two people will become immune (the former source of infection and the one who became infected from it), but with the development of the epidemic process, immunity will develop in many people, and the number of immune people is directly dependent on the scope of the epidemic process. Thus, the epidemic process leads to the development of not individual, but population immunity.

As already mentioned, a person gets sick as a result of infection with parasites of animals. This is possible because a number of animal parasites do not have a strict adaptation fixed in evolution to life in the body of a particular host species, since the populations of many animals are rather rarefied and the existence of parasitic species at their expense is practically unrealistic. Some biological similarity with animals, primarily with warm-blooded ones, led to the fact that from similar pathogens can affect a person. In such cases, we speak of zoonoses. In zoonoses, the epizootic process, if people are involved in the circulation of the pathogen, forms

an epidemic process. The scheme of such a transformation may look as shown in pic. 9.3.



Pic. 9.3. Formation of the epidemic process in zoonoses.

In cases where the epizootic process develops among domestic animals (including birds), they speak of **anthropurginic** foci. Anthropurgic should also include foci that are formed due to the so-called synanthropic animals, that is, not domesticated, but living near a person - in his houses or settlements (rats, house mice, pigeons, sparrows and etc.).

The presence of epizootics among wild animals indicates the existence of natural focal infections that can be dangerous to humans. Summarizing many of his expeditionary studies in various regions of the USSR and on the territory of Iran, as well as summarizing the data of world science, E. N. Pavlovsky formulated the **theory of the natural** foci of many diseases. According to this doctrine, natural foci of diseases formed in certain climatic and landscape conditions due to the historically established biocionotic relationships between various inhabitants who have adapted to live in these conditions (wild animals, including in some cases birds, reptiles, amphibians, fish, molluscs, arthropods, etc.). Various parasitic species have adapted to these biocionotic relationships in evolution, which, in essence, become one of the constituent components of these biocionotic relationships.

The causative agents of natural focal diseases can cause the formation of secondary anthropurgic foci, including synanthropic (for example, pigeons, sparrows, which form foci of Japanese encephalitis among urban residents) and domestic (dogs with rabies) animals in the circulation.

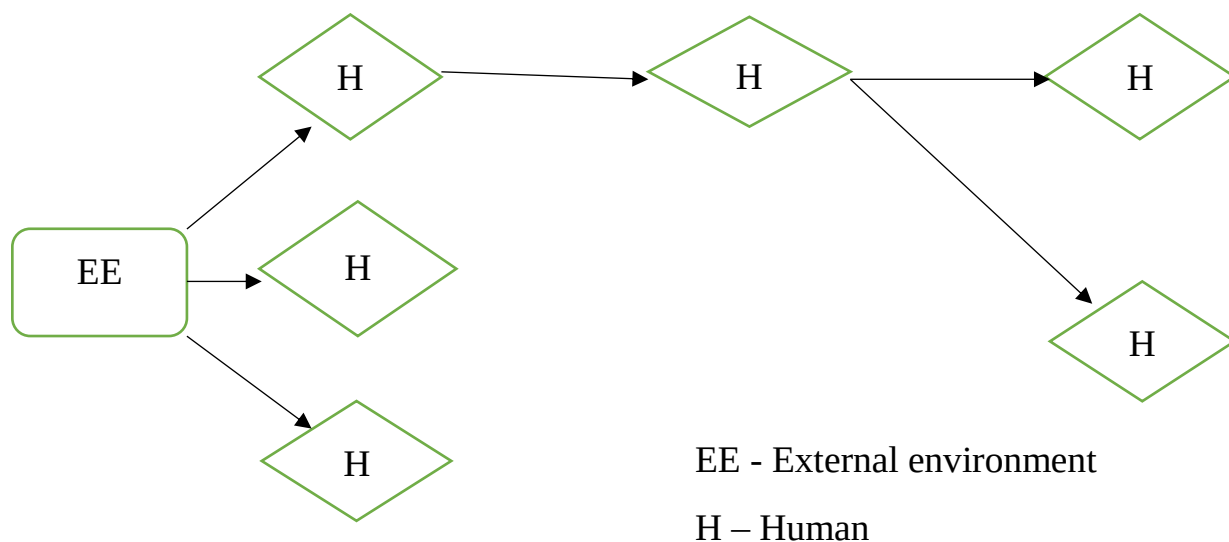
Among animals, infectious agents mix according to the general law of a single system - the localization of the pathogen in the body and the mechanism of transmission, however, often due to the impossibility of the existence of the parasite due to one mechanism of transmission, the epizootic process is supported by several localizations and, consequently, therefore, several transmission mechanisms. It is possible that there is a main mechanism in this sum, but in different situations, as observations show, the significance of the main and additional can change. Thus, tularemia exists in natural foci, undoubtedly due to the transmissible mechanism of transmission (ixodid ticks), but in some specific situations, the epizootic process among rodents is supported by the transmission of the pathogen by food and water. Human infection is carried out in some cases in accordance with the transmission mechanism that has developed in natural conditions among animals, in others it can occur in a different way. So, anthrax in animals is a typical intestinal infection, anthrax in humans in 98 - 99% of cases develops in the form of a skin form, i.e., infection is most often realized by contact (care for animals, indirect contact due to objects of animal origin - leather, skins, wool, etc.).

A person with zoonotic infections is most often a biological dead end - the continued existence of the parasite becomes impossible. This is due to the fact that a person as a source of infection, as a rule, cannot compete with infected animals in terms of danger to others. In the conditions of society, that is, in the conditions of communication among people, the transmission mechanism that manifests itself in the animal world cannot be realized. Finally, although this needs further study, it is possible to think that passage through the human body may reduce the virulence of the pathogen.

Only in very rare cases (in Fig. 9.3 this is displayed not as a connecting line, but as a dotted line) does the danger of a person become real. This is evident in some tropical diseases - yellow fever ("yellow fever of the cities") and dengue disease. Cases of infection from people sick with Crimean hemorrhagic fever are also described (the disease is recorded in the south of the country in the plains and foothills located between the Black and Caspian Seas). The blood of patients in whom hemorrhages and bleeding are possible contains a virus, therefore, when caring for and assisting patients, as well as during various medical procedures, it is possible to infect others, in particular medical personnel. But, of course, these episodes cannot ensure the preservation of the pathogen in nature.

As already mentioned, a person can suffer when infected with facultative parasites, for which the main habitat is the external environment. Such nosoforms received a not entirely successful term - sapronoses, reflecting a certain inconsistency of choice. Although all these agents are characterized by a saprophytic way of feeding (they exist due to the utilization of inanimate organic substrates), it was hardly correct to take this trait as a basis, since the other two groups (anthroponoses, zoonoses) are named after their main habitat. Кроме того, надо иметь в виду, что

целый ряд облигатных паразитов также обладает сапрофитическим способом питания (многие обитатели кожных покровов и просвета кишечника). При сапронозах формирование эпидемического процесса можно представить в виде схемы (рис 9 4).



Pic 9.4. Formation of the epidemic process in sapronoses.

Picture 9.4 shows that people become infected when a pathogen from the external environment enters (for example, pathogens of gas gangrene and tetanus, which penetrate into wounds from the soil), but sometimes infection from a person is possible (outbreaks caused by free-living worms are recorded in hospitals). the external environment with *Pseudomonas aeruginosa*, which are the result of infection of patients from each other due to violations of the rules of asepsis and antisepsis during medical manipulations).

Completing the description of the three groups of infections, it is necessary to point out some terminological inconsistency, which is often found in the literature. We are talking about what zoonotic infections are proposed to be called zooanthroponoses or even anthropozoonoses, since these diseases are dangerous for humans and the population suffers from them (as opposed to only animal infections, i.e., truly zoonotic ones). The evolutionary approach, however, has in mind to designate groups on the basis of not an accidental defeat of a person, but on the basis of the main host, which ensures the existence and preservation of the parasitic species. If random phenomena are used for differentiation, then one can reach the point of absurdity. So, for example, the plague would have to be designated as saprozoo-anthroponosis, since, according to modern data, the plague pathogen, like other *Yersinia*, lives mainly in the external environment, that is, it, apparently, should not be attributed to obligate, but to facultative parasites (for more details, see the section "Private epidemiology"). Or, say, *Salmonella*, which can cause major food poisoning due to reproduction and accumulation in the food product, should be attributed to

the causative agents of zoonoses. One exception can be distinguished from this rule: for a number of biohelminths (wide tapeworm and some others), humans and animals (cats, etc.) can be the main hosts, i.e. the evolution of the parasite has led to adaptability to life in parallel as in the human body, and animals. In other words, and apparently, these are true zoonoses.

Questions for chapter 9

1. Components (internal structure) of the epidemic process
2. 3 Links of the epidemic process
3. Source of infection
4. primary and secondary (immune) carriage,
5. Transmission mechanism
6. Susceptible organism
7. Formation of the epidemic process in zoonoses
8. Theory of natural foci

Chapter 10

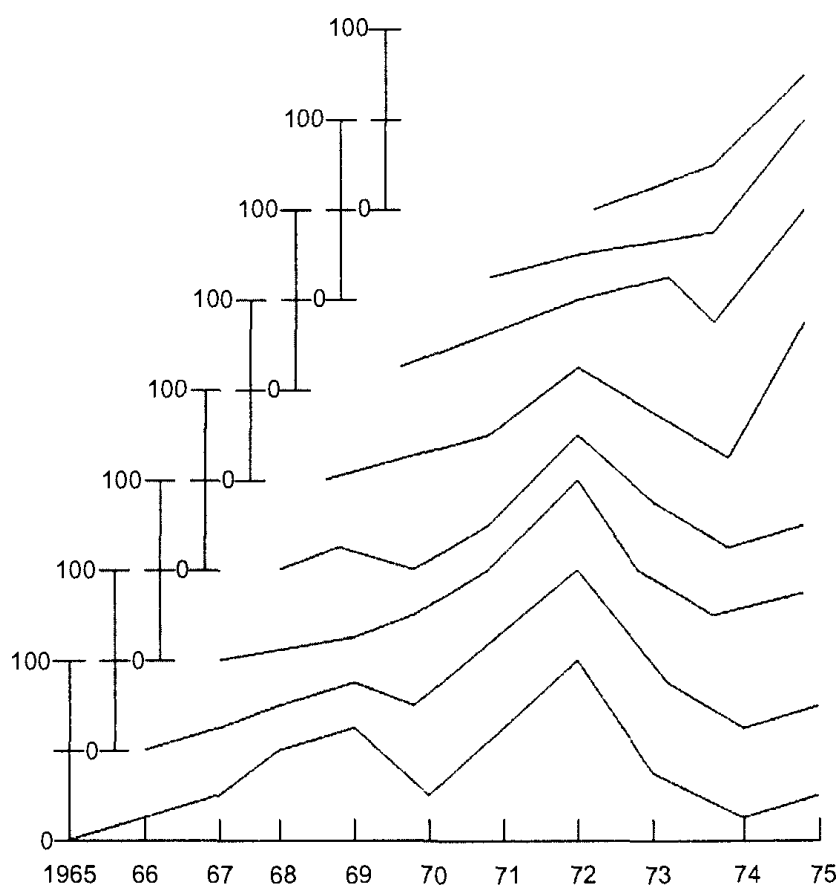
POPULATION IMMUNITY AND THE THEORY OF SELF-REGULATION OF THE EPIDEMIC PROCESS.

Population immunity (formerly it was most often called collective immunity) is an acquired state of specific protection of a population (of the entire population, its individual groups), which is made up of the immunity of individuals included in this population.

The level of population immunity consists of the total protection of individuals and is characterized by the proportion of such individuals in the population. If all people in the population are immune, population immunity is 100%, in which case the development of the epidemic process is impossible. However, this ideal situation during the natural development of the epidemic process (clinically expressed forms of infection, carriage) either does not occur at all, or is extremely rare (a similar situation sometimes occurs among local residents living in natural foci), although artificially with the help of vaccination, it is quite possible to create such a situation.

The development of population immunity primarily depends on the mechanism of transmission, on its activity: the more people are involved in the circulation of the pathogen, the higher the population immunity. The most active mechanism of transmission is characterized by a group of airborne infections, therefore, with these diseases, population immunity, all other things being equal, develops especially rapidly. Accordingly, for the spread of airborne infections, the importance of population immunity is especially great - it plays a decisive inhibitory role in the development of the epidemic process. Experience shows that the counteraction of population immunity during the spread of airborne infections does not necessarily manifest itself with the immunity of the entire population (100%), its role can be noticeable already when only a certain part of the population is protected. one case of measles and diphtheria, i.e., to completely exclude the development of the epidemic process, it is necessary to protect at least 96-98% of susceptible people with the help of vaccination. This is due to the fact that as the epidemic develops

process and, accordingly, an increase in the number of immune people, susceptible to this parasite and immune discharge each other. Epidemiological observations have shown that the epidemic process loses its activity much earlier than all



susceptible people are involved in it (according to the figurative expression J1. V. Gromashevsky - "combustible material"). This can be confirmed, in particular, by observing the long-term dynamics of the incidence of children born in a particular year (age cohort). On pic. 10.1 presents data on the incidence of mumps in the Vyborg district of Leningrad.

Pic. 10.1. The incidence of mumps in conditional groups of 1000 children born in 1965-1975. in the Vyborgsky district of Leningrad (P. X. Yafaev, G. I. Grishanova).

Each long-term curve is the incidence in a group (cohort) of those born in the same year (indicators per 1000 population of the corresponding cohort). From pic. 10.1 shows that the children of each cohort are involved in the epidemic process several times - in the years of the next rise in the incidence. Thus, among children born in 1965, 1966, 1967, during the observed period (up to 1975 inclusive), the incidence increased three times (not all susceptible people were involved in each rise). The next rise in the incidence occurred in years when the density (concentration) of non-immune people in the population due to the newly born and dying of immune people of the older generation reached some kind of "critical mass", i.e. population immunity was the smallest. From pic. 10.1 also shows that in a city of many millions, in the absence of intervention in the epidemic process (at the time described, there were no vaccinations against mumps), the epidemic process does not fade, only level fluctuations take place. In small populations, after the next introduction of the pathogen, the epidemic process may completely stop (until the next introduction).

The smaller the population, the higher the probability of a complete cessation of the epidemic process.

With infections of the external integument, infections of the gastrointestinal tract (with the exception of enterovirus infections, in particular poliomyelitis), blood (transmissible) atroposes, the inhibitory effect of population immunity on the development of the epidemic process usually does not affect, since the number (relative number) of immune is insufficient for a real impact on the circulation of the parasite.

From the foregoing, it can be concluded that population immunity, formed under conditions of spontaneous circulation of the parasite (without active human intervention), affects the course and development of the epidemic process, i.e., its certain regulatory function is manifested.

V. D. Belyakov and his co-workers pointed out that the epidemic process is regulated by more complex mechanisms involving the parasite population and the host population.

The theory of self-regulation of the epidemic process

V. D. Belyakov with employees in the 70s. 20th century based on his own research and generalization of world science data, he formulated a theory (concept) of the internal self-regulation of the epidemic process, which determines its self-development. The main thing in this theory, which is undoubtedly fundamental and universal, is an indication that the epidemic process, i.e., the interpopulation relationship between the parasite and the host, is a system that is subject to internal self-regulatory processes.

Biology, medicine, in particular, have long established that every living organism is a complex self-regulating system, but ideas about self-regulation have never gone beyond the organismic level.

The mechanism, the essence of self-regulation, given by the authors, consists of the following components.

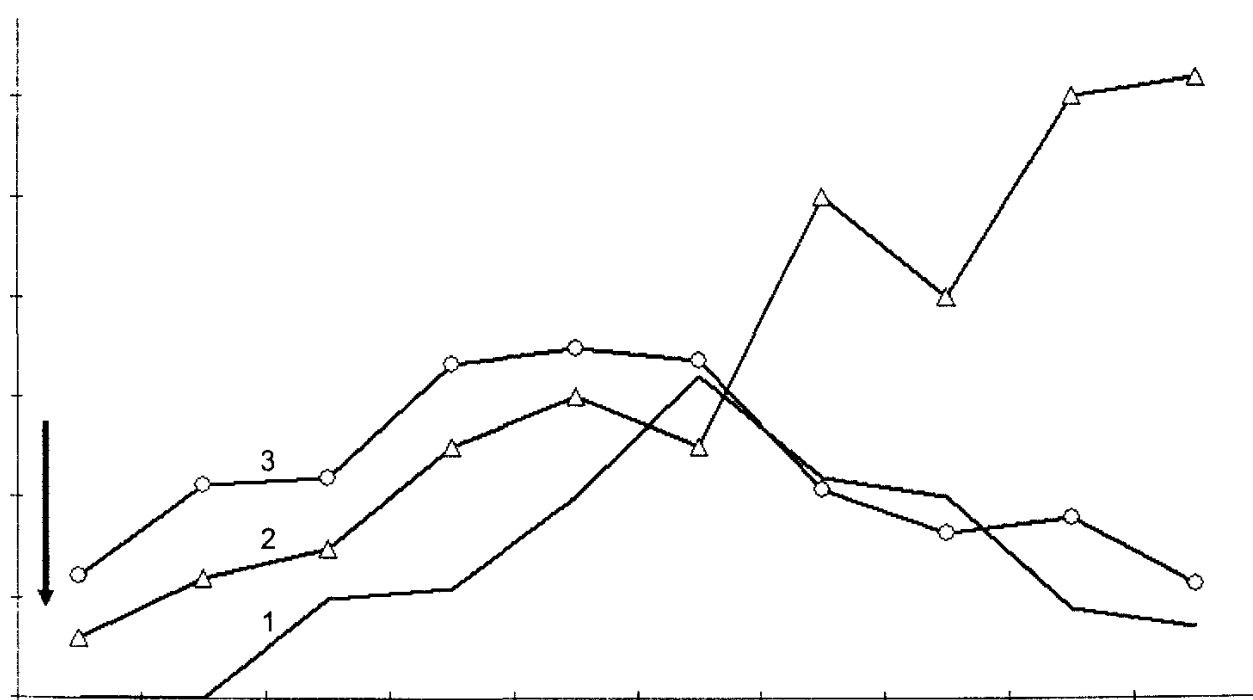
1. Host and parasite populations are heterogeneous in genotypic and phenotypic properties that characterize their relationship to each other.

As you know, all units, any component of the material world are not homogeneous, but the authors defined this phenomenon as the main cause (base) of self-regulatory processes. In each population there are resistant and susceptible to infection people, due to the latter, the existence of the parasite is ensured. On the other hand, in the parasite population there are virulent and non-virulent races.

2. In the epidemic process, there is an interdependent variability of the biological properties of both interacting populations.

Above are data on changes among the population during the spread of diseases transmitted by airborne droplets: the formation of population immunity, which has an inhibitory role in the circulation of the pathogen. Examples of variability in the course of the epidemic process of the virulence of the pathogen are known. So, for

example, in diphtheria during the epidemic period, virulent varieties of the pathogen (gravis type) are mainly isolated, in the inter-epidemic period - mainly the weakly virulent type of mitis. The authors of the theory provide convincing materials that characterize changes in the course of the development of the epidemic process in the virulence of hemolytic streptococcus A (Fig. 10 2). The figure shows that after the formation of the team, there was an increase in the level of carriage of group A streptococcus. The first patients with tonsillitis appeared only a month later. In parallel, there was an increase in the virulence of group A streptococcus. Then the picture changed: the incidence of angina and the virulence of group A streptococcus synchronously decreased, and the carriage continued to grow. Thus, the authors conclude that the change in the incidence rate during the epidemic process is associated with a change in the virulence of the pathogen.



Pic. 10.2. Change in the virulence of group A streptococcus during the epidemic process (Khodyrev A.P., Belyakov V.D., 1988).

On the abscissa axis - the order of examination of people in the team from 10 11 to 11 05 (the arrow indicates the time of formation of the team), on the y-axis - dynamics in terms of visibility 1 - incidence, 2 - carriage 3 - virulence of group A streptococcus.

On pic. 10.3 shows how the virulence of *Pseudomonas aeruginosa* changed, which caused an outbreak in a urological hospital.

Pseudomonas aeruginosa

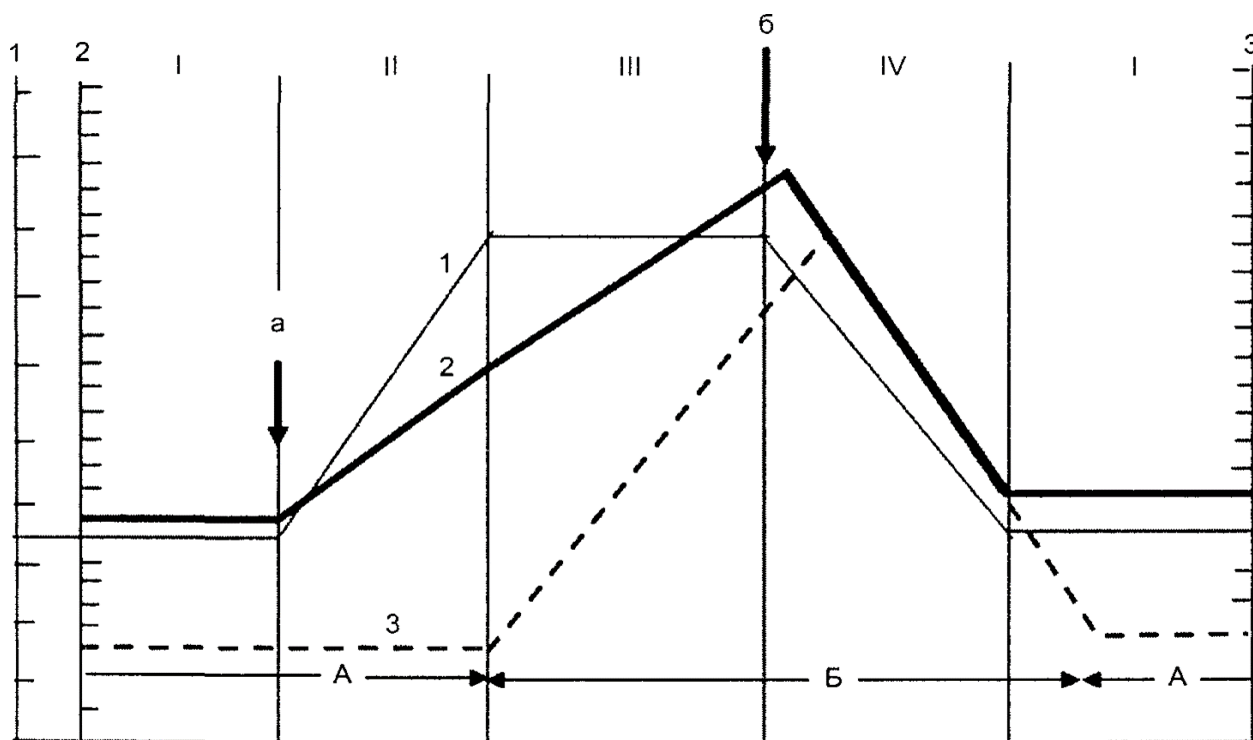
Pic. 10.3. The incidence of *Pseudomonas aeruginosa* infection in the urological hospital and the virulence of isolated strains (L. P. Zueva) *Pseudomonas aeruginosa* virulence index.

Against the background of regular isolation of weakly virulent races of *Pseudomonas aeruginosa*, before the outbreak, an increase in the incidence was detected, which was synchronized with an increase in the virulence of the isolated cultures of the pathogen, and a decrease in the virulence of the isolated cultures was accompanied by a gradual decrease in the incidence.

In favor of the above regulatory mechanism, there is evidence for airborne infections in relation to the host population (formation of population immunity), in relation to the parasite population - in airborne infections, which are characterized by the development of the infectious process both in the manifest and in the symptomatic form, as well as in diseases that are caused by opportunistic bacteria. However, the universality of this mechanism involved in self-regulation requires further study and confirmation, since there are facts that do not fit into the analyzed scheme. For example, with measles (an obligate pathogenic parasite), diseases, if it is not possible to intervene in the course of the infectious process, are almost always difficult both in the epidemic and in the inter-epidemic period (although, of course, it is difficult to imagine that the measles virus, which has unlimited opportunities for rapid reproduction and generational change, would not be subject to changes during the epidemic process, but other properties of the parasite may change). It is not clear the possibility of such a regulatory mechanism in infections of the digestive system, as well as infections in which The role of immunity (syphilis, yuroporea, HIV infection, mycoses, helminthiasis, etc.).

3. There is a phase self-restructuring of the parasite population, which determines the uneven development of the epidemic process.

It is this position that has been sharply criticized, although it is possible that the theory under discussion in this part, apart from the postulated strict sequence of the number and significance of phases, was to some extent ahead of the time of existing ideas and stereotypes. The authors believe that in the parasite population there are 4 consecutive phases * of reservation, epidemic transformation, epidemic spread and, finally, reservation transformation. On the example of acute airborne infections, the authors present a schematic diagram of the phase change (pic. 10 4).



Pic. 10 4. Phase changes in the pathogen population (scheme)
(V. D. Belyakov, G. D. Kaminsky, 1987).

On the abscissa axis - time periods, on the ordinate axis on the left - indicators of virulence (1) and abundance (2) of the pathogen population in arbitrary units on the right - incidence rates (3) in arbitrary units Arrows indicate the beginning of the change in the habitat of the pathogen a - reaching the quantitative threshold of susceptible b - achievement of a quantitative threshold of immune in the circulation chain of the pathogen Phase I - reservation II - epidemic transformation ill - epidemic distribution IV - reservation transformation Periods A - off-season (inter-epidemic) B - seasonal (epidemic).

An attempt to extend the presented scheme to all infectious diseases was subjected to especially strong criticism, and forced the authors to agree with the possibility of deviations from the picture shown in pic. 10.1 and in Table YL. Of course, in all cases it is very difficult to connect the development of the epidemic process with the given faunal transformations of the parasite, their sequence and significance. This applies to a number of intestinal infections, infections of the external integuments, and many chronic infections.

Phase Changes in the Parasite Population (on the Example of Infectious-Immunological Relationships with the Host Population).

Phase.	Habitat	Corresponde nce environment a habitat.	Degree heterogeneit y.	Selection type.	Virul ence.	Number.	Manifestation epidemic process.

Reserv ation.	host immune organisms	Corresponds .	Relative homogeneity .	Stabilizing.	Low.	low, stable.	End epidemic (seasonal) recession incidence and the main part inter-epidemic (off-season) period.
epidem ic transfor mation.	Passage (beginning) through susceptible individuals of the host. Immunolo gical trace	Not matches.	Generation of heterogeneit y followed by homogenizat ion.	Directed.	Grow ing.	Increasing (differential survival).	Pre-epidemic (preseason) period.
epidem ic spreadi ng.	Susceptibl e organisms. rise collective immunity	Corresponds .	Relative homogeneity .	Stabilizing.	High.	High increasing.	Epidemic (seasonal) rise in incidence.
Reserv ation convers ion.	Passage through immune individuals	Not matches	Generation of heterogeneit y followed by homogenizat ion.	Directed.	Decre asing.	Decreasing (differential death) after achievement s maximum numbers	The peak of the epidemic seasonal rise and the period of decline in the incidence.

4. The influence of social and natural factors on the formation and development of the epidemic process, which is generally recognized.

Self-regulatory processes in the scheme presented by V. D. Belyakov and co-workers are evident in anthroponotic airborne infections. In other groups of anthroponoses, there is no doubt that self-regulation processes also operate, but their mechanism is different (for example, in typhoid fever, to ensure the existence of a parasitic species, after suffering an acute infectious process, a certain group of carriers is formed, some of them retain the pathogen all their lives). Self-regulatory processes, in accordance with their own laws that have developed in evolutionary development, take place during zoonotic infections (for example, encapsulation of *Trichinella* larvae in the host's muscle tissue).

With regard to facultative parasites, one can apparently also speak of the possibility of self-regulation. When parasitizing among people, self-regulation is limited to the small space where facultative parasites live (for example, departments of hospitals are a place where conditions are formed for the preservation of conditionally pathogenic microorganisms due to self-regulatory processes, and this is obvious even with active influence on these microorganisms). It should be noted that the non-parasitic phase (ie, the existence of a facultative parasite in the external environment) is also in the conditions of self-regulation, but the factors that ensure the preservation of the agent are different, adequate to the external environment.

So, parasitic systems exist due to self-regulatory processes, but their nature is specific to each system.

Questions for chapter 10

1. Theory of self-regulation of the epidemic process
2. Population immunity
3. Phase changes in the pathogen population
4. Influence of social and natural factors on the formation and development of the epidemic process

Chapter 11

CLASSIFICATION OF INFECTIOUS DISEASES

Classifications are necessary to streamline the system of understanding and knowledge of the subject, as well as to organize a reasonable and consistent practical solution to the problems that have arisen. The meaning of the classifications lies in the fact that, first of all, a certain one cardinal sign is selected, according to which the differentiation of groups (in our case, infections) is possible, and then specific phenomena, events (individual nosoforms) are distributed among the groups. A multi-stage classification is possible. Attempts to carry out the classification of infectious diseases (infectious conditions) were carried out repeatedly. This was done by clinicians, microbiologists and other specialists, each time having in mind the solution of specific problems of the profession. However, these classifications were not universal.

The World Health Organization created the "Statistical Classification of Diseases, Injuries and Causes of Death", which is now accepted for use in many countries around the world. This classification is constantly being modernized (the classification of the Yuth revision is now in force) and is of great importance for the unification of the registration and accounting system: with its help, it is possible with a high degree of certainty (unfortunately, not only registration unification is important, but also the quality of accounting) comparison of morbidity in different countries. However, in this statistical classification there is no single system in the grouping of nosoforms (there is a separate group of infectious diseases, and then there is a grouping according to the localization of the pathological process - diseases of the circulatory system, respiratory organs, etc., which also include infectious diseases, for example, endocarditis, pneumonia, etc.).

Classification by etiology is possible (viral, bacterial infections, rickettsiosis, mycoses, helminthiasis, etc.). Differentiation into groups according to etiology is of great scientific and practical importance; it is not by chance that entire areas have developed - virology, helminthology, mycology, etc.

It is important to differentiate on the basis of the evolutionarily formed main host (main habitat) - into anthroponoses, zoonoses \ sapronoses.

L. V. Gromashevsky proceeding from the evolutionary basis; parasite localization and, accordingly, the transmission mechanism (see Table 8. proposed his own classification - the division of all infectious diseases into 4 groups. This classification is the most productive, although, as modern data show, it is practically suitable only for anthroponoses, however, there are some exceptions here (for example, *Staphylococcus aureus*, group A streptococcus, herp < type 1 virus exist as a species under the action of not one, but two transmission mechanism - airborne and contact). It is not always possible to apply this classification to zoonotic infections, as already mentioned, since in the animal world the existence of parasites

due to how many mechanisms of transmission is quite natural. In addition, it should be taken into account that human infection with animal parasites often occurs under the action of not an evolutionarily established mechanism of transmission, but random transmission routes. Meanwhile, it must be borne in mind that zoonosis] in the animal world is also supported by the evolutionarily developed mechanism (s) of transmission. And this provides a basis for classification (taking into account the choice of the leading transmission mechanism, if there are several of them). Despite some difficulties, the classification of L. V. Gromashevsky in relation to anthroponoses has firmly entered; our science and practice as the best available at the present time.

Questions for chapter 11

1. Classification of infectious diseases
2. Differentiation on the basis of an evolutionarily formed main host
3. Classification based on the evolutionary basis of the main localization of the parasite and, accordingly, the transmission mechanism

Chapter 12

CHARACTERISTICS OF THE EPIDEMIC PROCESS MANIFESTATIONS.

The epidemic process, its manifestations can be described (represented) both in terms of its origin (morbidity, constantly recorded in the observed population, or the penetration of the pathogen into the population from outside), and taking into account its quantitative, including dynamic, characteristics.

When the pathogen is introduced from the outside, they speak of **exotic** (exotic) diseases and morbidity. Thus, we classify as exotic for our country cholera, various tropical fevers (fortunately, the latter, when introduced, do not give further spread of diseases due to the lack of conditions for the transmission of the pathogen) and some other nosological forms. Exotic can include influenza caused by a new type of influenza A virus that originated outside our country, a new type of coronavirus infection (SARS). The WHO Regional Office for Europe set the task of achieving the elimination in European countries of the so-called indigenous (i.e. , and not adventitious) measles. It should be noted that nosoforms can be exotic for the population not of the whole country, but for residents of individual regions, regions, territories and smaller administrative units.

Endemic (endemic) refers to nosological forms that are constantly recorded in our country, i.e., the incidence of which occurs due to their own sources of infection. This modern concept of endemicity differs from the former interpretation of the term. Previously, nosoforms were considered endemic, which were constantly recorded among the population of only one region of the globe, but under certain circumstances spread among residents of other countries, previously free from the pathogen. These nosoforms always included cholera, which has long constantly affected the population of the Hindustan Peninsula (modern India, Pakistan, Bangladesh), but sometimes went beyond its permanent focus, causing pandemics, i.e., the incidence of the population of many countries and continents.

A proposal was also made to refer the concept of endemicity only to natural focal diseases, but this recommendation was not supported.

Modern infectious morbidity of the population and most of the nosological forms are endemic. The exclusion of such diseases from the category of endemic is possible only through the active, and most often very energetic and expensive intervention of society (vaccination of non-immune children, and in case of diphtheria and natural focal diseases - also adults; bringing the sanitary and hygienic state, in particular communal improvement, settlements in accordance with modern requirements, strengthening quarantine measures at the borders, etc.). It is also important to prevent the spread of morbidity due to internal foci, i.e., the formation of endemicity in case of drifts (exotic infections).

The quantitative characterization of the epidemic process has already been described to some extent (see the section "Method of Epidemiology"). Below are some additions. **Ordinary morbidity** is the prevailing level of morbidity under the influence of fairly stable social, natural and biological factors.

The calculation of the ordinary was proposed by V. D. Belyakov, based on the possible applicability in this case of the law of normal distribution. His proposal boils down to determining the arithmetic mean ($\bar{X}$) of several (5-8) years or months (depending on the goal: calculating a multi-year or intra-annual ordinary), and then calculating the standard (root-mean-square) deviation (σ). An indicator is taken as an ordinary $\bar{X} + 2\sigma$.

$$\sigma = \sqrt{\sum (X_i - \bar{X})^2 / (n-1)},$$

where $\bar{X}$ is the sign of the sum; X_i - each indicator taken to calculate $\bar{X}$, n - number of years (months) taken to calculate $\bar{X}$.

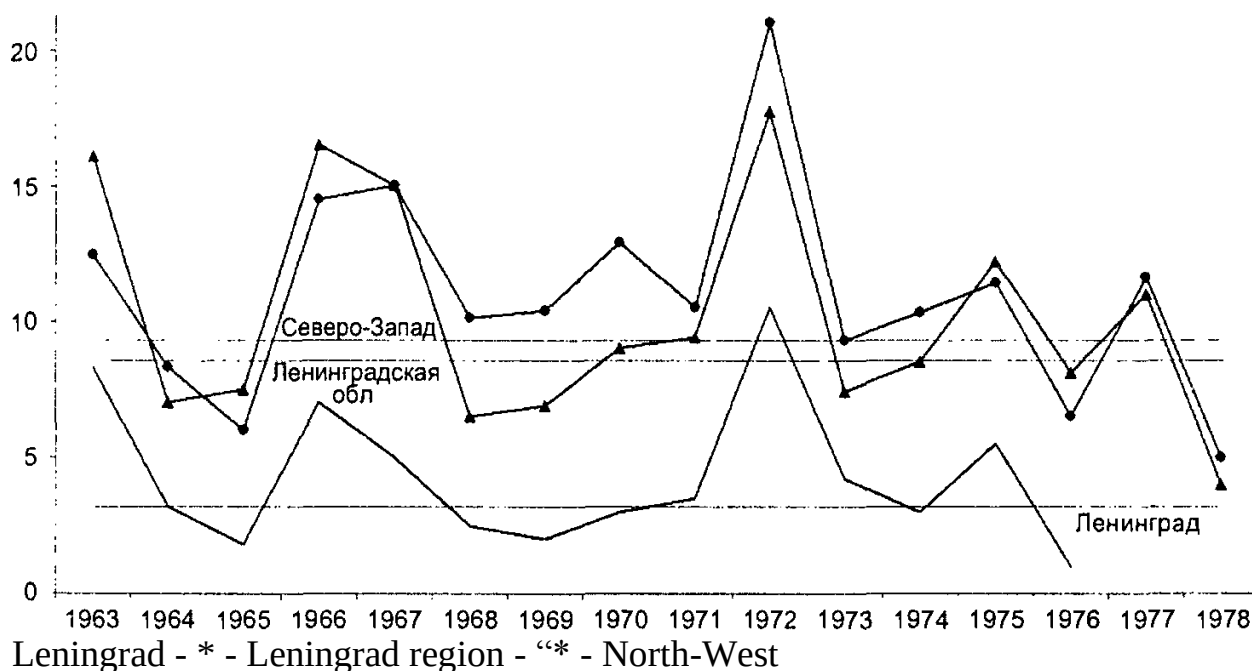
However, the above formula is not quite suitable, since the calculation of the ordinary does not provide for the determination of the spread of indicators from the average value, but the possible fluctuations of the average value itself, so the formula will be different:

$$\bar{X} + 2m,$$

where the average error $m = \sigma / \sqrt{n-1}$

There are a number of computer programs through which you can determine the ordinary.

The ordinary can be used to compare the significance of various nosoforms for the population of a country or individual territories (for example, comparing the ordinals of typhoid fever, dysentery, and viral hepatitis A); the significance of any one nosoform for different groups of the same population (children, adults, etc.) or for the population living in different territories; assess the origin of the disease (for exotic diseases, the ordinal is 0). Ordinary morbidity, apparently, cannot always be opposed to epidemic (an exception is exotic diseases), since an ordinary level can also indicate an unfavorable epidemic situation. Pic 12.1 shows that the incidence rate of dysentery in the Leningrad region and in the North-West of the country was significantly higher than in Leningrad.



Pic. 12.1. Dynamics of the incidence of dysentery in 1963-1978.

Apparently, in the first two cases, we are talking about a chronic water epidemic in many settlements. It is better, obviously, to talk about ordinary morbidity and morbidity above the ordinary. This refers, firstly, to cyclical rises (seasonality in relation to the intra-annual ordinary and rises in individual years within the framework of a multi-year cyclicity), and secondly, **outbreaks, epidemics and pandemics** that go beyond the cyclicity.

An **outbreak** is an increase in the incidence of the disease above the prevailing ordinary in some limited group (children's institution, school, some kind of enterprise, etc.), without the spread of diseases in space outside the affected group

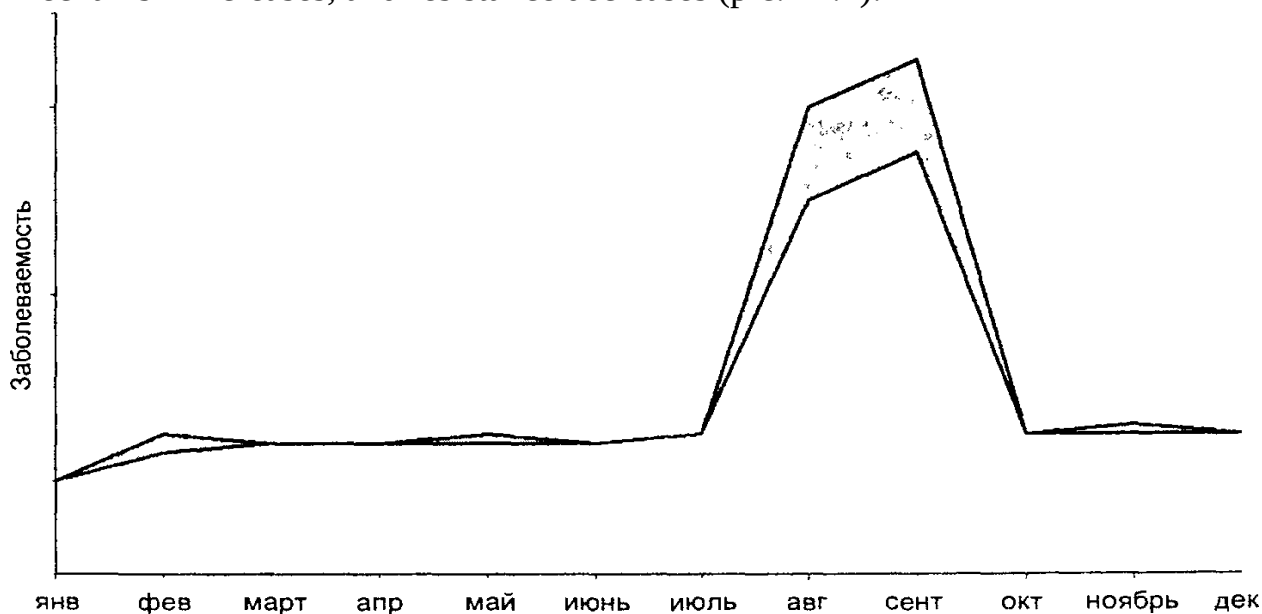
Epidemic - an increase in the incidence above the ordinary in a large population (city, district, region, etc.)

Pandemic - involvement in the epidemic process, which leads to an incidence above the ordinary, the population of many countries, continents or the entire population of the Earth.

It is necessary to dwell on one more term (concept) - **sporadic incidence**. This term is perceived ambiguously, some epidemiologists identify this concept with the ordinary (in particular, JI. V. Gromashevsky adhered to this point of view), others understand the appearance of diseases that do not have an obvious epidemic connection with each other, that is, about sporadic incidence is said in the absence of foci (the dominant idea of sporadic incidence). Meanwhile, it should be noted that sometimes in the form of sporadic cases, the sum of which leads to an increase in the ordinary level, an epidemic can develop. This is observed in cases where a sufficiently powerful source of infection, which led to the disease of many people who are not related to each other, is at some distance from the diseased (for example,

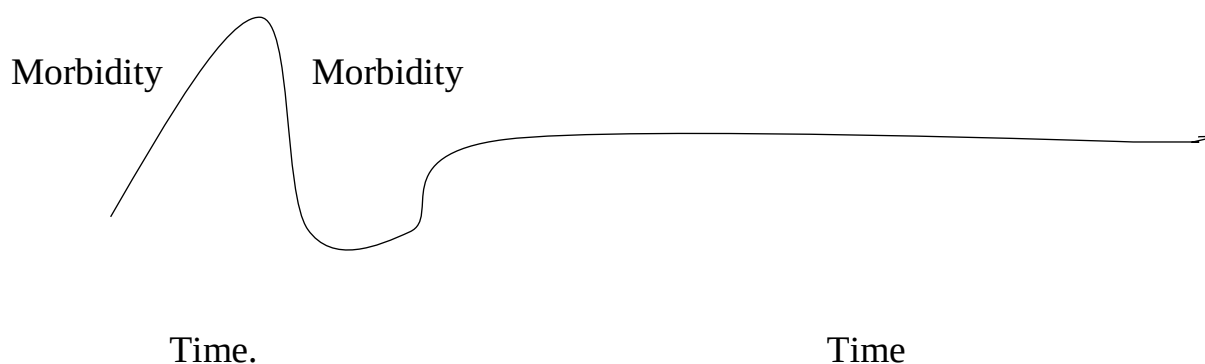
infection by a source of infection at an enterprise of some food product, which then goes to retail, etc.).

Speaking of outbreaks and epidemics, it should be noted that the likelihood of their occurrence during the seasonal rise is higher than in the off-season, since the number of infection sources increases, in some cases the activity of the transmission mechanism increases, and resistance decreases (pic. 12.2).



Pic. 12.2. Intra-annual dynamics of morbidity.

The ordinary is usually characterized only in static indicators (incidence, prevalence), since it is calculated using data from several weeks, months, years, i.e. it already reflects the average level of indicators that have changed over time. Outbreaks and epidemics, in contrast to the ordinary, are characterized not only in statics (the absolute number of cases, incidence), but also in dynamics: in time (acute, chronic - pic. 12 3) and in space (during outbreaks and epidemics).



Pic. 12.3. Acute and chronic epidemics.

The epidemic process during pandemics is characterized in exactly the same way - both in statics and in dynamics (in time and space - the sequence and degree of damage to the population of various countries and continents).

Questions for chapter 12

1. Characteristics of the manifestations of the epidemic process
2. Exotic diseases
3. Endemic diseases
4. Outbreak, epidemic and pandemic
5. Sporadic incidence.

Chapter 13

FACTORS OF THE EPIDEMIC PROCESS.

The possibility of the emergence and spread of morbidity among the population depends on three factors - **biological, social and native**.

The biological factor is the evolutionarily established character of the population relationships of biological species - the parasite and the genus. The biological factor reflects the specificity of the epidemic process (for example, each of the nosoforms - dysentery, measles, typhus, syphilis - have their own specific features of occurrence and distribution among people). The biological factor has a role in the formation of seasonality, in some cases - on the scale of the epidemic process (it determines - depending on the state of population immunity or the virulence of the pathogen, the incidence rate). This is especially evident in "children's" infections (children suffer - the non-immune part of the population), with natural diseases (newcomers, who have not been subjected to epidemics, are most often ill), the emergence of a new variety of para influenza A, the appearance of which leads to the development of pandemics (see .j cases "Influenza and acute respiratory infections"). The social factor is various forms of communication between people that contribute to or hinder the manifestation of parasitism (the degree to which people are centered in families, settlements, enterprises, educational and health institutions, sanitary and hygienic development of labor, life, places of recreation, the system and capacity of transport depending on the level of culture and material security of the population, the composition of the health care system, etc.)

The social factor determines the possibility and extent of the development of the epidemic process, it has an impact on the evolution of the parasite.

A general assessment of the social factor can be carried out according to the incidence or prevalence (and prevalence) of the population. At the present time, those infeu are the most dangerous and most common. for the pathogens of which the maximum possible distribution is ensured by the totality of the relationships of people in society. Close and diverse contacts of people in modern society lead to a high (highest) incidence of airborne diseases.

pelny (respiratory tract) infections, i.e. it is for this group of infections that modern social relations are the most adequate.

Very often, those nosoforms are designated as social, the distribution of which is associated with low material security and household disorder (tuberculosis, etc.) or violations of the existing sanitary and hygienic conditions (dysentery, typhus, etc.). In the case of these nosoforms, we are talking about the fact that some group of people differs in material or everyday characteristics from the largest possible part of the population (in our example, * a higher incidence of tuberculosis, dysentery, typhus), or the population of some regions or regions have communal amenities that do not meet modern requirements (in Pic. 12.1, the higher incidence of dysentery in

the Leningrad region and in the North-West of the country, compared with the ordinary in Leningrad, most likely reflects the consequences of poor-quality water supply). The examples given show the significance of some specific social conditions included in the general concept - the social factor, and reflect their significance in the spread of certain nosological forms or groups of diseases. Thus, the selective affection of certain groups or the population of certain regions serves as an indicator of the significance of one or another specific component of the social factor. In some cases, it is possible to conduct a targeted epidemiological assessment of the selective significance of a certain social factor. So, for influenza, which spreads especially rapidly in cities, in the 70s. 20th century a mathematical predictive model for the spread of the epidemic in the USSR was developed. The model was based on transport, mainly aviation, communications between the cities of the country. This model makes it possible to accurately predict the spread of influenza caused by new varieties of the group A virus across the country.

In some cases, the significance of the social factor acquires a particularly sinister meaning; wars and economic cataclysms lead to the mass spread of many infectious diseases, in particular parasitic typhus, venereal diseases, intestinal infections, and in some cases some natural focal diseases. This is also seen in the example of HIV infection. With HIV infection, which so far leads to the death of almost all those infected, the conditions that are developing in society (sexual promiscuity and perversion, drug addiction becoming more widespread) put the population of the country in a position of defenselessness, since natural sexual intercourse is very actively involved in the transmission of the virus. mechanism of transmission and intrauterine infection of the fetus. So far, our society, as it turned out, is not yet ready to resist the spread of HIV infection. Urgent energetic intervention of the state and society in the fight against this terrible disease is required (development, no matter how expensive, of means of prevention and treatment, extensive explanatory work, a more serious and consistent fight against drug addiction and drug business, etc.)

The natural factor is the climatic and landscape conditions, which, along with the social factor, contribute to or hinder the development of the epidemic process. This factor is especially important in natural focal diseases and in some transmissible anthroponoses (malaria, etc.). The natural factor, as well as the social one, influences through the biological essence of the epidemic process, affecting the population of both the host and the parasite, as well as the transmission mechanism (the latter is especially pronounced in transmissible infections). The role of the natural factor affects the development of seasonality. In addition, it is necessary to indicate the value of solar radiation, in particular, its fluctuations.

Questions for chapter 13

1. Factors of the epidemic process
2. Biological factor
3. Social factor
4. Natural factor

EPIDEMIOLOGICAL SURVEILLANCE

The anti-epidemic service, which was created to prevent the occurrence of infectious diseases, as well as to combat emerging infectious diseases, builds its work, taking into account the specifics of each nosoform, on the basis of epidemiological surveillance data.

Epidemiological surveillance is a continuous assessment of the state and trends in the development of the epidemic process in order to determine the reasons for its development and make timely decisions that ensure the implementation of measures adequate to the situation.

In other words, the diagnostic activity of the anti-epidemic service, designed to carry out targeted measures, is organizationally implemented in the system of epidemiological surveillance. Epidemiological surveillance is carried out in anti-epidemic institutions of all levels, and a mandatory exchange of information between institutions of adjacent levels is provided.

The success of diagnostic work depends, first of all, on the accuracy and reliability of registration and accounting of patients. However, it must be borne in mind that so far nowhere and never has there been absolute accuracy and reliability. This is due, as already mentioned (see "Method of epidemiology"), with a number of circumstances:

1. Diagnosis of diseases, which determines their further registration, depends on the qualifications of clinicians and their attitude to recording not only clinically pronounced cases, but also mild, "atypical" forms (such "atypical", mild diseases can dominate in some nosological forms). Currently, in order for mild forms not to pass by specific diagnostics and registration, the so-called "standard case definition" is being developed and proposed, which indicates all possible features of the manifestation of the corresponding nosoform. Unfortunately, in natural conditions, if the disease proceeds easily ("atypically"), the possibilities for differentiating different nosological forms are narrowed, since identical or almost identical manifestations can be in various diseases.

In a number of cases, epidemiological data are important, and sometimes decisive: most often in the context of a developed or developing outbreak, especially a local one, as well as in mass morbidity, for example, during an influenza epidemic.

Laboratory, especially microbiological, studies help (the latter, as a rule, only with positive results, and also by no means always, since against the background of the development of a mild form of one disease, carriage of other pathogens is possible). Laboratory methods are often useful in dysentery, diphtheria (isolation of a toxigenic strain of diphtheria bacillus) and some other nosological forms. Unfortunately, such microbiological confirmation of the disease is not always possible. In particular, with viral infections, laboratory tests are usually not used for individual diagnostics (an exception is HIV infection) because of the high cost, duration of the study, and the need to have an appropriate, well-equipped laboratory. However, virological

studies are used to determine the nature of the emerging epidemic, especially in influenza epidemics. With helminthiases and diseases caused by protozoa, a diagnosis without laboratory confirmation is impossible.

The use of immunological methods for some infections gives satisfactory results (paired sera test). Unfortunately, these methods are often belated, so they are not always important when solving operational problems.

So, the diagnosis of mild forms of infection largely depends on the qualifications of the doctor, who, in particular, must take into account laboratory data and the epidemic situation. Great difficulties arise when it is necessary to take into account asymptomatic forms. This problem has arisen most acutely in connection with the spread of HIV infection. The existing system of laboratory examinations, mainly of risk groups (drug addicts, homosexuals) and pregnant women, cannot characterize the state of affairs in society, since the natural route of transmission (heterosexual contacts) is gradually becoming dominant. The same, but less painful for society, situation has developed with regard to the carriage of hepatitis B and C viruses (the same natural sexual transmission).

2. The completeness of registration and accounting of patients depends on the behavior of the patients themselves. In some cases, sick people do not consider it necessary to seek medical help. This applies, of course, primarily to people suffering from mild forms of illness.

Non-working people often find themselves outside the boundaries of official registration and accounting, since for them the issues of social insurance become relevant only when hospitalization is necessary.

3. Conscious underestimation of morbidity rates, which, unfortunately, still occurs. This deliberate underestimation of the registration and registration of patients, especially those suffering from mild forms of illness, takes place not only in the practice of polyclinics and anti-epidemic institutions, but also in hospital conditions. We are talking about purulent-septic infections (GSI), which are caused by opportunistic pathogens and therefore, at first, often develop in a mild form. However, such non-severe forms of HSI, which are not given due attention, quite often conceal a great epidemic threat. Lack of attention to them (or insufficient attention), leading to a decrease or even neglect of the requirements of asepsis and antisepsis, especially outside the operating unit - in the dressing room, procedural, etc., inevitably leads to the formation of hospital virulent strains that cause nosocomial, sometimes severe infections and even outbreaks.

Such incomplete registration (which, of course, must be combated by selecting adequate, but by no means always strict administrative measures) in each place, in each administrative unit, has a certain, more or less constant value, i.e., an error in accounting carries in itself to some extent a standard, systematic error. As a result, if it is required to evaluate events developing over time, then it is sometimes possible to obtain a relatively reliable picture of the dynamics of the epidemic process in

epidemiological diagnostics. However, all these shortcomings in registration and accounting can lead to a fatal error and conclusions when comparing the incidence in different administrative territories, therefore, when determining areas (places) of risk, great care is required and a thorough study of the existing system of registration and accounting for each taken for comparison. territory.

Thus, the first task of practical institutions in diagnostic work is the streamlining of registration and accounting, their unification in different territories, that is, the development of uniform criteria in this respect and their strict implementation.

The actual diagnostic work consists of two closely related and complementary components - operational and retrospective epidemiological analysis.

14.1. Operational analysis

Operational analysis is carried out taking into account the general epidemiological assessment formulated on the basis of a retrospective analysis (see below). Operational analysis, which organically includes the epidemiological examination of foci, as the name itself shows, provides for constant, continuous monitoring of the epidemic situation.

We are talking about daily, weekly, and sometimes monthly (operational analysis) recording of registration data, i.e., the incidence rate is constantly assessed, taking into account the structure (the degree of BOBJ in the epidemic process of various population groups), the territorial distribution of diseases, as well as the dynamics over time . The latter is caught mainly in the evaluation of weekly and monthly indicators. However, in acute, most often food, outbreak> daily dynamics is of great importance. In essence, operational analysis is based on the idea of constant monitoring of possible changes in the epidemic situation.

So, the task of operational epidemiological analysis is to quickly (immediately) identify the fact of a change in the current level of morbidity and establish the causes of this change, i.e., you mean determining the development of outbreaks (both local and diffuse> deciphering their essence.

That is why, in order to assess changes, it is necessary to have an idea of the usual indicators characteristic of a given time and period, i.e., one should have information about the ordinary (for operational analysis, depending on the nosological form and the observation period of daily, weekly, sometimes monthly) on favorable stages (see page 129). The ordinary level serves as a standard, according to which possible changes in the development of the epidemic process are established.

As a rule, along with information about the general ordinary level, it is necessary to have an idea of the ordinary levels for various groups of the population (different age groups attending and not attending childcare facilities, residents of different territories, etc. Data are not only of the general ordinary level, but also of differentiated for various population groups contribute to a more accurate assessment of possible changes in the epidemic situation, in particular when

identifying outbreaks during a seasonal rise, since it is very difficult to determine outbreak incidence against the background of a general rise in incidence. different groups of the population in a more or less prosperous period, as well as at the stage of a low seasonal rise.

On the basis of registration data, which are entered into a computer or a special journal, epidemiologists set themselves two napaj ly performed tasks:

1. For each nosoform, an epidemiological scheme is compiled, which can be based on a weekly period of time (Table 14.1).

Approximate Accounting Worksheet Schema

table 14.1

	1 Week			Similar to 2-4 weeks	Total for 4 weeks	
	Data for days 1, 2, 3, 4, 5, 6.7	total	Differences with the established ordinary (yes / no)		total	Differences with the established ordinary (yes / no)
Total						
Children under two years of age, including those attending kindergartens, including those in orphanages						
Children aged 3-6, including those attending kindergartens, including those in orphanages						
Schoolchildren, including those living in boarding schools, orphanages, etc.						
Adult students, including those living in hostels						
Professions						
Professions						
Place of residence (city / village, district,						

conditional division of the controlled territory, etc. - it is advisable to use symbols)			
Foci (two or more cases) in the family, in a children's institution, etc. - use symbols			

Notes. 1-When calculating the ordinari, it is necessary to use the weekly indicators of ordinars in prosperous months

2-To assess events during the period of seasonal rise, it is necessary to determine the ordinary level for this time in prosperous years, i.e., with a low seasonal rise

3-preschool educational institution - children's health institution

2. Generalization (systematization) of data from an epidemiological survey of foci to determine specific, sometimes dominant, causes of diseases
 Exceptions are data on isolated cases of exotic diseases that pose an epidemic danger (chollera, maparia, etc.), sometimes natural focal diseases, as well as manageable infections, including infections from outside (measles, poliomyelitis, etc.). In addition, an epidemiological survey of single (sporadic) cases is necessary with a diffuse distribution of diseases, the total number (or incidence) of which obviously (significantly) exceeds more or less the established ordinary. In such a situation, i.e., in the event of the occurrence of many single foci, an epidemiological examination is mandatory and provides for the indispensable detection of some common factor (using the logical method of similarity). For example, one that gives a similar picture of possible contamination (use of the same dairy product made at the same dairy, etc.). In some cases, there may be more than one such common factor. In such situations, it is necessary to establish the level of significance of each factor, i.e., to determine the percentage of its occurrence: the higher this indicator, the more likely its etiological significance. Thus, the growth of sporadic morbidity, which determines the incidence rate above the ordinary, indicates the development of an outbreak and, therefore, in each focus, during an epidemiological examination, it provides for the search for a possible cause (this work in such a focus differs from the epidemiological examination of a single focus, which does not change the overall level of incidence).

Examination of multiple foci (2 or more cases) is carried out in the system of operational analysis on a mandatory basis, since in such foci there is a certain probability of finding the cause of the diseases that have arisen. In this case, it is advisable to use graphs, diagrams, put on paper or a computer screen the spatial distribution of diseases. The epidemiological survey system is presented in the diagram (p. 24 in the section "Method of Epidemiology").

Below are the variants of the tables that are filled out on the basis of the data of the epidemiological survey of the foci (Tables 14.2 and 14.3).

The mentioned scheme (p. 24), which is intended for entering epidemiological survey data, in case of transmissible anthroponoses, primarily in case of typhus, should reflect all aspects of the sanitary and hygienic state of dwellings, places of usual stay, as well as places of casual stay (departure to disadvantaged regions), the presence of body lice, etc.

In natural focal diseases, depending on the nosoform, a specific set of information is used. For example, in case of hemorrhagic fever with renal syndrome (HFRS), visits to forest or shrub moist areas, living in summer cottages or in garden plots, the presence of rodents (voles) in the last ones, the density of rodent colonization of premises, etc. should be reflected.

If tick-borne encephalitis or borreliosis is suspected, data on the population density of ixodid ticks, visits to forest areas, tick attacks, the duration of bloodsucking of attacked ticks, and other data that can help, first of all, clinical and then epidemiological diagnosis, are evaluated.

With hepatitis B and C, HIV infection, when it comes to adults and adolescents, information is needed on sexual (especially casual) relationships, on the use of intravenous drugs; for all about blood transfusions and other invasive medical manipulations.

Table 14.2

Approximate scheme of the table for intestinal infections, filled out on the basis of the examination of foci (separately for each nosoform*)

	1 Week		Similar to 2-4 weeks	Total for 4 weeks
	Data for days 1, 2, 3, 4, 5, 6, 7	total		
Purchase of products: ■ at the store ■ on the market ■ own production				

Manufacturers of used dairy products (name, No.): ■ milk ■ sour cream ■ Other foods that may be of epidemic importance (meat, for pseudotuberculosis - fruits, etc.)			
The nature of the water supply: ■ plumbing ■ well • open reservoir ■ occasional water source			
Data (if any) of a microbiological study of water in the area of diseases that have arisen			
Bathing (what body of water)			
Place of occurrence of the disease (house, number of preschool educational institution, number of the orphanage, orphanage, boarding school, school number, etc.)			
Compliance with the requirements of the sanitary and hygienic regime (especially when cooking) - it is			

advisable to use symbols			
The first case of the disease, the second, third, etc. in the focus (symbols can be used)			

The table is compiled separately for dysentery Sonne, Flexner (with type designation), VGA, OKINE.

During the epidemiological examination of the focus, various laboratory techniques are widely used that allow (help) to establish epidemic links, identify sources and transmission factors, determine the most vulnerable groups of the population, and in some cases predict the situation. Microbiological and, in some nosoforms, immunological studies are especially important. Microbiological methods are used not only to establish the fact of pathogen circulation, but also for intraspecific typing of a microorganism (determining the features of the antigenic structure, antibiogram characteristics, sensitivity to a set of diagnostic phages, virulence, including toxigenicity, etc.). This makes it possible to establish epidemic links and transmission factors during epidemiological examination of foci, and with constant monitoring, to predict the epidemic situation. Immunological methods can be useful for clarifying the diagnosis of the disease, identifying vulnerable groups (individuals), and with constant monitoring of the state of population immunity (airborne and natural focal diseases, poliomyelitis) - predicting the epidemic situation and assessing the quality of the specific prophylaxis carried out.

Table 14.3

Approximate scheme of the table for airborne infections, filled on the basis of the epidemiological survey of foci (separately for each nosoform)

	1 Week		Similar to 2-4 weeks	Total for 4 weeks
	Data for days 1, 2, 3, 4, 5, 6.7	total		
Location of disease (home,				

No. preschool educational institution, orphanage, orphanage, school, etc.)			
Terms of isolation (hospitalization) from preschools, schools: etc. after the onset of the disease (number of days)			
First (second, third, etc.) case in the outbreak			
In the presence of specific prophylaxis, patient compliance with the vaccination schedule (vaccination, revaccination) - yes / no			
The presence of susceptible people among those who communicated (had not previously been ill, not vaccinated, vaccinated in violation of the vaccination and revaccination regulations) - yes / no			

So, although the epidemiological examination of foci often does not allow us to find the cause of diseases, when entering its data into a specially prepared generalizing (summary) table, the materials of the latter contribute to solving the problem of operational analysis. This refers to the possibility of epidemiological diagnosis when comparing the materials of this generalizing table with the data of the above accounting table.

14.2. Retrospective analysis

The meaning of a retrospective analysis is that, firstly, it gives an exhaustive description of the epidemic process in statics (the level in a selected period of time) and in dynamics over the past period. Secondly, it reveals (should reveal) the causes and leading tendencies of their action, which determined the epidemic situation in the past (not the recent past).

These trends are usually stable, so they allow extrapolating the data obtained for the next period. In addition, retrospective analysis determines the effect of the actions taken, especially if any changes were made to them during the analyzed period.

A retrospective epidemiological analysis is carried out annually - in time it coincides with the annual report on the activities of the anti-epidemic institution, but this does not mean at all that it cannot be carried out if necessary at any time of the year.

It is especially valuable if a retrospective analysis is carried out for many years (annually) according to a single scheme. With such a system of work, as a rule, the main (stable) trends in the nature and causes of the development of the epidemic process are well established, and the effect of some random phenomenon (outbreak) that distorts the overall picture of the development of the epidemic process is also traced. However, in a retrospective analysis, it is only possible to state the fact of an outbreak that has taken place; its causes, as already mentioned, can only be established with a professionally conducted operational analysis. It should also be noted that only on the basis of long-term data it is possible to assess the situation for the expiring (expired) year. Retrospective analysis is largely based on data that is collected and systematized constantly during operational analysis, therefore, both the effectiveness of retrospective analysis and the amount of work performed in this depend on the quality of the latter.

In addition, the following information is required for retrospective analysis'

- detailed general records of infectious diseases, including those that could not be used in operational analysis;
- data on the demographic characteristics of the population,
- data on social and natural factors, on their possible changes (for example, on differences in the level of average summer air temperature in certain years);
- data on the sanitary and hygienic characteristics of the water supply system, food, housing, children's institutions, etc.;
- data on compliance with legislation on specific prophylaxis.

At the level of regional, regional, cities of Moscow and St. Petersburg specialized anti-epidemic institutions, the so-called monitoring of the possible development of the epidemic process in the actual groups of infectious

diseases is constantly carried out (some airborne infections, especially controlled by means of specific prophylaxis, poliomyelitis, natural - focal diseases). The data of such tracking (characteristics of population immunity, taking into account age characteristics, in case of natural focal diseases also territorial distribution; the level of carriage of virulent varieties of the pathogen; the density and infestation of populations of wild animals and arthropods - sources and carriers of pathogens of natural focal diseases, etc.) are also important in retrospective analysis.

A retrospective analysis is carried out in relation to each noso-form separately. In those cases when, under one officially recognized clinical nosoform, diseases caused by various pathogens are combined, along with a general assessment, there is a need for a separate analysis of various etiological forms (general dysentery, Flexner and Sonne dysentery, coli-enteritis in total and coli- enteritis caused by E. coli of various antigenic variants, etc.).

The retrospective analysis consists of 4 sequentially implemented parts (stages):

1. Drawing up an analysis program taking into account the specifics of the nosoform.
2. Grouping the collected material into tables (filling in the tables) and then visualizing these tables in the form of diagrams, graphs, cartograms, etc. in accordance with the developed program.
3. A descriptive stage for stating facts (a general description of the epidemic process in statics and dynamics - in time and space; the incidence of different population groups also in statics and dynamics).
4. Analytical stage (the actual analysis to identify cause-and-effect relationships).

The first stage is the compilation of a program that allows characterizing the incidence of the population as a whole and its various groups not only in statics, but also in dynamics - in time and space. In essence, the program is a collection of stencil tables. Thus, the program provides in the future, i.e. in ripo-during the implementation of a retrospective analysis, identification of risk groups, places (territory) of risk, time of risk, and at the analytical stage also risk factors - establishing the causes of current epidemic situation. This set of stencil tables is generally standard for each nosoform, it is prepared in advance on the basis of available scientific and practical data, which is why a long-term retrospective analysis is possible (Tables 14.4, 14-5). However, it must necessarily take into account local characteristics and the current situation, which may have certain specifics. In addition, this set should be constantly amended, taking into account the latest theoretical and practical data.

Table 14.4

Long-term dynamics of morbidity (incidents) in terms of age

Age groups	sick	Years				
		20..	20..	20..	20..	20..
0-2 years	abs					
	Incidence (per 100 thousand of this age group)					
3-6 years old	abs					
	Incidence (per 100 thousand of this age group)					
7-14 years old	abs					
	Incidence (per 100 thousand of this age group)					
15-19 years old	abs					
	Incidence (per 100 thousand of this age group)					
20 years and older	abs					
	Incidence (per 100 thousand of this age group)					
Total	abs					
	Incidence (per 100 thousand of this age group)					

Notes. 1 In modern reporting documents, two groups most often appear - the total number of cases, including children under 14. This is acceptable for obtaining generalized information, but cannot serve analytical purposes

2 In some cases, it is important to divide the 0-2 year group into two - up to 1 year and from 1 year to 2 years. This division is advisable for meningococcal infection, coli-enteritis and other diseases in which children under 1 year old are the most vulnerable group of the population (risk group) But this is possible if the group of children under 1 year old is not too small.

Table 14.5

Long-term dynamics of incidence in various groups (per 100 thousand of the population of the corresponding group)

Age groups	social group	Years				
		20..	20..	20..	20..	20..
0-2 years	Complete home education					
	Visiting preschool					
	Living in children's homes					
3-6 years old	Complete home education					
	Visiting preschool					
	Living in orphanages, orphanages					
7-14 years old	Pupils					
	Children of boarding schools or other closed institutions					
15-19 years old	Pupils					
	Children of boarding schools or other closed institutions					
	Students of secondary specialized educational institutions, universities					
	Including 1st year students living in a hostel					
	Workers, employees					
20 years and older	Students of secondary specialized educational institutions, universities					
	Food business workers					
	Medical workers					
	Other workers and employees					
	Working in the field of agriculture (livestock)					
	Non-working (pensioners, etc.)					

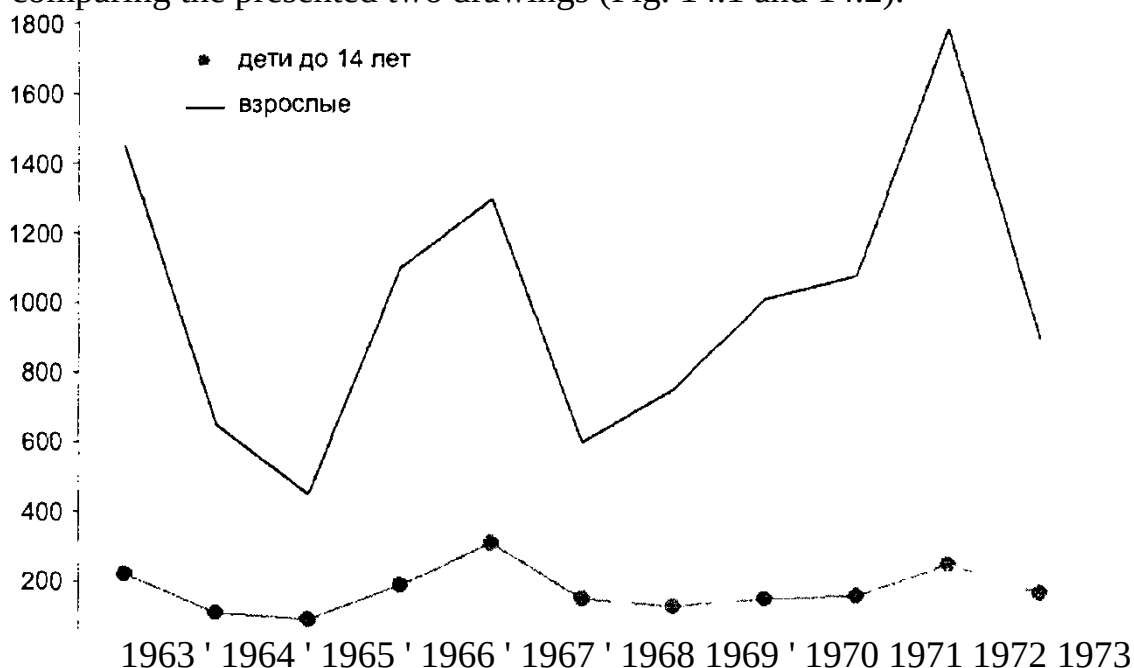
Notes. 1 Professional and other social grouping in a number of cases is determined by local conditions and therefore may have individual characteristics, for example, if a large enterprise is, as they say now, a city-forming enterprise, that is, it significantly determines the way of life of the majority of the population, then —need to differentiate part of the population by work in various functional parts of the enterprise, etc.

2 Differentiation of the population into social groups with different nosological forms may differ. In particular, with intestinal infections, parasitic typhus and zoonoses, it most often does not make sense to single out a group of students (students) of the 1st year living in a hostel (although without dividing into courses, the social group “accommodation in a hostel ”may have a certain meaning)

The group “workers of food enterprises”, if we consider airborne infections, can be excluded, it can also be excluded from the analysis of the causes of the development of the epidemic process in viral hepatitis A

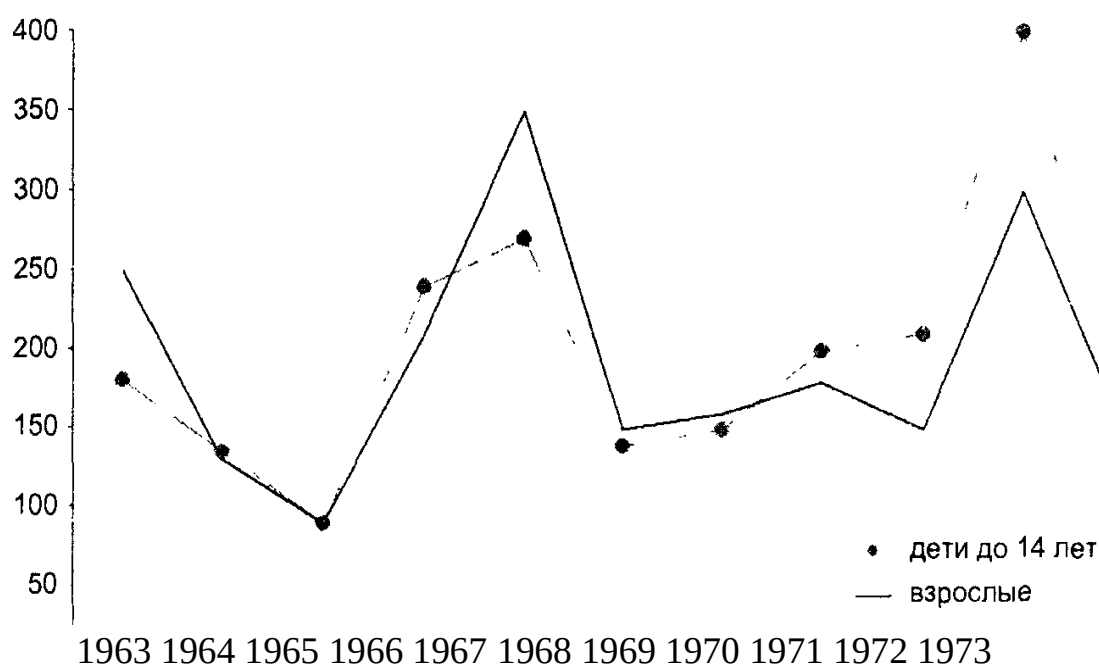
The group “working in the field of agriculture, especially animal husbandry” is important for zoonotic infections and sometimes for streptococcal infections

In a number of cases, when assessing long-term dynamics in different population groups, in order to identify a trend, it is advisable to present the material not in intensive indicators, but in so-called visibility indicators, taking for each group the incidence in any year as 100% (for all groups the original, i.e., 100%, must be the same year). This can be demonstrated by comparing the presented two drawings (Fig. 14.1 and 14.2).



Pic. 14.1. Dynamics of the incidence of dysentery in adults and children under

**14 years of age
in the Kalininsky district of Leningrad in 1963-1973.(per 100 thousand of the
corresponding age group)**



Pic. 14.2. Dynamics of the incidence of dysentery in adults and children under 14 years old in the Kalininsky district of Leningrad in 1963-1973. (in terms of clarity)

In case of nosoforms, for the prevention of which specific prophylaxis means (vaccination and revaccination) are used, as already mentioned, a table for accounting for the percentage of vaccination coverage is introduced into the retrospective analysis program (Table 14.6). In addition, since, if possible, selective immunological studies are carried out approximately six months after vaccination of persons who, according to the plan, were (should have been) vaccinated and revaccinated, the program should include a table reflecting this activity (Table 14, 7). Indicators of the usefulness of the specific prevention carried out are of great importance at the analytical stage.

Table 14.6

Vaccination coverage percentage (vaccination and revaccination)

	Years				
	20..	20..	20..	20..	20..
Vaccination					
1st revaccination					

2nd revaccination					
Adults					

Table 14.7

Data of selective immunological testing of the quality of ongoing specific prophylaxis

	% of individuals with protective titers or geometric mean titer				
	20..	20..	20..	20..	20..
Population age of vaccination					
Population at 1st revaccination age					
2nd revaccination age population					
Revaccination age population					
Adults					

All of the above templates of tables should be prepared not only for data characterizing the population of the study area as a whole, but also for individual places included in this territory (urban residents - residents of rural areas, residents of different cities; residents of different districts of the city; residents of different rural areas, residents of places with different climatic conditions, residents of industrial zones - residents outside the industrial zones, etc., etc.).

Along with the long-term dynamics of morbidity in a retrospective analysis, the assessment of intra-annual dynamics is of great importance. It is important not only to establish the magnitude and duration of the seasonal rise, but also to determine causal relationships, since in many nosoforms a high annual incidence rate is usually determined by a high level of seasonal rise. In other words, to understand the reasons for the high annual level, it is necessary to decipher the reasons for the high seasonal rise in the incidence. In some cases (for example, with meningococcal infection), when searching for the causes of a change in the epidemic situation, it is important to compare not only the indicators of the seasonal rise, but also the off-season level that has developed in different years. In addition, as already mentioned, when studying the intra-annual dynamics, it is possible to state the fact of an outbreak that took place if it was outside the established time of risk. That is

why the retrospective analysis program includes stencils of tables characterizing the intra-annual dynamics of the incidence of the entire population (Table 14.8), as well as its various groups (age, living in different territories, etc., etc.). In other words, monthly dynamics must be available not only for the entire population as a whole, but also for all groups that were presented in Table. 14.5, i.e., at the stage of program development, all these table templates must be prepared. In the same way, tables of monthly dynamics should be prepared for the population of different places in the aggregate and differentiated for individual groups (in strict accordance with the division in assessing long-term dynamics).

Table 14.8

Distribution of diseases by months (intra-annual dynamics) last year

	months of the year												
Abs	I	I	II	I	V	V	VI	VII	I	X	X	XI	total
	I	I	I	V		I	I	I	X		I	I	
In % of the annual total													
In intensive terms (per 100 thousand population)													

Notes, 1. The distribution of diseases by months is possible in any given variant (absolute numbers,%%, intensive indicators), in some cases all variants are necessary

2 Intensive indicators are appropriate only if the main migration processes are under control during the observed year (summer trips to summer cottages, summer recreation facilities, etc.) If it is possible to take into account these migration processes, then intensive indicators reflect intra-annual dynamics particularly accurately.

When studying the nature of the development of the epidemic process, foci are important (it can be used to judge local - in the focus - conditions for the spread of diseases, about vaccination work with noso-forms controlled by means of specific prevention, etc., etc. and,), therefore, at the stage of program development, appropriate stencils of tables should be prepared (Table 14.9) and indices should be proposed to evaluate this phenomenon.

Table 14.9

Quantitative characteristics of foci

	Foci with number of cases				Total foci
	1	2-4	5-10	over 10	
Among the general population					
In families					
in preschool					
In the children's homes					
In orphanages					
In schools					
In boarding schools and other closed educational institutions					
In children's summer health institutions					
In dormitories of secondary specialized and higher educational institutions					
At enterprises					

Notes. 1. Data in the table is entered as a fraction: in the numerator - the number of outbreaks, in the denominator - the number of cases.

2 In everyday practice, a system has been adopted for recognizing foci as multiple if 5 or more cases of the disease are recorded in them. Such a system may be convenient, but it will never allow us to understand the true cause of focality, which operates in a given population.

$$\text{average number of cases per outbreak} = \frac{\text{total number of cases}}{\text{total number of foci}}$$

$$\text{proportion of the number of cases in multiple foci} = \frac{\text{number of cases in multiple foci}}{\text{total number of cases}} \times 100\%$$

$$\text{mean number of cases in multiple lesions} = \frac{\text{total number of cases in multiple lesions}}{\text{total number in multiple lesions}}$$

$$\text{specific gravity of the number of multiple foci} = \frac{\text{number in multiple lesions}}{\text{total number of foci}} \times 100\%$$

There are other indicators that characterize focality. When developing a retrospective analysis program for some nosological forms, it is necessary to take into account the possibility of disability and death. In this regard, stencils of additional tables are being prepared (Table 14.10). They provide for the registration of the absolute numbers of the dead, as well as columns for calculating mortality and mortality for the entire population and for risk groups (for example, with meningococcal infection for children under 1 year old or up to 2 years old; with tick-borne encephalitis - for visitors to natural hearth zone, etc.

Table 14.10

Data on deaths in absolute numbers and mortality rates

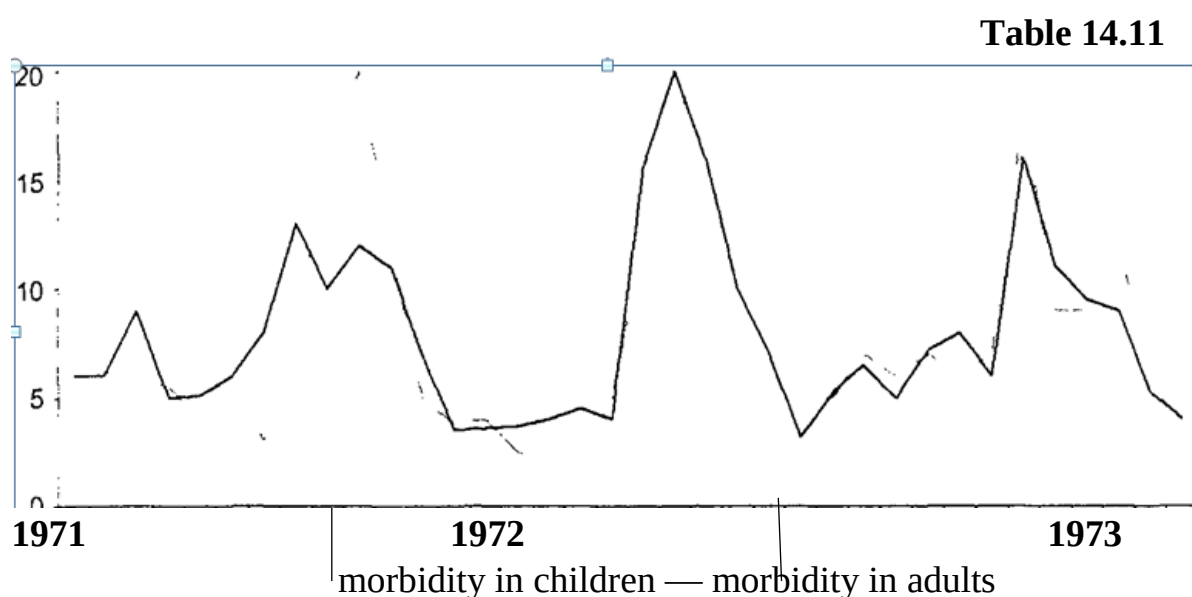
Age groups	Years				
	20..	20..	20..	20..	20..
0-2 years					
3-6 years old					
7-14 years old					
15-19 years old					
20 years and older					
Total					

Notes 1 Data on deaths are given as a fraction of the absolute number of deaths / mortality per 100 thousand of the population of the corresponding group

2 Most often, mortality (due to the small number of deaths) is given only for the entire population, and for certain age groups only absolute numbers of deaths can be indicated. But if an abnormal number of deaths is found in any age group, then for this part of the population, mortality should be also presented

In some cases (meningococcal infection, poliomyelitis, tick-borne encephalitis, etc.), when drawing up a program, it is necessary to provide for the definition of disability (see Appendix 1) and disability, both for the entire population and for the most vulnerable groups of the population The last index (a fraction in which the numerator indicates the number of disabled people among the population, multiplied by the selected coefficient - 100, 1000, etc., the denominator - the total number of the population) allows us to determine the social significance of the nosoform. Here are some, but by no means all necessary tables - their number and structure are determined by the nature of the studied nosoform and the task

The second stage of the retrospective analysis is filling in the stencils of the tables, calculating the indices and, for clarity, a graphical representation of the data compared groups of the population, it is often expedient to use indicators as a percentage in relation to any year, taken as 100%, or in relation to the annual total, taken as 100%. Such a system allows you to get visual comparable data in cases where when different population groups have significant differences in incidence. This is especially demonstrative when using a graphical representation of data (Fig. 14 3)



Pic. 14.3. Monthly dynamics of the incidence of Sonne dysentery in children and adults(in terms of visibility)

Intra-annual dynamics can be presented in aggregate for a number of years (say, for 5 years) or for a year. In the latter case, with high indicators in the first months of the year, it is advisable to compare them with the data of intra-annual dynamics in the previous year, since the indicators in the first months of the year under study can reflect the epidemic process, the beginning of which was laid earlier. This often occurs with viral hepatitis A.

This is due to the fact that the epidemic year does not correspond to the calendar - it usually begins in September-October.

At this stage, all indicators of incidence, prevalence, focality, disability, lethality, mortality, etc. are calculated. In some cases, it may be difficult to determine the incidence. This is due to the fact that the population may change (migration especially intra-annual - summer vacations, etc. However, despite the difficulties, this indicator must be calculated, since without it it is impossible to count on the effectiveness of retrospective analysis Mortality, which indicates the severity of the infectious process or, in some cases, as therapeutic measures, as already mentioned, it is presented as a percentage of deaths among those who fell ill with one or another nosoform. However, it must be remembered that the mortality rate significantly depends on the accepted system of clinical and laboratory diagnosis of infections and, accordingly, registration and recording casualties On the other hand, with the help of the indicator

mortality, it is possible to compare the consequences of the disease not only for population groups that are fully (or almost completely) taken into account, but also for those whose total number may not be known (migrants, refugees, homeless people, etc.). The above indices (coefficients) make it possible in the future to judge the essence of the potential opportunities for the development of the epidemic process in the affected populations (collectives), as well as, in some cases, the timeliness and effectiveness of the anti-epidemic measures taken in the event of unfavorable conditions.

It should be noted that sometimes it is possible to use extensive indicators for the convenience of perception. For example, having data on the incidence of bacteriologically confirmed dysentery, it is possible to represent the role of individual pathogens as a percentage (for example, Flexner's dysentery - 40%, Sonne's dysentery - 60%).

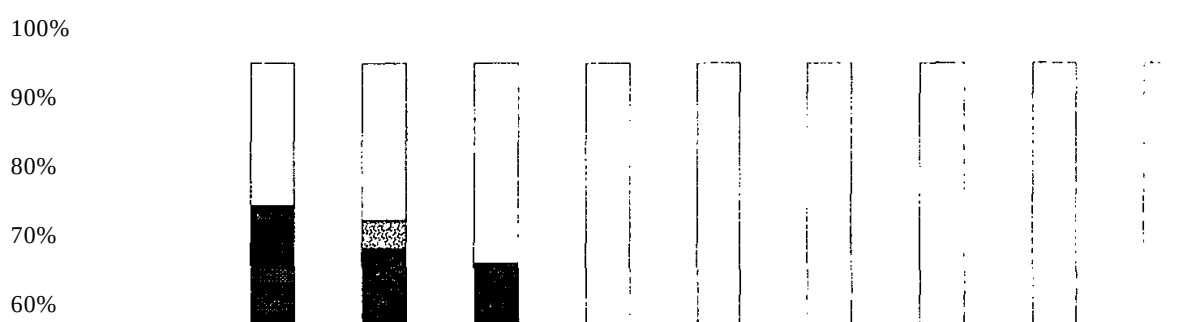
With a long-term developing infectious process (chronic infections), there are many difficulties in registration and accounting and, accordingly, in further analysis. This is due to many factors - long-term incubation (with leprosy, for example, up to several years), slow development of symptoms of the disease, widespread carriage (asymptomatic infection), which occurs either in parallel with manifest forms of infection (for example, with viral hepatitis B) , or precedes the manifestation (in particular, with HIV infection). These features and many risk factors (internal, for

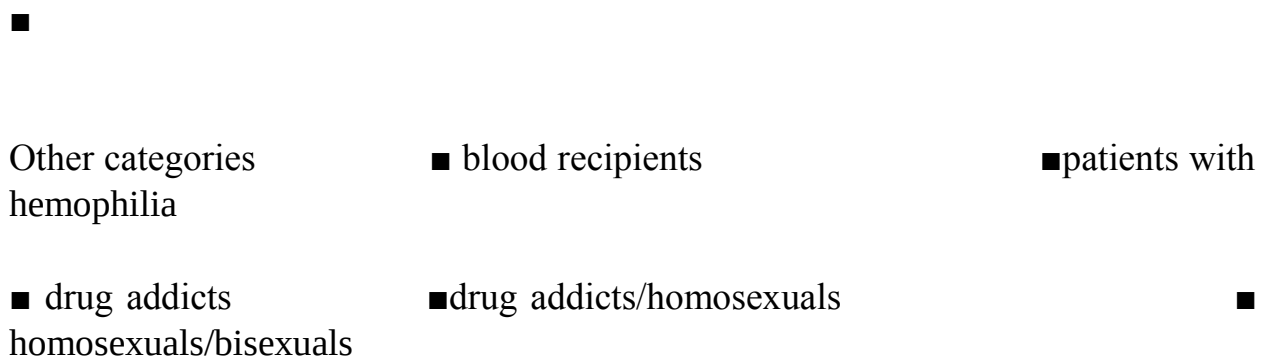
example, in tuberculosis, genetic factors, the presence of immunodeficiency, diabetes and some other diseases; external - poor socio-economic living conditions, etc.) force, firstly, to resort to the widespread use of not only incidence indicators, but also prevalence, and secondly, to apply extensive indicators. The latter can be useful not only at the descriptive, but also at the analytical stage of diagnostic work, since it is often impossible to calculate frequency indicators for some population groups (homeless people, migrants, refugees, drug addicts, etc.). Thus, the WHO European Office, in order to identify risk groups for HIV infection, had to resort to characterizing the situation with the help of extensive indicators (Fig. 14.4).

The figure shows that among those infected with the HIV virus, drug addicts dominated in Spain and Italy, and homosexuals dominated in England, France, Germany and some other Western European countries. There is no doubt that against the background of the impossibility to determine the relative number of drug addicts and homosexuals among the general population, extensive indicators among HIV-infected people give reason to consider the mentioned groups of people as risk groups * it is obvious that there is no such relative number of drug addicts among the general population and homosexuals, as has been observed among HIV-infected people.

It should be noted that with this group of infections, differentiation into different social groups has a specific, individual character. In addition, due to many risk factors and the impossibility of

slow impact on them (socio-economic conditions, etc.) falls on the next stages of analysis, along with a statement of facts, i.e., characteristics of the manifestations of the epidemic process, give in a general formulation the state of risk factors and their impact on morbidity, and, finally, to provide a forecast for the development of the epidemic process. So far, specific recommendations based on identified causal relationships cannot always be implemented.





Pic. 14.4. Extensive indicators of risk groups among AIDS patients

The third stage - descriptive - provides for the definition of risk groups, places (territories) of risk, as well as the time of risk. This is possible when comparing table data and graphic material.

Let us present some simplified scheme of the descriptive and then the analytical stage of the retrospective analysis on the example of the estimate of the incidence of dysentery in 1963-1973. in the Kalininsky district of Leningrad (we emphasize that this is an example, a ire template suitable for all occasions).

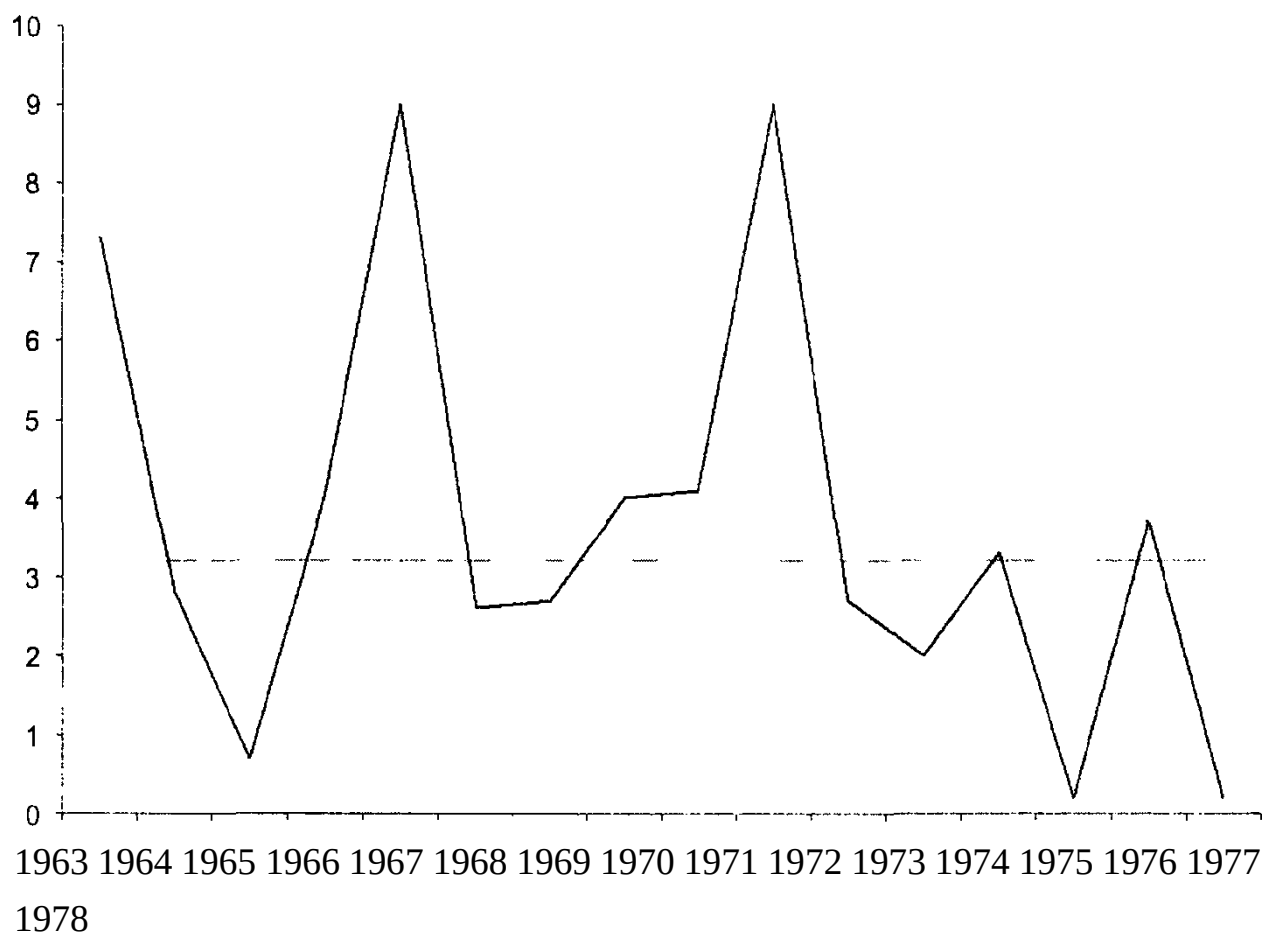
Long-term dynamics of the incidence of the population as a whole, which is presented in Table 14.11 and in Fig. 14 5, testifies to the unevenness of the level, and in the observed period there were ? noibe\u with an interval of 4 and 5 years.

The long-term dynamics of the incidence of Zonpe dysentery and F ICKC pen in the Kalininsky district of Leningrad in terms of imi chyadn "kmi (pn incidence in 1963 was taken as IJ), as well as in intensive is presented in Table 14.12 and pa pic 14 6 and 14.7

Table 14.11

Long-term dynamics of the incidence of dysentery (including cases based on clinical data only)

years	1963	1964	1965	1966	1967	1968	1969	1970	1971	1972	1973
Abs cases	1497	797	567	1302	2010	968	1001	1379	1371	2349	1205
Incident	5230	2786	1691	3945	5911	2616	2634	3480	3427	5872	3010

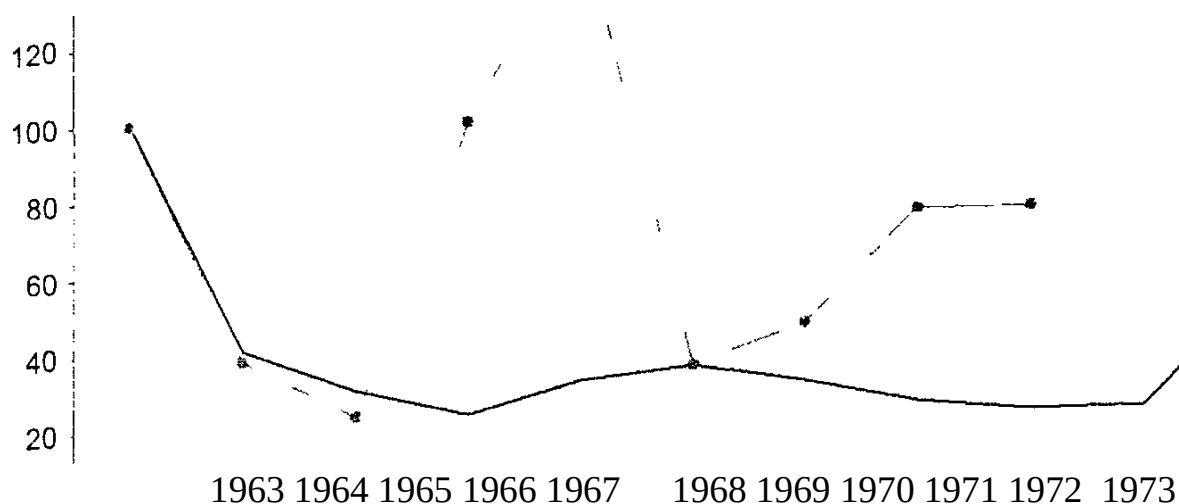


PIc. 14 5 Dynamics of the incidence of dysentery in 1963-1978

Table 14.12
Incidence (incident per 100 thousand population) of Sonne and Flexner dysentery in the Kalininsky district of Leningrad

years	1963	1964	1965	1966	1967	1968	1969	1970	1971	1972	1973
Sonne	2284	955	537	2360	3564	889	1006	1698	1718	3593	1328
Flexner	440	191	142	144	158	177	154	110	102	108	263

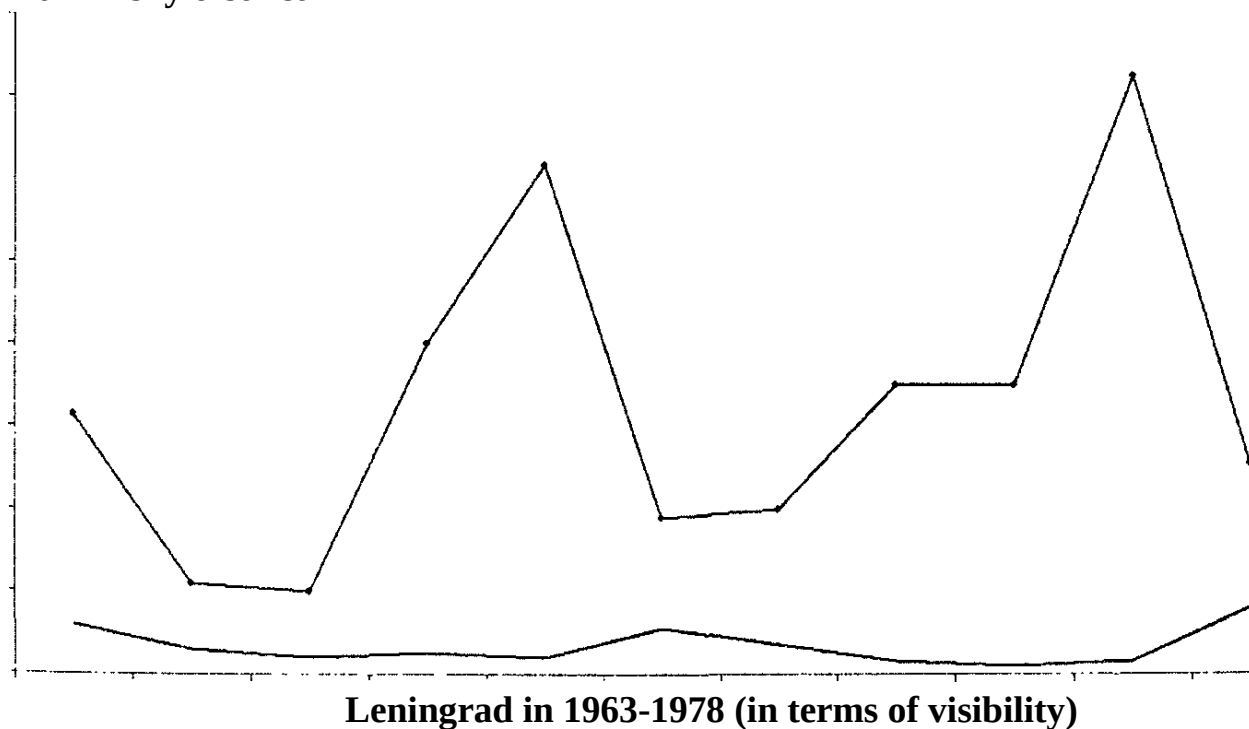
in the Kalininsky district of Leningrad



Sonne's dysentery"

- Flexner's dysentery

Pic 14.6 Dynamics of the incidence of Sonne and Flexner dysentery in the Kalininsky district



Sonne's dysentery"

- Flexner's dysentery

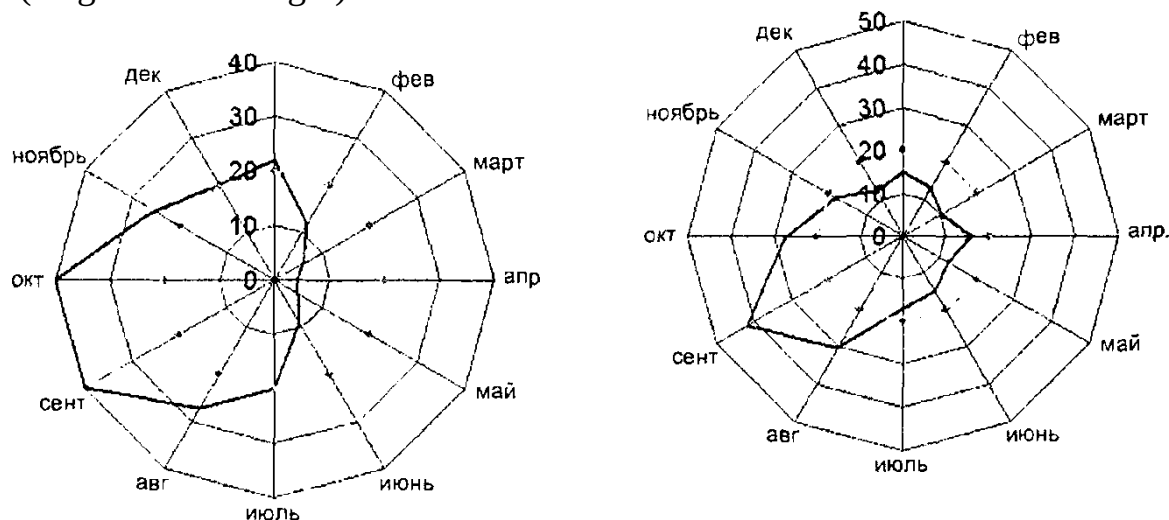
Pic 14.7 Dynamics of incidence (incident) of Sonne and Flexner dysentery (per 100 thousand population)

Comparison of the presented tables (14.11 and 14.12) and figures (14.6 and 14.7) gives grounds to draw the following conclusions:

1. The dominant pathogen is *Shigella Sonne*.
2. The long-term dynamics of the incidence of dysentery reflects the dynamics of the incidence of Sonne's dysentery (apparently, bacteriologically unconfirmed, so-called clinical, dysentery is largely also Sonne's dysentery).

3. The incidence of Flexner's dysentery had, compared with other years, high rates only twice - in 1963 and 1973, and the first relative rise coincided with the high incidence of Sonne's dysentery.

Average long-term seasonality is shown in fig. 14.8, which indicates that, although the seasonality of Sonne and Flexner dysentery has much in common, nevertheless, there is a difference: with Sonnedysentery (diagram on the left), the shift in high incidence to the autumn period is more noticeable than with Flexner dysentery (diagram on the right).



Pic 14.8. Monthly distribution of dysentery cases

Monthly incidence differed from this typical seasonality in 1967, when the maximum number of diseases occurred in January and February: 680 cases were registered in January, 227 in February (46% of the total number of patients per year), with Sonne's shigellosis was registered 490 and 217 times, respectively (58% of the annual accounting). An increase in the incidence of Flexner's dysentery was not observed at this time.

From Table. 14.13 shows that the incidence of children in all observed years is significantly higher than the incidence of adults, although the dynamics of the epidemic process is the same (see Fig. 14.3).

The seasonality of the incidence of dysentery in children and adults is more or less similar, only the difference in the autumn period is obvious: if the incidence of adults in comparison with summer ethane is steadily decreasing, then the incidence of children is maintained at this time even at a sufficiently high

juice level. This autumn shift in the incidence of children was associated almost exclusively with Sonne-dysentery.

In table. 14.14 materials of incidence of children of different age categories are given.

Table 14.13

Long-term dynamics of morbidity in children and adults (incidence per 100 thousand of the population of the corresponding groups) in the Kalininsky district of Leningrad

years	1963	1964	1965	1966	1967	1968	1969	1970	1971	1972	1973
Children under 14	1458,1	666,6	461,4	1102,0	1316,3	620,3	754,1	1028,0	1070,7	1780,3	870,4
adults	227,4	124,8	86,9	181,3	317,2	162,4	134,2	167,5	163,4	270,3	161,2
Incidence ratio in adults and children	1:6,4	1,5,3	1,5,3	1:6,0	1:4,1	1,3,8	1,5,6	1:6,1	1:6,5	1:6,5	1:5,4

Table 14.14

Morbidity (incident) of dysentery in children of different age groups

years	1964	1965	1966	1967	1968	1969	1970	1971	1972	1973
Up to 1 year	2264,2	1051,1	2036,2	1210,4	924,7	1051,1	1471,8	1263,1	1390,4	563,3
1-2 years	1461,1	1092,5	2263,9	2444,0	1533,7	1762,1	2535,4	2870,1	3400,3	1728,2
3-6 years old	1061,1	673,6	2046,2	1681,6	908,0	1032,3	1510,2	1378,3	2450,1	1002,0
7-14 years old	230,5	176,8	451,3	1230,1	371,5	376,7	520,3	544,2	1204,4	600,3

From Table. 14.14 it can be seen that children aged 1-2 years are the most at risk (only in 1964, children under one year old were more affected, which, it is possible, is associated with outbreaks among children in this age group) In 1967, the increase in incidence was especially significant among children 7-14 years old. It is interesting that the incidence of children of other age categories in 1967 was significant, but compared with the previous year it was either lower (children under 1 year old and 3-6 years old) or insignificantly higher (children 1-2 years old). The following year, the incidence of children aged 7-14 fell sharply (in other age categories, the indicators also decreased, but not so significantly).

In table. 14.15 presents data on the long-term dynamics of the incidence of dysentery for the last three observed years among children under 3 years old and children 3-6 years old, both organized, that is, attending children's institutions, and exclusively home education. These years accurately reflect the patterns of all

observed years, and are taken into account as a year of high incidence (1972), as well as years of relative well-being

Table 14.15

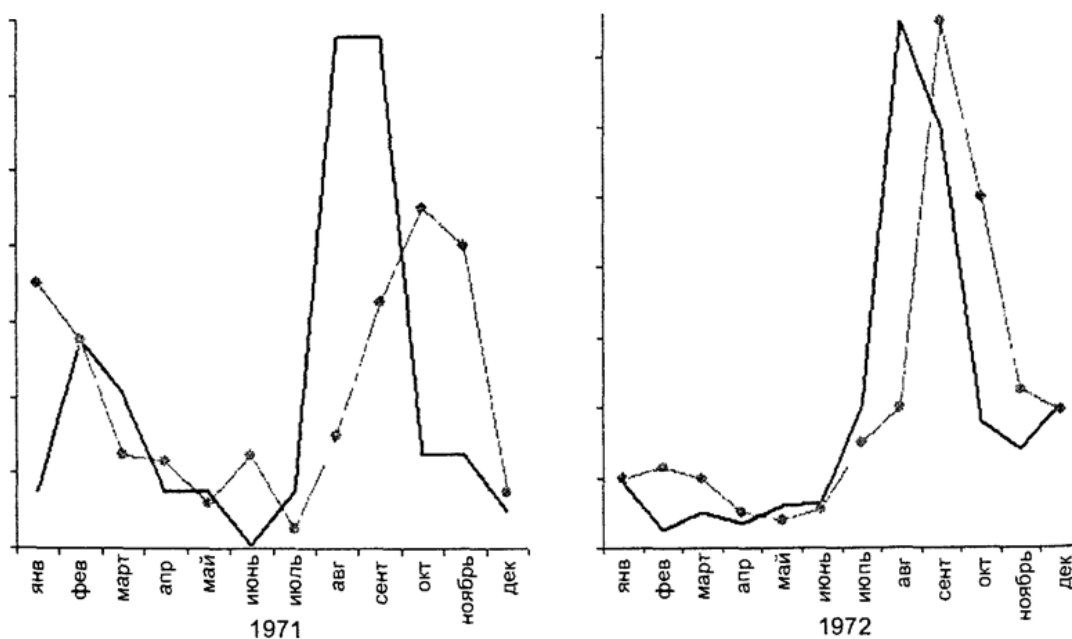
The incidence of dysentery in organized and unorganized children of different age groups (per 1000 people in the corresponding group)

Incident	1971 y	1972 y	1973 y.	Average for 3
Organized up to 3 years	36,8	50,7	20,3	35,9
Unorganized under 3 years	10,5	14,2	9,8	8,2
Organized 3-6 years	15,6	35,5	13,6	21,6
Unorganized 3-6 years	6,7	9,6	4,7	7,0

The materials given in Table 14.15 show:

- 1) the incidence of dysentery of organized children is higher than that of unorganized ones, and this is typical for all children (from 0 to years), and for both groups separately;
- 2) the incidence in children aged 0 to 3 years is higher than in children 3-6 years old - this applies to both organized and unorganized children;
- 3) 1972 was a year of high incidence among all children, i.e. this year was a time of risk.

Intra-annual dynamics of the incidence of organized and unorganized children aged 3-6 years in terms of clarity is presented on the example of two years in fig. 14 9.



Pic. 14 9 Monthly incidence of dysentery in organized and unorganized children (in terms of visibility)

The data in Fig. 14 9 testify

- 1) summer seasonality is typical for both organized and unorganized children,
 - 2) the autumn high level is typical only for the incidence of organized children
- Data on the number of diseases in single and multiple foci at home and in children's institutions are given in Table 14.

Table 14.16

Focal morbidity at home

years	Number diseases	Number foci	Number of single foci	Number of diseases in them	Number of multiple foci	Number of diseases in them
1971	1371	1295	1237	1237	58	134
1972	2349	2128	2053	2053	128	296
1973	1205	1145	1100	1100	45	105

Table 14.17

Focal morbidity in children's institutions

years	Number diseases	Number foci	Number of single foci	Number of diseases in them	Number of multiple foci	Number of diseases in them
1971	724	167	47	47	120	677
¹ 972	919	602	512	512	90	407
1973	499	326	293	293	33	206

Table 14.18

Indicators characterizing focality at home and in children's institutions

years	Average number of cases per outbreak		Average number of cases in multiple		Specific gravity of the number of cases in multiple foci, %		Specific gravity of multiple foci, %	
	made y conditi	institutio	made y e	instit	made y condition	instit	made y conditi	instit
1971	1 06	4 36	2 31	5 64	9 77	93,51	4 48	71,86
1972	1 1	1 53	2 31	4 52		44 29	6 06	14 95
1973	1 05	1 53	2 33	6,24	8 71	41,28	3 93	10 12

Table 14.18 shows that in 1971 there was an unfavorable situation in children's institutions: 71.86% of the foci were multiple, they accounted for 93.51% of cases of diseases. d - the year of relative prosperity - turned out to be fatal for children's institutions: 46.6% of all morbidity in the region fell on focal morbidity in them. In 1972, which was characterized by a very high incidence and the highest seasonality of incidence, on the contrary, compared with other analyzed years, the importance of focality at home increased: in multiple foci there were 12.6% of cases of diseases. In 1973 - the most prosperous year - there were relatively few multiple foci in children's institutions, but they accounted for 41.28% of cases of the disease, which is why this year there was a record indicator of multiple foci - 6,24, i.e., on average, there were 6.24 cases of diseases in multiple foci.

Evaluation of the significance of multiple foci in the incidence of dysentery Sonne and Flexner managed to trace in 1967-1973. Multiple foci in Sonne-dysentery accounted for 7.9 to 29.8% of cases (the last in 1967). With Flexner dysentery 3 years out of

There were no 6 multiple foci at all, for 3 years there were 2 and 3 cases of multiple foci, only in 1970 there were 14 cases (28.6%) in multiple foci.

The significance of multiple foci in assessing intra-annual dynamics is presented on the example of data for 3 years (Table 14.19).

Table 14.19

Relative number of cases of diseases that occurred in multiple foci (% of the total number of diseases in the corresponding month)

	J	F	M	A	M	I	I	A	S	O	N	D
1971	6 0	19,1	64	8,2	8,2	2,1	2,8	4, 9	15,3	14,5	11,0	7,1
1972	0	15 0	5,4	9,7	18,1	3 3	7,1	12,7	15,6	16,2	16,9	15,0
1973	3 2	14,1	3,1	4,3	4,3	12,5	83	4,4	6,7	26,0	5 2	3 5

Gabl materials. 14 19 indicate that the relative number of patients in multiple foci increases most often in autumn, when children's institutions begin to function after the summer break. Along with this, one can note the fact of an increase in the relative number of patients at any time year, but outside the seasonal rise, this, as a rule, is not accompanied by an increase in the general incidence

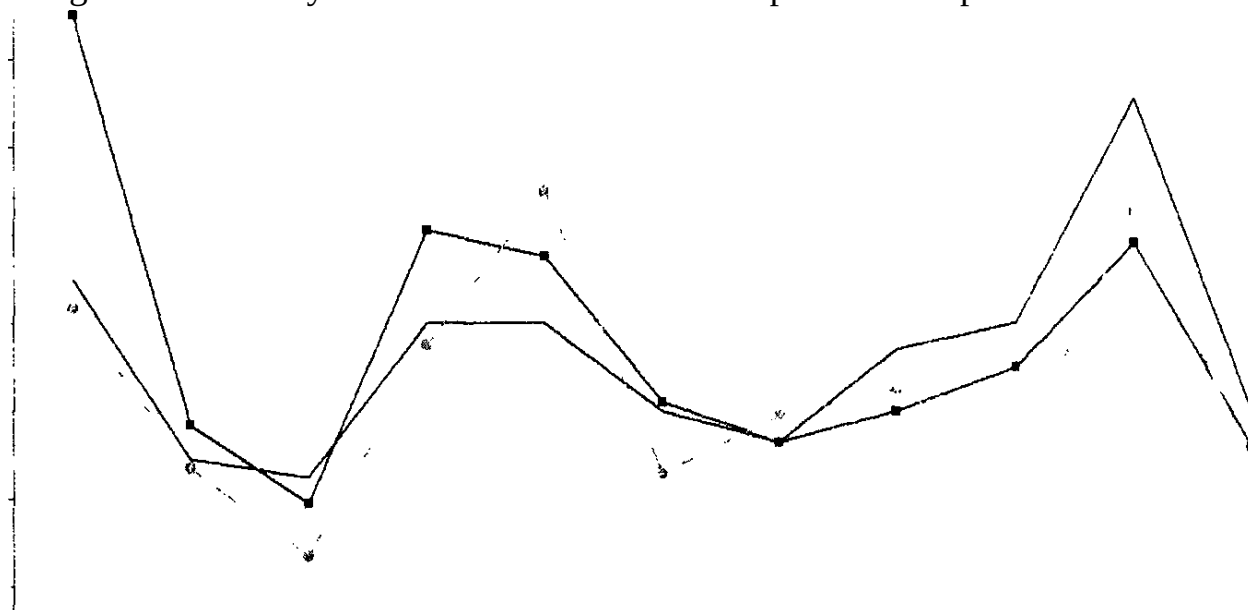
Kalininsky district of Leningrad for assessing the characteristics of the incidence of dysentery, in particular the territorial distribution

Plot No. 1 - a territory dominated by the old pre-revolutionary housing stock, where people lived mainly in communal apartments;

Plot No. 2 is a territory with individual rural-type residential houses without internal water supply (water use from wells and water intake street columns) and sewerage systems;

Plot No. 3 - a territory built up mainly with modern comfortable houses

Long-term morbidity data for these three areas are presented in pic. 14.10.



1963	1964	1965	1966	1967	1968	1969	1970	1971	1972	1973
— section No. 1			section No. 2 *			section No. 3				

Pic. 14.10. Dynamics of the incidence (incident) of dysentery in the district

From fig. 14.10 it can be seen that there is a fairly clear synchronization of the epidemic process, and with almost identical incidence (the exception is 1963 - there is some connection with an unusual rise in the incidence of children under 1 year old). In other words, the incidence - the incidence in all years and long-term dynamics - was practically the same in all territories.

The fourth stage - analytical - allows you to identify (should identify) causal relationships using logical methods, most often using the method of concomitant changes (correlation analysis) and comparative techniques, that is, comparisons (method of difference and similarity) . At this stage, the use of biostatistical techniques is mandatory (determining the reliability of differences or similarities, in some cases case-control or retrospective cohort studies are used)

In the analyzed example of studying the causes of the development of the epidemic process of dysentery in the Kalininsky district of Leningrad, a retrospective analysis provides (as in other infections of the intestinal tract) to identify transmission routes (primarily dominant) and the causes of the seasonal rise. Sources of infection, with rare exceptions, are not established, the solution of this problem is practically possible only with operational analysis.

The data obtained at the third stage of the retrospective analysis allow us to say that the water route of transmission in this case is of no fundamental importance. This is evidenced by the following data:

- ◆ The incidence of children of all age groups, especially children under 6 years old inclusive, is higher than that of adults. A position based on common sense (children, it is believed, unlike adults, as a rule or at least more likely to receive disinfected water than adults) is considered an axiom. In this case, the actual data are consistent with the above consideration.

- ◆ Morbidity in site No. 2, which differs significantly from sites No. 1 and No. 3 in the water supply system, turns out to be the same in terms of level and dynamics as the incidence in other sites. The very fact that it is impossible to use the difference method as applied to the territorial distribution of morbidity (in this case it cannot be argued that inadequate water supply means high morbidity, satisfactory water supply in relation to the causative agent of dysentery is low morbidity) indicates that the water factor in the current situation cannot be of significant importance.

There is no doubt that contact-household transmission occupies a certain place in the spread of the causative agent of dysentery. This is evidenced by a higher incidence of children attending children's institutions than the incidence of children exclusively at home (here the method of difference is applicable: the probability of

infection in children's institutions due to contact with a certain number of sick or sick children is undoubtedly higher than with limited contact with people at home). The contact-household route of transmission is also supported by the fact of an increase in the incidence in autumn due to children attending children's institutions, among whom the focality is also growing at this time. In other words, contact-household transmission in the conditions of communication in children's institutions is quite real. However, if we analyze the situation among the population as a whole, and not just children attending children's institutions, then we have to admit that it is not this mode of transmission that determines the current incidence. Firstly, the incidence in different areas that differ in the living conditions of the population (comfortable modern houses, communal apartments, rural-type houses) is identical both in statics and dynamics. In this case, again, it is impossible to use the logical device of difference. Second, it dominates

The population of the region has a sporadic incidence, and, as is known, with contact-household transmission, there must be focality, since in the absolute majority of cases this path operates over a short distance.

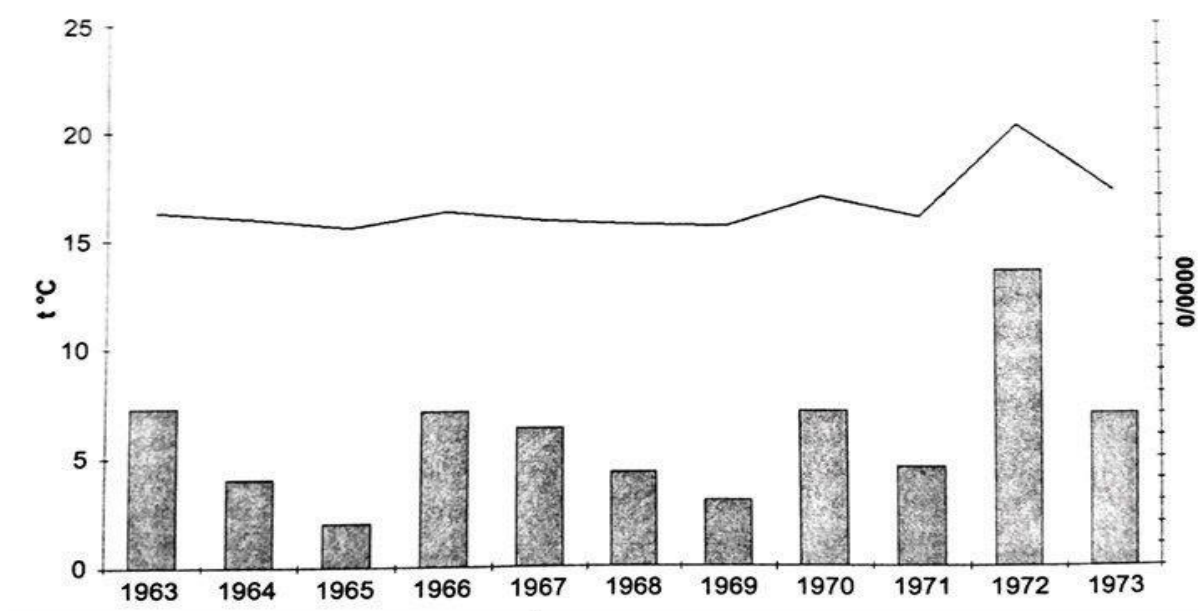
The above materials indicate that the leading route of transmission is food. With regard to the transmission of dysentery pathogens, dairy products are the main products, and in the summer, the importance of greens - fruits and vegetables - may increase. In this case, there is clear epidemiological evidence in this regard. At the time being analyzed, the population is supplied with the products of one or two dairy enterprises (dairy plants), that is, the population of all sections was provided, as it were, from a single center. In other words, the similarity method indicates the same type of conditions for infection with differences in the water supply system (site No. 2 is special in this respect) and in the household provision of the population (all 3 sites are not similar to each other). The dominant sporadic incidence indicates the food way, which is realized due to the contamination of the product outside the dwelling. Contamination of products in the process of their manufacture. However, in the absence of conditions for the reproduction of the pathogen (or with its mat accumulation in the product), it must inevitably manifest itself in the form of sporadic morbidity.

The fact that at that time the danger of contamination of dairy products at the manufacturing enterprise was obvious (however, it still exists), was evidenced by occasional outbreaks (there are opportunities for the pathogen to multiply in the product). In particular, an increase in the incidence in January-February 1967 was deciphered by operational analysis - it was an outbreak associated with the accumulation of *Shigella Sonne* in a dairy product before it was put on sale.

Solving the problem of seasonality in the incidence of dysentery, of course, goes beyond the usual retrospective analysis carried out in anti-epidemic institutions - this is, in essence, a global scientific task. However, even in the system of epidemiological surveillance, it is possible to obtain the necessary information that

will help predict the situation and then take the necessary adequate measures. Correlation analysis for comparing annual incidence rates (obvious outbreaks were excluded - each of them was taken as one episode of infection) for 11 years and the average temperature (June-August) showed an obvious statistical relationship - the correlation coefficient was 0,7 (pic. 14.11).

Thus, the method of concomitant changes showed that the high temperature in summer is the cause of high head morbidity. Indeed, the years of high morbidity are the periods of a high level of summer seasonal rise in morbidity (this is most defiantly seen in the example of 1972). In such years, all groups of the population are equally involved in the summer seasonal rise - adults, children of home education and those in childbirth (in each group, the increase in the incidence in relation to the incidence of frost in the months that fell is approximately the same).



■ Incidence of dysentery.
— Temperature

Pic 14.11 Comparison of the average summer incidence of dysentery with the average summer air temperature (June - August)

This gives reason to think that the reason lies not in the ways of transmission (for example, for each population group in the summer, there may be features when infected in one way or another - for example, when bathing, which is less likely for young children attending children's institutions than for adults and adolescents, etc.). It is likely that the high summer temperature reduces the resistance of the human body (and, indirectly, increases the virulence of the pathogen) Such a conclusion, of course, does not reveal (even if it is true) the inner essence of the phenomenon, but it allows, in conditions of high summer temperatures (or in anticipation of it), to intensify the implementation of measures, and in relation to all groups of the population methods such as case-control and retrospective ("historical") cohort research. The general structure of epidemiological surveillance is shown in picture 14.12.

Questions for chapter 14

1. Epidemiological surveillance is
2. Stages of epidemiological surveillance
3. Standard case definition
4. Operational analysis
5. Retrospective analysis

Chapter 15

PREVENTIVE AND ANTI-EPIDEMIC MEASURES.

The practical service implements preventive and anti-epidemic measures. The first are carried out in anticipation of the possible emergence of diseases, the second in the conditions of the development of the epidemic process. Both of them are built taking into account the internal structure of the epidemic process, that is, in relation to the sources of infection, the mechanism of transmission and the susceptible population. These activities can be carried out on the basis of the achievements of science and practice based on general guidelines. But, as a rule, they are carried out on the basis of epidemiological surveillance data, i.e., after specific causal relationships have been established as a result of diagnostic activity.

15.1. General structure of preventive and anti-epidemic measures.

In table. 15.1 and 15.2 shows the general structure of preventive and anti-epidemic measures.

However, along with the provision that measures should be based on the findings of diagnostic activities, the following should also be borne in mind. As already mentioned, activities are carried out in relation to all three links, but this does not mean that one must always adhere to this principle. The structure of the epidemic

process (its elementary cell) consists of three interconnected successive parts. From what has been said, it follows that the neutralization of any of these three links automatically excludes the possibility of the development and existence of an epidemic process. In some cases, when there are no sufficiently effective means of struggle, it is necessary to work with respect to all three links, which makes it possible as a result to obtain a product of efficiency in relation to each link. However, this is connected, as it were, with the “dispersal” of forces and means of anti-epidemic and other services and often does not give the desired result. If it is possible to concentrate efforts on one link (or sometimes two), against which there are effective means of struggle, then it is advisable to use this particular setting. At the same time, it must be borne in mind that the strategy and tactics of struggle in the system of preventive and anti-epidemic work may differ.

Table 15.1

Preventive actions.

	Anthroponoses	Zoonoses	Sapronoses
Source of infection	Isolation and hospitalization of patients Active identification of patients with manifest forms, carriers (survey, clinical examination, microbiological and other laboratory studies of IT e)	Isolation, treatment (sometimes destruction) of economically valuable animals Destruction of sick animals that are not valuable in the economic respect Deratization,	Isolation and treatment of patients Microbiological control over objects of the external environment of hospitals for the selection of objects and methods of disinfection.

Transmission routes	Strengthening general sanitary measures (in relation to nutrition, water supply, sewage removal, etc.) current and final дезинфекция Возможная санитарная обработка (паразитарные тифы)	Gain sanitary and veterinary events Current and final disinfection. Usage	Sterilization, current and final disinfection in a hospital and other facilities Strengthening the regime of asepsis and antisepsis
Susceptible organism	Emergency prophylaxis (chemo-, phage-, antibiotic prophylaxis, passive immunization) Vaccination according to epidemic indications	Vaccination of risk groups Passive immunization of persons under attack ectoparasite - carrier pathogen (tick-borne	Vaccination according to epidemic indications (tetanus).

Table 15.2

Anti-epidemic measures

	Anthroponoses	Zoonoses	Sapronoses
Source of infection	Isolation and hospitalization of patients Active identification of patients with manifest forms, carriers (survey, clinical examination, microbiological and other laboratory studies of IT e)Observational and quarantine activities in the hearth	Isolation, treatment (sometimes destruction) of economically valuable animals Destruction of sick animals that are not economically valuable Deratization, including, if possible, in a natural focus	Isolation and treatment of patients Microbiological control over objects of the external environment of hospitals for the selection of objects and methods of disinfection

Transmission routes	Strengthening general sanitary measures (in relation to nutrition, water supply, sewage removal, etc.) current and final дезинфекция Possible sanitization (parasitic typhus)	Gain sanitary and veterinary activities Current and final disinfection Use of protective clothing and repellents in the wild	Sterilization, current and final disinfection in a hospital and other facilities Strengthening the regime of asepsis and antisepsis
Susceptible организм	Emergency prophylaxis (chemo-, phage-, antibiotic prophylaxis, passive immunization) Vaccination according to epidemic indications	Vaccination of risk groups Passive immunization of persons who have been attacked by an ectoparasite - a carrier of the pathogen (tick-borne encephalitis)	Vaccination according to epidemic indications (tetanus)

Preventive and anti-epidemic work must be planned, since activities thought out in advance can provide for all necessary and possible general and private measures. In cases where the solution of the problem is realistic only with the participation of various services and departments, as well as in some cases authorities, epidemiologists initiate the preparation of so-called complex problem-thematic plans or problem-targeted plans. Plans are being prepared for the own work of the epidemiological department or specialized epidemiologists. All plans provide for deadlines, executors (responsible executors), in complex problem-thematic and problem-targeted plans - also administrative and material support.

15.2. Disinfection

15.2.1. Disinfection (decontamination)

Disinfection is a system of knowledge and practical activities aimed at removing and destroying pathogens of infectious diseases in the external environment, their carriers (arthropods) and rodents.

The term "disinfection" has two meanings: firstly, it is the destruction of the pathogen in the external environment, and secondly, the term is collective, which implies the combination of three functions *

- 1) actual disinfection, i.e., the destruction of the pathogen in the external environment;
- 2) the destruction of arthropods (insects, mites) that are involved in the transmission of the pathogen during transmissible (blood) infections or themselves cause pathology (scabies); this section is called **disinfection** ;
- 3) the fight against rodents, which in some nosological forms are sources of infection; this section is called **deratization**.

This collective understanding of disinfection has developed as a result of the practical expediency of combining all three functions in one service. Apparently, historically, this comes from the Middle Ages, when complex measures were taken in Europe in the centers of the plague by a small number of specially admitted people in protective clothing. These people had to carry out the actual disinfection, and disinsection (destruction of fleas), and deratization (destruction of rats). Subsequently, all three functions were combined and performed by the same service. With the development of science and practice, the strategy and tactics of carrying out disinfection measures have changed. First of all, the role of preventive disinfection, i.e., measures in the absence of diseases or their small number, has increased. In particular, disinfection of water in the water supply system has become a practice. Such decontamination provides well-being and protection from infection in infections with a fecal-oral transmission mechanism and in some natural focal diseases (tularemia, leptospirosis, etc.). Modern data show that the incidence of typhoid fever, viral hepatitis A depends entirely on the quality of water disinfection. In addition, the principles of protection against food contamination are used (dairies, food industry, etc.). Preventive disinfection also dominates in hospital settings.

The range of disinfection measures in the outbreaks that have arisen is gradually limited, the former tactics of total disinfection of all objects is gradually transformed into the disinfection of only those objects that can act as a transmission factor. The range of nosofoms under which disinfection is carried out has narrowed. With a low resistance of the pathogen, the need for disinfection of the external environment itself disappeared. However, the refusal of disinfection in these cases is not always simple and easy. Population studies have shown the senselessness and futility of disinfection in foci of measles, meningococcal infection and some other diseases. However, in our practice this is not always taken into account. There are no convincing epidemiological data on the advisability of disinfection in diphtheria foci. Now, the widespread use of insecticides (chemicals that have the ability to kill arthropods) in the open nature is practically abandoned. This is due to environmental and economic considerations. In addition, experience shows the futility of these measures (for example, it is practically impossible to kill mosquitoes in open nature),

or there is a rapid recovery (in 2-3 years) of the arthropod population (this is evidenced by attempts to widely use DDT and some other insecticides in the foci of tick-borne encephalitis). This, of course, does not exclude the local (small areas near settlements) use of insecticides, although even in this case one cannot hope for a good success of the event.

Until recently (in the USSR), field deratization was widely used in natural plague foci, but there is still no reliable data indicating the epidemic and, especially, epizootic effect of the event.

On the other hand, disinfection measures are being taken more vigorously in hospital conditions, mainly to protect against purulent-septic infections.

For various groups of infectious diseases, certain disinfection measures are carried out (Table 15 3).

Table 15.3

The main directions of disinfection measures for various groups of infectious diseases.

Groups of infections	Disinfection measures
-----------------------------	------------------------------

Intestinal infections with fecal-oral transmission mechanism Disinfection of multiple transmission factors (water, food products - vegetables, fruits, etc. utensils, kitchen utensils, excretion of patients, etc.)	Disinsection rare (destruction of flies)
Respiratory tract infections with airborne transmission mechanism	Disinfection of household items in some foci (tuberculosis)
Transmissible blood infections	Disinsection
Infections of the external integument with a contact mechanism of transmission	Disinsection of household items in the foci of scabies Disinfection of household items (linen, upholstered furniture, bath, etc.) for some bacterial (staphylococcus, etc.) and fungal (epidermophytosis, etc.) diseases
Zoonoses in which rodents are the source of infection	Deratization
Hospital infections with artificial routes of transmission	Disinfection at various levels Sterilization

Types of disinfection

Preventive disinfection is carried out in the absence of detected sources of infection, but assuming their presence. It is carried out in medical and preventive, children's institutions, in public places, at food and production facilities, in baths, hairdressers, etc. The purpose of preventive disinfection is to reduce the contamination of environmental objects, thereby reducing the risk of human infection.

Focal disinfection is carried out in epidemic foci.

The purpose of focal disinfection is to prevent infection of persons surrounding the patient, and to prevent the removal of the pathogen outside the focus. Depending on the conditions of carrying out, there are current (in the presence of a source of infection) and final (after removal of the source) disinfection.

Current disinfection is carried out continuously throughout the infectious period. It is carried out in apartment centers, in hospitals, in isolation wards.

Depending on the location of the patient, current disinfection is carried out by instructed carers or medical workers.

Final disinfection is carried out after hospitalization, recovery or death of the patient. In chronic infections (tuberculosis) after the patient has moved to a new place of residence.

The final disinfection, as a rule, is carried out once by the employees of disinfection stations, medical personnel of health facilities, children's institutions, as well as instructed persons.

Both during the current and, especially, during the final disinfection, some items are subject to chamber disinfection, that is, some things (mattresses, other bedding, sometimes clothes) are taken out of the hearth (care must be taken to prevent infection of personnel or contamination of objects from external sources). environment).

In foci of especially dangerous infections, the final disinfection is carried out in closed suits of the appropriate type, depending on the nature of the infection. After completion of work, all members of the team are required to undergo sanitization.

Disinfection methods

The following disinfection methods are available

- mechanical,
- physical,
- chemical

Mechanical methods include shaking, knocking out, vacuuming, washing and washing, airing and ventilating rooms, filtering water, sweeping. They are designed to reduce the concentration of microorganisms on objects. Given the fact that the dose of the pathogen is important for the manifestation of infection, this measure can be very effective in some cases.

Physical methods are based on the destruction of microorganisms under the influence of physical factors. These include incineration, calcination, roasting, boiling, the use of dry hot air, sunlight, radioactive radiation, etc.

Physical impact on microorganisms can also be carried out in combination with chemical methods in special gas chambers. Depending on the active substance, the chambers are divided into:

- steam;
- steam-formalin;
- hot-air;
- gas.

Gas chambers must be securely sealed.

Due to its high toxicity to humans, chamber gas treatment is rarely used (for processing documents and antiques). However, gas chambers have become increasingly used for the sterilization of instruments and some other items in the central sterilization departments (CSOs) of hospitals.

Chemical methods of disinfection are based on the use of chemicals that have a bactericidal, sporicidal, virucidal and fungicidal effect on microorganisms.

For disinfection, drugs are used that differ in the mechanism of action. Most often, oxidizing agents, halogen preparations, quaternary ammonium compounds (QAC), alcohols, aldehydes, etc. are used,

It should be understood that disinfection measures are of great importance in the fight against infectious diseases, however, their effect is most often manifested in combination with other ongoing measures.

In hospital conditions, sterilization measures, i.e., the complete destruction of pathogens at various objects (a set of measures for asepsis and antisepsis), are the main ones for preventing purulent-septic infections.

15.2.2 Disinsection

Disinsection - the destruction of insects and ticks that are carriers of pathogens of infectious and parasitic diseases, as well as other arthropods that cause anxiety and inconvenience to humans.

In the general complex of preventive measures aimed at reducing infectious diseases, pest control occupies a significant share. The choice of methods and means by which pest control measures are carried out must be done taking into account the biological and ecological characteristics of each type of arthropod.

In addition, in accordance with the requirements for the protection of the environment from pollution by pesticides, and taking into account the development of resistance of arthropods to the drugs used.

Types of disinsection.

Disinsection, as well as disinfection, is divided into *preventive and focal*.

Preventive pest control is carried out in order to prevent the breeding of insects and ticks, as well as the settlement of residential and outbuildings by them.

Focal disinsection is carried out in the foci of transmissible infectious and parasitic diseases and scabies, as well as in intestinal infections in the presence of flies in the foci.

Disinsection methods.

The following disinsection methods are available:

- mechanical;
- physical;
- chemical;
- biological;
- combined.

Mechanical methods of disinfestation in some cases include the removal of arthropods along with dust and debris when sweeping walls, sweeping floors, vacuuming, cleaning yard areas.

An important place is occupied by methods based on preventing arthropods from entering the room by screening windows, doors, and destroying them in various ways (adhesive tapes, flytraps, special traps, etc.).

Physical methods of pest control include the use of heat, such as dry or humid air, steam, hot or boiling water. In recent years, it has been proposed to use ultrahigh frequency currents (UHF), ultrasound, and ionizing radiation.

Chemical pest control methods use substances to kill insects (insecticides), mites (acaricides), larvae (larvicides), insect eggs and mites (ovicides). Chemicals, depending on the goals and objectives of pest control, can be used in the form of dusts, emulsions, suspensions, soaps, ointments, solutions, aerosols, poisoned baits, special pencils, varnishes, paints, etc.

Insecticides can enter the organism of arthropods in various ways. Depending on the routes and methods of penetration, insecticides are divided into the following groups:

- ◆ *Contact* - which penetrate into the body of arthropods through the outer integument (cuticle) as a result of direct contact of the arthropod (whole body or parts of it) with an insecticide.

- ◆ *Intestinal* - which penetrate the body of an arthropod when it enters the body with food or water.

- ◆ *Fumigants* —* penetrate through the respiratory system.

- ◆ *Systemic* - capable of destroying a blood-sucking arthropod (lice, fleas, mosquitoes, ticks, etc.) through single or multiple contact with a host receiving a certain dose of a drug that is detrimental to an arthropod.

Some insecticides by action on arthropods can be assigned simultaneously to two or three groups.

*To protect against attack by arthropods (insects, ticks), and not for destruction (in situations where this is not possible), **repellents are used** (drugs that repel arthropods or act in other ways).*

Repellents are most often used in the field, but can be used indoors (mosquito repellent, etc.).

Biological methods of disinsection. In the last decade, biological means have become important in the fight against arthropods.

These include causative agents of arthropod diseases: *bacteria, viruses, fungi, protozoa, helminths*.

The most promising are bacteria. Research continues to develop modes of chemical sterilization of insects.

The main criterion for assessing the quality of ongoing pest control measures is the density of arthropods on environmental objects.

15.2.3. Deratization

Initially, the term "deratization" (from Latin *rattus* - rat + negative prefix *de*) meant the destruction of rats.

*At present, **deratization** is a system of preventive and extermination measures aimed at destroying or reducing the number of rodents that are dangerous in an epidemic sense and bring economic damage.*

Types of deratization measures

Rodent control includes preventive and extermination measures. The leading role belongs to preventive measures.

They are aimed at depriving rodents of shelters and making it difficult for them to access food. These are construction and technical measures that prevent the penetration of rodents into the premises, depriving them of access to water and food, as well as cleaning up populated areas, depriving rodents of shelters and food sources, timely harvesting, destruction of weeds.

Extermination measures are measures aimed at a decline in the rodent population. Deratization measures are carried out in settlements (dwellings, warehouses, household buildings) or in places adjacent to human habitation. The expediency of field deratization in natural plague foci needs a serious epidemiological assessment. The most effective organizational form of rodent control is continuous **systematic deratization**.

Deratization methods

There are the following deratization methods:

- mechanical;
- chemical;
- biological.

The mechanical method is based on the use of traps and traps. This method of extermination of rodents is safe for humans, is objective and illustrative, therefore it is used to study the effectiveness of deratization.

The chemical method consists in poisoning rodents with poisonous substances - rodenticides (from Latin *rodentis* - gnawing and *caedo* - I kill). These substances act when they enter the intestines or lungs (fumigants).

Acute poisons, chronic poisons and gases are used for deratization.

The biological method of struggle is based on the use of the characteristics of predators (cats, foxes, kites, etc.) - the natural enemies of rodents.

The issues of disinfection and sterilization in medical institutions (po-clinics, hospitals, medical units, etc.) will be discussed in the chapter on the epidemiology of hospital infections.

15.3 Specific prophylaxis of infectious diseases

Specific prophylaxis is the artificial creation of immunity in individuals or population immunity, although most often these tasks are solved in parallel.

Distinguish between active and passive artificial immunity. *The first is created with the help of vaccines, the second - with the help of drugs containing antibodies against some pathogen.*

The basis of specific prevention is the desire to artificially more or less fully reproduce the natural processes that occur in the body in the fight against an invading parasite. In other words, specific prophylaxis has certain limitations * it cannot be used for syphilis, fungal diseases, helminthiasis and for some other groups or individual nosological forms, in the pathogenesis of which the protective function of immunity is either negligible or absent altogether.

When choosing a strategy and tactics for the use of specific prophylaxis in modern conditions, several provisions are taken into account.

1. The more active the mechanism of transmission of the pathogen, the more indicated the use of specific prophylaxis. In infections, the causative agents of which are spread due to particularly active, practically uncontrollable, airborne transmission, often the only way to prevent the spread of diseases among the population or a limited population (children, military groups, etc.) is the use of specific prophylaxis. ki. If for any airborne infections there is effective protection due to vaccination, then they speak of diseases “managed” with the help of specific prophylaxis (measles, diphtheria, etc.). Sometimes other mechanisms of transmission can also get out of control (in the event of wars, other social disasters, etc.).

d.). In such cases, there may also be a need for universal (or limited to some collectives) vaccination. Very often, due to the high risk of infection and the inability to control the likelihood of infection of people, vaccinations are widely used in natural foci (tick-borne encephalitis, tularemia, etc.).

2. Specific prophylaxis should be abandoned if the problem of combating one or another nosoform can be solved (successfully solved) by other means. Vaccination is the introduction of a foreign agent into the body, which can lead to unwanted side reactions (non-specific painful reaction, which can sometimes be severe; allergic reaction; provoking existing chronic diseases; when using vaccines containing attenuated, i.e. e. weakened, but alive, pathogen - a specific reaction, etc.). The fight against typhoid fever in the recent past was solved with the help of vaccination of the entire population or some groups (troops), but now the incidence has been reduced to low levels by gradually bringing the water supply in line with existing sanitary and hygienic requirements - the need for $\neg$ vikakh disappeared.

3. It is necessary to introduce vaccination even with a low incidence (if it is impossible to actively intervene in the epidemic process by other means) against those nosoforms that are often characterized by a severe course of the disease, there are no effective treatments, but they have a high social significance. We are talking

about assessing the consequences of morbidity: what is the lethality, disability, mortality, disability (an indicator that characterizes the relative number of people with disabilities among the population). The incidence of poliomyelitis (meaning severe, paralytic forms, often leading to death) in the pre-vaccination period rarely rose to 10 per 100,000 population. However, high lethality and disability forced the development and use of a vaccine against this disease.

4. It is advisable, if possible, to narrow the circle of people to be vaccinated, identifying risk groups as precisely as possible. Such a system especially effective in zoonotic infections. Only those groups of the population that have a direct relationship with animals (care, grazing, treatment, etc.) or are engaged in the processing of animal raw materials are subject to vaccination. With natural foci th diseases are vaccinated by persons who go to work or rest in the zone of an actively operating focus.

5. In very rarely recorded cases of diseases with nosological forms, even if they are quite severe and not always amenable to specific treatment, they prefer not to vaccinate, since loading the body of a huge number of people with foreign agents that can cause unwanted reactions, due to for the rarest cases of disease, often looks inappropriate. Thus, in the foothills and adjacent plains of the North Caucasus from the Black Sea to the Caspian Sea, in some years, from one to several cases of Crimean hemorrhagic fever (CHF) are recorded. Of course, it is hardly advisable to vaccinate the entire population living in this region against the CHF virus. Perhaps, after more accurate epidemiological mapping of the area, there will be a need to develop a drug and specific prophylaxis for a limited circle of people located in the area of action of a precisely established and delineated natural focus (or several such isolated foci).

As already mentioned, specific prophylaxis (first of all, vaccination) can have two tasks: ensuring individual protection of those vaccinated and creating population immunity. In case of zoonotic infections (including natural focal infections), sapronosis (tetanus), trips to regions or countries that are unfavorable in relation to any diseases, specific prevention aims to provide exclusively individual protection. In anthroponoses, primarily in infections, the causative agent of which is transmitted by airborne droplets, as well as in the activation of other transmission mechanisms as a result of the action of some unfavorable social factors (wars - a possible high incidence of typhus; unfavorable water supply - a high level incidence of viral hepatitis A, etc.), specific prophylaxis should provide both individual protection and the formation of a high level of population immunity.

A good effect after vaccination is determined by a number of conditions.

1. The quality of the drug (in this case, we mean non-compliance with the regime and conditions during the production, transportation and storage of the drug - this is mandatory and, of course, and its ability to create immunity due to the biological and chemical properties). There are a number of very effective, reliable vaccines

available. For example, vaccines against tularemia, yellow fever, and smallpox are considered the standard of highly effective drugs. On the other hand, there are drugs that cannot fully meet the demands of practice. A search for a more effective drug against coccyx is required.

lusha, need to improve the vaccine against influenza, cholera, typhoid fever and some others.

2. Compliance with the regimen (regulation) of drug administration. There must be a strict discipline of compliance with the timing of the introduction of drugs (age of people to be vaccinated, allowable time intervals between individual injections of the drug in the course of vaccination and between vaccination and revaccinations). The choice of the date of vaccination is determined, if we talk about children - who, as you know, are the first to be vaccinated - the current epidemic situation. The age of children to be vaccinated established by law, based on a long-term assessment of the epidemic situation, was selected for each nosoform. Only when the epidemic situation worsens, the regulations can be temporarily changed - children of an earlier age are vaccinated. In addition, when developing the vaccination schedule, the age-related feature of the maturation of the immune system of children in relation to a particular pathogen or its waste products (exotoxins) must be taken into account. Thus, children at the age of 1 year are vaccinated against measles (the epidemic situation forced this period to be legalized, although immunity develops more fully when children who have reached the age of 1.5 years are vaccinated). The same legislation provides for the vaccination of 6-month-old children in the event of a worsening epidemic situation. In this case, we see a compromise solution, taking into account the importance of both factors. Against hepatitis B and tuberculosis, vaccination is carried out immediately or shortly after birth (in the first week of life), against diphtheria, whooping cough and tetanus - 3 months after birth, etc., etc.

Most specific prophylaxis drugs only imitate the natural infectious process, therefore, vaccination, as a rule, is not able to provide the level, quality and duration of immunity that is formed after an illness, i.e. it is not equivalent to that which protects people who have been ill. This forces, firstly, to select the largest tolerated dosages of the drug, and secondly, to often use a system of repeated administration of the drug, including revaccination. The problem of insufficiency (to obtain a good immune response) of tolerable dosages and the forced repeated administration of inactivated and chemical vaccines is to some extent solved if subcutaneous preparations are used, with the help of added adjuvants (adjuvants). Adjuvants are adsorbents that are indifferent to the body (aluminum hydroxide is most often used), which at the injection site create, as it were, a depot of the vaccine and, due to slow desorption, provide tolerance to sufficiently large dosages, as well as long-term immunization irritation, which makes it possible to reduce the number of injections for both vaccination and revaccination. It is possible that the positive effect of adjuvants is associated not only with the phenomena of adsorption - desorption.

1 in

Revaccinations due to the already mentioned booster effect lead to a rapid increase in immunity indicators, and to levels that are significantly higher than those formed after primary vaccination. The vaccination-revaccination system often provides a more reliable formation of the so-called ground (main) immunity, which, due to T- and B-memory lymphocytes, often makes it possible to protect the previously vaccinated even after a long time after vaccination.

3. A high percentage of vaccination coverage of the population, providing reliable herd immunity. This condition does not matter if it is required to protect people traveling to places where epidemic trouble is developing with the help of specific prophylaxis. There is no need to create population immunity in case of zoonotic, including natural focal, infections and sapronoses (tetanus). With these groups of diseases, it is important to achieve full vaccination coverage of people at risk. Population immunity, as an inhibitory factor in the development of the epidemic process, is important in airborne infections or other anthroponoses, the mass incidence of which, due to unfavorable social conditions, becomes threatening. The positive role of population immunity affects not only the fact that people with artificial immunity have a chance not to forget oh-fly, but also in the fact that with a high degree of population immunity, the risk of infection decreases. The latter is explained by a decrease in the circulation of the pathogen due to the impossibility or decrease in the likelihood of the formation of new sources of infection. In addition, under conditions of rather intense, but not absolute, population immunity (not 100% of the population is stable), due to the rarefaction of susceptible (or insufficiently protected) among the dominant immune part of the population, there is a real chance that they will not encounter the pathogen at all, and upon encountering it, they will become infected with doses insufficient for the development of the disease. Thus, population immunity can to some extent neutralize the lack of effectiveness of the drug at the individual level.

To create artificial **active** immunity, several groups of vaccines are used.

Live vaccines that contain a weakened (attenuated) strain of the pathogen. Reliable, genetically determined attenuation is most often selected empirically during passages on artificial nutrient media, on specially selected cell cultures, or on animals. Cultivation conditions are also selected, which may differ from the usual ones.

Live vaccines are considered one of the best - they often imitate the natural infectious process quite well, often causing the formation of a fairly reliable immunity. These vaccines are not expensive, because the initial dosage of the drug is not large (calculation for the reproduction of the vaccine strain in the body, which ensures resulting in a vigorous and long-term effect on the body's immune system). The advantages of live vaccines should also include the fact that the frequency of drug administration is usually not large, there are not many revaccinations, and rather

long periods are provided between vaccination and revaccination. Unfortunately, vaccine strains can sometimes, although extremely rarely, cause clinical forms of a specific infectious process. In some cases, this leads to the rejection of the use of live vaccines in favor of killed (inactivated) or chemical vaccines. In particular, a number of countries have switched to vaccination against poliomyelitis using an inactivated vaccine, which is inferior in effectiveness to live.

In work focused on the creation of immunity with the help of live vaccines, additional opportunities have appeared when using recombinant processes (the exchange of genetic material), which are observed in some pathogens. In particular, this technique is applicable in the preparation of live influenza vaccines, since the influenza virus genome consists of 8 fragments that are not very tightly linked to each other. With the joint cultivation of wild and attenuated (weakened) strains due to recombinant phenomena, the exchange of genetic material (genome fragments) is possible. At present, it is possible to obtain recombinant strains (they are called reassortant vaccine strains), which contain two fragments of the genome of wild strains responsible for the formation of surface H- (hemagglutinin) and N- (neuraminidase) antigens. These antigens are necessary for the formation of a protective immune response specific to wild strains of the virus.

Killed (inactivated) vaccines are widely used because they do not cause a specific reaction that can develop after the introduction of a live vaccine. However, since the killed vaccines contain a large number of microbial bodies (viral corpuscles), the vaccinated often develops a non-specific painful reaction to the administration of the drug, sometimes quite severe. This reaction is occasionally accompanied by an exacerbation of chronic diseases, which led to the need to develop a list of diseases (chronic pathological conditions) that determine the so-called medical exemptions from vaccinations. Unfortunately, the practice of widespread use of the system of medical exemptions (often without proper reason) has led not only to an increase in the number of people who are defenseless against certain diseases, and very dangerous ones (whooping cough), but also to a sharp decrease in population immunity.

The inactivation mode is selected in such a way that the most important antigenic components of the pathogen are preserved without any violations of the chemical structure, including the spatial structure. Sparing physical and chemical influences or their combinations are used - temperature not more than 56-58 ° C and other physical agents, formalin, phenol and other substances in minimal concentrations. Vaccination with killed (inactivated) vaccines is one of the expensive measures, since the concentration of the microbe in the preparation, as already mentioned, must be high, in addition - and this is the main thing - to obtain reliable immunity, vaccination with repeated administration of the drug and revaccination (sometimes several) is required also with multiple injections of the drug. Such a complex immunization system creates many difficulties in organizing vaccinations and often

leads to violations of vaccination schedules, and often for objective reasons (departure, illness) and also because of psychological barriers on the part of the vaccinated or their relatives.

Despite all the shortcomings, killed vaccines, since specific reactions to the pathogen are excluded, occupy an important place in the system of specific prevention.

Chemical vaccines. The idea of using chemical vaccines (the so-called subunit vaccines) arose on the basis of the data that not all components of a microbial cell (viral corpuscle) possess immunogenic properties, i.e., properties to induce protection against a pathogen. In it, along with antigens responsible for the formation of the body's defense, there are substances (antigens) that are not related to the creation of immunity, but often lead to nonspecific painful reactions (essentially, these are ballast, unnecessary, and sometimes dangerous ingredients). At present, the meningococcal chemical vaccine and some others have come into practice. Sometimes some chemical components extracted from the microbe are additionally introduced into the killed vaccines, which enhances the immunogenic properties of the drug.

Genetically **engineered vaccines** have been developed and continue to be developed. When using the principles of genetic engineering, the genome of a harmless microbe (*E. coli*, yeast, etc.) is introduced and fixed with a gene responsible for the formation of an antigen that is crucial in the development of immunity against the pathogen from which the said gene was obtained (for example, the gene for surface antigen hepatitis B virus). Genetic engineering allows you to get a pure antigen, that is, it is a kind of chemical vaccine. But on the basis of genetic engineering, one can also count on the use of non-hazardous live vaccines (a harmless microbe will produce the antigen necessary for immunization during vegetation in the body itself). In some nosoforms in the pathogenesis of the disease, the defeat is not from the microbial cell itself, but from the products of its vital activity - exotoxins (diphtheria, tetanus, botulism, gas gangrene). In this regard, for the prevention of such diseases, preparations containing neutralized exotoxin - **toxoid** are used.

In the system of specific prophylaxis, in order to simplify immunization, in particular, to minimize the number of vaccinations, **associated preparations** are widely used, which contain antigens of several pathogens. Associated vaccine preparations from live attenuated pathogens have also been created. The possibility of effective use of associated drugs has been proven in many experiments and in epidemiological experiments, it also has a theoretical justification: each antigen introduced into the body stimulates the activity of only a certain clone of lymphocytes (each antigen has its own clone, which is intact with respect to other antigens). On the same basis, simultaneous immunization with various drugs is possible.

Specific prophylaxis is organizationally implemented in the form of scheduled vaccinations and vaccinations according to epidemic indications. Routine vaccinations are carried out against a number of airborne infections (diphtheria, whooping cough, measles, mumps, rubella, tuberculosis), against tetanus, poliomyelitis, viral hepatitis B. These vaccinations are carried out regardless of the current epidemic situation, since the latter can at any time change for the worse. Scheduled vaccinations for certain population groups (risk groups) are carried out on the basis of local legislation against a number of zoonotic infections (including natural focal). According to epidemic indications, vaccinations are carried out against any nosological forms (if a vaccine exists), including against those that are controlled by routine vaccination.

For **passive** immunization, not native human and animal sera are currently used, but only those fractions that contain antibodies (mainly the **gamma globulin fraction**). Ideally, it is desirable to have pure antibodies. Preparations of animal origin have proteins that are alien to humans, therefore, due to the high risk of developing allergic reactions, they are forced to refuse. Currently, the number of preparations of animal origin is reduced to a minimum, only in cases where it is necessary to have preparations with a very high concentration of antibodies while they have to be used. Recently, there has been a quite reasonable trend towards a gradual abandonment of the widespread use of passive immunity for preventive purposes. This does not exclude the use of purified serum preparations for therapeutic purposes, including the administration of specific gamma globulins to bitten, possibly rabid, animals and in natural foci of tick-borne encephalitis - to persons in whom a stuck tick was found.

Questions for chapter 15

1. Preventive and anti-epidemic measures
2. General structure of preventive and anti-epidemic measures
3. Preventive measures
4. Anti-epidemic measures
5. Disinfection. Disinsection
6. The main directions of disinfection measures for various groups of infectious diseases
7. Deratization
8. Specific prevention of infectious diseases
9. Types of vaccines.

CONTENT

INTRODUCTION	3
List of abbreviated words	5
Part I. GENERAL EPIDEMIOLOGY	6
1. SUBJECT OF EPIDEMIOLOGY	6
1. 1. DEFINITION OF THE SCIENCE OF EPIDEMIOLOGY	6
1. 2. THE SUBJECT OF EPIDEMIOLOGY. THE PLACE OF EPIDEMIOLOGY IN THE STRUCTURE MEDICAL SCIENCES, MEDICAL EDUCATION AND PRACTICAL HEALTH CARE	10
2. EPIDEMIOLOGICAL METHOD	14
2.1. EVOLUTION OF EPIDEMIOLOGICAL RESEARCH TECHNIQUES. MODERN STRUCTURE OF THE EPIDEMIOLOGICAL METHOD	14
2.2. METHOD OF EPIDEMIOLOGICAL EXAMINATION OF NIDUS	18
2.3. EPIDEMIOLOGICAL ANALYSIS METHOD	24
2.4. EXPERIMENTAL RESEARCH TECHNIQUES	70
2.5. USE OF TECHNIQUES EPIDEMIOLOGICAL DIAGNOSIS IN EVIDENCE-BASED MEDICINE	84
Part II. EPIDEMIOLOGY OF INFECTIOUS DISEASES.	85
3. TEACHING ABOUT EPIDEMIC PROCESS	86
3.1. DEFINITION OF THE EPIDEMIC PROCESS	86
3.2. COMPONENTS (INTERNAL STRUCTURE) OF THE EPIDEMIC PROCESS.	102
3.3. POPULATION IMMUNITY AND THE THEORY OF SELF-REGULATION OF THE EPIDEMIC PROCESS.	114
3.4. CLASSIFICATION OF INFECTIOUS DISEASES	122
3.5. CHARACTERISTICS OF THE EPIDEMIC PROCESS MANIFESTATIONS.	124
3.6. FACTORS OF THE EPIDEMIC PROCESS	129

3.7. EPIDEMIOLOGICAL SURVEILLANCE	132
3.8. PREVENTIVE AND ANTI-EPIDEMIC MEASURES	167
CONTENT	186
GLOSSARY	188
REFERENCES	195

GLOSSARY

Analytical epidemiological methods - (gr.analysis-spread, spread) these methods are used in order to determine the causes of the appearance and spread of the disease, that is, dangerous factors.

Analytical epidemiological methods are those used in the examination of epidemiological theories, hypotheses about dangerous factors.

Anthroponoses - (gr.anthropos-human-posos-disease) causative agent are infectious diseases that live mainly in the human body.

b) the risk of spreading the triggering epidemic variant.

Biological species is the sum of natural populations fused into a single gene pool. The types of infectious disease triggers are determined by their phenotypic signs in laboratory conditions.

Biosenosis - (gr.bios-life+koipos-general) the adaptation of various species of creatures and living beings to living in one environment due to evolutionary progress. Parasitic system and parasitocenosis, belong to the concept of biocenosis.

Classification of infectious diseases - scientific grouping of infectious diseases. An International Statistical Classification of infectious diseases has been adopted. For the epidemiological classification of infectious diseases, a sign of phylogenetic and ecological proximity of pathogens is taken as a basis. The epidemiological classification of infectious diseases is based on the mechanism of transmission of the causative agent of this disease and the location of the causative agent in the human body.

Conditionally pathogenic microorganisms are microorganisms that constantly live or freely live in the organism of the host, which cause disease only under certain conditions. The human organism is not considered a permanent habitat for these microorganisms.

Contagiousness is the property of the pathogen in the species circle. The degree of contagion of specific types of pathogens varies at different stages of the development of the epidemic process and is determined by the characteristics of the interaction of the pathogen with the host's organism.

Continuous cold chain- in a special temperature mode (+2s - +8s) from the moment of production of vaccines to the vaccinated population.

Deratization – (derived from the French word-des-negation, loss, rattus-squid), loss of rodents.

Desinsection - (derived from French-insecta-insect, des-negation, loss) loss of arthropods (insects) that spread infectious disease triggers.

Disinfection-French-des-negation, loss, and Latin infectio - means disease-calling, destruction of pathogenic microorganisms (bacteria, viruses, rickettsiae, simpling animals, fungi) in the environment.

Epidemic furnace is the location of the causative source of the disease within the probability of transmission of the causative agent and the environmental objects surrounding it.

Epidemic is an outbreak that exceeds sporadic levels or occurs where the same disease has not occurred before.

Epidemic outbreaks are simultaneous outbreaks of a number of people in a limited area (outbreaks in separate communities or groups, which are mutually epidemiologically related).

Epidemic process -1) the manifestation of the causative parasite and the interaction of the population of people in certain social economic and natural conditions in the form of solitary or numerous outbreaks. 2) the process of emergence and spread of infectious diseases among people.

Epidemic trend is the main direction of the intensity of change in the perennial dynamics of the epidemic process.

Epidemiological control is a modern form of Organization of anti-epidemic work, aimed at preparing the population for anti-epidemic protection and ensuring its successful implementation, collecting information, analyzing and assessing certain conditions, setting a goal, making management decisions and formalizing them, giving clear instructions to the executors and checking their implementation.

Epidemiological diagnosis - determination of the epidemiological status and incidence of the population using epidemiological research methods.

Epidemiological method is a set of methods used to identify risk factors, aimed at studying the distribution of disease across regions, among different groups of the population, and aimed at identifying preventive problems.

Epidemiological state of the population is the sum of data that characterizes the manifestation of the epidemic process and the factors of its development.

Epidemiology as a science of General Medicine - a science that studies the causes, conditions and mechanisms of spread of diseases of the population, its distribution among different groups of the population and in different seasons of the year, and, analyzing this data, develops measures (prevention) to prevent and combat the disease.

Epidemiology is a science about the epidemic process, about the laws of its development and forms of manifestation.

Epizootia is a disease of animals belonging to a particular region.

Furnace of anthropurgical infection - (gr. anthropos-man + ergon-activity, impact) is an epidemic furnace formed due to the activity of people.

Gene pool is the sum of genes in individuals in a single population.

General epidemiology is the sum of theoretical, methodological, practical and organizational knowledge used in disease prevention. General epidemiology consists of 5 sections. 1) the science and methods of Epidemiology 2) the doctrine of the epidemic process. 3) epidemiological diagnosis. 4) anti - epidemic measures. 5) Organization of anti-epidemic work.

Genotype - (gr. genos-generation, origin +tipos-type, type) is the sum of individual-specific genes. The genotype of microorganisms is determined by clones, the sum of genes specific to micropopulations.

Genotypic and phenotypic heterogeneity of parasitic and host populations is the diversity of excitatory and human populations according to their genotypic and phenotypic characteristics. Symptoms of the parasite include the characteristics of pathogenicity, infectivity and immunogenicity, predisposition to the signs of the host, the characteristics of generating immunity.

Heterogeneous population—(gr. heterogenes-diverse, not homogeneous) for example, the fact that people in a community are not homogeneous in their susceptibility to disease.

Hospital infections (intra-hospital infection or nosocomial infection or yatrogenic infections) are infectious diseases that occur and develop in hospitals.

Host is an organism that is considered a living environment and a source of nutrients for the parasite.

Immunity - (lot. immunos) the ability of a person to resist the action of infectious disease pathogens and their toxins, developed as a result of the interaction of antigen with the body. An immune discrepancy occurs after infection and after

vaccination. By the mechanism of development-there will be anti-toxin, antimicrobial, humoral, cellular, general and local immunity. Human population is diverse in terms of generating and maintaining immunity.

Immunogenicity is the property of the causative agent (immuno+gr-genes –fertile, born) to develop one or another type of immunity in the master (human) body.

Immunological composition of the population is the distribution of individuals into populations by whether they have immunity.

Infection - (lot.infectio-damage or infection) 1) infectious process 2) type of infectious disease 3) specific infectious disease.

Infectious disease triggers are microorganisms, viruses, prokaryotes, mycoplasmas, chlamydia, ricketts, bacteria, spirochetes that cause infectious diseases in humans.

Infectious diseases are diseases that arise as a result of the proliferation and life activity of viruses and prokaryotes that fall into the body of people. The type of diseases is determined by the type of causative agent.

Infectious process is the process of interaction of the causative parasite and the organism of the master (human or animal). The manifestation of the disease in an unmarked or obvious (manifest) form, that is, in the manner of bacterial transport.

Intra-hospital infection-infectious diseases that arise and develop in a treatment-preventive institution. In order for a hospital to have an intra-hospital infection, the source of the causative agent must be associated with the hospital, which will have to take into account the latent period of the disease when diagnosing these diseases.

Invasion-damage with vomiting (common animals), cases of their infection.

Loss of infection - complete termination of the type of infectious disease due to the elimination of the causative agent as a biological species in the global Mashtab.

Manifestation of infection-pronounced characteristic signs characteristic of each type of infectious disease. These clinical signs are determined by the degree of pathogenicity of the excitatory population and the degree of predisposition of the population of people.

Natural epidemiological experiment is an epidemiological study used to assess morbidity under extreme conditions, to assess the effects of external factors in groups with high or low morbidity rates.

Natural factor, in Epidemiology, is the sum of abiotic and biotic elements in the external environment.

Natural furnace-1) the geographical landscape is a branch of the territory, in which the transmission, spread of the pathogen among wild animals is observed. 2) regardless of the activity of humans in nature vertebrates that is, the residence of the host's population, a place where there are natural conditions for the reproduction of the pathogen in his organism.

Nozoareal is an area where there is potential for the development of an infectious disease. Global and regional nozoareals are distinguished.

Operational epidemiological analysis (OPA) - an immediate assessment of the development and dynamic state of the epidemic process, the results of the OPA form the basis for making decisions to carry out rapid measures against the disease.

Pandemic - (gr.pandemos - all people) the peak of the development of the epidemic process, the spread of an infectious disease to a huge number of countries, continents or the entire globe.

Parasite - (gr.parasitos is a living micro organism that uses another living organism (the host organism) as its habitat and source of nutrients. Parasites can be pathogenic, conditionally pathogenic, or non-pathogenic. The causative agents of infectious diseases will be absolute or facultative parasites.

Parasitic diseases are infectious diseases caused by pathogenic eukaryotes (fungi, viruses, common animals, arthropods).

Parasitism is a form of interspecific relationship, the process of using the second (master) organism of a living organism as a living and feeding environment.

Pathogenicity - (gr.pathos-disease+ genes-emergence) is the property of the causative parasite to cause disease in another organism (host organism).

Phenotype-the sum of all the properties and signs that the organism has formed in the process of individual development, the phenotype is determined by the conditions of the living environment.

Population - (lat.population-population) is a population community or isolated population community that differs from another in its natural life activities.

Potential effectiveness is the measure of the outcome of measures acquired at a certain stage of Science and practice, which are important in reducing diseases. Efficiency is represented by the index of protection and the index of efficiency. Clear (practical) effectiveness-prevention of the disease is the result of measures

taken by practical health authorities to reduce or end it. The epidemiological, economic and social effectiveness of anti-epidemic measures is disputable.

Predisposition 1) the development of a pathological process in the organism of the host (man, animal) in response to the causative agent, reproduction and living life, the property of the host to ensure the emergence of an infectious disease in a clear (manifest) form or in an unmarked form.

Private epidemiology is a complex of knowledge about the epidemiology of individual types of infectious diseases.

Psychrophils are microorganisms that tend to reproduce at low temperatures.

Reservoir of the causative agent of infection is the sum of the conditions that ensure the survival of the natural habitat and excitatory population of the causative agent. In anthroponosis, the reservoir of the causative agent is the human organism, in Zoonoses the animal organism, and in sapronoses the objects of the external environment.

Resistance is the resistance of people to infectious diseases, not infecting them, without dependence on specific factors of immunity. Determined by genotypic and phenotypic factors.

Retrospective epidemiological analysis (REA) is an analysis of the previously occurring incidence rate, structure, perennial and annual dynamics in a given area, ensuring the resolution of epidemiological diagnostic issues in order to justify the planning of epidemic response measures.

Risk areas are areas with high incidence rates. Risk-threatening communities-1) organized communities with high incidence rates 2) Organized Communities in which the trigger is maintained during the inter-epidemic period and an epidemic option is formed.

Risk factors - 1) aggravating the risk of the appearance of diseases, social and natural factors and specific features of the functioning of people, as well as the state of the internal system of the body. 2) conditions that shape the disease: a) the risk of the occurrence of the triggering epidemic variant.

Sapronoses are infectious diseases, the source of which are the objects of the external environment.

Saprophytes are free-living microorganisms that feed on plant and extinct animal organs.

Seasonality-in the annual dynamics of infection with infectious diseases, there is always a certain season (winter, summer, etc.) rise.

Social factor, in Epidemiology, is the sum of social relationships, contacts that have an accelerating or slowing effect on the epidemic process, preventing or helping the manifestation of self-control mechanisms developed as a result of the evolution of infectious disease triggers.

Source of infection (the source of the causative agent of infection) is the natural habitat (environment) of the causative parasite, a sick person or animal who infected the patient with the disease, in sapronous diseases, objects of the external environment.

Sporadic morbidity is a morbidity that occurs singly. Corresponds to the lowest incidence rate in the season period of the year.

The mechanism of transmission of infection is the process of the transition of the causative agent from the source of infection to the body of a healthy person, which occurs during evolution. The mechanism of transmission is carried out in three stages (the release of the pathogen outside the patient's body, its presence at the objects of the external environment and entry into the body of a healthy person)

Trigger elimination is the complete elimination of a trigger as a biological species in a given area.

Virulence is the degree of pathogenicity of the causative agent (lat-virulentus - poisonous). Inflammatory populations are characterized by a severe-mild course of the diseases that they call.

Zoonoses - (gr.zoon-animals+nosos-disease) infectious diseases in which the main source of the causative agent is animals.

REFERENCES

Main references

1. Брико Н.И., Покровский В.И. Эпидемиология. Учебник. М.: «ГЭОТАР-Медиа», 2015. (эл.вер)
2. Миртазаев О.М., Зуева Л.П., Матназарова Г.С. - Эпидемиология. Тошкент, 2016
3. Миртазаев О.М., Зуева Л.П., Матназарова Г.С. - Эпидемиология. Тошкент 2020
4. Покровский В.И. Инфекционные болезни и Эпидемиология. Москва, 2008
5. Покровский В.И., Брико Н.И. Общая эпидемиология с основами доказательной медицины. Москва, 2010

Additional references

6. Bhopal R. Concepts of epidemiology.- Oxford University Press., 2003
7. Leon Gordis. Epidemiology. Philadelphia: Saunders., 2018
8. Беляева Н.М, Трякина И.П., Синикин В.А., Никитина Г.Ю. КОРЬ Учебное пособие Москва 2015
9. Брико Н.И. Руководство по формированию практических умений по эпидемиологии. Москва, 2017
10. Даминов Т.О. ОИТВ инфекция. Ташкент, 2010
11. Жаҳон соғлиқни сақлаш ташкилотининг «Вакциналар ёрдамида бошқарилувчи юқумли касалликлар ва иммунизация» дастури бўйича тиббиёт ходимлари ва педагоглар учун қўлланмаси. Тошкент -2014.
12. Зуева Л.П., Яфаев Р.Х. Эпидемиология. Санкт-Петербург, 2006
13. Красавцев Е.Л., Романова Е.И., Анищенко Е.О. Детские инфекции. Учебно-методическое пособие. Гомель 2008.

- 14.Лысенко А.Я., Кондрашин А.В., Ежов М.Н. Маляриология. Копенгаген, 2003
- 15.Миртазаев О.М. ва хаммуаллифлари. Профилактик эмлаш тизимида узлуксиз совуқлик занжири. Тиббиёт олий ўқув юртлари педагоглари учун ўқув-услубий қулланма. Тошкент 2020й
- 16.Мусабаев И.К. Руководства по кишечным инфекциям. Ташкент, 1980
- 17.Онищенко Г.Г. Заболеваемость паразитарными болезнями в Российской Федерации: научное издание // Эпидемиология и инфекционные болезни.-М., 2007.
18. Покровский В.И., Брико Н.И. Руководство к практическим занятиям по эпидемиологии. Москва, 2005
- 19.Руководство по эпидемиологическому надзору корью, краснухой и синдромом врожденной краснухи в Европейском регионе ВОЗ Обновленное издание, 2012 г.

Legal documents

- 20.Ўзбекистон Республикаси «Аҳолининг санитария-эпидемиологик осойишталиги тўғрисида»ги Қонуни. - Т.: 26.08. 2015-й.
- 21.Ўзбекистон Республикаси санитария-эпидемиологик осойишталик ва жамоат саломатлиги хизмати фаолиятини ташкил қилиш чоратадбирлари тўғрисида. ПФ-4790.2020 йил. 9 сентябрь
22. Ўзбекистон Республикаси СанҚваМ №_0239-07/4, 27.07.2021.Ўзбекистон Республикаси Соғлиқни сақлаш вазирлигининг 11.04.2006 даги 148-сонли буйруғи –Республиканинг барча омборларида вакциналарни тўғри сақлаш ва самарали бошқариш стандарт ишчи муолажалари тўғрисида
- 23.Ўзбекистон Республикаси Соғлиқни сақлаш вазирлигининг

27.01.2015 йилдаги 36-сонли буйруғи — «Бошқарилувчи юқумли касалликлар иммунопрофилактикасини ташкил қилиш» тўғрисида.

24. Ўзбекистон Республикаси Соғлиқни сақлаш вазирлигининг 27.08.2018 йилдаги 542-сонли буйруғи «Вирусли гепатитлар эпидемиологияси, эпидемияга қарши ва профилактик чора тadbирларни ташкиллаштириш»