

## NEW APPROACHES TO ANTIBACTERIAL TREATMENT OF CHRONIC LUNG DISEASES

**Annotation**

Chronic respiratory diseases, which began in childhood, are the cause of disability not only for children, but also for the adult population. Thus, according to the latest data, the incidence of obstructive pulmonary disease has increased by 3.2 times. Some mechanisms for the development of their progression in children have not been fully disclosed. In recent years, the number of antibiotic-resistant strains of microorganisms has increased, which contributes to the progression of lung tissue damage and worsens the prognosis of the disease. In solving the problem of the rationality of antibiotic therapy, an extremely important place is occupied by the issue of creating effective therapeutic concentrations of an antibiotic in a chronic focus of pulmonary inflammation. The effect of antimicrobial therapy is determined not only by the correct choice of the drug, but also by the method, its dose and frequency of administration. One of the effective methods that improve the results of treatment is physiotherapy procedures used in the complex treatment of CLD.

**Key words:** chronic lung diseases, patients, microbial flora, antibiotic therapy.

**Аннотация**

Хронические респираторные заболевания, начавшиеся в детстве, являются причиной инвалидности не только у детей, но и у взрослого населения. Так, по последним данным, заболеваемость обструктивными заболеваниями легких увеличилась в 3,2 раза. Некоторые механизмы развития их прогрессирования у детей до конца не изучены. В последние годы увеличилось количество антибиотикорезистентных штаммов микроорганизмов, что способствует прогрессированию повреждения легочной ткани и ухудшает прогноз заболевания. При решении проблемы рациональности антибиотикотерапии крайне важное место занимает вопрос создания эффективных терапевтических концентраций антибиотика в хроническом очаге воспаления легких. Эффект антимикробной терапии определяется не только правильным выбором препарата, но и методом, дозой и частотой его применения. Одним из эффективных методов, улучшающих результаты лечения, являются физиотерапевтические процедуры, применяемые в комплексном лечении ХЗЛ.

**Ключевые слова:** хронические заболевания легких, пациенты, микробная флора, антибиотикотерапия.

For more than 100 years, the attention of pediatricians has been attracted by the problem of treating chronic nonspecific lung diseases and their complications in children [1,5,9,10,13,21]. In modern conditions, the role of rehabilitation is increasing, since the reform of the healthcare system implies a reduction in the length of the patient's stay in the hospital and a shift in the

emphasis of medical care to the rehabilitation and outpatient stages [3,7,11,18]. Therefore, works devoted to the search for new treatment regimens for Chronic Lung Disease (CLD) in children are relevant for pulmonology.

Treatment of CLD is complex and includes antibiotic therapy, muco- and bronchodilators, vitamin therapy, kinesitherapy, physiotherapy, sports, and treatment of its complications. [4,6].

According to modern concepts, infection is the cause of exacerbation of CLD in 50-60% [2,14,20]. The problem of antibiotic therapy of chronic inflammatory lung diseases constantly attracts the attention of pediatricians. The detection of the causative agent of a bacterial infection in chronic inflammatory lung diseases is one of the main prerequisites for rational antibiotic therapy [6,8,10]. It should be noted that the spectrum of bacterial flora in chronic inflammatory lung diseases has changed significantly. *Staphylococcus* was previously the most common causative agent of pneumonia, according to most authors, today it has lost its primary role [4,10,15].

In the last decade, the results of bacteriological studies carried out in chronic lung diseases in children have shown a variety of isolated flora. Most often, *pneumococcus*, *influenza bacillus*, *staphylococcus*, *streptococcus* are found in the respiratory tract, less often other types of pathogens [4,16,17].

Studies of bronchial secretion samples, performed by a quantitative method using selective nutrient media for the isolation of pneumotropic pathogens, showed that the main etiological significant pathogen in chronic pyoinflammatory lung diseases in children is *pneumococcus*, isolated in monoculture and in association in 66% of patients, and *coli influenza*, which occupies the second place in the frequency of inoculation (45%) and occurs both in monoculture and in association with *pneumococcus* [19].

As observations show with a mild exacerbation of chronic bronchitis, the most common clinically significant microorganisms are non-typable and non-encapsulated forms of *H. Influenzae*, *S. Pneumoniae*, *M. Catarrhalis* [1,6]. With more severe exacerbations, often requiring hospitalization in intensive care units, the proportion of the above microorganisms decreases and the proportion of *H. Influenzae* producing  $\beta$ -lactamase, gram-negative bacteria, in particular various species of *Enterobacteriaceae*, *P. Aeruginosa*, increases.

According to Ageikin V.A. [1] in the sputum of patients with chronic inflammatory lung diseases in children, two predominant pathogens are found: *Haemophilus influenzae* in 60-70% and *pneumococcus* in 35-40% of patients. In a small number of children (5-10%) *Moraxella catarrhalis* is sown, which is sown both in monoculture and in associations. The author also claims that *Haemophilus influenzae* is sensitive to protected penicillins (amoxicillin), as well as cephalosporins of 2-3 generations.

The authors point out that serological research methods were not inferior to microbiological seeding in terms of sensitivity and specificity, and their complex use is most effective for determining the etiological significance of *Haemophilus influenzae* in the development of exacerbation of chronic bronchitis. The combined use of microbiological and immunological methods makes it possible to detect not only microorganisms, but also the products of their destruction and the reaction of the immune system to the corresponding irritation. Summarizing the above literature data, it can be noted that bacteriological monitoring in chronic inflammatory lung diseases in children is one of the criteria for the severity of the pathological process and helps to choose a rational antibiotic therapy regimen.

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One of the reasons for the transition of acute pneumonia to chronic is a decrease in the sensitivity of pathogens to antibiotics. This is due to the widespread use of various antibiotics, in connection with which the selection of resistant forms of microorganisms takes place [19].

Determining the sensitivity of the microbe to antibiotics is of particular importance in chronic inflammatory diseases of the lungs, in which, due to repeated and prolonged antibiotic

treatment, the sensitivity of the microbial flora often changes. The data of the above literature once again confirm that antibiotic therapy is the main method of treatment and elimination of exacerbation of chronic inflammatory lung diseases.

The basis for prescribing antibiotic therapy for chronic inflammatory lung diseases is the diagnosis of the infectious nature of the exacerbation, which meets the criteria of Anthoniesen N.R. et al. [21] the presence of 3 main signs: an increase in sputum volume, an increase in its "purulence" and an increase in shortness of breath (I type of exacerbation). An indication for the appointment of AP may also be the presence of two of the above signs (type II exacerbation), but purulent sputum should be a mandatory sign. The observations made by Stockley R.A. et al. showed that in chronic nonspecific lung diseases there is a close correlation between purulent sputum and the presence of microorganisms in it.

The effectiveness of antibiotic therapy in chronic inflammatory lung diseases remains an urgent problem. At the same time, it is known that the cure of a focal infection can be achieved only if the site of its direct action is adequately provided with an antibiotic. However, it is not easy to create the necessary therapeutic concentrations in the lung in chronic diseases, since drugs hardly penetrate into the foci of chronic infection. This is due to the development of pronounced fibro-sclerotic changes and impaired vascularization of the lung tissue, the presence of persistent bronchial dyscrinia and obstruction. Therefore, it is important to choose a method of therapy that maximizes the focus of inflammation in the lungs with antibacterial drugs.

Taking into account the prevailing pathogens and their drug sensitivity in chronic lung diseases in children, antibiotics of the penicillin and cephalosporin series, macrolides are used [2,6,11,12,18,21].

In the treatment of chronic inflammatory lung diseases in children and adolescents Volkov I.K., Katosova L.K. [13] give preference to parenteral administration of drugs and the appointment of the maximum allowable therapeutic doses. For this purpose, the authors used Rocephin in 67 children with COPD in children at a dose of 50-80 mg/kg once a day intravenously. The duration of the course ranged from 7 to 13 days. During treatment with Rocefin, complete eradication of *M. catarrhalis*, *S. Pneumoniae* and *S. Aureus* was noted. In 8.9% of patients, the seeding of *H. infuenzae* remained and in 2.9% of patients - *P. Aeruginosae*. Side effects were detected in 3% of children who had dizziness on the background of jet administration of the drug, in 3% of children - intestinal dysfunction, in 10.5% of patients an increase in the amount of *Candida* fungal flora in sputum was noted.

Bronchoscopic and intratracheal methods of drug administration significantly increase the effectiveness of therapy, especially in the bronchiectasis form of chronic pneumonia and in severe purulent lesions of the draining bronchus. In a very severe course of the disease, there is a positive experience with the introduction of antibiotics into the pulmonary artery system.

It has been established that the distribution of the antibiotic in the lungs depends on the nature of tracheobronchial secretion, on the partial binding of the drug to serum proteins and bronchial secretions, on the degree of endobronchitis activity and the individual characteristics of the child's body [11,21]. Inadequate concentration of antibiotics is one of the main components that adversely affect the results of the treatment of chronic lung diseases. [12,18,25].

In order to develop optimal antibiotic therapy regimens for chronic pneumonia in children during the period of maximum activity of the infectious-inflammatory process in the bronchi, intramuscular antibiotics were used for 10–12 days [2]. At the same time, the same drug in the average age daily dosage is administered endobronchially with an interval of 3 days. As the activity of endobronchitis subsided, the intramuscular administration of the antibiotic was canceled, and the drug was administered only endobronchially at the age-specific daily dosage after 5 days.

Traditional methods of antibiotic therapy do not always provide the desired results. This is due to the difficulty of eliminating the infection from the focus of chronic pulmonary inflammation, frequent relapses of bronchitis, a decrease in the activity of local airway protection factors and an increase in the number of antibiotic-resistant strains of microorganisms

(6,12,18,26). The parenteral route of administration of antibiotics does not allow to obtain the desired result, since the antibiotics circulating in the blood do not penetrate in the required amount through the fibrous-modified lung tissue into the focus of infection. The introduction of large doses of antibiotics does not solve the problem of treating chronic lung diseases in children. This increases the possibility of toxic and allergic reactions [12,21,24].

In recent years, endobronchial administration, ultraviolet laser irradiation, ozone therapy in combination with antibiotics, and subanesthetic endobronchial ultrasonic injection-aerosol spraying of antibiotics have begun to be used in the treatment of chronic pneumonia [2,11,19]. However, the widespread use of antibiotics has contributed to significant changes in the nature of the microbial flora. There is an increase in antibiotic-resistant strains of microorganisms and an increase in pathogenic properties and potentially pathogenic microorganisms [6,11,12,22]. All this requires a periodic review of some principles of antibiotic therapy, among which the principle of the effect of antibiotics on bronchopathogens is of particular importance.

Thus, one of the reasons for the low efficiency of traditional methods of antibiotic therapy is the impossibility of creating the optimal concentration of antibiotics in the lymphatic system, which is the main route for the spread of infection [2,11,18,19,23]. An attempt to create high concentrations of antibiotics in the lymphatic system by traditional methods is accompanied by toxic and allergic reactions, leading to immunodeficiency [2,12,16]. Therefore, the effect of antimicrobial therapy is determined not only by the correct choice of the drug, but also by the method, its dose and frequency of administration. One of the effective methods that improve the results of treatment is physiotherapy procedures used in the complex treatment of CLD. At present, the impact of ultrasonic (US) waves has become widely used. Ultrasound therapy has an anti-inflammatory effect, affects blood and lymph circulation, the state of nervous regulation, and proliferative-trophic processes in the body.

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