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ISSUES OF ETIOPATHOGENESIS AND DIAGNOSTICS OF BRONCHO-OBSTRUCTIVE SYNDROME IN CHILDREN (LITERATURE REVIEW)

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Annotation: *Modern data on the characteristics of broncho-obstructive syndrome in children are presented. Etiological causes and pathogenetic mechanisms are given, risk factors that contribute to the development and predispose to a recurrent course, clinical characteristics, and diagnostic studies for broncho-obstructive diseases are discussed. The characteristics of the most common causes of bronchial obstruction in children - acute bronchitis, acute bronchiolitis and bronchial asthma - are given.*

Key words: *broncho-obstructive syndrome, children, acute bronchitis, acute bronchiolitis, bronchial asthma.*

Broncho-obstructive syndrome (BOS) continues to be an urgent problem in pediatric pulmonology, which is due to its high prevalence in children, the complexity of differential diagnosis, and an ambiguous prognosis [20].

Worldwide, about 50% of all young children have at least one episode of obstruction, while more than half of them (57.5%) have recurrent episodes of obstruction, despite this, only 30-40% of them at an older age, bronchial asthma (BA) will develop [9].

Thus, the problem of studying this problem in children is due to the high prevalence of BOS, the early age of onset of the disease, the difficulty in carrying out diagnostic treatment measures, which will contribute to the timely detection of the recurrent course of the disease and the development of preventive measures.

Definition, etiology, pathogenesis and phenotypes of broncho-obstructive syndrome in children.

Broncho-obstructive syndrome (or bronchial obstruction syndrome) is a symptom complex associated with impaired bronchial patency of a functional or organic origin. Not being an independent nosological form, BOS can accompany many pathological conditions [13].

In the English literature, the term “wheezing” is used to denote the condition of difficulty breathing in children - wheezing, in which “wheeze” (whistle) is a high-frequency sound heard on exhalation (sometimes on inhalation), in some cases with the participation of auxiliary respiratory muscles, which is the result of narrowing of the bronchi (intrathoracic airways) [41], which corresponds to the terms “bronchial obstruction” and “broncho-obstructive syndrome” used in domestic pediatrics.

Airway obstruction is also defined as narrowing or occlusion of the airway, which may result from accumulation of material in the lumen, wall thickening, contraction of bronchial muscles, decreased lung retraction forces, destruction of the airway without corresponding loss of alveolar tissue, and/or airway compression [23].

BOS is associated with a violation of bronchial patency of a functional or organic origin, which can be caused by acute or chronic pathology of the bronchopulmonary system, hereditary diseases, and developmental anomalies. It is important to note that BOS is not an independent nosological form of the disease and cannot be used as the main diagnosis [13].

On average, 60% of preschool children, when infected with respiratory pathogens, have manifestations of bronchial obstruction syndrome, and at the age of under 3 years, obstruction is registered in every third child [34]. In childhood, in most cases of respiratory diseases, BOS is a manifestation of obstructive bronchitis (OB), acute bronchiolitis (AB) and bronchial asthma.

For most patients of early and preschool age, the main provoking factor in the occurrence of broncho-obstructive syndrome is viral infections, less often - viral-bacterial associations. The main causative agents of viral respiratory infections, which are characterized by the occurrence of this syndrome, are: rhinoviruses, adenovirus, human metapneumovirus, coronoviruses, bocavirus, parainfluenza virus. It was revealed that infants hospitalized in infectious diseases hospitals for bronchiolitis of respiratory syncytial etiology had repeated episodes of bronchial obstruction in their follow-up, and subsequently during the first decade of life they more often developed BA compared to children without a history of infection caused by this virus [33]. The role of rhinovirus infection in the development of recurrent biofeedback and the formation of asthma cannot be ruled out [24].

A number of viral infections, such as RS virus and rhinovirus, can cause periodic BOS throughout childhood. However, a similar picture is also typical for the onset of bronchial asthma, which makes differential diagnosis difficult in young children [2]. It is known that most exacerbations of airway obstruction in children are provoked by respiratory viral infections [Babushkina, 2011]. A number of scientists have confirmed the significant role of mixed infections of viral etiology in the development of biofeedback [10]. The results of recent studies based on the

PCR diagnostic method have confirmed the increasing role of viral respiratory tract infections in the development of broncho-obstruction and asthma [35].

In children over 3 years of age, in 10–40% of cases, acute obstructive bronchitis is caused by Mycoplasma pneumonia, and in 27–58% by Clamydophila pneumonia [1].

The causes and pathogenetic mechanisms of the development of bronchial obstruction can be very diverse and depend on the age of children, their anatomical, physiological and immunological characteristics, the course of the antenatal and early postnatal periods [3]. In the pathogenesis of acute bronchial obstruction in children, swelling of the mucous membrane of the bronchi and bronchioles, hypersecretion of mucus and, to a lesser extent, the development of bronchospasm come to the fore. Long-term exposure to a provoking factor on the respiratory system and associated inflammation leads to hyperplasia of the mucous membrane. Hypersecretion of mucus and desquamation of the ciliated epithelium, in turn, leads to impaired mucociliary clearance. This condition is also aggravated by imperfect collateral ventilation of the child's respiratory system [21]. The main components of obstruction in the infectious etiology of broncho-obstructive syndrome are swelling of the bronchial mucosa, inflammatory infiltration, hypersecretion of mucus, bronchial dystonia, spasm of bronchial smooth muscles; swelling of the lungs, increasing obstruction due to compression of the airways. Spasm of bronchial smooth muscles is less pronounced than during exacerbation of atopic bronchial asthma. The significance of each component in a particular sick child depends on the etiology of the disease and individual characteristics of reactivity. The appearance of biofeedback largely depends on the etiology of the disease that caused it. The genesis of BOS involves various pathogenetic mechanisms, which can be divided into functional or reversible (bronchospasm, inflammatory infiltration, edema, mucociliary insufficiency, hypersecretion of viscous mucus) and irreversible (congenital bronchial stenosis, obliteration, etc.) [4]. Currently, most researchers recognize the heterogeneity of biofeedback [5]. The formation of biofeedback is influenced by various factors: age, etiology and individual characteristics of the reactivity of the child's body [25,26].

There are a number of anatomical and physiological features of the structure of the bronchopulmonary system in young children, which, unlike adults, contribute to a more rapid development of their biofeedback during ARVI. Thus, the bronchi and bronchioles have a relatively small diameter, which leads to higher peripheral resistance in the airways. There is poor development of the muscular and elastic tissue of the lungs and a reduced number of collateral airways, which aggravates the obstruction of the bronchi and bronchioles, and also increases the risk of developing atelectasis. The chest, trachea and bronchi are pliable in infants and

young children, and the diaphragm is positioned horizontally rather than obliquely, as in adults, which increases the likelihood of shortness of breath and respiratory disorders [6].

The most significant morphological feature of the respiratory tract in early childhood is considered to be a relatively reduced lumen of the bronchi, which significantly affects aerodynamic resistance. In the first year and a half of life, 80% of the total surface of the lungs is in small bronchi (less than 2 mm in diameter), while in children aged 6 years it is only 20%. In addition, young children are characterized by the pliability of the cartilage of the bronchial tract, low rigidity of the bone structure of the chest, which freely reacts by retracting compliant places to increase resistance in the airways, as well as features of the position and structure of the diaphragm [7,8]. The course of biofeedback in childhood is significantly influenced by the structural features of the bronchial wall: a large number of goblet cells that secrete mucus, as well as the high viscosity of bronchial secretions associated with an increased level of sialic acid [32].

The adaptive immune system, which is controlled by both immunological and non-immunological mechanisms, also plays an important role in the pathogenesis of BOS. When the respiratory tract is exposed to an infectious antigen or allergen, lymphocytic infiltration of the submucosal membrane first develops, followed by damage to epithelial cells, necrosis and ulceration of the mucous membrane. The result is the proliferation of fibroblasts, myofibroblasts, epithelial cells, smooth muscle cells and mesenchymal progenitor cells, which leads to subtotal or complete obliteration of the airway lumen [34]. In addition, the period of early childhood is accompanied by a critical period of development of the immune system, when an inadequate or even paradoxical immune response develops to antigenic influences [7,9].

The early development of asthma in children may be facilitated by intrauterine sensitization of the fetus due to increased permeability of the fetoplacental barrier caused by various influences. During the prenatal period, during which lung formation and maturation occurs, even minimal effects on fetal airway development can have a major impact on the risk of developing AOB and asthma in the future [8,10]. In addition, during postnatal sensitization, excessive antigenic exposure in the first years of a child’s life is important [1].

Most researchers recognize the influence of premorbid background factors on the development of obstruction. These are toxicosis of pregnant women, complicated childbirth, hypoxia during childbirth, prematurity, a burdened allergic history, hereditary predisposition to atopy, rickets, thymic hyperplasia, early artificial feeding, excess body weight, and previous respiratory disease at the age of 6-12 months [14]. Among the unfavorable environmental factors that can influence the development of biofeedback, an important role is given to

unfavorable environmental conditions and passive smoking in the family [15]. Under the influence of tobacco smoke, hypertrophy of the bronchial mucous glands occurs, mucociliary clearance is disrupted, and the movement of mucus slows down. Passive smoking contributes to the destruction of the bronchial epithelium. In addition, tobacco smoke is an inhibitor of neutrophil chemotaxis [6]. In 2008, the working group of the European Respiratory Society (ERS) proposed dividing BO syndrome in preschool children into phenotypes [19]: episodic (viral) - wheezing is observed for a limited period, often associated with upper respiratory tract infections and with the absence of symptoms between episodes, recurrent and multi-trigger BO syndrome, caused by a number of factors (viral infections, tobacco smoke, allergens, aerosols, crying, laughter, physical activity, etc.), the division of which is still used today. The literature uses a division into phenotypes that takes into account the clinical outcome of broncho-obstructive syndrome: episodic and recurrent, or persistent, bronchial obstruction [29,30].

Criteria for diagnosing broncho-obstructive syndrome in children.

General clinical signs of bronchial obstruction in children include tachypnea, expiratory shortness of breath with the participation of auxiliary muscles, noisy wheezing, chest bloating, wet or paroxysmal, spasmodic cough. Auscultation reveals scattered moist fine rales, dry wheezing, and with bronchiolitis - crepitus; percussion - boxy shade of percussion sound, narrowing of the boundaries of cardiac dullness. Physical signs in the presence of BO are due to the fact that increased intrathoracic pressure is required to produce exhalation, which is ensured by increased work of the respiratory muscles. Increased intrathoracic pressure contributes to compression of the bronchi, which leads to their vibration and the occurrence of whistling sounds [22]. Young children cannot make complaints, so it is worth paying attention to indirect signs indicating dyspnea, such as anxiety or, conversely, lethargy, confusion, a forced position, and an unreasonable decrease in appetite [21].

The absence of typical clinical manifestations outside the acute state of bronchial obstruction complicates diagnostic measures or, conversely, can lead to overdiagnosis. Various laboratory and functional research methods have little information content for identifying the etiological causes of biofeedback in children. There is a need not only to evaluate diagnostic indicators, but to form a comprehensive picture of a particular patient, taking into account a detailed study of his life history [28].

To determine wheezing characteristic of biofeedback, an integral diagnostic method is auscultation of the chest organs. However, the results of this study are subjective. It is worth noting that there are modern acoustic methods using computer technologies that allow obtaining reliable diagnostic information [18].

Various medical instruments are used to assess the severity of dyspnea, although their use in young children is limited [26]. Thus, spirometry is considered the most informative non-invasive method for assessing external respiratory function, which must be carried out exclusively according to strict rules to obtain reliable data. However, the use of this procedure in children under five years of age is difficult due to the complexity of performing forced maneuvers and the required commands [24].

The next no less important sign by which the severity of BOS is assessed is oxygen saturation - pulse oximetry measuring heart rate (pulse) and blood oxygen level (SpO2) in a person's blood. This is one of the few objective diagnostic methods. [20,21]. When conducting an X-ray examination of the chest in patients with biofeedback, there is swelling of the lungs, increased bronchovascular pattern, and areas of decreased transparency of the lung tissue.

Thus, when examining children with broncho-obstructive conditions, the main task of the doctor is to identify the leading clinical symptoms and syndromes of the disease, determine the cause-and-effect relationships of their occurrence, to assess the necessary diagnostic measures and the adequacy of the treatment.

The problems of differential diagnosis of obstructive conditions, which are quite complex in children of the first years of life, are extremely important. This is largely determined by the characteristics of pulmonary pathology in early childhood, a large number of possible etiological factors for the formation of AOB and the absence of highly informative distinctive signs in bronchial obstruction of various origins. Diseases occurring with biofeedback include acute obstructive and recurrent bronchitis, asthma, bronchiolitis; bronchopulmonary dysplasia; malformations of the bronchopulmonary system; foreign bodies of the trachea, bronchi, esophagus; aspiration syndrome; diseases of the cardiovascular system of congenital and acquired nature; hereditary metabolic abnormalities; diseases of the central and peripheral nervous system; immunodeficiency states that occur with lung damage; thymomegaly; helminthiases [15,16].

Modern ideas about the main nosological diseases manifested by broncho-obstructive syndrome in children.

Currently, the incidence of bronchitis averages 75–250 cases per 1,000 children per year, while in 50% of young children, respiratory infections occur with a clinical picture of obstructive bronchitis of varying severity [19]. According to the accepted classification of clinical forms of bronchopulmonary diseases in children, they are distinguished [17]: Acute bronchitis - acute inflammation of the bronchial mucosa, caused by various infectious, less often physical or chemical factors (J20.0 - J20.9). Diagnostic criteria: Clinical: low-grade fever, cough, diffuse dry and variable moist rales in the lungs. X-ray: changes in the pulmonary pattern (possibly increased and increased transparency) in the absence of infiltrative and focal

shadows in the lungs. Recurrent bronchitis (J40.0) – repeated episodes of acute bronchitis 2-3 times or more during the year against the background of respiratory viral infections. The criteria for diagnosing an acute episode correspond to the clinical and radiological signs of acute bronchitis. It occurs, as a rule, in children in the first 4-5 years of life. Chronic bronchitis (J41) is a chronic widespread inflammatory lesion of the bronchi. Diagnostic criteria: Clinical: productive cough, moist rales of various sizes in the lungs in the presence of at least 2-3 exacerbations of the disease per year for 2 or more years in a row. The cause of acute bronchitis in children in 90% of cases is respiratory viruses, primarily parainfluenza viruses, influenza viruses, respiratory syncytial (RS) virus, rhinovirus, adenovirus, metapneumovirus [23,30]. Up to 10% of cases of OB in childhood, especially in schoolchildren and adolescents, are caused by bacterial pathogens such as Mycoplasma pneumoniae, Chlamydophila pneumoniae and Bordetella pertussis [31,32]. Bronchitis is an inflammatory disease of the bronchial mucosa, the causes of which are most often infectious, less often chemical and physical factors. Acute bronchitis in most cases (about 90%) is a manifestation of ARVI. Clinically, bronchitis is manifested by cough and diffuse wheezing in the lungs in the absence of focal and infiltrative changes on the radiograph. Acute bronchitis can develop at any age. If it is not accompanied by signs of obstructive syndrome, it is usually referred to as acute simple bronchitis. In the presence of bronchial obstruction syndrome, acute obstructive bronchitis is diagnosed. Acute obstructive bronchitis occurs with a syndrome of bronchial obstruction caused by swelling of the bronchial mucosa, hypersecretion of mucus, which reduces the lumen of the bronchi, thereby sharply increasing aerodynamic resistance in them [14,15].

Acute bronchiolitis (J21) is defined as an inflammatory disease of the lower respiratory tract primarily affecting the small bronchi and bronchioles and develops in children under 2 years of age [35,40]. The main etiological factors of acute bronchiolitis are respiratory viruses, most often respiratory syncytial virus. The onset of the disease is acute with catarrhal symptoms, body temperature is normal or subfebrile. Clinical signs of biofeedback may appear both on the first day and 2–4 days after the onset of the disease. In infants, especially premature infants, apnea may occur, usually early in the disease, before respiratory symptoms manifest [26,42,43]. In children of the first year of life, bronchiolitis may develop, which is accompanied by damage to the intrapulmonary airways up to the alveolar ducts and leads to the development of severe respiratory failure [38,40]. The symptom complex of acute bronchiolitis includes obstruction of the lower respiratory tract, which occurs against the background of an acute respiratory viral infection (or when exposed to irritants) and is accompanied by cough and signs of respiratory failure: difficulty groaning, tachypnea, retraction of the intercostal

spaces and/or hypochondrium, flaring of the wings of the nose and bilateral wheezing. in the lungs [3].

Epidemiological studies indicate that from 4 to 8% of the population suffer from asthma; in the pediatric population this figure is up to 5-10%, which dictates the need for special attention to this pathology [12]

Asthma is a multifactorial disease [37,38] characterized by chronic inflammation of the airways, the presence of respiratory symptoms such as wheezing, shortness of breath, chest congestion and cough, which vary in time and intensity, and appear together with variable airway obstruction that develops during child growth under the influence of causal factors,

It should be emphasized that the diagnosis of asthma in children is clinical: it is based on observation of the patient and assessment of symptoms (wheezing, coughing, shortness of breath, as well as the development of symptoms at night or upon awakening) with the exclusion of other causes of asthma, the presence of risk factors for the development of asthma (including family history), as well as response to therapy aimed at controlling the disease.

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