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# Modern Ideas About the Clinical and Immunological Features of Modern Juvenile Rheumatoid Arthritis and Methods of Its Therapy.

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**ABSTRACT**

The article presents data on the clinical and immunological features of modern juvenile rheumatoid arthritis and methods of its therapy. One of the urgent problems of modern rheumatology is chronic inflammatory diseases of the joints in children, united under the general term "juvenile arthritis" or, in accordance with the international classification of 2017 - "juvenile idiopathic arthritis". In domestic rheumatology, the term "juvenile rheumatoid arthritis" (JRA) is widely used. The etiology and pathogenesis of JRA are still unknown. This disease is characterized by pronounced clinical polymorphism and genetic heterogeneity, in connection with which it combines independent inflammatory diseases of the joints in children, different in course and prognosis, and possibly having certain equivalents in adults.

**Keywords:**

rheumatoid arthritis, rheumatology, joint diseases, juvenile arthritis, joint inflammation.

JRA is a chronic inflammatory joint disease characterized by a complex autoimmune pathogenesis, a steadily progressive course, possible involvement of internal organs in the process, and frequent development of disability in children. One of the variants of JRA without systemic manifestations is polyarticular JRA of seronegative (without rheumatoid factor) and seropositive (with RF) subtypes. Along with this, it is possible to identify variants of the course of JRA associated with provoking infectious agents. Research by A.G. Lyskin showed that in young children (up to 5 years old) suffering from JRA, the latter is often (up to 74%) associated with a bacterial viral and mixed infection, which aggravates the course of the underlying disease. So, along with the bacterial and viral nature of such, a high frequency of infection of patients with the articular form of JRA with opportunistic flora is known: chlamydia (in 83%), bacteria of the

intestinal group (in 33%), *Helicobacter pylori* (in 90%).

According to the results of various studies, the prevalence of JRA in different countries ranges from 0.05% to 0.6%, and the incidence is from 2 to 19 cases per year per 100,000 children. The prevalence of JRA in the Russian Federation is 62.3 per 100,000, the primary incidence is 16.2 per 100,000. In adolescents, the prevalence of JRA is 116.4 per 100,000. The frequency of the disease varies in different ethnic groups, and therefore, in its etiology a role of genetic predisposition is assumed. It is known that in JRA, combined and genetically determined disorders in the main links of specific immunity (cellular and humoral) are most often noted. It should be noted that, in contrast to the quantitative and qualitative indicators of specific lymphocytic immunity, to a certain extent studied in JRA, in the modern scientific literature there is not

enough information about the functional activity of neutrophilic blood leukocytes in this disease. Meanwhile, the expediency of studying neutrophils in JRA is due to the fact that the indicators of the functional state of these cells characterize the activity of the pathological process and reflect its dynamics. Data from the literature of recent years indicates the complex nature of the effect of JRA with a provoking virus and a bacterial provoking agent on the activity and quantitative composition of the active components of the neutrophil cytoplasm. In this regard, there is a need to search for more sensitive and informative diagnostic methods, assess the degree of activity of the pathological process and the effectiveness of the measures taken. All of the above determined the need for this study. RA depending on provoking dependent factors.

**Purpose of the study:** To study the clinical and cytochemical features of JRA depending on the provoking factors.

**Research objectives:** To study the frequency of detection of infections preceding juvenile rheumatoid arthritis in children. To study the state of the microbicidal function of neutrophils in children with JRA, taking into account provoking factors. In this work for the first time: An important role of exposure to viral, bacterial and urogenic infections in the development of JRA in children has been established. A study was made of the phagocytic and microbicidal function of peripheral blood neutrophils in children with various types of JRA in terms of the activity of alkaline and acid phosphatase, myeloperoxidase, the content of non-enzymatic cationic proteins and the oxidase microbicidal system in spontaneous and stimulated NBT-test.

The analysis of changes in the parameters of the phagocytic and digestive functions of peripheral blood neutrophils depending on the type of JRA provoking factors (bacterial infection, viral, opportunistic) was studied. A computer morphometric analysis of DNA of neutrophils and lymphocytes in children with JRA was carried out. The diagnostic information content of the obtained data on the

functional and metabolic activity of peripheral blood neutrophilic leukocytes was determined depending on the provoking factor.

**Practical significance of the work:** Identification of various infections preceding JRA, followed by their therapy, is an important measure for the prevention of this disease and the prevention of exacerbation. The revealed features of the functional activity of peripheral blood neutrophils in JRA provoked by various infectious factors are objective diagnostic markers of the degree of disturbances in the system of neutrophilic leukocytes in this disease. In patients with JRA, there is a significant activation of the nuclear apparatus of neutrophils and lymphocytes in comparison with persons in the control group. The use of the results of the work in clinical practice will improve the diagnosis of the nature of the course of JRA and the ongoing therapy. Rheumatic diseases of childhood (rheumatic fever, diffuse connective tissue diseases, juvenile arthritis, systemic vasculitis, etc.) occupy one of the important places in the structure of childhood morbidity, among which juvenile rheumatoid arthritis (JRA) is one of the urgent problems in due to a significant increase in the proportion of the disease among the child population in recent years.

JRA is part of a heterogeneous group of chronic inflammatory joint diseases in children ("juvenile chronic arthritis") along with psoriatic arthritis, spondyloarthritis, and chronic arthritis of unspecified nosology. These diseases are united by a tendency to a chronic progressive course, which has a significant impact on the quality of life of the child and a high probability of his early disability. The still unclear etiology of the disease and the complex, predominantly autoimmune pathogenesis, the involvement of internal organs in the process in a number of patients, create significant difficulties in the treatment of JRA. The disease can begin at any age, including in children of the first years of life, which are characterized by a predominance of seronegative forms, an acute onset, early generalization with a pronounced exudative component in the joints, and a severe course. In this case, the early diagnosis of JRA is

especially difficult due to the variability of the clinical picture, the difficulty of using generally accepted diagnostic criteria, and the lack of awareness of pediatricians regarding the characteristics of the disease at an early age. This, in turn, determines the relevance of further study of the features of JRA in young children in order to early verify the diagnosis and prescribe adequate therapy to patients, assess its effectiveness and safety. The situation is complicated by the fact that the modern arsenal of antirheumatic drugs is not always a guarantee of successful treatment of JRA and has many adverse reactions in the form of damage to the mucous membrane of the gastrointestinal tract, increased blood pressure, neutropenia, and agranulocytosis. This leads to a constant search for new drugs that can have a disease-modifying effect and improve the prognosis of the disease. In this regard, immunotropic therapy is of great importance, since in JRA, combined and genetically determined disorders in the main links of specific immunity are most often noted.

The most characteristic immunological picture of JRA in young children is defined as a decrease in the content of CD8-expressing lymphocytes, an increase in the content of CD4-, CD 19-, CD95-positive cells with an increase in the concentration of pro- and anti-inflammatory cytokines in the blood serum, which indicates the instability of the immune response. At the same time, in the early age group (1-6 years) there is a significant violation of the T-cell immunity of children with JRA due to a significant predominance of Th-1 cells, associated with systemic manifestations in the early stages of the disease. It is important to note that the nature of immunological disorders is largely determined by the duration of the disease: with a JRA duration of more than 7 years, there is a maximum functional activity of neutrophils with depletion of their reserve capabilities, a predominance of Th2-lymphocytes and a high level of IgA, IgE, accompanied by exacerbation of joint inflammation, exudation, progression of destructive processes. In turn, this necessitates taking into account the age characteristics and

duration of the disease in the diagnosis and prediction of the course of various JRA variants.

In modern scientific literature, there is not enough state of the functional activity of neutrophilic leukocytes in young children with oligo- and polyarticular arthritis, which makes it expedient to conduct such studies. Of particular interest in this case is the assessment of the microbicidal function of neutrophils, as "professional" phagocytes, which reflects the intraleukocyte potential of their biocidal activity, which is realized both during intracellular digestion of antigens and in extracellular killing.

The results of the study served as the basis for modifying the existing classification and diagnostic criteria for JRA. Signs of an unfavorable prognosis in the early stages of the disease were revealed, and the need to take into account the variant of the onset and course of JA when choosing the tactics of treating patients was substantiated. The expediency of determination of ACCP in the blood serum at the early stages of the disease to predict the nosological affiliation and the nature of the course of the disease is shown. All of the above is important not only for rheumatologists, but also for pediatricians.

The results of the work were introduced into the practice of the children's department of the Institute of Rheumatology of the Russian Academy of Medical Sciences and became the basis for modifying the classification and testing of JRA diagnostic criteria in relation to modern conditions and using them in everyday work. The revealed diagnostic value of ACCP became the basis for the determination of these antibodies in patients with JA at the early stages of the disease in order to predict the polyarticular variant of the lesion and the development of JRA, as well as the early prescription of aggressive treatment in this group of patients.

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