**UDC 616.8-007.6-02:612.232**

# CHANGES IN THE CLINICAL STATE OF THE BODY WHEN NEUROLOGICAL DISORDERS AND BRONCHIAL ASTHMA COME TOGETHER

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✓ ***Resume***

***The publication provides a literature review reflecting the scientific substantiation of the mechanisms of the onset and development of mental disorders in bronchial asthma. A brief historical excursion to the study of the issue of bronchial asthma is presented. The data of epidemiological studies of bronchial asthma in the world are presented. The modern theories of the mechanisms of development of mental disorders in bronchial asthma are considered. Particular attention is paid to the role of perinatal lesions of the central nervous system, providing autonomic dysregulation in bronchial asthma in childhood. The diathetic model of stress explains the contribution of anxiety and depression to the formation of mental disorders in bronchial asthma.***

***Key words: bronchial asthma, mental disorders, perinatal damage to the central nervous system, neurological diseases.***

# ИЗМЕНЕНИЕ КЛИНИЧЕСКОЙ СИТУАЦИИ В ОРГАНИЗМЕ ПРИ СОПУТСТВУЮЩИХ НЕВРОЛОГИЧЕСКИХ ЗАБОЛЕВАНИЯХ И БРОНХИАЛЬНОЙ АСТМЕ

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✓ ***Резюме***

***В публикации представлен обзор литературы, отражающий научное обоснование механизмов возникновения и развития психических нарушений при бронхиальной астме. Изложен краткий исторический экскурс изучения вопроса бронхиальной астме. Приведены данные эпидемиологических исследований бронхиальной астме в мире. Рассмотрены современные теории механизмов развития психических нарушений при бронхиальной астме. Особое внимание уделено роли перинатального поражения центральной нервной системы, обеспечивающего вегетативную дизрегуляцию при бронхиальной астме в детском возрасте. Диатезная модель стресса объясняет вклад тревоги и депрессии в формирование психических нарушений при бронхиальной астме.***

***Ключевые слова: бронхиальная астма, психические расстройства, перинатальное поражение центральной нервной системы, неврологические заболевания.***

# NEVROLOGIK KASALLIKLAR HAMDA BRONXIAL ASTMA BIRGALIKDA KELGANDA ORGANIZIMDAGI KLINIK HOLATNING O’ZGARISHI

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***Nashrda bronxial astmada ruhiy kasalliklarning paydo bo'lishi va rivojlanish mexanizmlarining ilmiy asoslanishi aks ettirilgan adabiyotlar sharhi keltirilgan. Bronxial astma muammosini o'rganishga qisqacha tarixiy ekskursiya taqdim etilgan. Dunyodagi bronxial astma bo'yicha epidemiologik tadqiqotlar ma'lumotlari keltirilgan. Bronxial astmada ruhiy kasalliklarning rivojlanish mexanizmlarining zamonaviy nazariyalari ko'rib chiqiladi. Perinatal davrda bronxial astmada avtonom disregulyatsiyani ta'minlab, markaziy asab tizimining perinatal shikastlanishining roliga alohida e'tibor qaratiladi. Stressning diatez modeli tashvish va tushkunlikning bronxial astmada ruhiy kasalliklarning shakllanishiga qo'shgan hissasini tushuntiradi.***

***Kalit so'zlar: bronxial astma, ruhiy kasalliklar, markaziy asab tizimining perinatal shikastlanishi, nevrologik kasalliklar.***

## Relevance

The current course of asthma is characterized by significant severity, resistance to therapy, and more frequent development of asthmatic conditions [2]. This is largely due to the fact that AD belongs to the group of psychosomatic diseases, since in its origin mental and somatic factors are closely intertwined, creating complex causal relationships [5]. Bronchial asthma (BA) is an important public health problem in all countries of the world. Statistics indicate a steady increase in the prevalence of the disease. Despite the advances in his treatment, the increase in patients is 20-50% every ten years. The upward trend in mortality and disability continues [6]. The role of mental factors in the pathogenesis of AD is confirmed by data on the occurrence and provocation of seizures during emotional stress and psychological stress [11].

It should be noted that the neurogenic theory was one of the first in the history of the development of ideas about the etiopathogenesis of AD. Before the concept of allergy was formed, the pathogenesis of an asthmatic attack was explained by neurogenic spasm of smooth muscles. Currently, AD is considered as a heterogeneous disease, in the pathogenesis of which neuropsychiatric disorders play a certain role, with close interaction of somatic and neuropsychic factors [3].

The neuropsychic factor mediates its influence on the functional state of the bronchi through sympathetic and parasympathetic regulation mechanisms. Influences are transmitted along the vagus nerve that cause contractions of the smooth muscles of the bronchi; through the pulmonary sympathetic plexus - adrenergic influences, relaxing smooth muscles [10, 13]. Dysfunction of the autonomic nervous system, carrying out operational control and "adjustment" of bronchial tone to changing conditions of the external and internal environment, is one of the mechanisms of pathogenesis of altered reactivity of the bronchi and lungs, leading to bronchial obstruction [1]. Autonomic nerves regulate many functions of the respiratory tract, including lung muscle tone, secretory processes, blood circulation, microvascular permeability, migration and release of inflammatory mediators that are important in the pathogenesis of bronchial asthma [7–9].

Bronchial asthma is a chronic inflammatory airway disease in which many cells, including mast cells and eosinophils, play an important role. In sensitive individuals, this inflammation is the cause of symptoms that are usually associated with widespread but variable airflow restriction, which is often reversible spontaneously or under the influence of treatment and causes an interrelated increase in bronchial responsiveness to various stimuli (A.G. Chuchalin, 2007). Statistics indicate a steady increase in the prevalence of the disease. In the world, this disease affects 150 million people. Despite the advances in its treatment, the increase in patients is 20-50% every ten years [5]. The upward trend in mortality and disability continues - 1 million people die from AD every decade. The economic damage from the disease is associated not only with the cost of providing assistance, but also with the loss of working capacity, with the emergence of social and family problems in this regard [15].

As a rule, starting in childhood, the disease continues to occupy a leading position among chronic bronchopulmonary pathology in adulthood, often causing disability.

Like any chronic disease, AD has a significant impact on the patient's psyche. The factor of expectation of an attack, the need to use an inhaler, adherence to a diet can be a prerequisite for the difficult formation of social reputation up to the development of social isolation (I.S. Aron, 2000). The limitation in the emotional and social aspects of life caused by the disease may be more significant for the patient than the physical limitations or the symptoms of the disease themselves.

Allergic inflammation is recognized as the leading pathogenetic mechanism of AD [17]. At the same time, only a comprehensive approach to treatment, taking into account the changes that occur in the extrapulmonary sphere, makes it possible to obtain the most significant therapeutic effect. The development of questions of pathogenetically substantiated therapy of asthma is of great importance.

In a few publications, one can find indications of the influence of mental factors on the course of bronchial asthma, on the accompanying vegetative [5], deviations in the emotional-personal and intellectual-mnestic spheres.

We have not found any works analyzing neurological and psychoemotional disorders in AD in patients of working age in the available literature. There are reports [13] on the study of the autonomic status and psychoemotional disorders in BA patients without regard to age, the nature of the course of the disease, which

dictates the need to clarify these issues and determines the relevance of this study.

Recently, an opinion has been increasingly expressed about the serious contribution of hypoxic damage to the central nervous system (CNS) and prematurity in the genesis of the disease. The consequences of perinatal damage to the central nervous system (PPCNS) are functional instability of the cortical-subcortical interactions that regulate the respiratory complex. Prematurity leads to morphological and functional immaturity of the brain structures, which provide autonomous regulation of vital functions. Hypoxia and prematurity are factors of the imperfect immune response of the newborn, leading to frequent infectious diseases that disrupt the neurogenic regulation of the bronchi [8, 9]. In some studies, there is a correlation between the depth of CNS damage and the severity of AD symptoms caused by a more severe neuro-immune-endocrine imbalance [10]. Neurological and psychopathological disorders that develop as a result of PCNS naturally close the vicious circles of AD pathogenesis, limiting the patient's adaptive capabilities throughout life. In this regard, the study of the clinical and dynamic characteristics of neuropsychiatric disorders in children with BA is a very urgent task, since it can contribute to the improvement of methods of prevention and treatment of this disease.

With a high degree of probability, it can be assumed that understanding the mechanisms of development of mental disorders in AD can clarify the causes of the onset of the disease itself, and will make it possible to develop the principles of prevention and therapeutic intervention, and rehabilitation. At present, neurogenic inflammation with the participation of neuropeptides, dysfunction of the autonomic nervous system (ANS) [4], disturbances of the emotional sphere and damage to the suprasegmental structures of the brain [1] should be attributed to the most promising areas of establishing the pathogenesis of mental disorders in AD.

In recent decades, there has been a decline in the level of children's health in the Russian Federation. Leading experts associate this with a rapid increase in the frequency of pre- and perinatal pathology of the central nervous system. The most common cause of brain damage in the fetus and newborn is hypoxia associated with an unfavorable course of pregnancy and childbirth. Under conditions of hypoxia, hemodynamic and metabolic disorders occur, which disrupt energy supply. As a result, the modern child population is characterized by reduced stress resistance and compensatory-adaptive capabilities [18]. In 60–80% of mothers of children with asthma, complications of pregnancy are observed, accompanied by fetal hypoxia (gestosis, threat of premature birth, acute infectious diseases), which are unconditioned pathogenic factors leading to organic brain damage in the early stages of ontogenesis. The consequence of perinatal hypoxic lesions of the central nervous system is the functional instability of the cortical-subcortical and spinal structures of the brain and their connections that regulate the respiratory complex. In such children, in the perinatal period, respiratory and cardiovascular disorders occur, affecting the fetus and the brain of the newborn. With prematurity, the morphological and functional immaturity of the brain structures is noted, unable to provide adequate autonomous regulation of blood circulation and respiration in a newborn. Perinatal damage to the central nervous system and prematurity are often factors of a weak and imperfect immune response of the newborn, which contributes to the emergence of infectious diseases of the perinatal period, disrupting the neurogenic regulation of bronchial smooth muscle tone with damage to the ciliated epithelium. The consequence of this is an increased permeability of the mucous membrane for allergens, triggering of sensitization mechanisms, a sharp activation of specific and nonspecific hyperreactivity of the bronchi with the development of bronchospasm [7]. Perinatal CNS damage results in neurological disorders in the first year of life, delayed manifestation of cerebral disorders in the form of autonomic dysregulation, manifestations of hydrocephalus and syndrome of emotional-volitional and behavioral disorders against a background of attention deficit, delayed speech and sensorimotor development, hyperexcitability, increased mental fatigue associated with it exhaustion of active attention, restlessness, scattering, disinhibition, lack of self-control, difficulty in memorization, lack of adaptive capabilities in conditions of external discomfort, decrease in criticality [7]. As they grow older, symptoms of cerebrasthenic and asthenovegetative syndromes, behavioral disorders, learning difficulties, weakness in self-control, preschool and school maladjustment appear [12]. Domestic researchers believe that the brainstem structures, the limbic system, and the diencephalic region are the most sensitive to hypoxia and mechanical trauma [9]. The emerging microstructural changes in these centers lead to a violation of autonomic and

hormonal regulation, dysontogenesis of the somatic and mental spheres [2]. Such violations are observed in severe extragenital pathology, smoking, drug use, severe complications of the mother's pregnancy [8]. Many researchers note the significant role of ANS in the development of asthma in children [7]. Normally, the autonomic nuclei of the brainstem regulate bronchial tone and its reactivity, including by changing the sensitivity of the respiratory tract receptors [3]. In conditions of disease (BA), the predominance of cholinergic (parasympathetic) influence is characteristic. In addition, there is evidence of a decrease in sympathetic regulation in patients with asthma at rest, while in response to emotional stress, patients with asthma demonstrate an increase in parasympathetic control. In the conditions of a respiratory test, a weakening of the activity of the sympathetic and / or an increase in the activity of the parasympathetic link is observed. Methacholine challenge tests lead to airway hyperresponsiveness with an increase in the parasympathetic modulation index [17]. Studies of autonomic regulation in adolescents with asthma, depending on the state of its initial tone, have demonstrated a number of features. Thus, with initial sympathicotonia, autonomic reactivity was observed with a significant increase in vagal influence with insufficient inclusion of the sympathoadrenal system during exercise. In the initial vagotonia, sympathicotonic and hypersympathicotonic regulation prevailed in the early onset of broncho-obstructive syndrome with a more severe course of an asthmatic attack. In adolescents with initial sympathicotonia, changes in the structure and function of membrane receptors, the formation of an unstable metabolism of mast cells and a disturbance in the antioxidant system of the body were noted [17]. Obviously, as a result of hypoxic lesions of the central nervous system, dissociative disorders occur in the links of the neuroimmunoendocrine complex [4]. Regulatory neuropeptides act as mediators of the emerging pathological systems, which are a link between the nervous and immune systems (they have receptors in the limbic system, hypothalamus, adrenal secretory cells and lymphocytes) [13]. in this case, the amygdala complex (MC) is assigned a special role. Damage to the basolateral and centromedial nuclei of the MC leads to discoordination of the most important vegetative centers of the brain and disruption of the normal reactions of the respiratory system in response to significant changes in the environment [17]. The limbic system is involved in the implementation of the endocrine, autonomic and behavioral response to the current situation, taking into account past experience. Thanks to MC, the activity of the most important autonomic centers of the brain is coordinated, providing the processes of visceral regulation and regulatory impulses are formed that determine the required level of activity of sympathetic and parasympathetic preganglionic neurons, as well as motor neurons of the respiratory system and sphincter areas [18]. In children with a deeper CNS lesion, there is an imbalance in the functional activity of the T, B-cell link of immunity, the phagocytosis system, the level of the main stress-limiting hormones, which contributes to the earlier manifestation of asthma and its severe course [8]. In children with asthma who have undergone hypoxic damage to the central nervous system, the level of substance P in the blood, as well as the values of the neuropeptide diagnostic coefficient, are significantly higher than in children of the comparison group, which indicates a more pronounced neurogenic inflammation [14]. The highest values of substance P and neuropeptide diagnostic coefficient are observed in children with attention deficit hyperactivity disorder [3]. It has been suggested that AD and allergic diseases can act as risk factors for the development of attention deficit hyperactivity disorder [11]. Additional factors are called - incomplete family, pathological types of upbringing, increased stress in the family, late start of asthma treatment.

## Conclusions

Thus, neuroendocrine shifts due to perinatal brain damage already in childhood cause a breakdown in autonomic regulation, leading to maladjustment and worsening of asthma.

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**Entered 09.09.2021**