FEDERAL STATE BUDGETARY EDUCATIONAL INSTITUTION
OF HIGHER EDUCATION
«BASHKIR STATE MEDICAL UNIVERSITY»
OF THE MINISTRY OF HEALTHCARE OF RUSSIAN FEDERATION

DEPARTMENT REPRODUCTIVE HUMAN HEALTH
WITH COURCE OF IMMUNOLOGY

APPROVED by
Head of the department

Kurcer M. A.
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Methodical recommendations For students
Independent work of students

Discipline: Clinical Immunology
Specialty: 31.05.01. «General education»
Course 4
Semester 5
Hours: 24

Ufa - 2021

Methodological instructions for professors for lectures in the discipline "Clinical Immunology " were developed by the faculty of the department in accordance with the work program of the academic discipline (Ufa, 2021), the curriculum (2021) and taking into account the requirements of the Federal State Educational Standard of Higher Education 3 ++ according to specialty 31.05.01. «General education» (M., 2020).

Authors:

1. Assistant of the department of reproductive human health with course of immunology Gaisina A. R.
2. Associate professor of the department of reproductive human health with course of immunology Gaisina A. F.

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Head of the department  (Kurcer M. A.)

Lesson 1

Тема: Fundamentals of Immunology:

Stages of formation of immunology. Immunity theories.

The purpose of studying the topic: it consists in mastering knowledge about the stages of formation of immunology.

Tasks: to study the stages of formation of immunology

Type of occupation: - independent extracurricular work (abstract).

Duration:- 8 hours.

The student must know before studying the topic:

1. Mechnikov's theory of immunity
2. Paul Ehrlich's theory of immunity
3. Theory of immunity Occasionally
4. Instructive theories of immunity

The student should be able to:

1. Use educational, scientific, popular science literature, the Internet.
2. To carry out the collection of material for immunological research.
3. Prepare micro-preparations.

The student must own:

Methods of microbiological diagnostics :

- microscopic
- bacteriological
- immunological
- allergological
- molecular biological.

Tasks for independent extracurricular work of students on this topic:

1. Get acquainted with the theoretical material on the topic of the lesson using the recommended educational literature.
2. Answer questions for self-control
3. Mechnikov's theory of immunity
4. Paul Ehrlich's theory of immunity
3. Theory of immunity Occasionally
4. Instructive theories of immunity

3. Test your knowledge using test control:

A. One of the founders of the development of the doctrine of immunity is not:

1. Thucydides
2. L. Pasteur
3. I.I. Mechnikov
4. B. Langenbeck answer: 4

B. Who first developed a practical method of standardization of diphtheria toxin and antitoxin preparations:

1. I.I. Mechnikov

2. P.Ehrlich
3. P.F. Zdrodovsky answer: 2

Q. Who developed the doctrine of human blood groups differing in red blood cell isoantigens and antibodies to them:
1. E. Jenner.
2. K. Landsteiner.
3. Louis Pasteur.
answer: 2

Complete tasks:
Task No. 1.
Purpose: Who is I.I. Mechnikov?
Answer:
I. I. Mechnikov developed the phagocytic theory of immunity - the body's immunity to infectious diseases. I. I. Mechnikov's research has shown that special macro- and microphage cells play an important role in the formation of immunity. These cells absorb and digest foreign particles, including bacteria. I. I. Mechnikov's research on phagocytosis has convincingly proved that, in addition to humoral, there is cellular immunity.

Task number 2.
Purpose: Who is P. Ehrlich?
Answer:
A great role in the development of immunology was played by the German chemist P. Ehrlich, who developed the humoral theory of immunity and the doctrine of antibodies
Task number 3.
Question: Who is the scientist K. Landsteiner?
Answer: Austrian scientist K. Landsteiner, discovered isoantigens
and blood groups and is the founder of immunogenetics
Forms of control: mastering tasks for independent extracurricular work on this topic - test tasks, control questions, situational tasks.

Lesson 2

Topic: The relationship of maternal and fetal immune systems
The purpose of the topic: to study the mechanisms of the relationship between the immune systems of the mother and fetus
Tasks: - to study the theory of immunity.
Type of occupation: - independent extracurricular work (abstract).
Duration:- 4 hours.
The student should know before studying the topic:
1. The difference between the fetus and the mother by histocompatibility antigens.
2. Conflicts between the immune systems of the mother and fetus.
3. The role of IgG and fetal protein alpha-fetoprotein in fetal development.
4. The role of the placenta as a buffer between two immune systems.
The student should be able to:
1. Use educational, scientific, popular science literature, the Internet.
2. To carry out the collection of material for immunological research.

3. Prepare micro-preparations.

The student must own:

Methods of immunological diagnostics:

Tasks for independent extracurricular work of students on this topic:

1. Get acquainted with the theoretical material on the topic of the lesson using the recommended educational literature.

2. Answer questions for self-control:

-The difference between the fetus and the mother by histocompatibility antigens.

-Conflicts between the immune systems of the mother and fetus.

-The role of IgG and fetal protein alpha-fetoprotein in fetal development.

- The role of the placenta as a buffer between two immune systems.

3. Test your knowledge using test control:

A. When does the differentiation of cells of the immune system of intrauterine development of the embryo occur?

1. 1 to 2 weeks of intrauterine development of the embryo
2. from 2 to 3 weeks of intrauterine development of the embryo
3. from 3 to 6 weeks of fetal development

, the answer is: 3

B. When are the first lymphoid cells detected in the fetal liver?

1. for 3 weeks
2. for 4 weeks
3. for week 5

, the answer is: 3

. Does thymus formation occur?

1. for week 5
2. for 4 weeks
3. for 6-7 weeks, the answer is: 3

G. Development of the thymus, implies:

1. Differentiation of two types of lymphocytes in it: immunologically immature (having a thymus antigen on its surface) and mature, located in the brain layer of the organ.
2. Differentiation of B-lymphocytes in it
3. Differentiation of macrophages

answer: 1

Complete tasks:

Task No. 1.

Objective: What physico-chemical properties of antibodies correspond to different classes of immunoglobulins?

Answer:

It was found that only Ig G is transmitted from mother to fetus, and its levels in the umbilical cord blood of the fetus reach concentrations found in the mother's blood. The principle of transmission of this class of immunoglobulin and the expediency of this process is extremely important, since the formation of its own Ig G in the fetus is quite low and even at the time of delivery does not exceed 1% of the synthesis of its mother. At first, it was assumed that the transplacental transmission of Ig G is peculiar only to the hemochoric type of placenta. However, later it turned out that it is determined by the ability of

cells to transport pinocyte vacuoles with proteins without their degradation during this process. Ig M also has a similar type of transmission, but the rate of vacuole diffusion is much slower, and therefore the concentration of this protein in the fetus is low.Physiologically, this is partially justified by a decrease in the penetration of the mother's isohemagglutinins belonging to this class to the fetus. Of all plasma proteins, Ig G has the highest rate of transition from mother to fetus. At the same time, it has been shown that the passage of proteins through the placenta does not depend on the molecular weight of the protein, but is the resulting rate of its sorption on placental cells, diffusion into the fetus, reverse diffusion to the mother and the degree of degradation by intracellular proteases. The mechanism of Ig G transport has much in common with the penetration into the cell of high-mass proteins, as well as DNA and RNA viruses and toxins of protein origin.The immunoglobulin molecule binds to a receptor on the syncytiotrophoblast. Trypsin-cleaved Ig G has the ability to diffuse through the placenta. The fab fragment Ig G obtained with pepsin also does not pass through the placental barrier. The theory of F. W. R. Brambell (1966), with subsequent additions, suggests the receptor transport of Ig G through the placenta. There are two types of pinocytic vesicles — large (macro-) and small (micropinocytic). It is shown that the small type of vacuoles is designed for selective binding of protein molecules, in particular Ig G.Such a vacuole passes through the cytoplasm of the cell and is ejected from it by exocytosis. Receptors for the Fc fragment of immunoglobulin were found on human chorionic trophoblast cells. Currently, it is customary to subdivide Ig G into several subclasses (Ig G 1-4). Their differentiation in practical conditions can be carried out by analyzing changes in antibody titers in native serum, after warming up, after contact with staphylococcus, after treatment with cysteine

Task number 2.

Objective: How do the immunological aspects of perinatal infections develop from the characteristics of a child's development?

Answer:

The immunological aspects of perinatal infections consist of the peculiarities of the child's development during the period (his contact with various infectious pathogens and antigens) and gradually decreasing maternal immunity. The state of immunity of the pregnant woman is not significantly impaired. A paradoxical effect is created — the fetus is not rejected as an allograft, due to the blockade of cellular immunity in relation to its tissues. However, in relation to other antigens, the mother's body responds with normal immune reactions.

Forms of control: mastering tasks for independent extracurricular work on this topic - test tasks, control questions, situational tasks.

Lesson 3

Topic: Features of antifungal, antiprotozoal immunity. The peculiarity of antitumor immunity

The purpose of studying the topic: to consider the main mechanisms of the formation of antifungal, antiprotozoal and antitumor immunity.

Objectives: to consider the main mechanisms of the formation of antifungal, antiprotozoal and antitumor immunity.

Type of lesson: - preparation for classes.

Duration:- 8 hours.

The student must know before studying the topic:

1) Acquired immunity, types (active, passive, artificial, natural, sterile, non-sterile, antibacterial, antitoxic, antiviral, local, etc.)
2) The main differences between innate and acquired immunity.
3) Forms of immune response.
2,after studying the topic:
1) Features of antifungal immunity.
2) Features of antiprotozoal immunity.
3) Features of antitumor immunity.

The student should be able to:

1. Use educational, scientific, popular science literature, the Internet.
2. To carry out the collection of material for immunological research.

The student must own:

Methods of immunological diagnostics:

Tasks for independent extracurricular work of students on this topic:

1. Get acquainted with the theoretical material on the topic of the lesson using the recommended educational literature.

2. Answer questions for self-control:

-Features of antifungal immunity.
-Features of antiprotozoal immunity.
-Features of antitumor immunity.

3. Test your knowledge using test control:

A. Do mushrooms belong to?
1. eukaryotes
2. prokaryotes
answer: 1

B. How can reproduction occur in fungi?
1. Sexually
2. Asexual way
answer: 1,2

Q. What are the diseases caused by fungi called?
1. Escherichiosis
2. Phimoses
3. Mycoses answer: 3

g. The main representative of the genus Candida causing specific candidiasis:
1. Candida albicans
2. Candida minimalis
3. Candida medium
answer: 1

D. What is the name of the outer rigid membrane of protozoa?
1. Pelicula
2. Vesucula
3. Falikula

Complete tasks:

Task No. 1.

Purpose: Give a brief description of the immune response in candidiasis?

Answer:

Fungal infections develop, as a rule, with a decrease in the overall immunoreactivity of the body or defectiveness of the T-link of immunity. With congenital T-cell immunodeficiency, skin and mucous membranes of Candida albicans, brain and meninges are often affected by cryptococci, lung pneumocysts. Pneumocystic pneumonia is one of the dangerous complications of AIDS. It is also known that a decrease in the functional activity of polymorphonuclear leukocytes (PMN) and T-lymphocytes, observed with fatigue, malnutrition, alcoholism, deficiency of trace elements (Fe, Cu, Zn), diabetes mellitus, tuberculosis, is often accompanied by the development of such a harmless fungus that constantly lives on the skin and mucous membranes as Candida albicans.With fungal infections, as a rule, reduced indicators of the cellular link of immunity are detected, and vice versa, the development of a fungal infection (for example, the appearance of thrush) is the first reliable clinical sign of a disorder in the cellular link of immunity. Children with congenital deficiency of humoral immunity show high resistance to fungal lesions. Probably, antibodies are not any significant factor in protecting against fungal infection. These data indicate that with the development of fungal infection, immunotherapy should be aimed primarily at normalizing and stimulating the work of the T-link of the immune system.

Phagocytes, T cells, and NK lymphocytes take part in the elimination of fungi. Polymorphonuclear cells play a major role in the phagocytosis of fungi and their destruction among phagocytic cells . In this process, antibodies and complement (C3b) can act as opsonins. Any functional disorders associated either with genetic defects or acquired as a result of adverse effects on the body of physical, chemical or other factors (drugs–corticosteroids, antibiotics) can create the basis for the development of recurrent fungal infections.

Some fungi are destroyed as a result of direct lytic (fungicidal) action of NK cells and T lymphocytes. On the example of cryptococci, this ability of NK cells has been demonstrated in vitro.Many fungal infections are accompanied by the development of hypersensitivity reactions of types I and IV. The development of hypersensitivity significantly complicates the course of an infectious disease, can give it a new character. So, with fungal lung lesions, this can lead to chronic granulomatosis and fibrosis.

Task number 2.

Purpose: Give a brief description of the protective mechanisms of fungi?

Answer:

The protective mechanisms of fungi differ little from those of bacteria and include a capsule that protects fungi from phagocytosis (for example, in cryptococci), resistance to digestion in macrophages (for example, in histoplasmas) and the ability to destroy PMYALS (for example, in coccidia).

Task No.3.

Purpose: Give a brief description of the simplest?

Answer:

Protozoa consist of a single eukaryotic cell. From the outside, the body of the protozoa is covered with a rigid membrane – a pellicle. Adjacent to it is an outer denser and more homogeneous layer of cytoplasm – ectoplasm. In some species, the pellicle may contain supporting fibrils and even a mineral skeleton. The set of organelles located in the more liquid endoplasm is identical to that of cells of multicellular organisms; the exception may be the presence of several nuclei in some species. Many protozoa are able to actively move due to pseudopods, flagella or cilia. In unfavorable conditions, cysts form. Protozoa use humans as a power source. In humans, protozoa can cause acute (for example, African sleeping sickness) and chronic (for example, giardiasis) diseases. The life cycle of parasitic protozoa often includes the formation of intermediate forms in the body of various hosts, which gives them the opportunity to infect susceptible organisms more effectively. Protozoa spread over long distances by

insect vectors, parasitize intracellularly, are characterized by high variability of surface antigens, and in the process of their development have an immunosuppressive effect on the host organism. Among the protozoa, malaria pathogens, African and American trypanosomes, and leishmania are the greatest danger to humans. A number of protozoa (amoeba dysentery, giardia, isospores) cause mild to moderate intestinal lesions.

Task No.3.

Purpose: Give a brief description of antitumor immunity?

Answer: On the way to creating an effective vaccine, there are real difficulties associated with the nature and characteristics of antitumor immunity.

Antitumor immunity is a system that includes two lines of defense with different characteristics and functions. The first of them – natural (natural, nonspecific) immunity – reacts to the presence of an alien origin in the body, including altered (mutated) cells that can be potential sources of tumor development. The second, adoptive (specific) immunity, serves to implement an immune response by forming a population (clone) of lymphoid cells designed to fight a developing tumor. For this purpose, adoptive immunity, unlike natural immunity, has characteristic properties – immunological memory in relation to a specific tumor factor (antigen) and the ability to recognize this factor (i.e. specificity), as a result of which an immune response is formed and maintained, and ultimately tumor cells atypical for the body are destroyed. It is on the basis of specificity and immunological memory that the creation of any vaccines is based.

Natural immunity is realized due to several types of cells:

1) large granular lymphocytes – NK cells, natural killers (from the English killer – killer);

2) mononuclear cells (monocytes of circulating blood and tissue macrophages);

3) neutrophilic granulocytes.

The function of natural immunity consists,

firstly, in the recognition and destruction of microbial, virus-infected, malignant cells by phagocytosis (leukocytes, mononuclears) or cytotoxic effect (NK lymphocytes) and,

secondly, in the presentation (presentation) of foreign material to the system of adoptive immunity.

For the presentation, a structure is formed consisting of an antigen fragmented during phagocytosis and elements of a monocyte-macrophage cell – the main histocompatibility complex (MHC). Intercellular interaction with the participation of MNS determines the further development of the response in the system of adoptive immunity: the formation of a cytotoxic cellular reaction and the production of specific antitumor antibodies.

Lymphocytes involved in the reactions of adoptive immunity have various functions: for example, helpers produce factors that stimulate the function of killers; killers produce toxic factors that destroy tumor cells. Various types of cells involved in immunological reactions interact with each other through the secretion of relevant factors (tissue mediators) – cytokines (lymphokines – for lymphocytes, monokines – for monocytes and macrophages).

Natural and adoptive immunity are, as already mentioned, links of a single mechanism of immunological protection, the implementation of which is aimed at maintaining the constancy of the internal environment of the body and neutralizing foreign substances, including transformed cells.

Modern science has data on the nature of a complex that recognizes a tumor antigen and can cause the development of an effective immune response. This complex combines several factors. Tumor antigen, phagocytized and processed by cells of natural immunity, is a peptide molecule that is associated with various histocompatibility molecules represented on monocytes or tissue macrophages (classes of molecules are called MHC-1 or MHC-2). In this form (tumor peptide + histocompatibility molecules +

auxiliary factors), the antigen interacts with the corresponding receptors of lymphocytes – T helper cells and T cells, precursors of cytotoxic cells.

Дfor each type of cell, the connection of the tumor antigen with its histocompatibility molecule is necessary: for T-cytotoxic cells – with MHC-1,

for helpers – with MHC-2.

CD markers are receptor structures (differentiation antigens) on the surface of T–lymphocytes that determine their functional properties (various subpopulations of lymphocytes: CD8 helper cells, CD4 cytotoxic cells);

B7 (CD28/B7) – auxiliary molecules necessary for cell interaction and transmission of a stimulating signal;

IL-2 is a factor of inter–lymphocytic interaction that provides activation of cytotoxic (antitumor) response. The effect of IL-2 is realized by increasing the number of activated lymphocytes (lymphokine-activated cells, LAC), which, in comparison with NK cells, have more pronounced antitumor cytotoxicity. The activity of IL-2 was established in animal experiments, and subsequently the therapeutic effect of this factor was convincingly shown in relation to some types of human tumors, in particular metastatic foci in melanoma and kidney tumors. Treatment gives positive results in 15-20% of cases, and in about half of them there is complete resorption of metastases (Rosenberg S.A., 2001). IL-2 stimulates the growth of the LAC subpopulation with the combined cultivation of lymphoid cells with antigens from tumor tissue. Even with a multiple increase in the concentration of IL-2, it does not have a direct cytotoxic effect (i.e., without the participation of LAC) in relation to malignant cells. This leads to the conclusion that IL-2, unlike chemotherapy drugs, is an antitumor immunomodulator.

All the necessary factors of antitumor protection are inherent in the nature of the immunity of a healthy person, and nevertheless the developing tumor manages to overcome this barrier. Why is this happening?

The problem lies in the nature of the tumor itself and the patterns of malignant growth.

Firstly, the tumor originates from the tissues of the body and its difference (degree of foreignness, antigenicity) from healthy cells is not so significant as to cause the development of a pronounced immune response. Tumor antigens (OAA – tumor–associated antigens) are weak antigens, unlike the antigens of bacteria or viruses, which show more pronounced differences, i.e. stronger antigenic properties, which are used in the creation of effective (antibacterial, antiviral) vaccines.

Secondly, the developing tumor has its own protective mechanism for selecting cells that can most effectively counteract the immune surveillance system (Deichman G.I., 2000). This mechanism includes an active antioxidant system and prostaglandin E2 synthesis.

These factors resist the mechanisms of anticancerogenesis (including immunity), support the survival of transforming cells and thus contribute to the formation of their clone forming a tumor.

Thirdly, a growing tumor has a depressing effect on the immune system by the mass of its cells and the products of their vital activity, including those that suppress immunity and have a general toxic effect on the patient's body.

Fourth, the immunosuppressive effect of antitumor chemotherapy and radiation is added.

So, the reasons for the insufficient effectiveness of immunological defense mechanisms during the development of tumor disease are:

- weak antigenicity of OAA
- selection of tumor cells as malignancy increases
- tumor production of immunosuppressive factors
- the general toxic effect of the tumor process on the patient's body

• side effect of immunosuppressive therapy

The listed factors, which manifest their effect at different stages of the oncological process, indicate the features that determine the insufficiency of antitumor immunity: the escape of malignant cells from immune surveillance and the increase in their resistance to the action of immune mechanisms as the tumor mass increases. Calculations show that with the number of tumor cells at the level of 109, immunological defense mechanisms are insufficient. Meanwhile, this amount is close to the minimum for the manifestation of the first symptoms of neoplasm. With a cell mass of 108, the tumor does not yet clinically detect itself, although it is available for diagnosis by determining the appropriate markers – cancer embryonic antigen (REA), CA-125 (for ovarian cancer), etc. Understanding these patterns allows us to draw an important conclusion that it is fundamentally possible to use immunotherapy as a method of anti-relapse and antimetastatic treatment when the bulk of the tumor has been removed and the prognosis of the disease depends on the effective suppression of the surviving malignant cells. And from here it logically follows the conclusion about the possibilities and prospects of the use of antitumor vaccines.

Forms of control: mastering tasks for independent extracurricular work on this topic - test tasks, control questions, situational tasks.

Lesson 4

Topic: The peculiarity of antitumor immunity.Immunotherapy: Immunomodulators Immunobiotechnology

The purpose of studying the topic: to study the basic principles of the action of immunomodulators

Tasks: to consider

-the main mechanisms of action of immunomodulators;

- classification of immunomodulators.

Type of occupation: - independent extracurricular work (abstract).

Duration:- 4 hours.

The student must know before studying the topic:

1) Acquired immunity, types (active, passive, artificial, natural, sterile, non-sterile, antibacterial, antitoxic, antiviral, local, etc.)

2) The main differences between innate and acquired immunity.

3) Forms of immune response.

The student should know after studying the topic:

-immunomodulators (immunostimulants and immunosuppressants)

-characteristics of the main immunomodulators;

- immune modulators of microbial origin;

-immunomodulators of endogenous convergence

-synthetic immunomodulators

The student should be able to:

1. Use educational, scientific, popular science literature, the Internet.
2. To carry out the collection of material for immunological research.
3. Prepare micro-preparations.

The student must own:

Methods of immunological diagnostics:

Tasks for independent extracurricular work of students on this topic:

1. Get acquainted with the theoretical material on the topic of the lesson using the recommended educational literature.

2. Answer questions for self-control:

1) the main mechanisms of action of immunomodulators;
2) classification of immunomodulators

3. **Test your knowledge using test control:**

A. Do immunostimulants include?
1. thymus preparations,
2. interleukins, interferons
3. interferon inducers, biologically active peptides
4. polysaccharides of some fungi, therapeutic vaccines
answer: 1,2,3,4

B. Do probiotic microorganisms (bifidobacteria and lactobacilli) have immunostimulating activity?
1. Bifidobacteria
2. Lactobacilli
3. E. coli
answer: 1,2

V. Does thymus formation occur ?
1. for 5 weeks
2. for 4 weeks
3. for 6-7 weeks, the answer is: 3

G. Peptide immunomodulators are:
1. Antibiotics
2. Thymus preparations, such as thymalin, thymogen, thymotropin
3. Aminoglycosides
Answer: 1,2

Complete tasks:

Task No. 1.

Purpose: To list immunostimulants?

Task number 2.

Purpose: To list immunosuppressants

Forms of control: mastering tasks for independent extracurricular work on this topic - test tasks, control questions, situational tasks.

Solving situational problems:

Task 1

During the biotechnological process, a genome was isolated from the cell nucleus of a pathogenic microorganism for humans, in which a certain gene (a site of the nucleic acid of the microorganism) was selected. This gene was propagated using PCR. In the database of antimicrobial agents, one was selected, interaction with which suppressed the activity of the gene most effectively. Then the antimicrobial agent selected from it was tested in action on the whole microbial cell of the original microorganism, causing a pronounced suppression of its vital activity.

1. Determine the type of antimicrobial structure screening for a specific pathogen.
2. Highlight the main stages of screening, determine their significance during screening.
3. What this type of antimicrobial structure screening is used for.
4. What will serve as a continuation of this process?
Answer:
1. In this example, targeted screening is used.
2. Sequential stages of targeted screening:
1) Gene selection. At the first stage, a gene is selected using bioinformatics data on the role of the gene and the significance of its expression product in cell metabolism, as well as structural and comparative genomics.
2) Gene amplification. At the second stage, the DNA of the selected gene is amplified (multiplied) using polymerase chain reaction (PCR) in order to obtain a sufficient amount of the gene for further studies. The accumulated DNA matrix undergoes transcription and translation in a cell-free ribosomal matrix system in order to obtain a sufficient amount of the gene product (target).
3) Determination of the specific activity of the target in the cell-free system. Natural metabolites and synthetic substances with antimicrobial action from libraries of antimicrobial agents are tested for the ability to suppress the activity of the target.
4) Selection of the antimicrobial agent with the highest
5) Investigation of the mechanism of interaction of the selected antimicrobial agent with the whole microbial cell. An important stage of the study, since in practice the antimicrobial substance may not penetrate the cell, undergo enzymatic inactivation or interact with other macromolecules of the cell.
3. Targeted screening is formed as a new strategy in the field of screening pathogen antagonists and the creation of innovative antimicrobial drugs with a fundamentally different mechanism of action than antibiotics selected during primary screening for activity on laboratory nutrient media. A distinctive feature of the new strategy is that the search work begins not with inhibitors of a particular metabolic process of the pathogen, but with possible targets for potential antimicrobial agents using knowledge about the genome and gene.
4. In the future, the value of a particular gene for the vital activity and reproduction of a pathogenic microorganism is determined by its

Task 2.
The fermentation stage is central among the stages of industrial production. Fermentation is understood as the whole set of sequential operations from the introduction of inoculate into a pre-prepared and thermostated medium to the completion of growth, biosynthesis or biotransformation processes.
1. What two types of fermentation do you know?
2. What equipment is used for fermentation? Its main elements, a schematic representation.
3. How does the technological design of industrial biotechnology processes depend on the ratio of the producing microorganism to oxygen? Three groups of bioreactors.
4. Ways to control the fermentation process.
Answer:
1. Surface and deep fermentation.
2. Fermentation takes place in special containers called fermenters or bioreactors. The main elements of the fermenter are double walls, the gap between which is filled with cooling or heating liquid, inlet openings for gas and liquid flows, a control system for the composition of the nutrient medium and conditions inside the reactor.
3. The technological design of industrial biotechnology processes is largely determined by the ratio of the producing microorganism to oxygen. When using aerobic cultures, the fermentation equipment and the

norms of the technological regime are selected in such a way that mass transfer (oxygen transfer from the gas to the liquid phase) ensures the supply of oxygen to the cells in quantities necessary and optimal for a given culture in a given growth phase. The industrial use of facultative anaerobes does not pose the task of absolute exclusion of oxygen from the environment. In the initial phase of these processes, it is only necessary to remove oxygen from the gas phase above the culture liquid, which can be achieved by introducing an inert gas or simply displacing air with carbon dioxide released by cells during metabolism. The technological design of strictly anaerobic processes is more complicated than for fermentation processes, since in this case it is necessary to completely exclude the possibility of oxygen entering the gas, and from there into the liquid medium.
Bioreactors are divided into three main groups:
1. reactors with mechanical mixing;
2. bubbling columns through which air is passed to mix the contents;
3. airlift reactors with internal or external circulation; mixing and circulation of the culture medium in them is provided by an air flow, due to which a density gradient occurs between the upper and lower layers of the culture medium.
4. The simplest way to control the fermentation stage in a periodic mode is to change the concentrations of the components of the medium and its pH, as well as the introduction of the necessary additives according to a pre-developed program implemented by the technologist in each fermentation cycle. It is also important to maintain a certain composition of the nutrient medium. In continuous biosynthesis processes, the technologist's task is to maintain the concentration of all nutrients (and oxygen) and the dosed introduction of acid or alkali to pH-statize the system at a given level

Task 3
An important component of biotechnology is genetic engineering. Genetic engineering methods transform bacterial, yeast and mammalian cells into "factories" for the large-scale production of any recombinant protein.
1. Define recombinant DNA.
2. What enzymes do you know that are used in the construction of recombinant DNA?
3. Features of quality control of genetically engineered drugs, quality indicators.
4. The role of vector in genetic engineering.
5. Characteristics of vector systems important for the transfer of necessary genes into mammalian cells.
Answer.
1. Recombinant means DNA formed by combining in vitro (in vitro) two or more DNA fragments isolated from various biological sources.
2. The enzymes used in the construction of recombinant DNA can be divided into several groups:
- enzymes that produce DNA fragments (restrictases);
- enzymes synthesizing DNA on a DNA matrix (polymerases) or RNA (reverse transcriptases);
- enzymes connecting DNA fragments (ligases);
- enzymes that allow changing the structure of the ends of DNA fragments.
3. Quality control of genetically engineered drugs has its own characteristics. Medicinal products obtained by recombinant technology should be identical to the structures of the human body and contain a minimum of permissible impurities in order to avoid immunological and allergic reactions, should also not contain toxins, pyrogens, which is achieved by using pure biological material and high-quality purification of the finished product.
The control of recombinant protein drugs is carried out according to the following indicators:
a. authenticity and purity;
b. biological activity;

c. apyrogenicity;
d. absence of acute and chronic toxicity;
d. biological and immunological identity, which is determined by international standard samples, and the standard sample is always used recombinant.

4. In genetic engineering, foreign genes are cloned in so-called shuttle vectors. These vectors are replicated with equal success in the cells of several hosts. The vectors were obtained by a combination of in vitro plasmid fragments. It is convenient to embed a gene in a special vector for expression, which already contains regulatory elements that ensure active expression after the introduction of a recombinant plasmid into a bacterial cell. Such effective regulatory sites include, for example, a strong promoter of the beta-lactamase gene (the penicillin resistance gene, which is part of the pBR 322 plasmid).
5. Convenience of gene delivery - the problem of delivering foreign DNA in vitro is practically solved, and its delivery to target cells of different tissues in vivo is successfully solved (mainly by creating structures carrying receptor proteins, including antigens specific to certain tissues), then other characteristics of existing vector systems are integration stability, regulated expression, without
There are two types of gene therapy: substitution and corrective. Gene replacement therapy consists in introducing an intact gene into the cell. The inserted copy will replace the defective gene preserved in the patient's genome by function. All clinical trials conducted today use the introduction of additional amounts of DNA into the cell.
With corrective therapy, it is assumed that the defective gene will be replaced by a normal one as a result of recombination. While this method is at the stage of laboratory testing, since its effectiveness is still very low.

Forms of control: mastering tasks for independent extracurricular work on this topic - test tasks, control questions, situational tasks.

The main literature

Serial №	**Title**	**Author(s)**	**Year, place of publication**	**Number of copies**	
				In library	At the department
1	2	3	4	7	8
•	**Basic Immunology: Functions and Disorders of the Immune System [Текст] :** [учебноеиздание]	**A. K. Abbas, A. H. Lichtman, S. Pillai.**	Elsevier, 2016 – 335 p.	80	0

Additional literature

Seria l№	**Title**	**Author(s)**	**Year, place of publication**	**Number of copies**	
				In library	At the departme nt
1	2	3	4	7	8
3.	Lectures in immunology: курс лекций	Maianskii, A. N.	N. Novgorod: Publishing house	40	0

			NSMA, 2004 – 256 p.		
•	**IMMUNOLOGY**	**Khaitov R.M.**	**2008 – 256 c.on-line.**	**access mode:** ЭБС «Консультант студента» http:// www.studmedlib.ru/book/ ISBN9785970407042.html	unlimited access
•	**Fundamental Immunology.**	**Lippincott Williams & Wilkins**	**2008 –on-line**	**access mode:** Database«LWW Medical Book Collection 2011» http:// ovidsp .ovid.com	unlimited access