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Features of SARS-COV-2 infection and directions of drug and vaccine creation

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Introduction: Until the beginning of the 21st century human coronaviruses were known as the cause of typical seasonal acute respiratory disease. Highly pathogenic coronaviruses were identified as the cause of severe acute respiratory syndrome (SARS) with high mortality in 2002 – SARS-CoV, and then in 2013 as the causative agents of Middle East respiratory syndrome – MERS-CoV. They have caused severe respiratory disease in humans because of their ability to adapt to the host, increasing affinity for human airway receptors. The emergence of a new coronavirus in 2019 caused a rapid increase in the incidence of severe acute respiratory syndrome and turned into a pandemic.

Background: The new coronavirus SARS-CoV-2, which causes Covid-19 (coronavirus infection disease), was first detected in December 2019 in Wuhan, the capital of Hubei province, from where it quickly spread to China and continued to spread to Italy and other countries of Europe and after around the world, the number of confirmed new cases is increasing daily. **Rationale:** Coronaviruses are members of the order Nidovirales of the family Coronaviridae and divided into 4 genera: α - and β -coronavirus, which infect only mammals, and γ - and δ -coronavirus, which mainly affect birds. The central place is occupied by the genus β -coronavirus, which includes especially dangerous pathogens of lethal human pneumonia – SARS-CoV, MERS-CoV, SARS-CoV2. In turn, β -coronavirus divided into four subgenres: A, B, C, D. SARS-CoV-2 is β -coronavirus, subgroup B, Sarbecovirus. Coronaviruses affecting humans currently have 7 species. They divide into 2 groups. 1st group has 4 common types of coronaviruses that cause about 15% of typical seasonal SARS: HCoV-229E, NL63, OC43 and HKU1. Usually these types cause mild forms of upper respiratory tract diseases in children (and less often in adults), but in some cases (like other SARS viruses) cause interstitial pneumonia (in newborns, children with immunodeficiency, people with cancer, patients who take immunosuppressive therapy, the elderly with heart failure and chronic lung disease). 2nd group has 3 types of coronaviruses, which in a large percentage of cases SARS. 1. SARS-CoV – the epidemic began in China in November 2002 from live animal markets in Foshan (Guangdong Province), spreading to Asia and the world. Considered, horseshoe bats can be the natural reservoir of SARS-CoV. SARS-CoV affected 32 countries for 9 months, 8096 people became ill, of which 774 died (9% mortality). No new cases of SARS-CoV have been reported since 2004. 2. Another type of coronavirus that caused SARS in humans, MERS-CoV, first detected in Saudi Arabia in 2012. Considered bats can be the natural reservoir of MERS-CoV, and single-humped camels can be vectors. MERS-CoV has been found in patients in 27 countries, mainly in the Middle East, and remains endemic in many of them due to circulation in camels. The last outbreak of MERS occurred in South Korea in 2015, where the virus was imported from Kuwait (186 became ill and 33 died – the elderly). As of November 2019, MERS-CoV caused 858 deaths out of 2494 laboratory-confirmed cases (33% mortality). 3. SARS-CoV-2, like SARS-CoV and MERS-CoV, can cause severe respiratory disease with a high mortality rate. Horseshoe bats considered the natural reservoir of SARS-CoV2 (as well as SARS-CoV). There are two versions for SARS-CoV2: the first is that it is bat coronavirus and it has spread from the seafood market, can cross the interspecies barrier and become pathogenic to humans; second, that during an experiment at the Institute of Virology in Wuhan, the coronavirus accidentally struck an employee in an aerosol, who became the "first patient". **Discussion:** The virion of coronaviruses is covered with a lipid shell that clearly visible on electron microscopic images club-shaped spikes length of 10 nm. Coronaviruses contain a positive single-stranded RNA genome with a length of 26 to 32 thousand nucleotides (the largest known RNA virus) and four structural proteins – spike (S), envelope (E), membrane (M) and nucleocapsid (N). Protein S binds to target cell receptors and triggers the infectious process, protein M plays a role in shell formation and virion formation, and protein E forms pentameric ion channels that destroy cell membranes during viral budding. SARS-CoV-2 uses as receptors for cell penetration CD147 – glycoprotein and angiotensin converting enzyme type 2 (angiotensin converting enzyme 2 – ACE2). CD147 expressed in the cell membrane of epithelial and endothelial cells and T lymphocytes. Monoclonal antibodies against CD147 prevent infection of SARS-CoV2 cells in vitro. Analysis of cell samples for the presence of RNA sequences SARS-CoV-2 reveals significant RNA transcription in the nasal epithelium and less in the cells of the lower respiratory tract and alveolar epithelium. This suggests that the upper rather than the lower respiratory tract is the initial site of SARS-CoV-2 infection. ACE2 localized in type I and II pneumocytes, vascular endothelial cells and enterocytes (therefore symptoms from the respiratory tract are often accompanied by symptoms from the gastrointestinal tract – nausea, diarrhea, etc.). SARS-CoV2 infection leads to cytopathic effects, including apoptosis, cell lysis, and syncytium formation in lung tissue. After penetration into the host cell, the SARS-CoV-2 genome attaches to the ribosomes, leading to the translation of viral polyproteins, which subsequently processed by viral proteolytic enzymes. As a result, of proteolysis the protease-mediated virus 3CLpro (chymotrypsin-like protease) and PLpro (papain-like protease), polyproteins are broken down into smaller components, which plays a major role in mediating the replication and transcription of viruses and promotes infection. Another RdRp (RNA-dependent RNA-polymerase) enzyme, replicase, is important for viral genome replication and products of new virions. Therefore, these enzymes can be considered as potential drug targets for the development of therapeutic agents, as they are crucial for the survival, replication and transmission of SARS-CoV-2. Therapeutic strategies using for the treatment of Covid-19 mainly divided into immune and antiviral. S, E, M, N proteins, two replicase isoforms (RdRp1a and RdRp1ab) and proteases (3CLpro and PLpro) can be considered as potential targets for drugs and vaccines against SARS-CoV-2. Despite the many directions in the search for effective drugs for treatment Covid-19, today the most effective strategy in therapy is access to oxygen and well-staffed supportive care reduces mortality more than any medicinal product. **Conclusion.** The sudden appearance of SARS-CoV-2 and the pandemic caused by this virus have posed a threat to the security of the global health system. The scientific community around the world is working hard to find effective drugs and vaccines against the new coronavirus. In an effort to find the cure for Covid-19, WHO has developed the SOLIDARITY concept, an international clinical trial as a common global platform for improving scientific links and accelerating information exchange. On the basis of Mechnikov Institute of Microbiology and Immunology National Academy of Medical Sciences of Ukraine also began the study of the peculiarities of immunity Covid-19 for further development of the therapeutic and vaccine strategies.

Keywords: SARS-CoV-2; genome; pathogenesis; therapeutic strategies

Autoimmune rheumatic diseases and autoinflammatory syndromes, facets of contact

21-30

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Introduction The peculiarity of the development of inflammation, its acute and chronic course, various combinations of inflammatory mediators, the nature and severity of the immune response is largely arise from the genetic characteristics of the organism. It would be logical to assume the key role of small mutations of genes in initiating the development of autoaggression, activation of signaling molecules, immunocompetent cells with violation of their cooperation, production of pro-inflammatory cytokines, as a consequence of the effect of persistent viral-bacterial infection and non-infectious agents. In this regard, the comparative analysis of pathogenetic mechanisms of development, clinical symptoms of autoimmune rheumatic diseases and genetically determined autoinflammatory syndromes (AIDs), the mutation of genes in the development of many of them has already been proved, would be interesting. **Material & methods** The article is compiled based on the publications review. **Results & discussion** At the heart of the development of autoimmune rheumatic diseases lie mostly the changes in the system of immunobiological surveillance, the adaptive link of immunity. The elimination of T-lymphocyte anergy to autoantigens, increased activity and expansion of clones of T and B lymphocytes, the production of circulating autoantibodies upon activation of signaling pathways / molecules, the secretion of proinflammatory cytokines (IL-1,6, TNF- α) are the key links in immunopathogenesis of rheumatic diseases. The spectrum of autoimmune rheumatic diseases differs in adults and children. Only children suffer from juvenile idiopathic arthritis, juvenile dermatomyositis, neonatal lupus, Kawasaki disease, and acute rheumatic fever. Both children and adults suffer from systemic lupus erythematosus, systemic vasculitis, antiphospholipid syndrome, and systemic scleroderma. Dominant symptoms in the debut of autoimmune rheumatic diseases are prolonged fever, skin-vascular syndrome, serositis, arthralgia, arthritis, myalgia, myositis, high laboratory activity indicators. In contrast with most autoimmune disease auto-inflammatory syndromes usually present during childhood. AIDs is a heterogeneous group of rare, genetically determined states characterized by unprovoked attacks of inflammation and manifested by fever and clinical symptoms resembling rheumatic ones in the absence of autoantibodies and / or antigen-specific T-lymphocytes. Diseases of this group have both common and distinctive features that correspond to the Eurofever register of more than 21 nosological forms, including congenital recurrent febrile syndromes, cryopyrin-associated periodic syndromes, granulomatous and pyogenic diseases, proteasome deficiency, chronic recurrent multifocal osteomyelitis. Unlike of autoimmune diseases, the main role in the initiation of autoinflammatory syndromes is played by mutations in genes involved in the realization of the immune response of the innate immunity system, as well as non-antigen-induced antibody synthesis or activation of T and β -lymphocytes. A special place, as a trigger mechanism, in the development of autologous means, belongs to the multilayered cytoplasmic complex formed in neutrophils and macrophages - an inflammasome regulating the secretion of pro-inflammatory cytokines and, as a consequence, triggering an inflammatory response upon contact of cells with infectious and non-infectious agents. The composition of the inflammasome includes proteins encoded by genes, the specific mutations of which cause the development of AIDs. Most clearly, the inflammasomes role in the pathogenesis of AIDs can be traced to the example of Cryopyrin-associated Periodic Syndromes (CARS), including Familial Cold Auto-inflammatory Syndrome (FCAS), Muckle-Wells Syndrome (MWS) and Chronic Infantile Onset Neurological Cutaneous Articular/ Neonatal Onset Multi-systemic Inflammatory Disease - CINCA / NOMID syndrome. All three problems are caused by a mutation of the CIASI gene located in the long arm of the first pair of chromosomes and encoding the cryopyrin protein (NLRP3). Despite differences in pathogenesis and distinctive features of a course of diseases, the targets of inflammatory reaction in the compared groups of autoimmune rheumatic diseases and autoinflammatory syndromes are identical: the skin, joints, serous coverings, and the central nervous system. The complication of both syndromes is the development of AA-amyloidosis, and multi-organ failure. **Conclusion** Perhaps the disclosure, the understanding of more subtle mechanisms of development, the cyclicity of the autoinflammatory process, the spontaneous arrest of the inflammatory response, unprovoked relapse attacks, as well as the determination of the carriage of pathogenic mutations of genes responsible for the development of AIDs in patients with autoimmune rheumatic diseases, will help to identify that disturbed link in the general chain of interconnection of cells of congenital and adaptive immunity, which is a key factor in the development of autoaggression. So in order to deepen our understanding of human innate immunity, and to offer more targeted therapies for patients with autoimmune rheumatic diseases, further studies on the genetics and molecular pathophysiology of autoimmune rheumatic and autoinflammatory diseases are essential.

Keywords: Autoimmune rheumatic diseases, autoinflammatory syndromes, facets of contact

Nuclear localization signal peptides (NLS) and their role in viral pathogenicity

31-40

Nosalskaya Tatiana Nikolaevna, Martynov Artur Viktorovich, Bomko Tatiana Vasilievna

The review provides data about nuclear localization signal peptides (NLS) and their function in the cell, incl. with a viral infection process. The binding, penetration, assembly, and budding of viruses are currently being intensively studied in many systems. However, the stages of nuclear transport during the penetration and release of the virus have remained practically unexplored. NLS were first identified in the large T antigen virus SV40 and from nucleoplasmin, and then were identified in a large number of proteins. They usually contain short base peptides includes lysine or arginine residues in the form of mono- or bipartite signals. NLSs include the "pat4" motif, which consists of a contiguous stretch four essential amino acids (arginine and lysine). Both coronaviruses and arteriviruses show similar genomic organization and belong to Nidovirales. Although both families encode nucleoproteins (N-proteins), the main function of which is to bind viral RNA, NLS-containing proteins has different sizes and do not have significant homology. The review provides the characteristics and structure of NLS for many viral proteins, and shows their role in the pathogenicity of viruses.

Keywords: Nuclear localization signal, viruses, coronaviruses, influenza, hepatitis, virulence

Some aspects of studying the state of the oral microflora

41-44

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The study of the microflora of the oral cavity plays an important role in establishing the pathogenetic mechanisms of purulent-inflammatory diseases of periodontal tissues. The human oral microbiome includes more than 700 species of microorganisms that inhabit various habitats, including teeth, gums, tongue, cheeks, hard and soft palate, and tonsils. The term "microbiome" was coined in 2001 by Joshua Lederberg to denote the ecological set of commensal, symbiotic and pathogenic microorganisms in our body that play the role of "determinants of health and disease". Under the influence of various factors in the qualitative and quantitative composition of the microflora of the oral cavity there are changes. Her condition is influenced by lifestyle, age, human nutrition, compliance with the rules of oral hygiene, as well as the presence of various diseases, including various disorders and diseases in the oral cavity, and other factors. Because there is a constant flow of microorganisms that enter the oral cavity from the environment, it is necessary to distinguish them from endogenous species, which Theodore Rosebury called local microbes or normal microflora. It is believed that the difference between them cannot be established directly by studies of human isolates alone. It is necessary to compare them with isolates from the external environment to determine which clones are rapidly restored in the host organism, or in the environment. Analysis of the oral microbiome of healthy people using the latest advances in sequencing technology revealed that most species of bacterial microorganisms in healthy people are identical. Based on international research in recent years, a database of phylogenetic data on the human oral microbiome - Human Oral Microbiome Database (HOMD), which includes about 700 taxa (individual species and subgroups) and 13 types of Actinobacteria, Fusobacteria, Chlamidia, Chloroflexi, Furiarchaeota Proteobacteria Spirochaetes, SR1, Synergistetes, Tenericutes and TM7. HOMD is the first phylogenetic base of microbiome results, which aims to understand the health and development of human oral diseases (including caries, purulent-inflammatory periodontal

diseases and others). In order to determine the relative number of taxa and to identify new species of oral microbiota, 36,043 clones of 16S rRNA genes with more than 1000 isolates were analyzed. The results revealed 1,179 taxa, of which about 280 species of bacteria were isolated culturally and received an official name, about 8% - cultivated but not named, and 68% were non-cultivated. Thus, it was confirmed that more than half of the species of bacteria existing in the oral cavity cannot be cultured on nutrient media. As for the classical bacteriological methods of research, they are obviously used to the greatest extent in routine practice, to study the state of the human microbiome, including the oral cavity. The search for new methods of prevention and treatment of purulent-inflammatory periodontal diseases is inextricably linked with the isolation of pure cultures of pathogens and the study of their biological properties: sensitivity to antibiotics, exposure to various physical factors (ultraviolet, laser radiation, relativistic electrons, etc.) cells.

Keywords: oral microflora, studying, review

Experimental works

Immunological features of umbilical cord blood of newborns born to women with different implementation of intrauterine infection

45-49

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Introduction. Perinatal infections (PNI) have been increasingly referred to as one of the causes of adverse effects of pregnancy recently, accompanied by an inflammatory process, which is based on a highly integrated immune response. Immunopathological reactions cause destabilization of the whole homeostasis and create a favorable basis for the periodic exacerbation of infectious and inflammatory diseases, and the inability of the pregnant woman's body to adequate immune response is the cause of the pathological course of pregnancy.

Determination of immunological parameters in the umbilical cord reflects the degree of formation of the immune system of the fetus and thus characterizes the level of anti-infective protection, which depends on the risk of infectious abnormalities. **Objective:** To investigate the immunological features of umbilical cord blood of newborns born to women with different implementation of intrauterine infection (IUI).

Materials and methods. The study involved examination of 180 pregnant women divided into 3 groups depending on the presence and nature of the detected infection: Group I - viral (CMV, herpes simplex virus types 1,2,6), Group II - bacterial (chlamydia, ureaplasma, mycoplasma) and Group III - mixed (viral and bacterial) infection. Each of these groups was divided into 2 subgroups: with subsequent implementation of the infection in newborns (1) and without it (0). This group was the main one in the study. Control group included 50 patients with physiological pregnancy. In clinical trials, samples of umbilical blood obtained during childbirth from women with signs of IUI after the use of different treatment regimens depending on the etiological factor of PNI were studied. **Results and discussion.** Studies have shown a significant decrease in the total number of CD3⁺T lymphocytes, their subpopulations CD4⁺T-helpers, CD8⁺T suppressors, as well as CD25⁺ regulatory T-cells in newborns with the implementation of IUI. The activity of cytotoxic natural killer cells (CD16⁺NK), which implement anti-infective protection, was higher in the main groups than in the control, which is apparently due to the effect on the fetus of a large number of antigens. The percentage of B-lymphocytes in the umbilical blood of newborns with infectious abnormalities was in the range of reference values, but in Group I-0 of newborns the number of cells producing immunoglobulins was significantly higher than in the same group with the implementation of IUI, which may be associated with increased production of own immunoglobulins due to insufficient transplacental transfer of IgG from the mother. The increased concentration of IgM in the umbilical blood, which was found in various clinical groups, indicates the activation of humoral responses in the newborn in response to an infectious agent and is a marker of IUI. In the groups with IUI implementation, the concentration of IgM and IgG in the umbilical blood was lower by 20–30% and 13–17%, respectively, than in similar comparison groups, which is an important factor in reducing the anti-infective resistance of newborns. The level of IgA in the clinical groups did not differ statistically, although it exceeded the reference values. **Conclusion.** The functional activity of umbilical blood phagocytes in groups with clinical manifestations of IUI was characterized by a significant decrease in the ability of neutrophilic umbilical blood granulocytes to actively absorb and fully digest antigens. Such a defect in the phagocytic protection of the fetus may be one of the probable factors increasing the risk of infection.

Keywords: perinatal infections; implementation of intrauterine infection; umbilical cord blood; immunopathological reactions.

Determination of the presence of specific antibodies against SARS-CoV-2 school-age children in Kharkiv in September 2020

50-55

Volyansky A. Yu., Kuchma I. Yu., Davydova T. V., Kuchma M.V., Yudin I.P.

Introduction. Recently, the world community and modern medical science have faced the challenge of the emergence new human coronavirus SARS-CoV-2 capable of causing severe acute respiratory syndrome. WHO has named the disease caused by this virus Covid-19 (coronavirus infection disease). SARS-CoV-2 was first detected in December 2019 in Wuhan, from where it quickly spread to China and further around the world. Due to the high contagiousness and pathogenicity of SARS-CoV-2, WHO declared the global pandemic Covid-19 in early March 2020. The features of the pathogenesis of Covid-19 determine the significant frequency cases of this disease with a severe course. The severity course of the disease and the consistency and completeness of the immune response are interrelated: excessive and continued activation of innate immunity factors with an increase in the cytokine profile is observed in patients with severe course, and the transition to the stage of production the specific antibodies is characterized by an improvement in the patient's condition and recovery. The specific humoral response is important in the formation of collective post-infection and post-vaccination immunity and is an indicator of overcoming epidemic processes in the population. The study is conducted in the Mechnikov institute of microbiology and immunology National Academy of Medical Sciences of Ukraine has one of the tasks of determining specific antibodies to SARS-CoV-2 in different age groups and monitoring the formation of the immune layer during the epidemic process, as well as the duration of detection of specific antibodies. **Material & methods.** A study was conducted to determine specific total immunoglobulins, IgA, IgM and IgG to SARS-CoV-2 by enzyme-linked immunosorbent assay (ELISA) among schoolchildren Kharkiv gymnasium №X for 27-28 weeks of the pandemic (21-24/09/2020). The object of the study were 439 samples of serum from children aged 6 to 16 years. **Results & discussion.** This phase of the study the presence of specific SARS-CoV-2 antibodies in certain groups held at a time when the territory of Ukraine still it was not observed a significant increase in the number of patients with Covid-19 compared to Western Europe, China, the USA and others, but with almost 6 months have passed since the beginning of the pandemic. Most of the patients (98.4 %) in a survey questionnaire and not noted the manifestations of acute respiratory illness, excessive fatigue, temperature rise or other manifestations characteristic of Covid-19. The study revealed total SARS-CoV-2 antibodies in 20.3% of children, questionable levels total antibodies were found in almost 9 %. IgA was detected (positive and questionable) in 15.2 % of children, IgM – 7.7 %, and IgG – 14.3 %. In serum samples total SARS-CoV-2 antibody positive/questionable in 23.6% of cases were identified only one of the classes of immunoglobulins: IgA at 5.6 %, IgM – 3.3 %, IgG – 14.7 %. In most samples two classes of antibodies were detected simultaneously – 67.4 % of samples and in 9.02% all three classes of immunoglobulins were detected simultaneously. An interesting fact is predominantly simultaneous presence in serum IgA and IgG in 60 samples (46.9%) with total serum antibodies to SARS-CoV-2. Simultaneous detection IgM and IgG was noted much less, only in 29 samples – 22.7%, the combination of simultaneous presence IgA and IgM without presence IgG was detected in one sample (0.78%). **Conclusion.** The data obtained indicate that more than 20% of school-age children in the randomized sample had antibodies to SARS-CoV-2 at 27-28 weeks of the pandemic (21-24/09/2020), despite the fact that at the time of this study, our country has not yet faced an avalanche of rising morbidity, which was observed in this period. Covid-19 is known to be milder, asymptomatic or asymptomatic in children, which is

consistent with our lack of evidence in most children for 6-8 weeks prior to the study, although it is possible to assume that the infection occurred earlier. However, the simultaneous presence in the serum SARS-CoV-2 IgA and IgG in 60 samples (46.9%) and IgM and IgG in 29 samples – in 22.7%, which is approximately three quarters of all children, which had positive antibodies to SARS-CoV-2, according to traditional notions about the frequency of the formation humoral response suggests a higher probability of infection during this period to the coin determination of antibodies in blood serum. Obtained in this study data provide an understanding certain features of the formation SARS-CoV-2 post infectious immunity in school-age children and delivered important issues that require further research.

Keywords: Covid-19 school-age children; antibodies to SARS-CoV-2

Identification of the Oxa-48 Gene Coding For Carbapenem Resistance in *Klebsiella pneumoniae* and *Escherichia Coli* at Dr. Muhammad Hoesin Central General Hospital, Palembang Muhammad Fitrizal

56-62

OXA-48 is a class D β -lactamase which is not inhibited by *clavulanic acid*, *tazobactam* and *sulbactam*, because their activity may be inhibited in vitro by NaCl. Some *b*-lactamase enzymes hydrolyze carbapenem and are therefore defined as hydrolysis of class D carbapenem *b*-lactamase. Carbapenem-resistant *Klebsiella pneumoniae* isolates were found in Istanbul, Turkey, in 2001. OXA-48 produces isolates that have the ability to fight drugs and cause very beneficial resistance to β -lactams, including widely available *cephalosporins*, *cephamycins*, and *monobactam* and carbapenem. The OXA-48 gene is found on plasmids. Antibiotic resistance is a phenomenon taken from the discovery of antibiotics where there is a very good adaptability for bacteria which are treated with various antibiotics. It has bacteria that have the ability to mutate as a protection for survival. This study is a case study involving the OXA gene as an encoder for carbapenem in *Escherichia coli* and *Klebsiella pneumoniae* using the Polymerase Chain Reaction (PCR) method to use genotypes used in hospitals that can be used in Dr. RSUP. Mohammad Hoesin Palembang. Bacterial isolates derived from patients with *Klebsiella pneumoniae* and *Escherichia coli* infections in the period September-November 2017 were identified using Vitek 2 Compact. bla_{OXA-48} gene was detected by PCR, followed by visualization through electrophoresis. The detection results were then analyzed by comparing the pattern of antibiotic resistance. From 24 samples tested only 1 (4.7%) positive samples were obtained from the *bacterium Klebsiellapneumoniae* and no positive gene was found in *Escherichia coli*. This study identified 1 (4.2%) samples that had a positive OXA-48 gene while 23 (95.8%) samples had a negative OXA-48 gene.

Keywords: *Klebsiella pneumoniae*, *Escherichia coli*, OXA-48, Carbapenem

Theoretical confirmation of prospectivity of application of metabolic complexes of lactobacilli and saccharomycetes in the fight antibiotic resistance of bacteria

63-69

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Introduction. The global problem is the increase in the number of infectious diseases caused by antibiotic-resistant pathogens. Measures to control these microorganisms should be aimed at preventing the formation of antibiotic-resistant populations of microorganisms and at inhibiting already established resistant populations. The aim of the work is to substantiate the perspective of using metabolic complexes of lactobacilli and saccharomycetes to control antibiotic resistance of bacteria. **Material & methods.** Cellular structures of lactobacilli and saccharomycetes (L / S) were received by irradiation with low-frequency ultrasonic waves (generator G3-109) of suspensions of *Lactobacillus rhamnosus* GG (from symbiotic PREEMA®, Schonen, Switzerland) and *Saccharomyces boulardii* (from probiotic drug BULARDI®, Schonen, Switzerland). The metabolites of *L. rhamnosus* GG (ML) and *S. boulardii* (MS) were received in their own cellular structures. The combination of lactobacilli with saccharomycetes (MLS) and metabolites of saccharomycetes (LS) in the cellular structures of lactobacilli. Suspensions of microorganisms (resistant to antibiotics) gram-negative *Pseudomonas aeruginosa* PR, *Acinetobacter baumannii* PR, *Klebsiella pneumoniae* PR, *Lelliottia amnigena* (*Enterobacter amnigenus*) PR, gram-positive *Staphylococcus aureus* PR, *Staphylococcus haemolyticus* PR, *Enterococcus faecalis* PR, *Corynebacterium xerosis* PR, the cultures *Corynebacterium spp. tox* +, *Streptococcus viridans*, *Streptococcus pneumoniae* with an optical density of 5,0 units on the McFarland scale (Densi-La-Meter (PLIVA–Lachema Diagnostika, (Czech Republic)) was added to L / S / ML / MLS / MS / LS (experimental samples) or to 0.9% sodium chloride solution (control samples) in a ratio of 1: 1. All samples were incubated for 1 hour at a temperature of + 35 ± 1 ° C, then the optical density was adjusted to 0.5 McFarland. Sowing was carried out on Mueller–Hinton medium. After disks with antibiotics (imipenem, vancomycin, cefotaxime, gentamicin, erythromycin, ciprofloxacin, ampicillin, chloramphenicol, ampicillin, ceftazidime, ceftriaxone, tetracycline, levofloxacin, amoxiclav, azithromycin), incubated (35 ± 1 ° C, 24 hours), measured the zones of growth retardation of microorganisms under the discs with antibiotics. **Results & discussion.** Potentiation of antimicrobial activity in the combined use of experimental samples with antibacterial drugs occurred in 88% of combinations with ML, 83 % – with MLS, 85 % – with MS, 73 % – with LS. Without increase in activity was substances with gentamicin, ampicillin, ceftazidime were administered against *A. baumannii* PR and with levofloxacin against *S. aureus*. Samples of ML over L (P = 0,005) and MLS over L (P = 0,008) had the advantage of a general increase in the diameters of the zones of growth inhibition of all tested pathogens. These results indicate a statistically significantly greater inhibition of growth of selected strains when combining antibiotics with metabolic complexes than with cellular structures. Excellent enhancement was observed when combining different antibacterial drugs with ML (on 5,5 ± 0,7, P < 0,05), MLS (on 4,95 ± 0,6, P = 0,01) and MS (on 3,96 ± 0,6, P = 0,001) relative to control. More inhibition of growth was observed of antibiotics with MLS than with MS (P = 0,02). A difference between the efficacies of the metabolic complexes ML and MLS was not found (P = 0,09). The presence of a large number of combinations of metabolic complex – antibiotic with the ability to therapeutically significant indicators to increase the antibacterial activity testifies the effectiveness of the combined use of metabolites *L. rhamnosus* GG and *S. boulardii* with different drugs. **Conclusion.** Theoretically confirmed of prospectivity of application of metabolic complexes of lactobacilli and saccharomycetes in the fight against antibiotic resistance of bacteria. Synergistic combinations of lactobacilli and saccharomycetes with antibiotics have been established. A therapeutically significant increase in their combined antimicrobial activity has been proven. This efficacy for different antibiotic-resistant strains indicates the perspectives of using metabolic complexes of lactobacilli and saccharomycetes to develop multifunctional antimicrobials preparations with consequence the possibility of inhibiting antibiotic resistance to already formed bacterial populations and at preventing the formation of antibiotic-resistant populations of microorganisms.

Keywords: lactobacilli, saccharomycetes, multidrug-resistant microorganisms, potentiation of antibiotics, combinations metabolites with antibiotics, synergistic antibacterial activities.

Activity of the COVID-19 pathogen transmission mechanism and means of its interruption in modern conditions

70-75

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Introduction. During the 21st century, three coronavirus-related pandemics have been reported. In 2019, a new virus called severe acute coronavirus 2 syndrome (SARS-CoV-2) was confirmed. Currently, the incidence of COVID-19 is growing daily and fatalities are registered in many parts of the world, including Ukraine. The introduction of quarantine somewhat halted the spread of the virus, but led to enormous economic losses. Therefore, the introduction of personal protective equipment could help break the chain of the COVID-19 epidemic process. However, misconceptions about the transmission mechanism of SARS-CoV-2 and myths about personal protective equipment have led the population of Ukraine, including medical workers, to ignore the routine wearing of masks and respirators indoors and in transport,

and to keep a distance of 1.5 - 2 meters. Therefore, the purpose of the work was to study the aerosol-aspiration mechanism of transmission of the SARS-CoV-2 virus based on extrapolation from experimental studies and proof of the effectiveness of personal protective equipment in interrupting the transmission of the pathogen COVID-19. **Material & methods.** The results of an experimental study of the mechanism of transmission of pathogens through the air in the laboratory of the State Institution "Institute of Epidemiology and Infectious Diseases. L.V. Gromashevsky National Academy of Medical Sciences of Ukraine". The motion of the aerosol cloud and its vorticity was recreated. The formulas were used to determine the aerodynamic characteristics of the process, in particular, time, distance, speed, acceleration and deceleration, cutting size, aspiration flows and directions of aerosol cloud movement. The risk of infection in a mobile atmosphere compared to a stationary indoor atmosphere was calculated using a certain formula, which included the number 3.14; the distance between a sick (or carrier) and a healthy person; a factor of 0.4 that is equal to the maximum diameter ("diameter") of the aerosol cloud. **Results & discussion.** The mechanism of transmission of the causative agent of infectious diseases is realized through three stages - the isolation of the pathogen from the body, its stay in the factors of transmission and entry into a new organism. It was found that during expiratory acts, the droplets do not scatter in a cone, but are released in separate portions - aerosol clouds of irregular shape about 40 cm in diameter. The movement of these clouds is characterized by a fading inertial run up to 90 cm long, and having overcome this distance, they fall into nearby air currents and, depending on the direction of the wind, can move in different directions. In a closed room, on the way of its movement, an aerosol cloud changes within 1 - 7 seconds. Super-large droplets in the range of 500 - 1000 microns fly about 1 meter per second along ballistic curves and fall to the floor, slightly smaller droplets with a radius of 50 - 100 microns have time to dry out, decrease in diameter and settle within the next few seconds. Droplets in the 25 - 50 micron range settle in two and a half minutes, and even smaller droplets can stay in the air for tens of minutes or even hours. In confined spaces, the ventilation flows directed towards the exhaust hood can prevent transmission of SARS-CoV-2 coronavirus. There is a misconception that it is not possible to become infected with the SARS-CoV-2 virus outdoors. The study showed that the risk of infection in the open at a distance of 1 meter is 12%, at a distance of 2 and 4 meters, respectively, 6.3% and 3.3%. The rapid spread of the COVID-19 pandemic against the background of the susceptible population contributed to the smoothing of annual seasonality, but its pronounced manifestation in the long-term dynamics is not excluded. Large dispersed droplets have been shown to settle mainly in the upper respiratory tract and cause subclinical forms with symptoms of acute respiratory viral infection and carrieris, while small ones can enter the lower respiratory tract, causing severe acute pneumonia. The chain infectious process is dose-dependent, and is largely determined by the nature of the pathogen. The pattern of dose-dependence of the infectious process is especially important for understanding the epidemic and infectious processes in COVID-19. The two-week incubation period suggests that the coronavirus population may grow rather slowly. Therefore, it can be assumed that in the current COVID-19 epidemic process, SARS-CoV-2 virus infection occurs at doses close to those that cause the carrieris, ie relatively small doses. And the conversation is a variant of the aerosol-aspiration mechanism of transmission of the pathogen, which causes the transmission of small doses, and hence the pandemic spread of asymptomatic and subclinical forms of coronavirus infection. Therefore, in our opinion, the most adequate and effective means of protection against COVID-19 is the routine use of masks and respirators that meet the State Standard of Ukraine. **Conclusion.** The spread of COVID-19 occurs through aerosol clouds mainly indoors (buildings, structures, transport), but the risk of infection also remains on the street and in parks where there are crowds. The severity of the disease depends on the loading of the aerosol cloud with the SARS-CoV-2 virus, the dose and characteristics of the aerosol droplets that enter the body. Large droplets, which get into the body when talking, even in small doses, cause subclinical forms and carriers, and fine - severe forms of COVID-19. Total mask regimen interrupts the aerosol-aspiration mechanism of SARS-Cov-2 transmission by stopping its transmission from a COVID-19 patient to a healthy person.

Keywords: COVID-19, pathogen transmission mechanism, interruption in modern conditions

The effect of using whitening creams that contain mercury in the community

76-82

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Background: Mercury is usually added to skin lightening products because of its whitening effect. However, many cosmetics contain mercury above 1000 ppm to enhance the whitening effect. **Objectives:** This research aimed to determine the effects of mercury use in whitening creams for the general public. **Methods:** This research used descriptive-qualitative approach, the method that used in this research is literature study which implemented by recording the previous findings regarding to the variables of conflict. **Results:** Skin lightening products that contain mercury are available for sale via the Internet, promoted online on social media sites, and for sale via mobile applications. WHO states that more than 90 creams from 15 countries have detectable mercury concentrations below 1 ppm. **Discussion:** Thirty-four creams (10% of the sample) were found to have high mercury levels, that is, above 1 ppm, in four of the 13 samples from Indonesia, overall, mercury concentrations in this particular product ranged from 93 ppm to over 16,000 ppm. Long-term adverse effects of using mercury cream on health include kidney damage, skin rashes, skin discoloration, and scarring, decreased skin resistance to bacterial and fungal infections, anxiety, and depression.

Keywords: Health Effects, Cosmetics, Mercury, Whitening Cream, Skin.

Case Report

Cataract Extraction on One Seeing Eye in Patient with Behcet's Disease

83-87

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Introduction : Behcet's Disease is autoimmune relapsing systemic vasculitis of unknown that can cause uveitis and affect the anterior and posterior segment of the eye. Cataract is the most common complication of anterior segment caused by recurrent uveitis. This case was to report the outcomes and complications of cataract surgery in patients with Behcet's disease. **Case report:** A of 35 years old man complained progressive visual loss since 6 months before admission with VA 1 meter finger counting and NLP. There was history of recurrent redness on both eyes accompanied by blurred vision and pain, oral aphthosis, and genital aphthosis since three years before admission but didn't seek help because of low access to healthcare in his previous home. From anterior segment examination there was posterior synechia, cloudy lens, pupil seclusion, rubeosis iridis, flare and cell suggesting chronic uveitis. There was elevated IOP of 43.4 mmHg on left eye. Retinal vasculitis was found on posterior segment examination. **Result:** After combination of methylprednisolone and azathioprine for one year, there were improvement of quieter condition on both eyes and decreased left eye IOP of 37.2 mmHg. Lens extraction with iris retractor was done after three months of no inflammatory response. Despite uneventfull surgery and combination of immunosuppressive medication, the visual acuity are not much improved and there was optic atrophy from the complication of chronic Behcet's disease. **Conclusion:** In patient with chronic Behcet's disease, ocular involvement can affect both anterior and posterior segments with poor visual outcome regarding its complication

Keywords : Behcet's disease, Cataract extraction, one-seeing eye