DRUG-RESISTANT FORMS OF PATHOGENIC MICROORGANISMS: CAUSES AND MECHANISMS OF ADAPTATION AND RESISTANCE

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Introduction. The problem of the formation of resistance of microorganisms to antimicrobial (including antiviral, antifungal and antiparasitic) drugs (AMR) and other types of resistance began to acquire its relevance in the last two decades of the last century in countries with a developed healthcare system and intensive agriculture. More than half a century of antimicrobial chemotherapy, with all its obvious successes in the fight against severe bacterial infections, served, in turn, as a powerful factor of evolutionary importance and led to a significant increase in the rate of variability of pathogenic microorganisms, which is a reflection of the highest adaptive capabilities of prokaryotes. According to international experts, antimicrobial resistance is the cause of more than 700 thousand deaths in the world every year, of which 22 thousand cases occur in European countries. According to international experts, this figure is expected to increase to 10 million by 2050.

Aim. Determination of the main causes and mechanisms of the formation and spread of resistant forms of microorganisms.

Materials and methods. Analyze the scientific literature and the results of the advanced research in the field of microbiology and pathophysiology regarding the causes, conditions and mechanisms of the formation of antimicrobial-resistant microorganisms.

Results and discussion. The spread of AMR and other types of resistance is one of the most pressing problems of our time, posing biological and economic threats to all countries. AMR and other types of resistance reduce the effectiveness of measures for the prevention and treatment of infectious and parasitic diseases of humans, animals and plants; lead to an increase in the severity and duration of these diseases, which contributes to an increase in mortality and deterioration of health indicators among the population, death of animals and plants. The problem of the formation of AMR and other types of resilience began to acquire its relevance in the last two decades of the last century in countries with a developed health care system and intensive agriculture.

The main reasons for the emergence and spread of AMR and other types of resistance are:

- irrational and (or) uncontrolled use of antimicrobial drugs, chemical and biological agents in health care, agriculture;
- insufficient availability of diagnostic tools for the resistance of microorganisms to drugs in practical health care;
- violation of the qualitative and quantitative composition of the normal microbiota of humans or animals;
- environmental pollution and the emergence of new biological threats associated with the use of genetically engineered microorganisms and harmful plant organisms.

A long period of virtually uncontrolled use of antimicrobial drugs in medicine, veterinary medicine and agriculture has led to the spread of forms of microorganisms, including pathogens of infectious diseases, with genetic characteristics that determine resistance to antimicrobial drugs, including antibiotics, anti-tuberculosis, antiviral and antifungal drugs, as well as disinfectants, including sterilizing, disinfecting, antiseptic, insecticidal and acaricidal agents.

The development of resistance is an inevitable consequence of the widespread use of antimicrobial drugs as a selective factor. According to a number of experts, the laws of evolution indicate that, in the end, microorganisms will become resistant to any antibiotic.

It is important to note that antibiotics do not have the ability to directly grossly disorganize the chemical structure of the target cell, as is typical for many antiseptics. Antibiotics manifest their effect through selective blocking of one of the components of the plastic or biochemical function of the microorganism, which creates the prerequisites for the survival of the pathogen at the population level and the formation of a resistant strain. The variety of known mechanisms of acquired drug resistance of microorganisms can be reduced to several types.

Types of mechanisms of acquired resistance of microorganisms:

1.Enzymatic antibiotic inactivation (betalactams, aminoglycosides, chloramphenicol, fosfomycin, lincomycin)

2. Modification of the structure of the intracellular target on which the drug acts (aminoglycosides, betalactams fluoroquinolones, erythromycin, lincomycin, rifampicin, tetracyclines, glycopeptides),

3.Changing the permeability of the outer membrane structures of the cell for drugs (macrolides, tetracyclines, fluoroquinolones, chloramphenicol, etc.)

4. Active excretion (release) of the drug from the cell (multiple resistance to drugs of different chemical classes: tetracyclines, fluoroquinolones, macrolides, chloramphenicol, etc.)

5. The relatively recently discovered mechanism of active energy-dependent elimination of antibiotics is of general biological significance. It is based on the concept of universal maintenance of cellular homeostasis by systems of active release of xenobiotics from the cell, which made it possible to reveal the widespread mechanisms of resistance. This phenomenon is based on a significant increase in the cytoplasmic membrane of the amount of specific proteins, conventionally called "pumps".

Improvement of measures to control the circulation of antimicrobial drugs, chemical and biological agents provides for: introduction of restrictions excluding the uncontrolled use of antimicrobial drugs, chemical and biological agents, including: improving control over prescription dispensing of antimicrobial drugs for medical and veterinary use; taking measures to ensure the rational prescription and use of antimicrobial drugs in health and veterinary medicine; taking measures to prevent the inappropriate use of antimicrobial drugs for prophylactic and other purposes; settlement of issues of distance selling of antimicrobial drugs and pesticides; prohibition of advertising of antimicrobial drugs, etc. And what is no less important is to find a way to create qualitatively new antimicrobial drugs.

A new class of antibiotics was last developed 30 years ago. The bacteria have developed resistance to all existing species. The production of antibiotics is costly, and it takes a long time from development to implementation. In 2017, the public health service in England issued a warning that an urgent need to address the problem of antibiotic resistance, otherwise, by 2050, due to this problem, 10 million people will die every year in the world. As a result, the global decline in labor productivity will cost the global economy $ 100 trillion. Therefore, healthcare organizations in different countries urge doctors and patients to stop abusing antibiotics.

Conclusions. AMR is a complex issue and requires a collective multisectoral approach. One Health is about bringing together a wide range of sectors and stakeholders dealing with human health, terrestrial and aquatic animals and plants, food and feed production and environmental protection,

allowing them to interact and jointly develop and implement programs, strategies, legislation measures and research aimed at improving the health indicators of the population.

The most important challenge is to drive innovation and capital investment in areas such as operational research, the discovery and development of new antimicrobials, vaccines and diagnostics, especially for the most serious gram-negative bacteria, in particular carbapenem-resistant Enterobacteriaceae and Acinetobacter baumannii.

WAYS TO IMPROVE THE DIAGNOSIS OF PARASITIC INVASIONS

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Introduction. According to the WHO, the problem of infectious pathology has not lost its relevance. As before, infectious diseases, including new ones, pose a threat to human development, as they are the cause of a third of the world's total annual deaths. According to the World Bank, in recent decades there have been 50% of deaths of children under 5 years of age caused by infectious diseases (respiratory pathology, intestinal infections, measles, malaria, AIDS, etc.), and in the structure of morbidity in this age group infectious diseases 80%. According to the World Health Organization, mortality from infectious diseases in some countries ranks second in the structure of overall mortality. In addition, the ability of pathogens to mutate and the formation of resistance to chemotherapeutics should be noted. Among the factors of infectious diseases, special attention is drawn to the pathogens of protozoal diseases: malaria, leishmaniasis, trypanosomiasis and others. Pathogens that have overcome the species barrier are especially dangerous. Babesiosis is recognized as such a pathogen that can cause disease in humans. Babesiosis is a group of emergent obligate-transmissible, naturally-mediated hemoparasitic protozoan anthro-pozoonoses, which are transmitted by blood-sucking arthropods - mites of the superfamily *Ixodoidea* of the family *Ixodid*. The onset of the disease can be fatal in most cases. The vector is a tick, in the body of which the virus persists for life, as a result of which it can be transmitted transovarially. The clinical course of babesiosis infection is diverse, which should be associated with different types of babesia: *Babesia bovis, Babesia divergens, Babesia odocoilei, Babesia microti* and *Babesia duncani*. The variety of etiological factors complicates the diagnosis and requires improvement of methods for identifying the causative agents of babesiosis.

Aim. To analyze the current state of diagnosis of the disease and identify promising ways to improve laboratory diagnosis of babesiosis.

Materials and methods. Systematic and content analysis (analysis of domestic and foreign publications on the study of babesiosis pathogens), as well as the method of generalization (formation of conclusions) were used during the study.

Results and discussion. According to the literature, the taxonomic position and diversity of species determines the peculiarity of the causative agent of babesiosis. It is known that babesiosis is caused by a pathogen from the class of spores, and, when ingested, is concentrated in the center of erythrocytes, as well as on the periphery of the cell structure. Thus, babesia begin to multiply inside the erythrocytes, resulting in a hemolytic crisis, accompanied by the appearance of hemoglobin in the