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MODERN METHODS OF IMMUNOTHERAPY OF OBSTRUCTIVE BRONCHITIS IN CHILDREN

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This monograph is devoted to the problems of obstructive forms of acute bronchitis (acute obstructive bronchitis, acute bronchiolitis) in young children. In the monograph, the author provides data on the important role in the development of broncho-obstructive syndrome of excessively high functional-metabolic activity of neutrophilic leukocytes, which is confirmed by a high level of chemiluminescence, and a direct correlation with the content of free and protein-bound oxyproline in blood plasma, reflecting a violation of collagen metabolism and the degree of destruction in the bronchopulmonary apparatus. The monograph is intended for pediatricians, general practitioners, masters and all those interested in this issue.

ISBN:

LIST OF ABBREVIATIONS

AOM - activated oxygen metabolites

ABL-antigen-binding lymphocytes

BOS-bronchial obstructive syndrome

BSOP-protein-bound hydroxyproline

Gl - glycogen

α-GPDH - α-glycerophosphate dehydrogenase

IL - interleukins

AI - absorption index

CP - cationic proteins

CK - creatine kinase

AP - acid phosphatase

MP - miyeloperoxidase

NL - neutrophilic leukocytes

NBT-test - nitroblue tetrazolium reduction test

AOB - acute obstructive bronchitis

AOBl - acute obstructive bronchiolitis

OP - oxyproline

PCP - percentage of completion of phagocytosis

SDH - succinate dehydrogenase

FOP - free oxyproline

FR - free radicals

FA - phagocytic activity

PI - phagocytic index

CL - chemiluminescence

ALP - alkaline phosphatase

INTRODUCTION

This monograph provides the reader with the opportunity to gain knowledge on issues of improving the quality of diagnostics and immunocorrection of children with acute obstructive bronchitis.

Respiratory diseases are an important problem in pediatrics, due to their leading role in the overall structure of childhood morbidity. The high prevalence of acute pathology of the upper and lower respiratory tract is a pressing social and important medical problem, especially among young children. Acute bronchitis has occupied and continues to occupy a leading position among acute pathologies of the respiratory tract. The review examines the data of domestic and foreign researchers on the issue of studying the prevalence, classification, and features of the course of acute bronchitis and bronchiolitis in children. Based on the nature of the bronchial lesion and the features of the clinical course, acute bronchitis, acute obstructive bronchitis and acute bronchiolitis. The clinical picture of acute bronchitis and bronchiolitis depends on the clinical form of the disease and the etiology of the disease. The most severe form is acute bronchiolitis, the main causative agent of which is the respiratory syncytial virus. Acute bronchitis affects children of all ages, but this pathology is more common in preschool and school-age children. Having studied the literature on this issue, it can be noted that the frequency of bronchitis and bronchiolitis in domestic and foreign literature coincides.

The indisputable advantage of the monograph is that it can be used as a reference by any doctor who encounters these diseases. The monograph is of interest to students of medical universities, general practitioners, and pediatricians.

CHAPTER I. MODERN CONCEPTS OF ACUTE OBSTRUCTIVE BRONCHITIS IN CHILDREN.

§ 1.1. Causal aspects of acute obstructive bronchitis in children at the present stage.

Today, respiratory diseases occupy the first place in childhood pathology, exerting a significant impact on infant mortality and the formation of persistent deviations in the health of children [5,7,59,80], among which a significant role is given to acute obstructive bronchitis, the frequency of which depends on the season, place of residence, and epidemiological situation [3,34,61]. Diseases of the lower respiratory tract are characterized by various clinical and morphological manifestations, which are caused by the anatomical and physiological characteristics of the child's body, often leading to bronchial obstruction and the etiologic agent of the disease. Often, broncho-obstructive syndrome is the initial manifestation of various pathological conditions of the respiratory organs, at the same time determining both the severity of the underlying disease and its prognosis [19,67,69,101]. According to a number of researchers, the development of acute obstructive pulmonary disease is significantly influenced by the premorbid background: allergic diseases, perinatal pathology of the central nervous system, rickets, nutritional disorders, poor feeding, frequent colds, hereditary pathology of the bronchopulmonary system [99,107]. According to Achilova D.N. (2019) and other researchers, an unfavorable environmental situation and parental smoking in the family contribute to the development of acute obstructive pulmonary disease. Under the influence of tobacco smoke, hypersecretion of the bronchial glands of the bronchial mucosa increases, resulting in impaired mucociliary clearance, resulting in a slowdown in the outflow of mucus through the bronchi and the destruction of the bronchial epithelium [3,120,121]. Currently, an unfavorable environmental situation is a fairly important etiological factor in the formation

of acute obstructive pulmonary disease in children [80,104]. There are studies that prove that children whose parents abused alcohol may develop fetal alcohol syndrome, in which bronchial tone decreases or disappears completely, mucociliary clearance is impaired, immunological responses slow down, and protective development contributes to the development of broncho-obstructive syndrome. Organic and inorganic substances in the environment have a toxic, sensitizing effect on the mucous membrane of the respiratory tract, contributing to respiratory pathology. In young children, the high incidence of respiratory infections is due to the degree of development of the immune system, high contagiousness with viral agents, and the immaturity and instability of immunity to them [3,62,64,118]. It is generally accepted that the main etiological factors for the development of acute respiratory obstruction in children are respiratory viral infections [6,23,68]. Acute obstructive disease, mainly bronchitis, is caused by multifactorial pathogenic microorganisms, as well as chemical and physical factors [7,44,57,59]. Many authors in their scientific papers indicate that during epidemic outbreaks of acute respiratory viral infections, the incidence rates of acute obstructive bronchitis in children reach peak values [50,69,79,83, 96]. In most preschool children, subsequent acute respiratory viral infections after acute obstructive bronchitis occur with symptoms of broncho-obstructive syndrome, that is, the disease often becomes recurrent [109]. 15 Recently, in 30-50% of cases, acute obstructive bronchitis becomes recurrent, and in 15-30%, bronchial asthma develops [71,110,116,119]. The term “atypical pathogens” first appeared in pulmonology and eventually was introduced into other areas of medicine. Diseases caused by atypical microflora, in particular Chl. Pneumoniae and Myc. Pneumoniae, were characterized by an atypical course of clinical symptoms, with mild clinical, auscultatory, radiological and laboratory indicators that were not amenable to therapy with cephalosporin antibiotics

[75,76,110,113]. The etiological role of atypical microflora in the development of acute obstructive pulmonary disease is to a certain extent due to the intracellular existence of these pathogens [11,16,20,26,32,33,41]. character As a result of numerous studies, the structure and morphology of atypical pathogens were identified, pathogenicity factors were studied, the taxonomic position of the pathogen was determined, the features of clinical manifestations, course options, as well as the principles of therapy were determined, so each of these infections began to acquire its characteristic classical features and a certain clinical picture [25,51,55,58]. Nowadays, chlamydia and mycoplasmosis remain one of the most common infectious diseases in the world [72,110,109,111,117]. Analysis of foreign and domestic literature on the role of viral and atypical bacterial pathogens in the development of acute obstructive bronchitis in preschool children showed that the most common of them are chlamydial, mycoplasmal, respiratory syncytial virus infections. An important feature is mixed infections and they account for 20 to 70% of the disease, the layering of which can be accompanied by a severe course of the disease [106,109,120]. 16 Chl. pneumoniae and Myc. pneumoniae are intracellular pathogens, occupying the second and third place in the number of pathogens of acute respiratory infections and often become chronic (74%) and lead to a severe course of the disease [21], due to long-term persistence and a tendency to recurrence of the inflammatory process in the bronchi [65,66]. Chl. pneumoniae and Myc. pneumoniae, when affecting the respiratory tract, often lead to a protracted course, block and paralyze the mechanisms of mucociliary clearance, contributing to an increase in bronchial reactivity and disrupt immunoregulation [80,82,89,90]. In women of childbearing age and pregnant women, the high prevalence of urogenital tract diseases caused by chlamydial and mycoplasmal infections may result in high infection rates with these microorganisms in young children, which may create

conditions conducive to the development of diseases in newborns and early childhood [94,97,104,106]. Despite the research findings on respiratory diseases of mycoplasmal etiology, the subject remains relevant in pediatrics. The achievements of many years of research into Myc. Pneumoniae have made it possible to explain many of the features of mycoplasma infection. M. Pneumoniae is specific in that the human body does not always recognize the antigenic structure of the agent. There is currently compelling evidence on the formation of acute respiratory viral infections in respiratory mycoplasmosis [75,86,87,95, 96,110,117,119,120]. The entry points for M. Pneumoniae are the mucous membranes of the upper respiratory tract, and in respiratory mycoplasmosis, a significant decrease in the cleansing function of the respiratory tract from mucus and other foreign microflora is observed for a period of 1 to 3 years after the disease, as well as a decrease in the functional system of the respiratory tract and mucociliary activity of the bronchial epithelium, which increases the degree of invasiveness of the agent, leads to the formation of reinfection and penetration of pathogenic microflora, mixed infection [13,24,78]. Romanovskaya O.F. et al. cite data in their works that M. Pneumoniae are prokaryotes and opportunistic microorganisms, their small size, small genome, and lack of a rigid cell wall, this ability makes them more protected from the effects of both humoral and cellular immune defense mechanisms of the body. The absence of a rigid cell wall of this pathogen determines not only their cell polymorphism, but also their resistance to penicillin antibiotics [57,74,75]. G.A. Samsygina (2019) indicate that coinfections of M. pneumoniae and RS virus lead to more pronounced histological changes with destruction of the tracheal epithelium. The chlamydial- mycoplasmal association, in turn, is characterized by a more severe course, in which the mechanisms of such mutual influence remain undisclosed [80]. Myc. pneumoniae differs from Chl. pneumoniae in that they

parasitize the eukaryotic membrane, which determines the pathogenesis of the disease. Currently, more than 100 species of Myc. pneumoniae are known, of which 14 species affect the human body. However, Myc is of particular interest. Pneumoniae, which has the highest pathogenicity, is the causative agent of respiratory mycoplasmosis, accounting for up to 16% of acute respiratory diseases in children [78,79,98]. Mycoplasma infection predominates in preschool and school-age children and is recorded in 9.8% of children under 1 year of age, in 21.1% of 1-2 year-olds, in 44.4% of 3-6 year-olds, and in 61.6% of children over 7 years of age. The disease occurs year-round; its incidence is considered rare in summer. The source of infection is patients in the acute phase of the disease or people with asymptomatic course of the disease. Route of transmission: airborne, the incubation period is on average 3-11 days (sometimes up to 3 weeks). A child can become infected from an infected mother during childbirth, passing through the "infected" birth canal. Mycoplasma infections progress differently in children and adults. For example, in children, the bronchopulmonary tree is most often affected, with inflammation of the pharynx, nose, bronchi, and lungs developing. The incidence and severity of the disease depend primarily on the state of the child's immune system; children with "low immunity" infected with Myc. Pneumoniae are more likely to become ill and have a more severe course of the disease. Children can usually become infected with mycoplasma in preschools, schools, or in crowded places, transmitted by airborne droplets [12,42,63,75]. After infection with mycoplasma, the body develops specific humoral and cellular immune responses aimed at eliminating the pathogen. However, the resulting immunity is short-lived, which means that reinfection cannot be ruled out [13,21]. In recent decades, studies have shown significant changes in the microbial spectrum of respiratory tract infections, as well as an increasing role of Chl. Pneumoniae in the development of acute respiratory

infections [8,9]. Infection with Chl. pneumoniae usually occurs in preschool and school age, and reinfection can occur at any period of subsequent life. In children aged 5-14 years, Chl . Pneumoniae is the etiologic agent of acute respiratory infections in 21-35% of cases, and in adolescents and individuals aged 19-23 years - in 16-20% of cases [21,26,37,76]. There are studies indicating that Chl. pneumoniae, due to its high tropism for the epithelium of the respiratory tract, disrupts protective functions, contributing to the risk of infection of the bronchi by pathogenic microorganisms, penetration of allergens and toxic substances through the bronchial mucosa. The main feature is that the structure of the cell wall of Chl. Chl. pneumoniae has some similarities with gram-negative bacteria. As mentioned above, Chl. pneumoniae have affinity for the villous epithelium of the bronchi and completely immobilize the villi within 48 hours after infection. At the same time, manifestations of acute respiratory infections are possible in the clinical picture [41,46,48]. In recent years, the importance of Chl. pneumoniae in the structure of respiratory infections in children has increased. The causative agent is low in toxicity, therefore, as the disease develops, symptoms of toxicosis are not expressed. Characteristic signs are a prolonged cough (up to several weeks), which can be paroxysmal. Moist rales of different calibers are heard on auscultation. Radiologically, an increase in the pulmonary pattern and infiltrative opacities are detected. Infection of children most often occurs from mothers suffering from urogenital chlamydia, which can be a source of infection for children, which can serve as a differential diagnostic criterion for the disease [57,58,59]. After mycoplasma or chlamydial infection, children experience repeated respiratory infections, often accompanied by biological reactions and a protracted, recurrent course. This fact is likely associated with altered immunological reactivity and decreased resistance to pathogens that arise during the disease, creating a favorable environment for the persistence

of microorganisms, contributing to chronicity and the development of a complicated course of the disease. Antibacterial therapy for the disease in most patients, while temporarily suppressing the activity and growth of pathogens, does not contribute to the correction of the resulting immunological changes, increasing the likelihood of a recurrent course of the disease. Most authors prove that acute obstructive pulmonary disease caused by chlamydial and mycoplasmal infections is characterized by a severe course of the disease, but the mechanisms leading to a severe course remain not fully understood, and problems associated with diagnosis and treatment persist [51,63,71,72,78,86,90]. Of interest is the further study of risk factors and clinical and immunological features of acute obstructive pulmonary disease with atypical microflora in children, which requires further research using modern diagnostic criteria that allow their use to justify the examination [81,100,116]. Thus, there is no doubt that further study of the impact of atypical microflora (Myc. pneumoniae, Chl. pneumoniae) on the clinical and immunological picture of acute obstructive pulmonary disease in childhood is necessary.

§ 1.2. Clinical course of acute obstructive bronchitis in children depending on etiological factors.

It is well known that the inflammatory process in the bronchi in young children is manifested mainly by acute obstructive bronchitis and acute bronchiolitis [6]. Acute obstructive bronchitis is characterized by inflammation of the bronchial mucosa and development due to deeper edema and hyperplasia of the mucous membrane, obstruction of the airways, hypersecretion of mucus or the development of bronchospasm. In preschool children, obstruction is mainly caused by hypersecretion of viscous and thick mucus, as well as hyperplasia of the mucous membrane. Bronchospasm is more pronounced in children over 4 years of age [5,6,7,108]. It should be

emphasized that most researchers evaluate broncho-obstructive syndrome as a pathophysiological concept characterizing the violation of bronchial conductivity against the background of acute and chronic respiratory diseases [2,15]. In the English-language literature, bronchial obstruction is referred to as "wheezing" - wheezing syndrome [40,103]. AOB is characterized by the development of obstructive syndrome on days 1-3, with catarrhal manifestations. A painful spasmodic cough lasting about 10-14 days, expiratory dyspnea, noisy, wheezing breathing, and oral wheezing are the main clinical symptoms of the disease. In young children, the clinical picture of AOB is characterized by a syndrome of impaired bronchial patency with the presence of unproductive cough, pronounced catarrhal manifestations, dyspnea of a mixed or expiratory nature, a box-like sound is noted on percussion, and upon auscultation, the phenomenon of prolonged expiration, expiratory dry wheezing, and sometimes various-caliber wet rales of a diffuse nature. Localization of auscultatory changes is most often detected bilaterally; in 8-10% of subjects, localization of auscultatory changes in the axillary and subscapular regions is possible. BOS lasts 4-10 days, with gradual disappearance, parallel to the elimination of physical changes in the lungs [2,3,5,19,24,50]. Acute obstructive bronchitis is clinically characterized by symptoms of respiratory failure: expiratory dyspnea, distant wheezing, cyanosis of the nasolabial triangle, retraction of the intercostal spaces, involvement of the accessory muscles of the lungs. Most often, the disease begins gradually against the background of a satisfactory general condition of the child with an infrequent dry cough. An increase in temperature, an increase in catarrhal phenomena and the development of respiratory failure are recorded on the 2-3 day from the onset of the disease. A constant symptom in this category of patients is an abundance of moist and crepitant rales on inspiration and dry wheezing on expiration throughout the lung fields. Perioral or

generalized cyanosis, distant wheezing are one of the important signs of obstructive bronchitis. The severity of the disease determines the severity of the disease. The course of the respiratory infection determines the intensity of the intoxication syndrome and the temperature curve [67,69,70,79,80,85,93]. 22 Regardless of the etiologic factor, the main clinical manifestations of BOS are a painful cough with scanty sputum, expiratory dyspnea with a sonorous wheezing, a symptom complex of respiratory failure, the appearance of dry wheezing and wet wheezing of various sizes in the lungs [18,40,44,59]. In children of the first months of life, acute obstructive bronchitis is severe, often with the development of acute respiratory failure grade II-III, which has a high probability of a fatal outcome, amounting to up to 1% in respiratory syncytial infection, and up to 4-7% of the number of hospitalized patients in parainfluenza and adenovirus infections. In children aged 5-7 years, repeated cases of development of acute obstructive bronchitis reach up to 50% [43,101]. Despite all the studies on the formation of acute obstructive bronchitis in children, the question of the causes of its relapses remains open. The issues of studying the risk factors for the occurrence, age-related and clinical characteristics of the course of acute obstructive bronchitis depending on the etiology of the atypical infection remain poorly studied [64]. The significance of clinical and immunological characteristics of the course of mixed viral-bacterial infections, including the main agents in the etiological structure of recurrent obstructive bronchitis in children, has not been determined [7,47,55]. Thus, the presented results of scientific research in the field of acute obstructive bronchitis of atypical etiology are diverse and contradictory. There are few studies in the available literature on the regional patterns of respiratory infections, including those associated with acute respiratory viral infections. When confirming a diagnosis, while prioritizing laboratory diagnostic methods

for atypical infections, we often encounter ambiguous clinical results, which are the target of further research.

§ 1.3. Laboratory and instrumental diagnostics of bronchial obstruction in children.

Generally accepted laboratory and instrumental methods are used to diagnose bronchial obstruction syndrome. To determine and clarify the severity of broncho-obstruction, an assessment of the functional state of the lungs is carried out. In addition to functional methods for the differential diagnosis of bronchial obstruction, spirography methods are used. However, spirography is limited in pediatric practice, especially in young children, since it requires the active participation of the child in the examination [111,114,119]. The peak flowmetry method is simple to perform, can be used in outpatient settings, by determining the volumetric air velocity during forced expiration, allows you to predict BOS before clinical manifestations, which can be used in disease monitoring [56,113]. Just like the spirography method, the use of peak flowmetry is limited by the age range of children (not earlier than 6 years) [65,81]. A method of bronchophonography which is based on the analysis of the amplitude- frequency characteristics of the respiratory noise spectrum by recording 28 curves of acoustic noise arising during breathing, with subsequent mathematical processing. The method allows to expand the functional assessment of the lungs obtained by routine examination methods, to objectively assess the severity of bronchial obstruction syndrome in children [18,19]. The results of the study in children showed the high information content of bronchophonography in children, primarily with obstructive disorders in the respiratory system. The features and patterns of distribution of bronchophonography indicators depending on gender, age and nosological form of the disease have been established [45]. The X-ray picture of the lungs in BOS is not specific, changes characteristic of the underlying disease are

determined (bronchitis, bronchiolitis, bronchial asthma) [5, 12,81.]. In the study of sputum in bronchitis in children aged 3-6 years, the growth of Staphylococcus was determined aureus, at the age of 7-12 years - Streptococcus pneumonia, at the age of 13-18 years – Staphylococcus aureus. The data obtained can be used to select treatment tactics for this pathology. In the acute phase of BOS, sputum microscopy can reveal eosinophils and neutrophils [89]. Thus, the diagnosis of acute obstructive bronchitis with atypical microflora in children should be comprehensive. Currently available diagnostic methods are highly specific and sensitive, allowing for verification of the etiology of the disease and the possibility of early initiation of etiotropic treatment to improve the prognosis.

CHAPTER II. CLINICAL ASPECTS AND IMMUNOMODULATORY THERAPY OF YOUNG CHILDREN WITH BRONCHO-OBSTRUCTIVE SYNDROME

§ 2.1. Immunological aspects of acute obstructive bronchitis in children.

Modern aspects of the etiology and pathogenesis of acute obstructive bronchitis take into account the development of a pathological inflammatory process in the bronchi as a result of exposure to external and internal environmental factors, mainly infectious ones; the immunoregulatory mechanisms of the body are of great importance [69,73]. At present, the study of cytokine regulation in various pathological conditions, including respiratory diseases, remains relevant [61,62]. Cytokine profile indicators are fundamentally important for clarifying the most important pathogenetic links of acute obstructive bronchitis in children, which are necessary for improving the diagnostic and prognostic criteria of the disease, which is necessary for conducting optimal immunocorrective therapy. The regulatory function of cytokines is to regulate embryogenesis, including the immune system, the regulation of the main physiological functions of the body; regulation of the body's defense reactions and regulation of tissue regeneration processes. Cytokines, interacting with other links of the immune system improve metabolic processes of the body, which reflects the state of the immune response. Blood cytokines bind to specific receptors damaging the cytoplasmic membrane of cells, causing a cascade of pathological reactions, lead to strengthening or suppression of the activity of regulated genes [1,17,25]. In infectious and inflammatory processes occurring in respiratory pathology, cytokines affect the formation of the pathological process. Cytokines formed in the cells of the immune system perform a mediator function, 24 intercellular cooperation, thereby participating in and regulating the inflammatory and immune response [25]. There are several types of cytokines: 1. Interleukins -

they perform humoral communication between leukocytes; 2. Interferons - they protect the body from viruses; 3. Colony-stimulating factors - they are necessary for the production of formed elements of the blood; 4. Tumor necrosis factors perform anti-inflammatory, immunostimulating and hematopoietic functions; 5. Factors that transform cell growth, which have anti-inflammatory properties, inhibit antibody formation and differentiation of cytotoxic cells; 6. Growth factors, including fibroblast , epidermal and platelet growth factors, regeneration of damaged tissues. Depending on the function, cytokines are divided into 2 groups: anti-inflammatory (IL-4, IL-10, IL-2, IFN-γ) and pro-inflammatory (IL-6, IL-8, TNF-a), and pathogenic microorganisms and allergens affect the state of the cytokine status. Thus, the indicators of the cytokine status reflect the state of the immune response and the body's defensive response [28,34,36]. The basis of the pathogenesis of the impact of atypical infections is the launch of the cytokine cascade, in the form of proinflammatory and anti-inflammatory cytokines, the balance of which determines the characteristics of the course and prognosis of diseases [13,20.] To date, the immunoregulatory functions of the main cytokines in various infectious diseases have been studied in sufficient detail [110]. In obstructive bronchitis, which is characterized by the development of bronchial obstruction, pathogenic microorganisms, when interacting with macrophages, affect the balance of cytokines [1]. 25 Currently, the role of the cytokine profile in obstructive bronchitis of atypical etiology in children has been practically not studied. However, the study of cytokine indicators is significant for determining the various links in pathogenesis and improves diagnostic capabilities in obstructive bronchitis in children. Determination of immune changes in obstructive bronchitis can be quite significant criteria for conducting optimal immunocorrective therapy. The study of these issues allows us to determine the risk groups for recurrent course in children with

newly developed acute obstructive bronchitis, which would determine the approach to optimal methods of anti-relapse treatment in children [10,23,60]. The most important role in the pathogenesis of the disease belongs to the activation of inflammatory mediators, including interleukins, which stimulate the activation of mast cells, basophils, eosinophils and B cells [11,69]. In recent years, the study of the importance of interleukins in the development of recurrent course of acute obstructive bronchitis has continued. In children, high levels of IL-8 and IFN-β are determined in acute obstructive bronchitis, which indicates the predominance of the cellular phase of the immune response over the humoral one. The presented data indicate that high values of IL-6 and IL-8 may be immunological markers of acute obstructive bronchitis, which confirms the importance of cytokines in the pathogenesis of bronchial obstruction [15]. A study of proinflammatory cytokines showed that in children with acute respiratory viral infections, the levels of IL-8, IL-1β and IL-4 were increased, while IFN α was decreased, indicating suppression of cellular mechanisms of the immune status [34,36]. IL-6 promotes the proliferation of thymocytes and B lymphocytes, activating the formation of inflammatory phase proteins [1,119]. In viremia, IFNα differentiates antigen-activated T helpers into Th1 cells , which are responsible for the cellular immune response, thus creating antiviral protection. Another type of interferon, IFN 26γ, leads to the activation of macrophages, increases the production of anti-inflammatory cytokines and is an antagonist of IL-4, which promotes the synthesis of IgE. It is believed that changes in interferonogenesis are detected during respiratory viral infections [22,31]. IFNα, being one of the factors of the innate immune response of the organism, reacts to the introduction of the virus, performing a regulatory function in maintaining homeostasis in the human body. IFNα, due to the direct antiviral effect, suppresses the growth and development of intracellular microorganisms,

subsequently exerting an immunoregulatory effect, preventing apoptosis, which leads to the differentiation of antigen-activated T-helpers, promoting the maturation of functionally active antigen- presenting dendritic cells [35,39]. Undoubtedly, it is necessary to take into account the fact that chlamydia themselves can alter the reactivity of the host organism to pathogens and thereby can influence the course of the infectious process and the outcome of the disease [21]. Many foreign authors cite the results of laboratory data of patients with chlamydial infection. In the general blood test, a relative decrease in the number of neutrophils and lymphocytes, as well as a decrease in the monocytic- lymphocyte ratio are noted [26,41]. It has been proven that with respiratory chlamydia, local production of secretory IgA, activation of cytotoxic T-lymphocytes and the formation of antibodies of the IgM, IgA, IgG classes to the chlamydial antigen develop [35,39]. When determining the nature of immunological disorders (IgA, IgG, IgM) in children with acute obstructive bronchitis and evaluating immunocorrection with the drug ismigen, a violation of the immunological reactivity of the body was revealed and the effectiveness of therapy in relation to the state of the immune system in children was shown [35,39]. When treating bronchopulmonary pathology in children, it is necessary to take into account the pathogenetic focus, in this regard, it is necessary to take into account the main indicators of the immune status of the body [36]. 27 Interferons are produced and found in all nucleated cells of the blood and mucous membranes, and are constant natural factors in human anti-infective defense, including immunostimulating and antiviral mechanisms [68,83]. When analyzing the interferon status in respiratory viral infections, it was proven that recombinant interferon alpha 2b with antioxidants allows for the normalization of the level of IFNα production, with an increase in the synthesis of IFN-γ [84,91]. Thus, existing studies on the role of cytokine status in acute obstructive bronchitis in children, depending on the

etiological factor, indicate the inconsistency of the results obtained and the need for further study of the issue.

§ 2.2. Modern aspects of clinical immunomodulatory therapy of young children with broncho-obstructive syndrome.

The fight against ARVI, as follows from the literature, is one of the priority tasks in the Republic of Uzbekistan in the field of pediatrics. Young children are especially sensitive to ARVI, they get sick 3 times more often than preschool children, and 5 times more often than adults. According to M.M. Khaidarova, in 45% of young children, cases of ARVI are complicated by bronchopulmonary diseases. According to official statistical reporting with a cumulative total since the beginning of the year, the share of causes of death of newborns in the republic was from respiratory distress syndrome, in 2018 - 47.1%, in 2019 - 13.08%, at the age of up to one year, ARVI - in 2018 23.55%, in 2019 - 23.38%.

At the same time, as follows from the literature, there is a stable tendency to increase the frequency of BOS cases in ARVI, bronchiolitis, bronchitis, pneumonia, bronchial asthma, as well as against the background of congenital and hereditary pathology. According to various authors, the frequency of BOS in ARVI is up to 25%. The prevalence of BOS in ARVI in Uzbekistan ranges from 10 to 40%. The relevance of studying BOS is associated not only with its increasing frequency (27-31%) in ARVI in young children, frequent relapses of bronchial obstruction in them, but also with the complexity of therapy and often refractoriness to it.

Some authors note that ARVI is more often complicated by bronchitis and bronchiolitis than by pneumonia, which at the beginning of the disease can sometimes be difficult to distinguish from pneumonia. Hyperdiagnosis of pneumonia is accompanied by unjustifiably excessive hospitalization of children, and even powerful antibacterial treatment, which is unnecessary for

bronchitis. At the same time, it is indicated that among acute bronchopulmonary diseases of viral origin, bronchitis accounts for 30-40%.

Environmental problems are an important factor in increasing the frequency of BOS. Thus, E.A. Lyutaya (2010) during examination of 126 children aged 1 to 14 years admitted to the allergology department of the Tashkent Pediatric Medical Institute from the ecologically unfavorable district of Chirchik, in comparison with 120 children of the same age living in the Yunus-Abad district of Tashkent, where there are no large industrial enterprises, revealed that the frequency of BOS in young children under 3 years in Chirchik was 88.6 %, in Tashkent 78.2%, bronchiolitis, respectively 6.4 and 5.4%. It was also established that the course of diseases with broncho-obstructive syndrome in children living in an unfavorable area differs from that in the control group by a more pronounced severity and sluggishness.

Many authors believe that circadian fluctuations in the secretory activity of peripheral glands play an important role in the development of broncho-obstructive pulmonary diseases.

Some authors note that children with AOB have an aggravated premorbid background - allergic diathesis was found in 46.7% of children, unfavorable obstetric history - in 89.5%, anemia - in 93.5%, rickets - in 67.8%, and hypotrophy - in 11.3%. Most children (72.3%) were admitted to the clinic in the first 3 days from the onset of the disease and almost all in the first 2-3 days after the onset of acute obstructive bronchitis. Severe broncho-obstruction syndrome was observed in 70.5% of patients: pronounced expiratory dyspnea, wheezing, tachypnea (more than 60 breaths per 1 min.), perioral cyanosis, profuse wheezing, often fine bubbling rales in the lungs. The authors believe that the pathogenetic and clinical essence of the obstructive syndrome is close to asthmatic bronchitis and bronchial asthma. A proposal is made to consider children with BOS as threatened by bronchial asthma, considering it a “pre-

asthma" condition, with the resulting conclusions about the need to carry out appropriate treatment and preventive measures.

Other authors share the same opinion. At the same time, some authors categorically object to considering BOS as a clinical manifestation of pre-asthma. At the same time, they point out that, whatever the triggers - allergic, infectious, etc., the most probable factors in BOS, as follows from the definition, will be bronchospasm, edema and hypersecretion. Therefore, the main therapeutic measures in BOS are aimed at relieving bronchospasm, eliminating edema, reducing hypersecretion and improving the rheological properties of bronchial secretions.

Currently, a new classification of clinical forms of bronchopulmonary diseases in children is used, adopted in Moscow at a symposium on improving the classification of non-specific lung diseases in children and confirmed at the 11th International Congress of Pulmonologists of Central Asia, as well as on September 19-23, 1998, at the Congress of the European Respiratory societies (European Respiratory Society-ERS), whose representative from the CIS countries, in particular Uzbekistan, was Academician A.M. Ubaidullaev, as well as other leading pulmonologists of the republic.

According to this classification, acute bronchitis with obstructive syndrome and acute obstructive bronchitis are distinguished as independent forms of bronchitis. It is emphasized that acute bronchitis with obstructive syndrome is an acute form of bronchitis with obstructive syndrome, characterized by prolonged and difficult exhalation and noisy breathing. Acute bronchitis with obstructive syndrome is a severe form of acute bronchitis with obstructive syndrome and severe respiratory failure caused by obstruction of small bronchi. In radiographs of patients with acute bronchitis with obstructive syndrome and acute obstructive bronchitis, focal and infiltrative shadows are absent. It should be noted that most foreign authors consider all cases of acute

bronchitis with obstructive syndrome to be acute bronchitis with obstructive syndrome, while acute bronchitis is not distinguished separately as a form of the disease.

Among the main etiologic factors of respiratory infections associated with the development of BOS are respiratory syncytial viruses (RS viruses), influenza and parainfluenza viruses. They contribute to the disruption of the mucous epithelium of the bronchi and the penetration of inflammatory factors through the mucous membrane barrier. There is convincing evidence that RS viruses have the ability to persist in the blood for a long time, which contributes to the sensitization of the body. Most patients have an increased tendency to recurrence of bronchial obstruction with another acute respiratory viral infection, and some - later and in response to non-infectious allergens.

And analyzing the WHO data, it was noted that 1/3 of fatal outcomes in young children are due to respiratory diseases. The leading place among them is occupied by the RS virus and parainfluenza viruses of 1, 2, 3 strains, and the RS virus affects 11-25% of children in the first year of life and 43-50% of the second year of life. Epidemic serotypes of adenoviruses affect mainly children under 3 years of age.

As follows from the literature data of the last decade, most authors adhere to the unanimous opinion that AOB and AOBl are mainly caused by the RS virus, adenovirus, parainfluenza virus and, less frequently, by the influenza virus, rhinovirus, and herpes virus. In some studies, the RS viral nature of bronchiolitis is established in 45% of sick children. Other authors, when examining newborns with bronchiolitis, confirmed the RS viral etiology of the disease in 69.5%.

Sharma B. S. and co-authors in their studies showed that BOS is observed in 91% of cases with PC -virus infection, in 50% with adenovirus infection, and in 45% with parainfluenza infection. Zhang L. with a group of

authors, It was established that with PC virus infection, bronchiolitis mainly develops, and adenovirus infection is often combined with pneumonia.

Some authors are inclined to believe that obstructive syndrome in ARVI is the main cause of the severity of the disease and the occurrence of respiratory failure. Due to thickening of the walls of small bronchi due to inflammatory edema and infiltration, hypersecretion and accumulation of secretions, their lumen narrows, which leads to a sharp increase in respiratory resistance, impaired bronchial patency and alveolar ventilation. Maintaining an adequate minute volume of breathing in the acute period of the disease is achieved by increasing the frequency of breathing with a decrease in the respiratory volume.

A number of researchers associate the development of acute obstruction syndrome in acute respiratory viral infections with the appearance of bronchospasm.

In the opinion of Simonova O.I., Gorinova Yu.V., Bakradze M.D. Narrow airways and pliability of bronchial walls contribute to the development of broncho-obstruction syndrome in young children. Narrower airways are more easily affected by mucosal hyperplasia, edema, and hypersecretion than wide ones, which increases bronchial resistance. This process is facilitated by physical data - in children under 3 years of age, the pectoral muscles are poorly developed, so they cannot play a major role in the development of bronchospasm in bronchiolitis.

When analyzing the literature, it was noted that for the diagnosis of bronchial obstruction, the presence of symptoms such as retraction of the compliant areas of the chest during breathing (especially in the area of the jugular fossa), cyanosis, and distinct swelling of the lungs during X-ray examinations are necessary.

Some authors indicate that the severity and clinical form of non-specific diseases of the bronchopulmonary system in children, including the development of acute obstructive pulmonary disease, are largely determined by morphofunctional disorders of various organs and systems, and primarily by the state of higher mechanisms (sympathetic-adrenal, parasympathetic and humoral) of the autonomic nervous system. It is indicated that the parasympathetic phase is characterized by reparative-anabolic processes that are controlled by the insular apparatus of the pancreas, STH, ACTH, ADH, etc. The reparative-metabolic focus of this phase is reflected in the structural-functional stabilization of various organs and systems, primarily at the bronchopulmonary level.

The originality of the solution to this issue lies in the fact that the author proposes to treat diseases of the bronchopulmonary system in depending on the predominance of the tone of the nervous system. Thus, in the sympathetic-adrenal phase, many authors recommend using drugs with antioxidant, antiphospholipase action, NSAIDs, dosage forms that improve the rheological properties of blood, the microcirculation system, membrane stabilizers, bronchorrhea stimulants, as well as drugs that block the pathophysiological effects of sympathetic vegetative- visceral shifts in the body of children. In the parasympathetic phase, the author suggests using anticholinergic drugs (possibly in combination with sympathotonic drugs), dosage forms with a broad metabolic effect and, first of all, stabilizers of the structural and functional organization of cell membranes, as well as agents that improve the properties of bronchial secretions and the function of mucociliary clearance, immunomodulators.

A.N. Kokosova revealed the relationship between vegetative homeostasis and broncho-obstructive syndrome. It was established that the drug saltos had a more pronounced therapeutic effect in patients with a

moderate sympathetic nervous system (72%) than in patients with vegetative balance (34%). The importance of prescribing membrane stabilizers, antioxidants is based on the possibility of a key role of lipid peroxidation (LPO) processes in damaging cell membranes, inhibiting membrane-dependent enzyme complexes, developing inflammation and broncho-obstruction.

E.A.Kharabadzhakhyan, A.Yu.Antipov, when examining 60 children suffering from obstructive bronchitis, revealed a significant imbalance in the LPO system and antioxidant protection in peripheral blood leukocytes before and after treatment. Clinical observations made it possible to the conclusion that during the treatment with antioxidants (vitamin E and Essentiale) on the 3-4th day there was a significant decrease in cough, sputum production, the number of moist rales in the lungs, and an improvement in the well-being of children. Clinical recovery was also observed 3-4 days earlier than when treating children with traditional methods.

S.S.Shchuka, studying the features of endoscopic and cytomorphological changes during the period of exacerbation of recurrent obstructive bronchitis, revealed a connection between disorders in the bronchi and the secretory function of the bronchial tract and destructive processes in the ciliated epithelium of the bronchi. It was established that the low content of alveolar macrophages in the bronchial secretion in the examined children indicates a decrease in local protective properties, contributing to the recurrent nature of the inflammatory process in the bronchi.

It should be noted that the inflammatory process in the bronchi during broncho-obstruction develops in response to the effects of various damaging agents, the most common of which are microorganisms, their exo- and endotoxins, other aggressive factors, components of the bacterial cell wall (lipopolysaccharides, peptidoglycans, taichoic acids).

According to L.R. Sha-Akhmedova et al., the development of BOS in children is influenced by nutritional factors, as well as anamnestic data on the pathological course of pregnancy (in 92% of mothers), colds (in 48% of women) and improper nutrition of women during pregnancy (in 72.7%). In 60 **%** cases of BOS developed as a result of severe nutritional disorders: young children were given citrus juices, strawberries, bread, cookies, and whole cow's milk too early.

The basis of bronchial damage under the action of these etiologic factors is the inflammatory reaction, which prevails over all others in acute obstructive bronchitis. At the height of broncho-obstruction, the adequacy of the reaction is regulated by intercellular interactions through the synthesis of various mediators, including cytokines, interleukins (IL), growth factors and expression of their receptors, as well as through direct intercellular contacts, which creates powerful para- and autocrine regulation loops.

According to some authors The initial stage of broncho-obstruction in acute obstructive bronchitis is a mediator reaction, which breaks down into two links - neuro- and lipid-mediator, the final result of which is considered to be a change in the microcirculatory bed, increased emigration of leukocytes and their chemotaxis into the forming focus of inflammation.

It has been recently established that in the first seconds after the development of broncho-obstruction in the experiment, sensory peptidergic nerve fibers involved in nodiception secrete special sensory neuropeptides: substance P, calcitonin-related gene peptide, and protein gene peptide. These substances have a powerful vasodilatory effect, induce expression of intercellular adhesion molecules (ICAM -1, IV CAM - I) on the surface of leukocytes and endothelial cells, thereby facilitating leukocyte migration. It has been noted that under the influence of sensory neuropeptides, accumulation of neutrophils, macrophages, and T-lymphocytes in the inflammation focus

sharply increases. Calcitonin-related gene peptide stimulates endothelial cell proliferation, and substance P induces production of tumor necrosis factor (TNF-α) in macrophages, which leads to enhanced angiogenesis. Sensory neuropeptides have an effect influence the function of macrophages, increasing their production of cytokines, and also model the proliferation of T cells and influence the production of antibodies.

It is now well established that opportunistic microorganisms expressed in the bronchial lumen cause the release of biologically active compounds, inflammatory mediators, which enhance bronchoconstriction. These include prostaglandins (PG), prostacyclins, thromboxanes, leukotrienes, fatty acid peroxides, and platelet activating factor. The spectrum of lipid mediators depends on the enzymatic pathway of arachidonic acid conversion, formed under the influence of phospholipase A2 from membrane lipids of damaged cells. The cyclooxygenase pathway produces prostonoids: PG, prostacyclins, and thromboxanes. PG act as synergists of inflammatory mediators such as histamine, serotonin, and kinins. They increase vascular permeability, bronchoconstrictor effect, bring sensory peptidergic nerve fibers into a state of hypersensitivity, which causes bronchial spasm, hypersecretion, initiate an inflammatory reaction. Prostacyclins and thromboxanes in turn affect the bronchial mucosa, vascular walls, change platelet aggregation (prostacyclins reduce, and thromboxanes increase aggregation).

The lipoxygenase pathway produces eicosanoids: leukotrienes, peroxides, and hydroperoxides of fatty acids. Leukotrienes are strong chemotactic agents and promote the migration of neutrophils to the site of inflammation. These effects are most pronounced in leukotriene B4 and are found in inflammatory exudate in bronchial lavage fluid, in bronchial sputum in sick children with broncho-obstruction. It is significant that even before the onset of broncho-obstruction, a number of cytochemical and morphological

features are detected in peripheral blood leukocytes. It has been established that at the onset of broncho-obstruction and at the height of clinical manifestation, the activity of a number of neutrophil enzymes increases - alkaline and acid phosphatases, NADPH dehydrogenases, determined by the level of nitroblue tetrazolium reduction, the content of cationic protein, glycogen, and myeloperoxidase activity decreases. At the same time, euchromatization of nuclei and the activity of DNA metabolism enzymes in neutrophils increase.

According to S.V. Lukyanov et al., ATP formed during the breakdown activates both A_1 and A_2 -adenosine (purine, xanthine) receptors. Stimulation of A_1 -receptors leads to a decrease in the intracellular content of cAMP, an increase in the level of calcium ions in the cytoplasm and bronchoconstriction. In children with broncho-obstructive diseases, a violation of adenosine reception is observed, expressed in an increase in the ratio of A_1/A_2 receptors.

$_1$ /A $_2$ ratio is associated with a decrease in the number of A $_2$ receptors and, to a lesser extent, with an increase in the content of A $_1$ receptors.

There are convincing evidence that an important link broncho-obstruction is the insufficiency or blockade of β_2 - adrenoreceptors, which is manifested by the inadequacy of adenylate cyclase or a violation of the action of cyclic nucleotides (cAMP, cGMP). In this case, a decrease in the activity of β-receptors promotes the activation of receptors and the implementation of the action of mediators through cyclic nucleotide GMP.

An important trigger for broncho-obstruction and inflammation development are interleukins IL - IL - 1, IL - 6, TNF - α and IL - 8. Under the influence of triggering proinflammatory IL in the bronchi, activation of both different types of leukocytes and cells of other origin - endothelium, fibroblasts, creatocytes - occurs. The effect of IL - 1, IL - 6, TNF - α, IL - 8 enhances the main functions of neutrophils, cytotoxic NK cells, stimulates the

release of histamine by basophils and mast cells, the synthesis of PGE $_2$ by creatocytes. High levels of PGE $_2$ IN the body of patients with broncho-obstruction act as an inhibitory autocrine mediator. It has been established that PGE 2 inhibits the proliferation of T cells and their production of IL-2 and γ-IFN. Like IL-4, PGE $_2$ switches the synthesis of immunoglobulins, inhibiting the formation of IgG and suppressing — lgM. It is possible that during the period of broncho-obstruction, a decrease in the amount of PGE $_2$ leads to an imbalance in the immune system.

A.A. Eyubova et al., having conducted a clinical and immunological assessment of the use of T-activin in obstructive bronchitis in children aged 1 to 3 years with an aggravated premorbid background (frequent acute respiratory viral infections, malnutrition, anemia, rickets), before treatment revealed a significant decrease in cellular immunity indicators, IgA levels against the background of increased IgM content , decreased T-total ROC, T-active ROC, suppression of the functional activity of T-lymphocytes, and dysfunction of B-cells. The use of T-activin at a dose of 1.3 μg per 1 kg of body weight led to the normalization of all studied parameters of the immune system. Along with this, a statistically significant initially increased decrease in IgM was noted.

Some authors, when studying the dynamics of T- and B-systems immunity in young children with ARVI complicated by acute and obstructive bronchitis revealed a sharply reduced relative and absolute content of T-lymphocytes. At the height of obstructive bronchitis, the relative and absolute number of T-lymphocytes was significantly higher than at the initial stage of the disease. Unlike acute bronchitis, with obstructive bronchitis, at the height of the disease, a further increase in B-cells in the peripheral blood was observed. According to the RBTL with FGA, with AOB, compared with acute bronchitis, a more pronounced decrease in T-lymphocytes was observed in

combination with significant inhibition of their functional activity. At the same time, an increase in the spontaneous ability of T-lymphocytes to form blasts was noted with obstructive bronchitis.

In acute bronchitis and acute obstructive bronchitis in young children, there are significant changes in the immunological status of the body. The onset of the disease is accompanied by suppression of the functional activity of T cells by a decrease in their absolute and relative number.

of B cells increases with the increase in the concentration of immunoglobulins. It is noted that it is necessary to develop a method for influencing the immune system in acute obstructive bronchitis. Some authors, studying the frequency of cases of obstructive bronchitis in acute respiratory viral infections and the possibility of their transformation into respiratory allergosis, found that the acute period of obstructive bronchitis in young children is accompanied by a deficiency of the T-immune system, which is characterized by a reliable decrease in the content of T (CD3) lymphocytes, T (CDD) helpers, T (CD3) suppressors and an increase in the number of B (CD_{19}) lymphocytes. The inclusion of a 0.01% solution of immunomodulin at the rate of 0.3 ml per 10 kg, 0.5 ml per 10-30 kg of body weight, intramuscularly for 10 days, led to a pronounced an increase in the relative content of T-lymphocytes. At the same time, a differentiated analysis of the number of B (CD_{19}) -lymphocytes showed that after one course of immunomodulin therapy, this indicator normalized only in patients without a history of recurrent obstruction. This allowed the authors to recommend immunomodulin as an immunocorrective drug in the treatment of young children with obstructive bronchitis.

Luss L.V., studying the effectiveness of immunomodulin in sepsis and obstructive conditions in children, revealed, along with a reliable decrease in T-lymphocytes (SD_3), helpers (SD_4), suppressors (SD_8) and an increase in B-

lymphocytes (SD_{19}) and killers (LNK-16), a significant increase in antigen-binding lymphocytes (ABL) in obstructive syndrome, which indicates profound disturbances in the specific link of immunity. At the same time, it was noted that in children with obstructive bronchitis, the humoral link of immunity changes, as evidenced by data on a significant increase in IgG, IgA and a decrease in IgM. The administration of immunomodulin for 10 days (at the rate of 0.1 ml per 10 kg of body weight) had a corrective effect on the impaired links of the immunological reactivity of the body of children with bronchoobstruction.

Considering the issue of introducing immunomodulin into clinical practice for the treatment of young children with acute obstructive bronchitis, we noted that the effect of this drug on the cellular link of immunity in this pathology has not been fully studied.

The prescription of immunomodulin is based, as follows from the works of Rizopulu A.P. and Garib F.Yu., on the fact that in non-specific inflammatory diseases of the lungs, which include acute bronchitis, acute obstructive bronchitis and bronchiolitis, changes in quantitative and qualitative parameters of the immune status: the number of T cells (CD3+), their functions (RBTL on PHA, Con A, the content of T-suppressors ($CD8_+$) and their functions (ConA-induced suppression), the number of T-helpers ($CD4_+$), the number of B-lymphocytes ($CD19_)$ and their functions (concentrations of immunoglobulins of classes G , A , M , PBTJI on PWM), the formation of IL-1 and 2, the content of neutrophils, alveolar macrophages and their functions (phagocytic number, phagocytic index), the activity of humoral factors of non-specific anti-infective resistance (lysozyme, complement, properdin system, (3-lysine), the activity of antibody-dependent and natural killers, the severity of autoimmune reactions (lymphocyte migration inhibition reaction, RBTL, etc.) on the pulmonary antigen and the formation of autoantibodies against it.

V.K. Tatochenko and a group of co-authors justify the use of immunocorrectors based on the nature of immunological disorders in non-specific inflammatory lung diseases. It has been established that local immunity is suppressed in patients. Indirect evidence of the involvement of immunological mechanisms in the pathogenesis of lung disease is the establishment of the fact of an increased number of reliable correlations between the parameters of the immune system in the acute period of the disease and a decrease in their number during remission. At the same time, a number of researchers point to the need for careful use of immunocorrectors in the treatment of non-specific lung diseases (NSLD).

An important argument against immunocorrection in the therapy of NVZL is the absence of immunomodulators with selective action on individual links of the immune system, including specific populations and subpopulations of lymphoid cells and specific clones. lymphocytes. The rationale for using non-specific immunomodulation is the existence in the body of a physiological system for regulating specific immunological reactions, which include Fab fragments of homologous IgG, interleukins, interferons, leukocyte integrins, leukotrienes, prostaglandins, the complement system, myelopeptides, thymus peptides, and low-molecular nucleic acids.

All these factors are not capable of inducing an immune response on their own, but they can control its severity. Therefore, when immunomodulators are introduced into the body, in some cases, some natural physiological situations are reproduced. Thus, according to a number of authors, sodium nucleate has the ability to influence the synthesis of RNA, DNA, protein, ATP, ADP, glycolysis, oxidative phosphorylation, amino acid catabolism, glycogen synthesis, oxygen metabolism, collagenolytic processes, and the cyclic nucleotide system. Polysaccharide and lipopolysaccharide preparations intensify the synthesis of protein, DNA, adenylate cyclase, stimulate the

activity of glycolytic dehydrogenases and lysosomal enzymes. The general effect of the preparations was expressed in the mobilization of the pituitary gland - adrenal cortex system, lymphoid cells and macrophages. These preparations are capable of causing the formation of prostaglandins E, suppressing the synthesis and release of leukotrienes.

The metabolic action of levamisole also turned out to be quite pronounced. Its ability to stimulate the activity of hexose monophosphate shunt enzymes, protein iodination in neutrophils, DNA and protein synthesis in lymphocytes, macrophages, increased secretion of glucosidase and catapsin D in phagocytes, accumulation of intracellular cGMP in peripheral lymphocytes and granulocytes. Muramyl dipeptide was able to activate various lysosomal enzymes, causing an increase in the level of sputum cyclic AMP, prostaglandins, and stimulate DNA synthesis. Polyelectrolytes in tissue culture are able to synthesize DNA and RNA.

The synthetic polymer stimulator polyoxidant causes activation of glycolysis of hexose monophosphate shunt, cyclourea, lysosomal hydrolases in phagocytic cells, enhances expression of various cellular receptors. Synthetic RNA increases inclusion of - thymidine in lymphoid and other cells, stimulates formation of cAMP. Methyluracil and pentoxyl activate cholinesterase, formation of protein and nucleic acids in tissue culture.

In recent years, preference has been given to natural correctors isolated from the thymus gland of animals: T-activin (Russia), thymostimulin, thymuvocol (Germany), thymomodulin (Italy). At the same time, thymus derivatives and myelopeptides potentiate the synthesis of protein and nucleic acids in various cells. At the same time, they are regulators of lipid metabolism, reduce the glucose content in the blood, normalize liver tests - ALAT and AS AT. Thymus activity decreases with age, and its highest immunoregulatory capacity is manifested in the fetus several weeks before birth. The drug

obtained from the thymus of fetuses several weeks before birth has increased biostimulating and immunocorrective activity.

According to F.Yu. Garib, immunomodulin is the first domestic drug obtained with a high degree of purification from the thymus of sheep fetuses, approved by the Main Directorate for Quality Control of Medicines and Medical Equipment M3 of the Republic of Uzbekistan for use in medical practice as a biostimulating and immunocorrective agent. It has been established that immunomodulin has the ability to restore damaged links of the immune system in acute infectious diseases, increase the activity of T-lymphocytes, phagocytes, stimulate the production of interferon, antibody genesis, and enhance hematopoiesis. The drug is non-toxic and compatible with other drugs.

There are reports that immunomodulin can be used for acute respiratory viral infections to combat viruses, restore the functions of the immune system and prevent complications of the bronchopulmonary system.

According to N.N. Volodin and M.V. Degtyareva, when using immunoglobulin preparations and thymus preparations for infectious diseases in newborns, treatment periods are reduced, the effectiveness of therapy and the body's resistance to unfavorable environmental factors are increased.

It has now been proven that immunomodulators simultaneously affect both the immunological and biochemical and clinical status. According to some authors, the inclusion of pharmacological and non-drug immunocorrection in the usual basic therapy significantly increases the effectiveness of traditional treatment. The combination of immunocorrectors with different mechanisms of action and the combination of non-drug effects with modulators are more effective if the immunocorrector is prescribed at an earlier stage of the disease, at the height of immunological disorders in the body.

Thus, the analysis of the literature review shows that in recent years, much attention has been paid to immunocorrectors due to the insufficient effectiveness of antibacterial and anti-inflammatory therapy. However, they are not yet widely used due to the lack of clear criteria for their appointment, as well as methods for assessing the effectiveness of immunomodulatory therapy. At the same time, the development of such criteria should be carried out on the basis of studying the clinical manifestations of the disease and research into systemic and local factors of immunological reactivity. In this regard, important data for assessing the effectiveness of the treatment and prognosis of the disease can be the indicators of the cytochemical activity of neutrophilic leukocytes.

In recent years, the domestically produced drug immunomodulin has been used to correct metabolic disorders in tissues in bronchopulmonary pathology, including in children with acute bronchitis. However, there is virtually no data in the literature on its effect on cytochemical indices of neutrophils. In this regard, a clinical study of the effect of the domestic drug immunomodulin to correct the immune status in young children with acute obstructive bronchitis will help to increase the effectiveness of their treatment, reduce the frequency of severe complications and relapses of the disease.

was carried out based on the results of three years of research work (1998-2000) conducted at the 1st somatic department of the Tashkent City Children's Clinical Hospital and the Central Scientific Research Laboratory of the First Tashkent State Medical Institute.

A total of 95 young children aged 1 month to 3 years (mean age 1.5±0.63 years) were examined. Of the total number of children examined, 59 (62.1%) were boys and 36 (37.9%) were girls.

The largest number of sick children were aged from 1 month to 2 years, with an equal number of both boys and girls. Consequently, the development

of BOS does not depend on gender, but on age, and the disease is mainly detected in children under 2 years of age.

It should be noted that in order to evaluate the studied biochemical *and* clinical parameters and the reliability of the obtained data, we selected groups of patients using a random sampling method in such a way that they could be compared both by age and gender.

The diagnosis of non-specific lung diseases was based on the clinical course of the disease in accordance with the proposed and currently valid classification of clinical forms of bronchopulmonary diseases in children, adopted in Moscow at the symposium "Non-specific lung diseases in children" (November 1995).

In this case, anamnestic data, premorbid background indicators, clinical, laboratory and instrumental tests, and functional and radiological examination data were taken into account to establish a diagnosis.

Children with bronchial asthma, as well as children with simple acute bronchitis and bronchopneumonia were excluded from the number of examined patients. For the examination, we selected mainly children with the first episode of obstructive bronchitis, in whom the infectious process - ARVI - prevailed in the genesis of broncho-obstruction.

According to the modern classification, we diagnosed AOB and AOBl in children who fell ill for the first time, whose X-ray images in dynamics did not show focal and infiltrative shadows in the lungs, and showed a pronounced cough, dry and moist rales during auscultation, prolonged and difficult exhalation, and noisy breathing. AOB was diagnosed in 63 (66.3%) children, and AOBl in the remaining 32 (33.7%). It should be noted that in patients with bronchiolitis, in contrast to patients with AOB, the disease was more severe, with obstructive syndrome and severe respiratory failure caused by obstruction of small bronchi.

The distribution of patients depending on the form of the disease, gender and age is presented in Table 2 and Fig. 2. From Table 2 and Fig. 2 it is clear that AOB mainly occurs at the age of 1 month to 2 years, almost equally in both boys and girls.

Consequently, AOB is equally often observed in boys and girls mainly at the age of 1 to 12 months. In children aged 2 to 3 years, this indicator decreases. AOBl is observed in the same number of boys and girls up to 12 months, and at the age of 12 months to 2 years, mainly boys are affected. AOBl has not been diagnosed in children aged 2 to 3 years. In the general structure of BOS in children aged 1 to 3 months and 4-6 months, AOBl predominates, and from 7-9 months to 3 years - AOB.

The clinical characteristics of BOS depending on the form of the disease are presented in Table 1.

We have established that upon admission to the clinic, 62 children, including 42 (66.7%) with acute obstructive bronchitis and 20 (62.5%) with acute obstructive bronchitis, had clinical signs of catarrh of the upper respiratory tract against the background of normal temperature in 31, subfebrile temperature in 44, which was observed for 2-3 days, and in some patients - 15, the disease began with a febrile temperature. Cough and wheezing were observed in all patients with acute obstructive bronchitis examined by us. Only dry (whistle and buzzing) wheezing were observed in 42, as well as a combination of dry and moist medium bubbling - in 21, moist small bubbling - in 32 children. The latter were heard in all examined children with acute obstructive bronchitis. According to literary data, acute bronchitis in young children is mainly diffuse.

Table 1

Clinical characteristics of BOS depending on the form of the disease upon admission of children to hospital

Sign	AOB (n =63)	AOBL (n =32)
1	2	3
Age (year)	1.69±0.82	1.35±0.51
Severity of the general condition: Moderate severity Heavy	 8 (12.7) 55 (87.3)	 32 (100)
Normal temperature	26 (41.3)	8 (25.0)
Subfebrile temperature	31 (49.2)	15 (46.9)
Febrile temperature	6 (9.5)	9(28.1)
Dyspnea	58 (92.1)	32 (100)
Perioral cyanosis	41 (65.1)	27 (84.3)
Respiratory failure 1st degree II degree III degree	 4 (6.3) 59 (93.7)	 27 (84.4) 5 (15.6)
Cough: dry	31 (49.2)	6(18.7)
Wet, with sputum production	32 (50.8)	26 (81.3)
Extended exhalation	49 (77.8)	32 (100)
Participation of accessory muscles in the act of breathing	42 (66.7)	32 (100)
Remote wheezing	63 (100)	32 (100)
Percussion (lung distension)	48 (76.2)	32 (100)
Wheezing: Dry	42 (67.7)	
Dry and wet medium bubble	21 (33.3)	
Fine bubbles	---	32 (100)
Catarrh of the upper respiratory tract	42 (66.7)	20 (62.5)
Normal white blood cell count	29 (46.0)	9 (28.1)
Leukocytosis	8 (12.7)	5(15.6)
Leukopenia	26 (41.3)	18(56.3)
Neutrophilia	11(17.5)	8 (25.0)
Eosinophilia	17 (27)	3 (9.3)
Increased ESR	28 (44.4)	13 (40.6)
X-ray examination (absence of focal and infiltrative shadows)	63 (100)	32 (100)

It should be noted that dyspnea was detected in 90 sick children, including 58 (92.1%) children with moderate dyspnea (40 breaths per minute) and 32 (100%) children with acute obstructive pulmonary disease (AOBL) with severe dyspnea, sometimes reaching 60 breaths per 1 minute. When analyzing the blood, we found that sick children with BOS do not have any specific features in the change in the blood formula. A normal number of leukocytes was determined in 38 examined children, moderate leukocytosis was noted in 13 children, including 8 (12.7%) with acute obstructive pulmonary disease and 5 (15.6%) with AOBL. Leukopenia was also noted in 44, including 26 (41.3%) sick children with acute obstructive pulmonary disease and 18 (56.3%) with AOBL. Relative neutrophilia was detected in 19 examined children, of which 11 had a left shift.

In general, relative neutrophilia was observed in the group of children with acute obstructive pulmonary disease - in 11 (17.5%), in children with acute obstructive pulmonary disease (AOBL) - in 8 (25.0%). ESR was moderately elevated in 28 (44.4%) children (more than 10 mm/hour) with acute obstructive pulmonary disease and in 13 (40.6%) children with acute obstructive pulmonary disease. In children with acute obstructive pulmonary disease, chest X-ray showed bilateral enhancement of the pulmonary pattern and expansion of the lung roots, low position of the flattened domes of the diaphragm. In children with acute obstructive pulmonary disease, increased transparency of the lung fields, especially in the periphery, low position of the diaphragm, horizontal position of the ribs, small areas of compaction of the lung tissue, probably due to subsegmental atelectasis, compaction of the alveoli were determined, but confluent infiltrative shadows were absent.

Analysis of case histories revealed that almost all examined patients had an aggravated premorbid background. Thus, 19 (20%) children were breastfed, 11 (11.6%) were mixed fed, and 24 (25.3%) were bottle fed.

At the same time, it was revealed that 23 (24.2%) children with BOS had an unfavorable obstetric history, including 21 (22.1%) children born with asphyxia during childbirth. Anemia was established in 56 (58.9%) sick children, rickets - in 21 (22.1%), exudative-catarrhal diathesis - in 24 (25.3%), lymphaticohypoplastic diathesis - in 10 (10.5%), hypotrophy of I - II degree - in 6 (6.3%), syndrome of impaired intestinal absorption - in 7 (7.3%) and perinatal encephalopathy - in 24 (25.3%). It should be noted that an unfavorable premorbid background was equally often detected in sick children with AOB and with AOBl.

It should be noted that 54 (56.8%) sick young children were admitted to hospital on the 1st–2nd day of illness, and 41 (43.2%) within 4–6 days.

Depending on the form of the disease and treatment, the patients were divided into groups (Table 2). The effectiveness of the basic therapy was studied in 53 patients with BOS, including 38 with AOB and 15 with AOBl (comparison group). The main group consisted of 25 children with AOB and 17 with AOBl. Children from this group, along with basic therapy, were additionally prescribed immunomodulin from the moment of admission to the hospital. The control group consisted of 20 healthy children from 1 month to 3 years old.

To correct the impaired immune system in young children with BOS, immunomodulin was prescribed according to the method proposed by Khaidarova M.M. et al. - 10 ml of 0.01% solution per 10 kg of body weight for 5-7 days, depending on the severity of the disease and the effectiveness of treatment.

Table 2

Distribution of young children depending on the form of the disease and treatment

Group	Form of the disease		Total
	AOB	AOBL	
Comparable	38	15	53 (55.8%)
Main	25	17	42 (44.2%)
Control	-	-	20

When conducting basic therapy, it was important to quickly normalize the patency of the airways and ensure adequate pulmonary ventilation. Treatment was mainly aimed at eliminating the main pathophysiological mechanisms of its formation:

- liquefy and remove mucus from the trachea and bronchi,
- relieve swelling of the bronchial mucosa,
- eliminate oxygen deficiency,
- improve the immune status of the body.

In order to thin viscous sputum and reduce swelling of the bronchial mucosa, children over 2 years of age were prescribed thermal steam, soda (1-2% sodium carbonate solution), saline-alkaline (1-2% sodium bicarbonate solution and 1-2% sodium chloride solution) inhalations, as well as inhalations of Borjomi mineral water, decoctions of medicinal herbs (chamomile, sage, wild rosemary, coltsfoot), and plenty of warm drinks (tea, milk mixed with alkaline mineral water). To improve sputum evacuation, it was recommended to change positions in bed more often and pick up the child. In case of severe anxiety, sedative therapy was prescribed (bromine preparations, valerian, phenobarbital, seduxen).

Distraction procedures such as hot baths and warm wraps had a good therapeutic effect.

Due to the fact that in a significant number of cases, BOS occurs against the background of acute respiratory viral infections, leukocyte interferon was prescribed 3-4 times a day during the acute period or during an exacerbation of obstructive bronchitis.

In acute obstructive pulmonary disease, mucolytic drugs and proteolytic enzymes were prescribed. The indication for their prescription was persistent, unproductive cough. Mucolytic drugs - N -acetylcysteine or its analogues (mukomist, mucosalvan) - were used intramuscularly (10% solution of 0.5-1 ml). Bromhexine (0.004) was prescribed to children over one year old orally at 1/2 tablet 3 times a day, biosalvan at 1/2 tablet 2 times a day for children under 1 year; over 1 year old at 1 tablet 2 times a day or in aerosols - 2 ml per one inhalation dose; rinatiol - only orally at 1 teaspoon 4 times a day.

Proteolytic enzymes, causing protein hydrolysis, also help to reduce the viscosity of sputum, clear the bronchi of mucus. Along with this, they help to regenerate and epithelialize the mucous membrane of the respiratory tract. In the presence of mucous sputum, it was recommended to use trypsin and chymotrypsin (2.5 mg intramuscularly), pancreatin (1/4-1/2 tablet 3 times a day). Exercise therapy was prescribed individually, taking into account the phase of the disease.

For the treatment of bronchospasm, berodual was used - a combination drug containing 0.5 mg of the adrenergic drug fenoterol hydrobromide and 0.25 mg of the anticholinergic agent ipratropium bromide per 1 ml. It was prescribed as 1 dose 3 times a day. Antispasmodics were recommended parenterally: euphyllin, no-shpa. The daily dose of euphyllin was 2-6 mg/kg/day. After achieving sufficient patency of the airways, oxygen therapy was started, which was carried out in the oxygen chamber DIP-1. Oxygen was supplied humidified, at a concentration of no more than 40% and combined with aeroionotherapy (the use of light negative ions in the oxygen chamber).

In the absence of a therapeutic effect and increasing respiratory failure, 4 children from the comparison group were prescribed glucocorticoid hormones: prednisolone at a dose of 1-2 mg per 1 kg or hydrocortisone 5 - 1 0 mg/kg. Corticosteroids were recommended to be administered intravenously in a short course for 3-5 days.

In the presence of symptoms of heart failure, the administration of cardiac glycosides (corglycon, digoxin, strophanthin) was recommended.

Some children from the comparison group were prescribed Essentiale as part of the treatment course to improve the functional activity of the myocardium, which helps stabilize biological membranes. The drug was administered intravenously in a single dose of 0.2 ml/kg 1-2 times a day, drip in a *5%* glucose solution at the rate of 1 ml Essentiale - 50 ml of glucose. The complex treatment included antibiotic therapy with penicillin drugs, as well as vitamins, absorbable drugs. Nystatin and lactobacterin were prescribed to prevent complications of antibiotic therapy. Children with AOB were prescribed ampiox, infusion therapy with drip hemodesis with sequential drip administration of glucose and saline solutions.

§2.3. Principles of therapy for chlamydial and mycoplasma infections

Currently, despite ongoing research and improvement of bronchitis therapy, practicing physicians often encounter their insufficient effectiveness in clinical practice. The resistance of pathogenic 29 microorganisms is constantly increasing, which is associated, among other things, with irrational antibacterial therapy and indicates the need for further research to improve pathogenetic therapy [14,19,21,22]. Etiotropic tactics and Determination of the etiological factor of acute respiratory infections is of crucial importance for adequate etiotropic therapy in the early stages of the disease [11]. The development, course and outcome of diseases caused by Chl. pneumoniae and Myc. pneumoniae are largely determined by the state of the child's body, the

characteristics of its homeostasis, immunological reactivity, the presence of concomitant diseases, the biological properties of the pathogenic agent, including its ability to long-term persistence and many other factors [16,32,33]. Considering modern concepts about the role of pathogens, diagnostics and issues of differential diagnostics depending on the etiologic factor, the algorithm of initial antibacterial therapy, the author noted that in recent years, the irrational use of macrolides and oral cephalosporins in the initial therapy of respiratory diseases has persisted. Thus, in community-acquired pneumonia, the use of β- lactam antibiotics in atypical pneumonia, carried out in 81% of patients, turned out to be ineffective [29,30,88]. The effectiveness of etiotropic therapy for AOB can be assessed by the elimination of clinical symptoms of the disease, normalization of hemostasis analysis and elimination of the pathogen [77]. The problem of rational use of antibacterial therapy remains, caused by verification of the diagnosis of AOB, taking into account the identification of new and variability of existing etiologic agents, including atypical flora [4,29]. 30 It is necessary to develop rational approaches to the prescription of antibacterial drugs, in the absence of which or the use of outdated data, there is a risk of an unsatisfactory prognosis of the disease and the emergence of resistant strains of microorganisms, especially in atypical etiologies. Treatment of sick children with chlamydial and mycoplasmal infections is carried out taking into account regional sensitivity, age, toxicity, tolerability for a particular child, previous and concomitant pathology and the nosological form of the disease [78]. Myc. pneumoniae and Chl. pneumoniaea have several common properties: they cannot be detected by conventional microbiological methods, are obligate or facultative intracellular parasites and cause extrapulmonary symptoms and, since they do not have a peptide glycan cell wall, they do not respond to β- lactam antibiotics. At the same time, they respond to drugs that inhibit protein synthesis, such as macrolides and

tetracyclines, or to inhibitors of DNA synthesis, such as fluoroquinolones [13,115]. Macrolides have the ability to accumulate in tissues and lesions; it must be taken into account that this process occurs most intensively in the tonsils, lymph nodes, and lung tissue, which determines their choice for the treatment of chlamydia. The role of macrolides in the treatment of respiratory diseases has significantly increased. A feature of pharmacodynamics Macrolides is their long-lasting post-antibiotic effect. Three groups of macrolides are most widely used: Group 1 - 14-membered (erythromycin, oleandomycin, clarithromycin, roxithromycin); Group 2 - 15-membered (azithromycin); Group 3 - 16-membered (josamycin, spiramycin, midecamycin). Macrolides (azithromycin, josamycin, roxithromycin, clarithromycin, midecamycin, spiramycin) have a bacteriostatic effect at medium doses and a bactericidal effect at high doses of the drug, while being effective against most gram-positive bacteria, anaerobes, spirochetes, chlamydia and mycoplasmas [27,82]. Macrolide antibiotics remain the most effective and frequently used drugs against mycoplasma and chlamydia infections. Myc. Pneumoniae and Chl. Pneumoniaea parasitizes outside the cell and does not have a cell wall, the main purpose of which is to suppress and disrupt the protein synthesis of the microorganism. The first-generation macrolide drug erythromycin was first used to treat Myc. Pneumoniae and Chl. Pneumoniaea in children, due to its good antibacterial properties, can at the same time cause more obvious side effects in the digestive tract, even cause phlebitis and local pain, long-term treatment can cause liver and kidney damage [107,115]. Macrolides, with their long period of elimination, retain their antibacterial activity for 4-5 days after antibacterial therapy. Since chlamydia and mycoplasma are obligate intracellular parasites, prone to long-term persistence in the body of a child with transient immunological deficiency. In this regard, single courses of macrolides do not always lead to

eradication chlamydial and mycoplasmal infections. Therefore, the use of immunomodulatory drugs is indicated in the treatment of almost all forms of chlamydial infection in children [105,120]. However, with the emergence of macrolide- resistant strains of Myc. pneumoniae and Chl. pneumoniae, the total duration of febrile days, the course, and the time of hospitalization of children increased. At the same time, there are more inflammatory reactions and complications [46,105,117]. Currently, macrolides in general and clarithromycin in particular are included in the recommendations for the treatment of respiratory tract infections caused by "atypical" pathogens, which is due, on the one hand, to the high antimicrobial activity of macrolides against 32 chlamydia and mycoplasmas and the absence of significant problems with the resistance of the above-mentioned pathogens, and on the other hand, to the favorable safety profile of macrolides and the possibility of use in children from a very early age [27,97,102]. In recent years, there are studies indicating disturbances in the immune status in bronchopulmonary diseases and, in some cases, the presence of primary and the development of secondary immunodeficiency states, which indicates the need for immunocorrective therapy for AOB in children [39,54]. Among the new generation immunomodulators, the domestic drug Galavit deserves special attention [49,70]. According to literature, Galavit has immunomodulatory and anti-inflammatory properties associated with the regulation of the functional and metabolic activity of innate and adaptive immune cells. The drug restores the phagocytic activity of monocytes and macrophages, enhances the bactericidal activity of neutrophils, and increases the cytotoxic activity of NK cells. Galavit enhances the body's resistance to infectious diseases of both bacterial and viral origin, accelerates the elimination of pathogens from the body, reducing the incidence and duration of illness. It also enhances and improves the functional activity of antibodies, and improves the production of interferons (IFN-α and

INF-γ). In inflammatory diseases, Galavit inhibits the pathological synthesis of tumor necrosis factor-α, interleukin-1, interleukin-6 and other proinflammatory cytokines, their cyclicity for an average of 6-8 hours, and also reduces the intoxication syndrome in patients [52,54,92]. However, no data on the use of Galavit in combination with Clarithromycin in children with obstructive bronchitis and its effect on the state of cellular and humoral immunity were found in the literature available to us. In this regard, the aim of our study 33 was to evaluate the effectiveness of Galavit on clinical and immunological parameters in children with acute obstructive bronchitis. Atypical flora in children with AOB that is not timely diagnosed and treated leads to a repeated episode and a protracted course of the disease, re-hospitalization, which requires additional economic costs and can lead to unfavorable outcomes with the possibility of developing chronic diseases. Currently, the relevance of research in children with acute obstructive pulmonary disease (AOB) with atypical microflora lies in the identification and improvement of diagnostic and prognostic clinical and laboratory research methods, as well as the refinement of therapeutic measures to develop a personalized approach to patient management [53,58]. Summarizing the review of literary sources, we concluded that interest in acute obstructive pulmonary disease (AOB) with atypical microflora in childhood is highly relevant. Despite the introduction of modern diagnostic methods and the study of patterns of clinical and immunological changes, these remain insufficiently studied, which determines the need for research to optimize the diagnosis and treatment of the disease. The search for methods for early diagnosis and improvement of treatment effectiveness can be adopted as a priority area.

CHAPTER III. MATERIALS AND METHODS OF THE RESEARCH

§ 3.1. General characteristics of clinical observations.

This dissertation is based on data obtained as a result of three years of research conducted at the 1st somatic department of the Tashkent City Children's Clinical Hospital and the Central Scientific Research Laboratory of the First Tashkent State Medical Institute. Ninety-five young children aged 1 month to 3 years (mean age 1.5 ± 0.63 years) were examined. Of the total number of children examined, 59 (62.1%) were boys and 36 (37.9%) were girls.

1 show, the greatest number of affected children were between the ages of 1 month and 2 years, with equal numbers of boys and girls. Consequently, the development of BOS depends not on gender but on age, and the disease is primarily diagnosed in children under 2 years of age.

It should be noted that in order to evaluate the studied biochemical *and* clinical parameters and the reliability of the obtained data, we selected groups of patients using a random sampling method in such a way that they could be compared both by age and gender.

The diagnosis of non-specific lung diseases was based on the clinical course of the disease in accordance with the proposed and currently valid classification of clinical forms of bronchopulmonary diseases in children, adopted in Moscow at the symposium “Non-specific lung diseases in children”. [79,80].

In this case, to establish a diagnosis, anamnestic data, premorbid background indicators, clinical, laboratory and instrumental tests, and data from functional and radiological examinations were taken into account.

Children with bronchial asthma, as well as children with simple acute bronchitis and bronchopneumonia, were excluded from the study group. For the study, we primarily selected children with a first episode of obstructive bronchitis, in whom the predominant underlying cause of bronchoconstriction was an infectious process (acute respiratory viral infection).

According to the current classification, we diagnosed acute obstructive pulmonary disease (AOB) and acute obstructive pulmonary disease (AOBL) in children with newly diagnosed cases. Their radiographs showed no focal or infiltrative pulmonary shadows, but a pronounced cough, dry and moist rales on auscultation, prolonged and labored expiration, and noisy breathing. A total of 63 (66.3%) children were diagnosed with acute obstructive pulmonary disease (AOB), while the remaining 32 (33.7%) had acute obstructive bronchitis (AOBL). It should be noted that patients with bronchiolitis, unlike those with acute obstructive bronchitis, had a more severe course of the disease, with obstructive syndrome and severe respiratory failure caused by obstruction of the small bronchi.

Distribution of patients by disease type, gender, and age. Consequently, AOB is observed equally frequently in boys and girls, primarily between the ages of 1 and 12 months. In children aged 2 to 3 years, this rate decreases. AOB is observed in equal numbers of boys and girls under 12 months, and between the ages of 12 months and 2 years.

Boys are predominantly affected. AOB has not been diagnosed in children aged 2 to 3 years. In the overall structure of BOS, AOB is predominant in children aged 1 to 3 months and 4 to 6 months, while OOB is predominant in children aged 7 to 9 months to 3 years.

The clinical characteristics of BOS depending on the form of the disease are presented in Table 3.

We found that upon admission to the clinic, 62 children, including 42 (66.7%) with acute respiratory distress syndrome and 20 (62.5%) with acute respiratory distress syndrome (RDS), had clinical signs of catarrh of the upper respiratory tract against the background of normal temperature in 31, subfebrile temperature in 44, which was observed for 2-3 days, and in some patients (15), the disease began with a febrile temperature. Cough and wheezing were observed in all patients with AOS examined by us. Only dry (whistle and buzzing) wheezing were noted in 42, as well as a combination of dry and wet medium bubbling rales in 21, and wet small bubbling rales in 32

children. The latter were heard in all examined children with AOS. According to literary data [25,26,64], acute bronchitis in young children is mainly diffuse in nature.

It should be noted that dyspnea was detected in 90 sick children, including moderate dyspnea (40 breaths per minute) in 58 (92.1%) children with acute obstructive pulmonary disease and severe dyspnea in 32 (100%) children with acute obstructive pulmonary disease, sometimes reaching 60 breaths per minute. Blood analysis revealed that sick children with BOS do not have any specific features in the change in the blood formula. A normal number of leukocytes was determined in 38 examined children, moderate leukocytosis was observed in 13 children, including 8 (12.7%) with acute obstructive pulmonary disease and 5 (15.6%) with acute obstructive pulmonary disease. Leukopenia was also noted in 44 children, including 26 (41.3%) with acute obstructive pulmonary disease and 18 (56.3%) with acute obstructive pulmonary disease. Relative neutrophilia was detected in 19 examined children, of which 11 had a left shift. In total Relative neutrophilia was observed in the group of children with AOB - in 11 (17.5%), in children with AOBl - in 8 (25.0%). ESR was moderately elevated in 28 (44.4%) children (more than 10 mm / hour) with AOB and in 13 (40.6%) children with AOBl (Table 3). In children with AOB, chest radiography showed bilateral enhancement of the pulmonary pattern and expansion of the roots of the lungs, a low position of the flattened domes of the diaphragm. In children with AOBl, increased transparency of the lung fields, especially in the periphery, a low position of the diaphragm, horizontal position of the ribs, small areas of compaction of the lung tissue, probably due to subsegmental atelectasis, compaction of the alveoli, but confluent infiltrative shadows were absent.

An analysis of the case histories revealed that almost all of the patients examined had a complicated premorbid background. Thus, 19 (20%) children were breastfed, 11 (11.6%) were mixed-fed, and 24 (25.3%) were formula-fed.

Table 3.

Sign	OOB (n = 63)	OOBL (n = 32)
Age (year)	1.69+0.82	1.35+0.51
Severity of general condition: Moderate severity Heavy	8 (12.7) 55 (87.3)	32 (100)
Normal temperature	26 (41.3)	8 (25.0)
Subfebrile temperature	31 (49.2)	15 (46.9)
Febrile temperature	6 (9.5)	9(28.1)
Dyspnea	58 (92.1)	32 (100)
Perioral cyanosis	41 (65.1)	27 (84.3)
Respiratory failure I degree II degree III degree	4 (6.3) 59 (93.7)	27 (84.4) 5 (15.6)
Cough: Dry	31 (49.2)	6(18.7)
Wet, with sputum production	32 (50.8)	26 (81.3)
Extended exhalation	49 (77.8)	32 (100)
Participation of accessory muscles in the act of breathing	42 (66.7)	32 (100)
Remote wheezing	63 (100)	32 (100)
Percussion (lung distension)	48 (76.2)	32 (100)
Wheezing: Dry	42 (67.7)	
Dry and wet medium-bubble	21 (33.3)	
Fine bubbles	---	32 (100)
Upper respiratory tract catarrh	42 (66.7)	20 (62.5)
Normal white blood cell count	29 (46.0)	9 (28.1)
Leukocytosis	8 (12.7)	5(15.6)
Leukopenia	26 (41.3)	18(56.3)
Neutrophilia	11(17.5)	8 (25.0)
Eosinophilia	17 (27)	3 (9.3)
Increased ESR	28 (44.4)	13 (40.6)
X-ray examination (absence of focal and infiltrative shadows)	63 (100)	32 (100)

At the same time, it was revealed that 23 (24.2%) children with BOS had an unfavorable obstetric history, including 21 (22.1%) children born with asphyxia during childbirth. Anemia was established in 56 (58.9%) sick children, rickets - in 21 (22.1%), exudative-catarrhal diathesis - in 24 (25.3%), lymphaticohypoplastic diathesis - in 10 (10.5%), hypotrophy of I - II degree - in 6 (6.3%), syndrome of impaired intestinal absorption - in 7 (7.3%) and perinatal encephalopathy - in 24 (25.3%). It should be noted that an unfavorable premorbid background was equally often detected in sick children with AOB and with AOBl.

It should be noted that 54 (56.8%) sick young children were admitted to hospital on the 1st - 2nd day of illness, and 41 (43.2%) within 4-6 days.

Depending on the form of the disease and treatment, patients were divided into groups (Table 4). The effectiveness of the conducted basic therapy was studied in 53 patients with BOS, including 38 with AOB and 15 with AOBl (comparison group). The main group consisted of 25 children with AOB and 17 with AOBl. Children from this group, along with basic therapy, were additionally prescribed immunomodulin from the moment of admission to the hospital. The control group consisted of 20 healthy children from 1 month to 3 years old.

To correct the impaired immune system in young children with BOS, immunomodulin was prescribed according to the method proposed by Khaidarova M.M. et al. [75] - 0.01% solution per 10 kg of body weight for 5-7 days, depending on the severity of the disease and the effectiveness of treatment.

Table 4

Distribution of young children depending on the form diseases and treatments

Group	AOB	AOBl	Total
Comparable	38	15	53(55,8%)
Main	25	17	42 (44,2%)
Control	-	-	20

During basic therapy, it was important to quickly normalize airway patency and ensure adequate ventilation. Treatment was primarily aimed at eliminating the underlying pathophysiological mechanisms of its development:

- liquefy and remove mucus from the trachea and bronchi,
- relieve swelling of the bronchial mucosa,
- eliminate oxygen deficiency,
- improve the immune status of the body.

To thin viscous sputum and reduce swelling of the bronchial mucosa, children over 2 years of age were prescribed warm steam, soda (1-2% sodium carbonate solution), saline-alkaline (1-2% sodium bicarbonate solution and 1-2% sodium chloride solution) inhalations, as well as inhalations of Borjomi mineral water, herbal decoctions (chamomile, sage, wild rosemary, coltsfoot), and plenty of warm fluids (tea, milk mixed half and half with alkaline mineral water). To improve sputum evacuation, it was recommended to change position in bed more often and pick up the child. In case of severe anxiety, sedative therapy was prescribed.

Distraction procedures such as hot baths and warm wraps had a good therapeutic effect. Due to the fact that in a significant number of cases, BOS occurs against the background of ARVI, leukocyte interferon was prescribed

3-4 times a day during the acute period or during an exacerbation of obstructive bronchitis.

In acute obstructive pulmonary disease, mucolytic drugs and proteolytic enzymes were prescribed. The indication for their prescription was persistent, unproductive cough. Mucolytic drugs - N -acetylcysteine or its analogs (mukomist, mucosalvan) - were used intramuscularly (10% solution of 0.5-1 ml). Bromhexine (0.004) was prescribed to children over one year old orally at 1/2 tablet 3 times a day, biosalvan 1/2 tablet 2 times a day for children under 1 year; over 1 year old - 1 tablet 2 times a day or in aerosols - 2 ml per one inhalation dose; rinatiol - only orally at 1 teaspoon 4 times a day.

Proteolytic enzymes, by causing protein hydrolysis, also help to reduce the viscosity of sputum and clear the bronchi of mucus. They also promote regeneration and epithelialization of the respiratory tract mucosa. In the presence of mucous sputum, trypsin and chymotrypsin (2.5 mg intramuscularly) and pancreatin (1/4-1/2 tablet 3 times daily) were recommended. Physical therapy sessions were prescribed individually, taking into account the phase of the disease.

Berodual, a combination medication containing 0.5 mg of the adrenergic drug fenoterol hydrobromide and 0.25 mg of the anticholinergic agent ipratropium bromide per ml, was used to treat bronchospasm. One dose was prescribed three times daily. The daily dose of euphyllin was 2-6 mg/kg/day. Once sufficient airway patency was achieved, oxygen therapy was initiated in the DIP-1 oxygen chamber. Oxygen was administered humidified, at a concentration of no more than 40%, and combined with aeroionotherapy (the use of light negative ions in the oxygen chamber). If there was no therapeutic effect and respiratory failure worsened, glucocorticoids were prescribed to four children in the comparison group: prednisolone at a dose of 1-2 mg/kg or hydrocortisone at a dose of 5-10 mg/kg. Corticosteroids were

recommended to be administered intravenously for a short course of 3-5 days. In the presence of symptoms of heart failure, the administration of cardiac glycosides (corglycon, digoxin, strophanthin) was recommended.

Some children in the comparison group were prescribed Essentiale, a drug that helps stabilize biological membranes, to improve myocardial function. The drug was administered intravenously at a single dose of 0.2 ml/kg 1-2 times daily, and by drip in a *5%* glucose solution at a rate of 1 ml Essentiale per 50 ml glucose. Antibiotic therapy was included in the combined treatment.

Penicillin-based medications, as well as vitamins and absorbable medications, were administered. Nystatin and lactobacterin were prescribed to prevent complications from antibiotic therapy. Children with acute obstructive pulmonary disease (AOBl) were given ampiox and infusion therapy with hemodesis drips and sequential glucose and saline drips.

§ 3.2. Characteristics of cytochemical blood tests.

To clarify the pathogenesis of the disease and evaluate the data of immunocorrective therapy when prescribing immunomodulin, we conducted special cytochemical studies of leukocyte blood cells in sick young children.

Capillary blood samples up to 2.0 ml were used for the study. Blood was collected in the morning on an empty stomach. The studies were conducted before and after treatment on days 10–12. The average treatment duration was 8–12 days.

The activity of acid phosphatase (AP) was studied by the Burston azo coupling method (modified by Yu.F.Rudens, I.M.Buikis, 1965), alkaline phosphatase (AP) according to M.P.Shchubich (1965), myeloperoxidase (MP) according to R.P.Nartsissov (1964), glycogen content (GL) according to A.L.Shabadash (1974), cationic proteins (CP) by the bromophenol blue method according to M.P.Shchubich (1974), the activity of succinate

dehydrogenase (SDH) and α-glycerophosphate dehydrogenase (α-GPDH) according to Nachlas in the modification of R.P.Nartsissov, creatine kinase (CK) according to V.A.Saks and Yu.I.Voronkov (1974). Functional activity of neutrophilic leukocytes (NL) was assessed using the NBT test by B.S. Nagaev. Phagocytic activity (PA), phagocytic number (PN), phagocytic index (PI), percentage of phagocytosis completion (PPC) and digestion index (DI) were determined simultaneously. Calculation of the CB, MP, CP, ALP, GL, as well as SDH, α-GPDH and NBT test indicators was carried out according to L. Kaplow (1955), the average cytochemical coefficient - in conventional units.

It should be emphasized that all the listed methods are well known, standardized and described in detail in the reference book "Laboratory Research Methods in Clinical Practice" (edited by prof. V.V. Menshikov) [54]. Therefore, we did not describe in detail the essence of cytochemical reactions. At the same time, we decided to dwell in detail on the method of isolating leukocytes and determining their metabolic activity. Neutrophils were isolated from heparinized venous blood (10 units of heparin per 1 ml of blood) of healthy donors. The cells were obtained on a double Ficoll-Verografin gradient ($d_1 = 1.077$; $d_2 = 1.119$), washed with Hanks' solution and suspended in RPMI -1640 medium ("Serva", Germany) with 10% fetal calf serum and gentamicin (40 μg/ml).

The study used a cell suspension containing more than 90% neutrophils with a viability (by trypan blue absorption) of at least 95%.

Neutrophil reactive oxygen species production was measured chemiluminometrically using a HLMC-01 instrument (Russia) in the presence of luminol (Sigma, USA). The luminol solution was prepared by serially diluting a commercial preparation in dimethyl sulfoxide (Sigma, USA) and Hanks' solution to a luminol concentration of 250 μM (dimethyl sulfoxide concentration 2.3 vol.%).

100 µl of luminol were added to measuring vials containing 800 µl of neutrophil suspension (500 x 10^3 cells in 1 ml). The vials were placed in thermostatic cell of the HLMC-01 device and kept for 10 min until the tubes were warmed up. After recording spontaneous chemiluminescence, 100 µl of zymosan solution were added to the experimental vials, and 100 µl of Hanks' solution to the control vials, and the luminescence was recorded for 3 min. The measurements were expressed as impulses per 1 s (imp/s) [91].

To assess the activity of proliferative processes in the connective tissue of the lungs in children with acute obstructive pulmonary disease, we used the method of determining oxyproline (OP) in blood plasma by M.A. Osadchuk and V.M. Kapustin [71].

Procedure: 0.4 ml of absolute ethanol was added to 0.1 ml of blood plasma to precipitate the protein. After mixing, the tubes were centrifuged at 3000 rpm for 15 minutes. The supernatant was washed off, then 6 ml of concentrated HCl was added and mixed. The contents of the tubes were then poured into 50 ml flasks with a reflux condenser, placed in a sand bath, and left at boiling for 4 hours. Upon completion of hydrolysis, 3 ml of liquid were removed from the flasks with hydrolysates, placed in centrifuge tubes, neutralized with 6 N NaOH, and the total volume was brought to 8 ml with distilled water. Then, 1 ml of oxidizing agent (chloramine B in acetate-citrate buffer pH -6.0) was added. After 4 min, 3 ml of Ehrlich's reagent (2 g of n - dimethylaminobenzaldehyde dissolved in 3 ml of 57% perchloric acid) was added and placed in a water bath at -60 °C. After 30 min, the tubes were cooled and the volume was brought to 10 ml with isopropyl alcohol. After thorough mixing, spectrophotometry was performed on an SF 46 (Russia) in cuvettes with an optical path length of 10 mm at a wavelength of 558 nm against water. The OD content in each sample was calculated using the formula:

A=E x 84.6, where

A - amount of OP, μg/ml.

E - optical density, nmol.

84.6 is a calibration coefficient calculated based on the calibration curve data using standard solutions.

Statistical processing of the obtained cytochemical and biochemical parameters was performed. Statistical characteristics such as arithmetic means (M) and standard error (m) were determined, and the reliability of the parameters was assessed using Student's t - test using the Microsoft Excel software package.

Since no significant differences were found in the normative indicators depending on gender and age, we did not divide them into age groups.

CHAPTER IV. CLINICAL ASPECTS OF IMMUNOMODULATORY THERAPY IN CHILDREN WITH OBSTRUCTIVE SYNDROME

§ 4.1. Evaluation of the effectiveness of immunomodulin by indicators characterizing respiratory failure in sick children with acute obstructive bronchitis and bronchiolitis

As follows from the literature review, bronchitis in the Republic of Uzbekistan is one of the main pathologies in the structure of lower respiratory tract lesions, especially in young children. At the same time, the leading place among bronchitis is occupied by acute obstructive bronchitis, bronchiolitis, which are characterized by a tendency to repeated episodes of exacerbation, the development of severe complications, and a recurrent course.

It is important to note that in recent years certain progress has been achieved in the study of the etiology, pathogenesis, clinical picture, diagnostics, and treatment of acute obstructive bronchitis and bronchiolitis. At the same time, as the clinical experience of practicing pediatricians shows, on whom timely diagnostics of the disease largely depends, the prescription of adequate pharmacotherapy, and individual prevention of relapses are largely complicated by the insufficient number of pathogenetically substantiated treatments. Despite the availability of highly effective drugs, their widespread use is hampered by the lack of sufficient knowledge about their pharmacological properties at the cellular-subcellular, organ-altered level. The drug immunomodulin has been insufficiently studied, especially in acute obstructive bronchitis and acute obstructive bronchitis in young children. We present information on the definition and justification of the inclusion of immunomodulin in a complex of therapeutic measures for sick children of early age with acute obstructive bronchitis and acute obstructive bronchitis.

The effectiveness of the drug immunomodulin was assessed by the period (days) of disappearance of symptoms of respiratory failure and

intoxication in children during the treatment period. Objective symptoms of respiratory failure in the clinical picture in children with acute obstructive pulmonary disease and acute obstructive pulmonary disease were severe dyspnea with the participation of accessory muscles in the act of breathing and flaring of the wings of the nose, cyanosis of the nasolabial triangle, high respiratory rate, pale skin, tachycardia, prolonged exhalation, distant wheezing, as well as determined by auscultation - in children with acute obstructive pulmonary disease dry whistling and buzzing, with acute obstructive pulmonary disease mainly an abundance of fine bubbling rales, cough (at the beginning dry obsessive, and during the treatment wet to productive).

Objective symptoms of intoxication of the body in children with acute obstructive pulmonary disease and acute obstructive pulmonary disease during the treatment period were high body temperature, lethargy, adynamia, capriciousness and anxiety, sleep disturbance, poor appetite, catarrhal symptoms (rhinitis, pharyngitis, nasopharyngitis), leukopenia, neutrophilia, and increased ESR.

It should be noted that the severity of the disease in children with AOB according to clinical signs was significantly higher than in children with AOB, which required more intensive therapy with the inclusion of not only bronchodilators, sedatives, but also significantly more mucolytic drugs, as well as in some cases antibiotics, glucocorticoid hormones (IV short course for 3-5 days).

The difference in the therapy administered between patients with AOB and AOBl is noted in the following examples.

Patient Sh., 9 months old. Acutely fell ill: body temperature quickly rose to 38.5°C, difficulty breathing through the nose appeared, vomiting occurred once during the day. On the 2nd day, cough, shortness of breath, profuse

serous-mucous discharge from the nose developed; the child became restless, capricious, and lethargic. Sleep and appetite were disturbed. At home, he took biseptol, mucaltin, his throat was treated with furacilin solution, but fever, cough, lethargy, and shortness of breath persisted. On the 3rd day, he was examined by a local doctor and sent for treatment to the Tashkent City Children's Clinical Hospital, where he was hospitalized in serious condition in the 1st somatic department. On admission, body temperature was 38.8°C, he was pale, lethargic, indifferent, severe shortness of breath and cyanosis of the nasolabial triangle were observed. Remote wheezing was heard. Mucous discharge from the nose. Persistent wet cough. The mucous membrane of the oropharynx is hyperemic. RR - 58 per 1 min. Abundance of silent fine-bubble rales are heard over the lungs on inspiration and at the very beginning of expiration, whistling dry rales on expiration. Percussion sound over it has a box shade. Heart sounds are muffled, tachycardia. Pulse is rhythmic 152 per 1 min. The abdomen is soft, painless. The liver protrudes from under the rib by 1 cm with a sharp elastic edge. The spleen is clearly palpated. Stool and diuresis are not disturbed.

In the blood: Hb - 128 g / l, Er - 3.8 x $^{10\,12}$ / l, Color. p. - 1.0, L - 11.0 x 10 ^{9} / l, p.a. - 4%, s.a. 33%, eosinophils - 5%, lymph. - 52%, mon - 4%, ESR - 14 mm / h. Radiography - increased transparency of the lung fields, low position of the diaphragm are observed.

The study of specific indices of local immunity revealed the following: KB - 2.11 conventional units; MP - 1.56 conventional units; CP - 0.51 conventional units; ALP - 0.39 conventional units; GL - 0.48 conventional units; SDG - 0.71 conventional units; α-GPDH - 1.62 conventional units; CC - 6.53 IU/10 ^{9} L; CL - 885.54 imp/s/10 ^{9} L; NST-test - 16.21 conventional units; FA - 73.25%; FC - 3.26%; FI - 3.58%; PZF - 75.23%; IP - 2.50%; SOP - 7.18 μg/ml; BSOP - 20.14 μg/ml.

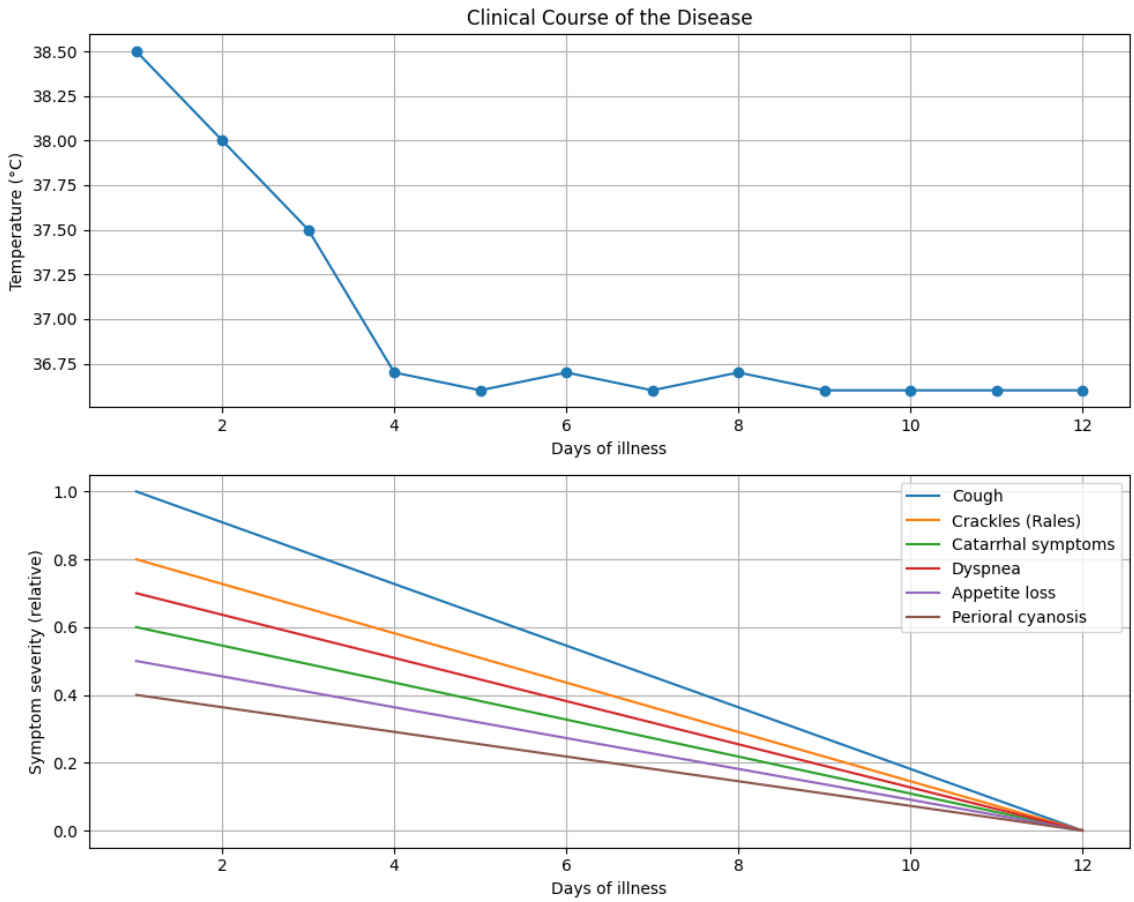


Fig. 1. Clinical characteristics of the course of the disease of patient Sh.

Based on clinical and instrumental data, a diagnosis was made: Acute obstructive bronchiolitis, grade II respiratory failure.

Subsequently, against the background of pathogenetic therapy, the condition gradually began to improve: the temperature returned to normal by the 3rd day of illness, wheezing in the lungs by the 8th day, cough by the 10th day. Shortness of breath disappeared on the 5th day, appetite improved on the 6th, catarrhal symptoms - on the 5th.

Received: penicillin, euphyllin, vitamin therapy, broncholitin, hemodez, a mixture of no-shpa with diphenhydramine, calcium chloride, a short course of prednisolone.

After treatment: KB - 1.37 conventional units; MP - 1.65 conventional units; CP - 0.43 conventional units; ALP - 0.33 conventional units; GL -1.69 conventional units; SDG -1.36 conventional units; α-GPDH - 1.10 conventional units; CC - 8.03 IU/10 ^{9} L; CL - 707.35 imp/s/10 ^{9} L; NBT-test -

13.75 conventional units; FA - 71.22%; FC - 4.29%; FI - 2.91%; PZF - 76.96%; IP - 1.66%; SOP - 5.92 μg/ml; BSOP - 16.22 mcg/ml.

The child was discharged from the hospital on the 12th day in satisfactory condition.

Patient D., 1 year old. The disease began with malaise, dry cough, nasal congestion. On the 3rd day, the body temperature rose to 38.2°C, shortness of breath appeared. The child's condition worsened, he became lethargic, capricious. At home, she was treated with ampicillin (tab), bromhexine, paracetamol. Despite this, the child's condition worsened, shortness of breath increased, cough intensified, sleep was disturbed. On the 4th day, the child was hospitalized in serious condition in the 1st somatic department of the Territorial City Children's Clinical Hospital.

On examination at the clinic, the body temperature is 38.3°C, the skin is pale and warm. Perioral cyanosis is noted. When breathing, the wings of the nose are distended, distant wheezing is heard. Respiration is rapid, 54 per 1 min. Dry whistling and moist medium-bubble moist rales are heard above the lungs. Heart sounds are muffled, tachycardia. Pulse is 148 per 1 min. The liver and spleen are not enlarged. Stool and diuresis are regular.

In the blood: Hb - 106 g / l, Er - 3.6 x 10^{12} \l, color.p. - 0.9, L - 8.0 x 10^{9} /l, p.c. - 3%, s.c. 37%, eosinophils - 6%, lymph. - 47%, mon. - 7%, ESR - 10 mm / h. Cytochemical parameters of blood before treatment: KB - 1.92 conventional units; MP - 1.72 conventional units; KF - 0.53 conventional units; ALP - 0.40 conventional units; GL - 0.77 conventional units; SDG - 0.85 conventional units; α-GPDH - 1.33 conventional units; KK - 6.88 IU/10^{9} L; CL - 835.91 imp/s/10^{9} L; NST-test - 14.44 conventional units; FA - 82.90%; FC - 3.47%; FI - 3.44%; PZF - 93.95%; IP - 2.75%; SOP - 6.62 μg/ml; BSOP - 17.72 μg/ml.

Radiography - bilateral enhancement of the pulmonary pattern and expansion of the roots of the lungs, increased transparency of the lung fields.

Based on clinical and instrumental studies, the diagnosis was: acute obstructive bronchitis, grade II.

Cytochemical parameters of blood after treatment: CB - 1.51 conventional units; MP - 2.08 conventional units; CP - 0.39 conventional units; ALP - 0.31 conventional units; GL - 1.88 conventional units; SDG - 1.37 conventional units; α-GPDH - 1.16 conventional units; CC - 8.86 IU/10 ^{9} L; CL - 612.39 imp/s/10 ^{9} L; NBT-test - 12.37 conventional units; FA - 60.54%; FC - 5.36%; FI - 2.30%; PZF - 73.48%; IP -1.61%; SOP - 5.86 μg/ml; BSOP - 16.05 mcg/ml.

Recovery was slow. Temperature lasted for 2 days, shortness of breath - 4 days, cough -8, wheezing - 7 days. Appetite returned to normal by the 5th day, sleep by the 6th day. Discharged by the 9th day in satisfactory condition.

The examples given show that the clinical picture of children with AOB and AOBl differed significantly when treated with the traditional method. The duration of treatment for children with AOBl was 12 days, and for children with AOB 9 days, despite the fact that the patients underwent a full range of modern treatment measures. Under the influence of traditional treatment, a number of indicators - lethargy, adynamia, lack of appetite, enlarged peripheral lymph nodes, pale skin, distant wheezing, as well as wheezing determined by auscultation, cough - persisted for quite a long time.

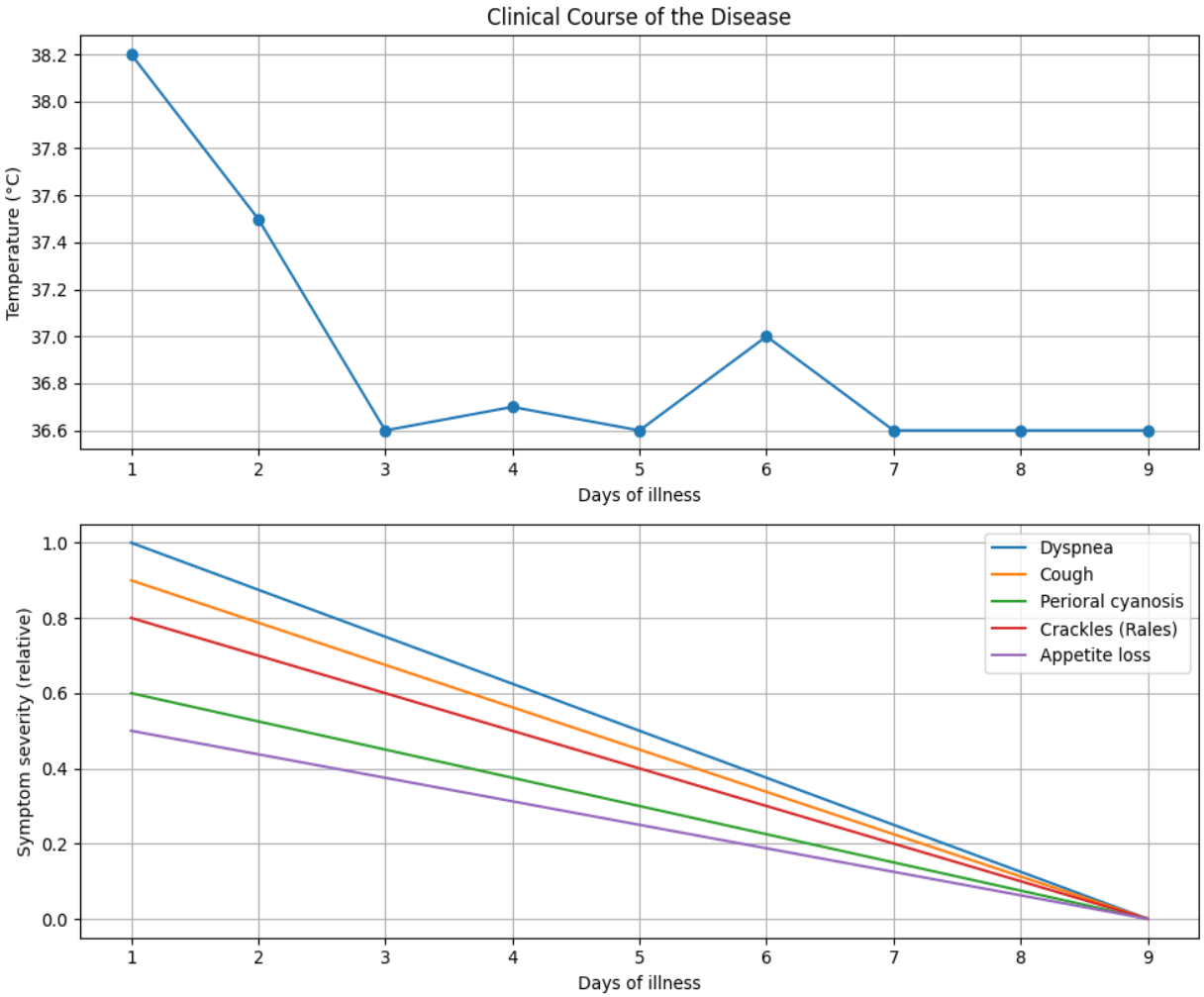


Fig. 2. Clinical characteristics of the course of the disease in patient D.

In this case, the severity of clinical and laboratory signs in patients with AOBl were characterized by a longer aggressive course than in children with AOB. Additional inclusion of the drug Immunomodulin in the complex of therapeutic measures made it possible to significantly reduce the time of disappearance of clinical signs of respiratory failure compared to such data noted in children treated with the traditional method (Tables 3 and 4).

The time of disappearance of clinical signs, assessed by indicators characterizing respiratory failure in children with acute respiratory distress syndrome during the period of treatment with the additional inclusion of immunomodulin, was reduced compared to the group of children treated with the traditional method.

Table 3

Time (days) for the disappearance of clinical signs of respiratory failure in children with acute obstructive pulmonary disease during the treatment period (M+ m)

Clinical sign	Traditional therapy (n =38)	Trad. therapy + immunomodulin (n =25)	Effect, %
Expiratory dyspnea with the involvement of accessory muscles	3.4±0.81	2.3±0.15*	32.4
Restoring the respiratory rate	3.9±0.27	2.7±0.16*	30.8
Cyanosis of the nasolabial triangle	2.8±0.16	2 , 1 ± 0 , 12 *	25.0
Paleness of the skin	5.7±0.12	4.9±0.23*	14.0
Tachycardia	3.2±0.22	2.5±0.18*	21.9
Remote wheezing, and	4.9±0.28	3.5±0.26*	28.6
also determined by auscultation	7.4±0.39	5.3±0.28*	28.4
Cough until it disappears completely	7.9±0.23	5.8±0.26*	26.6
Average value			26.0±2.21

- P<0.05

Thus, expiratory dyspnea with the participation of accessory muscles disappeared 1.1 days earlier, and the clinical effect increased by 32.4%, the restoration of the respiratory rate decreased by 1.2 days, and the clinical effect increased by 30.8% (Table 4).

Table 4

Time (days) for the disappearance of clinical signs of respiratory failure in children with acute respiratory failure during the treatment period (M+ m)

Clinical sign	Traditional therapy (n =15)	Traditional therapy + immunomodulin (n = 17)	Effect, %
Expiratory dyspnea with the involvement of accessory muscles	4.5±0.28	3.1±0.20*	31.1
Restoring the respiratory rate	4.7±0.19	3.3±0.14*	29.8
Cyanosis of the nasolabial triangle	3.6±0.20	2.7±0.18*	25.0
Paleness of the skin	7.8±0.33	6.3±0.45*	19.2
Tachycardia	4.9±0.27	3.5±0.21*	28.6
Remote wheezing, as well as	6.7±0.39	5.3±0.26*	20.9
determined auscultatory	11.6±0.33	8.9±0.35*	23.3
Disappearance of percussion sound with a boxy tone or boxy sound	7.8 ±0.34	6.4±0.17*	18.0
Cough until it disappears completely	10.5±0.26	8.8±0.14*	16.2
Average value			23.6±1.67

* - P<0.05

The disappearance of cyanosis of the nasolabial triangle was noted 0.7 (P<0.05) days earlier, the effect increased by 25.0%, pallor of the skin by 0.8 (P<0.01), tachycardia by 0.7 (P<0.001), distant wheezing by 1.4 (P<0.001), as well as determined by auscultation by 2.1 (P<0.002), cough decreased - by 2.1 (P<0.002) days, and the clinical effect increased by 14.0%, 21.9%, 28.6%, 28.4% and 26.6%, respectively.

When assessing the effectiveness of treatment in children with acute respiratory distress syndrome based on indicators characterizing respiratory failure, it was found that the period of disappearance of expiratory dyspnea was shorter in patients treated with immunomodulin by 1.4 days (P<0.002), and the treatment effectiveness indicator increased by 31.1%. Restoration of respiratory rate, disappearance of cyanosis of the nasolabial triangle, pallor of the skin, tachycardia, distant wheezing, as well as characteristic percussion pulmonary sound with a box shade determined by auscultation, cough decreased by 1.4 (P < 0.002), 0.9 (P < 0.001), 1.5 (P < 0.002), 1.4 (P < 0.002), 1.4 (P < 0.002), 2.7 (P < 0.002), 1.4 (P < 0.002) and 3.7 (P < 0.002) days, respectively, and the effectiveness of treatment increased by 29.8%, 25%, 19.2%, 28.6%, 20.9%, 23.3%, 18.0% and 16.2%.

Thus, the analysis of the obtained data on the study of clinical signs of the disappearance of respiratory failure in patients with AOB and AOBl showed that the effectiveness of treatment with the inclusion of immunomodulin is significantly higher than in patients treated with traditional therapy.

§ 4.2. Evaluation of the effectiveness of immunomodulin by indicators characterizing intoxication in children with acute obstructive bronchitis and bronchiolitis

When assessing the effectiveness of treatment of children with acute obstructive pulmonary disease based on indicators characterizing the degree of intoxication, the following was revealed during treatment with immunomodulin and the traditional method.

The time of disappearance of high body temperature decreased by 0.7 days (P<0.001), lethargy and adynamia - by 2.1 days (P<0.002), capriciousness, anxiety - by 0.7 days (P<0.001), sleep disturbance - by 1.1 days (P<0.02), lack of appetite - by 1.6 days (P<0.001), catarrhal phenomena - by 0.8 days (P<0.001), leukocytosis, leukopenia, neutrophilia and increased ESR

- by 1.3 (P<0.002), 1.2 (P<0.002), 1.2 (P<0.002) and 1.4 (P<0.002) days, respectively, the effectiveness of treatment increased, respectively, by 33.3%, 42.9%, 20.6%,30.6%,34.0%,24.3%,29.6%,26.7%,25.5%,31.1% (Table 5).

Less pronounced, the time of disappearance of intoxication symptoms in children with acute respiratory distress syndrome during the period of treatment with immunomodulin was reduced compared to the data on clinical signs of respiratory failure.

Table 5

Time (days) for the disappearance of clinical signs of intoxication in children with acute obstructive pulmonary disease during the treatment period (M± m)

Symptom of intoxication	**Traditional therapy (n =38)**	**Trad. therapy + immunomodulin (n =25)**	**Effect, %**
Increased body temperature	2.1±0.16	1.4±0.09*	33.3
Lethargy, adynamia	4.9+0.30	2.8+0.08*	42.9
Capriciousness, anxiety	3.4±0.19	2.7+0.13*	20.6
Sleep disturbance	3.6+0.25	2.5+0.07*	30.6
Lack of appetite	4.7±0.31	3.1+0.08*	34.0
Catarrhal phenomena (rhinitis, pharyngitis)	3.3±0.16	2.5+0.11*	24.3
Leukocytosis	4.4±0.15	ЗД±0.08*	29.6
Leukopenia	4.5±0.06	3.3+0.09*	26.7
Neutrophilia	4.7±0.30	3.5+0.07*	25.5
Increased ESR	4.5+0.22	3.1+0.10*	31.1
Average value			29.9±3.19

* - P<0.05

At the same time, compared with the indicators obtained with traditional treatment, a significant difference was noted in the reduction in the duration of symptoms of intoxication of the body.

Thus, the time of disappearance of intoxication symptoms was shorter in children with acute obstructive pulmonary disease who received immunomodulin compared to the traditional treatment group: high body temperature - by 0.5 days ($P < 0.01$), lethargy and adynamia, capriciousness and anxiety, sleep disturbance, lack of appetite, catarrhal phenomena, leukocytosis, leukopenia, neutrophilia, increased ESR - respectively, by 1.5 ($P < 0.05$), 0.8 ($P < 0.01$), 1.3 ($P < 0.002$), 1.4 ($P < 0.002$), 1.8 ($P < 0.002$), 1.2 ($P < 0.002$), 0.5 ($P < 0.05$), 0.9 ($P < 0.02$) and 1.7 ($P < 0.002$) days, and the effectiveness of treatment increased by 19.2%, 11.4%, 17.8%, 25.5%, 28.6%, 17.4%, 24.5% and 9.8%, 17.3% and 20.9% (Table 6).

It should be noted that the effectiveness of immunomodulin in AOB is not as high as in AOB, as can be seen from the table of the effectiveness of treatment with immunomodulin by signs.

The effectiveness of treatment with immunomodulin based on signs of intoxication of the body in children with acute respiratory distress syndrome was significantly lower by 18.7% ($P<0.002$) than based on clinical signs assessing respiratory failure.

At the same time, the effectiveness of therapy established by signs of intoxication in children with acute respiratory failure treated with immunomodulin was significantly higher by 13.05% ($P<0.05$) compared to those with respiratory failure. Such a difference in indicators is associated with the peculiarities of pathomorphological changes in the bronchopulmonary system and in the body as a whole, which determines the severity of the disease and, accordingly, the body's resistance to the treatment.

It should be noted that the criterion for assessing the effectiveness of treatment with immunomodulin was chosen conditionally and cannot fully reflect the depth of clinical changes in the body of children for assessing clinical recovery.

Table 6

Time (days) for the disappearance of clinical signs of intoxication in children with acute obstructive pulmonary disease during the treatment period (M± m)

Symptom intoxication	**Traditional therapy (n =15)**	**Trad. therapy + immunomodulin (n =17)**	**Effect, %**
Increased body temperature	2.6 ± 0.19	2 , 1 ± 0 , 11 *	19.2
Lethargy, adynamia	4.4±0.23	3.9±0.17*	11.4
Moodiness, restlessness	4.5±0.26	3.7±0.20*	17.8
Sleep disturbance	5.1±0.17	3.8±0.14*	25.5
Lack of appetite	4.9±0.13	3.5±0.09*	28.6
Catarrhal phenomena (rhinitis, pharyngitis)	4.6±0.22	3.8±0.12*	17.4
Leukocytosis	4.9±0.16	3.7±0.10*	24.5
Leukopenia	5.1±0.27	4.6±0.18*	9.8
Neutrophilia	5.2±0.18	4.3±0.15*	17.3
Increased ESR	8.1±0.25	6.4±0.13*	20.9
Average value			19.3±2.01

* - P<0.05

To do this, it is necessary to introduce an indicator of the clinical recovery period.

CHAPTER V. CLINICAL TRIAL RESULTS

§ 5.1. Evaluation of the effectiveness of immunomodulin therapy according to the algorithm of respiratory failure, intoxication and clinical recovery indicators

As shown by the results of the study, the average clinical recovery rate of children with AOB treated by the traditional method was 8.7±0.21 days, while with the inclusion of immunomodulin in the complex therapy - 6.3±0.16 days. The effectiveness of treatment increased with treatment with the additional inclusion of immunomodulin, compared with the group of sick children treated by the traditional method - by 27.6%. In children with AOB, the period of clinical recovery with traditional therapy was 12.6±0.13 days, and with the inclusion of immunomodulin in the course of therapy 10.4±0.92 days, i.e. the treatment period was reduced by 2.2 ± 0.01 days. The effectiveness of treatment increased by 17.5%.

As can be seen from the above, the effectiveness of therapy is higher in children with AOB than with AOBl, which to a greater extent coincides with such dynamics when assessing clinical signs in children with AOBl treated with immunomodulin, and does not coincide in the direction of clinical signs in children with AOB treated with immunomodulin.

In order to give a correct, objective assessment of the effectiveness of treatment with the additional inclusion of immunomodulin, compared with the method of traditional therapy, we have compiled a database of average indicators of effectiveness, assessed by clinical signs of respiratory failure, the degree of intoxication and the criterion of the timing of clinical recovery. This allowed us to create an algorithm for statistical processing and objectively assess, taking into account the sum of all indicators, the increase in the effectiveness of treatment with the additional inclusion of immunomodulin.

As the results showed, the effectiveness of treatment in patients with AOB increased with the inclusion of immunomodulin by 27.8 ± 1.42%, and in patients with AOBl - by 20.1 ± 1.50% compared to the data obtained with treatment by the traditional method.

Thus, a high rate of treatment effectiveness is noted with the inclusion of immunomodulin, compared with traditional treatment, but in patients with AOB it is 27.7% higher than in children with AOBl.

The differences in the effectiveness of immunomodulin treatment in children with AOB and AOBl are shown in the following extracts from case histories.

Patient U., 5 months old. Became acutely ill. Body temperature suddenly rose to 38.1°C, runny nose, mild cough were noted, shortness of breath and cyanosis of the nasolabial triangle appeared on the 2nd day. The condition deteriorated sharply. Hospitalized.

On examination at the clinic, the following were noted: elevated temperature up to 38.6°C, pale skin, cyanosis of the nasolabial triangle, dyspnea. The pharynx is hyperemic. Flaring of the wings of the nose is observed during breathing. Accessory muscles participate in the act of breathing. The number of breaths is 62 per 1 min. The cough is frequent, wet. Numerous fine bubbling rales are heard in the lungs. Percussion sound is boxed. Heart sounds are muffled. Pulse 142 per 1 min. The liver is not enlarged.

In the blood: Hb - 112 g / L, er - 3.8 x 10^{12} / L, color.p - 0.8, L - 13.0 x 10^{9} / L; p.a. - 8%, s.a. 36%, eosinophils - 8%, lymph. - 46%, mon - 4%, ESR - 16 mm / h. When studying the parameters of local immunity revealed: KB - 2.11 conventional units; MP - 1.55 conventional units; CP - 0.53 conventional units; ALP - 0.42 conventional units; GL - 0.56 conventional units; SDG - 0.78 conventional units; a-GPDH - 1.83 conventional units; KK - 7.10 IU/10^{9} L;

CL - 910.18 imp/s/10 ^{9} L; NST-test - 16.12 conventional units; FA - 77.14%; FC - 3.22%; FI - 3.70%; PZF - 88.50%; IP - 2.50%; SOP - 7.93 μg/ml; BSOP - 22.30 μg/ml.

Chest X-ray - increased transparency of the lung fields, low position of the diaphragm, horizontal position of the ribs.

Taking into account the above symptoms, acute obstructive bronchiolitis, stage III respiratory failure, was clinically diagnosed.

Symptomatic therapy was performed with the inclusion of immunomodulin at 0.1 ml of 0.01% solution intramuscularly for 9 days, against the background of which from the 2nd day of illness the temperature returned to normal and appetite was restored, from the 5th day shortness of breath was not observed, from the 6th day perioral cyanosis disappeared, and from the 8th day the cough stopped, from the 6th day there were no wheezing in the lungs.

At the same time, cytochemical and metabolic parameters were restored to control values: KB - 1.42 conventional units; MP - 2.50 conventional units; CP - 0.40 conventional units; ALP - 0.27 conventional units; GL - 1.98 conventional units; SDH - 1.73 conventional units; α-GPDH - 0.96 conventional units; CC - 9.35 IU/10 ^{9} L; CL - 508.03 imp/sec/10 ^{9} L; NBT-test - 15.31 conventional units; FA - 50.78%; FC - 4.98%; FI - 2.26%; PZF - 62.26%; IP - 1.61%; SOP - 5.39 μg/ml; BSOP - 13.28 mcg/ml.

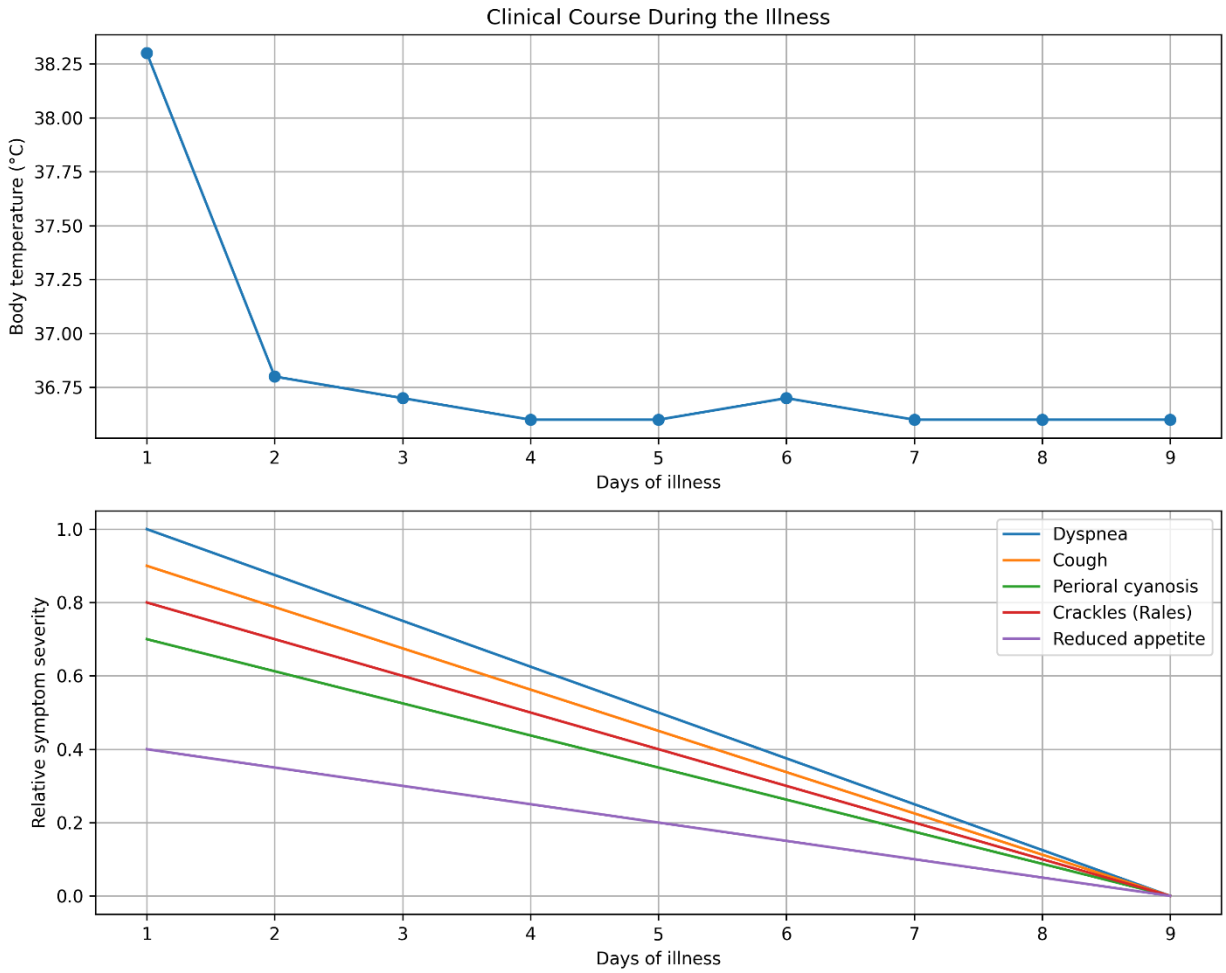


Fig. 3. Clinical characteristics of the course of the disease of patient U.

Discharged in satisfactory condition on the 9th day.

Patient T., 1 year 8 months. The disease began with a rise in temperature to subfebrile, cough, runny nose, lethargy. On the 3rd day of the disease, the body temperature rose to 38.5 ° C, the cough intensified, shortness of breath and distant wheezing appeared. The condition worsened and the child was hospitalized in serious condition. On examination, lethargy, pallor, cyanosis of the nasolabial triangle, runny nose, shortness of breath were observed. Body temperature increased to 38.7 ° C. The mucous membrane of the oropharynx and posterior pharyngeal wall is hyperemic. Distant wheezing is heard. Respiratory rate is 48 per 1 min. Dry whistling and moist medium-bubble rales are heard in the lungs against the background of harsh breathing. Muffled heart sounds, tachycardia. The liver is not enlarged.

In the blood: Hb - 132 g / L, er - 4.2 x 10^{12} / L, color.p - 1.0, L - 9.5 x 10^{9} / L; p.c. - 7%, s.c. 38%, eosinophils - 3%, lymph. - 44%, mon - 8%, ESR - 8 mm / h. Cytochemical and metabolic parameters: CB - 1.88 conventional units; MP - 1.78 conventional units; KF - 0.56 conventional units; ALP - 0.42 conventional units; GL - 0.74 conventional units; SDG - 0.89 conventional units; α-GPDH - 1.39 conventional units; KK - 7.51 IU/10^{9} L; CL - 841.64 imp/s/10^{9} L; NST-test - 16.02 conventional units; FA - 81.44%; FC - 3.13%; FI - 3.75%; PZF - 92.50%; IP - 2.56%; SOP - 6.52 μg/ml; BSOP - 19.22 μg/ml.

Chest X-ray - increased pulmonary pattern and widened lung roots, increased transparency of lung fields. Clinically established diagnosis: acute obstructive bronchitis, stage II respiratory failure.

Subsequently, against the background of pathogenetic therapy with the inclusion of immunomodulin at 0.1 ml intramuscularly for 6 days, the boy's condition gradually began to improve: the temperature decreased and returned to normal by the 2nd day; catarrhal symptoms by the 3rd; perioral cyanosis by the 2nd; shortness of breath by the 3rd, wheezing by the 4th; cough by the 5th, appetite on the 4th day.

Cytochemical and metabolic parameters of blood after treatment: CB - 1.41 conventional units; MP - 2.51 conventional units; CP - 0.38 conventional units; ALP - 0.32 conventional units; GL - 2.08 conventional units; SDG - 1.65 conventional units; α-GPDH - 0.90 conventional units; CC - 9.61 IU/10^{9} L; CL - 498.12 imp/sec/10^{9} L; NBT-test - 15.23 conventional units; FA - 59.29%; FC - 3.62%; FI - 2.57%; PZF - 80.66%; IP - 1.42%; SOP - 4.98 μg/ml; BSOP - 12.84 mcg/ml.

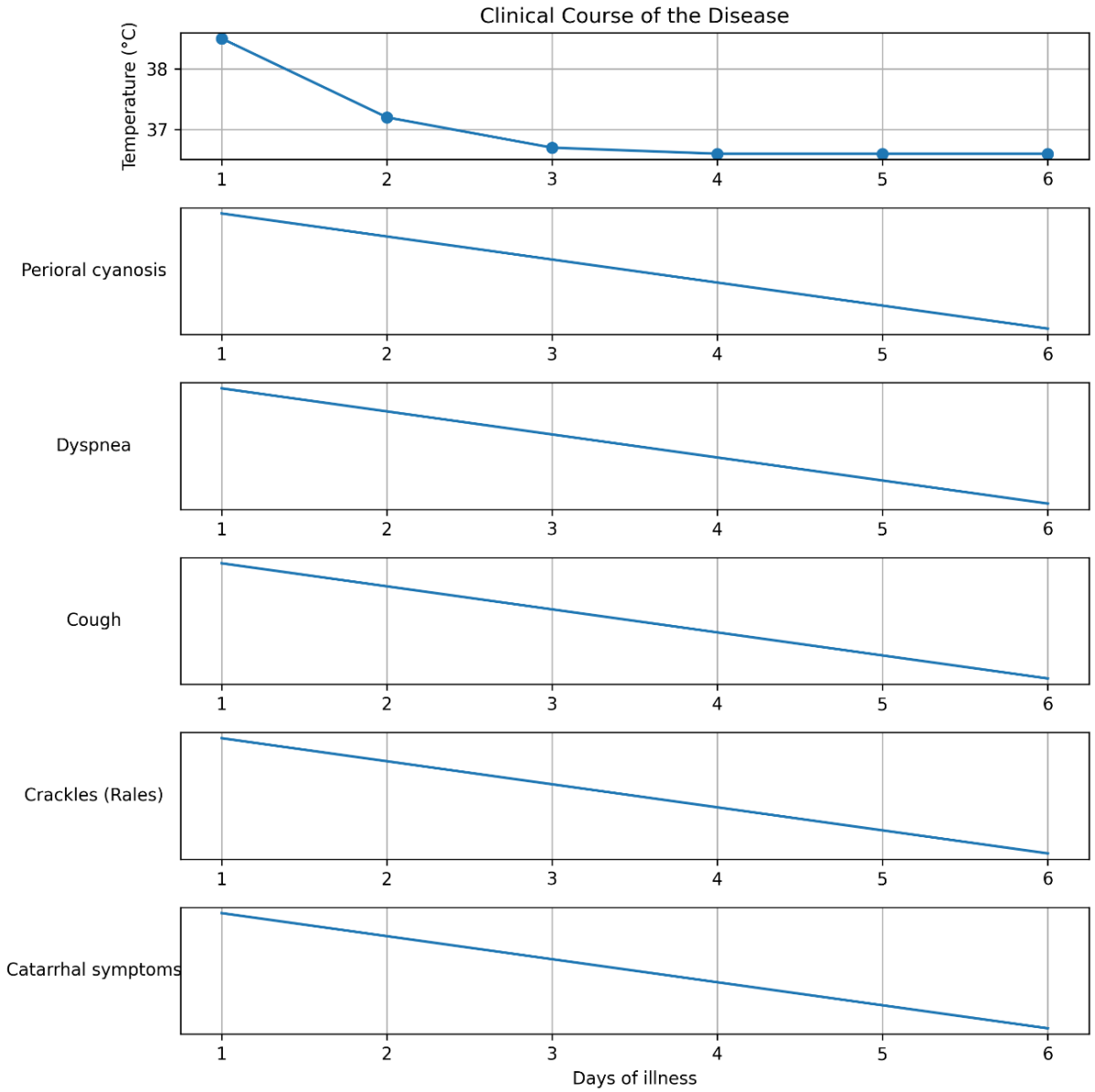


Fig. 4. Clinical characteristics of the course of the disease of patient T.

On the 6th day, the patient was discharged from the hospital in satisfactory condition.

It can be assumed that the high therapeutic effect associated with the introduction of immunomodulin into the course of treatment, compared with the traditional method, is associated with the peculiarity of the immunocorrective action of the drug and its influence on the functional metabolic processes in the body of children with acute obstructive pulmonary disease and acute obstructive pulmonary disease.

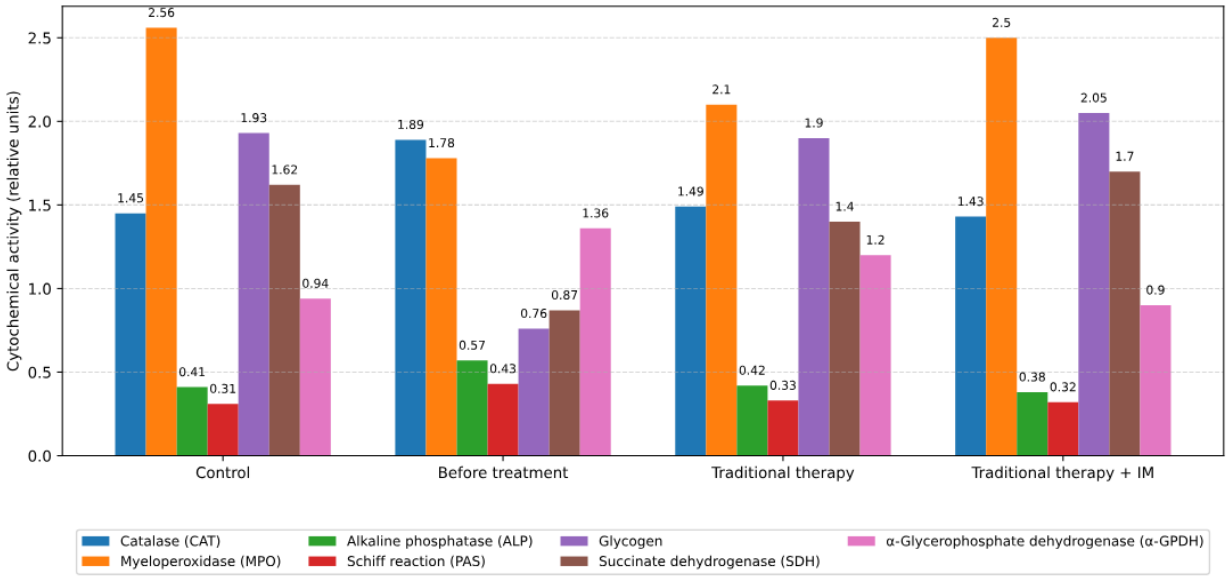
Thus, the effectiveness of treatment in young children with acute obstructive pulmonary disease and acute obstructive pulmonary disease increases with the additional inclusion of immunomodulin in the course of treatment. At the same time, clinical symptoms characterizing the state of respiratory failure, intoxication of the body and the timing of clinical recovery are reduced at an earlier stage. All this justifies the inclusion of immunomodulin in a complex of therapeutic measures in the treatment of young children with acute obstructive pulmonary disease and acute obstructive pulmonary disease.

§ 5.2. Cytochemical and metabolic criteria of the effect of immunomodulin therapy in young children with acute obstructive bronchitis and bronchiolitis

Analysis of the obtained research results showed that at the end of the course of therapy with the traditional method, young patients with acute obstructive pulmonary disease still experience disturbances in individual indicators of the cytochemical activity of NL.

The activity of MP and SDH remains reduced by 18.0 and 13.6%, while the α-GPDH indicator is higher - by 26.6% compared to the data in the control (Fig. 9).

AOB



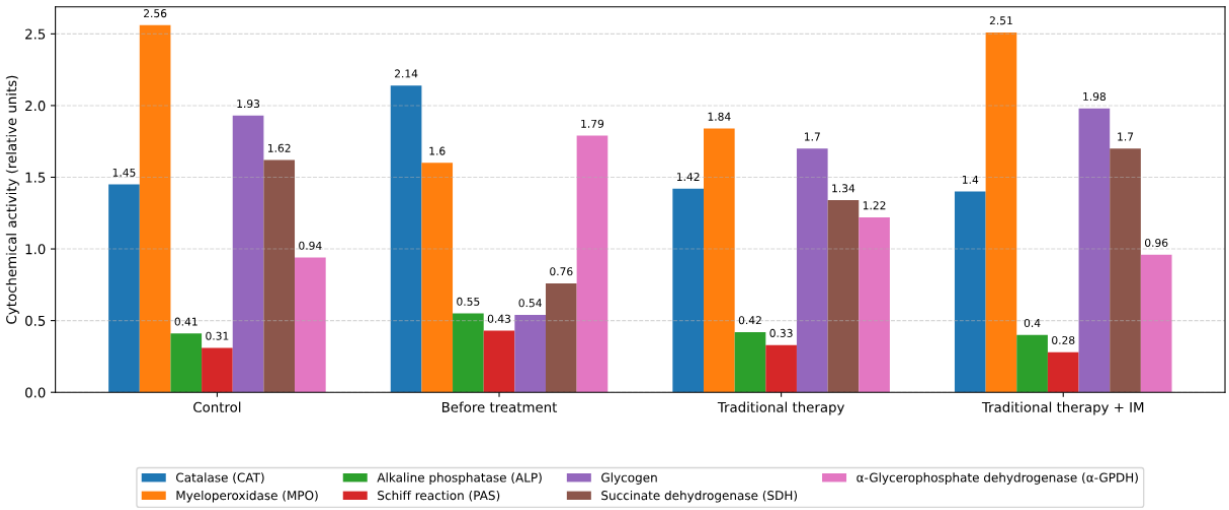


Fig. 9. Dynamics of cytochemical activity indices of NL (%) of blood in children with AOB and AOBl before treatment

Similar data were obtained in the treatment of children with acute obstructive pulmonary disease using traditional methods.

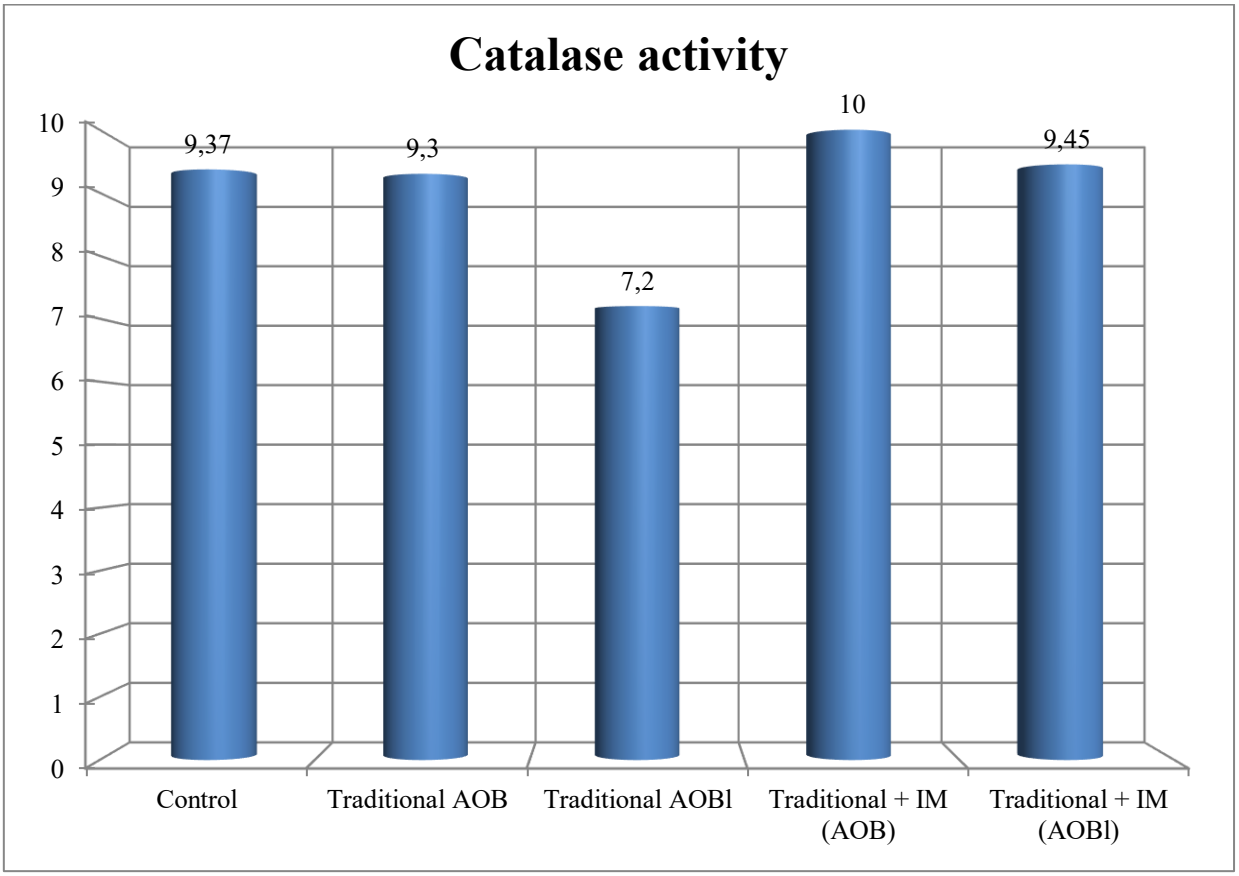
Thus, the activity of MP is reduced by 28.1%, SDG by 17.3%, and α-GPDH is higher than the control by 29.8%. In children with AOB treated with the traditional method, a statistically significant ($P < 0.01$) low content of glycogen in the NL was noted - lower by 11.9%. When immunomodulin was included in the basic therapy, complete restoration was observed in children with AOB, and with AOB, approach to the control of all the studied parameters of the cytochemical activity of NL.

Consequently, by the end of the course of treatment of young children with AOB and AOBl using the traditional method, not all studied indicators of the cytochemical activity of NL are restored, whereas when immunomodulin is included in the complex treatment, all values of the cytochemical activity of NL are normalized.

When studying the level of CC in both study groups, it was found that with traditional treatment this indicator was within the control limits only in patients with acute obstructive pulmonary disease, whereas with the inclusion of immunomodulin, it approached the control level (Fig. 10).

Consequently, with treatment including immunomodulin, by the end of the course of therapy the CC indicator is restored to control values in the groups of children with acute obstructive pulmonary disease and acute obstructive pulmonary disease, and with treatment using only the traditional method - only in children with acute obstructive pulmonary disease.

When analyzing the results of studies of the state of metabolic activity of the NL by changes in the level of CL, it was noted that with traditional treatment we were unable to restore this indicator to control values in both children with AOB and with AOBL. By the end of the course of therapy, its level was higher than the control values by 17.5% and 32.7%, respectively. At the same time, when immunomodulin was included in the complex treatment, the CL indicator in the NL group of children with AOB and OOBL was within the control limits.



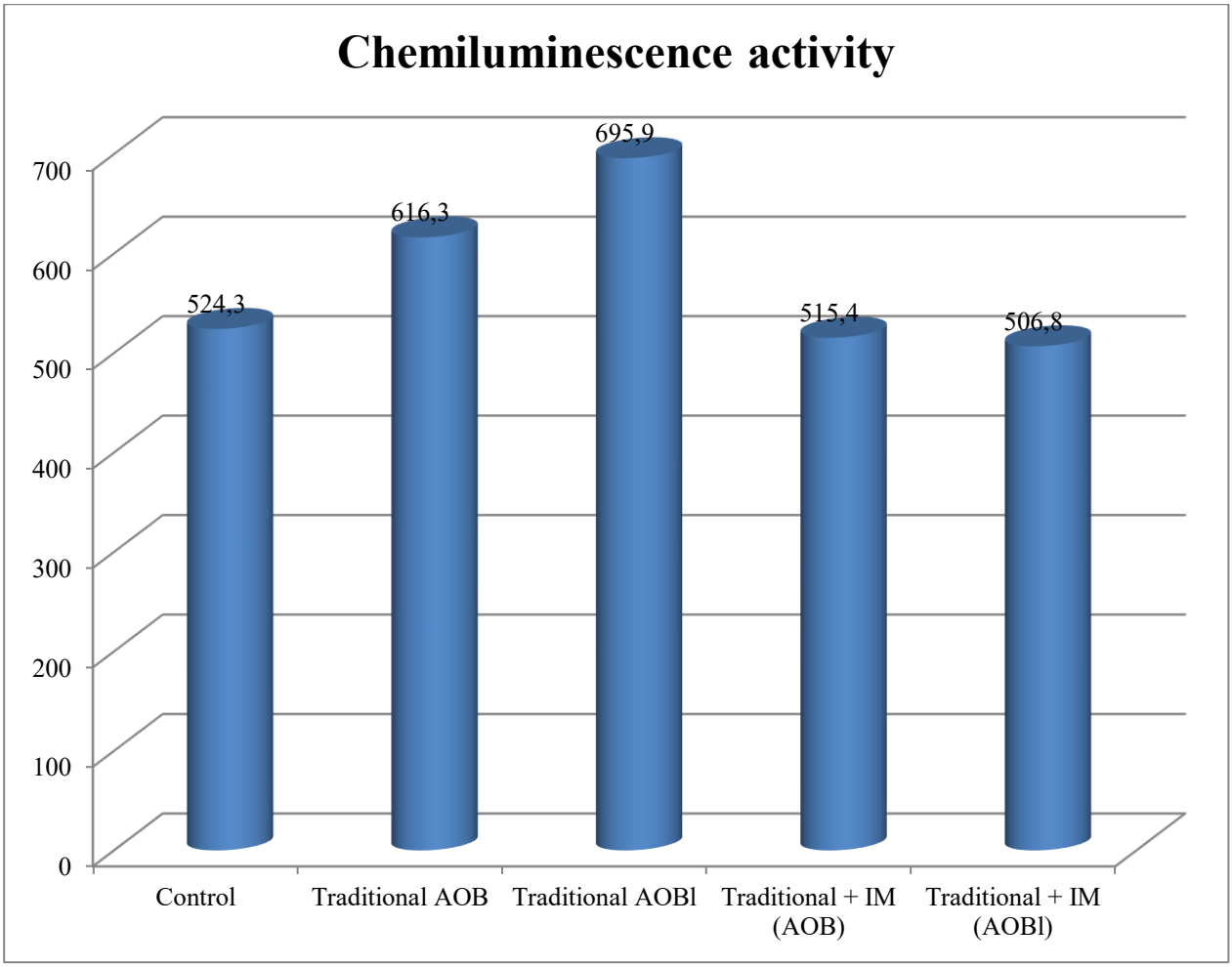


Fig. 10. Dynamics of the KK and HL indices in the NL among the examined young children

Consequently, with traditional treatment, the metabolic activity of the NL in children with AOB and AOBl and the HL index are not restored, whereas with the additional inclusion of immunomodulin in the complex treatment, they return to the control level.

In children with AOB after traditional basic therapy, all indicators of phagocytosis completion were within the control values. At the same time, in children with AOB, a number of indicators reflecting the state of phagocytosis were higher than the control - NST test - by 8.9% ($P < 0.05$), FA - by 13.3%, FI - by 17.4%, PZF - by 10.9% ($P < 0.05$), IP - by 14.7% (Fig. 1 1).

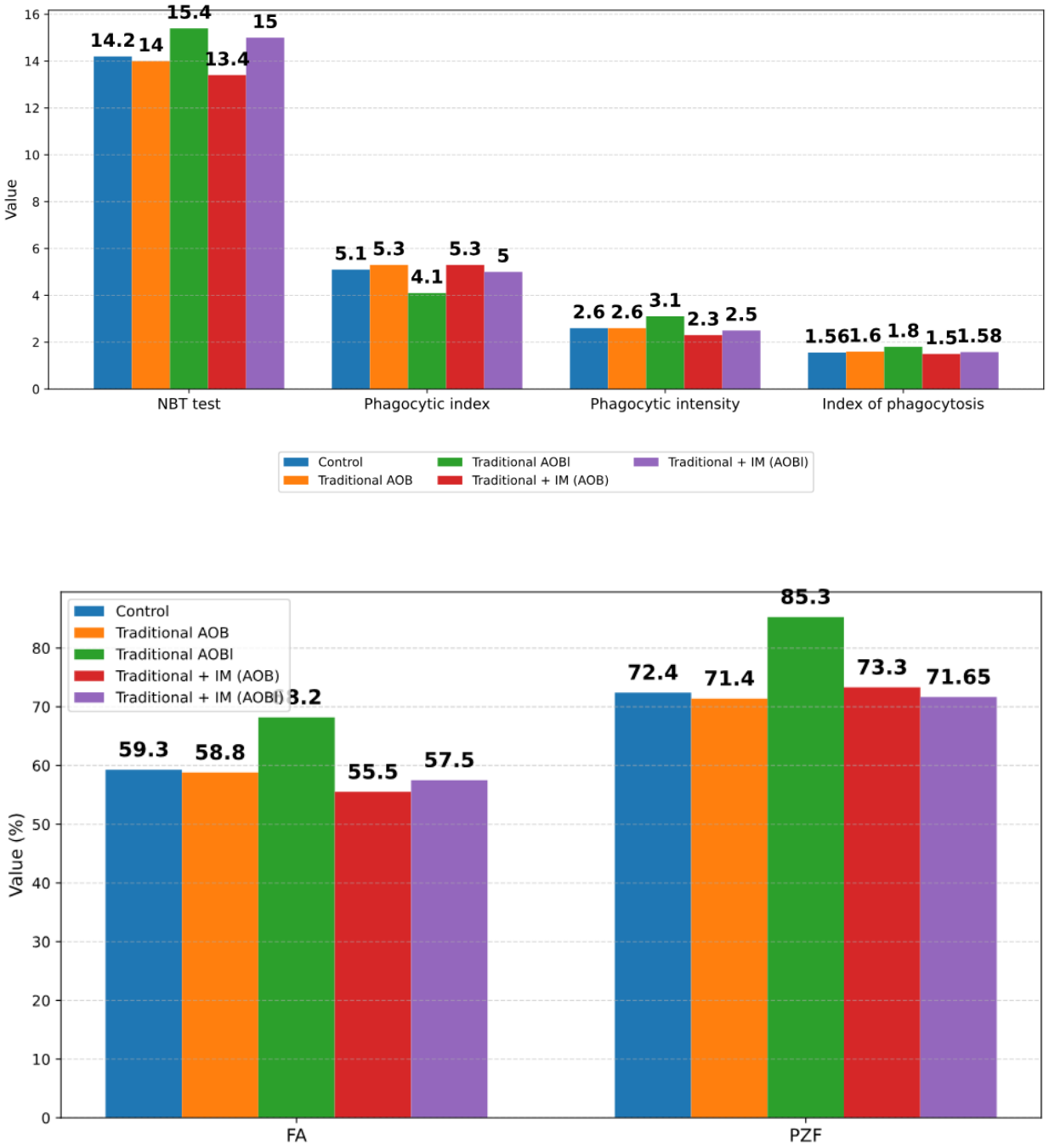


Fig. 11. Dynamics of functional-metabolic activity indicators in the NL among the examined young children during the treatment process

When assessing the data on the phagocytic activity of NL by the end of the course of treatment using the immunomodulin immunocorrector, it was noted that in both examined groups they were within the control values.

Consequently, traditional therapy does not restore the indices of phagocytic activity of NL to control values in children with AOBl, whereas in children with AOB they were within the control limits. With the additional

inclusion of immunomodulin in the complex treatment, the level of phagocytic activity of NL is restored in both groups.

It should be noted that when analyzing all the studied parameters (cytochemical, energy-generating, metabolic, phagocytic activity) by the end of the course of treatment in children treated by the traditional method, deviations of certain parameters from the control were noted - in 5 (13.2%) of 38 with acute hepatitis B and in 5 (33.3%) of 15 with acute hepatitis B. At the same time, when including immunomodulin, changes from the norm in the parameters of cytochemical, energy-generating and phagocytic activity were observed in 1 (4%) of 25 with acute hepatitis B and in 2 (11.7%) of 17 with acute hepatitis B.

It can be assumed that the relative dynamics of the indices of cellular immunity in different methods of therapy could have a special effect on the data characterizing the state of the bronchopulmonary system in patients with acute broncho-obstructive syndrome. Indeed, as the results of the studies showed, the level of OP, both free and protein-bound, in children with AOB treated with the traditional method was within the control values, whereas in patients with AOBl, SOP exceeded the control values by 14.6%, and BSOP - by 19.6%.

By the end of therapy with the inclusion of immunomodulin, the studied parameters of SOP and BSOP in blood plasma were within the control limits.

Consequently, the inclusion of the immunomodulin immunocorrector provides a more pronounced therapeutic effect aimed at eliminating the process of destruction in the bronchopulmonary system in children with acute obstructive pulmonary disease and acute obstructive pulmonary disease than the traditional method, which was mainly effective only in the group of children with acute obstructive pulmonary disease.

Evaluating the results of treatment in a comparative aspect between groups of patients with AO and AO, treated with the traditional method and the method with the additional inclusion of immunomodulin according to the indicators of the frequency of cases of restoration of OP in the blood plasma, we noted that they do not at all coincide with the data on the state of cellular immunity.

Thus, after a course of treatment of children using the traditional method, deviations from the control values of free and protein-bound OP were observed in 3 (7.9%) of 38 with AOB and in 3 (20%) with AOBl (Fig. 12).

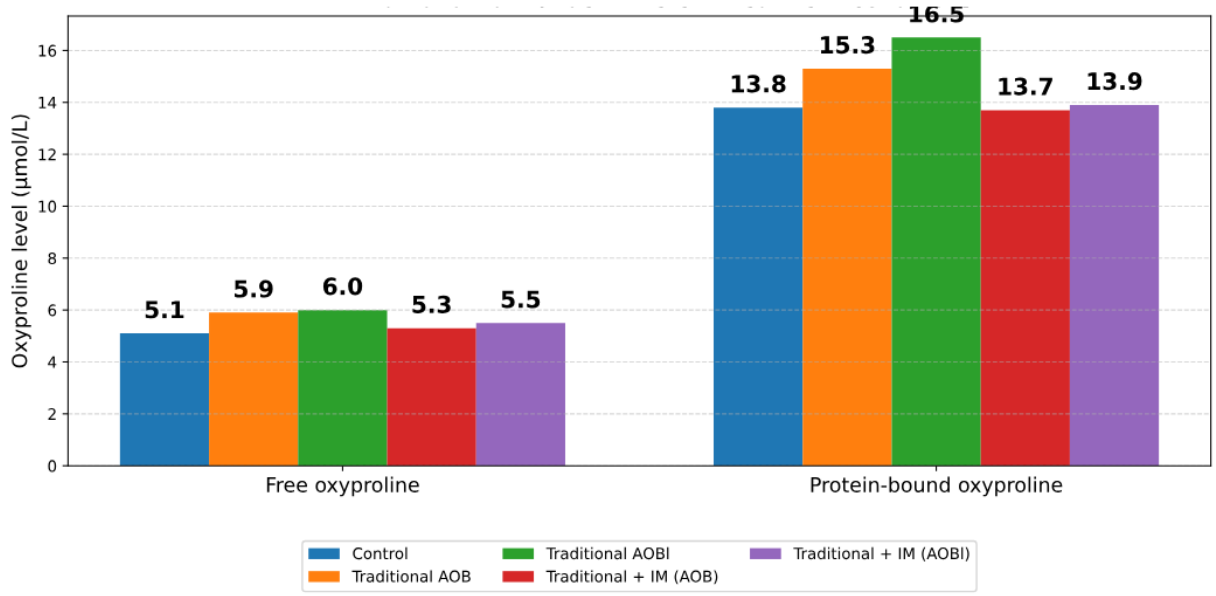


Fig. 12. Dynamics of free and protein-bound oxyproline levels in blood plasma in young children with acute obstructive pulmonary disease and acute obstructive pulmonary disease during treatment

At the same time, in children with AOB who had recovered and were treated with additional inclusion of immunomodulin, a high level of SOP and BSOP was not detected. In patients with AOB, only 1 (5.9%) out of 17 showed an increase in the level of these indicators.

Consequently, additional inclusion of immunomodulin in complex treatment promotes restoration of the index of destruction of the bronchopulmonary system - OP - to control values in a larger number of sick children with AOB and AOBl than with the traditional method of therapy.

Thus, before the treatment, children with acute obstructive pulmonary disease and acute obstructive pulmonary disease showed a significant disruption of the state of cellular immunity and a high degree of destructive processes in the bronchopulmonary tissue assessed by the level of free and protein-bound OP in the blood plasma.

Restoration to control values of the studied parameters of cytochemical, energetic, metabolic, phagocytic activity or the level of OP was more often observed in children with acute obstructive pulmonary disease and acute obstructive pulmonary disease treated with the inclusion of the drug immunomodulin in the complex therapy compared to such data obtained with basic therapy.

It is possible that the varying degrees of disturbances and restoration of the studied parameters of cellular immunity and bronchodestructive processes reflect the degree of clinical manifestations depending on the form of the disease before treatment and the effectiveness by the end of the therapy in young children with acute obstructive pulmonary disease and acute obstructive bronchitis.

CHAPTER VI. RESULTS OF CYTOCHEMICAL AND METABOLIC STUDIES

§ 6.1. Diagnostic and prognostic value of cytochemical studies of blood leucocytes in the functional assessment of acute obstructive bronchitis

In recent years, despite the progress of medical science, cytochemical methods for studying the enzymatic activity of blood leukocytes remain one of the most important and informative methods for diagnosing and predicting acute and chronic diseases of the bronchopulmonary system in pediatrics. The main advantage of studying the enzymatic activity of blood leukocytes is the ability to obtain important diagnostic and prognostic information in the absence of any shifts in the morphological composition of the white part of the blood. These methods, along with high diagnostic sensitivity, are relatively cheap, easy to perform, do not require special bulky equipment and allow you to obtain the necessary information in a relatively short period of time (on average 2 - 3 hours).

In most research papers, blood leukocytes are considered as cells that characterize the state of the body's immunological reactivity. At the same time, undeservedly little attention is paid to such a phenomenon of leukocytes as high intensity of aerobic metabolism. Due to this property, the leukocyte, as well as other aerobic cells (neuronocyte, hepatocyte, myocardiocyte, etc.), is a cell highly sensitive to changes in the oxygen regime in the body.

Among the subcellular structures, the first to react to insufficient oxygen supply to the cell are mitochondria. This is due to the fact that it is in them that the reactions of oxidative phosphorylation and tissue respiration occur, ensuring an adequate level of energy generation in the cell. A decrease in the oxygen supply to the mitochondria is accompanied by a change in the activity of enzymes catalyzing mitochondrial bioenergetic reactions. At the same time, the processes of ATP synthesis catalyzed by water-soluble enzymes are easily

accessible for analysis and can serve as models for studying the extremely complex processes of mitochondrial phosphorylation. One of such enzymes is creatine kinase (CK), which catalyzes the reversible reaction of ADP phosphorylation with the formation of ATP and free creatine. Under physiological conditions, CK ensures the constancy of the ATP level in the cell.

Literature data indicate that the activity of mitochondrial dehydrogenases of blood leukocytes are sensitive indicators of oxygen deficiency in tissues. The most informative and objective criteria for tissue hypoxia in the body of young children are such mitochondrial enzymes as succinate dehydrogenase (SDH) and α-glycerophosphate dehydrogenase (α-GPDH) of blood leukocytes.

SDH is a key enzyme of the Krebs cycle, which is the main “focus” of all metabolic pathways in the cell. SDH activity is a marker of the intensity of aerobic bioenergetic processes in mitochondria, since it is directly related to the intensity of oxidative phosphorylation.

Mitochondrial α-GPDH is an enzyme of the central oxidation-reduction reaction of glycolysis associated with the formation of ATP. Mitochondrial α-GPDH takes part in the glycerophosphate shuttle mechanism that provides electron supply to the Krebs cycle reactions, and therefore its activity reflects the synchronicity of glycolysis and biological oxidation processes. The glycerophosphate shunt plays the role of a powerful competitor of LDH and thereby helps maintain steady-state concentrations of pyruvate, which is necessary to launch reactions of the tricarboxylic acid cycle. Determination of only the average activity of mitochondrial dehydrogenases of leukocytes significantly reduces the interpretation of cytochemical parameters.

Based on the mathematical method of processing proposed by V.Yu. Urbach, R.P. Nartsissov introduced a number of indicators into cytochemical

analysis that characterize the structure of the population of the leukocyte - lymphocyte system of an individual by their enzymatic activity. Such indicators include the asymmetry coefficient, which characterizes the measure of balance of cell pools with high and low enzymatic activity, the variation coefficient, which reflects the enzymatic heterogeneity of lymphocytes, and the excess coefficient, which gives an idea of the abundance of cells with typical enzymatic activity for a given individual.

At the same time, it should be noted that the most important property of mitochondrial enzymes of peripheral blood leukocytes is their close correlation relationship with the activity of similar enzymes in internal organs. This property is expressed in the existence of ergonic correlations, characterizing the correspondence of the functional activity of some cells and systems to the work of other body systems.

Moreover, an organ in a state of functional stress has more such correlations with leukocytes.

In light of the above, leukocytes, in our opinion, can be regarded as cells whose enzymatic systems reflect the state of mitochondrial bioenergetics in aerobic cells of the body. It should be emphasized that changes in the activities of mitochondrial dehydrogenases of blood leukocytes precede similar shifts in enzymatic activity in internal organs. This makes it possible to “catch” this hypoxic process in a timely manner and carry out targeted therapeutic correction.

In recent years, the reactions of leukocytes as effectors of inflammation to a stimulus have been studied in clinical practice not only by SDH and α-GPDH indices, but also by the activity of acid and alkaline phosphatase (AP and ALP), myeloperoxidase (MP), glycogen (GL), cationic proteins (CP), etc. However, as an analysis of modern literature shows, each of the above cytochemical features characterizes only individual links in the complex

apparatus of cellular reactivity. For example, one cannot draw general conclusions about their phagocytic activity as a whole based on the absorption and digestion of any one strain of a microbe by neutrophils.

In the last decade, the nitroblue tetrazolium test (NBT test) has been increasingly used as an integral test for assessing the potential microbiocidal capacity of phagocytes. The molecular basis of the NBT test has been studied quite thoroughly. Its principle is based on the ability of neutrophils to absorb nitroblue tetrazolium, which is reduced to an insoluble dark blue deformazan in the cell phagosomes. In phagosomes, NBT serves as an acceptor of electrons that are formed during the oxidation of NADPH to NADP during glucose conversion in the pentose cycle. NADPH oxidation, in turn, is associated with the production of highly reactive activated oxygen metabolites (AOM): hydrogen peroxide (H_20_2), superoxide anion ($O_2\uparrow$), singlet oxygen (O_2T), hydroxy hydrogen (OH') and a series of less stable hydroxy radicals.

Granulocytes have two bactericidal systems that use the products of the "respiratory burst": the myeloperoxidase system and the oxygen-dependent cytolytic system, which does not depend on this enzyme. The myeloperoxidase system is largely associated with the NADPH-cytochrome P-450-dependent electron transport system of leukocytes, the functional activity of which is associated with the metabolic activity of leukocytes and is aimed at ensuring chemical homeostasis of the cell, protecting it from the damaging effects of toxic metabolic products formed during phagocytosis and digestion of bacteria, detoxification of bacterial toxins, cytotoxicosis, tissue decay products activated by the action of lysosomal enzymes during detoxification of xenobiotics, etc.

To assess the metabolic oxygen-dependent bactericidal and myeloperoxidase activity of leukocytes, along with cytochemical activity, the methods of chemiluminescence (CL), fluorometry, spectrophotometry and the

NBT test are widely used. The NBT test has advantages over other cytochemical reactions. Firstly, the NBT test reveals components that are absent (or almost absent) in a resting neutrophil. They arise only upon stimulation, therefore, they allow to differentiate intact and activated cells. Secondly, the NBT test reflects the final reaction of one of the key enzyme systems responsible for the cytochemical potential of the neutrophil. Impaired ability to restore NBT coincides with pathology of oxygen-dependent bactericidal mechanisms.

It should be noted that leukocytes take an active part in protecting the body in infectious diseases. They not only destroy foreign agents, but also influence the course of many of the most important reactions of the body, being a cellular-humoral effect of inflammation in response to a wide range of stimulating effects. Leukocytes are able to quickly rebuild their metabolism, carry out adhesion, degranulation, migration, phagocytosis and endocytosis, activation of a number of humoral systems of the body. In infections, leukocytes influence the development, course and outcome of the disease, often determining its prognosis.

In obstructive bronchitis, leukocytes, migrating into the lung tissue, play a vital role in eliminating the pathogen, phagocytizing and digesting both bacteria and the released products of macrophage decay.

Acute bronchitis as a condition associated with increased energy expenditure of the child's body is accompanied by a transformation of bioenergetic homeostasis. This is reflected in a change in the enzymatic activity of blood leukocytes in young children with acute bronchitis.

According to some authors, before the development of BOS, there is an increased activity of mitochondrial dehydrogenases of leukocytes, which is due to adaptation mechanisms to upper respiratory tract infection. Probably, such an interpretation of cytochemical data by the authors is due to the fact that

the comparison of the indicators of SDH, α-GPDH, ALP, CP, GL in leukocytes was carried out in sick children at the onset of the disease. At the same time, N. Mazureket, N.M. Grubbaueretal showed that the acute period of development of obstructive bronchitis is accompanied by suppression of SDH and activation of α-GPDH, CP, ALP, KB lymphocytes in comparison with similar indicators in young children with simple acute bronchitis and pneumonia, which indicates an increase in oxidative processes. The development of complications in the body of children after BOS is accompanied mainly by inhibition of mitochondrial enzyme systems of leukocytes. This is confirmed by a number of cytochemical and biochemical studies.

Of particular interest are the data concerning the relationship between the indices of enzymatic activity of leukocytes, lymphocytes in the blood of children and immune processes in the body with BOC. D. Olivieriet. al. based on the study of eosinophilic alveolitis in immunological interstitial lung diseases and the correlation between the activity of SDH, lymphocytes in the blood of young children established that the depression of the enzyme in the macrophages of the lungs is combined with the suppression of its activity in the lymphocytes of the blood. In addition, a reliable correlation relationship was revealed between the activity of SDH in the lymphocytes of the blood in the acute period of broncho-obstruction and the activity of this enzyme in macrophage alveocytes. These data served as the basis for using the determination of the enzymatic activity of lymphocytes in the diagnosis and prognosis of hypoxic complications in young children with AOB.

The study of the enzymatic activity of blood lymphocytes in young children with BOS showed that broncho-obstruction is accompanied by a sharp activation of enzymes catalyzing both anaerobic and aerobic bioenergetic reactions. Thus, D. Ukenaetal., T. Nicolai, A. PoI indicate a reliable increase

in the activity of LDH, α-GPDH, CP, ALP, KB in lymphocytes. At the same time, SDH, the level of GL and MP were significantly reduced at the height of the disease. The enzymatic status of blood lymphocytes in sick children of early age on the first day of BOS is characterized by the maximum peak of increase in LDH, α-GPDH, CP, ALP and KB and a deep depression of SDH, followed by their recovery on the 10-14th day from the moment of treatment.

A number of researchers at the height of the disease revealed the presence of an imbalance in the enzymatic structure of lymphocytes [148,152]. In young children who have suffered from AOB for the first time, high activity of α-GPDH in lymphocytes is maintained for another 2-3 months, which may be an important reason for the reduced reactivity of the body and the undoubted addition of a secondary infection.

Disruption of enzymatic activity is inextricably linked with cellular-humoral immunity. As a non-specific reaction in the development of acute obstructive pulmonary disease, quantitative and qualitative changes in the parameters of the immune status act as an important pathological link: the number of T cells (CD^{3+}) and their function (RBTL on PHA, ConA), the content of T suppressors (CD^{8+}) and their function (ConA-induced suppression), the number of T helpers (CD^{4+}), the number of B lymphocytes (CD^{19+}) and their function (the concentration of immunoglobulins of classes G, A, M, RBTL on PWM), the formation of interleukins 1 and 2, the content of neutrophils, alveolar macrophages and their function (phagocytic number, phagocytic index), the activity of humoral factors of non-specific anti-infectious resistance (lysozyme, complement, properdin system, (3-lysines), the activity of antibody-dependent and natural killers, the severity of autoimmune reactions. (lymphocyte migration inhibition reaction, RBTL, etc.) to the pulmonary antigen and the formation of autoantibodies against it.

The nature of immunological disorders in non-specific inflammatory lung diseases is that local immunity is suppressed, especially in severe cases of the inflammatory process. In this case, patients experience a decrease in the number and inhibition of T-lymphocyte functions, especially T-suppressors, an imbalance in the B-link of immunity and humoral factors of natural anti-infective resistance, and the formation of pronounced autoimmune reactions against lung tissue. According to A.M. Zemskov et al., indirect evidence of the involvement of immunological mechanisms in the pathogenesis of lung diseases is the establishment of the fact of an increased number of reliable correlations between the parameters of the immune system in the acute period of the disease and a decrease in their number during remission.

In recent years, an important place in the formation of BOS has been given to the suppression of the antioxidant system against the background of activation of lipid peroxidation. Thus, E.A. Kharabadzhakhyan, A.Yu. Antipov, when examining 60 children with acute bronchitis, revealed a significant increase in the intensity of LPO, suppression of SOD activity and, at the same time, an increase in the rate of reactions of glutathione-B-transferase and glutathione transferase in leukocytes of the peripheral blood. They noted the presence of a connection between the dynamics of the disease and the activity of antioxidant enzymes. The imbalance in the LPO-antioxidant enzymes system developing during BOS has its own characteristics in different age groups of children.

V.D.Delyan et al., when disclosing the pathogenesis of acute obstructive leukemia in young children, revealed a significant increase in spontaneous induced chemiluminescent-dependent luminescence of polymorphonuclear leukocytes. Children with high CL values in the acute period of the disease with their subsequent decrease by the time of clinical recovery were characterized by a recurrent course of acute obstructive leukemia. Different

levels of CL in neutrophilic leukocytes in the peripheral blood during the peak of acute obstructive leukemia and by the time of clinical recovery make it possible to predict the development and outcome of acute obstructive leukemia during the first examination of children.

A.A. Savchenko et al., when studying the functional activity of blood leukocytes in children with recurrent acute bronchitis and atopic dermatitis, found that the high information content of the CL method (including in the dynamics of treatment) makes it a necessary means of monitoring the level of nonspecific reactivity of the body, especially when prescribing treatment.

A number of researchers have found a positive correlation between the content of LPO products and the duration of the disease and a negative one between the activity of antioxidant enzymes and the severity and duration of acute obstructive pulmonary disease. An inverse relationship has also been established between the content of T-cells, T-suppressors, and T-helpers and the intensity of LPO in leukocytes. There is some evidence that the concentration of biogenic amines is in an inverse reliable correlation with the indices of antioxidant protection and in a direct correlation with the content of LPO products.

In recent years, the intensification of LPO has been given an important place in the mechanism of oxyproline metabolism (OP) disorders. OP is one of the important components of lung collagen. Compared with other parenchymatous organs, the collagen content in the lung is the highest. When OP metabolism is disrupted, unfavorable conditions are created for the stability of the pulmonary framework of the alveolar surfactant system and the performance of the lungs' main gas exchange function.

A number of researchers explain the disruption of collagen synthesis regulation during inflammatory processes in the lungs by shifts in

immunological reactivity. At the same time, excessive collagen formation is associated with the manifestation of lymphocyte autotoxicity.

The dependence of collagen production activation on the damaging effect of T-cells of lymphocytes has been revealed. A number of researchers associate the intensity of collagen formation in acute inflammatory lung diseases with metabolic disorders, namely protein-bound OP, and not its free fraction. In the case of a protracted course of the disease, a high level of protein-bound OP in the blood plasma against the background of a fairly good clinical condition of patients may indicate an unfavorable prognosis.

Thus, the presented literature data indicate high diagnostic and prognostic significance of cytochemical and metabolic activity of leukocytes in assessing the clinical course, effectiveness of therapy and the state of the body of young children with acute obstructive pulmonary disease. At the same time, there are practically no data in the literature on the effect of immunomodulin on the exchange of OP, CC, the intensity of lipid peroxidation in the body of young children with acute obstructive pulmonary disease and acute obstructive pulmonary disease. High information content of determining OP, CC, lipid peroxidation intensity and the availability of scarce data justify conducting studies to assess the severity of the development of destructive processes in the lungs, the effectiveness of the immunocorrective therapy and the prognosis of the course of the disease in young children with acute obstructive pulmonary disease and acute obstructive pulmonary disease.

To clarify the pathogenesis of the disease and evaluate the data of immunocorrective therapy when prescribing immunomodulin, special cytochemical studies of leukocyte blood cells were carried out in sick young children.

The material for the study was capillary blood up to 2.0 ml. Blood was collected in the morning on an empty stomach. The studies were conducted

before and after treatment on the 10th - 12th day. The duration of treatment was on average 8-12 days.

The activity of acid phosphatase (AP) was studied by the Burston azo coupling method (modification of Yu.F. Rudens, I.M. Buikis, 1965), alkaline phosphatase (AP) according to M.P. Shchubic (1965), myeloperoxidase (MP) according to R.P. Nartsissov (1964), glycogen content (GL) according to A.L. Shabadash (1974), cationic proteins (CP) by the bromophenol blue method according to M.P. Shchubic (1974), the activity of succinate dehydrogenase (SDH) and α-glycerophosphate dehydrogenase (α-GPDH) according to Nachlas in the modification of R.P. Nartsissov (1969), creatine kinase (KK) according to V.A. Saks and Yu.I.Voronkov (1974). The functional activity of neutrophilic leukocytes (NL) was assessed using the NBT test by B.S.Nagaev (1983). At the same time, the phagocytic activity (FA), phagocytic number (PN), phagocytic index (PI), percentage of phagocytosis completion (PPC) and digestion index (DI) were determined. The values of KB, MP, CP, ALP, GL, as well as SDG, α-GPDH and NBT tests were calculated according to L.Kaplow (1955), and the average cytochemical coefficient was calculated in arbitrary units (AU).

It is necessary to emphasize that all the listed methods are well known, standardized and described in detail in the reference book “Laboratory Research Methods in Clinical Practice” edited by Prof. V.V. Menshikov (1987).

Neutrophils were isolated from heparinized venous blood (10 units of heparin per 1 ml of blood) of healthy donors. The cells were obtained on a double Ficoll-Verografin gradient (d1 = 1.077; d2 = 1.119), washed with Hanks' solution and suspended in RPMI - 1640 medium (Serva, Germany) with 10% fetal calf serum and gentamicin (40 μg/ml).

The production of active oxygen forms by neutrophils was recorded chemiluminometrically using the HLMC-01 device (Russia) in the presence of luminol ("Sigma" USA).

To assess the activity of proliferative processes in the connective tissue of the lungs in children with acute obstructive pulmonary disease, we used the method of determining oxyproline (OP) in blood plasma by M.A. Osadchuk and V.M. Kapustin.

Since no significant differences were found in the normative indicators depending on gender and age, we did not distribute them into age groups.

§ 6.2. Cytochemical activity of neutrophilic leukocytes before and after treatment in young children with acute obstructive bronchitis and bronchiolitis

As can be seen from the literature review, obstructive forms of acute bronchitis (AOB, AOBl) in young children occupy one of the leading places in the structure of childhood morbidity and mortality in the Republic of Uzbekistan. Due to the widespread prevalence of this disease, the high frequency of severe complications and early disability of children, this problem has not only medical but also important socio-economic significance.

A number of authors associate the development of obstructive forms of acute bronchitis with disorders of the cellular-humoral link of immunity. Neutrophilic leukocytes (NL) occupy an important place in this process. It has been established that, depending on the period of the disease, they are able to quickly rebuild their metabolism, carry out adhesion, degranulation, migration, phagocytosis and endocytosis, and activate a number of humoral systems of the body. There is some information that in bronchopulmonary pathologies, NL affect the development, course, and outcome of the disease, often determining its prognosis. All this determines a targeted search for effective methods for correcting the identified disorders in leukocytes, in the cellular link of immunity.

The arsenal of drugs used in the treatment of acute obstructive pulmonary disease is constantly updated. Of particular interest are immunomodulatory drugs, the use of which is justified by a significant impairment of the immune system in children with BOS. In this regard, the most promising drug for the treatment of patients with acute obstructive pulmonary disease is immunomodulin. At the same time, its effect on the cytochemical indices of NL in the blood of young children with acute obstructive pulmonary disease has not been studied.

As is known, the important components reflecting the cytochemical activity of NL are KB, MP and lysozyme. Acid and alkaline phosphatase actively participate in the degradation of microorganisms, the formation of cellular decay products, and glycogen is an important energy and plastic material of the phagocytic cell. An important indicator of the cytochemical activity of neutrophils is the content of SDH and α-GPDH in them, which are different pathways for energy supply to cells (SDH is the main enzyme of the Krebs cycle, α-GPDH is an enzyme of the glycerophosphate shuttle system, which carries out the relationship between glycolysis and mitochondrial oxidation). Their determination allows us to assess the state of intracellular energy as a whole and the predominant involvement of the main or reserve pathway of energy formation in the process.

The analysis of the obtained results of the study showed that before the treatment, young children with AOB and AOBl had significant disturbances in the cytochemical activity of NL. Moreover, in children with AOBl, these shifts were expressed more significantly, compared to sick children with AOB.

Thus, in young children with AOB before treatment, compared with the control group, there is a significant increase in the activity of KB, CP, ALP and α-GPDH (by 30.3%, 39.0%, 38.7% and 44.6%, respectively) and a decrease in the values of MP, GL and SDD by 60.7%, 30.5% and 46.3%,

respectively). At the same time, in patients with AOB, the activity of KB, CP, ALP and α-GPDH exceeded the control data - by 47.6%, 34.1%, 38.7% and 90.4%, and the MP, GL and SDH indicators decreased - by 37.5%, 72.0% and 53.1%, respectively (Fig. 5).

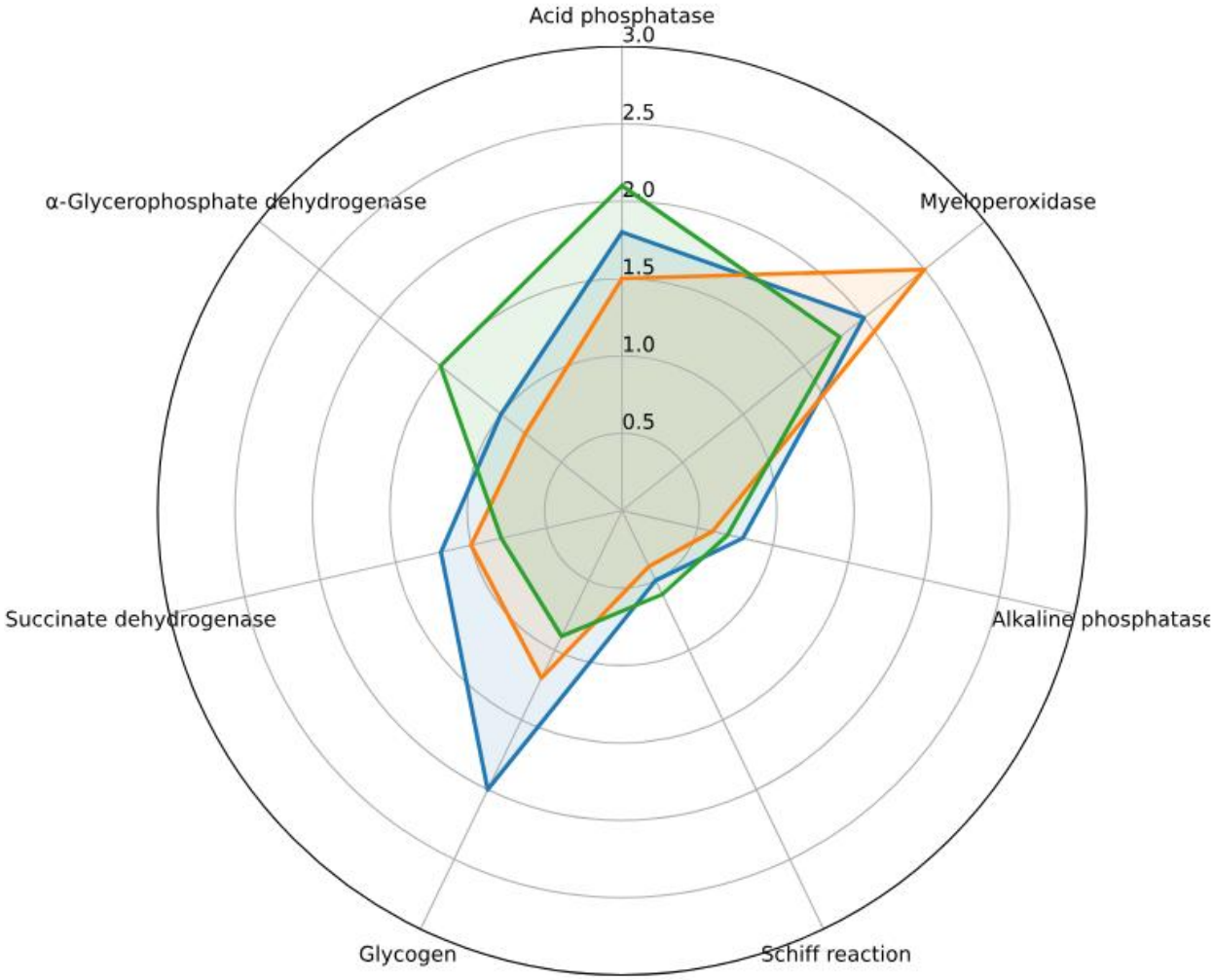


Fig. 5. Indicators of cytochemical activity of NL (%) of blood in children with AOB and AOBl before treatment

Therefore, before the treatment, significant disturbances in the cytochemical activity of enzyme systems, reflecting different levels of oxidative processes and energy supply in cells, are observed in young children with AOB and AOBl in the NL. More pronounced changes in the cytochemical activity of the NL were observed in children with AOBl.

Perhaps an important link in the disruption of the cytochemical activity of NL in children with AOB and AOBl is the shift in the formation of ATP.

Currently, for an objective assessment of the energy supply of the cell, the activity of the enzyme KK-ATP (creatine-H-phosphate transferase - CP 2.7.3.2) is determined, which catalyzes the reversible reaction of ADP phosphorylation with the formation of ATP and free creatine. Under physiological conditions, KK ensures the constancy of ATP in the cell. Violation of the energy supply can lead to a decrease in oxygen consumption and shifts in glucose oxidation in the reactions of the hexose monophosphate shunt.

As shown by the analysis of the obtained research results before the treatment, i.e. in the exacerbation phase, the activity of CC in children with acute obstructive pulmonary disease was lower than the control values by 23.3%, and in patients with acute obstructive pulmonary disease - by 29.0% (Fig. 6).

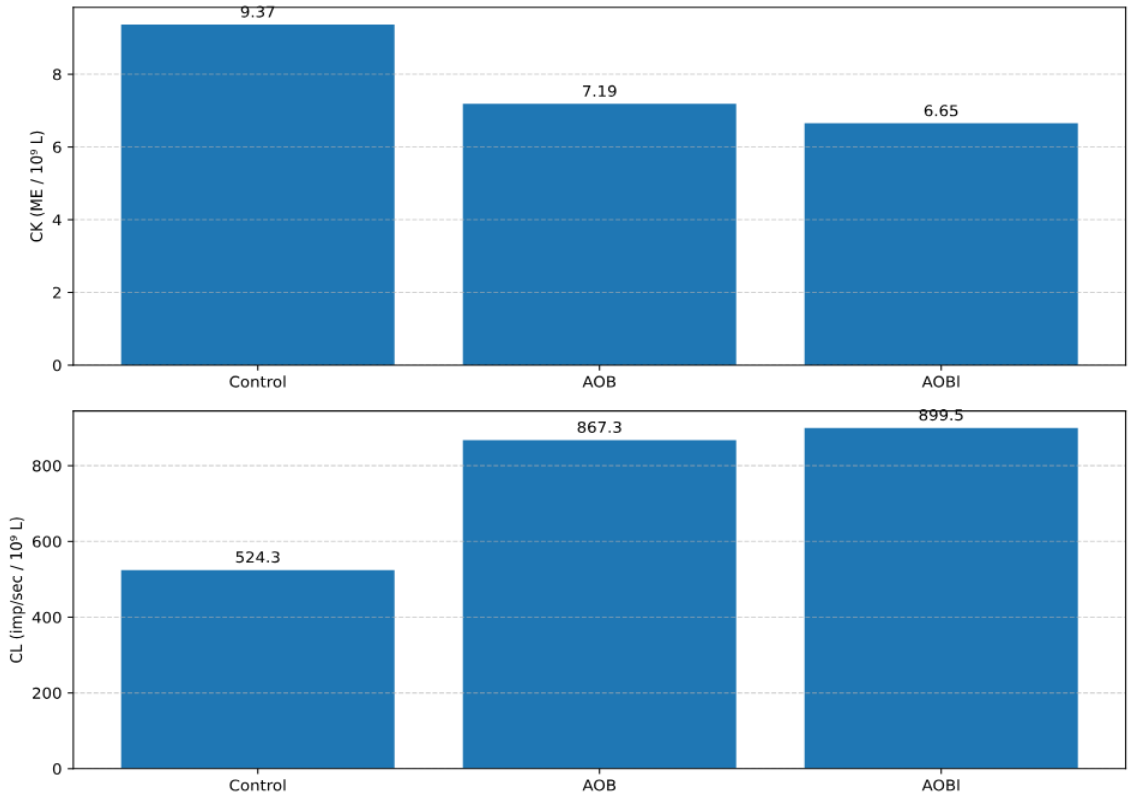


Fig. 6. Indicators of CK and CL activity in NL (%) of blood in children with AOB and AOBl before treatment

Therefore, it can be assumed that one of the reasons for the disturbances in the cytochemical activity of the NL in children with AOB and AOBl are

changes in the energy supply of the cell with ATP due to the suppression of the catalytic activity of the enzyme KK. The noted more significant suppression of KK in patients with AOBl is probably one of the reasons for the more profound shifts in the cytochemical activity of the NL in the blood of this group of children, compared with the group of children with AOB. A decrease in energy supply can lead to a change in the oxygen-dependent bacteriocidal system of the NL and, as a consequence, in the performance of their main function - phagocytosis. In this regard, we simultaneously studied not only the cytochemical activity, but also the phagocytic function of the NL.

As the results of the study showed (Fig. 7), before the treatment in the blood of young children with acute obstructive pulmonary disease, an increase in the following indicators was noted: NST test - by 17.1%, FA - by 28.5%, FI - by 46.6%, PZF and IP by 26.1% and 75.0%, respectively.

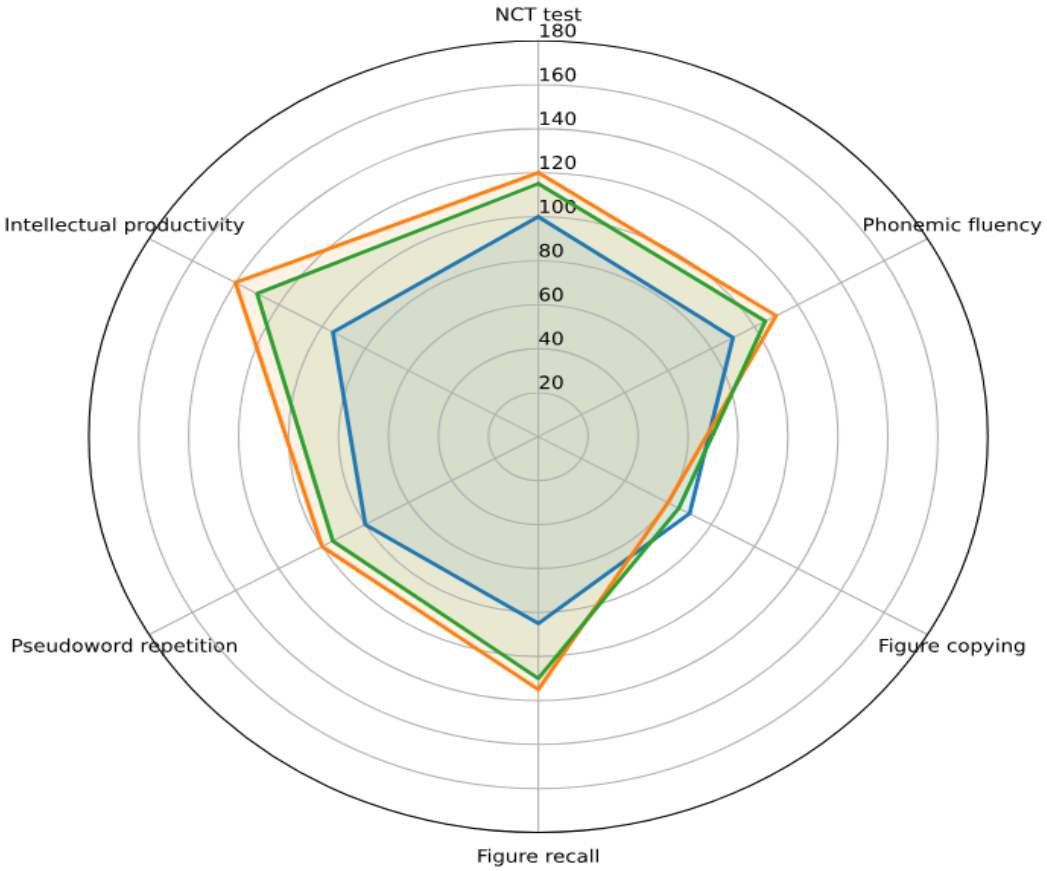


Fig. 7. Indicators of functional and metabolic activity in the LL among the examined young children

At the same time, the value of the FC decreases by 33.3%. In children with OOBL, the level of the NST test increased by 13.8%, FA - by 20.9%, FI - by 38.3%, PZF - by 19.6%, IP - by 61.5%, and the FC decreased by 37.5%.

Consequently, in general, the functional activity of the neutrophils in young children with AOB and AOBl increases. However, as can be seen from Fig. 14, not all phagocytosis indices increase, which indicates the intensity of this process in the neutrophils. At the same time, in children with AOBl, the phagocytosis process is less pronounced than in children with AOB.

It has now been established that during the development of the inflammatory process under the influence of bacterial toxins, biogenic amines, and tissue protein breakdown products, activation of the NL occurs, which consists in increased oxygen consumption. At the same time, a number of aggressive, biologically active forms of oxygen are produced: superoxide anion radical, hydroxyl radical, hydrogen peroxide, and singlet oxygen. Granulocyte activation has the character of a “respiratory explosion”.

As noted in the literature review, there are two bactericidal systems in the NL, which produce the products of the “respiratory explosion”: the myeloperoxidase - NADPH-dependent redox system and the oxygen-dependent cytolytic non-enzymatic, spontaneous system of activation of active oxygen forms. The increase in CL products reflects, namely, reflects the non-enzymatic, spontaneous system of activation of active oxygen forms. This process is associated not only with the participation of NL in phagocytosis, but also with the cytotoxic effect on tissues not involved in the pathological process.

As our studies have shown, in sick young children before treatment, there is an intensification of the processes of metabolic phagocytic activity of NL. This is evidenced by the high content of CL products in them, which exceeds

the control value in children with AOB by 1.65 ($P < 0.002$) times, and in children with AOBl - by 1.72 ($P < 0.002$) times.

Consequently, in sick children with AOB and AOBl, along with violations of cytochemical, phagocytic activity, significant shifts in the metabolic activity of the blood NL are observed. At the same time, the metabolic activity of CL production in the blood NL of sick children with AOBl is significantly higher than in children with AOB, which possibly determines the form and course of the disease, the development of destructive processes in the bronchopulmonary system.

§ 6.2. Clinical significance of oxyproline determination for assessing the severity and outcome of the disease in young children with acute obstructive bronchitis and bronchiolitis

Of particular interest to us is the study of the level of oxyproline (OP). It has now been established that OP is one of the important components of pulmonary collagen. Compared to other parenchymatous organs, the collagen content in the lung is the highest. When OP metabolism is impaired, unfavorable conditions are created for the stability of the pulmonary framework of the alveolar surfactant system and the performance of the lungs' main gas exchange function. In this regard, this chapter is devoted to the study of the OP content in the blood of children with AOB and AOBl before treatment.

In recent years, a certain place in the disruption of collagen synthesis regulation in inflammatory processes in the lungs has been given to shifts in immunological reactivity. In this case, excessive collagen formation is associated with the manifestation of leukocyte autotoxicity. A dependence of collagen production activation on the damaging effect of T-cells and lymphocytes has been revealed. A number of researchers explain the intensity of collagen formation in acute inflammatory diseases in the lungs with protein-related metabolic disorders, in particular with OP. In a protracted course of the

disease, a high level of OP in the blood plasma against the background of a fairly good clinical condition of patients may indicate an unfavorable prognosis for the disease.

As our studies have shown, in young children with acute obstructive pulmonary disease, before treatment, there was an increased content of both free and protein-bound OP in the blood plasma - by 30.4% and 35.2%, and in children with acute obstructive pulmonary disease - by 44.2% and 49.8% (Fig. 8).

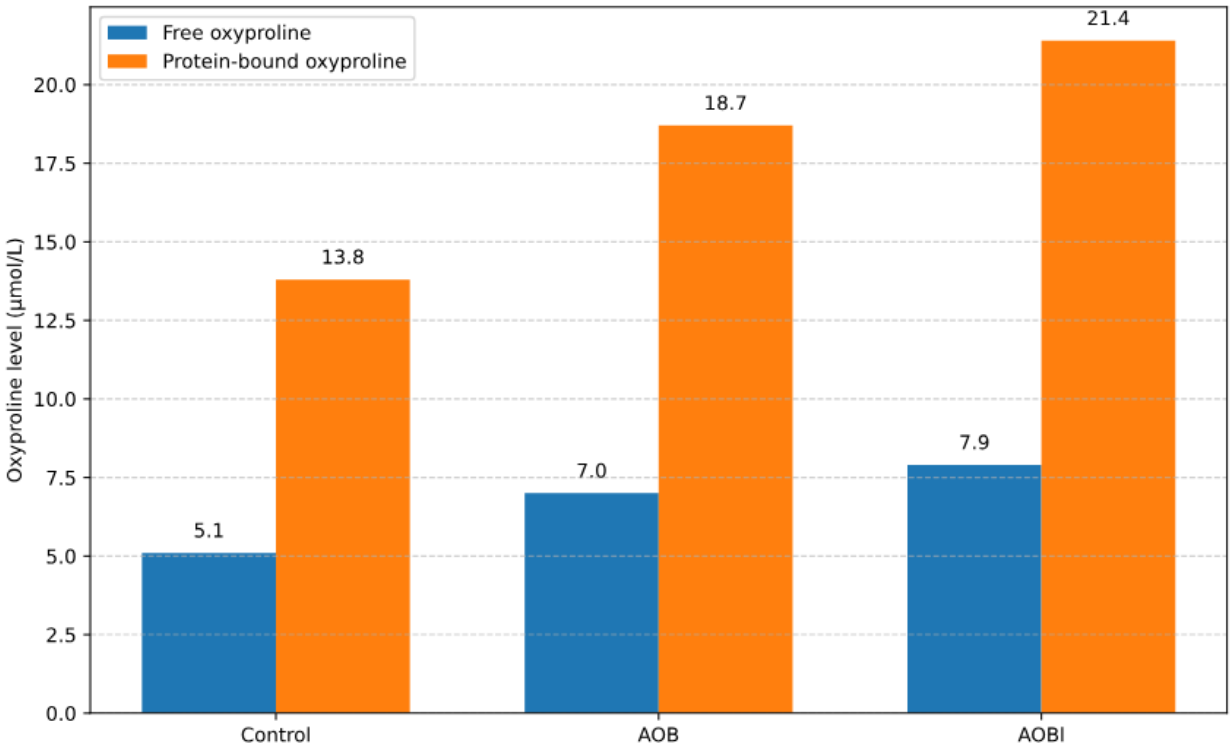


Fig. 8. Level of free and protein-bound oxyproline in blood plasma of examined young children

Therefore, before treatment, children with AOB and AOBl show a significant increase in the blood plasma of protein-bound and free OP.

To prove that the increase in OP in blood plasma is associated with the activity of NL, we conducted a correlation analysis between the indicators of the functional-metabolic activity of NL and the level of protein-bound and free OP.

Table 7

Indicators of the correlation relationship between parameters reflecting the cytochemical, functional and metabolic activity of NL and the level of free (FB) and protein-bound (PB) OP in the blood plasma of children with acute obstructive pulmonary disease before treatment (M+ m)

Parameters	SOP (n = 63)		BSOP (n = 63)	
	G	R<	G	R<
KB, ue. ed.	+0.25	0.05	+0.29	0.02
MP, specific unit	-0.29	0.02	-0.30	0.02
KF, u.e.	+0.30	0.02	+0.36	0.01
[AP, specific units]	+0.21	0.1	+0.25	0.05
GL, u.e.	-0.48	0.001	-0.52	0.001
SDG, ue. units	-0.40	0.001	-0.37	0.01
α-GPDH, specific units	+0.36	0.01	+0.41	0.001
KK, ME/10 ^{9}L	-0.26	0.05	-0.26	0.05
HL, imp/s/10 ^{9}1	+0.51	0.001	+0.49	0.001
NST test, uel. units	+0.25	0.05	+0.28	0.05
FA, %	+0.27	0.05	+0.25	0.05
FC, %	-0.31	0.02	-0.30	0.02
FI, %	+0.26	0.05	+0.24	0.05
PZF, %	+0.25	0.05	+0.25	0.05
IP,%	+0.32	0.01	+0.27	0.05

All the indicators of the correlation dependence between the functional-metabolic activity of the NL and OP were reliable. Moreover, its level was significantly higher in patients with AOBl than in children with AOBl. It should be noted that in patients with AOBl and AOBl, there is a reliable direct, positive (+) correlation dependence between the indicators of KB, CP, ALP, a-GPDH, CL, NST-test, FA, FI, PZF and IP, and a reliable negative (-) correlation dependence between the values of MP, GL, CC and FC.

Table 8

Indicators of the correlation relationship between parameters reflecting the cytochemical, functional and metabolic activity of NL and the level of free (FB) and protein-bound (PB) OP in the blood plasma of children with AOBL before treatment, (M+ m)

Parameters	SOP (n =32)		BSOP (n =32)	
	G	R<	G	p<
KB, ue. ed.	+0.34	0.05	+0.36	0.05
MP, specific unit	-0.31	0,1	-0.37	0.05
KF, u.e.	+0.35	0.05	+0.42	0.02
ALP, specific units	+0.37	0.05	+0.38	0.05
GL, u.e.	-0.53	0.01	-0.54	0,001
SDG, ue. units	-0.46	0.01	-0.45	0.01
α-GPDH, specific units	+0.45	0.01	+0.42	0.02
KK, ME/10 ^{9}1	-0.32	0,1	-0.34	0.05
HL, imp/s/10 ^{9}1	+0.55	0,001	+0.49	0.01
NST test, uel. units	+0.29	0,1	+0.40	0.02
FA, %	+0.34	0.05	+0.38	0.05
FC, %	-0.42	0.02	-0.39	0.05
FI, %	+0.36	0.05	+0.35	0.05
PZF, %	+0.34	0.05	+0.32	0,1
IP,%	+0.36	0.05	+0.36	0.05

Consequently, it can be assumed that the development of destructive processes in the bronchopulmonary system, evidenced by an increase in the level of free and protein-bound OP, is based on shifts in the functional-metabolic activity of the NL.

The identified changes in the functioning of the NL (suppression of MP, CC and a sharp increase in CL) indicate a violation of the cellular link of

immunity and the need for targeted correction of this system in young children with acute obstructive pulmonary disease and acute obstructive pulmonary disease.

Currently, as we have already noted, immunomodulin is widely used in the treatment of bronchopulmonary pathology. It has been established that the drug has the ability to restore damaged links in the immune system: the activity of T-lymphocytes, immunomodulatory T-helpers and T-suppressors, B-lymphocytes, phagocytes, stimulates interferon production, antibody genesis, and enhances hematopoiesis. The drug is non-toxic and compatible with other drugs. At the same time, as literary data show, it is still unclear how immunomodulin will act on the cytochemical, metabolic processes of the cellular link of immunity in a clinical setting, in particular, during the development of acute bronchopulmonary pathology.

Thus, in sick children, before the treatment, significant shifts in the cytochemical, energy-generating, phagocytic, metabolic activity of blood NL, an increase in the level of protein-bound and free OP are observed.

CONCLUSION

The relevance of the problem of treating acute obstructive pulmonary disease in young children is due to the high frequency and prevalence of this pathology and the insufficient effectiveness of existing conservative treatment methods, which in some cases leads to the development of severe complications and even unfavorable outcomes of the disease.

Among the possible causes of acute pulmonary obstructive pulmonary disease, regardless of the etiologic factor, is a decrease in immune defense and reactivity of the organism of young children. Leukocytes are the first cellular elements mobilized by the organism during the development of acute inflammation in the lungs. The nature of the development and outcome of the disease largely depend on the functional state of leukocytes, which react to shifts in the internal environment and act as a powerful effector organ of the system for ensuring structural homeostasis.

Evaluation of functional and metabolic features of leukocytes in acute obstructive pulmonary disease is necessary to clarify the pathogenesis of the disease, control the course of inflammation and the effectiveness of treatment, and predict the outcome of the pathological process in the body. This is due to the fact that leukocytes clearly express the connection between metabolic and functional disorders in pathology. According to D.N. Mayansky, leukocytes are capable of accurately reflecting various homeostasis disorders during inflammation, since they are replaced every 10 hours. This means that all shifts that occurred during this period will be recorded by leukocytes. Only adequate methods are needed to detect changes in the functional appearance of cells. In this regard, a more informative method is the study of the cytochemical activity of leukocytes (SDH and α-GPDH, KB, CP and ALP, lysozyme, MP and GL). No less valuable is a comparative study of intraleukocyte components and indicators of the activity of spontaneous absorption and reduction of nitroblue

tetrazolium by neutrophil granulocytes (NBT test), as well as other data - FA, FC, FI, PZF, IP characterizing the biochemical basis of the phagocytic function of leukocytes.

Important indicators for assessing the state of functional-metabolic activity of leukocytes are the intensity of ultra- weak luminescence (ULG), the activity of the enzyme KK, which is mainly responsible for the energy supply of the cell. During acute inflammation in the bronchopulmonary system, the process of destruction of lung tissue occurs, which is characterized by a violation of collagen metabolism. In this regard, an informative method for assessing the degree of destruction in the lungs is determining the level of oxyproline in the blood.

Literature data on the cytochemical properties of neutrophils, their functional and metabolic activity in acute obstructive leukemia are insufficient and sometimes contradictory. Activation of peroxidases and acid hydrolases in acute obstructive leukemia, a decrease in their activity, and the absence of changes are reported. At the same time, there are practically no data indicating a violation of the cytochemical, functional and metabolic activity of leukocytes, the state of collagen metabolism in the development of BOS and in the dynamics of its treatment, including when prescribing immunocorrectors to young children with acute obstructive leukemia and acute obstructive leukemia.

In this regard, we have set the following research objectives:

- to find out the pattern of changes in the cytochemical, functional-metabolic activity of leukocytes, shifts in collagen metabolism in the bronchopulmonary system during the development of BOS;

to evaluate the effectiveness of therapy in the treatment of young children with acute obstructive pulmonary disease and acute obstructive pulmonary disease using the generally accepted basic method and the method

with the inclusion of the drug immunomodulin in the complex of measures, based on clinical indicators of cytochemical, functional and metabolic activity in leukocytes, and shifts in collagen metabolism;

based on the obtained data on disorders in the cellular link of immunity, their pathogenetic significance in the development of BOS, to substantiate the need to include immunomodulin in complex therapy as an adequate and clinical-pathogenetic agent in the treatment of young children with acute obstructive pulmonary disease and acute obstructive pulmonary disease;

The results of the study showed that all clinical signs characteristic of AOB and AOBl were observed before treatment in 95 examined patients aged from 1 month to 3 years (mean age 1.5+0.63 years). We diagnosed acute obstructive bronchitis based on the clinical course of the disease, results of general clinical, cytochemical, special biochemical studies in accordance with the classification of clinical forms of bronchopulmonary diseases in children adopted in Moscow at the symposium "Nonspecific lung diseases in children" (November 4, 1995). According to this classification, for our examinations we selected, by random sampling, children with AOB who were newly ill, who had no focal or infiltrative shadows in the lungs on radiographs, and had a pronounced cough, dry and moist rales on auscultation, and an extended and difficult exhalation (see Table 3). In patients with severe acute bronchitis with obstructive syndrome (AOB), the disease process proceeded with severe respiratory failure caused by obstruction of the small bronchi.

It should be noted that in most children, acute obstructive pulmonary disease and acute obstructive pulmonary disease proceeded against the background of acute respiratory viral infection. Even before treatment, many of them had clinical signs of catarrh of the upper respiratory tract with normal body temperature (in 34), with subfebrile (in 46), febrile (in 15). When analyzing the blood of sick children with acute obstructive pulmonary disease

and acute obstructive pulmonary disease, an ambiguous reaction of shifts in the leukocyte formula was noted. In 38 sick children, a normal number of leukocytes was observed, in 13, leukocytosis, and in 44, leukopenia. Neutrophilia and eosinophilia were noted to the same extent in children with acute obstructive pulmonary disease and acute obstructive pulmonary disease (Table 3). In all cases, ESR was elevated - more than 10 mm / h in 28 children with acute obstructive pulmonary disease and in 13 with acute obstructive pulmonary disease.

It is characteristic to note that almost all the examined patients had an aggravated premorbid background. In infancy, 25.3% of the children were bottle-fed, 11.6% were mixed-fed, and 20% were breast-fed. An unfavorable obstetric history was established in 24.2% of the children, including 22.1% of children born with birth asphyxia. Anemia was detected in 58.9% of patients with BOS, rickets - in 22.1%, exudative catarrhal diathesis - in 25.3%, grade I - II hypotrophy - in 6.3%, SNCE - in 7.3%, and perinatal encephalopathy - in 25.3%. An unfavorable premorbid background was equally detected in children with both AOB and AOBl.

Children were mainly admitted to hospital on the 1st-2nd day of illness. In 43.2% of children hospitalized after 4-6 days, the clinical picture of BOS was neglected and more pronounced than in children admitted on the 1st-2nd day of illness. When evaluating special studies, it was found that before the treatment, i.e. during the period of admission of children to hospital, significant deviations from the control values of all studied cytochemical activity indices were observed (an increase in KB, CP, ALP and α-GPDH indices, a decrease in MP, GL and SDH indices) (see Fig. 12), while a high level of CL in leukocytes (see Fig. 15) and both SOP and BSOP content in the blood were noted (Fig. 16). When analyzing the indicators characterizing phagocytic

activity, an increase in the NST test, FA, FI, PZF and IP and a decrease in the level of FC were noted (see Fig. 14).

Moreover, shifts in the cytochemical, functional-metabolic activity of leukocytes, the process of phagocytosis and destruction of lung tissue assessed by changes in the level of OP in the blood plasma were more pronounced in patients with AOBl than with AOB.

Consequently, a clear pattern of dependence between the degree of cytochemical activity, functional metabolic shifts, phagocytosis disorders in leukocytes, destructive processes in the bronchopulmonary system and the clinical course, the form of BOS in children in the active period of development of acute obstructive pulmonary disease and acute obstructive pulmonary disease is noted.

Since we have identified significant disturbances in the cellular link of immunity, which is consistent with the literature data of recent years on significant shifts in the T and B-system of immunity in young children with acute obstructive pulmonary disease, we naturally faced the problem of introducing the drug immunomodulin into the course of treatment and studying its clinical efficacy. Immunomodulin is the first domestic drug, highly purified, obtained from the thymus of sheep fetuses. There is some information on its high therapeutic efficacy aimed at increasing the humoral link of immunity in young children with acute obstructive pulmonary disease. Immunomodulin for the correction of the disturbances in the immune system that we identified in young children with acute obstructive pulmonary disease was prescribed according to the recommendations of M.M. Khaidarova et al. - 0.1 ml of 0.01% solution per 10 kg of body weight for 5-7 days, differentiated depending on the severity of the disease, the effectiveness of the immunomodulatory therapy.

The results of the studies showed that in young children with acute obstructive pulmonary disease and acute obstructive pulmonary disease with

the basic method, clinical signs of BOS persisted for quite a long time - up to 5-6, and sometimes up to 8-10 days clinical signs of BOS. They had respiratory failure - dyspnea with the participation of accessory muscles in the act of breathing and flaring of the wings of the nose, cyanosis of the nasolabial triangle, high respiratory rate, pale skin, tachycardia, distant wheezing, including those determined by auscultation, dry wheezing, cough in children with acute obstructive pulmonary disease, prolonged exhalation and mainly an abundance of fine bubbling rales, cough (at the beginning of treatment, dry obsessive, and during treatment, wet productive) in sick children with acute obstructive pulmonary disease. In addition, symptoms of intoxication were detected - high body temperature, lethargy, adynamia, loss of appetite, catarrhal phenomena (rhinitis, pharyngitis, nasopharyngitis).

It should be noted that the severity of the disease in children with AOB was significantly higher than in children with AOB, which required more intensive therapy with the inclusion of not only bronchodilators, antibiotics, sedatives, but also significantly more mucolytic drugs, exercise therapy procedures, and in some cases glucocorticoid hormones. On average, the clinical recovery rate of children with AOB treated with the traditional method was 8.7+0.21 days, and in children with AOB - 12.6+0.13 days ($P<0.01$).

Despite the fact that all the studied parameters of clinical signs returned to normal and the children were discharged from the hospital in a satisfactory condition, when analyzing the cytochemical, functional-metabolic, bioenergetic indicators of the state of the OP level, it was established that a number of indicators differed significantly from those in the control. Thus, from Table 11 it is clear that of the cytochemical parameters, the indicators of SDH and α-GPDH, MP did not reach the norm, a fairly high intensity of ultra-weak luminescence in leukocytes, determined by the level of CL, remained (Fig. 19), which indicated a violation of the activity and tension of cellular

immunity and, as a consequence, a reduced reactivity of the child's body, which under unfavorable conditions of detention can lead to a relapse of the disease.

The above once again convincingly demonstrates the need to include immunomodulators in the complex treatment of young children with BOS.

Indeed, as the results of our studies have shown, the inclusion of immunomodulin in the course of treatment, from the first days of admission of patients with BOS, an improvement in the clinical picture of the disease is noted. Thus, in children with acute obstructive pulmonary disease, treated with the additional inclusion of immunomodulin in the complex of therapeutic measures, compared with the group of children where the therapy was carried out using the basic method, the time of disappearance of clinical signs of respiratory failure on average decreased by 1.3 ($P < 0.05$) days, the effectiveness increased by 26.0% (see Table 5), and clinical symptoms of intoxication - by 1.2 ($P < 0.05$) days, the effectiveness increased by 29.9% (Table 7). At the same time, in children with acute respiratory failure, the time of disappearance of clinical symptoms of respiratory failure and intoxication decreased on average by 1.8 ($P<0.02$), 1.1 ($P<0.05$), and clinical efficacy increased by 23.6% and 19.2%, respectively (see Tables 6, 8) before treatment.

Considering the noted disturbances in the cellular link of immunity in children with BOS in the context of the subcellular and organismic level, it can be confidently stated that regardless of the etiological factor (in our studies, most sick children with AOB and AOBl were admitted to the clinic with ARVI), the pathogenetic link in the dysfunction of leukocytes is shifts in energy supply. This is evidenced by the data on the increase in catabolic processes in the cell, the transition of glycolytic processes to the unfavorable path of glucose oxidation, since the main reserve of glucose - glycogen in leukocytes was significantly lower than the control at the height of the disease in children with AOB and AOBl - by 60.6% ($P < 0.002$).

The development of catabolic processes in the cell is indicated by the data of discrepancy in the change in the activity of the enzymes SDG and α-GPDH. At the height of BOS in sick children with AOB and AOBL, a decrease in SDG of the main enzyme of the Krebs cycle and the inclusion of a reserve unfavorable pathway of glycolysis, activation of the enzyme α-GPDH are noted. Activation of the enzyme α-GPDH, apparently, as well as a decrease in the activity of the enzyme KK participating in the processes of ADP phosphorylation with the formation of ATP and free creatinine, were among the important reasons for the decrease (or increased consumption of GL during activation of α-GPDH) and its inhibition, as a consequence of a decrease in energy formation with low activity of the enzyme KK in leukocytes of GL.

A decrease in energy production and respiratory processes with the inclusion of gluconeogenesis processes, as follows from literary data, is accompanied by an increase in tissues of underoxidized metabolic products, including non-esterified fatty acids, which are good substrates for the intensification of free radical oxidation processes. In our studies, this is characterized by an increase in the level of free luminescence of CL in leukocytes.

Uncontrolled process of regulation of free radical oxidation, as evidenced by sharp inhibition of MP activity, can be assumed to be one of the pathogenetic links in the launch of lysosomal enzymes - KB, CP and ALP. This to an even greater extent contributes to the formation of a chain of free radical processes, which, apparently, were one of the important mechanisms of compensated increase in the phagocytic activity of neutrophilic leukocytes, as evidenced by the data on the increase in the FA, FC, FI and PZF indicators. At the same time, IP turned out to be reduced, which indicates a significant violation of the important function of phagocytosis - neutralization of toxins, suppression of microbiocidal activity - bactericidal, bacteriostatic effect.

The noted elevated level of CL, on the one hand, can be considered as a positive fact of high metabolic activity of leukocytes in inflammatory processes, which, apparently, was characterized in children with BOS by an increase in the main indicators of phagocytosis (FA, FC, FI, PZF), on the other hand - as an important factor in aggression on intact tissue, in particular the bronchopulmonary system. The inflammation process in the bronchopulmonary apparatus stimulates the formation of chemoattractants that attract leukocytes to the area of damage. Their activation is associated with the so-called respiratory burst, accompanied by active absorption of oxygen from the surrounding tissues and the synthesis of active oxygen forms: O_2 , H_2O_2 , OH, singlet oxygen (O_2^1), hypochlorous acid, etc.

Therefore, it can be assumed that an increase in the content of free and bound OP, along with the direct or indirect effects of infection, their waste products, and toxic metabolic products, is associated with an increase in the level of CL in leukocytes.

There is convincing evidence in the literature of the experimental and clinical nature of the increase in the bronchi and accumulation of a large number of leukocytes, macrophages during the development of BOS in the bronchi and peribronchial tissues. Some authors noted that the intensification of free radical oxidation in leukocytes and, as a consequence, in the bronchi can be one of the important pathogenetic links in the bronchoconstruction of the development of hypoxia in the lung tissues during BOS. Based on the obtained results of the study and literary data, we proposed a hypothetical scheme for the participation of impaired leukocyte function in the mechanisms of BOS in young children with AOB and AOBl.

Therefore, the above data indicate an important pathogenetic role of changes in the cellular link of immunity in the development of BOS. The degree of disturbances in leukocytes (cytochemical, functional-metabolic,

phagocytosis) in young children with BOS apparently determines the different levels of destruction in lung tissue, bronchoconstrictor, hypoxic effect, clinical signs of respiratory failure and intoxication of the body and, as a consequence, the clinical form of the disease - AOB and AOBl.

Thus, the analysis of our own research results showed that an important pathogenetic factor in the development of BOS in young children with acute obstructive pulmonary disease and acute obstructive pulmonary disease is a violation of the cellular link of immunity - cytochemical, functional- - metabolic, energy activity of leukocytes. Changes in leukocytes lead to shifts in the performance of their main function - phagocytosis. An increase in the uncontrolled level of free radical processes can be an important link in the destruction of cellular membranes of the bronchopulmonary system, broncho- and vasoconstriction, the development of hypoxia and, as a consequence, BOS.

Basic, generally accepted therapy is insufficient to restore the impaired functional activity in the cellular link of immunity in children with BOS to control values, which justifies the inclusion of immunocorrectors in the complex of therapeutic measures. The introduction of immunomodulin into the complex treatment reduces the time of clinical recovery and increases the effectiveness of treatment. Clinically and pathogenetically, this proves the need to include this drug in the course of treatment of young children with AOB and AOBl.

LIST OF REFERENCES

1. Angoulvant F., Bellettre X., Milcent K., Teglas J.P., Claudet I., Le Guen C.G. et al. Effect of Nebulized Hypertonic Saline Treatment in Emergency Departments on the Hospitalization Rate for Acute Bronchiolitis: A Randomized Clinical Trial. JAMA Pediatr. 2017; 171(8):171333. doi: 10.1001/jamapediatrics.2017.1333.

2. Azkur D., Özaydin E., Dibek-Misirlioglu E., Vezir E., Tombuloglu D., Köse G., Kocabaj C.N. Viral etiology in infants hospitalized for acute bronchiolitis. Turk. J. Pediatr. 2014; 56(6): 592–6.

3. Achilova D. N. Clinical and immunological aspects and optimization of diagnostic methods for obstructive bronchitis in children, 2019, pp. 17-41

4. Alibekova M.B. Features of diagnosis and treatment of mycoplasma pneumonia in young children//Bulletin of emergency medicine 2013. № 3.- P.86-89.

5. Alibekova M.B. Clinical and immunological features of mycoplasma pneumonia in young children: Abstract of Cand. Sci. (Medicine). Tashkent, 2012. - 17 p.

6. Alibekova M.B., Mukhammedova H.T., Kamalov Z.S., Mansurova F.Z., Ismailova G.Kh. Nosichenko L.E. Changes in some indicators immune status in mycoplasma pneumonia in young children // Immunocorrection with cycloferon. Physiology and pathology of the immune system. Immunopharmacogenomics. - 2010. - No. 2. - P. 34-38.

7. Antimicrobial therapy at the crossroads of medical sciences//Bulletin of the practical doctor. – 2012. – Vol. 2, No. 1. – P. 3-4.

8. Akhmatova Yu.A., Akhmatov A. Forecasting the development and early diagnosis of pyelonephritis of TO RCH etiology in children: scientific publication// Infection, immunity and pharmacology. - Tashkent, 2017. - No. 5-6. P. 63-64.

9. Bardennikova S.I., Zaitseva O.V., Melnikova E.A. Rational antibiotic therapy of lower respiratory tract diseases in pediatric practice: problems and opportunities “Effective pharmacotherapy//Pediatrics. - 2014. - No. 2 (16). - P. 38-44.

10. Barinsky I.F., Makhmudov F.R., Mordvintseva E.Yu., Sergeev O.V. Specific inactivated vaccines and immunomodulators as a means of emergency prevention of acute viral infections and relapses of chronic viral diseases // Terra Medica. - 2014. - No. 4. - pp. 22-26.

11. Belan E.B., Sadchikova T.L. Acute respiratory viral infections: a current view of the problem and a modern approach to treatment. RMJ. Medical Review. 2018. No. 11. P. 60–64.

12. Belova E.V., Kapustina T.A., Parilova O.V., et al. Efficiency of cyclic polyantibiotic therapy for chlamydial lesions of the paranasal sinuses in children // Children's infections. - 2016. - No. 3. - P. 3841.

13. Belevsky A.S., Knyazheskaya N.P. Thiamphenicol glycinate acetyl cysteine: some aspects of use in acute and chronic pulmonary diseases. Practical Pulmonology, 2017, No. 3.P. 122;

14. Belykh N.A. et al., Clinical and epidemiological features of mycoplasma infection in children of the Ryazan region // Russian Medical Biological Bulletin named after Academician I.P. Pavlov.-2018.-V.26.-№2.P.258-267.

15. Belyaev D.L., Babayants A.A., Frolova I.S., Khatuntseva N.V. Participation of chronic mixed infections with herpes group viruses in the formation of severe syndrome of mixed infections of microbial-viral etiology // Rus. Allergology journal. - 2011. - No. 4, issue 1. - P. 49-50.

16. Bondarenko G.M., Fedorovich T.V. Clinical, epidemiological and immunopathogenetic characteristics of urogenital mycoplasmosis and optimization of methods for the treatment of mycoplasma infection//

Dermatovenereology. Cosmetology. Sexopathology. - 2018. - No. 1-4. - P. 19-24.

17. Bontsevich R.A., Subina T.L., Vinyukov V.A., Gavrilova A.A. Features of mycoplasma infection of the respiratory organs in clinical practice// Consilium medicum , 2020. No. 3. –P. 40-45.

18. Volovik I.K. Differential diagnostics of broncho-obstructive syndrome in children // Critical Care Medicine. 2013. No. 1. P. 125–128.

19. Volkov I.K. Differential diagnostics of broncho-obstructive syndrome in children. Emergency Medicine. No. 1 (48) 2013. P.-125-126 18. Vysochina I.L., Kramarchuk V.V. Evidence base of the efficacy and safety of flavonoids and the opinion of outpatient physicians in the focus of choosing approaches to treating ARVI// Modern ped i atr i ya. Ukraine, 2020.- 6 (110). P.62-68.

20. Galimova L.F., Pikuza O.I., Zakirova A.M., Suleimanova Z.Ya. Features of the cytokine profile in community-acquired pneumonia in children caused by atypical pathogens. Reproductive health of children and adolescents / 2017, No. 2-3. P.-55-56

21. Gladkikh R.A., Molochny V.P., Malinovskaya V.V., Polesko I.V., Obukhova G.G. Dynamics of cytokine and neopterin levels in young children with acute respiratory viral infections using recombinant interferon alpha-2 b with antioxidants (tocopherol acetate and ascorbic acid) Pediatrics 2017 Vol. 96, No. 4, pp. 17-18

22. Geppe N.A., Ivanova I.A., Kamaev A.V., Kolosova N.G., Kondyurina E.G., Malakhov A.B. et al. Bronchial obstruction due to acute respiratory infection in preschool children: diagnostics, differential diagnostics, therapy, prevention. Moscow: MedKom-pro, 2019;78 p.

23. Golub A.V., Kozlov R.S. Macrolides for the treatment of community-acquired lower respiratory tract infections//Medical Council. - 2013.-№5.-26-30.

24. Golovacheva E.G., Afanasyeva O.I., Osidak L.V., Obraztsova E.V., Voloshchuk L.V. Influence of the interferon system on the direction of polarization of the immune response to influenza in children. Pediatr. 2014; 5 (3): 137–141.

25. Gonchar M.A. et al., Macrolide-resistant mycoplasma infection in children: concept of formation, modern principles of diagnosis and treatment// Child health. 2018.-№3.-Vol.13.-P.294-301.

26. Gorelov A.V., et al. Interferon preparations in the treatment of acute respiratory viral infections and influenza in newborns and children in the first months of life//Attending physician. - 2015.-№1.-P. 7-13.

27. Gorelov A.V., Tselipanova E.E., Alimova I.L. Use of the drug Genferon® light in children of different ages with ARVI//Effective pharmacotherapy. - 2016.- No. 21.-P.12-17.

28. Gorina L.G. et al. Identification of markers of mycoplasma infection in children with rheumatoid arthritis//Infectious diseases. - 2016.-№2.-P.13-17

29. Geppe N.A., Dronov I.A., Kolosova N.G. Efficiency of using thiamphenicol glycinate acetyl cysteine in acute bronchitis in children. Russian Medical Journal 2016; 3:386–390].

30. Guliev N.D., Ragimova N.D. Polymorphism of cytokine genes in newborns with intrauterine infections. Rossiyskiy Vestnik Perinatology and Pediatrics, 6, 2015. P.-42

31. Dautov F.F. Environmental factors and population health, 2010

32. Danilov A. I., Petrochenkova N. A., Kovaleva L. A. Modern features of community-acquired pneumonia caused by Clamydophyla pneumoniae, Attending Physician No. 3/2019. C-93-95

33. Dobrynin A.S., Shakhov K.V., Khismatullina E.R., Nikogosyan A.R. Mycoplasma pneumonia during an outbreak of respiratory mycoplasmosis in a children's group // Proceedings of the All-Russian scientific forum of students with international participation "Student Science - 2020", Special issue. - 2020.- vol. 3. - P. 673-674.

34. Drannik G.N. Clinical immunology and allergology: A manual for students, interns, immunologists, allergists, and general practitioners of all specialties. K., 2010.-552s.

35. Eshmolov S.N., Sitnikov I.G., Melnikova I.M. Cytokines TNF- α , IFN - γ , IL-1, IL-4, IL-8 and their role in the immune response to infectious lesions of the central nervous system in children//Children's infections. - 2018.- Vol.17.-№1.-P.17-22.

36. Zhukova O.V., Kononova S.V., Konyshkina T.M. The influence of diagnostics of intracellular microorganisms on the incidence rates of recurrent obstructive bronchitis and bronchial asthma in the population of children of the Nizhny Novgorod region // Problems of standardization in health care, 7-8, 2013.

37. Zaitseva O.V. Issues of diagnostics and treatment of respiratory infections caused by “atypical” pathogens // Difficult patient. - 2010. - No. 9. - P. 4-8

38. Zaitseva O.V. Infection and immunity: current issues in pediatric practice//Children's infections. - 2015. - No. 1. - P. 36-43.

39. Zaitseva S.V., Zastrozhina A.K., Murtazaeva O.A. Mycoplasma infection in children (literature review)//Russian Medical Journal. 2017; 5:327-334.

40. Zaitseva, S.V. Therapy of acute obstructive syndrome in children with acute respiratory diseases [Electronic resource] / S.V. Zaitseva, S.Yu. Snitko, O.V. Zaitseva [et al.] // Attending physician. - 2013. - No. 11

41. Zaplatnikov A. L., Koroid N. V., Girina A. A., Neiman I. V. Principles of antibacterial therapy of community-acquired respiratory tract infections in children//VSP. - 2012. - P. 22-29.

42. Zaplatnikov A.A., Maikova I.D., Lepiseva I.V., Respiratory mycoplasmosis in the practice of a pediatrician. Journal: Medical Council. No. 1.2016. -P.157-161.

43. Zryachkin N.I. et al. Azithromycin in the treatment of community-acquired pneumonia in children//Children's infections. - 2016.-№1. - P. 45-48.

44. Ivanova O.N. Clinical case of mycoplasma pneumonia in a 14-year-old child / O.N. Ivanova // The Path of Science. - 2016. - No. 28. - P. 69-70.

45. Ivanova N.A. Recurrent bronchial obstruction and bronchial asthma in children of the first five years of life. Russian Bulletin of Perinatology and Pediatrics. - 2016; 64-66.

46. V.V. Ivanov. Study of the concentration of cytokines produced by Th 2 lymphocytes in patients with parainfluenza. Medicine: challenges of today. Proceedings of the international scientific conference (Chelyabinsk, June 2012). - Chelyabinsk, 2012. - P. 39-41.

47. Ilyenko, L.I. New opportunities to improve the quality of health of frequently ill children / L.I. Ilyenko, I.N. Kholodova, T.N. Syryeva // RMJ. - 2011. - No. 16. - P. 11-66

48. Kaitmazova N.K. Clinical and immunological characteristics of children with obstructive bronchitis and methods for improving treatment tactics, 2013. P.-15-23

49. Kapustina T.A., Belova E.V., Kin T.I. Frequency of detection of chlamydia in the nasopharynx of schoolchildren using the direct immunofluorescence method // Children's infections. - 2013.- No. 2.-P.39-42.

50. Kapustina T.A., Belova E.V., Markina A.N., Parilova O.V. et al. Clinical and epidemiological features of chlamydial infection of the upper respiratory tract in children. – Krasnoyarsk: Versona, 2014.-118 p.

51. Karzhavina L.I. Difficulties in diagnosing community-acquired pneumonia in children with mycoplasma infection / L.I. Karzhavina, E.S. Timokhova, M.S. Arbuzova // Current issues in pediatrics. - 2015.- No. 1.-P. 53-56.

52. Karimova N.N. et al. Modern view on the treatment of TORCH infection: abstracts of reports of the IX Congress of Obstetricians and Gynecologists of Uzbekistan (November 28-29, 2017, Tashkent) // News of dermatovenereology and reproductive health. - Tashkent, 2017. - Vol. 79-80.- No. 3-4 (2). - P. 147.

53. Karpov I.A., Kachanko E.F. Clarithromycin: possibilities of clinical use//Medical news. -2012.-№1.-68-72.

54. Kiliceva T.A. Mycoplasma pneumonia: scientific publication // Infection, immunity and pharmacology. - Tashkent, 2017. - No. 3. - P. 108-113.

55. Kolosova N.G., Geppe N.A., Dronov I.A. Approaches to the treatment of bacterial respiratory tract infections taking into account modern data on the microbiome. Russian Bulletin of Perinatology and Pediatrics, 2019; 64:(1), P125

56. Kokoreva S.P., Razuvaev O.A. Predicting the development of pneumonia in children during an outbreak of respiratory mycoplasmosis. Kazan Medical Journal. 2017. No. 6. Vol. 98. P. 921-927.

57. Kornienko MN, Karazhas NV, Rybalkina TN, Feklisova LV, Savitskaya NA. The role of opportunistic infections in the etiology of acute respiratory diseases with complicated course in frequently ill children. Childhood infections. 2012;11(3): 54-61.

58. Koshkarina E.A., Kvashnina D.V., Shirokova I.Yu. Clinical, epidemiological and immunological characteristics of mycoplasma pneumonia//Journal of Epidemiology. - 2019.-№1(23)-P.7-18.

59. Krivopustov S.P., Cherniy E.F., Loginova I.A., Shcherbinskaya E.N., Volynets O.V. Bronchial obstruction syndrome in children: issues of differential diagnosis and treatment // Journal "Children's Doctor". - 2011. - No. 6 (13). - P. 5-11.;

60. Kuvardina L.V., Kharlamova F.S., Polesko I.V., The role of combined mycoplasma and herpesvirus infection in skin lesions in children//Children's infections.- 2019.-№18(3).-P.5-10.

61. Lapshin V.F. Therapy of respiratory infections: features pharmacokinetics and advantages of the original clarithromycin//Health of Ukraine. - 2011.-№5(258).-P.1-7.

62. Lesina O.N. et al. Clinical, epidemiological and laboratory characteristics of mycoplasma infection in children//Infectious diseases: news, opinions, training. – 2016. - No. 16.- P. 49-53.

63. Lebedev A.B., Ryvkin A.I., Antonova S.N. Methods of treatment of severe broncho-obstructive syndrome in young children // 12 Nat. Congress on Respiratory Diseases: Abstracts of the report. – Moscow, 2015.

64. Luss L.V., et al. Interferon treatment in combination therapy and prevention of influenza and respiratory infections // Effective pharmacotherapy. Allergology and immunology – 2014. - No. 1 . –P.14-19.

65. Lukashevich, M. G. Broncho-obstructive syndrome in young children: what a general practitioner should know / M. G. Lukashevich // Collection of articles of the V Congress of Primary Healthcare Physicians of the South of Russia, XI Conference of General Practitioners (Family Physicians) of the South of Russia. - 2016. - P. 173-182

66. Malinovskaya V.V., Chebotareva T.A., Parfenov V.V. Clinical efficacy of Viferon in the treatment of influenza and acute respiratory viral infections in adults. Almanac of Clinical Medicine. 2014; 35: 120-129.

67. Maidannik V.G. Community-acquired pneumonia in children: Use of azithromycin from the standpoint of evidence-based medicine // International Journal of Pediatrics, Obstetrics and Gynecology. - 2012. - Vol. 2, No. 1. - P. 95-111.

68. Mayorov R.V., Ozerova I.V., Getmanov S.D., Nezhdanova E.V. The influence of atypical microflora on the development of respiratory pathology in children. Bulletin of new medical technologies -2017 Vol. 24, No. 4 - P. 105-109. 67. Mukhammedova Kh.T. Bakhodirova A.N. Alibekova M.B. Algorithm for diagnosing mycoplasma pneumonia in young children // Proceedings of the 9th Republican scientific - practical conference, /Shoshilinch tibbiyot akhborotnomasi/), Navoi 2012, - P.18-19.

69. Malakhov A.B. Dronov I.A. Pharmacotherapy of cough in children with respiratory infections. Consillim Medicum//Pediatrics. - 2014. - No. 1. - P. 45-49.

70. Malakhov, A.B. Modern approaches to the diagnosis and treatment of diseases accompanied by bronchial obstruction syndrome in early childhood / A.B. Malakhov, N.A. Geppe, L.S. Starostina // Difficult patient. - 2011. - Vol. 9. - No. 4. - P. 3-7

71. Macharadze D.Sh ., Yanaeva H. A., Peshkin V.I. ARVI. Treatment Features. Attending Physician No. 1/2018; Page numbers in the issue: 38-41;

72. Melekhina E.V., et al. Rational approach to the treatment of acute respiratory viral infections in children with recurrent respiratory tract infections: a comparative study of the efficacy and safety of treatment and preventive regimens with Genferon® light and Arbidol® // Pediatrics. Journal named after G.N. Speransky. - 2016.; Vol. 95. - No. 5. - P. 134-140.

73. Mizernitsky Yu. L. Macrolides in community-acquired pneumonia in children: modern therapy trends//Pediatrics. - 2011. - No. 4. - P. 11-15.

74. Mizernitsky Yu. L. Use of an innovative domestic interferon inducer for the prevention and treatment of acute respiratory viral infections in children//Medical Council. - 2016. - No. 1. - P. 50-53.

75. Mizernitsky Yu.L. Differential diagnostics and differentiated therapy of acute bronchial obstruction in acute respiratory viral infections in young children. Practical medicine. - 2018.- No. 9 (85) P.-85-86.

76. Mizernitsky Yu.L. Environmentally conditioned respiratory diseases in children. - In the book: Environmental pediatrics / edited by A.D. Tsaregorodtsev, A.A. Viktorov, I.M. Osmanov. - Public Chamber of the Russian Federation. - Moscow: Triada-X, 2011. - P. 102-119

77. Mayansky N.A., Melnichuk O.S., Filyanskaya E.G., et al. Multiplex analysis of cytokines in children with febrile infections // Problems of diagnostics in pediatrics. 2011. Vol. 3, No. 4. P. 15–19.

78. Mukhammedova H.T., Alibekova M.B., Mansurova F.Z., et al. Features of the course of MP in young children//Medical and organizational aspects of providing assistance to children and adolescents: materials of the Republican scientific and practical conference. Tashkent. 2011. pp. 201-202.

79. Nagovitsyna E.B., Knizhnikova E.V., Polubartseva V.V., Lebedko O.A. A case of a family outbreak of respiratory mycoplasmosis during the autumn-winter season of increase in incidence// Bulletin. - 2018.-Issue 70.- P.98-103.

80. Nazirova Ya.K. Suppositories based on local raw materials in the treatment of chlamydial infection and herpes simplex virus in newborns and their mothers: scientific publication//International symposium "National model of maternal and child health care in Uzbekistan: Healthy mother - healthy child", collection of abstracts. - Tashkent, 2011. - P. 92-93.

81. B.S. Nagoev. On the role of cytokines in the regulation of the immune system in infectious diseases / B.S. Nagoev, M.Kh. Kambachokova // Proceedings of the III Annual All-Russian Congress on Infectious Diseases (Moscow, March 28-30, 2011) // Infectious diseases. - Volume 9, Supplement No. 1. - 2011. - P. 260.

82. Nesterova I.V. Immunomodulatory therapy with targeted action: current reality and prospects//Allergology and immunology. 2016. Vol.17.-No.1.-P.18-20.

83. Nosulya E.V. Acute respiratory viral infection - difficulties in diagnosis and treatment. Medical Council. 2013; 3 (2): P. - 13-20.

84. Ovsyannikov D.Yu. Broncho-obstructive syndrome in children. Asthma and allergy, No. 1/2014. P-14

85. Orlov A.V., et al. Bronchoadenitis in mycoplasma pneumonia in a child: differential diagnosis and treatment//Vestnik Severo-Western State Medical University named after I.I. Mechnikov - 2019.- T.11.-№2.-P.71-78.

86. Acute respiratory tract infections in children. Diagnosis, treatment, prevention. Clinical guidelines. Moscow: MedKom-Pro; 2018. 200 p.

87. Osmirko T.V. Clinical and epidemiological substantiation and determination of risk factors for the birth of children with TORCH syndrome//Medical almanac.- 2015.-№5(40).-P.75-79.

88. Okhotnikova E.N., Ponochevnaya E.V., Sharikadze E.V., Usova E.I. Urgent issues of rational antibiotic therapy of inflammatory diseases of the lower respiratory tract in pediatric practice//Child health. - 2015. - No. 2 (61). - P. 141-148.

89. Okhotnikova E. N. Pathogenetic features of broncho-obstructive syndrome in children and modern possibilities of emergency therapy, Asthma and Allergy, No. 2 • 2013. P. 54-55.

90. Ochilova S.S., Aliyev Sh.R., Yodgorova N.T. Etiological role and analysis of mycoplasmas in children with acute and chronic pneumonia//Electronic scientific journal "Biology and integrative medicine ". 2016.-№5.-P.74-84.

91. Ochilova S.S., Yodgorova N.T., Ernaeva G.Kh. The role of Mycoplasma Pneumoniae as an etiologic agent in respiratory tract diseases. Electronic scientific journal "Biology and Integrative Medicine". 2017. No. 4. P. 110-128.

92. Petlenko S.V., Osidak L.V., Smirnov V.S. Comparative clinical and laboratory effectiveness of drugs for the pathogenetic treatment of acute respiratory viral infections// Questions of Virology.- 2016.№61(6).-P.263-269.

93. Poznyak A.L., Sidorchuk S.N., Tarasov A.V. Chlamidophila pneumoniae infection as a risk factor for the development of atherosclerosis (literature review) // Journal of Infectology. - 2013. - V. 5. No. 1. - P. 18-27.

94. Pochivalov A.V., Pogorelova E.I. Features of the treatment of obstructive bronchitis and bronchial asthma in young children with chlamydial infection//Applied information aspects of medicine. – 2015. – Vol.18, No. 6. – P. 20-23.

95. Plotnikova M.A., Klotchenko S.A., Egorov V.V., Nikulenkov K.P., Vasin A.V., Kiselev O.I. Application of solid-phase enzyme-linked immunosorbent assay in microchip format for quantitative determination of cytokine levels. Medical Immunology. 2012, Vol. 14, N 4-5, pp. 415-418].

96. Razuvaev O.A., Kokoreva S.P., Trushkina A.V. Features of mycoplasma infection in outbreak and sporadic morbidity in children // Treatment and prevention. - 2015-№4 (16). - P. 5-9.

97. Razuvaev O.A. Diagnostics and prevention of pneumonia of mycoplasma etiology in children: Diss. Cand. Med. Sciences. - Voronezh. - 2018, 160 p.

98. Razuvaev O.A., Kokoreva S.P., Makarova A.V. Humoral immune response to mycoplasma pneumonia in children. Applied information aspects of medicine. 2017. Vol. 20. No. 3. P. 60-65.

99. Rachina S.A., Bobylev A.A., Kozlov R.S., et al. Complications of community-acquired pneumonia caused by Mycoplasma pneumonia: literature review and results of own research // Clin. microbiol. Antimicrob. Chemotherapy. - 2013. - Vol. 15, No. 1. - P. 4-13.

100. Macrolide-resistant mycoplasma infection in children: concept of development, modern principles of diagnosis and treatment. Child Health. - 2018. - No. 3. - P. 294-301.

101. Chlamydophila respiratory infection Pneumonia in children. Approaches to diagnosis and treatment// Child health.- 2013.-№8(51).- P.127131.

102. Rishuk S. V., Smirnova I. O., Mirsky V. E. Features of the pathogenesis of urogenital mycoplasma infection//Bulletin of the Orenburg Scientific Center of the Ural Branch of the Russian Academy of Sciences. 2013. No. 1. P. 1-22.

103. Samsygina G.A. Acute respiratory diseases in children. Moscow: GEOTAR-Media, 2019.-P. 44.

104. Savenkova M., Savenkov M. Chlamydial-mycoplasmal infections in children. Moscow: Miklosh. - 2012. - 291 p.

105. Savenkova M.S., Savenkov M.P., Samitova E.R., Bullikh A.V., Zhuravleva I.A., Yakubov D.V., Kuznetsova E.S. Mycoplasma infection: clinical forms, course features, diagnostic errors // Issues of modern pediatrics. - 2013. - Vol. 12, No. 6. - P. 108-114.

106. Samorodnova E.A., Pikuza O.I. Chlamydia in children: the unknown about the known//Practical medicine.- 2014.-№9(85).-P.60-66.

107. Samal T., Maskalenko T. Treatment of obstructive forms of acute bronchitis in young children. Science and Innovations, No. 3 (121), 2013. P. 66–67

108. Senatorova A.S., Logvinova O.L. et al. Macrolide-resistant mycoplasma infection in children: concept of formation, modern principles of diagnosis and treatment// Child health.- 2018.- Vol.13.-№3.P.294-301.

109. C. A. Sokolov, O. V. Shamsheva. Immune status and cytokine profile indicators in frequently ill children and optimization of approaches to the prevention of acute respiratory infections. Children's infections 2013, No. 3, p. 9

110. Simonova O. I. Mucolytics in pediatric practice: rational choice, therapeutic effects and features of therapy. Issues of modern pediatrics. 2013; 12 (4): 24-29.

111. Simonova O. I., Gorinova Yu. V. Non-mucolytic properties of a well-known mucolytic. Issues of Practical Pediatrics. 2014; 9 (5): 52-57.

112. Simonova O. I., Gorinova Yu. V., Bakradze M. D. Efficiency of inhalation of hypertonic solution in children with bronchitis and bronchiolitis. Issues of modern pediatrics. 2014; 13 (4): 12-18.

113. Simbirtsev A.S. Cytokines in the pathogenesis and treatment of human diseases. St. Petersburg: Foliant, 2018: 512 p.

114. Simbirtsev A.S. Cytokines in the pathogenesis of infectious and non-infectious human diseases / / Medical Academic Journal, - 2013. - Vol. 13, No. 3. - P. 18-41.

115. Simovanyan E.I., Denisenko V.B. Improving the therapy of acute obstructive bronchitis associated with ARVI in young children // G.N. Speransky Journal "Pediatrics". 2018. Vol. 97. No. 1. P. 65–70.

116. Simonova O. I., Gorinova Yu. V., Alekseeva A. A., Tomilova A. A. Broncho-obstructive syndrome in children: a new solution to an old problem. Issues of modern pediatrics. 2015; 14 (2): 276–277.

117. Simonova A.Yu. Use of clarithromycin in the treatment of acute respiratory diseases in children//issues of modern pediatrics. - 2012. - Vol. 11. - No. 1. - P. 152-157.

118. Sokolov S. A., Shamsheva O. V. Indicators of immune status, cytokine profile in frequently ill children and optimization of approaches to the prevention of acute respiratory infections. Children's infections 2013, No. 3. P.-9

119. Sokolov S.A., Shamsheva O.V. Indicators of immune status, cytokine profile in frequently ill children and optimization of approaches to the prevention of acute respiratory infections // Children's infections. - 2013. - Vol. 12, No. 3. - P. 9-15.

120. Spichak T.V. Mycoplasma pneumonia in a child, what is the problem? // Medical Council. - 2018. - No. 6. - P. 71-76.

121. Spichak T.V. Respiratory mycoplasma infection in children: how far have we progressed in solving problems // Pediatrics. 2015; 94(6):128133.

122. Stetsyuk O.U., Andreeva I.V., Kozlov R.S. Safety and tolerability of antibiotics in outpatient practice. Clinical microbiology and antimicrobial chemotherapy 2011;13(1):67-84.

123. Timchenko O.L. Chlamydial infections occurring with damage to the respiratory tract//Infectious diseases: news, opinions, training. 2015. - No. 4. - P. 43-50.

124. Tatochenko V.K. For the pediatrician for every day. Handbook. Moscow: Borges. 2012. 274 p.

125. 127. Trushkina A.V. Clinical and laboratory substantiation of a differentiated approach to etiotropic therapy of acute respiratory diseases in children: Diss. ... Cand. of Medicine. - Voronezh, 2015.- 142 p.

126. Ubaidullaeva S.A. Increasing the effectiveness of measles vaccination in children with obstructive bronchitis: Abstract of a PhD thesis. Tashkent, 2010. - P. 21.

127. Feklisova L.V. et al. Clinical and laboratory effectiveness of the use of the domestic combined immunobiological drug Genferon Light in the complex treatment of children with acute respiratory diseases. - Moscow, 2013. - 50 p.

128. Feklisova L.V., Tselipanova E.E. Diagnosis and treatment of respiratory mycoplasmosis in children with obstructive syndrome and prolonged cough. Study guide. – M. 2015.-P.24.

129. Khadisova M.K., Feklisova L.V., Meskina E.R. Mycoplasma pneumoniae, Chlamydophila pneumoniae herpesvirus infections in children with recurrent respiratory diseases. Almanac of Clinical Medicine. 2017, 45 (1). -P.8-13.

130. Khaitova R.M., Ilina N.I. Clinical immunology and allergology: federal clinical guidelines. M., 2015. 91 p.

131. Khanin A. L., Chernushenko T. I. Problems of respiratory diseases and possible solutions at the municipal health care level // Pulmonology. - 2011. - No. 2. - P. 115-118.

132. Kharlamova F.S. et al. The role of combined mycoplasma and herpesvirus infection in the formation of cardiovascular and central nervous system pathology in children//Pediatrics. Journal named after G.N. Speransky. - 2017. - No. 4. - P. 48-59.

133. Khakimova R. A., Mamarasulova D. Z., Maksumova D. K., Botirova B. T., Abdullaev M. B., Askarov I. S. Laboratory features of

pneumonia caused by atypical pathogens in comparison with those in tuberculosis in children. Bulletin of Biological and Medical Problems – 2016 – Issue. 1, Volume 2 (127). P. 124-127.

134. Kharlamova FS, Shamsheva OV, Vorobyeva DA, Romanova YuV, Valts NL, Denisova AV. Mycoplasma infection in children: modern diagnostics and therapy. Pediatric infections. 2016;15(3): 50-57.

135. F. S. Kharlamova , O. V. Shamsheva , D. A. Vorobyova , Yu. V. Romanova , N. L. Waltz , A. V. Denisova , Mycoplasmosis - a trigger in the formation of somatic pathology in children, Attending physician.

136. F.S. Kharlamova, O.V. Shamsheva, I.V. Polesko, R.Yu. Yudin, O.S. Ostapushchenko, E.R. Samitova, D.A. Vorobyova, E.V. Simonova, N.L. Valts, N.K. Karaseva, A.A. Zakharova. The role of combined mycoplasma and herpesvirus infections in the formation of cardiovascular and central nervous system pathology in children.

137. Chebotareva T.A., Vyzhlova E.N., Zakharova I.N., Zaplatnikov A.L. Therapy of influenza and acute respiratory infections in children with altered health status. International Journal of Pediatrics, Obstetrics and Gynecology. 2013; 3 (2): 94–104.

138. Huaibin Liu, Jie Min, Haomiao Sun, and Chong-Lin Zhang. A study of the correlation between genes and respiratory diseases in children. ExpTherMed. – 2017, Aug. – Volume 14, No. 2. - WITH . 1463–1466. Published online - 2017 Jun 22. doi: 10.3892/etm.2017.4643 PMCID: PMC5526194.;

139. Shakhgereeva L.D., Truntsova E.S., Kasatkina N.V. Features of the course of obstructive bronchitis in young children. Scientific Review No. 2, 2019. P.-11-12

140. Yulish E.I., et al. Features of the clinic, diagnosis, treatment of mycoplasma pneumonia in children// Child health. - 2014. - No. 1. - P. 97-10

141. Marcello Bergamini, Ahmad Kantar, Renato Cutrera and Italian Pediatric Cough Interest Analysis of the Literature on Chronic Cough in Children. Group Int J Equity Health. – 2017. – Vol. 16. – R. 70. Published online 2017 May 4. doi: 10.1186/s12939-017-0566-2 PMCID: PMC5418843

141. Christian Madsen, Siri Eldevik Haberg, Maria C. Magnus, Geir Aamodt, Hein Stigum, Stephanie J. London, Pregnancy exposure to air pollution and early childhood respiratory health in the Norwegian Mother and Child Cohort Study (MoBa). Wenche Nystadand Per Nafstad Sensors (Basel). – 2017, Aug. – Vol. 17, No. 8. – R. 1780.

142. 141.Marcello Bergamini,Ahmad Kantar, Renato Cutrera and Italian Pediatric Cough Interest Analysis of the Literature on Chronic Cough in Children. Group Int J Equity Health. – 2017. – Vol. 16. – P. 70. Published online 2017 May 4. doi: 10.1186/s12939-017-0566-2 PMCID: PMC5418843

143. 142.Christian Madsen, Siri Eldevik Haberg, Maria CMagnus,Geir Aamodt, Hein Stigum, Stephanie J. London, Pregnancy exposure to air pollution and early childhood respiratory health in the Norwegian Motherand Child Cohort Study (MoBa). Wenche Nystadand Per Nafstad Sensors (Basel). – 2017, Aug. – Vol. 17, №8. – P. 1780.

144. Romanova, E. A. Bronchitis and tracheitis. How to deal with them / E. A. Romanova. - M .: AST, VKT, 2018. - 128 p.

145. Sagynbaeva B.A. Changes in chemiluminescent properties of blood in sick children with protracted obstructive bronchitis during treatment with immunomodulin// Pediatrics. - T., 2010. - No. 2-3. - P. 194-196.

146. Samsygina G. A. Respiratory tract infections in young children. - M.: MIKLOSH Publishing House, 2006. - 280 p.

147. Samsygina G.A. Chronic cough in children and its treatment // Consilium Medicum. Pediatrics. 2015. No. 02. P. 24–28.

148. Simovanyan E.I., Denisenko V.B. Improving the therapy of acute obstructive bronchitis associated with ARVI in young children // G.N. Speransky Journal "Pediatrics". 2018. Vol. 97. No. 1. P. 65–70.

149. Simovanyan E.N., Kharabadzhakhyan E.A., Denisenko V.B. Efficiency of using the recommended interferon α-2 β (Viferon) in acute obstructive bronchitis in children // Pediatrics - M., 2007. - V.87. - No. 1. - P. 105-114

150. Simonova O.I., Gorinova Yu.V., Bakradze M.D. Efficiency of inhalation of hypertonic solution in children with bronchitis and bronchiolitis. Issues of modern pediatrics. 2014; 13(4): 33–9.

151. Bronchial obstruction syndrome in young children with respiratory infections of various etiologies: features of clinical manifestations and immune response / V. K. Kotlukov, B. M. Blokhin, A. G. Rumyantsev et al. // Pediatrics. - 2006. - No. 3. -P. 14-21.

152. Skachkova M.A., Tarasenko N. F. et al. Differential diagnostics of recurrent bronchitis in children / Pediatric pulmonology: problems and solutions Edited by Yu. L. Mizernitsky, A. D. Tsaregorodtsev Issue 6. – Moscow 2006. – p. 17

153. Smirnov I.E., Mityushin I.L., Kucherenko A.G., Bakradze M.D. Cytokine profile in bacterial and viral infections in children. Russian Pediatric Journal. 2014; 17(4): 14–9.

154. Soroka Yu.A. Broncho-obstructive syndrome in pediatric practice. Journal “Child’s Health” 2(2) 2006 – p. 3.

155. Spichak T.V. Postinfectious obliterating bronchiolitis in children. M. Scientific world. 2005. 96 p.

156. Tatochenko V.K. Respiratory diseases in children. Practical guide. Edited by V.K. Tatochenko. Moscow: PediatrЪ. 2012. 480 p.

157. Tatochenko V.K. Practical pulmonology of childhood. – M.: Nauka, 2010. – 256 p.

158. Truntsova E.S. Prevention of acute respiratory infections among preschool children using enteral oxygen therapy // Health and education in the 21st century. 2014. Vol. 16. No. 4. P. 241–243.

159. Truntsova E.S., Avasova G.Z. Bronchitis in young children (features of diagnosis and treatment). Astrakhan: FGBOU VO "Astrakhan State Medical University of the Ministry of Health of the Russian Federation", 2017. 122 p.

160. The level of proinflammatory cytokines and cellular composition of bronchoalveolar lavage fluid in children with chronic bronchiolitis / Murigina G.L., Boytsova E.V. et al. // Pediatrics. - M., 2001. - No. 5. - P. 24-27

161. Fedorov A. V., Ponomareva I. A. Broncho-obstructive syndrome in children / Medical newspaper No. 8 of 02/06/2009; No. 9 of 02/11/2009.

162. Shchetinin M.N. Diseases of the bronchi and lungs - M.: Book Club 36.6, Metaphor, 2017. - 152 p.

163. Pike, S. S. Endoscopic picture and cytomorphology of bronchoalveolar lavage fluid in children with recurrent bronchitis [Text] // Pediatrics. - 1998. - n 3. - pp. 8-11.

164. Eyubova A.A., Nasrullaeva G.M. Efficiency of the Influvac vaccine in the prevention of influenza in frequently ill children. Pediatrics. 2004; 83 (2). – P. 45- 48

CONTENT

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MODERN METHODS OF IMMUNOTHERAPY OF OBSTRUCTIVE BRONCHITIS IN CHILDREN

Monography

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