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CORONAVIRUS INFECTION IN CHILDREN WITH TYPE 1 DIABETES MELLITUS. A CASE REPORT

Abstract:

The course of COVID-19 among children is usually not severe and can often be asymptomatic, but in some cases, the basis for which is still an open question, the SARS-CoV-2 virus is associated with the manifestation of type I diabetes in children, and has a more severe course in the presence of a concomitant chronic disease. The issue of treatment tactics and care for such children in general is still important and open. The article reviews the foreign literature, namely, statistical studies of changes in the number of patients with newly diagnosed type I diabetes mellitus, the possibility of developing complications in such patients with COVID-19, and the need for special care for such patients. The importance and safety of vaccination against SARS-CoV-2 virus in patients with diabetes mellitus is noted and considered. A clinical case from the author's own practice is presented, highlighting the approach to the diagnosis and treatment of COVID-19 in the Chernivtsi Oblast Clinical Hospital.

Keywords: *COVID-19, SARS-CoV-2, type I diabetes mellitus, children*

Recent studies show that SARS-CoV-2 is capable of directly and indirectly inducing pancreatic β-cell destruction, and the incidence of newly diagnosed diabetes after COVID-19 has increased in both adults and children. [1,3] In addition, patients already suffering from type I diabetes mellitus are at increased risk of diabetic ketoacidosis and hyperosmolar hyperglycaemia with the same frequency as patients with newly diagnosed diabetes, but the latter are at risk of developing severe diabetic ketoacidosis due to delayed diagnosis of diabetes. [2] The reasons for such a significant increase in blood glucose levels, which often leads to ketoacidosis in patients with type I diabetes mellitus infected with SARS-CoV-2, are still not fully understood, but the study by Wu, Z. et al. identified factors such as direct viral infection, metabolic dysfunction and aggressive immune response that may be associated with the development of type I diabetes in children after COVID-19. [4] The study by Karavanaki, K et al. notes that when treating such patients in an inpatient setting, it is necessary to take into account not only the need to treat the underlying (COVID-19) and concomitant (in this case, type I diabetes) diseases, but also to monitor the behaviour and mood of the child and parents, as the detection of a chronic disease and isolation measures negatively affect the mental state of the patient and his or her relatives or carers. [3] Over the past year, almost every study has noted a significant increase in the detection of type 1 diabetes in children with COVID-19, an increase in the frequency of ketoacidosis symptoms during the disease and the need for intensive care. [5-7] This is the reason why special attention should be paid to paediatric patients who are suffering from or have already had COVID-19 for early diagnosis and timely treatment of its possible complications, such as, in this case, type I diabetes. However, complications can be prevented by raising awareness among the population about the need and importance of vaccination against SARS-CoV-2, especially in children and adults with chronic diseases such as diabetes. [8] In their study, Gouda, N. et al. investigated the possible risks of vaccinating children and adolescents with type I diabetes against the SARS-CoV-2 virus, concluding that vaccination is safe and has no association with immediate blood glucose imbalance. [9]

The aim of the study is to investigate the features of the course, determine its severity and identify the risk of possible complications, as well as to determine the further tactics of COVID-19 treatment in patients with type I diabetes mellitus in a specific clinical case.

Materials and methods. Patient E., 11 months old, was under our observation. She suffers from type I diabetes mellitus, was born full-term via caesarean section from the first pregnancy and delivery. Birth weight - 3900 g, body length - 56 cm. BCG vaccination was performed in the maternity hospital, all other vaccinations were performed according to the age according to the vaccination schedule; she was not vaccinated against SARS-CoV-2 virus. Epidemiological history includes contact with family members with similar respiratory manifestations. On the second day of the illness, the girl and her mother were admitted to the emergency department of the Chernivtsi Oblast Clinical Hospital with complaints of fever to febrile levels (40˚C), lethargy, runny nose, and pale skin. The condition was assessed as moderate due to manifestations of intoxication, upper respiratory tract catarrh. The skin was pale and clean. Turgor and tissue elasticity were slightly reduced. Meningeal signs were negative. Nasal breathing was difficult. The pharynx was hyperemic. Rigid breath sounds over the lungs, symmetrical in both lungs, no wheezing. Diuresis was reduced. Laboratory testing identified the SARS-Cov-2 virus and confirmed the diagnosis of COVID-19. The haemogram showed significant lymphocytosis (72%). Urine sugar was detected, 28 mmol/l. Ultrasound of the liver showed reactive changes in the liver, moderate hepatomegaly. NSG showed signs of small pseudocysts of vascular plexuses on both sides. No radiography was performed due to the

presence of classical symptoms and a positive laboratory test, which allowed for a preliminary and later final diagnosis: COVID-19 confirmed by laboratory testing (Ag COVID-19+ from 30.09.2024). Acute nasopharyngitis, moderate severity. Type I diabetes mellitus. Bilateral pseudocysts of the cerebral vascular plexus. Moderate hepatomegaly.

Immediately after admission, the child received infusion therapy (NaCl 0.9%) up to 200 ml under the control of peripheral blood sugar level to reduce the level of sugar. Subsequently, the child was administered Novorapid (according to the food regimen) and Protafan (according to the regimen). A consultation with a paediatric endocrinologist was held to correct the continuation of treatment of type I diabetes. The patient was also prescribed symptomatic treatment, namely: saline nasal rinse and antipyretic (paracetamol) in case of fever (38˚C and above); it was recommended to continue breastfeeding.

The patient's condition improved rather slowly during treatment despite compliance with the treatment plan, but no negative dynamics was observed. The child is breastfed, suckles well, has stiff lungs, the pharynx remains hyperaemic, blood glycaemia ranged from 20 to 12 mmol/l, as a result, the child's hospital stay is extended until her general condition improves and her blood sugar level stabilises within the optimal range.

The peculiarity of this case is the presence of type I diabetes mellitus, which requires a special approach to the patient's treatment.

Conclusion. Thus, in patients with type I diabetes mellitus who have not been vaccinated against the SARS-CoV-2 virus, the risk of developing ketoacidosis and/or hyperosmolar hyperglycaemia is quite high, which complicates the course and makes treatment difficult, as seen in this case. Although the treatment is selected correctly in accordance with the age and existing comorbidities and complications, the recovery process is very slow, but there is no negative dynamics, which in this case can already be considered a marker of effective therapy. It is important to monitor glycaemic levels several times daily, which will ensure early detection of possible complications and allow for early implementation of the necessary treatment measures. It is advisable to disseminate information about the importance of vaccination against SARS-CoV-2 to avoid unwanted complications and to promote the mildest possible course of the disease in children with and without chronic diseases.

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HYPERTENSION: THE ROLE OF EARLY DIAGNOSIS AND PREVENTION OF THE DISEASE

Abstract:
Hypertension or its other name arterial hypertension (AH) is a disease of the cardiovascular system that manifests itself in a systematic increase in blood pressure. According to the latest data, more than a third of people in the WHO European region aged 30-79 suffer from hypertension. Hypertension is a major risk factor for cardiovascular disease, which can lead to serious complications, including heart attack and stroke. This article discusses the role of early diagnosis and prevention of the disease.

Keywords: *hypertension, arterial hypertension, hypertension, disease, diagnosis, prevention.*

Taking into account the peculiarities of the etiology, there are two types of arterial hypertension: primary or essential (hypertension); secondary or symptomatic.

Symptomatic hypertension is also divided into: renal; endocrine; caused by coarctation of the aorta; associated with neurological causes (brain tumor, encephalitis, sleep apnea, Guillain-Barré syndrome); caused by pregnancy; caused by increased cardiac output (increased wall stiffness in the elderly, aortic valve insufficiency, arteriovenous fistula, non-healing of the arterial duct, Paget's disease, beriberi).

In most cases, the onset of hypertension goes unnoticed. If blood pressure rises gradually, headaches and dizziness are usually ignored.

High blood pressure can be accompanied by generalized weakness, irritability, and drowsiness. Similar symptoms are inherent in completely different ailments, which is why patients visit a specialist late when hypertension is detected by chance during a visit to a doctor for other reasons.

Hypertension is diagnosed when repeated measurements in the doctor's office give a value of 140/90 mm Hg or higher. The diagnosis should be confirmed by 24-hour outpatient blood pressure (BP) monitoring or home measurement. The pressure in the arterial bed, which ensures the movement of blood from the heart to the organs, is the product of cardiac output and total peripheral vascular resistance. These parameters change under the influence of a wide range of pathophysiological factors. [1]

If a patient has high blood pressure, the first thing to do is to find out the cause. There may be situations when the pressure has increased, but it cannot yet be considered a disease: against the background of severe emotional stress, alcohol consumption, after significant physical exertion. However, in a healthy person, the body compensates for the effects of all these factors and keeps blood pressure normal.

Hypertension develops as a result of both genetic mechanisms and exogenous factors, such as excessive salt intake, psychoemotional stress, and obesity. People with close relatives under 55 years of age with hypertension have a fourfold increase in the risk of developing hypertension.

The role of excessive sodium (salt) intake in the development of hypertension has been clearly demonstrated in Japan. Thanks to the implementation of the National Education Program to limit salt intake, the incidence of hypertensive cerebrovascular accidents (heart attacks, strokes, etc.) has been significantly reduced over 20 years. [2]

Non-pharmacologic measures are an important component of the prevention and treatment of hypertension. Recommended lifestyle measures that are shown to lower blood pressure include weight control, a healthy diet, salt restriction, regular physical activity, and moderate alcohol consumption. Unfortunately, only a small proportion of adults change their lifestyle after being diagnosed with hypertension. Thus, community-based strategies that accelerate the implementation of health-promoting policies can create an environment where people are more likely to adopt or continue healthy behaviors and can have the greatest impact on health outcomes. Starting in childhood at home or at school to learn a healthy lifestyle. [3]

Restricting sodium in the diet has been shown to lower blood pressure and reduce the risk of cardiovascular disease. The WHO recommends reducing sodium intake to <2 g/day for children and 5 g/day of salt for adults. In general, the population should be encouraged to eat a healthy, balanced diet containing vegetables, fresh fruit, fish, whole grains, low-fat foods and unsaturated fatty acids, and reduce consumption of refined sugar, saturated fat and cholesterol. The role of excessive sodium (salt) intake in the development of hypertension has been clearly demonstrated in Japan. Thanks to the implementation of the National Education Program to limit salt intake, the frequency of hypertensive cerebrovascular accidents (heart attacks, strokes, etc.) has been significantly reduced over 20 years. [4]

American scientists have shown that increasing potassium intake lowers blood pressure, especially among people who consume a lot of sodium, thus reducing the risk of cardiovascular disease [5].

Excessive weight gain is associated with increased blood pressure, and obesity is closely linked to diseases that may be secondary causes of hypertension, such as obstructive sleep apnea and frequent use of NSAIDs due to early arthritis associated with being overweight. Weight loss also improves the effectiveness of antihypertensive drugs.

Reducing tobacco use through effective tobacco control programs is important for reducing the cardiovascular burden of disease. Education about tobacco dependence and its negative consequences should start at an early age through school programs. Tobacco taxation and pricing, banning tobacco advertising, and banning smoking in public places.

It is likely that prolonged stress-induced high blood pressure is the result of neurohormonal trophic factors of hypertrophy or atherosclerosis. Relaxation techniques are increasingly used in the treatment of patients with hypertension. Depression is a typical feature of patients with uncontrolled hypertension, which may contribute to poor control. Screening for depression in patients with hypertension is a simple and cost-effective tool.

Conclusions: Hypertension is a serious medical condition that requires timely diagnosis and prevention. Early detection of hypertension allows taking effective measures to prevent the development of complications such as stroke, heart failure, and other cardiovascular diseases. Important aspects include regular blood pressure monitoring, screening programs and raising public awareness of the risks associated with high blood pressure. A comprehensive approach to prevention, including lifestyle changes, pharmacotherapy and regular medical check-ups, is key to reducing morbidity and improving quality of life.

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COVID-19 IN UKRAINE

Abstract:
Coronavirus disease 2019 (COVID-19) is an infectious disease that was first detected in humans in December 2019 in Wuhan, Central China. The disease began acutely as an outbreak that developed into a pandemic. The family Coronaviridae (CoV, coronaviruses) includes two subfamilies, 5 genera and approximately 40 species. Many of these viruses cause disease in mammals and birds, and can be transmitted from animals to humans. In this article, we discuss the epidemiological features of the spread of SARS-CoV-2 in Ukraine.

Key words: *SARS-CoV-2, virus, morbidity, infection, prevalence.*

Human coronaviruses (hCoV) were first described in 1965. At the end of December 2019, a new pathogenic human beta-coronavirus, called SARS-CoV-2, was first detected in Wuhan, China. It is the third human coronavirus to have allegedly come from an animal source in the last two decades. Respiratory transmission is the dominant route of transmission. The virus can be spread from the mouth or nose of an infected person as small liquid particles (ranging in size from large droplets to smaller aerosols) when a person coughs, sneezes, sings, or talks. Bats and snakes are suspected to be the primary source and reservoir of the infection, from which the pathogen has been transmitted to humans in a way that is not yet clear. The spread of the disease in Ukraine began on March 3, 2020, when the first case was confirmed in the Chernivtsi region. On March 11, the Cabinet of Ministers introduced quarantine in Ukraine from March 12 to April 3. On March 12, 2 more cases of the disease were detected in Ukraine - in Chernivtsi and Zhytomyr regions. A state of emergency was declared in the Zhytomyr district center of Radomyshl, where a woman of retirement age was diagnosed with coronavirus disease. The first Ukrainian woman dies in Italy. The first fatal case of coronavirus disease in Ukraine in 2019 was the death of a 71-year-old woman from the Zhytomyr region who was hospitalized on March 12 after returning from Poland. It later became known that the day before, on March 8, she had attended a liturgy in a local church and kissed an icon.

In August 2024, the Ministry of Health registered 26,000 cases of the disease (Chief Sanitary Doctor of Ukraine Ihor Kuzinsaid during the telethon). According to him, in June, the Ministry of Health registered 2,300 new cases, in July - 11,500, and in the first half of August - 26,000. The chief sanitary doctor noted that the increase in the number of cases was caused by the new sub-variant of COVID-19, Omicron-FLiRT.

Epidemic season 2024/25: the incidence of SARS, influenza and COVID-19 among children and adults increased by 5%. During the first two weeks of the epidemic season in Ukraine (from September 30 to October 13), 233,059 Ukrainians fell ill with SARS, COVID-19 and influenza. During this time, 17 fatalities due to COVID-19 complications among adults have been registered. Last year, during the 2023/2024 epidemic season, 4,715,963 Ukrainians fell ill with SARS, influenza, and COVID-19. The number of deaths from influenza, COVID-19 and ARVI in Ukraine during this period was 1,028: 82 cases due to flu complications and 946 cases among people who tested positive for COVID-19.

Course and complications. The COVID-19 coronavirus disease can have various manifestations and health consequences. In particular, it primarily affects the cardiovascular and respiratory systems. At the same time, neurological and mental complications can occur both during the disease and after recovery. During the post-covid period, which can develop within 5-12 weeks after the acute course of coronavirus, patients may experience headaches, dizziness, taste or smell disturbances, delirium, nervous agitation, fatigue, difficulty concentrating, sleep disturbances, neuropsychiatric symptoms, and cognitive impairment.

One study [1] shows that the mortality rate among patients with at least one of the neurological manifestations is 27%. The elderly are particularly vulnerable to the disease. The prevalence of stroke in patients with COVID-19 is 1.2%. COVID-19 can also have neurological and mental consequences. Moreover, they can occur even if the coronavirus disease is asymptomatic. A meta-analysis of 28 studies [2] shows that the most common consequences of COVID-19 were fatigue or muscle pain (63%). In addition, 26% of people have trouble sleeping, and 23% have anxiety and depression. Difficulty walking is reported by 24% of people who have had the coronavirus. At the same time, another meta-analysis [3] of studies indicates that fatigue occurs in 32% of coronavirus cases, muscle pain in 20%, headache in 13%, headache with dizziness in 12%, changes in smell or taste in 19% and 21%, respectively, confusion in 11%, and nervous agitation in 45%.

Vaccination. Since the introduction of the COVID-19 vaccine in December 2020, mortality due to the pandemic has decreased by at least 57%, saving more than 1.4 million lives in the WHO European Region. Most of those saved were aged 60 and older, the group at highest risk of severe illness and death from the SARS-CoV-2 virus. The WHO estimates that the first vaccine saved 700,000 lives. It is estimated that 2.5

million people died from COVID-19 in the WHO European Region, but without the vaccine, it would have reached 4 million [4,6].

The World Health Organization has approved for emergency use the following vaccines available in Ukraine:

AstraZeneca is a vector vaccine developed by the Swedish-British company AstraZeneca together with the University of Oxford. For full immunization, you need to receive two doses of the vaccine 12 weeks apart.

Comirnaty/Pfizer-BioNTech is an mRNA vaccine against COVID-19 developed by the German biotechnology company BioNTech in collaboration with the American pharmaceutical concern Pfizer. For full immunization, you need to receive 2 doses with an interval of 21-28 days. CoronaVac / Sinovac Biotech is an inactivated vaccine developed by a Chinese biopharmaceutical company that researches, develops, manufactures and markets vaccines to protect humans from infectious diseases. For full immunization, it is necessary to receive two doses with an interval of 14-28 days. [5]

Conclusions. The WHO emphasizes that the virus has not disappeared, people continue to get sick, and the infection is likely to remain in the human population as a respiratory disease. Vaccination is the most effective way to prevent severe illness and death from COVID-19.

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DISORDERS OF PSYCHOSEXUAL DEVELOPMENT IN WOMEN: AN ANALYSIS OF CONTEMPORARY SCIENTIFIC LITERATURE

Abstract.
Disorders of psychosexual development in women are a relevant issue in modern medicine and psychology. These disorders can affect women's overall health, psycho-emotional state, and social relationships. The article examines the main factors influencing the development of such disorders, analyzes current scientific research, and suggests effective approaches to their diagnosis and treatment. Focus is placed on the biological and psychosocial aspects of psychosexual disorder formation. Recommendations are provided to improve psychotherapeutic and medical care for women with these conditions.

Keywords: *psychosexual development, psychosexual disorders, sexual dysfunction, gender identity, psychotherapy, sexual health.*

Introduction.

Psychosexual development is a key element in the formation of a healthy personality and normal sexual behavior. In women, this process encompasses both biological aspects, related to the functioning of reproductive organs and hormonal changes, as well as psychosocial factors, which shape their perception of themselves as sexual beings and their interactions with partners [1]. Disorders of psychosexual development often go undetected or are ignored due to societal taboos surrounding discussions on sexual topics, contributing to chronic psycho-emotional problems and sexual dysfunction.

Recent studies indicate that psychosexual development disorders may have both biological and psychosocial causes, necessitating a multidisciplinary approach for their diagnosis and treatment [2]. This article will analyze the key factors contributing to the development of these disorders and propose modern methods of treatment and prevention.

Research Objective. The aim of this study is to analyze contemporary scientific approaches to the study of psychosexual development disorders in women. The primary objectives of the research include:

1. Describing the biological and psychosocial factors contributing to psychosexual development disorders.
2. Analyzing current approaches to diagnosing psychosexual disorders in women.
3. Reviewing treatment methods and psychotherapeutic strategies used to correct these disorders.
4. Identifying prospects for further research to improve the diagnosis and treatment of psychosexual disorders in women.

Materials and Methods. The material for this study comprised scientific articles and monographs dedicated to the issues of psychosexual development in women, published over the last 10 years. Special attention was given to works focusing on the clinical aspects of psychosexual disorders, as well as the analysis of etiological factors and treatment methods. The analysis included Ukrainian and international publications from the fields of psychology, psychiatry, sexology, and social medicine [3, 5, 7, 9].

The research methods involved theoretical analysis of scientific literature, as well as data synthesis on the biological and social aspects of psychosexual disorders.

Research Results and Discussion.

1. **Biological Factors of Psychosexual Development Disorders.** Biological aspects are one of the primary factors influencing psychosexual development. Hormonal imbalances, for instance, can negatively impact sexual desire, the ability to experience arousal, and orgasm in women. According to research by Gomez-Lobo et al. (2016), women with developmental disorders or hormonal imbalances are more likely to encounter difficulties in forming gender identity and sexual behavior [8].

Studies also show that physiological issues, such as abnormalities in genital development or nervous system damage, can lead to serious psychosexual disorders. For example, Shynder V. V. (2014) notes that couples in which the male partner suffers from epilepsy often experience significant sexual disharmony, which also affects the psychosexual development of the woman [1].

2. **Psychosocial Factors.** Psychosocial factors, including family influence, social environment, and cultural expectations, play an important role in shaping female sexuality. Family upbringing, particularly in patriarchal cultures, can instill negative attitudes

toward one's sexuality, leading to sexual disorders in adulthood [6].

For instance, Yakovenko O. K. (2009) points out that women raised in conservative families with strict control over sexual behavior often face challenges in their sexual lives due to low self-esteem and feelings of shame [6]. Social stereotypes about female sexuality also frequently cause women to suppress their sexual desires or feel uncomfortable in sexual relationships.

3. **Clinical Manifestations of Psychosexual Disorders.** Psychosexual disorders in women can manifest in various forms: decreased sexual desire, difficulty achieving orgasm, pain during intercourse (dyspareunia), or involuntary vaginal muscle spasms (vaginismus) [5]. Orgasmic dysfunction is one of the most common disorders among women, accompanied not only by sexual issues but also by emotional disturbances, such as anxiety and depression [2]. Research by Yakymenko O. Y. (2012) showed that emotional support from a partner is an important factor in shaping sexual behavior in girls at different stages of psychosexual development [3]. Lack of support can lead to reduced self-esteem, which negatively impacts sexual activity and satisfaction.

4. **Treatment of Psychosexual Disorders.** The treatment of psychosexual disorders in women involves various therapeutic approaches. Medical therapy may include hormone replacement therapy if the disorder is related to hormonal imbalances [8]. In cases where the disorder is linked to psychosocial factors or emotional trauma, psychotherapy is the most effective treatment. Cognitive-behavioral therapy (CBT) has proven effective in treating psychosexual disorders by correcting negative thought patterns and behaviors that contribute to sexual dysfunction [9]. Sex therapy is also an important component of comprehensive treatment, especially in cases where the woman struggles with communication with her partner or has had negative relationship experiences [5]. Research shows that women who have experienced sexual violence or other types of traumatic events require specialized support to overcome the consequences of the trauma. Herasymenko L. O. (2014) notes that such women often suffer from co-occurring mental disorders that complicate the treatment of sexual dysfunction [5]. Therefore, it is important to provide comprehensive care, including both psychotherapeutic and medical interventions.

5. **Psychosexual Development and Society.** The social environment and its attitude toward sexuality play a crucial role in women's psychosexual development. Modern cultural and media processes shape standards of female beauty and sexuality, which influence women's self-esteem and sexual behavior [2]. In some cases, this leads women to feel pressured to conform to these standards, contributing to the development of psychosexual disorders. Sexual education, aimed at fostering a healthy attitude toward one's body and sexuality, plays an important role in preventing psychosexual development disorders. Research shows that sexual education programs promoting openness and awareness help reduce the incidence of sexual disorders among adolescents and young women [4].

Conclusion. Psychosexual development disorders in women are a complex phenomenon that encompasses both biological and psychosocial aspects. Effective treatment requires a comprehensive approach, including both medical therapy and psychotherapy. Timely diagnosis and support for women in their development are crucial, as they can significantly improve their quality of life and mental health. Psychosexual disorders can be prevented through appropriate sexual education and by expanding opportunities for open discussions about sexuality without stigma or judgment.

Prospects for Further Research. Further research should focus on studying the impact of innovative psychotherapeutic methods on the treatment of psychosexual disorders**,** as well as developing sexual education programs that consider cultural and social aspects of development. Research should also concentrate on examining the influence of modern technologies and media on women's psychosexual development, particularly in the context of shifting social standards and expectations.

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EFFECTIVENESS OF PREVENTIVE PROGRAMS IN MENINGOCOCCAL INFECTION.

Abstract.

The most effective preventive measure against N. meningitidis is vaccination. Five meningococcal serogroups are responsible for almost all forms of meningococcal disease in humans. Today it is possible to vaccinate against all five serogroups of meningococcus: A, B, C, Y, W135. For more than 30 years, polysaccharide vaccines against meningococcus have been used in the world. Bivalent (groups A and C) or tetravalent (groups A, C, Y, W135) polysaccharide meningoB coca vaccines have satisfactory immunogenicity in adults and children older than two years. The conjugate vaccine against meningococcal group C has been used in the world since 1999, has demonstrated safety and efficacy in the fight against meningococcal infection. To date, also licensed conjugate vaccine against meningococcus group A and tetravalent conjugate vaccine against meningococcus groups A, C, Y, W135. Conjugate meningococcal vaccine induces adequate antibody production and immunological memory formation in infants vaccinated at 2-4 months of age. Conjugate meningococcal vaccine can be used in children starting from 2-3 months of life, with the introduction of three doses in the first year of life or one dose of vaccine in adolescence. A polysaccharide vaccine against meningococcal groups A and C may be recommended for vaccination in children over two years of age.

In Ukraine, a conjugated tetravalent vaccine against meningococcal groups A, C, Y, W135 and polysaccharide vaccine against meningococcal groups A and C. vaccination against meningococcus for health reasons is indicated in patients with primary and secondary immunodeficiencyB we are at high risk of developing invasive forms of meningococcal infections, including meningitis (deficiency of the complement system, asplenia, HIV infection). Vaccination against meningococcus is recommended in the epidemic rise in incidence with generalized forms to persons living on endemic teritoB swarms and in foci of infection caused by meningococcus of the corresponding serogroup.

Keywords: *meningococcal disease, children, prevention, treatment, vaccination.*

Meningococcal disease is a serious bacterial disease that is caused by the bacteria Neisseria meningitidis (meningococci). It is especially dangerous for children, because it can develop very quickly and lead to serious consequences. Meningococcus can cause meningitis (inflammation of the meninges) and sepsis (blood poisoning). The infection is transmitted through droplets that are released by coughing, sneezing or close contact with a carrier of bacteria. Healthy people can be carriers without showing symptoms, but transmit the infection to others.

The latest approaches to the prevention and treatment of meningococcal disease in children are focused on improving vaccination, improving the effectiveness of antibacterial therapy and early diagnosis. Thanks to modern research, medicine has been able to achieve significant success in the fight against this dangerous infection.

The purpose of the study is an objective analysis of scientific sources on the specific prevention of meningococcal disease**.**

Materials and methods.

A literature review based on articles published in PubMed and National Library of Medicine databases.

Results.

Meningococcal infection is one of the dangerous bacterial infections that can cause mortality in childhood. Therefore, the main direction of preserving the health of small patients is early detection of such patients and specific prevention. Vaccination is the most effective means of preventing meningococcal disease, especially in children who are the most vulnerable population. Several types of vaccines have been developed in recent years covering different meningococcal serogroups. A review of vaccines and prevention programs assesses their effectiveness and impact on reducing disease rates.

Meningococcal polysaccharide vaccines. These are older vaccines containing purified polysaccharides from the shells of Neisseria meningitidis bacteria. They are used to prevent infections caused by serogroups A, C, W, and Y. Disadvantages: limited duration of protection (about 3-5 years), less efficacy in young children and lack of protection against serogroup B.

Conjugate vaccines. These vaccines have significantly higher efficacy compared to polysaccharide vaccines because the bacteria antigens are bound to a protein that stimulates a stronger immune response. Vaccines are available for serogroups A, C, W and Y. Examples of vaccines: Menactra, Menveo, Nimenrix. Advantages: longer immunity, high efficiency in young children, as well as the possibility of inclusion in routine immunization programs.

Serogroup B vaccine. Serogroup B was previously unattainable for vaccination due to the specificity of antigens of this group. However, the latest developments have led to the emergence of effective vaccines such as Bexsero and Trumenba. These vaccines contain several protein components that contribute to the formation of an immune response against serogroup B. Feature:

These vaccines are particularly important for regions where serogroup B is the most common cause of meningococcal disease.

Effectiveness of preventive programs

Inclusion of vaccines in national immunization programmes. In many countries, vaccines against meningococcal serogroups A, C, W, Y and B are included in national vaccination calendars. This significantly reduced the incidence among children and adolescents.

For example, in the UK, the introduction of vaccination against serogroup C led to the almost complete elimination of cases of infection caused by this serogroup. Vaccination against serogroup B also proved effective in significantly reducing the number of cases of the disease.

Targeted vaccination in risk areas

In areas with a high prevalence of meningococcal disease, vaccination is extremely effective in reducing the risk of outbreaks. This applies to both endemic regions and certain social groups, such as schoolchildren and students living in hostels, where the risk of transmission is higher. In Africa, where meningococcus was previously responsible for significant epidemics, a mass vaccination program against serogroup A (MenAfriVac vaccine) has significantly reduced the number of cases.

The role of vaccination in reducing mortality and complications

Meningococcal disease, untreated or detected too late, has a high rate of lethality and complications such as loss of limbs, neurological disorders and deafness. Preventive programs based on vaccination can prevent severe disease and significantly reduce mortality.

Conclusions.

Meningococcal disease vaccines are a powerful tool in the fight against a dangerous disease, especially among children. The effectiveness of preventive programs is confirmed by a significant reduction in morbidity and mortality in countries where vaccination is widely used. The most effective are conjugate vaccines and serogroup B vaccines, which can protect children from various strains of Neisseria meningitidis.

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GENDER ASPECTS OF THE PATHOPHYSIOLOGY OF SEXUAL DYSFUNCTIONS

Abstract.
The article explores the importance of gender aspects in the pathophysiology of sexual dysfunctions, as understanding these differences is key to effective diagnosis and treatment. Sexual disorders impact the quality of life of patients, making their study highly significant. The literature review emphasizes the physiological, psychological, and sociocultural factors that shape sexuality in men and women. Incorporating gender aspects into clinical practice allows for the development of more personalized therapeutic strategies, enhancing treatment effectiveness and improving the psycho-emotional well-being of patients.

Keywords: *gender aspects, pathophysiology, sexual dysfunctions, psycho-emotional factors, hormonal changes, sociocultural influences, treatment, diagnosis, sexuality.*

Introduction.

Sexuality is an important component of human life, influencing physical, psychological, and social health. Sexual dysfunctions, which include disturbances in sexual desire, arousal, and orgasm, pose a serious problem for many individuals, both men and women. Various studies indicate that sexual disorders can significantly negatively impact quality of life, relationships, and an individual's psycho-emotional state. However, it is worth noting that the manifestations and causes of sexual dysfunctions can differ significantly based on gender, highlighting the necessity of a gendered approach in their study and treatment [3, 8, 11].

The relevance of studying gender aspects of the pathophysiology of sexual dysfunctions is increasing in modern society, where issues of sexual health are gaining particular importance. Many men and women encounter difficulties in their intimate lives, often caused not only by physiological factors but also by psychological and sociocultural influences. For example, stress, anxiety, depression, and societal stereotypes regarding gender roles can significantly affect sexual function [7, 10].

Gender differences in the pathophysiology of sexual dysfunctions also suggest that men and women may have different needs in diagnosis and treatment. While erectile dysfunction may be a common issue among men, women often face challenges related to decreased sexual desire or absence of orgasm. This requires a comprehensive treatment approach that takes into account the specifics of each gender [10].

There are already several studies in the scientific literature exploring the gender aspects of sexual disorders. However, questions remain open, particularly regarding the mechanisms underlying different types of dysfunctions in men and women, as well as the effectiveness of therapeutic strategies. This underscores the need for further research in this area to provide evidence-based recommendations for clinical practice [5].

As part of this article, a review of contemporary scientific research related to gender aspects of the pathophysiology of sexual dysfunctions will be conducted. The focus will be on analyzing the pathophysiological mechanisms that cause sexual disorders, as well as assessing the impact of psychological and sociocultural factors. Clinical recommendations for the diagnosis and treatment of sexual dysfunctions will also be discussed, with an emphasis on gender differences [9].

In summary, the importance of studying gender aspects of sexual dysfunctions not only reveals the complexity of these issues but also contributes to the development of more effective and personalized approaches to their treatment. As a result, understanding these aspects can significantly improve the quality of life for individuals suffering from sexual disorders and help them restore healthy intimate relationships [1, 2, 6].

Research Objective. To analyze the scientific literature regarding gender aspects of the pathophysiology of sexual dysfunctions in order to identify key factors affecting sexual health in men and women.

Materials and Methods. The research utilized materials from scientific articles, monographs, reviews, and meta-analyses published in peer-reviewed journals over the past 10 years. The selection of literature was based on keywords such as "gender aspects," "sexual dysfunctions," "pathophysiology," "psychological factors," and "sociocultural influences." Analytical methods included systematic review and critical analysis, which allowed for the identification of key themes and trends in scientific research. Special attention was

given to gender differences in the manifestation and treatment of sexual dysfunctions. All selected articles were assessed for quality and relevance to the research topic.

Research Results and Discussion. As a result of the systematic review of the scientific literature, numerous gender aspects affecting the pathophysiology of sexual dysfunctions were identified. The main findings of the study can be divided into several key themes: physiological, psychological, and sociocultural factors.

1. **Physiological Aspects.** Research has shown that hormonal changes play a significant role in the development of sexual dysfunctions. In men, a decrease in testosterone levels is often associated with erectile dysfunction and reduced sexual desire. In women, menopause and changes in estrogen levels can lead to vaginal dryness and discomfort during intercourse, which also affects their sexual desire. According to the literature, these physiological changes can cause different types of dysfunctions in men and women, highlighting the importance of a gendered approach in therapy[7, 11].

2. Psychological Factors. Psycho-emotional aspects such as anxiety, depression, and stress have been identified as important factors affecting sexual function. Studies indicate that women are more likely to experience psychological difficulties related to sexuality, which can lead to decreased sexual desire or orgasmic disorders. Men, on the other hand, may be more prone to issues related to self-esteem, driven by social stereotypes about masculinity. This underscores the need for psychological support in the treatment of sexual dysfunctions [1,6].

3. Sociocultural Influences. Social stereotypes and cultural norms also have a significant impact on sexuality. Research demonstrates that societal expectations regarding gender roles can shape negative attitudes towards sexuality, which in turn may contribute to the development of dysfunctions. For example, men may feel pressure to conform to traditional notions of masculinity, which can lead to stress and, consequently, erectile dysfunction. In women, social norms may evoke feelings of guilt or shame regarding sexual desires, negatively affecting their sexual health [2, 3].

4. Gender Differences in Treatment. An important aspect identified during the study is the necessity of adapting treatment to the specifics of each gender. Men may be recommended pharmacological agents such as PDE-5 inhibitors, which have proven effective in treating erectile dysfunction. In contrast, women may benefit more from psychotherapeutic approaches, which can include cognitive-behavioral therapy and sexual therapy to overcome psychological barriers [4, 8].

Conclusion. Therefore, the findings of the study highlight the complexity of sexual dysfunctions and the importance of a gendered approach in their study and treatment. The identified physiological, psychological, and sociocultural factors interact and shape various aspects of sexual health, necessitating a comprehensive approach in clinical practice. This research opens new horizons for the development of individualized therapeutic strategies that can significantly improve patients' quality of life.

Prospects for Further Research. The literature analysis indicates the need for further studies that delve deeper into the gender differences in the pathophysiology of sexual dysfunctions. In particular, attention should be paid to the duration and quality of studies, as well as the impact of different therapeutic approaches on improving sexual health in both gender groups.

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ANTI-VACCINATION TRENDS IN PERTUSSIS PREVENTION. A NEW LOOK AT THE DIAGNOSIS OF RESPIRATORY INFECTION

Abstract

Whooping cough (or whooping cough) is a bacterial disease of the respiratory tract caused by the bacterium Bordetella pertussis. The relevance of the topic of pertussis in children remains high due to a number of factors associated with an increase in cases of morbidity, possible serious complications, as well as the influence of anti-vaccination moods. Despite the availability of an effective vaccine, pertussis is still a health threat, especially for children under 1 year of age, who have the highest risk of severe consequences.

Keywords: *whooping cough, Bordetella pertussis, children, vaccination, diagnosis*

In connection with the catastrophic situation with vaccinations in the state and epidemiological problems, parents with children who have manifestations of a seizure-like cough are increasingly turning to pediatricians or family doctors. A seizure-like cough is often accompanied by redness or even blue face and ends with the release of thick transparent mucus and vomiting. Such signs of the disease are mainly manifestations of whooping cough (whooping cough) - a children's acute infectious disease transmitted by airborne droplets. Often children are infected and from adult family members who for a long time cough and secrete microbes Bordetella pertussis, more often virulent serotype 1.0.3. It is important to remember that pertussis-like syndrome can be caused by other microorganisms, in particular B. parapertussis, B. halmesii, B. bronchoseptica, Mycoplasma pneumoniae, chlamydia, adenoviruses.

Every year in the world there are about 50 million cases of the disease, in developing countries, about 300 thousand children die. In Ukraine, 3-4 thousand cases of pertussis are recorded annually, mainly in children under the age of 1 year, in which the disease has a particularly severe course, with many complications and adverse consequences. The fact that the number of patients with pertussis will grow annually could be predicted.

Modern aspects of diagnosis and prevention of pertussis in children in the context of the growing anti-vaccination trend is an extremely important topic in pediatric medicine. Pertussis remains one of the most dangerous and common childhood infections, and the increase in the number of parents who refuse vaccination poses a serious threat to the health of children and society as a whole. In response to these challenges, modern medicine is developing new approaches to the diagnosis, treatment and prevention of the disease.

The aim of the study is to describe the main aspects of pertussis diagnosis and prevention

Materials and methods.

A literature review based on articles published in PubMed and the National Library of Medicine.

Results.

The main method of diagnosing pertussis remains the laboratory examination of nasopharyngeal swabs for the detection of Bordetella pertussis. The most effective method today is PCR (polymerase chain reaction), which allows you to detect the DNA of the pathogen even in the early stages of the disease. PCR has a high sensitivity and specificity, which makes it the gold standard for the diagnosis of pertussis, especially in conditions where the infection occurs atypically or with an erased clinical picture. Serological examination (detection of antibodies to Bordetella pertussis in the blood) is also used for diagnosis, especially in the later stages of the disease, when the bacteria are already difficult to isolate, but the immune system produces antibodies. Despite the importance of laboratory methods, the clinical manifestations of pertussis (convulsive cough with whistling breath) remain key for primary diagnosis, especially in young children.

The growth of the anti-vaccination trend threatens herd immunity, leading to an increase in the number of pertussis cases. To reduce the risk of morbidity, it is necessary to actively conduct educational campaigns among parents and debunk myths about the dangers of vaccination. The DTP vaccine (against pertussis, diphtheria and tetanus) is safe and effective, with minimal side effects. In response to concerns about the safety of whole cell vaccines (especially older pertussis vaccines), acellular (acellular) vaccines have been developed that cause fewer adverse reactions and are highly effective. They are used as part of the combined DTP vaccine. One of the most important modern approaches to the prevention of pertussis is the vaccination of pregnant women in late pregnancy. This makes it possible to transmit antibodies to newborns through the placenta, providing them with protection against pertussis in the first months of life, when they cannot yet receive a full dose of the vaccine. Revaccination of adolescents and adults. Immunity from the vaccine wanes over time, so many countries recommend revaccination of adolescents and adults to reduce the likelihood of infection and transmission to younger children who are not yet fully vaccinated. Immunocompromised children who cannot be vaccinated for medical reasons need to form herd immunity of the people around them.

Current research to develop vaccines that can provide longer immunity and require less revaccination is ongoing. The role of genetic factors in susceptibility to severe forms of whooping cough is also being studied, which may allow better development of individual prevention strategies.

Conclusion.

The conditions of the growing anti-vaccination trend create new challenges for the prevention of pertussis in children. Modern diagnostics and prevention focus on improving vaccines, raising public awareness and ensuring access to health services. An important role is played by educational campaigns that contribute to increasing the level of confidence in vaccination and the fight against misinformation. Thanks to such approaches, it is possible to reduce the incidence rate and protect children from severe complications of whooping cough.

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RESTRICTIVE CARDIOMYOPATHY

Анотація:

Рестриктивна кардіоміопатія (РКМ) — це гетерогенна група захворювань, що характеризуються рестриктивною патофізіологією лівого шлуночка (ЛШ), яка полягає у швидкому підвищенні тиску в шлуночках при незначному збільшенні об'єму наповнення через підвищену жорсткість міокарда. Визначальною ознакою РКМ є комбінація стійкої рестриктивної патофізіології, діастолічної дисфункції, нерозширених шлуночків та дилатації передсердь, незалежно від товщини стінки шлуночка та систолічної функції. Фенотипічний спектр РКМ є дуже широким. Розлади, що проявляються як РКМ, класифікуються за чотирма основними механізмами: 1) інтерстиціальний фіброз і внутрішня дисфункція міокарда, 2) інфільтрація позаклітинних просторів, 3) накопичення матеріалу в кардіоміоцитах, 4) ендоміокардіальний фіброз. Деякі розлади можуть демонструвати рестриктивну патофізіологію лише на початкових або термінальних стадіях, а інші — протягом усього свого розвитку. Крім того, у деяких пацієнтів можуть бути елементи як гіпертрофічного, так і рестриктивного фенотипу, що ускладнює класифікацію.

Рестриктивну патофізіологію можна виявити за допомогою катетеризації серця або доплерівської ехокардіографії. Конкретні стани зазвичай діагностуються на основі клінічних даних, 12-канальної електрокардіограми, ехокардіографії, ядерної медицини або серцево-судинного магнітного резонансу. Додаткові дослідження, такі як ендоміокардіальна біопсія та генетична оцінка, можуть бути необхідними для точного діагнозу. Терапія для РКМ є різноманітною і варіюється залежно від конкретного захворювання, причому модифікуюче лікування доступне лише для амілоїдозу серця і частково для кардіоміопатії, викликаної перенавантаженням залізом.

Abstract:

Restrictive cardiomyopathy (RCM) is a heterogeneous group of diseases characterized by restrictive pathophysiology of the left ventricle (LV), which consists of a rapid increase in ventricular pressure with a slight increase in filling volume due to increased myocardial stiffness. The defining feature of RCM is a combination of persistent restrictive pathophysiology, diastolic dysfunction, non-dilated ventricles, and atrial dilation, regardless of ventricular wall thickness and systolic function. The phenotypic spectrum of RCM is very wide. Disorders that manifest as RCM are classified according to four main mechanisms: 1) interstitial fibrosis and internal myocardial dysfunction, 2) Infiltration of extracellular spaces, 3) accumulation of material in cardiomyocytes, and 4) endomyocardial fibrosis. Some disorders may show restrictive pathophysiology only in the initial or end stages, while others may show restrictive pathophysiology throughout their development. In addition, some patients may have elements of both hypertrophic and restrictive phenotypes, which makes classification difficult.

Restrictive pathophysiology can be detected by cardiac catheterization or Doppler echocardiography. Specific conditions are usually diagnosed based on clinical data, a 12-channel electrocardiogram, echocardiography, nuclear medicine, or cardiovascular magnetic resonance imaging. Additional studies, such as endomyocardial biopsy and genetic assessment, may be necessary for an accurate diagnosis. Therapy for RCM is diverse and varies depending on the specific disease, with modifying treatment available only for cardiac amyloidosis and partly for cardiomyopathy caused by iron overload.

Ключові слова: *рестриктивна кардіоміопатія, захворювання міокарда, амілоїдоз*
Key words: *restrictive cardiomyopathy, myocardial diseases, amyloidosis*

Актуальність: Рестриктивна кардіоміопатія (РКМ) — це захворювання серцевого м'яза, яке характеризується жорсткістю стінок шлуночків, що спричиняє діастолічну дисфункцію, підвищення кінцевого діастолічного тиску та розширення передсердь. Шлуночки при цьому не розширені і мають нормальну товщину стінок, тому систолічна функція зазвичай збережена. Порушення структури та систолічної функції шлуночків може виникати лише на пізніх стадіях вторинного РКМ [14]. РКМ не є самостійним захворюванням і може бути наслідком різних успадкованих або набутих факторів. Як і в інших кардіоміопатіях, у РКМ виявлено генетичні мутації в генах, що кодують саркомерні білки. Епідеміологія цього захворювання недостатньо вивчена, але РКМ є найменш поширеною з кардіоміопатій. Ідіопатична форма, коли причина не встановлена, є рідкісною. Це захворювання може вражати людей будь-якого віку, причому діти мають найгірший прогноз, а дівчатка страждають частіше [20]. РКМ може бути як набутим, так і спадковим. У випадку спадкового захворювання для кожної причини було виявлено специфічні генетичні мутації.

Мета: дослідити особливості рестриктивної кардіоміопатії, описати можливі види діагностики та визначити ефективне лікування.

Матеріали та методи: Пошук літературних джерел здійснено за допомогою науково-статистичної бази. Проведено огляд літературних джерел до травня 2024 року, які стосуються огляду, клінічної картини, діагностики та лікування рестриктивної кардіоміопатії.

Результати дослідження:

Рестриктивна кардіоміопатія (РКМ) має найширший спектр причин і гістологічних особливостей серед кардіоміопатій, часто потребуючи катетеризації серця або ендоміокардіальної біопсії для точного діагнозу. Ситуація ускладнюється тим, що межі РКМ стають розмитими, оскільки багато генів, що викликають хворобу, спільні з іншими кардіоміопатіями, а серцеві фенотипи можуть змінюватися з часом. Хоча гемодинамічне визначення рестриктивної патофізіології є однозначним, співвідношення тиск-об'єм може змінюватися, а діагностичні порогові значення залишаються невизначеними. Новітні методи візуалізації, такі як серцево-судинний магнітний резонанс (CMR), сцинтиграфія з індикаторами кісток і позитронно-емісійна томографія, допомагають визначити конкретні причини пошкодження тканин (наприклад, амілоїдоз, хвороба Андерсона-Фабрі, гемохроматоз, саркоїдоз), навіть якщо рестриктивна патофізіологія ще не повністю зрозуміла [3].

Обмежувальна фізіологія ЛШ виникає через збільшення жорсткості міокарда, що спричиняє швидке підвищення тиску в шлуночках на початку діастоли при незначному збільшенні об'ємів наповнення або навіть критичному зменшенні об'ємів шлуночків аж до майже повної їх облітерації через масивну гіпертрофію стінки або ендоміокардіальну проліферацію [7]. Згідно з визначенням Європейського товариства кардіологів (ESC), іншими ознаками РКМ є "нормальний або знижений систолічний і діастолічний об'єм (одного або обох шлуночків)" і "нормальна товщина стінки шлуночка" [7]. Хоча це визначення концептуально правильне, його буквальне тлумачення може виключити багато розладів із загальною обмежувальною фізіологією, включаючи кілька форм РКМ.

Пацієнти з РКМ мають ригідний, некомплаєнтний ЛШ із порушенням діастолічного наповнення та високим тиском наповнення. Хронічно підвищений діастолічний тиск (ДТ) ЛШ зазвичай спричиняє легеневу гіпертензію, що посилює правосерцеву недостатність, особливо коли правий шлуночок (ПШ) уражений, як при амілоїдозі серця (АС). На ранніх стадіях РКМ систолічна функція ЛШ зазвичай зберігається, принаймні, якщо оцінювати її за фракцією викиду ЛШ (ФВЛШ), але з часом вона має тенденцію до погіршення. Поздовжня систолічна функція ЛШ часто знижується на ранніх стадіях, особливо при АС. Незважаючи на збережену ФВЛШ, ЛШ не може належним чином заповнитися, а розмір порожнини шлуночка може бути зменшений через значне потовщення стінки, що призводить до майже фіксованого ударного об'єму. В таких умовах єдиною адаптивною реакцією на фізичне навантаження, здатною збільшити серцевий викид, є збільшення частоти серцевих скорочень, яке може бути знижене у пацієнтів із супутньою вегетативною дисфункцією, що підвищує ризик гіпотензії під час фізичних навантажень. Крім того, ремоделювання та дилатація передсердь часто призводять до фібриляції передсердь (ФП), що зменшує внесок передсердь у наповнення ЛШ [9].

Гемодинамічний профіль, спільний для всіх форм РКМ, можна досить точно охарактеризувати за допомогою трансторакальної ехокардіограми. Першою ознакою обмежувальної патофізіології є поєднання двобічного розширення передсердь (без явних причин, таких як клапанні захворювання або фібриляція передсердь), нормальної або помірно зниженої фракції викиду лівого і правого шлуночків та нерозширених шлуночків. Доплерівське зображення може показати рестриктивну схему наповнення трансмітрального кровотоку з підвищеною швидкістю раннього діастолічного наповнення (хвиля Е) через підвищений тиск у лівому передсерді (ЛП) та зниженою швидкістю наповнення передсердь (хвиля А) через високий ДТ у шлуночках, зниження часу мітрального сповільнення та часу ізоволюметричного розслаблення. Крім того, співвідношення між систолічним і діастолічним кровотоком у легеневих венах помітно знижується через високий тиск в ЛП. Тканинна доплерографія зазвичай показує знижену ранню діастолічну швидкість міокарда (e′), що призводить до підвищення співвідношення E/e′. Застій нижньої порожнистої вени та печінкових вен, а також реверс діастолічного кровотоку в печінкових венах під час вдиху є звичайним явищем через нездатність ПШ адаптуватись до збільшеного венозного повернення [8,19,25].

Характерні зміни кожного розладу накладаються на загальний морфологічний і функціональний фенотип, що призводить до дуже гетерогенної картини. Кардіоваскулярний магнітний резонанс і гістологія міокарда дозволяють досліджувати надзвичайно гетерогенний субстрат міокарда. Навіть електрокардіографічна картина може сильно відрізнятися в спектрі РКМ. Можливим специфічним маркером РКМ, хоч і нечутливим, є ознака помітного двобічного розширення передсердь [3].

Клінічна картина РКМ може бути дуже різноманітною. Вона залежить від супутньої патології у випадку вторинних форм, але діастолічне порушення може вражати як лівий, так і правий шлуночок. Симптоми включають задишку, набряк легенів, серцебиття, втому, ортопное і біль у грудях [23]. Серцева недостатність (СН) і фібриляція передсердь (ФП) залишаються найпоширенішими симптомами. СН найчастіше правостороння або двокамерна зі збільшенням печінки, набряком нижніх кінцівок і асцитом [3]. При клінічному огляді часто спостерігаються розширення яремної вени, систолічний шум, третій тон серця, легеневі хрипи і периферичний набряк. Рідше зустрічаються гепатоспленомегалія, сам асцит і анасарка на пізніх стадіях хвороби [14].

Нещодавні дослідження показують, що у пацієнтів з РКМ серцева та периферична вегетативна дисфункція пов'язана зі зниженою чутливістю барорефлексу, що призводить до клінічного погіршення та аритмій. Наявність нормальної фракції викиду недооцінює прогресування захворювання [15,20]. Клінічно РКМ важко відрізнити від констриктивного перикардиту (КП). Історія кардіохірургії, травм, туберкульозу або злоякісних пухлин більше вказує на КП, тоді як високі рівні BNP у плазмі вказують на РКМ [1].

Близько 99% пацієнтів з РКМ мають аномалії на ЕКГ. Найчастішою аритмією є фібриляція передсердь (ФП), обумовлена збільшенням передсердь. Поширеною знахідкою є підвищений сегмент ST із зубчастими або двофазними пізніми зубцями Т. Також описано значне пригнічення ST з інверсією зубця Т, що імітує субендокардіальну ішемію, і пов'язано з підвищеним ризиком раптової серцевої смерті (ССД). Можуть спостерігатися передчасні серцеві скорочення як шлуночків, так і передсердь [10,14].

Найпоширенішим результатом рентгенографії грудної клітки є кардіомегалія, спричинена двостороннім збільшенням передсердь. Також можуть спостерігатися застій у легеневих венах, інтерстиціальний набряк і плевральний випіт [14]. А також кальцифікація перикарда або низький вольтаж QRS на ЕКГ підказують діагноз КП. Механіка ЛШ, визначена за допомогою відстеження тканин на ехокардіографії та CMR, може допомогти у розрізненні цих станів [21].

Зазвичай ехокардіографія показує відсутність гіпертрофії або дилатації шлуночків, збережену систолічну фракцію викиду ЛШ, двобічне збільшення передсердь та діастолічну дисфункцію. Американське товариство ехокардіографії (ASE) пропонує чотири параметри для ідентифікації діастолічної дисфункції:

- Індекс максимального об'єму лівого передсердя (LA) >34 мл/м;
- Пікова швидкість трикуспідальної регургітації (TRV) >2,8 м/с;
- Середнє співвідношення E/e' >14;
- Кільцева швидкість e' (перегородкова e' <7 см/с, бічна e' <10 см/с).

Співвідношення максимальної систолічної швидкості легеневої вени до максимальної діастолічної швидкості та зміни співвідношення E/A при маневрі Вальсальви використовуються для демонстрації підвищення тиску наповнення ЛШ. Деякі результати ехокардіографії також допомагають відрізнити ідіопатичну форму РКМ від вторинних (наприклад, саркоїдоз серця, гіпереозинофільний синдром, діабетична кардіоміопатія, склеродермія, ендоміокардіальний фіброз, вплив радіації, карциноїдна хвороба серця, метастатичний рак тощо). Крім того, ехокардіографія надає додаткову інформацію для диференціації РКМ від констриктивного перикардиту [17,18,22].

Магнітно-резонансна томографія серця (CMR) надає більше інформації, ніж ехокардіографія. Зокрема, вона корисна для ідентифікації специфічних закономірностей, характерних для захворювань, що викликають РКМ. Наприклад, дифузне субендокардіальне пізнє посилення гадолінієм (LGE) має приблизно 95% специфічність для діагностики амілоїдозу серця (АС). Крім того, LGE на CMR визнано цінним прогностичним фактором у пацієнтів з кардіосаркоїдозом або АС. Як і ехокардіографію, CMR можна використовувати для диференціації РКМ від констриктивного перикардиту [12,13].

Ендоміокардіальну біопсію зазвичай виконують, коли інші тести не дають остаточних результатів. Ця процедура може виявити, наприклад, наявність амілоїду або відкладення заліза, що допоможе підтвердити або виключити деякі вторинні форми РКМ. Проте, через неоднорідну структуру цього захворювання, корисно попередньо виконати LGE-CMR для точнішого керування біопсією та зменшення ймовірності хибнонегативного результату [14].

Лікування вторинних форм РКМ залежить від конкретної причини основного захворювання. Для ідіопатичної форми терапія спрямована на полегшення симптомів СН [24]. Для покращення наповнення шлуночків і зменшення діастолічної дисфункції можна застосовувати недигідропіридинові блокатори кальцієвих каналів (наприклад, верапаміл, дилтіазем) та бета-блокатори, які також сприяють розслабленню шлуночків. Аритмії слід лікувати, віддаючи перевагу відновленню синусового ритму; якщо це не вдається, призначають пероральні антикоагулянти. Імплантація дефібриляторів розглядається для запобігання раптовій серцевій смерті, хоча критерії відбору пацієнтів складно визначити [4]. Трансплантацію серця вважають єдиним остаточним методом лікування РКМ і рекомендується пацієнтам із СН, яка не піддається іншим методам

лікування. Деякі дослідники рекомендують включати пацієнтів до списку на трансплантацію навіть на ранніх стадіях захворювання, зокрема безсимптомних пацієнтів, через прогресуючий характер РКМ [6].

Петльові діуретики використовуються для зняття венозного застою в легеневому і великому колі кровообігу, асциту. Варто уникати високих доз, щоб не знизити надмірно попереднє навантаження, оскільки це може призвести до зменшення серцевого викиду та спричинити гіпотензію. Дигоксин слід застосовувати з обережністю через його аритмогенну дію [23].

Пацієнти зазвичай погано переносять брадикардію, і брадіаритмії можуть вимагати імплантації атріовентрикулярного кардіостимулятора. Препарати, що впливають на ренін-ангіотензин-альдостеронову систему, не показали прогностичної користі та можуть викликати гіпотензію [16]. Фібриляція передсердь є поширеною і часто погано переноситься через втрату участі передсердь у наповненні шлуночків. Контроль ритму є пріоритетом над контролем частоти, хоча досягнення та підтримання синусового ритму може бути складним. Пацієнти з синусовою аритмією та ФП мають високий тромбоемболічний ризик і повинні отримувати антикоагулянтну терапію незалежно від їхньої оцінки за шкалою CHA2DS2-VASc. Цей підхід слід застосовувати і в інших типах РКМ [3].

Імплантація вентрикулярного допоміжного пристрою є складною через малий розмір порожнини ЛШ та ризик обструкції при канюляції через верхівку ЛШ [11]. Трансплантація серця може бути розглянута для окремих пацієнтів з результатами, подібними до інших етіологій СН, за винятком амілоїдозу та радіаційно-індукованої кардіоміопатії, де результати зазвичай гірші [5]. Останнім часом, завдяки більш ранньому виявленню та лікуванню амілоїдозу, трансплантація серця була запропонована як ефективний варіант для ретельно відібраних пацієнтів з амілоїдозом, з результатами, подібними до пацієнтів, трансплантованих з інших причин СН [2].

Управління анестезією перед трансплантацією є складним завданням. Основні принципи передопераційного лікування включають: підтримку адекватного тиску наповнення, збереження синусового ритму, контроль електролітних порушень та управління системним судинним опором при відносно фіксованому серцевому викиді. Нещодавно стали доступні нові терапії для деяких форм РКМ, які змінюють перебіг захворювання та спрямовані на специфічні білки або нуклеїнові кислоти [3].

Висновок: Однією з найскладніших задач сучасної медицини є розрізнення різноманітних форм кардіоміопатій з клінічно значущого та здійсненного підходу до діагностики та розуміння цієї гетерогенної групи захворювань.

Основною характеристикою РКМ є постійна рестриктивна фізіологія, яка зазвичай супроводжується дилатацією передсердь і нерозширеними шлуночками, незалежно від товщини стінки шлуночка та систолічної функції. Обмежувальний шаблон наповнення на ехокардіографії сам по собі недостатній для діагностики РКМ, оскільки такий висновок може бути наслідком тимчасових гемодинамічних змін.

На відміну від товщини та дилатації шлуночків, які визначають гіпертрофічну та дилатаційну кардіоміопатії відповідно, рестриктивний характер наповнення може бути динамічним і змінюватися протягом коротких інтервалів часу (наприклад, при застосуванні діуретиків для зняття сильного застою). Тому доцільно вважати «постійною» рестриктивну патофізіологію за наявності рестриктивного шаблону наповнення щонайменше на двох повторних доплерівських ехокардіограмах: спочатку під час клінічного обстеження та повторно через певний період (наприклад, щонайменше через шість місяців).

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ACUTE OBSTRUCTIVE LARYNGOTRACHEITIS (CROUP) IN CHILDREN: CURRENT VIEWS AND UNRESOLVED ISSUES
(Literature review)

Resume.
This article highlights the topical issues of acute stenotic laryngotracheitis (ASLT) in children, this disease is one of the most common pathologies of the upper respiratory tract in childhood, of various etiologies, which can lead to serious complications. The authors note that timely diagnosis and treatment are crucial for reducing severe complications and reducing the risk of mortality.

Key words. *Laryngotracheitis, croup, airway obstruction, children.*

Abstract.
The aim of **work**. The aim of this work is analysis of of modern approaches to diagnosis and treatment of acute stenotic laryngotracheitis, study risk factors and the main etiological factors of the disease, and as well as development of recommendations for prevention and detection of laryngeal stenosis.

The essence of the topic.

Etiology and pathogenesis. Acute stenotic laryngotracheitis is most often caused by viruses, in particular parainfluenza viruses , less often influenza viruses, adenoviruses and respiratory- syncytial virus. lesions occur on the background of viral infection, which leads to inflammation of mucous membrane larynx, trachea and surrounding tissues. In children, larynx has narrow lumen, so even slight edema causes stenosis, that is accompanied by acute.

The pathogenesis of disease is· associated with development of inflammatory process, that includes swelling of mucous membrane of the larynx, increased secretion of mucus and spasm of m· muscles of the larynx . As a result of there is narrowing of the lumen of the airways, that leads to respiratory disturbance. The most typical symptoms include rough cough, hoarseness of the voice, noisy breathing and inspiratory shortness of breath. [4,6].

Clinical picture . The disease usually begins suddenly, often at night. The main symptoms are barking cough and stridor, hoarseness voice and sharp inspiratory dyspnea. In severe cases there may be symptoms of hypoxia, such as pallor, cyanosis of the skin and mucous membranes, disturbance of consciousness . Algover's index, that is used to assess the degree of respiratory failure, is an important criterion for making decisions about further therapeutic tactics.

Acute stenosing laryngotracheitis is often classified according to degrees of severity :

- Mild degree (I) - the presence of only hoarseness of the voice and barking cough.
- Medium (II) - inspiratory stridor is added, but there are no signs of hypoxia.
- Severe degree (III) - significant stridor, signs of hypoxia (cyanosis, tachycardia).
- Critical condition (IV) - extremely serious condition with a risk of asphyxiation, requires immediate intubation or tracheostomy. [1,7].

Principles of treatment. Treatment of GSLT includes several main approaches:

- Inhalation therapy: the use of nebulizers with bronchodilators and glucocorticoids helps quickly reduce edema and restore airway patency .
- Systemic therapy: in cases of moderate and severe severity is indicated administration of systemic corticosteroids, that effectively reduce inflammation.
- Oxygen therapy and intubation: in critical cases patients may require oxygen support and, as required, intubation to ensure adequate ventilation.

Children with AMLT, usually, recover within a few days provided that timely and adequate treatment is provided. However, it is, important to emphasize the need for early detection of severe forms of disease for with.[1,5,6].

Prevention. Preventive measures include reducing contact with infectious patients, strengthening - immunity vaccination against influenza and other respiratory infections, and as well as timely treatment of diseases of the upper respiratory tract. An important role in prevention is played by education of parents and medical staff to recognize early signs of laryngeal stenosis . [6,7].

Conclusions. Acute stenosing laryngotracheitis is a serious disease, that requires timely diagnosis and correct tactics treatment, especially in childhood age .

The main cause of development of stenosis is viral infection, which leads to edema and narrowing of the airways. Treatment should be complex based on the degree of severity of disease, including both drug therapy, and , if necessary , surgical methods. Timely treatment for medical assistance allows to avoid severe complications and reduce 2 the risk of fatal cases.

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MODERN ASPECTS OF ETIOLOGY, PATHOGENESIS, CLINICAL COURSE AND DIAGNOSIS OF LYME ARTHRITIS

Abstract.

Lyme borreliosis is a zoonotic infection with a vector-borne mechanism of transmission caused by Borrelia burgdorferi (less commonly B. mayonii). Rodents, birds, deer, and cattle are the natural reservoir of Borrelia burgdorferi. Ixodes ticks (Ixodes scapularis and I. pacifcus) are the main carrier of Borrelia between animals and humans: humans become infected by a tick bite infected with Borrelia. The possibility of human-to-human transmission of Lyme borreliosis has not been proven to date.

Lyme borreliosis is the most common vector-borne infectious disease characterized by a wide polymorphism of clinical manifestations. The largest number of cases is recorded in the spring and autumn period (May-October), which is associated with an increase in outdoor activities and seasonal activity of ticks (most active in April-June and August-October).

Keywords *: Lyme disease, lyme arthritis, erythema migrans, ixodid ticks.*

Etiology.

The causative agent Borrelia burgdorferi, a gram-negative DNA-containing microorganism, belongs to the order Spirochaetales, family Spirochaetaceae, genus Borrelia. Borrelia are motile Gram-negative spirochetes with 3-8 whorls. The genetic apparatus of Borrelia has no analogues among bacteria and consists of a single linear chromosome structure, a set of circular and linear plasmids, the latter being associated with the genetic plasticity of pathogens. Like other borreliae, B. burgdorferi is capable of repeatedly changing its antigenic structure in the course of its life in a living organism. Such antigenic mimicry allows it to persist in an infected organism for a long time. Two significant features of the disease are associated with the Borrelia genus: geographic distribution and clinical course: Borrelia burgdorferi sensu stricto is most commonly isolated in North America, less often in Europe, and more often leads to musculoskeletal disorders; B. afzelii is found in Europe and some regions of Asia and causes late skin manifestations, and B. garinii is widespread everywhere, with neurological symptoms predominating.

Borrelia have a large set of antigens that form antibodies of varying degrees of specificity; antigens contained in flagella provide cross-reactivity with other Borrelia, as well as Treponema and Leptospira. Among the surface membrane proteins, heat shock protein antigens deserve special attention. The outer membrane of borrelia contains lipoprotein and a lipoprotein substance that has a weak endotoxin-like effect.

Borrelia, which are highly sensitive to various disinfectants, do not survive in the external environment outside of a living organism, and die quickly under UV irradiation and boiling. They are microaerotrophs, with a growth optimum temperature of 33...+35 °C.

Modified Kelly's medium is optimal for growing borrelia; it takes at least 3 weeks to isolate and identify the pathogen. After 10 or more passages in culture, Borrelia can significantly reduce and even completely lose their infectivity, while retaining their antigenic properties.

In the body of a sick person, Borrelia borrelii CL are found in the skin, blood, cerebrospinal fluid, lymphoid tissue, synovial fluid, placenta, and even urine, but the probability of detecting them in certain organs and biological fluids is determined by the period of illness and the nature of organ disorders.

Epidemiology

Source of the infectious agent. Reservoirs and sources of borrelia in natural foci, and at the same time tick feeders, are about 200 species of wild animals, which are lifelong carriers of borrelia.

The main sources of the infectious agent are rodents - red and gray voles, house voles, forest mice, etc. in Ukraine - voles, house and field mice, common and lesser pika, in the United States - white-footed hamsters, deer hamsters, Mexican forest hamsters and other rodents. In anthropurgic centers with developed agriculture, spotted and white-tailed deer, cattle, dogs, and cats may be additional reservoirs, but their epidemiological significance is much less. Bird migration ensures the spread of ticks infected with Borrelia to new territories. The pathogen circulates through the animal-tick-animal route. Since the pathogens persist in ticks for life and are capable of transphasic and transovarial transmission, ticks are also reservoirs of Borrelia. Humans are infected by a transmissible mechanism when

they are in natural habitats, most often in deciduous forests with undergrowth, bushes and grass cover in the temperate climate zone.

Borrelia infection is possible through the dietary route - when consuming raw goat's milk and other dairy products without heat treatment; by contact - when rubbing the hemolymph of a crushed tick. The pathogen is not transmitted from a sick person to a healthy one, except for transplacental (vertical) transmission of borrelia from a sick pregnant woman to the fetus. The incubation period lasts from 3 to 32 days, can be extended up to 53 days, and averages 12 days.

Pathogenesis

During a tick bite, borrelia enter the skin with its saliva, where the primary reaction occurs, in which polymorphonuclear neutrophils and monocytes are initially most active. The spread of the infection in the skin is accompanied by an increase in the zone of hyperemia that forms at the initial stage, the appearance of rashes around the primary spot. The zone of hyperemia that expands around the primary lesion is due to the fact that borreliae move centrifugally from the focus, so they can be isolated more often from the edges of the affected area. The pathogens also penetrate the regional lymph nodes, which is accompanied by their enlargement.

As a result of further hematogenous dissemination, borrelia enter all organs and tissues. The appearance of secondary (migratory) rashes on different parts of the skin is primarily associated with the repeated release of Borrelia from various foci. The immune system is involved in the early stages: with the increase in the activity of polyclonal B lymphocytes, the level of IgM first increases (in weeks 1-3), peaking in weeks 3-8 of the disease. Later, IgG appears (weeks 3 to 8). At the stage of disseminated CL, damage to various organs and systems is mixed, with borrelia and immunopathologic reactions. At the same time, lymphocytic perivascular infiltration and vascular occlusion are formed. Borrelia can be detected in these infiltrates. Such lesions occur in the skin, muscles, heart, synovial membranes, and peripheral nervous system. Borrelia also penetrate the central nervous system, where an infiltrative inflammatory process with the active participation of T lymphocytes is formed. CNS lesions are accompanied by the production of IgM and IgG antibodies. In the late chronic stage of the disease, the leading mechanisms are immunopathological. The damaging effect is exerted by CEC, autoantibodies, interleukins. The most active production of interleukins, collagenase, prostaglandins is carried out in the presence of borrelia and their antigens, which gives grounds to speak of CL as a chronic, possibly lifelong, infection. However, it is believed that borrelia play the role of a trigger, and the lesions that occur in the chronic stage are realized through the immune system. It is very noteworthy that in the chronic stage, the level of IgM and IgG can be significantly higher in the areas of localization of the most severe organ damage (in arthritis - in the synovial fluid, in encephalitis - in the cerebrospinal fluid) than in the blood.

Clinical picture

Erythema migrans is a characteristic sign of infection, which is most often detected in 70% of patients. Migratory erythema is the only external manifestation of Lyme borreliosis that can be detected during clinical examination in patients with acute arthralgia. But in most patients with arthritis, erythema migrans never develops or goes unnoticed. Almost half of the patients have signs of systemic inflammation (malaise, fatigue, headache, arthralgia, myalgia, subfebrile body temperature, and lymphadenopathy). Usually, episodes of Lyme arthritis are short and affect one large joint, most often (90%) the knee joint is involved in the pathological process. Less commonly, the elbow, ankle, hip, and wrist joints are affected. Relapses of arthritis are noted over a period of several months to years in <50% of patients, even in those receiving adequate therapy. Arthritis usually begins suddenly with moderate pain (VAS 20 to 6 0 mm) and inflammatory syndromes.

A typical joint syndrome has the following signs

- involvement of large joints - hip, knee, shoulder;
- absence of axial skeletal lesions;
- mono-, oligo lesions;
- moderate synovitis;
- concomitant tendonitis, tendosynovitis, bursitis, fibrositis;
- muscle involvement - myositis, myalgia;
- neurological manifestations.

Sometimes in clinical practice, there are atypical cases of Lyme arthritis with hip involvement of the type of septic coxitis, especially in children, characterized by a significant increase in erythrocyte sedimentation rate (ESR) and the absence of fever.

Diagnosis

The history of the disease and clinical signs and symptoms, especially the appearance of erythema migrans, are important in the diagnosis. The main methods of diagnosing Lyme arthritis are laboratory verification of borreliosis infection, which helps to make a decision in a more complex case of the disease. IgM antibodies to Borrelia begin to rise 2 to 4 weeks after infection. High levels of IgM and IgG can persist in some patients for many years, even after treatment. A highly sensitive ELISA test should be used as a screening test; in case of a positive or doubtful result, confirmation by a specific immunoblotting test is required. The result is considered positive if 2 out of 3 antigenic bands are detected by IgM - arthritis is considered acute and 5 out of 10 bands are detected by IgG - arthritis is considered chronic. Borrelia DNA can be detected by polymerase chain reaction (PCR) in skin biopsy samples, synovial and cerebrospinal fluids, blood, and urine. The detection of Borrelia by PCR is highly specific, but the sensitivity in synovial fluid is no more than 85%.

Biopsy of the synovial membrane reveals fibrin deposits, villous hypertrophy, vascular proliferation, and marked plasma cell and lymphocyte infiltration. In some cases, silver staining reveals spirochetes. The number of leukocytes in the synovial fluid is 5 - 102-11 - 10*/ml, the largest proportion of them are segmented neutrophils. There is an increased protein content, normal or decreased glucose levels, and negative tests for

rheumatoid factor (RF) and antinuclear factor. The isolation of a spirochete culture allows for a reliable diagnosis, but this is rarely possible. Routine general clinical examinations reveal a slightly elevated ESR and C-reactive protein (CRP) levels.

Ultrasonography (US) of the joints reveals thickened synovium, increased fluid, combined periarticular tissue changes, tendonitis, enthesitis, muscle thickening, and swelling. Ultrasonography can be useful in detecting subclinical synovitis and determining the outcome of the disease, but this method is nonspecific and is not used in the differential diagnosis.

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ОГЛЯД: ПРОТИВІРУСНІ ПРЕПАРАТИ, ЕФЕКТИВНІСТЬ ЛІКУВАННЯ ВІРУСНИХ ЗАХВОРЮВАНЬ

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LOOK: ANTI-VIRAL DRUGS, EFFECTIVENESS OF L INVESTIGATION OF VIRAL ILLNESSES

Актуальність:

Вірусні епідемії та пандемії стимулювали розробку відомих і відкриття нових противірусних засобів. Близько сотні моно- та комбінованих противірусних препаратів вже схвалено, а тисячі знаходяться в розробці. В даній роботі було коротко розглянуто групи противірусних агентів та їх особливості. Ефективність противірусних препаратів залежить від багатьох факторів, включаючи тип вірусу, стадію захворювання, механізм дії препарату, а також індивідуальні особливості пацієнта. Противірусні препарати застосовуються для лікування різних вірусних інфекцій, таких як грип, ВІЛ, герпес, гепатит та інші.

Вступ: *У сучасній медицині противірусні препарати відіграють ключову роль у боротьбі з вірусними інфекціями, що становлять серйозну загрозу для здоров'я населення. Від грипу до ВІЛ/СНІДу, ці лікарські засоби забезпечують ефективні рішення для лікування та профілактики захворювань, що викликані різними вірусами. Розвиток нових противірусних терапій базується на глибоких дослідженнях вірусної патогенезу та механізмів дії препаратів, що дозволяє медичній спільноті адаптуватися до нових викликів у сфері охорони здоров'я. У цій статті ми розглянемо різні класи противірусних препаратів, їх механізми дії та перспективи розвитку у світлі нових наукових досягнень.*

Relevance: Viral epidemics and pandemics stimulated the development of existing and the creation of new antiviral agents zaobiv. Nearly hundreds of mono-combined antiviral drugs have already been approved, and thousands are in development. In this work, a brief look was taken at groups of anti-Russian agents and their characteristics. The effectiveness of antiviral drugs depends on a variety of factors, including the type of virus, the stage of infection, the mechanism of action of the drug, as well as the individual characteristics of the patient. Antiviral drugs are used to treat various viral infections, such as influenza, HIV, herpes, hepatitis and others.

Intro: In modern medicine, antiviral drugs play a key role in the fight against viral infections that pose a serious threat to the health of the population. From influenza to HIV/AIDS, medical professionals will provide effective solutions for the treatment and prevention of illness caused by various viruses. The development of new antiviral therapies is based on in-depth studies of viral pathogenesis and the mechanisms of drug action, which allows the medical profession to adapt to new trends in the health care field. This article will look at the different classes of antiviral drugs, their mechanisms of action and the prospects for the development of new scientific advances.

Ключові слова: *вірус, противірусний засіб, комбінація противірусних препаратів.*
Key words: virus, antiviral infection, combination of antiviral drugs.

Метою роботи є аналіз літератури, щодо вивчення особливостей та ефективності основних груп противірусних препаратів.

Матеріали і методи: До аналізу включалися тільки рецензовані статті, опубліковані англійською мовою, в яких досліджувалися групи противірусних препаратів, механізми їхньої дії, способи резистентності бактерій до антибіотиків.

Основна частина: Противірусні препарати є важливим інструментом у боротьбі з вірусними інфекціями. Вони діють на різні етапи вірусного циклу, заважаючи вірусам розмножуватися та поширюватися в організмі.

Основні групи противірусних препаратів:

1. **Інгібітори вірусної реплікації** : ці препарати блокують здатність вірусу до розмноження. Наприклад, інгібітори зворотної транскриптази (як для ВІЛ) або інгібітори РНК-полімерази (як для вірусів гепатиту).
2. **Інгібітори проникнення або виходу вірусу** : ці препарати перешкоджають проникненню вірусу в клітини або виходять з них. Наприклад, амантадин і осельтамівір використовують для лікування грипу.
3. **Імуностимулятори та імуномодулятори** : ці препарати не мають прямого противірусного

ефекту, але стимулюють імунну систему для боротьби з інфекцією. Наприклад, інтерферони застосовуються для лікування вірусного гепатиту С і В.

Переваги противірусних препаратів:

- **Цілеспрямованість** : Багато противірусних препаратів діють вибірково на вірусні клітини, не пошкоджуючи здорові клітини.
- **Зниження тривалості захворювання** : Використання противірусних засобів на ранніх стадіях може скоротити тривалість захворювання і зменшити тяжкість симптомів.
- **Зниження ризику ускладнень** : препарати зменшують ймовірність розвитку серйозних ускладнень, таких як пневмонія (у випадку грипу) або ураження хвороби (у випадку гепатиту).

Обмеження і проблеми:

1. **Резистентність вірусів** : Віруси здатні швидко мутувати, що може призвести до розвитку резистентності до противірусних засобів. Це особливо проблематично при лікуванні ВІЛ, грипу та герпесу.
2. **Час початку лікування** : Противірусні препарати найефективніші, коли застосовуються на ранніх етапах інфекції. Якщо лікування розпочато занадто пізно, його ефективність може суттєво знизитися.
3. **Побічні ефекти** : Деякі противірусні препарати можуть викликати серйозні побічні реакції, такі як пошкодження клітин, порушення обміну речовин, астено вегетативні прояви.
4. **Вартість лікування** : Багато вірусів протизасобів, особливо новітніх, можуть бути дорогими, що обмежує їх доступність для широких верств населення.

Приклади ефективних противірусних препаратів:

- Осельтамівір (Таміфлю) для лікування і профілактики грипу.
- Ацикловір і його аналоги для лікування герпесу.
- Антиретровірусна терапія (АРТ) для контролю ВІЛ.
- Софосбувір для лікування гепатиту С.

Озельтамівір, широко відомий як Таміфлю, є інгібітором нейрамінідази, який використовується для лікування та профілактики грипу. Останні дослідження продовжують вивчати його ефективність, особливо в порівнянні з іншими противірусними засобами.

1. **Ефективність** : у мета-аналізі 2023 року було виявлено, що озельтамівір потенційно скорочує тривалість госпіталізації пацієнтів із важким сезонним грипом на 1,63 дня порівняно з плацебо або стандартним лікуванням. Однак вплив на смертність залишається невизначеним через низьку достовірність доказів. Здатність озельтамівіру полегшувати симптоми в неускладнених випадках (таких як лихоманка, біль у м'язах або втома) підтверджується попередніми дослідженнями, але, знову ж таки, достовірність його впливу на зменшення тривалості симптомів є середньою або низькою. (https://secure.medicalletter.org/TML-article-1689a)
2. **Безпека** : побічні ефекти озельтамівіру добре задокументовані та включають нудоту, блювання та головні болі. У рідкісних випадках повідомлялося про нервово-психічні симптоми, такі як марення, хоча вони також можуть бути ускладненнями самого грипу. (https://secure.medicalletter.org/TML-article-1689a)
3. **Порівняння** : у прямих порівняннях дослідження показують, що озельтамівір може бути настільки ж або трохи менш ефективним, ніж нові противірусні препарати, такі як балоксавір марбоксил, у неускладнених випадках, але він залишається основним засобом через його більш широке застосування у важких випадках. (https://www.medrxiv.org/content/10.1101/2024.05.28.24307938v1)

Ці результати підкреслюють, що, хоча озельтамівір є корисним у багатьох випадках, особливо при застосуванні на ранніх стадіях інфекції, залишається невизначеність щодо його впливу на більш важкі результати.

Ацикловір (ацикловір) є одним із найбільш широко використовуваних противірусних препаратів для лікування герпесвірусних інфекцій, таких як симплексний герпес (HSV) та вітряна віспа/оперізуючий лишай (Varicella zoster, VZV). Ось деякі важливі аспекти сучасних досліджень цього препарату:

1.Ефективність при лікуванні герпесу :

- Ацикловір ефективно знижує активність вірусу герпесу та ускладнення швидкого загоєння шкірних висипів. У нещодавньому дослідженні підтверджено, що ацикловір значно знижує симптоми і тривалість захворювання у випадку з HSV-інфекцією при ранньому початку лікування.
- Однак було виявлено, що при тривалому застосуванні препарату можуть розвинутися резистентні штами HSV, особливо у використанні з ослабленим імунітетом. Це спонукало до пошуку альтернативних підходів, таких як використання нових препаратів або комбінації з ацикловіром. (https://ashpublications.org/blood/article/130/Supplement%201/3231/114851/Effectiveness-of-Acyclovir-Prophylaxis-Against)

2.Застосування в профілактиці після трансплантації :

- Одним із напрямків дослідження є профілактичне використання ацикловіру після трансплантації гемопоетичних стовбурових клітин (HSCT), коли ризик реактивації VZV є особливо високим. Згідно з метааналізом, ацикловір значно знижує ймовірність реактивації ВЗВ під час профілактичного застосування, але після припинення профілактики можливий «ефект відкату» — різке підвищення ризику інфікування. (https://ashpublications.org/blood/article/130/Supplement%201/3231/114851/Effectiveness-of-Acyclovir-Prophylaxis-Against)

3.Протидія резистентним штамам :

- З огляду на можливу резистентність до ацикловіру, особливо серед імунохроматографічних захворювань, досліджуються інші препарати, як-от **прителівір** , які можуть бути ефектив-

ними у випадках стійкості ацикловіру штамів герпесу. (https://www.yalemedicine.org/clinical-trials/pritelivir-versus-foscarnet-for-the-treatment-of-acyclovir-resistant-mucocutaneous-hsv-prioh-1)

Ці дані вказують на те, що ацикловір залишається ефективним засобом при лікуванні вірусних інфекцій, проте його тривале використання необхідно проводити ретельний моніторинг, особливо у заміні з новою ослабленою імунною системою.

Останні дослідження **антиретровірусної терапії (АРТ)** продемонстрували багатообіцяючі досягнення, особливо з використанням ін'єкційних препаратів тривалої дії. Традиційна АРТ, яка включає щоденний пероральний прийом ліків, була дуже ефективною для придушення ВІЛ приблизно у 70% пацієнтів. Однак для деяких може бути складно дотримуватися прихильності через такі проблеми, як психічне здоров'я, вживання психоактивних речовин і соціально-економічні бар'єри.

Одним із останніх проривів є використання ін'єкційних комбінацій тривалої дії, таких як каботегравір і рилпівірін. Клінічні випробування у 2024 році продемонстрували, що це лікування перевершувало щоденну пероральну АРТ у підтримці пригнічення вірусу у пацієнтів, які раніше мали проблеми з щоденним дотриманням режиму лікування. В одному дослідженні лише 7% учасників АРТ тривалої дії зазнали непригнічення ВІЛ у порівнянні з 25% у тих, хто щодня приймав таблетки. Крім того, він добре переносився, хоча деякі учасники повідомили про легкі реакції у місці ін'єкції. (https://www.nih.gov/news-events/news-releases/long-acting-hiv-treatment-benefits-adults-barriers-daily-pill-taking-adolescents-suppressed-hiv)

Ці висновки є важливими, оскільки вони показують, що АРТ тривалої дії може кардинально змінити ситуацію для людей, які стикаються з бар'єрами щодо щоденного прийому ліків, потенційно розширивши можливості лікування та зменшивши передачу ВІЛ у важкодоступних групах населення. Ця нова терапія пропонує більше зручностей і кращі результати для людей з проблемами прихильності, таким чином надаючи більше свободи і покращуючи результати для здоров'я для багатьох людей, які живуть з ВІЛ.

Ці терапії тривалої дії зараз розглядаються для ширшого використання за межами популяцій, для яких вони були спочатку схвалені, і дослідники сподіваються, що це може призвести до меншої кількості нових інфекцій і покращити рівень придушення вірусу в усьому світі.

Софосбувір, ключовий препарат у лікуванні гепатиту С, продовжує демонструвати високу ефективність в останніх дослідженнях. В одному значному дослідженні 2024 року розглядалося його використання в комбінованій терапії, як-от Софосбувір/Велпатасвір і Софосбувір/Велпатасвір/Воксилапревір, для пацієнтів із хронічним гепатитом С (ВГС). Комбіноване лікування досягло стійкої вірусологічної відповіді (SVR12) у 94-97% пацієнтів, що вказує на те, що майже всі пацієнти мали невизначуваний рівень вірусу через 12 тижнів після лікування.

Дослідження було зосереджено на особах, які раніше не отримували інших противірусних препаратів. Рівень успіху був дещо вищим у групі, яка отримувала софосбувір/велпатасвір/воксілапревір (97%) порівняно з групою, яка отримувала софосбувір/велпатасвір плюс рибавірин (94%). Обидва режими загалом добре переносилися, хоча спостерігалися легкі та помірні побічні ефекти, включаючи анемію та зміни печінкових ферментів. (https://eglj.springeropen.com/articles/10.1186/s43066-024-00321-y)

Ці висновки підтверджують роль Софосбувіру як високоефективного препарату для лікування різних штамів ВГС, навіть у складніших випадках, таких як попередня невдача лікування.

Висновки: На сьогоднішній день схвалено близько сотні моно- та комбінованих противірусних терапій, а тисячі перебувають у до- або клінічній розробці. Противірусні препарати залишаються основою лікування багатьох вірусних інфекцій, і їхня ефективність може варіюватися у залежності від типу вірусу, режиму лікування і стійкості до ліків. Застосування противірусних препаратів дозволяє розривати ланки патогенезу хвороб, тим самим сприяє більш ефективному лікуванню, та призводить до повного одужання, чи стійкої ремісії.

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LENNOX-GASTO SYNDROME, OR CHILDREN'S EPILEPTIC ENCEPHALOPATHY (LITERATURE REVIEW)

Abstract

Lennox-Gastaut syndrome (LGS) is considered as a pediatric epileptic encephalopathy and is defined by a triad of multiple drug-resistant seizure types, a specific EEG pattern showing bursts of slow spike-wave complexes or generalized paroxysmal rapid activity, and intellectual disability. According to estimates, the prevalence of LGS is 1 to 2% of all patients with epilepsy. The etiology of the syndrome is often divided into two groups: identified (genetic-structural-metabolic) in 65-75% of patients and LGS of unknown cause in others. Lennox-Gastaut syndrome can be considered as secondary network epilepsy. Seizures in the syndrome are usually drug-resistant, and complete seizure control with resolution of intellectual and psychosocial dysfunction is often not possible. The primary goal should be to reduce the frequency of the most incapacitating seizures (eg, drop attacks and tonic-clonic seizures). Many experts consider valproate, lamotrigine, and topiramate to be first-line drugs. Other effective antiepileptic drugs include levetiracetam, clobazam, rufinamide, and zonisamide. This syndrome is often associated with long-term negative consequences for intellectual development, social functioning, and independent living. [1, p.1-4]

Key words: *EEG, epilepsy, encephalopathy, convulsions, tonic seizures.*

Lennox-Gastaut syndrome (LGS) is a severe childhood-onset epileptic encephalopathy associated with high morbidity and profound impact on patients' quality of life.

LGS usually begins to manifest itself in children aged 1 to 8 years, most often at the age of 3-5 years. One of the characteristic features of the syndrome is the variety of types of attacks. These may include: Tonic seizures: These are seizures that occur during sleep and are characterized by muscle contractions that may last for seconds or minutes. Atonic seizures: A sudden loss of muscle tone that may cause the child to fall to the floor. Atypical absences: short-term loss of consciousness, during which the child does not respond to external stimuli. Myoclonic seizures: Rapid, uncontrolled muscle contractions that may affect one or more parts of the body. [1,2]

These attacks are often accompanied by cognitive impairment, reduced intellectual functions and slow development of the child. Patients with LGS are also at risk for behavioral disorders such as aggression, irritability, and hyperactivity. A universally agreed upon definition of LGS does not yet exist, and it has a wide range of clinical manifestations that continue to change and evolve over time. However, it has traditionally been defined as a "triad" of features that includes epilepsy with multiple pharmacoresistant seizure semiologies, a generalized wave-like discharge pattern on the EEG, and cognitive and behavioral impairments. [3, p. 3-5]

The reasons for the development of LHS can be diverse. In many cases, this is the result of brain damage in early childhood, which can be caused by the following factors:

1. Severe infections such as encephalitis or meningitis.
2. Head injuries during childbirth or at an early age.
3. Genetic mutations or metabolic diseases.
4. Disorders of brain development (cortical dysplasia). [4, p. 2-3]

However, in about 25-30% of cases, the exact cause of SLH cannot be established. One of the key aspects of the pathogenesis of this syndrome is the excessive excitability of brain neurons, which leads to generalized epileptic seizures. Also, less commonly, LGS may be associated with the rare genetic disorder tuberous sclerosis, inherited metabolic disorders, and other genetic disorders with a possible, though poorly defined, association with Down syndrome and Miller-Dieker syndrome. Indeed, LGS can represent the final stage of various epilepsies. [5, p. 8-11]

Diagnosis of LGS requires a comprehensive approach. Electroencephalography (EEG) plays an important role in determining the syndrome. Lennox-Gastaut syndrome is characterized by specific changes on the EEG, such as: slow waves: the presence of slow

waves in the range of 1.5-2.5 Hz, which appear both in the waking state and during sleep. Spike waves: high spike wave activity, indicating epileptic brain activity.

Magnetic resonance imaging (MRI) and computed tomography (CT) of the brain are also used for diagnosis to rule out structural changes in the brain. In addition, it is important to assess the child's cognitive development and behavioral characteristics, as developmental delay often accompanies SLH. [6, p. 9-10]

Treatment of SLH is challenging because the syndrome is usually resistant to standard antiepileptic drugs. The main methods of treatment include:

Antiepileptic drugs: sodium valproate, lamotrigine, topiramate, clonazepam and rufinamide are most often used. However, not all patients achieve complete seizure control with medication. Ketogenic diet: This is a high-fat, low-carb diet that sometimes helps reduce the number of attacks. It is believed that it changes the metabolism of the brain and reduces its excitability. Vagus stimulation: This method involves implanting a device that stimulates the vagus nerve and thus reduces the frequency of seizures.

Surgery: For severe cases, surgery (callosotomy) may be recommended, which involves cutting the corpus callosum to prevent the spread of epileptic activity between the brain's hemispheres. [7, p. 5-8]

The prognosis for children with Lennox-Gastaut syndrome is usually poor. Although some patients may achieve partial seizure control, complete seizure control is rarely possible. It is important to note that most children with LGS have moderate to severe mental retardation and behavioral problems that make it difficult for them to socialize and learn. Some children may improve as they get older, but seizures and cognitive impairment usually last a lifetime. This means that such patients need constant medical support and in many cases specialized care. [8, p. 4-7]

Conclusion: Lennox-Gastaut syndrome is a severe and complex form of epilepsy that significantly affects the quality of life of patients and their families. Despite advances in medicine, controlling seizures and improving cognitive development remains a challenge. The integration of drug treatment, diet, surgical methods and psychological support is the key to improving the condition of patients with this syndrome.

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HIV INFECTION: PATHOGENESIS, GLOBAL SITUATION, DIAGNOSIS AND TREATMENT

Abstract
Viral entry into host cells is a critical step in the viral life cycle. Entry of HIV-1 is mediated by the single surface envelope glycoprotein Env and is initiated by the interaction between Env and the host CD4 receptor. This interaction, referred to as the attachment step, has long been considered an attractive target for the discovery and development of inhibitors. The human immunodeficiency virus (HIV) is known to cause impairment of the human immune system and has been the leading cause of death until recently. It has been proven that the main target of HIV is T-lymphocytes. The virus inactivates T-lymphocytes by affecting a wide range of cellular and molecular targets, which leads to suppression of the immune system. We have analyzed various sources of information on HIV infection and summarized the main material in our article.

Keywords: *human immunodeficiency virus, AIDS, microRNA, exosomes, mechanisms of pathogenesis, diagnostic biomarkers.*

Introduction

Human immunodeficiency virus type 1 (HIV-1), a retrovirus that integrates its genetic information into host cells after infection, can lead to acquired immunodeficiency syndrome (AIDS) if left untreated.

The human immunodeficiency virus is currently causing a pandemic, resulting in an increase in the incidence of HIV infection, which is an important medical and social problem. Human immunodeficiency virus 1 (HIV-1) is a member of the retrovirus lentivirus family that causes human infection and dramatically reduces the number of CD4 T lymphocytes as the infection progresses. Consequently, affected subjects become highly susceptible to acquired immunodeficiency syndrome (AIDS). According to a report by the World Health Organization, since the discovery of HIV/AIDS, the number of people living with HIV/AIDS has reached 70 million, of whom 35 million have died. At the end of 2017, there were about 36.9 million people living with HIV worldwide.

Global use of antiretroviral therapy (ART), increasing prevention, and surveillance are being employed to contain the epidemic, but an effective vaccine is needed to end it.

Over the years, significant efforts have been made to study the pathogenesis of HIV infection; however, several aspects need to be clarified, including how the innate immune system acts in different anatomical compartments. Despite the molecular mechanisms were not completely understood, the importance of innate response in the progression of HIV infection was demonstrated by many studies on HIV-infected

Pathogenesis

HIV-1 entry into host cells

The HIV envelope protein (Env) is the only glycoprotein displayed on the surface of the HIV virion. Env forms a trimer, where each protomer is composed of a heterodimer of gp120 and gp41 subunits that non-covalently associate together. The gp120 subunit is responsible for recognizing and binding to the receptor CD4 on CD4+ T cells and macrophages. The binding of CD4 leads to conformational changes and exposure of the coreceptor binding site, which can then engage the coreceptors, CCR5 or CXCR4. The binding of CD4 and a coreceptor result in the shedding of gp120, and subsequent conformational changes in gp41 lead to the fusion of viral and host cell membrane, allowing the entry of the HIV capsid and genome into host cells.

The entry process is a critical aspect of the HIV-1 life cycle and a target of many therapeutic strategies, including but not limited to small molecule inhibitors and antibody modalities.

HIV-1 was shown to preferentially integrate into the gene bodies of actively transcribed regions of the host chromatin, in studies of cell lines, primary CD4+T cells, as well as in patient-derived CD4+T cells. Once integrated into the host chromosome, virus transcriptional regulation is dependent on the complex interplay of a plethora of host and viral factors, which will be the topic of this review. Cells that express high levels of viral RNA, proteins or virions are selected against, through cytopathic effects or immune-mediated cytotoxic killing. Latently infected cells, on the other hand, have little to no expression of viral RNA or proteins, and can survive by flying under the immune system's radar.

Unlike some other viruses that undergo latent stages, such as herpesviruses, HIV-1 does not have a

defined latency program. HIV-1 entry into latency is a complex and incompletely understood pathway. Factors implicated in driving the virus into latency include the depletion of the viral transactivator of transcription protein (Tat), a reduction in the availability of cellular transcription factors (TFs), an accumulation of epigenetic silencing marks surrounding the HIV-1 promoter, and the activity of additional chromatin regulators.HIV-1 enhances its own transcription and modulates the expression of cellular genes, and this is mainly due to the activity of the viral protein Tat. Tat serves as a molecular switch between latency and active transcription. This is primarily achieved through recruitment of the positive elongation factor (P-TEFb), relieving promoter-proximal stalling through phosphorylation of RNAPII, negative elongation factor (NELF) and DRB sensitivity inducing factor (DSIF).

Since inflammation and dysfunction of immune response are hallmarks of chronic untreated HIV disease, this could be a cause of serious non-AIDS events (SNAEs), and various clinical sequelae that afflict AIDS patients. There are some reports have documented the effect of early anti-retroviral therapy (ART) on the development of inflammatory diseases in AIDS. The impact of early ART on markers of inflammation is less clear. Early ART has been related to a significant decrease in the frequency of latently infected cells, which is more pronounced if ART is initiated within days to weeks (rather than months) following infection. Although early ART can potentially decrease serious non-AIDS events (such as inflammatory end-stage organ disease) and related mortality, longer prospective studies with clinical endpoints are still required to determine the benefits of early ART.

Markers of HIV infection

The main markers of detection are serological. For their detection, ELISAs are used to simultaneously detect antibodies to hiv 1/2 and hiv-1 p24 antigen (combined ELISAs) or to detect antibodies to hiv 1/2. Combined ELISAs are used to detect acute HIV infection, primarily during the examination of pregnant women, persons who have expressed a desire to become donors, and donors of blood, organs, tissues, cells. Combined DSTs are also used to establish HIV status in people with clinical signs of end-stage HIV infection;

The impact of different ART regimens on HIV persistence has been explored primarily at the level of RV. Historically, most studies compared RV between triple regimens consisting of two NRTIs plus an NNRTI or PI. The majority of these studies reported reduced viremia levels in individuals treated with NNRTI-based ART regimens

While no difference was observed between NNRTI-based and INSTI-based regimens ($p = 0.18$), PI-based treatment was associated with an increased frequency of detectable RV below the limit of quantification as compared to both NNRTI-based ($p = 0.013$) and INSTI-based ($p < 0.0001$) regimens.

As all current antiretroviral drug classes, including NNRTIs and PIs, are not expected to inhibit HIV RNA transcription or virus production, no differences in HIV transcription or virus production by regimen are expected if the drugs are equally potent in suppressing HIV replication. Therefore, the differences in cell-associated HIV RNA levels or RV by ART regimen would suggest that NNRTIs are more potent in suppressing HIV residual replication than PIs, resulting in smaller viral reservoir size. However, recently it has been shown that some NNRTIs, such as rilpivirine, efavirenz, and etravirine, can promote selective apoptosis of infected cells by inducing HIV protease-mediated cytotoxicity

If these NNRTIs are present in cells that are producing viral proteins, they may bind to the reverse transcriptase portion of a newly translated Gag-Pol polyprotein and promote its homodimerization, resulting in premature protease activation. This leads to a decrease in virus production and non-specific cleavage of multiple host proteins, including proteins that induce apoptosis . Accordingly, during in vitro HIV latency reversal, the addition of NNRTIs was associated with a large reduction in virus production . Although this mechanism will be nonfunctional in most reservoir cells as only a small proportion of the latter is producing HIV proteins, cells that become reactivated to do so in response to immune stimuli might be selectively killed by this NNRTI action, providing an alternative explanation for the observed lower levels of HIV transcription and virus production in individuals treated with NNRTI-based regimens.

Other groups were interested in comparing the ability of various NNRTIs to suppress HIV viremia. Some studies reported that nevirapine has a greater capacity to suppress RV when compared to the widely used NNRTI efavirenz. This observation could be explained by better penetration of nevirapine in some anatomical sanctuaries. Interestingly, nevirapine has shown very little in vitro HIV protease-mediated cytotoxicity, while efavirenz was very active , arguing that induction of apoptosis of infected cells may not be the major mechanism behind the more pronounced virological suppression by NNRTIs.Although many studies have been undertaken to better understand the effect of different ART regimens on the persistence of HIV reservoirs on therapy, a number of unanswered questions remain. First, the impact of the different regimens on immune dysfunction, such as immune activation, systemic inflammation, microbial translocation, mitochondrial dysfunction, and oxidative stress, is unclear. It has been suggested that heightened immune activation and inflammation may be both a cause and a consequence of HIV reservoir persistence and residual viral replication, in particular, in tissue. Therefore, ART regimens may have a direct and indirect effect on the host immune function. However, data on the influence of different ART regimens on immune activation and inflammation have so far been mixed . In a randomized trial, Hileman et al. observed more pronounced changes in systemic and vascular inflammation and monocyte activation markers after initiating INSTI-based compared with NNRTI-based ART

However, other randomized studies did not find differences in markers of inflammation, immune activation, T-cell senescence, and exhaustion between

INSTI-based and PI-based ART regimens. Besides, the switch from a PI-based to an INSTI-based regimen did not lead to a change in immune activation or inflammation markers

ART

Due to the success of ART, HIV has transitioned into a more long-term chronic disease in most countries, where the previous serious effects of AIDS are not now a major concern. Instead of addressing acute immune suppression that threatens patients' lives, clinical professionals now manage persistent disease, which may continue for several years. HIV care now requires clinicians and health care organizations to change from focusing on acute care, to long-term management. Clinical professionals not only require to be experts in antiretroviral control, but also require additional skills for the prevention and management of cardio-vascular disease, and other co-morbidities related to aging. Biomedical studies should also provide new approaches in this regard. One of the high priorities for handling HIV in the long term, is to understand the reasons for the persistent inflammation arising during ART, and how it results in morbidity and additional health problems. Moreover, there should affordable methods for preventing non-transmissible diseases and tuberculosis (TB) in populations who live in regions lacking robust care health systems.Seven classes of antiretroviral drugs, including protease inhibitors, nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs), non-nucleoside reverse transcriptase inhibitors (NNRTIs), integrase inhibitors, post-attachment inhibitors, CCR5 antagonists, and fusion inhibitors have been currently approved for the treatment of HIV-1 infection. Due to the high genetic diversity of HIV-1, monotherapy of any of the approved HIV-1 treatments usually leads to a selection of resistance mutations. Combination antiretroviral therapy (cART) that utilizes drugs from more than one class of HIV-1 drugs has proven to be very effective in controlling viral loads in HIV-1+ patients, rendering HIV-1 infection a lifelong chronic disease that is manageable for patients who have access to cART (~26 million patients based on the UNAIDS 2020 Fact Sheet). However, after decade-long cART treatment, patients can develop resistance to multiple classes of currently approved drugs and face viral rebound and disease progression.

Prevention

While chemoprophylaxis is effective on an individual basis, a preventive vaccine that leads to sustained immunity will play a crucial role in controlling and eventually eliminating HIV worldwide. A successful preventive vaccine, often described as the final step to ending the pandemic, is not on the horizon.

There is another major challenge to HIV vaccine prevention research that is often overlooked. Antibodies to gp120 have a short duration of action, as shown in primate and human vaccine studies (reviewed in Lewis et al., 2014), and attempts to increase resistance with adjuvants, viral proteins, or vectors have been unsuccessful and have instead sometimes resulted in increased activation of CD4 T cells. This activation can facilitate HIV infection, as these cells are the main targets of HIV. In the context of a vaccine, a proper balance of T cell responses is required (Fouts et al., 2015; Lewis et al., 2014). Some T cell activation is required for an effective adaptive immune response, but once a certain level is reached, the vaccine's effectiveness may be lost. Therefore, it is possible that a vaccine may be effective, but its effect may be obscured by increased susceptibility to HIV infection caused by the vaccine itself. Discovering why antibodies to glycoproteins such as HIV do not persist and identifying ways to address this problem without over-activating CD4 T cells should be an important major research priority.

Conclusion

HIV is primarily a sexually transmitted infection, but the overall risk per sexual exposure is low. One of the reasons for this discrepancy lies in the strong protection given by the mucosal innate immune system during the early steps of infection that need to be fully characterized. Understanding these protective mechanisms is crucial not only to better characterize HIV infection, but also because it could help the development of an effective prophylactic or therapeutic therapy.

Vaccination against oral transmission is a new field and requires more in-depth studies. Oral vaccines are attractive because they can induce high intestinal immunity, are relatively non-invasive, and can be administered on a large scale.

Understanding the pathogenesis of HIV from all sides allows us to see new aspects in the study of the infection and will help to reduce the number of HIV cases as soon as possible.

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LYME DISEASE: DISEASE MANIFESTATIONS, DIAGNOSIS

Abstract

Lyme disease (Lyme borreliosis) is a tick-borne, zoonosis of adults and children caused by genospecies of the Borrelia burgdorferi sensu lato complex. The ailment, widespread throughout the Northern Hemisphere, continues to increase globally due to multiple environmental factors, coupled with increased incursion of humans into habitats that harbor the spirochete. B. burgdorferi sensu lato is transmitted by ticks from the Ixodes ricinus complex. In North America, B. burgdorferi causes nearly all infections; in Europe, B. afzelii and B. garinii are most associated with human disease. The spirochete's unusual fragmented genome encodes a plethora of differentially expressed outer surface lipoproteins that play a seminal role in the bacterium's ability to sustain itself within its enzootic cycle and cause disease when transmitted to its incidental human host. Tissue damage and symptomatology (i.e., clinical manifestations) result from the inflammatory response elicited by the bacterium and its constituents. The deposition of spirochetes into human dermal tissue generates a local inflammatory response that manifests as erythema migrans (EM), the hallmark skin lesion. If treated appropriately and early, the prognosis is excellent. However, in untreated patients, the disease may present with a wide range of clinical manifestations, most commonly involving the central nervous system, joints, or heart. A small percentage (~10%) of patients may go on to develop a poorly defined fibromyalgia-like illness, post-treatment Lyme disease (PTLD) unresponsive to prolonged antimicrobial therapy. Below we integrate current knowledge regarding the ecologic, epidemiologic, microbiologic, and immunologic facets of Lyme disease into a conceptual framework that sheds light on the disorder that healthcare providers encounter.We have analyzed various sources of information on Lyme disease and summarized the main material in our article.

Key words: *Lyme disease, B. burgdorferi, PCR, biosensor, point-of-care, diagnostics, infectious disease.*

Introduction

Lyme disease is the prototype of an emerging infectious disease. The isolation of its etiologic agent, Borrelia burgdorferi, from humans in 1983 capped an intensive hunt for a pathogen that just a short time before had been cultured from a black legged (deer) tick, initially named Ixodes dammini but subsequently found to belong to a species, I. scapularis. The isolation of B. burgdorferi sparked an explosive increase in our knowledge of the bacterium, the disease it causes, and the enzootic cycle that sustains and creates risk to humans who intrude upon it.

We now know that Lyme disease (Lyme borreliosis) is the most prevalent tick-borne illness. Although the clinical manifestations of Lyme disease continue to be a source of considerable controversy, it is generally accepted that a relatively small number of syndromes dominate the clinical picture and that the vast majority of patients present with treatment-responsive acute illness. Serologic surveys conducted in high prevalence areas indicate that asymptomatic infection also is relatively common; thus, despite the bacterium's notorious reputation, benign outcomes often occur. The genomic sequence of B. burgdorferi revealed that the spirochete lacks genes encoding known toxigenic molecules as well as the secretory apparatus required to deliver them to the extracellular milieu it inhabits within its mammalian host.

Whereas reservoir hosts are unaffected by lifelong infection with Lyme disease spirochetes due to a poorly understood form of immunologic tolerance, infected humans often mount local and systemic inflammatory responses that make them ill. From this perspective, one can regard clinical Lyme disease in humans as an evolutionary "mismatch" between pathogen and the intolerant immune system of its incidental host. Beyond this reductionist view, however, we still have only a limited understanding of the microbial factors, pathogenic mechanisms, and immunologic responses that determine outcomes following the adventitious encounter of humans with this zoonotic microorganism.

Epidemiology

Lyme disease also is the most prevalent vector-borne illness in Europe, where it is widely, though non-uniformly, distributed. Remarkably, Lyme disease is not a mandatory notifiable disease in many European countries, complicating country by country comparison

of epidemiologic data. Although methods used to acquire surveillance and laboratory data vary greatly, an estimated 85,000 cases occur each year throughout Europe. In Europe, as in the U.S., new cases peak in the summer months of June through August, and underreporting is believed to be common. In Northern Europe, disease rates are highest in the Baltic states and Southern Sweden; in Central Europe, highest incidences are in Austria and Slovenia. At the southern limits of the disease range (e.g., Italy and the Balkans), incidence decreases rapidly from north to south. Disease rates across the Continent parallel the densities of I. ricinus ticks affected with the pathogenic species most frequently detected in patients, B. afzelii and B. garinii. Lyme disease rates are increasing in Europe for the same reasons as in North America—increased awareness, coupled with increasing distribution and abundance of I. ricinus due to the same environmental drivers, with climate change probably a major culprit.

Disease manifestations

The earliest manifestation of Lyme disease is the appearance of a typically bullseye-shaped rash, known as an erythema migrans, at the site of infection. While this rash is generally sufficient for Lyme diagnosis, it only occurs in 70–80% of cases, making it unreliable as a main indicator. Other than the erythema migrans, the most common symptoms are headaches and arthralgia, but these are far too general to indicate Lyme disease. As the disease progresses, Borrelia disseminate from the site of tick attachment and travel throughout the body, causing early disseminated symptoms that can include multiple erythema migrans, carditis, and meningitis. If left untreated for a prolonged period, Lyme disease may progress to a more severe late stage that can include encephalitis and arthritis, among other serious symptoms. While Lyme disease is easily treated with antibiotics if caught early, delayed diagnosis and/or treatment can prove more difficult to treat and lead to more serious health effects.

The most common presenting manifestation of Lyme borreliosis is an annular, expanding, erythematous skin rash termed erythema migrans (EM), which results from localized infection at the inoculation site after an incubation period of about 1 week (range, 3 to 32 days) after a tick bite. As the lesion expands, it may develop partial central clearing surrounded by a redder outer border, or classically, a "bull's eye" configuration with concentric rings of erythema alternating with partial clearing. However, if the patient is seen within days of rash onset, less distinctive lesions are more common. Typical appearances include expanding, homogeneous erythema, or expanding pale erythema surrounding a darker red center. In the United States, many patients with EM also have systemic symptoms, most frequently fatigue, arthralgia, myalgia or headache, and regional lymphadenopathy may be present. During the first days of infection, fever and chills may also be present, particularly in children. In some cases, multiple EM lesions occur, with a primary lesion at the site of the tick bite and secondary skin lesions resulting from hematogenous dissemination. Peripheral leukocytosis, leukopenia, anemia, or thrombocytopenia are not associated with EM, whereas lymphopenia or elevated liver function tests sometimes are.

Dissemination may also lead to noncutaneous organ involvement. If the patient is not treated with antimicrobial therapy, early Lyme neuroborreliosis may develop in approximately 15% of patients within weeks after initial infection, usually manifesting with cranial neuropathy (most commonly unilateral or bilateral facial nerve palsy), lymphocytic meningitis, or radiculitis. Within the same time frame, a less frequent (but potentially fatal) manifestation of early disseminated disease is Lyme carditis, usually causing atrioventricular conduction block in about 5% of untreated patients. In the northeastern United States, Lyme arthritis is the most common late manifestation of the disease, which occurs in approximately 60% of untreated patients, usually beginning months to as long as 2 years after untreated initial infection. Lyme arthritis typically affects only one or a few large joints, especially the knee. Affected knees usually have large joint effusions, with a neutrophilic leukocytosis in synovial fluid. Arthritis occurs only in a small proportion of European patients with Lyme borreliosis, often earlier in the disease course than in U.S. patients. In contrast, several later manifestations recognized with some frequency in Europe are rare or absent among North American cases, including acrodermatitis chronica atrophicans, borrelial lymphocytoma, and late encephalomyelitis.

In clinical practice today, most patients present with—and are treated for—erythema migrans, preventing later manifestations of the disease. Among cases reported to the Centers for Disease Control and Prevention (CDC) in recent years, 72% had EM, 28% had arthritis, 13% had neurologic involvement, and only 1.5% had carditis. In addition, among participants in a Lyme disease vaccine trial in the United States, 11% had asymptomatic infection. In Europe, as many as half of cases may be asymptomatic.

Diagnostic Tests

There are two broad categories of diagnostic tests for Lyme borreliosis: (i) direct detection methods, which detect the agent of infection in primary patient specimens, and (ii) indirect detection methods, which detect a host response to the infection. The first tests adopted for routine clinical diagnostic use were serum antibody tests (91). These indirect detection assays have evolved substantially in their methodology and chemistry (92), and they remain the most useful and widely available diagnostic aids. Despite prodigious recent advances in molecular methods for direct detection of other infectious agents, these and other direct detection strategies currently play little role in clinical diagnostics for Lyme borreliosis.

A specific antibody response against B. burgdorferi is not detectable during a "window period" of several days to a few weeks after initial infection. As the antibody response develops, IgM-class antibodies directed against a relatively limited repertoire of immunogenic antigens are produced, often with rapid IgM-to-IgG isotype switching.

While the IgM antibody response usually wanes and may become undetectable in late active disease, the IgG antibody response persists. However, in some cases, the IgM antibody response also persists, and therefore the presence of specific IgM antibodies does not necessarily indicate an infection of short duration or early-stage infection.

Current Methods of Diagnosis

In cases where an erythema migrans is not present or proves inconclusive, a global consensus of guidelines recommends the use of a standard two-tiered (STT) serology approach for the diagnosis of Lyme disease. This approach involves an initial enzyme immunoassay (EIA) or immunofluorescence assay (IFA) to measure antibody response to Borrelia antigens—often in the form of a whole-cell Borrelia sonicate. If this EIA/IFA returns a positive or equivocal result, then a follow-up Western blot is used to verify the presence of antibodies for a panel of specific Borrelia proteins. A meta-analysis of thirteen two-tiered serology studies across North America estimated the sensitivity of the approach at 46.3% for those with early-stage Lyme disease (symptoms for less than 30 days), 89.7% for those with early disseminated Lyme disease (30+ days), and 99.4% for those with late-stage Lyme disease. Specificity estimates for the two-tiered methodology were approximately 99% for all disease stages.

Recently, a modified two-tiered (MTT) approach, in which the western blot of the STT is replaced with a second immunoassay, was approved for use in the United States. Compared to the STT, the MTT demonstrates increased sensitivity for early Lyme disease, similar or slightly higher sensitivity for later stages of the disease, and similar specificity for all stages. A comparison of the STT and MTT approaches on several collections of sera from patients with erythema migrans and early Lyme disease estimated the sensitivity of the MTT test to be approximately 50%, while the sensitivity of the STT test on the same samples was approximately 40%.

While the sensitivity of the current two-tiered serology approaches is very high for disseminated Lyme disease, it remains quite difficult to detect the disease in its early stages. The development of anti-Borrelia antibodies can take upwards of three weeks to reach sufficient detection levels in the blood. Since the current standard relies on these antibodies, it is evident that a more direct method of detection is necessary to diagnose Lyme disease prior to its dissemination. The necessity of improved diagnostics is underscored by the recent and expected increases in Lyme disease, the potential for serious health difficulties, and the current diagnosis difficulties (e.g., misdiagnosis, false positives).

PCR

PCR is a biochemical technique used to amplify DNA sequences, providing millions of copies in a short period of time. Through PCR, scientists can amplify specific DNA samples to detectable levels in a manner analogous to sample preconcentration. PCR has been used to detect Lyme disease in clinical samples (e.g., blood, urine, cerebral spinal fluid). However, PCR-based tests typically have low sensitivity and are thus not typically used in clinical diagnosis. In addition, *Borrelia* is not effectively detected via PCR in humans due to its highly transient bacteremia phase and low concentrations in the body. PCR is commonly employed to confirm the presence of *Borrelia* in ticks and other hosts (e.g., deer), where bacterial concentrations are higher. It should be mentioned that PCR has seen many improvements since its introduction, and the development of new clinical PCR-based assays for Lyme disease is an area of active research.

Biosensors to the Rescue

Biosensors comprise a large and rapidly expanding collection of analytical devices that utilize biological components to detect biological and chemical analytes. All biosensors consist of two main components: A biorecognition element and a transducer. Biorecognition elements include antibodies, aptamers, enzymes, cells, and many other biological entities that interact specifically with a biological target. The role of these elements is to react, either chemically or physically, with an analyte of interest in order to indicate its presence in a sample. Since these biological interactions cannot necessarily be directly quantified, a transducer is required to convert these biological events into signals that can be recorded and analyzed in a coherent manner. Transducers may be optical, mechanical, piezoelectric, electrochemical, or any other method that can produce a measurable response.

In comparison to traditional diagnostic methods (e.g., ELISA, PCR), biosensors aim to provide several key advantages that make them ideal for infectious disease diagnosis. The use of highly specific biorecognition elements ensures biosensors have both high selectivity and sensitivity. The minuscule size of these elements allows functionalized surfaces to possess millions of potential interaction sites, leading to large linear response ranges. The use of relatively fast techniques (e.g., impedance) leads to rapid response times, providing results in as little as a few minutes. Biosensors are also typically low-cost, and many have the potential to be miniaturized into portable devices for in-field use.

The development of lightweight, portable biosensors for Lyme diagnosis would be invaluable considering that the disease disproportionately affects rural, heavily forested areas more often; these communities, though frequently exposed to the bacteria, often lack the complex equipment required to detect the disease. The current review aims to highlight the recent advances in the development of diagnostic biosensors for Lyme disease, with the goal of providing a clear outline for the future of Lyme diagnosis.

Conclusions

The key remaining questions are whether there can be found a better, more direct detection test to indicate the presence or absence of active B. burgdorferi, and whether additional controlled treatment trials using longer durations of treatment with the tetracycline or clarithromycin/hydroxychloroquine regimen, or regimens utilizing different antibiotics or combination of

certain antibiotics that might prove effective. The results of recent in vitro and early animal model experiments by Zhang and by Lewis) might hold promise of other potentially effective approaches to the management of patients with persistent symptoms of Lyme disease.

Of additional likely importance is the potential role of antibiotic tolerance as a mechanism of persistence and "resistance" of B.burgdoferi to treatment in patients with persisting symptoms. Recent results of experiments with other bacterial organisms that can persist demonstrate the likely role of antibiotic-tolerance as the mechanism by which they persist . This mechanism apparently relies on a ribonuclease produced by the organisms. If our preliminary results with BB0755, an annotated ribonuclease, that demonstrated cytotoxic activity with tissue-cultured cells of neural origin, is due to its ribonuclease activity, then this possibility might offer an explanation to B.burgdorferi's antibiotic tolerance.

There are additional questions that a better understanding of the pathophysiology of Lyme disease might lead to better approaches to the diagnosis and treatment of Lyme disease, especially in its persistent form. These include the possible role of antibiotic-tolerant persisters.

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FEATURES OF THE IMPACT OF TOXOPLASMOSIS ON HUMAN BEHAVIOR

Abstract.
Toxoplasmosis is a parasitic infection caused by the protozoan parasite Toxoplasma gondii. This parasite can infect both humans and animals, including birds and mammals. Toxoplasmosis is one of the most common parasitic infections worldwide. Toxoplasma gondii is the most common parasitic disease in developed countries. According to scientists, up to 90% of cats and dogs around the world are affected by toxoplasmosis pathogens. The toxoplasma infection rate is particularly high among rodents. In synanthropic foci, the source of infection is cattle, sheep, goats, camels, horses, donkeys, pigs, carnivores, ducks, geese, turkeys, guinea fowls, parrots and other animals. Toxoplasmosis can occur in acute and chronic forms, affecting the nervous and lymphatic systems, liver, spleen, and eyes. Toxoplasmosis is most dangerous in people with a weakened immune system, as it is acute and can damage the brain. When interviewing infected and healthy people, several differences in human behavior were found. Possible mechanisms by which T. gondii can affect human behavior include its effects on dopamine and testosterone.

Keywords: *toxoplasmosis, epidemiology, behavioral tests, dopamine.*

Etiology

The causative agent is Toxoplasma gondii (subkingdom Protozoa, type

Apicomplexa, order Coccidia, suborder Eimeriina, family Eimeriidae). T.gondii is an obligate intracellular parasite that exists in three forms: tachyzoite (endozoite or trophozoite), **bradyzoite** (cystozoite) and oocyst.

Tachyzoites (4-7 x 2-4 μm), shaped like a crescent with a rounded back end or a bow with a taut bowstring (toxon). Externally, the body of the pathogen is covered with a trimembranous pellicle. The cytoplasm is homogeneous with small granules. The nucleus is 1.5-2 microns in size. Reproduction of toxoplasmas occurs in cells of the macrophage-phagocytic system (MPS) by longitudinal

division or endodiogeny (internal budding). The multiplying parasites fill the cells, adhere tightly to each other and are surrounded by the membrane of the parasitoid vacuole. Due to the destruction of the affected cells, toxoplasmas are released, penetrate healthy cells, and the process repeats again.

Tachyzoites are sensitive to thermal, physical, and chemical agents. They die rapidly when heated to 55 °C for about 10 minutes, are not resistant to desiccation, and UV light. After 5-10 minutes, they die in a 50% alcohol solution, 1% phenol solution, 1% hydrochloric acid solution, and 2% chloramine solution. They tolerate low temperatures well: at 4-5 °C in milk they remain viable for several days, in donor blood - up to 30 days, and when frozen to -70 °C in an isotonic solution with serum and glycerol - for several months.

Epidemiology

Toxoplasmosis is an ubiquitous zoonosis. The final host and reservoir of parasites is the domestic cat or other members of the cat family (lynx, puma, jaguar, ocelot, Bengal cat, tiger, lion, etc.). About 1% of domestic cats shed oocysts in their feces. The disease in felines can be asymptomatic or with severe nervous system damage and fever. Intermediate hosts of toxoplasmas (humans, farm and domestic animals, rodents, birds, etc.) are an epidemiological dead end for the pathogen, except for those that are prey to felines. Mouse-like rodents and hares are especially often infected with toxoplasmosis, among which toxoplasmosis acquires the character of epizootics, forming natural foci of infection. Herbivores become infected by eating grass with oocysts on it.

The mechanism of toxoplasma transmission is mainly fecal-oral. The ways of its realization are alimentary, water, contact and household. The main factor of transmission is raw, insufficiently thermally processed meat (especially lamb and pork) containing pseudocysts of the pathogen. Infection is also possible by eating undercooked meat, unwashed vegetables and fruits. It is also possible to implement the contact mechanism of transmission through microtraumas of the external skin and close contact with contaminated animal raw materials (employees of meat processing plants, slaughterhouses, hunters, laboratory workers who work with contaminated material).

Cases of infection during organ transplantation and transfusion of blood products have been described. Sexual transmission is also theoretically possible during unprotected sexual intercourse, if the partners have mucosal defects and the blood of both participants in the act is in contact (if the blood of the infected person contains a highly virulent pathogen in large quantities).

Transplacental infection of the fetus (vertical transmission) is rare (one case per 1000-3500 deliveries). The most dangerous situation occurs when a seronegative mother is infected for the first time shortly before conception or while carrying a child. If a woman is infected 6 months or more before pregnancy, the risk

of congenital toxoplasmosis is very low. If the mother is infected during the first trimester of pregnancy with severe congenital toxoplasmosis, there is a high probability of miscarriage and stillbirth. Repeated infections and relapses are much less dangerous for the mother and fetus, as both are protected by circulating

antibodies. The condition of the placenta itself is also of great importance, since, according to the literature, toxoplasmas do not penetrate the intact placenta. The natural susceptibility to toxoplasmosis is high, although clinical signs of infection are more common in immunocompromised individuals. Toxoplasmosis is often an opportunistic infection in AIDS. Young people are more susceptible; toxoplasmosis is rare in people over 60 years of age.

Toxoplasmosis is widespread in many countries, especially in tropical regions. It has been established that in the northern regions of the globe (Iceland), the infection rate is in the range of 4-11%, and in tropical regions (Honduras, Tahiti) it reaches 64-68%.

Immunity in toxoplasmosis is non-sterile (the pathogen and antibodies against it are present), sufficiently intense, and it is believed that reinvasion does not occur.

Assessment of human behavior in toxoplasmosis

Since 1992, a series of studies have been conducted in the Czech Republic comparing the personality characteristics of individuals with anamnestic antibodies to *T. gondii*, thus suggesting that they have latent infection, with those without such antibodies. The personality questionnaires used in these studies , were the Cattell Inventory with 16 personality factors.

In general, differences in personality factors were greater in subjects of older age groups. In order to determine whether there was any correlation between personality change and duration of infection, personality test data were available for 190 men and 230 women who had been diagnosed with acute toxoplasmosis in the previous 14 years.

Differences in behavior between infected and healthy subjects were also studied using a panel of simple behavioral tests. For example, experiments designed to measure suspicion. They assessed a person's willingness to try an unfamiliar liquid, allow the experimenter to control their wallet, and sign a blank piece of paper. Similarly, experiments designed to measure self-control assessed whether a person arrived early or late for testing, how accurate the person's assumptions about the contents of their own wallet were, the time spent answering a computerized questionnaire, and knowledge of social etiquette.

The composite behavioral factors "Self-control" and "Neatness of clothing", similar to Cattell's factors Q3 (perfectionism) and G (supererogatory strength), showed a significant interaction effect between toxoplasmosis and gender, with infected men scoring significantly lower than uninfected men and a trend in the opposite direction for women. The effect of the interaction between toxoplasmosis and gender on the complex behavioral variable Relationships (similar to factor A, warmth) approached significance; infected men scored significantly lower than uninfected men, while there was no difference among women. All scores were made by raters who were unaware of the individual's *T. gondii* infection status.

Since animal studies *have* shown that mice infected with *T. gondii* have impaired motor activity, human studies were conducted on volunteer blood donors. A computerized simple reaction time test (reaction to the appearance of a white square) was performed in 60 adults who tested positive for antibodies to *T. gondii* and 59 adults who tested negative for such antibodies. Those with latent infection performed significantly worse (covariance analysis, $P = 0.011$) and seemed to lose concentration faster, although the effect of infection was moderate and explained less than 10% of the variation in performance.

Can minor changes in psychomotor performance have any impact on human behavior? To test this, blood sera were collected from 146 people in a Prague hospital who were believed to be responsible for causing road accidents, both as drivers and pedestrians. These sera were compared to 446 control sera collected at random in Prague. The difference in toxoplasmosis seroprevalence in these 2 samples suggests that subjects infected with *toxoplasma* have a 2.65-fold higher risk of road traffic accidents than subjects free of *toxoplasma* (Mantel-Haenszel test for age-stratified data, chi-square = 21.45, $P < 0.0001$). Factors that could lead to exposure *to T. gondii* and vehicle accidents cannot be excluded.

A recent study in Turkey also found higher levels of *T. gondii* antibodies among drivers involved in road traffic accidents. Among 185 such drivers, the prevalence of *T. gondii* IgG antibodies was 24.3% and IgM antibodies were 3.2%; among 185 age-matched controls, the prevalence of IgG antibodies was 6.5% and IgM antibodies were 0.5% (chi-square, $P < 0.05$).

Studies have also examined possible links between *T. gondii* infections and intelligence, education, and memory. Initial reports of associations with intelligence and education were found to be flawed when all confounding factors were taken into account. Two unpublished studies found no association between the infection and short-term memory.

It is known that T. gondii increases dopamine levels in rodents and that treatment of rodents with a selective dopamine uptake inhibitor changes the behavior of infected and uninfected rodents differently. In addition, the observed low level of novelty seeking in humans infected with toxoplasma or cytomegalovirus is likely due to high levels of dopamine in the ventral midbrain. The mechanism by which T. gondii increases dopamine levels is unknown, but it may involve inflammatory release of dopamine by increasing cytokines such as interleukin-2. An imbalance of dopamine between the mesolimbic and mesocortical regions of the brain is thought to play a role in the development of schizophrenia, which may explain the observed association between schizophrenia and toxoplasmosis.

Conclusion.

The results obtained over the past 15 years strongly suggest that latent toxoplasmosis affects the behavior of not only rodents but also humans. However, the neurophysiological mechanisms and practical

implications of these behavioral changes remain to be elucidated. **List of references**

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ВПЛИВ НАПРУЖЕНО-ДЕФОРМОВАНОГО СТАНУ КІСТКОВОЇ ТКАНИНИ НАВКОЛО ІМПЛАНТАТІВ, ЩО СЛУЖАТЬ ОПОРОЮ ПОВНОГО ЗНІМНОГО ПРОТЕЗА НА НИЖНІЙ ЩЕЛЕПІ ПРИ ЙОГО ТЕЛЕСКОПІЧНІЙ ФІКСАЦІЇ.

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INVESTIGATION OF THE STRESS-STRAIN STATE OF BONE TISSUE AROUND IMPLANTS SUPPORTING A COMPLETE REMOVABLE PROSTHESIS ON THE LOWER JAW, WITH ITS TELESCOPIC FIXATION

Анотація

Використання двоступеневих гвинтових дентальних імплантатів з метою, поліпшення фіксації знімних протезів на беззубої щелепи (особливо нижньої) набуло останнім часом все більшого поширення. З цією метою найчастіше використовується телескопічна або балочна система фіксації. Однак питання, який з них віддати перевагу, залишається відкритим на сьогоднішній день. Для досягнення поставленого завдання була побудована комп'ютерна модель, в якій в якості опори знімного протеза на нижній щелепі виступали два імплантати, встановлені в міжментальному відділі, із заданими параметрами.

Abstract

The use of two-stage screw dental implants in order to improve the fixation of removable dentures on the toothless jaw (especially the lower one) has recently become increasingly widespread. For this purpose, a telescopic or beam fixation system is most often used. However, the question of which one to give preference to remains open today. To achieve this task, a computer model was built in which two implants installed in the intermental department with specified parameters acted as a support for a removable prosthesis on the lower jaw

Ключові слова: *імплантати, кісткова тканина, телескопічна фіксація.*
Key words: *implants, bone tissue, telescopic fixation.*

Використання двоступеневих гвинтових дентальних імплантатів з метою, поліпшення фіксації знімних протезів на беззубої щелепи (особливо нижньої) набуло останнім часом все більше поширення [1]. З цією метою найчастіше використовується телескопічна або балочна система фіксації. Однак питання, який з них віддати перевагу, залишається відкритим на сьогоднішній день [2]. Для цього необхідно вивчити напружено-деформований стан кісткової тканини навколо імплантатів, які служать опорою повного знімного протеза при його телескопічній і балочної фіксації, і на підставі цього дати їх порівняльну характеристику [3-8]. Таким чином, на першому етапі наших досліджень метою роботи є вивчення напружено-деформованого стану кісткової тканини навколо імплантату, що служить опорою повного знімного протеза нижньої щелепи при його телескопічної фіксації.

Для досягнення поставленого завдання було побудовано комп'ютерну модель, в якій в якості опори знімного протеза на нижній щелепі виступали два імплантати, встановлені в міжментальному відділі, із заданими параметрами (довжиною 13 мм і діаметром 3,5 мм). Відстань між імплантатами при різних системах фіксації також задавалася однаковою, оскільки очевидно, що зміна цієї відстані істотно вплине на величину напружено-деформованого стану кісткової тканини навколо імплантатів.

В проведених дослідженнях нами не враховувався тип щелепи, оскільки очевидно, що довжина лінії, що з'єднує імплантат з дистальним краєм протеза, проведеної по альвеолярному гребеню, істотно впливає на напружено-деформований стан кісткової тканини навколо імплантату. Іншими словами, при зміні типу щелепи змінюються навантаження на імплантат.

При проведенні наших досліджень величина навантаження, що передається протезами на імплантатах, дорівнювала 200 Н, а кут, під яким вона передавалася, складав 125°, що відповідало нормогнатичному прикусу. При цьому передане навантаження було розкладено на вертикальну і горизонтальну складові.

Такий підхід дозволив створити єдину методику розрахунку, яка може бути застосована при будь-якій зміні кута передачі навантаження, що веде тільки до зміни вертикальної і горизонтальної складових навантаження на імплантат.

Моделювання та розрахунки виконувались в кінцево-елементному пакеті ANSYS. Для апроксимації моделей використали стандартний кінцевий елемент SOLID92 з бібліотеки елементів програми ANSYS, який є квадратичним елементом 2-го порядку, придатним для моделювання нерегулярних сіток. Елемент визначається десятьма вузлами, кожен з яких має три ступені свободи переміщення в напрямку осей X, Y, Z вузлової системи координат [5].

Імплантат на моделях позначали схематично (синім кольором), вивченню він не підлягав, і з метою відсутності в ньому деформації і навантаження моделювався зі значно більшим модулем пружності, ніж у інших компонентів моделі.

Результати дослідження та їх обговорення. Для досягнення поставленого завдання було всебічно обстежено побудовану модель і вивчено величину і характер розподілу навантажень і деформацій в системі кісткова тканина – імплантат при телескопічній фіксації повного знімного протеза нижньої щелепи. Для виконання поставленого завдання з визначення полів напружень і деформацій було проведено два варіанти розрахунку.

Варіант 1. Величина навантаження в системі кісткова тканина-імплантат представлена вертикальної складової.

Fверт = 114 Н.

Варіант 2. Величина навантаження в системі кісткова тканина-імплантат представлена горизонтальної складової

$F_{гор.}$ = 163 Н.

Отримані результати представлені в табл. і на рис. 1,2.

Таблиця

Значення переміщень в моделі і максимальне значення напружень в моделі, імплантаті, кістки

№ варіанту	Максимальне переміщення, мм	Максимальне навантаження, Н/мм^2 (МПа)		
		модель	імплантат	кістка
1	0,00833	26,81203	23,3421	8,1708
2	0,58443	292,51311	292,51311	126,7836

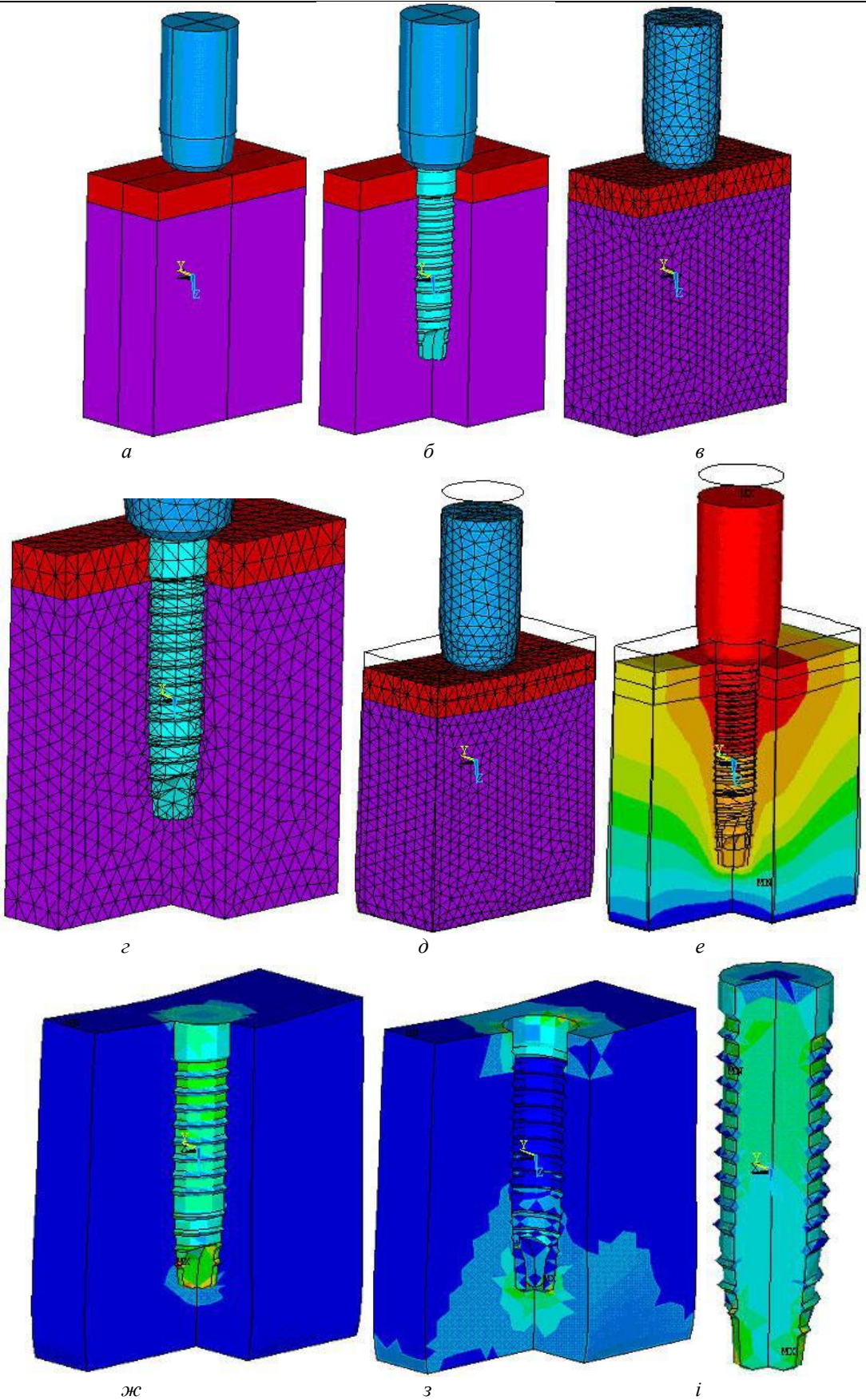

Рис. 1. Вертикальне навантаження на систему імплантат – кістка.
а – загальний вигляд моделі; б – модель в розрізі; в – загальний вигляд кінцево-елементної сітки на моделі; г – розріз моделі з кінцево-елементною сіткою; д – деформована форма; е – епюра переміщень в розрізі для всієї моделі; ж – епюра напружень в розрізі для всієї моделі; з – епюра напружень в кістці; і – епюра напружень в імплантаті.

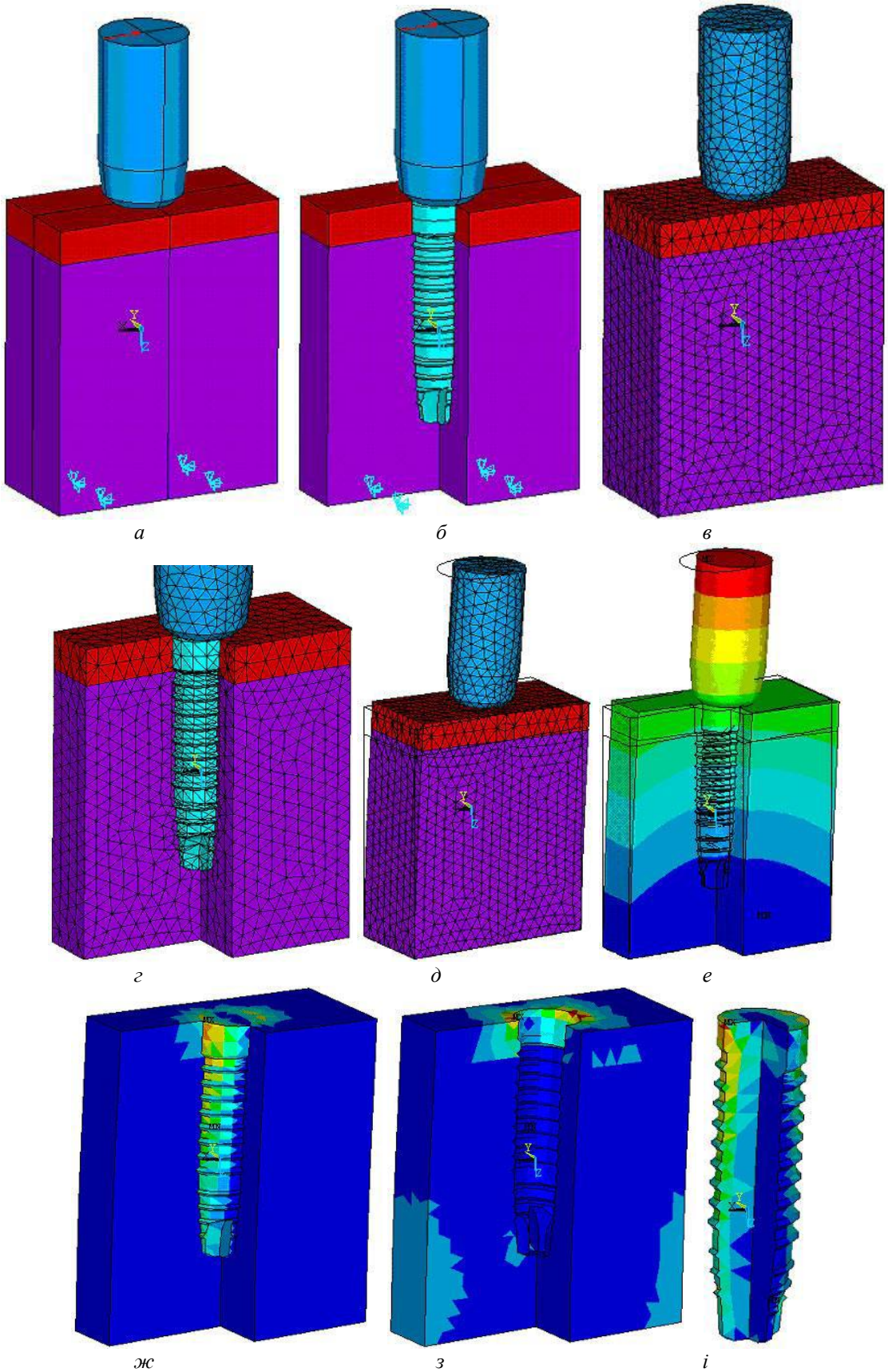

Рис. 2. Горизонтальне навантаження на систему імплантат – кістка.
а – загальний вигляд моделі; б – модель в розрізі; в – загальний вигляд кінцево-елементної сітки на моделі; г – розріз моделі з кінцево-елементною сіткою; д – деформована форма; е – епюра переміщень в розрізі для всієї моделі; ж – епюра напружень в розрізі для всієї моделі; з – епюра напружень в кістці; і – епюра напружень в імплантаті

Таким чином, на підставі проведених досліджень можна зробити наступні висновки. Величина горизонтальної складової, яка передається під кутом 125° на імплантат і служить опорою повного знімного протеза на нижній щелепі при його телескопічної фіксації, перевершує вертикальну складову тільки в 1,42 рази, а при цьому абсолютна величина максимальної напруги навколо внутрішньокісткової частини імплантату буде вище в 15,1 рази.

На підставі вищевказаного, можна зробити ще один висновок: ігнорування горизонтальної складової, а значить, величини кута змикання щелеп при плануванні хірургічної та ортопедичної складової лікування пацієнтів за допомогою знімних протезів, що опираються на двоступеневі гвинтові кореноподібні імплантати за допомогою телескопічної фіксації є грубою клінічною помилкою.

Варіант 1. Імплантат діаметром d = 3,5 мм і довжиною L =13 мм під дією вертикальної складової ($F_{верт}$ = 114,7 Н.) навантаження в 200 Н переданої під кутом 125° при телескопічній фіксації (рис. 1).

Варіант 2. Імплантат діаметром d = 3,5 мм і довжиною L = 13 мм під дією горизонтальної складової ($F_{гор}$ = 163,8 Н.) навантаження в 200 Н, який передається під кутом 125° (рис. 2).

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