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TRADITIONAL AND NEW REPRESENTATIONS ABOUT ETIOLOGY AND PATHOGENESIS OF INFECTIOUS DISEASES

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ABSTRACT

In the work, taking into account the accumulated data in the etiopathogenesis of infectious diseases, the number of pathogenetic mechanisms has been expanded. The existing traditional ones are joined by immune reactivity, microbiota, metabolic immunity, low molecular weight nucleic acids and cyclic nucleotides, which represent new possibilities for the prevention and treatment of pathological processes.

KEYWORDS: Immune reactivity, metabolic immunity, nucleic acids, microbiota.

INTRODUCTION

The relevance of this generalization is justified by the fact that 30-50 million people suffer from infections every year in the Russian Federation, which makes up more than 30% of all diseases. In fact, the real number of

infectious morbidity is significantly underestimated, because a number of pathological processes have an infectious component (some malignant neoplasms, coronary heart disease, peptic ulcer, Crohn's disease). New diseases and pathogens appear (legionnaires disease, mad cow disease, Ebola virus, SARS). Statistics do not take into account infectious complications in immunodeficiencies, allergies, lymphoproliferative processes, after vaccinations, in risk groups (children, pregnant women, puerperas, old people) and situations where this remains to be proved. The best diagnosticians in the world of pathologists claim that 50% of those who died in hospitals died from hospital infections.[1,2]

I. ETIOLOGY OF INFECTIONS

Inductors of infections are pathogenic, opportunistic pathogens and infectious agents. The latter include non-cellular life forms - viruses and prions and cellular - bacteria (prokaryotes), fungi, protozoa and helminths. Large microorganisms actinomycetes occupy an intermediate position between bacteria and fungi, and convoluted spirochetes fill the gap between bacteria and protozoa. Small intracellular parasites of rickettsia and chlamydia are located between viruses and bacteria, and mycoplasmas and ureaplasmas are bacteria, lost the cell wall during evolution. The etiological sources of diseases, for example, sapronoses, are their pathogens living in the external environment — microflora of soil, water, air, including leaves, legionella, etc., anthroponoses — bacteria and parasites that live only in humans (malaria, rash and relapsing fever, trench fever, fever pappatachi fever, vuchereriosis, brugiasis, loiasis), anthropozoonoses - pathogens of animals and humans (yellow fever, dengue fever, leishmaniasis, trypanosomiasis; plague, tularemia, pseudotuberculosis, anthrax, rabies), zoonoses - pathogens of infections that parasitize in certain types of animals, which are their natural reservoir, that infect humans (protozoa, viruses, bacteria, fungi, helminths, ticks).[3]

Soil microflora

It includes almost all microorganisms: spore, non-spore bacteria, actinomycetes, fungi, spirochetes, archaebacteria, protozoa, blue-green algae, mycoplasmas, viruses in the amount of up to 10 billion in 1 g. As a rule, pathogens in the soil are in various combinations - bacteria with fungi, with protozoa, with viruses. In this case, natural mechanisms of soil self-cleaning are possible. As a result, vegetative forms of microorganisms die in a few hours - months, spore-forming in decades.[4]

Soil microorganisms dangerous to humans are divided into 3 groups. 1. Pathogens for which the soil is a permanent habitat - bacteria, actinomycetes, fungi. 2. Spore microorganisms for

which the soil is a secondary reservoir (anthrax, tetanus, gas gangrene). 3. Pathogenic microorganisms that have fallen into the soil with excretions of humans and animals (E. coli, Salmonella, Shigella) with the preservation of viability for hours - days.

The cause of human sapronous diseases, for example, the disease of legionnaires, are legionella, surviving in water conditioners, Listeria and other pathogens.

Microflora of water

In principle, the microflora of water reflects the microbial landscape of the adjacent soil due to the entry of pathogens into the water with particles of the earth. In addition, biocenoses are formed in water - enterobacter, enterococci, clostridia; pathogens of intestinal infections - typhoid, paratyphoid, dysentery, cholera, leptospirosis; enterovirus infections, cryptosporidiosis; pseudomonads. Water way transmission have cholera vibrio, legionella, able to multiply in water. According to the degree of contamination by microorganisms, water is divided into 3 categories. Polysaprobic, dirty, containing more than 1 million pathogens in 1 ml; mesosaprobic - moderately contaminated - hundreds of thousands of microbes in 1 ml; oligosaprobic - pure, tens and hundreds of microorganisms in 1 ml.[5]

Microflora of air

It contains pathogens dangerous to humans - about 3.7% of pathogenic staphylococci, soil putrefactive flora, mold fungi and other pathogens. Indoors, representatives of the microflora of the human nasopharynx are identified, secreted with sputum, saliva, mucus: staphylococci, streptococci, tuberculosis mycobacteria, corynebacterium diphtheria, yeast, mycelial fungi, viruses, and others. A cloud of sneezing is formed around a person from a distance of 2 meters from microorganisms hanging about 1-2 hours.[6]

Etiological factors of zooanthroponosis

These include

Pathogenic staphylo- and streptococci causing abscesses, phlegmon, pyoderma, pyemia, septicemia, osteomyelitis, endometritis, and food toxicosis.

Pathogenic anaerobes C. tetani, C. botulinum, causative agents of gas gangrene, causing acute non-contagious wound infections in which the nervous system is affected by the exotoxin of the microbe.

Pathogenic enterobacteria of Escherichia, Salmonella, which, when a person is infected by an alimentary route, can cause entero - enteric forms of intestinal damage with septicemia.
Pathogenic Yersinia Y. pestis, Y. pseudotuberculosis, Y. enterocolitica are the causative agents of anthropozoonous plague, characterized by severe intoxication, damage to the lymphatic system, and a tendency to septicemia.

The causative agents of listeriosis, tularemia, which cause natural focal infectious diseases with the likelihood of developing degenerative lesions of parenchymal tissues.

The causative agents of brucellosis, which affect a person in direct contact with sick animals or when eating infected products.

The causative agents of leptospirosis, which cause infectious natural focal disease in animals and humans, characterized by fever, anemia, jaundice, hemoglobinuria, hemorrhagic diathesis, necrosis of the mucous membranes and skin, and atony of the digestive organs. The main transmission factor is water, contact and food routes.

Rickettsia causing Ku rickettsiosis (Q fever), which is a natural focal infectious disease characterized by short-term fever, the development of rhinitis, pneumonia, conjunctivitis.[7]

Microbiological etiological factors foodborne diseases

Food products are seeded by microorganisms as a result of vital infection of animals or as a result of their diseases, retention, processing and storage of products. Representatives of certain groups of microorganisms that can be found on food products, under certain conditions, can cause human diseases caused by Escherichia, Flavobacterium, Hafnia, Listeria, Mycobacterium, Proteus, Pseudomonas, Salmonella, Yersinia, microscopic fungi (mold).[4]

Foodborne diseases are divided into 2 groups: foodborne infections and food poisoning.

Food infections

These are infectious diseases that occur when there are live pathogen cells in the product. In food infections, food serves as a carrier of pathogens that do not propagate in products: Salmonella typhi, Shigella of bacterial dysentery, causative agents of zoonotic diseases Bacillus anthracis - anthrax, Brucella melitensis - brucellosis, Mycobacterium tuberculosis - tuberculosis and etc.

Food poisoning

These are diseases in which food plays a major role. Food intoxication (toxicosis) can occur in the absence of pathogen cells in food, when the cells themselves died, but their toxins were preserved. Distinguish between bacterial and fungal toxicosis. Bacterial toxicosis - botulism is caused by Clostridium botulinum, which is in the natural habitat - soil, and the products whose use can cause disease are raw smoked sausages, fish, ham, canned foods, mushrooms. The causative agent of bacterial staphylococcal toxicosis is Staphylococcus aureus, which can be in the oral cavity, on the nasal mucosa, in the air, on the skin. Often contain its products, the use of which causes the disease. These include canned meat, fish, cream, milk. Fungal toxicosis causes fungi Fusarium graminearum, Claviceps purpurea, forming mycotoxins, or fungal toxins. Sources of pathogens are cereal food, bread, soups, cereals from infected grains.[8]

II. ANTIBIOTIC RESISTANCE

Antibiotics are some of the most successful drugs ever made by humans. They transformed medicine and saved millions of lives. However, shortly after their discovery, it became apparent that antibiotic resistance may develop in microorganisms. For several decades, this problem was solved by the constant introduction of new drugs. In recent years, this trend has slowed significantly and, as a result, the prevalence of antibiotic-resistant bacterial pathogens has sharply increased.[7,9]

Antibiotic resistance is the ability of microbes to remain viable under the influence of therapeutic doses of antimicrobial chemotherapy drugs. Accordingly, bacteria should be considered resistant (or sustainable) if they are not neutralized by such concentrations of the drug that are actually created in the macroorganism during treatment. Antibiotic resistance can be natural and acquired.

Most often, antibacterial resistance is realized by the following ways. (1) Modification of an antimicrobial agent by bacterial enzymes by the addition or destruction of an active molecule. (2) By reducing the penetration of the antimicrobial agent into the bacterium by reducing the absorption of the active molecule. (3) Active release of antimicrobial agents from bacteria by substrate-specific and non-specific mechanisms. (4) Changes in the bacterial cell targets by protecting, modifying active centers to reduce affinity for the antibiotic molecule.

The loss of sensitivity of microorganisms to antibiotics, and according to forecasts this will completely happen in 10-25 years, will throw humanity into the pre-antibiotic era with unpredictable consequences. In recent years, "super bacteria - superbugs" with multidrug resistance have emerged, which is an evolutionary response to the uncontrolled use of antimicrobials.

According to WHO data, there is a steady increase in the accumulation of resistant, gram-positive and gram-negative microflora, mainly pathogens of nosocomial infections. In 2008 L. Rice identified a group of pathogens with a high level of antibacterial resistance that is responsible for the majority of nosocomial infections in the USA and gave it the name ESKAPE "run-and-save" (including Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa, Enterobacter species). These microorganisms are highly resistant to almost all available antibacterial drugs. Gram-negative bacteria with multiple antibacterial resistance pose a problem not only for adult patients, but also for children.

The highest level of total antibiotic resistance of microorganisms is registered in France, Germany, Russia, the USA, China, the lowest - in Denmark, Venezuela. The formation of antibiotic resistance of microflora is based on the irrational use of these drugs in production, which is 10 times greater than the use in medicine. Moreover, 80% of the same antibiotics are used in agriculture, animal husbandry, in hygienic, cleaning products, to prevent spoilage of fruits, vegetables, and in canning.

In medicine, there are often violations of the daily, course regulation of the use of these drugs, unjustified appointment for subfebrile conditions, acute respiratory and diarrheal viral infections, unreasonable combinations. Moreover, the frequency of antibiotic use in pediatrics is more than 90%. Subinhibitory concentrations of antibiotics, without exerting a therapeutic effect, cause horizontal gene transfer with increased virulence of infectious agents. The combination of antibiotic therapy with probiotics enhances the formation of microflora resistance in patients. In recent years, problems have arisen in creating new antibiotics. So, in 2000-2010, 5 new drugs were created, in 2015-2016 - not a single one.

Principles of combating the phenomenon of antibiotic resistance

Consist of a number of approaches. (1) Use of "old antibiotics" as starting preparations. (2) Temporary delayed appointment. (3) Inadmissibility of changes in the schedule of drug

administration during treatment. (4). Inadmissibility of substitution of specialized drugs with broad-spectrum antibiotics. (5). The use of a combination of drugs in special cases only according to indications.

Currently, several promising areas of the fight against antibiotic-resistant strains of microorganisms are being investigated: (1) Development of antimicrobial peptides of bacteriocins (cationic and amphiphilic peptides containing 20–50 amino acids with a wider range of targets). Their interaction with a negatively charged bacterial membrane causes the formation of transmembrane pores, which causes leakage of cell solutions and, ultimately, cell death. (2) Phage therapy - the use of phages to kill antibiotic-resistant bacteria. (3) Combination therapy (using a combination of antibiotics, for example, colistin in combination with tigecycline, aminoglycoside, meropenem), or a combination of an inactivating enzyme inhibitor and antibiotic, for example, clavulanate and amoxicillin. (4) Use of natural compounds such as flavonoids (isocytoside, eucalyptin), alkaloids (berberine), coumarins (asphodelin A), which exhibit a wide spectrum of antimicrobial activity against P. aeruginosa, E. coli, S. aureus, etc. (5) Expanded use of natural antibiotics of colicins, staphylocins, etc. (6) The use of additional methods of treatment for people at risk, which include pregnant women, puerperas, children, the elderly, chronic patients, patients with severe immunodeficiencies. These methods include passive immunoglobulin immunotherapy drugs, active immunotherapy with a combination of vaccines with non-specific modulators, as well as differentiated mono-, combined, alternative and complex immunomodulation. (7) Administration to patients with chronic bacterial infections resistant to antibacterial treatment with the formation of dysbacteriosis of combined immuno-metabolic therapy with the use of eubiotics.

III. MICROBIOTA

The most important factor in the etiopathogenesis of infections is also microbiota and its relationship with the body's immune reactivity. It includes bacteria, spirochetes, bacteriophages, mycoplasmas, chlamydia, rickettsia, viruses, prions and other microorganisms located in the five most important biotopes of the human body - the intestines, oral cavity, respiratory tract, skin integument and the genitourinary system. The occurrence, nature and outcome of infectious processes largely depend on the state of this microflora.

Since the intestinal microbiota is involved in the development of many diseases, various approaches are being developed for its correction. For this purpose, bacterial preparations based on living microorganisms of representatives of normal microflora - probiotics - are used. Probiotics are living microorganisms introduced into the human body: *Lactobacillus acidophilus, L. plantarum, L.casei, L. bulgaricus, Bifidobacterium longum, B. bifidum, B. breve, Enterococcus faecium*, etc. The hypothetical mechanism of action of probiotic preparations is due to microorganisms included in their composition, a number of functional properties. These include the ability to survive in an acidic environment, efficiently attach to the intestinal mucosal epithelial cells and colonize it, produce antimicrobial substances, stimulate the immune system, prevent excessive growth and reproduction of pathogenic microbes and restore normal intestinal microflora. A promising method for the prevention of severe forms of infectious diseases is fecal transplantation (FMT), in which a suspension of microorganisms from a normal microbiota from a healthy donor is introduced into the patient's intestines through an enema, colonoscope, nasogastric or nasoduodenal probe.

Microbiota is a complex and multicomponent complex, which, however, is covered in sufficient detail in our article[10], so we will not deal with it in detail.

IV. IMMUNE REACTIVITY

In the infectious process, this phenomenon is determined by the number and activity of lymphoid and phagocytic cells that are in circulation, the state of complement systems, parameters of non-specific resistance, killer cells, immune globulins, specific antibodies, cytokines and other parameters in a particular patient in the present point in time.[11,12] Immune reactivity causes three levels of anti-infection resistance.

NON-SPECIFIC, NATURAL RESISTANCE

It is a link with specific immune mechanisms. Its components are: (1) the barrier function of integumentary tissues - acid pH due to fatty and lactic acids, mucus, functioning of the ciliated epithelium, lymph nodes, inflammation; (2) protective local vascular reactions (spasm and/or vasodilation of microcirculation, exudation of the serous component of the blood); (3) fever, excretory reactions (cough, runny nose, sneezing, sweating, diarrhea), antagonistic effect of resident microflora, intestinal remodeling; (4) microbicidal exosecrets; (5) humoral bactericidal and lytic products of blood serum and tissue fluids, bronectin, collectins, interferons, normal antibodies; (6) intracellular mechanisms of resistance against pathogens; (7) cell factors - basophils, neutrophils, eosinophils, natural killers, mast cells,

dendritic cells, monocytes/macrophages. These mechanisms develop instantly or after a few hours.[13]

NON-SPECIFIC CONGENITAL IMMUNITY

It is a collective concept that includes the following categories.

Species immunity

By it is meant species-specific anti-infectious resistance due to the peculiarities of the temperature regime, the absence of adhesion receptors, food substrates for microorganisms, etc.

Maternal borrowed immunity

It is mainly caused by IgG antibodies.

Individual fetal immunity

It develops with intrauterine infection.

Actually innate immunity

Its signs are inheritance at birth, nonspecificity, stability, instantaneous realization.

Congenital, paleoimmunity

Inherent in all multicellular organisms - animals, plants, its "length" is about 1.5 billion years. The deployment of humoral and cellular components of innate immunity is carried out within seconds, minutes, hours, however, the formation of immune memory does not occur. Functioning is based on the recognition of not specific pathogens, but their images, which are either common structures of pathogenic microorganisms, or molecules that form when damage to their own cells. The first subgroup of molecules is associated with viruses, gram-positive and gram-negative bacteria, fungi, protozoa, parasites and is labeled as a marker of the "alien marker". The second is a marker of "changed his" under the influence of stress factors, etc. The removal of both is ensured by a complex of reactions, the most important of which is phagocytosis.[14,15]

Specific Adaptive Immunity (Ai)

Formed no more than 500 million years ago during the Cambrian evolutionary explosion during a massive attack of pathogenic microorganisms on vertebrates. It is determined only in 1.5% of animal species - cartilage, bone fish, amphibians, reptiles, birds, mammals. The formation of lymphoid organs has become a prerequisite for providing the basics of AI -

antigen-independent and antigen-dependent differentiation of T- and B-lymphocytes, which determined the survival of vertebrates. Adaptive immunity is not hereditary, but is acquired by an individual in the process of life, characterized by specificity, in some cases low tension and relative short duration, a certain temporary inertia (several days to weeks) for formation, due to humoral and cellular mechanisms (specific antibodies and sensitized lymphocytes). Preserves immune memory for repeated contact with the pathogen.[16]

CLASSIFICATION OF ADAPTIVE IMMUNITY

By origin

Natural

Natural passive

It is acquired passively when antibodies from the mother during fetal development are transmitted to the fetus through the placenta. Antibodies are transmitted against the causative agents of those diseases with which the mother was ill or against which she was immunized. If the baby is breast-fed, he also receives secretory immunoglobulins A.

Natural active

Acquired as a result of a disease. It is acquired individually, its duration is different, manifests itself in 1-2 weeks after the onset of the disease and can remain for months, years, for life.

ARTIFICIAL

Artificial passive

It is acquired when ready-made antibodies are introduced into the body. It occurs immediately, lasts 2-3 weeks if heterologous antibodies are used (from the horse), and 3-4 weeks if the antibodies are human.

Artificial active

With the introduction of vaccines, toxoids, transfer factor.

In connection with the pathogen

Sterile (post-infectious)

It remains after the elimination of the pathogen from the body (measles, diphtheria), non-sterile (infectious) exists as long as the pathogen is in the body (tuberculosis, syphilis).

Body coverage

General

It covers the whole body, the local - any organ. The main role belongs to IgA2. These immunoglobulins bind antigens, inhibit the adsorption of microbes, blocking their receptors.

By mechanism

Humoral, cellular, mixed (main)

Directionality

Antitoxic

Against exotoxins, enzymes - toxins, endotoxins. It is based on a humoral immune response.[13,17]

V. METABOLIC IMMUNITY

The next type of immunity is metabolic immunity, which in recent years we attach great importance to and which we consider as the ratio of the free radical oxidation of lipids and proteins and the antioxidant system in the regulation of immune homeostasis.

However, this problem is described in detail in our article[18] and we will not deal with it in detail. At the same time, we indicate that metabolic immunity in our opinion can also be one of the etiopathogenetic factors of infections, especially in association with a number of key mechanisms, including the system of oxidative and antioxidant activity, etc., which are also examined in detail in our article.[19] The proof of the role of metabolic immunity in the development of infectious diseases is the identification of certain correlative relationships between various indicators of the immune and metabolic systems of the body. So, in the acute period of deep pyoderma, the key parameters of immunopathology (CIC_3^+ NKC_3^+ $IL6_3^+$) led to a correlation with markers - 4 immune (IgM and IgG, medium-weight molecules (MWM_3^+), T cells) and 4 metabolic (Schiff bases, ceruloplasmin, oxidative activity blood plasma, common thiols). In another clinical model of purulent inflammation of pyelonephritis, key markers (B_3^+ MWM_3^+ $NSTsp_2^-$) "consistently changed" with the level of T-helper cells, CIC, IgM, malondialdehyde, vitamin E, superoxide dismutase. In chronic salpingo-oophoritis reference laboratory markers ($T_3^-IgM_3^+IL6_3^+$) were significantly dependent on CD95+ lymphocytes (apoptosis receptor), CD8+ cytotoxic/suppressor T lymphocytes, natural killer effectors (CD56+CD16+), IgM, Schiff bases, ceruloplasmin, ketodienes. And finally, in patients with peptic ulcer of the stomach and intestines, a direct

correlation was established between low molecular weight serum RNA and the level of T-cells, T-helper cells, IgA, and feedback with null lymphocytes.[20,21]

VI. Low Molecular Weight Nucleic Acids and Cyclic Nucleotides

Cyclic nucleotides

In the body, there is a single mechanism that regulates the biochemical processes and functions of cells belonging to various organs, including the immune system: 3´5´adenosine monophosphate (3′5′-AMP) and 3′5′ guanosine monophosphate (3′5′-GMP). These compounds can be considered as secondary intracellular messengers mediating the effect of extracellular factors. The formation of cyclic nucleotides is associated with the activity of enzymes — adenyl- and guanyl cyclases, which are components of cell membranes.[16]

Low molecular weight nucleic acids

In the process of development of any pathological and many physiological processes, the destruction of cells of various body tissues occurs as a result of the action of microorganisms, which is accompanied by the enrichment of the internal environment with fragments of low molecular weight nucleic acids, primarily RNA. This is confirmed by literature data that, for various infectious diseases, marked changes in the concentration of nucleic acids and, above all, RNA in blood plasma are noted. These include non-specific inflammatory lung diseases, acute dysentery, viral hepatitis, pyelonephritis, purulent processes, etc.[21] Wide biodynamic effects of low molecular weight RNA, their effect on microbial populations, infection and immunity, metabolism, tissue regeneration, etc. we considered in detail in article[22] and we will not present them in detail. We give only general laws of action.

Influence on infection

The accumulation of low molecular weight ribonucleotides in the body in the initial period of the infectious process causes the stimulation of reproduction of microorganisms of various taxonomic groups, the selection of virulent clones, the production of exotoxins, which is accompanied by the potentiation of the infection. Confirmation of this phenomenon is shown in model experiments with the administration of a wide range of gram-positive, gram-negative and other pathogens to susceptible animals simultaneously with RNA preparations, which caused an unconditional increase in infection, which was judged by a decrease in LD_{50} values, a decrease in the survival rate, and average rodent life expectancy , an increase in the area of skin necrosis during injection of exotoxins of pathogens of gas gangrene, etc.

Subsequently, the same nucleic preparations (including sodium salt of RNA-sodium nucleinate) caused an increase in antigenicity, immunogenicity, antibiotic sensitivity of microorganisms, specific immune defense factors, which was experimentally reproduced with the introduction of a nucleic stimulator 24 or less hours before infection of laboratory animals.

Influence on immunity

Powerful effects consisting of antiviral, detoxifying, adjuvant, immunomodulating and desensitizing effects were found in model experiments and clinical observations when using low molecular weight RNA preparations, an analogue of naturally released during infectious processes of ribonucleotides.[22,23] The drug enhanced the primary and repeated immune response to corpuscular and soluble bacterial and somatic antigens, induced a “revaccination" effect without adding antigen, and provided phenotypic correction of the low immune response in inbred lines that are highly responsive to animals.[22] This also indicates the importance of low molecular weight RNA as a new etiological link in infectious diseases.

Thus, at present, taking into account the accumulated data in the etiopathogenesis of infectious diseases, the number of pathogenetic mechanisms has been expanded. The existing traditional ones are joined by such as immune reactivity, microbiota, metabolic immunity, low molecular weight nucleic acids and cyclic nucleotides, which represent new possibilities for the prevention and treatment of these pathological processes.

REFERENCES

1. Pokrovsky V.I., Pak S.G., Briko N.I. Infectious diseases and epidemiology. Textbook. 3rd revised edition. Moscow, 2013; 1008.
2. Chereshnev V.A., Shmagel K.V. Immunology. Textbook for students. Educational institutions of higher professional education. Moscow. Publishing House: NP "Center for Strategic Partnership", 2014; 520s.
3. Gusev M.V., Mineev M. Microbiology. Moscow. Publishing Center Academy, 2003; 464s.
4. Vorobyev A.A., Krivoshein Y.S., Shirobokov V.P. Medical and Sanitary Microbiology. Manual. 4th edition. Moscow. Publishing Center: I. M. Sechenov First Moscow State Medical University, 2003; 464.

5. Vorobyev A.A., Krivoshein Y.S., Shirobokov V.P. Medical and Sanitary Microbiology. Manual. 4th edition. Moscow. Publishing Center: I. M. Sechenov First Moscow State Medical University, 2010; 464.
6. Vorobyov A.A. (Ed). Medical Microbiology, virology and immunology. Moscow. Publishing House: Medical Information Agency, 2008; 702.
7. Zverev V.V., Boychenko M.P. (Ed.) Medical microbiology, virusology and immunology. Moscow. Publishing House: GEOTAR-Media, 2010; 480.
8. Labinskaya A.S., Volina E.G. (Eds). Manual on Medical Microbiology. General and Sanitary Microbiology, Moscow: Publishing House: BINOM, 2008; book 1: 1077.
9. Tsarev V.N. (Ed). Microbiology, virusology, and immunology. Manual for Higher Education Institutions. Moscow. Publishing House: Practical Medicine, 2010; 543.
10. Zemskov A.M., Zemskov V.M., Zemskova V.A., Morozov A.N., Mamchik N.P. Immunology of infections at the present stage, microbiota and microbiota diseases. Internat J Curr Advanced Res, 2017b; 6(10): 6381-6386.
11. Zemskov A.M., Chereshnev V.A., Revishvili A.Sh., Zemskov V.M., Popov V.I., Zemskova V.A. Problems of Clinical Immunology in 21st Century. Moscow. Publishing House: Scientific Book, 2018a; 319.
12. Zemskov A.M., Chereshnev V.A., Revishvili A.Sh., Zemskov V.M., Popov V.I., Zemskova V.A. Problems of Clinical Immunology in 21st Century—II. Natural and Drug Regulation Mechanisms of Immunological Homeostasis. Moscow. Publishing House: Scientific Book, 2018b; 286.
13. Zemskov A.M., Zemskova V.A., Popov V.I., Karaulov A.V., Konoplya A.I. Immunology.Textbook. Moscow. Publishing and Printing Center: Scientific Book, 2013; 594.
14. Zemskov A.M., Zemskov V.M., Zemskova V.A., Zoloedov V.I., Kozlov V.A., Donzov A.V., Donzova E.V. Handbook of clinical immunologist "Modern the theoretical, practical, and applied aspects of clinical immunology". Moscow. Publishing House: Triada-X, 2015; 704.
15. Khaitov R.M., Ataullakhanov R.I., Shulzhenko A.E. (Ed.) Immunotherapy. A guide for doctors. 2nd edition revised and supplemented. Moscow. Publishing House: GEOTAR-Media, 2018; 768.
16. Novikov D.K., Novikov P.D. Clinical Immunopathology. Moscow. Publishing House: Medical Literature, 2009; 449.

17. Khaitov R. M. (Ed.) Immunology. Pharmacotherapy without errors. Guide for doctors. Moscow. Publishing House: E-noto. 2016; 504.
18. Zemskov A.M., Zemskov V.M., Donzov A.V., Donzova E.V., Zemskova V.A., Redkin A.N. Metabolic syndrome as a homeostasis modification factor. Internat J Curr Advanced Res, 2017a; 6(1): 1640-1644.
19. Lutskiy M., Zemskov A., Choporov O. Oxidative stress in immune cells in cerebrovascular diseases. Academic Publishing Deutschland: LAP LAMBERT, 2016; 223.
20. Zemskov A.M., Esaulenko I.E., Chereshnev V.A., Zemskov V.M., Suchkov S.V., Zemskova V.A. Cours of lectures on clinical immunophysiology. Textbook. Voronezh. Publishing House: Ritm, 2017; 1048.
21. Zemskov A.M. (Ed.) Fundamentals of Microbiology and Immunology. The average professional education. Textbook. Moscow. Publishing House: Knorus, 2019; 240.
22. Zemskov V.M., Neymann V.V., Pronko K.N., Zemskov A.M. Global role of low molecular weight nucleic acids in biological systems. Global J Med Res., 2020; 20(2): 5-10.
23. Zemskov A. M., Zemskov V. M., Chereshnev V. A. (Eds). Encyclopedia of immunology in 5 volumes. Moscow. Publishing House: Triada-X., 2013; 1962.