

**ROLE OF LOCAL AND SYSTEMIC IMMUNITY IN THE DEVELOPMENT OF
RESPIRATORY ALLERGOSES IN CHILDREN AND OPTIMIZATION TREATMENT**

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Annotation

The review reflects the etiology, pathogenesis and treatment of some diseases belonging to the group of respiratory allergoses on the basis of data from relevant sources and our own research. The main attention is paid to the reflection of the processes of allergic inflammation and its mediators of intercellular interaction-cytokines. Cytokines are secreted glycosylated polypeptides that regulate and determine the nature of immune responses in children. An important role in the pathogenesis of respiratory allergoses in children has an imbalance in the level of cytokines, which are involved in the processes of allergic inflammation.

The revealed violations in indicators of activity of phagocytosis, lysozyme, immunoglobulins, and also subpopulations of lymphocytes testify to presence of pathological reactions in processes of nonspecific protection of an organism, decrease in local and system immunity that also defines severity of a course and causes introduction of additional methods of correction of this pathology at children.

Violations in indicators of cytokine profile cause introduction of additional methods of correction of this pathology in children and inclusion in complex treatment of methods of immunocorrection and an assessment of efficiency of the carried-out treatment at respiratory allergoses in children.

Immunomodulatory effects of the drugs appear to increase the number of T-lymphocytes; in the restoration of the bactericidal activity of leucocytes; the effect on humoral factors (activation of compliment, the increase in the number of total and activated B-lymphocytes); the impact on phagocytosis.

It should be noted that, despite the huge attention of doctors to the problem of respiratory allergoses in children, this group of diseases still remains one of the most common allergic diseases in childhood. To develop methods of adequate therapy, it is necessary to continue a detailed study of pathogenesis, including the study of the cytokine system. Understanding the pathogenetic basis allows us to expand the range of modern therapies. In the structure of respiratory diseases in children of different age groups, bronchopulmonary pathology accounts for **30–40%** .

KEYWORDS: respiratory allergoses, cytokines, allergic inflammation, immunoglobulins, immunocorrection, Ismigen, Derinat, Amiksin.

Over the past ten years, there has been an increase in the number of patients in the dispensary group of frequently ill children (FIC). Among such children, **recurrent bronchitis** occupies one of the leading positions among respiratory system pathologies. In recent years, there has been a tendency toward recurrence of the pathological process in the bronchi, an increase in obstructive forms, and a prolonged course of the disease. Due to concomitant pathology of the respiratory, nervous, cardiovascular systems, and the musculoskeletal system,



the premorbid background in children often worsens. The etiological structure of pathogens is changing, and the effectiveness of drug therapy is decreasing due to the increasing resistance of pathogens .

The anatomical and physiological characteristics of pediatric patients, the increase in secondary immunodeficiency conditions associated with unfavorable environmental factors, non-compliance with sanitary and hygienic standards, and the sensitization of the child's body by pharmacological agents and allergen-containing foods are the main causes of the development of respiratory allergic diseases. Genetic predisposition should also be considered as one of the causes of respiratory allergies.

Today, specialists pay special attention to studying the causes of the development of recurrent obstructive syndrome and the progression of disorders of local and systemic immunity, as well as the induction of chronic forms of bronchial obstruction. Adequate interpretation of immune system disorders allows the selection of optimal therapy, and timely clinical diagnosis helps prevent complications .

Currently, there is an increase not only in the prevalence of respiratory allergic diseases but also in the number of patients with severe allergic conditions and those resistant to standard therapy. At the same time, the profile of clinical manifestations of allergies is changing. There is also underdiagnosis of a number of nosological forms. This indicates the relevance of studying immune system disorders in children with allergic pathology. This is confirmed by the growing number of publications on this topic. Domestic and foreign studies evaluate laboratory data in children with allergic diseases, including the determination of hypersensitivity to specific allergens . It has also been established that external factors influence the prevalence of allergic diseases .

Respiratory allergic diseases are a group of respiratory system disorders that include lesions of the **nose and paranasal sinuses, larynx, trachea, bronchi, and lungs**. Allergic immunological mechanisms are involved in their development. The immunological conflict depends on the action of the allergen and the immune response of the body, which is determined by genetic factors and hormonal influences.

Allergens are substances carrying signs of genetically foreign information that cause specific immune reactions. Allergens may be complete or incomplete (haptens) and may have infectious or non-infectious origins.

The main route of allergen entry into the body is **inhalation**.

House dust is usually considered the main inhaled allergen in respiratory allergic diseases. Its properties are determined by the microscopic mites of the genus **Dermatophagoides** contained in it. Respiratory allergic diseases in children can also be caused by plants, especially during the flowering period (for example, lamb's quarters in autumn and timothy grass in summer). Another important cause of allergy is animal hair. Poor sanitary and hygienic conditions of living spaces (mold, fungi, etc.) also play a role in the development of allergies.

Four types of allergic reactions are known:

Anaphylactic type. It is characterized by sensitization of tissue cells, mainly mast cells, and the interaction of antigen with antibody, which leads to the release of biologically active



substances. Mast cells are destroyed, blood vessels dilate, edema and infiltration occur, resulting in spasm of the bronchial smooth muscles.

Cytotoxic type. This is a humoral reaction of the immediate type involving immunoglobulin (Ig) E (for example, transfusion reactions during blood transfusion). This type of reaction does not play a significant role in respiratory organ damage.

Immune complex type. It is a humoral reaction of a semi-delayed type involving IgG. In this type of reaction, the complement system is activated.

Delayed cellular reaction. Humoral antibodies are not involved. It is characterized by slow development and gradual regression.

Often a combination of different types of reactions is observed with the predominance of one of them.

The characteristics of mediators of allergic reactions depending on their effects are presented in the table.

In some cases, the diagnosis of respiratory allergic diseases in children is difficult. Therefore, it is necessary to analyze the patient's medical history and consider genetic predisposition. Often, close relatives of children with **bronchial asthma** also suffer from allergic diseases. It is also important to remember accompanying allergic conditions that may accompany respiratory allergic diseases, such as **urticaria, atopic dermatitis, and helminthic infestations**. Respiratory allergic diseases in children are characterized by frequent relapses, occurring **one or two times per month**.

Indicators of **eosinophilia in peripheral blood** also play an important role. During the manifestation of the disease, the number of eosinophils usually does not exceed normal values and may sometimes decrease. After symptom relief, their number increases and remains elevated during remission.

The diagnostic algorithm may include determination of **IgE** levels and performing a **blast transformation reaction with a specific allergen**.

Below is a brief description of diseases related to respiratory allergic disorders.

Allergic rhinitis (AR) in children is rarely isolated; usually the process affects the sinuses, pharynx, larynx, bronchi, Eustachian tubes, and middle ear. AR is accompanied by sneezing, itching in the nose, coughing, and in some cases urticaria, laryngotracheitis, or Quincke's edema. Body temperature often increases, and rhinitis may recur.

Allergic rhinosinusitis. Against the background of frequent acute respiratory infections, polypoid changes occur in the mucous membrane of the nose and paranasal sinuses. Symptoms include difficulty breathing through the nose, mucous or mucopurulent discharge, headache, and subfebrile temperature. Recurrences are possible even after adenoid removal. Otorhinolaryngologists note cyanosis and swelling of the mucous membranes. X-ray examination reveals partial or complete shading of the sinuses. The level of eosinophils in the mucus may reach **80%**. Allergen tests are diagnostically significant.



Adenoid vegetations in most cases have an allergic etiology. Surgical treatment alone often does not provide the expected effect.

The **infectious-allergic nature of chronic tonsillitis** is confirmed by allergen testing. Chronic tonsillitis is often combined with allergic pharyngitis. Food allergens are considered etiological factors. One of the main features of the disease is the rapid development of symptoms after the consumption of allergens .

Allergic laryngitis develops acutely, and edema may lead to asphyxia. The cause is usually food allergy. The disease often occurs as a false croup and usually requires hospital treatment.

Acute and chronic otitis media have a recurrent course. Body temperature often rises to 39°C, and ear pain occurs. Relapses may occur up to **12 times per year** .

Allergic tracheitis and bronchitis are more common in children aged **3–6 years**. Allergic tracheitis often precedes bronchial asthma. Symptoms include sweating, increased salivation, and constricted pupils. Sinusitis is often present. The cough resembles whooping cough .

Allergic bronchitis has a persistent recurrent course. Body temperature is usually normal or subfebrile. Cough most often occurs at night, and the diagnosis is rarely made .

Allergic pneumonia develops either independently or in association with other allergic diseases, including bronchial asthma (in **3% of all asthma patients**). It is usually localized in the middle and lower lobes of the right lung. Blood eosinophilia and lymphocytosis are observed. The erythrocyte sedimentation rate may be normal or elevated. Body temperature is usually normal, and radiological changes regress rapidly.

Eosinophilic pulmonary infiltrate is usually asymptomatic and detected accidentally, most often in patients with bronchial asthma. In this case, the clinical condition does not correspond to the radiological findings. Blood eosinophilia is often detected .

In recent years, both domestic and foreign publications have discussed various aspects of the pathogenesis of respiratory allergic diseases. According to several authors, the **cytokine profile** should be studied in children with respiratory allergic diseases. Cytokine imbalance leads to a pronounced inflammatory process in the respiratory tract of children .

Cytokines are secreted glycosylated polypeptides that regulate and determine the nature of immune responses. They participate in almost every stage of immune and inflammatory reactions, including antigen presentation, bone marrow cell differentiation, cell recruitment and activation, expression of adhesion molecules, and acute-phase responses. There is no single classification of cytokines. Depending on their cellular source, they are divided into **mono- and lymphokines**, and according to biological activity they are classified as cytokines mediating humoral immunity, cellular immunity, allergic reactions, or possessing immunosuppressive properties .

One of the most important functions of cytokines is the **regulation of inflammation**.

Among pro-inflammatory cytokines, several subgroups are distinguished:

- cytokines with chemotactic activity that activate inflammatory cells;



- cytokines that destroy altered cells and stimulate proliferation and differentiation of inflammatory cells;
- cytokines that stimulate proliferation of bone marrow precursors and their release into the bloodstream;
- cytokines that suppress inflammatory cell function and inhibit inflammatory processes .

According to several authors, exposure to specific antigens leads to the differentiation of **T-helper cells into two subpopulations – Th1 and Th2**. Th1 cells secrete mainly **interleukin-1, interleukin-2, interferon-gamma, and tumor necrosis factors**, which participate in antiviral and antibacterial defense. Th2 cells synthesize **IL-4, IL-5, and IL-10**, which mainly induce humoral immune responses. Th1 cells predominate in healthy individuals, whereas Th2 cells dominate in patients with atopic diseases .

In severe bronchial asthma, an increased level of **IL-8** is detected in airway secretions .

The immune system of patients with bronchial asthma is characterized by a decrease in **T-lymphocytes with suppressor activity**, predominance of **Th2 immune response**, dysregulation of cytokine cascades, activation of eosinophils, and disturbances in neurogenic and endocrine regulation.

Thus, cytokines play an important role in the pathogenesis of bronchial asthma in children. However, data on the role of individual cytokines remain contradictory.

Despite progress in drug therapy, the number of patients with severe bronchial asthma continues to grow, which necessitates the development of new diagnostic and treatment methods.

The use of **immunomodulators** in children with respiratory allergic diseases has been studied. These drugs can reduce the activity of Th2 cells and increase Th1 activity, improving immune balance.

Clinical studies show that immunomodulators such as **IRS-19, Broncho-Vaxom, Ismigen, interferon preparations, Polyoxidonium, and Derinat** may reduce the frequency of exacerbations of bronchial asthma and acute respiratory infections in children.

Thus, the use of immunomodulators as part of complex therapy can **reduce the frequency of asthma exacerbations, prolong remission periods, decrease the incidence of respiratory infections, and positively influence immune responses in children with respiratory allergic diseases**.

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