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OBESITY-RELATED PRE-ECLAMPSIA - FETUS AND NEWBORN OUTCOMES (literature review)

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Abstract. The paper deals with the studying the epidemiology of risk factors of preeclampsia, including the delayed risk of preeclampsia associated with obesity. Obesity is a serious risk factor for preeclampsia. Throughout the world, hypertensive disorders in pregnancy and related complications are among the main causes of maternal and their fetuses/newborn morbidity and mortality. Fetal and neonatal outcomes associated with eclampsia and its complications are significant, including neonatal mortality and serious long-term neonatal morbidity.

Key words. pregnancy; preeclampsia; obesity.

For many years, PE remains one of the serious multisystem pathological complications of pregnancy, the frequency of which has no tendency to decrease. Still Hippocrates in the IV century BC He described the disease of pregnant women, the symptoms of which aligned with epilepsy. Only in 1827, R. Bright suggested that eclampsia (translated from Greek "lightning", "outbreak") is a kidney disease based on the definition of albuminuria. In 1843, J. Lever describes edema and headache for eclampsia. A. Delore in 1884 put forward an infectious theory and even identified the so-called Bacillus Eclampsiae. In 1886, E. Leyden, the term "nephropathy" was introduced, and in 1908 S. D. Minov "Preeclampsia". In 1905, J. de Lee suggested that eclampsia is the result of toxins, and W. Zangemeister described the classic triad: arterial hypertension, swelling, proteinuria, which is the basis for the diagnosis and assessment of the severity of PE [1,2].

Hypertensive disorders during pregnancy, including preeclampsia (PE), represent a wide range of conditions that are associated with significant incidence and mortality of mothers and their and fruits/newborns. According to various authors, the incidence of PE is from 3 to 10% of all pregnancies. All over the world, PE and related complications are one of the main causes of maternal mortality. Currently, there is a tendency to reduce maternal mortality due to preeclampsia in developed countries, however, the maternal incidence remains high and is the main factor that contributes to hospitalization in the intensive care unit during pregnancy [3].

Approximately 12-25% of the fetal growth restrictions and small for this gestational age of the fetus, as well as from 15 to 20% of all premature births are associated with preeclampsia. Contenting complications associated with PE are significant, including the mortality rate of newborn and serious long-term neonatal incidence. Despite the tangible successes of medicine, the only well-known pathogenetic treatment of preeclampsia is the completion of pregnancy regardless of the gestational age [3,4]. The purpose of this publication is to discuss the epidemiology of risk factors PE, including the delayed risk of PE associated with obesity.

Obesity is a rapidly increasing risk factor for preeclampsia, which dictates the need to understand the pathogenetic mechanisms that contribute to the increase and implement this risk.

Preeclampsia is a syndrome specific for pregnancy, in which many organs are affected, characterized by the development of hypertension and proteinuria, mainly detected from 20 or more weeks of pregnancy. According to various estimates, PE complicates from 2 to 8% of all pregnancies. Although the exact reason is unknown, the pathophysiological processes underlying this disorder are described in two stages. The first stage is characterized by reduced placental perfusion, possibly associated with abnormal placenta, violation of trophoblast invasion and inadequate remodeling of the spiral arteries of the uterus. The second stage refers to maternal systemic manifestations with inflammatory, metabolic and thrombotic answers, which are reduced to a change in vascular function, which can lead to a violation of the activities of several organs [5,6].

The exact classification of various hypertensive disorders during pregnancy remained complex due to the changing nomenclature, as well as geographical variations in accepted diagnostic criteria. For example, such terms as "toxemia" and "hypertension

caused by pregnancy” are now considered outdated.

In addition, discussions continued on various diagnostic PE criteria in different regions of the world. This applies to the degree of hypertension, the presence/absence of proteinuria and the classification of the severity of the disease. These inconsistencies led to problems when comparing and generalizing epidemiological and other results of major studies [6].

The classification system, based on the report of the “working group by high arterial pressure during pregnancy”, is most often used in the United States, which defines four main categories: gestational hypertension, preeclampsia/eclampsia, chronic hypertension and mesmeric hypertension of preeclampsia. Preeclampsia is defined as the first detected prolonged blood pressure (> 140 mm Hg Systolic or > 90 mm Hg of HG diastolic at least 2 dimensions with an interval of 4-6 hours and proteinuria (at least 1+ or at least 1+ or > 300 mg in a 24-hour urine collection after 20 weeks of pregnancy [7]).

The preeclampsia is considered severe if, in addition to the defining criteria for blood pressure and proteinuria, any of the following is present:

- blood pressure from 160 mm Hg. and higher
- systolic and/or diastolic from 110 mm Hg. and more.
- The excretion of five or more grams of protein with daily urine.
- neurological disorders (visual changes, headache, convulsions, coma). Pulmonary edema.
- liver dysfunction (increased liver transaminase or epigastric pain.
- impaired renal function, oliguria or increased concentration of creatinine in blood serum > 1.2 in women without indicating in a history of kidney disease.
- thrombocytopenia.
- placental detachment, restriction of the fetal growth or oligohydramnion.

Eclampsia refers to seizures that occur only in women with PE, and cannot be classified as other reasons.

Hellp syndrome is determined by the presence of hemolysis, increased liver transaminase and low platelets. Hellp is not necessarily manifested in the presence of hypertension or proteinuria, but it is believed that it is associated with preeclampsia.

Diagnosis of preeclampsia can be especially complicated in women with previously existing hypertension and/or chronic kidney disease, since both an increase in blood pressure and excretion of protein in urine increase to the end of pregnancy.

Thus, the diagnosis is based on a sudden increase in blood pressure or proteinuria and/or confirmation of a violation of the function of parenchymal organs [1,2].

The main reason for the critical assessments of various classification systems boils down to the fact that none of them has been independently appreciated in terms of the ability to identify those women who are at risk of adverse pregnancy outcomes. But recent studies were aimed at developing clinically significant definitions based on the forecast data of adverse outcomes [8–11].

A systematic review of the World Health Organization shows that hypertensive disorders in the structure of maternal mortality account for 16% of all maternal deaths in developed countries, 9% in Africa and Asia and up to 26% in Latin America and the Caribbean basin [12]. In regions with the highest MS, most deaths are associated with eclampsia, but not with preeclampsia. Based on the research data of the national study of the register of prescribed patients in the United States, the level of preeclampsia during childbirth and childbirth increased by 25% from 1987 to 2004, while the eclampsia indicator reduced I went out by 22%, although this indicator is not significant [4]. Severe complications of pre-eclampsia and eclampsia include renal failure, stroke, cardiac dysfunction or respiratory failure/arrest, coagulopathy, and liver failure. In a study of hospitals operated by Health Care America Corporation, preeclampsia was the second leading cause of pregnancy-related intensive care admissions after obstetric bleeding [3].

Fetal and neonatal outcomes associated with preeclampsia vary worldwide. Approximately 12 to 25% of fetal and small-for-gestational age growth restriction and 15 to 20% of all preterm births are associated with preeclampsia.

The associated complications in preterm infants are significant, including neonatal mortality and serious long-term neonatal morbidity. A quarter of stillbirths and neonatal deaths in developing countries are due to preeclampsia/eclampsia. Infant mortality due to preeclampsia is three times higher in low-resource health facilities than in high-income countries, largely due to a lack of facilities and capacity to provide neonatal intensive care [4].

A number of studies have reported a 7–20% chance of recurrence of preeclampsia in a subsequent pregnancy [12]. This risk is further increased if a woman has had preeclampsia complicated by two previous pregnancies, as well as if she developed preeclampsia at an earlier gestational age. Estimates of recurrence of preeclampsia vary greatly depending on the quality of the diagnostic criteria used. In an Icelandic study using strict diagnostic criteria for preeclampsia and other hypertension disorders, the likelihood of recurrent preeclampsia or superimposed preeclampsia in a second pregnancy was 13% [12]. Dr. Leon Chesley and his collaborators demonstrated that women whose even single pregnancies were complicated by eclampsia had a mortality risk that was two to five times higher over the next 35 years compared to those whose pregnancies were not complicated by preeclampsia. Other studies have also demonstrated an association between preeclampsia and cardiovascular disease and related mortality. The risk of cardiovascular disease was increased 8-fold in Scandinavian women who developed preeclampsia severe enough to require early delivery.

In a cohort of women who give birth in Jerusalem, the risk of mortality at 24–36 years of follow-up is twice as high in women with prior preeclampsia compared with women who have not been diagnosed [13]. Mortality was largely related to cardiovascular causes. These results were also confirmed in other populations [13]. Metabolic syndrome-hypertension, dyslipidaemia, insulin resistance, endothelial dysfunction, and vascular abnormalities have been observed months to years after preeclampsia, which also supported the concept of a link between preeclampsia and cardiovascular disease later on [13]. Whether these common risk factors lead to preeclampsia and then cardiovascular disease, or whether preeclampsia itself may contribute to this long-term risk remains unresolved. Based on these data, preeclampsia should be considered as a cardiovascular risk factor, and women with a history of preeclampsia should have ongoing, close surveillance to prevent and/or detect future cardiovascular disease. The epidemiology of preeclampsia reflects a wide range of risk factors, as well as the complexity and heterogeneity of the disease. Risk factors can be classified according to specific pregnancy characteristics and history. The increase in the frequency of preeclampsia may be associated with a higher prevalence of predisposing diseases such as chronic hypertension, diabetes mellitus, obesity, infertility, as well as the use of artificial reproductive technologies with a concomitant increase in multi-embryonic pregnancy [13].

According to a systematic review of controlled trials, first pregnancy is a significant risk factor, nearly tripling the risk of developing preeclampsia compared to repeat pregnancies. An estimated two-thirds of cases occur in first pregnancies after the first trimester. The relationship between first gestation and preeclampsia suggests an immunological mechanism that allows subsequent pregnancies to protect the mother's body from paternal antigens. In support of this concept, there is evidence that previous reproductive losses, prolonged sexual activity before pregnancy, or prolonged cohabitation before pregnancy are among the factors that reduce the risk of preeclampsia. On the contrary, the risk of preeclampsia increases with the use of barrier contraceptives, changing the future father, fertilization with donor spermatozoa. But even during a subsequent pregnancy, a change in sexual partner also increases the risk of preeclampsia [3].

Excessive volume of the placenta, as well as hydatidiform mole, multiple gestations are also associated with the development of preeclampsia. Early development of this complication may have more serious clinical manifestations [3,14].

The extreme age limits of childbearing age are also associated with preeclampsia. However, once a parity adjustment occurs in the young age group for recurrent pregnancies (because most first pregnancies occur at a younger age), the association between younger age and preeclampsia is lost. Multiple studies demonstrate a higher prevalence of preeclampsia in older women, regardless of parity; however, many do not control pre-existing medical health problems. After controlling for baseline differences, women aged 40 years and older had a two-fold risk of developing preeclampsia: an odds ratio of 1.68, (1.23–2.29) among primigravidas and 1.96, (1.34–2.87) among frequently pregnant women [13,14]. The connection between the African-American and American race and preeclampsia is explained by the higher prevalence in this group of chronic hypertension, often not diagnosed. Although some studies demonstrate a higher risk of preeclampsia among African American women, 32–34 large prospective research, which controlled the Association of the identified preeclampsia with other risk factors, did not find a significant connection between preeclampsia and African-American race. Heavier forms of preeclampsia can be associated with the negligent race of the mother [16].

Many risk factors for maternal mortality from preeclampsia are similar to the factors of cardiovascular diseases. The previous chronic hypertension, diabetes, obesity of vascular disorders, chronic kidney pathology, autoimmune states are associated with the risk of preeclampsia, and the degree of risk is seriously tied with the seriousness of the underlying chronic disease. Women with chronic hypertension have a risk of preeclampsia by 10-25% more compared to the general population [7]. This risk is increased to 31% in women with long-term hypertension from 4 and sick. With a diagnosis of gestational diabetes, the total risk of developing preeclampsia is approximately 21%. At the same time, the risk of 11-12% with diabetes lasting less than 10 years increases to 36-54% among women with longer diabetes leading to impaired microcirculatory homeostasis. In case of low kidney diseases (creatinine is a serum of 1.5 mg/DL), the risk of preeclampsia is estimated at 20-25%, but in more than 50% in pregnant women with severe renal failure.

Preeclampsia is more common in women with autoimmune states, such as systemic red lupus and antiphospholipid syndrome [7]. Family history according to preeclampsia is supposed to the risk of this formidable complication of pregnancy. Paradoxically, smoking cigarette is associated with a decrease in the risk of preeclampsia, possibly due to the modulation of angiogenic factors [14]. Obesity - an increased cetla index (BMI, kg/m²) is also associated with preeclampsia. Given the obesity epidemic in the United States and the world, this is one of the most significant and potentially variable risk factors for preeclampsia. In the United States, the proportion of women with overweight or obesity has increased by about 60% over the past thirty years [17]. The World Health Organization evaluates the prevalence of women with obesity and overweight (body mass index > 25 kg/m²) - in the United States of 77%, 73% in Mexico, 37% - in France, 32% - in China, 18% - 18% In India and 69% - in South Africa with wide variations on each continent [18]. The high prevalence of obesity and the predictable increase have significant consequences for pregnancy, since obesity is associated with infertility, spontaneous miscarriage, malformations of the fetus, thromboembolic complications, gestational diabetes, stillbirth, premature births, cesa -cross -section, macrosomia of the fetus and hypertension disorders [19]. Obesity increases the overall risk of preeclampsia by about 2-3 times [20]. The risk of preeclampsia is gradually increasing with an increase in BMI, even within the normal range. It is important to note that not only the late or light forms of preeclampsia are increasing, but also the early and severe preeclampsia, which are associated with greater perinatal incidence and mortality. Increased risk is present in both European and African-American women [21]. The connection between the risk of preeclampsia and obesity is also demonstrated in different populations around the world. The advanced concept that obesity can play a causal role is based on the fact that weight loss reduces the risk of preeclampsia. Some studies show that an excessive increase in the mass of mothers is associated with the risk of preeclampsia, although they can be refuted by the fact of fluid retention in interstition and cavities for preeclampsia, which contributes to weight growth. Although weight loss is not recommended during pregnancy, obesity refers to potential variable risk factors for preeclampsia [15]. Weight loss before pregnancy is recommended for women with overweight and obesity, which can help reduce the risk of adverse outcomes. According to American researchers, in a number of regions 30% the risk of preeclampsia is due to obesity. Obesity is a risk factor for both relatively preeclampsia and cardiovascular diseases [22]. In connection with the above, it is important to study the general mechanisms of the development of obesity and PE, which will ensure a deeper understanding of the pathophysiology of preeclampsia, potential areas for further research and possible goals of therapy.

According to estimates, insulin resistance is present in two-thirds of obese people. It is also a risk factor for cardiovascular diseases and type 2 diabetes [23]. Insulin resistance is more often found in preeclampsia and can persist until the age of seventeen after a pre-sequet of pregnancy, which increases the risk of cardiovascular diseases. Metabolic syndrome (obesity, hypertension, insulin resistance, impaired glucose tolerance and dyslipidemia) is also more often observed among women with a history of preeclampsia [23,24]. Regarding the metabolic syndrome, it was suggested that obesity contributes to hypertension in connection with many common pathogenetic mechanisms, including reducing the access of nitrogen oxide due to oxidative stress, an increase in sympathetic tone and ongotensinogen with fatty tissue. Dyslipidemia and an increase in the number of free fatty acids released from adipocytes also allegedly contribute to oxidative stress and insulin resistance [24].

Inflammation is a common pathogenetic mechanism of obesity, cardiovascular diseases and preeclampsia. Fat tissue generates several inflammatory mediators, which can disrupt the function of the endothelium and are more actively produced in obese people. C-reactive protein (CRP) is an inflammatory mediator produced by the liver, as well as adipocytes, its blood content is higher in obesity, it is associated with cardiovascular incidence. The circulating CRP rises at an early stage of pregnancy before the development of preeclampsia and, apparently, has a stronger connection with preeclampsia among women with obesity [25]. Inter-Lykin-6 is another powerful inflammatory mediator, which can lead to vascular damage and is associated with obesity, resistance to insulin and later-with cardiovascular disease. The concentration of the circulating CRP is also higher for preeclampsia associated with obesity, which indicates the potential connection of these pathologies [25]. The factor of tumor necrosis - alpha (TNF -A) is also produced by fat tissue and is associated with insulin resistance, endothelial damage and oxidative stress. Circulating concentrations increase both with the progressive severity of obesity and with preeclampsia [26]. Nevertheless, studies show that the TNF-A content is not higher in pregnant women with obesity compared to not suffering obesity [6,26]. As one of the important mechanisms of preeclampsia, oxidative stress is postulated, leading to a change in the function of the endothelium and the occurrence of vascular dysfunction. Obesity is also associated with oxidative stress, possibly secondary in relation to inflammation and free fatty acids, as well as to a lower concentration of circulating antioxidants [6,24]. Thus, oxidative stress can be a factor that contributes to the development of preeclampsia in fat women.

Leptin and adiponectin - two substances produced by adipose tissue affect metabolism and are associated with cardiovascular diseases. Obesity is characterized by an increased level of leptin and a reduced concentration of adiponectin [27]. Circulating leptin increases with preeclampsia and correlates with maternal BMI [27]. It should be noted that leptin is also produced by a placenta, probably representing the main source of circulating concentrations during pregnancy. Adiponectin has effects sensitive to insulin, its content decreases with obesity, and correctly correlates with cardiovascular risk. There is still no consensus regarding the concentration of adiponectin of pre -extraclampsia, since the studies had conflicting reports about higher and low concentrations [2,28].

Based on the mechanism of action and associations with cardiovascular diseases and obesity, these adipokins can matter in the mechanism of development of preeclampsia, especially among women with obesity or inclination to it.

The balance of circulating angiogenic factors changes in pregnant women with the risk of preeclampsia in comparison with normal pregnancy [2]. The levels of the placental growth factor (PGF) and the vascular endothelial growth factor (VEGF) are lower in women with preeclampsia. This is probably due to a higher concentration of the circulating soluble SFLT- an anti-egogenous factor that binds and inactivates PGF and VEGF [29]. Some studies showed that the levels of SFLT-1 and PGF are reduced in pregnant women with obesity, while in other studies it is stated that higher BMI is associated with higher SFLT-1 concentrations and a higher SFLT-1/PGF ratio indicating the predominance anti -angiogenic effects in the early stages of pregnancy [29]. Although the research results are not consistent with each other, an altered angiogenic environment with obesity can cause the development of preeclampsia. Features of lifestyle, such as diet, sleep disturbance and physical activity also have a close causal connection with obesity and cardiovascular diseases. Many of these factors are associated with preeclampsia, thus increasing the likelihood of the presence of some general pathogenetic mechanisms of obesity and preeclampsia, which contribute to an increase in preeclampsia. Violation of the synthesis of nitrogen oxide (NO) and bioavailability leading to vascular dysfunction - the general key mechanism of the pathogenesis of obesity and cardiovascular diseases [30]. Asymmetric dimethylarginin (ADMA) is a competitive agonist L-Arginin, the precursor of the synthesis of nitrogen oxide. ADMA functions as an inhibitor of nitrogen oxide synthesis, leads to a decrease in the formation of NO and an increase in the formation of superoxide. Increased adma concentrations are associated with inflammation, insulin resistance, dyslipidemia, obesity and cardiovascular diseases. Interestingly, the circulating adma, as shown, decreases with weight loss [30]. In several studies, higher concentrations of ADMA were demonstrated with preeclampsia and even before its development [10]. In a number of clinical studies, L-Arginine was used to cancel some effects of ADMA. It was safely used during pregnancy. One randomized controlled study showed that the frequency of preeclampsia was reduced with the introduction of a combination of arginine

and antioxidant therapy in a high -risk group compared to placebo or antioxidants [31]. Further research will be useful for clarifying the effects of L-arginine at the degree of risk of preeclampsia and in women with obesity. Thus, the best understanding of the relationship between obesity, preeclampsia and cardiovascular diseases can also shed light on the general mechanisms of pathogenesis and offer adequate treatment.

A wide range of risk factors for the development of preeclampsia emphasizes the heterogeneity of this syndrome. Obesity - a growing problem around the world - is a serious factor in the risk of preeclampsia, and the realized risk of PE of fat women can subsequently lead to cardiovascular complications and mortality from cardiac pathology. Further study of the mechanisms underlying these connections will develop recommendations to reduce these potential risks.

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INFLUENCE OF PERSONALITY OF CHILDREN AND ADOLESCENTS OF THE UZBEK POPULATION ON MANIFESTATIONS AND DEVELOPMENT OF NEUROCIRCULATORY DYSTONIA

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Abstract. The relevance of studying the personality characteristics of children with vegetative vascular dystonia (VVD) is dictated by the fact that many psychosomatic disorders (ischemic and hypertension diseases, bronchial asthma, gastric ulcer and 12 bc, neurodermatitis, etc.) originate in childhood and their primary manifestations are vegetative disorders. According to the literature, among the children with non-communicable diseases who go to the doctor, 50-75% are patients with VVD. Purpose of the study. Study of the influence of the mental state and personality characteristics of patients on the manifestations and development of NCD in children and adolescents of the Uzbek population. Material and methods. We studied 43 patients with NCD (18 boys and 25 girls) aged 7 to 16 years with hypotonic, hypertensive and cardiac types. In the examined group of patients with NCD, children with hypertensive (46.5%) type prevailed. Patients (39.5%) were diagnosed with hypotonic NCD, and in 14 patients with cardiac type. For the study of individual - typological and personal characteristics of children, in addition to clinical and pedagogical observations, traditional experimental - psychological methods were used, allowing the most differentiated approach to the analysis of the personality of a sick child. The results of the study were subjected to variational-statistical processing: mean values (\bar{X}), standard deviation (T) and its errors ($+m$), testing hypotheses from the normal distribution were tested by Student's t-test. Conducted correlation and dispersion analysis according to the program. Results: patients with NCD are characterized by a pronounced increase in emotional stress, difficulty in making interpersonal contacts and contributing to the violation of the psycho-vegetative regulation of the individual. The predominance of the desire for well-mannered forms of behavior, combined with conscious self-control, prevents the reaction of negative emotions, which contributed to the long-term preservation of emotional stress and further difficulties in adaptation. Patients with NCD usually had combinations of disharmonious personality traits, which led to the appearance of intrapsychic conflicts between dominant and mutually exclusive types of needs. The actual mental state of children with NCD determined by the Kettell method as a whole manifests itself as a personality of a highly neurotic response, which confirms the connection between NDC and personality traits. Conclusions: These intrapsychic conflicts underlay violations of social adaptation in the school and family spheres, and also prevented psycho-vegetative adaptation, which manifested itself in psychopathological and vegetative-somatic disorders in this disease.

Key words. neurocirculatory dystonia, children and adolescents, psychosomatics, personality.

Introduction. Cardiovascular diseases consistently occupy the first place in the structure of morbidity and mortality worldwide. Currently, the emphasis in the study of cardiovascular diseases has been shifted to childhood [1–3]. The ever-increasing prevalence of cardiovascular disease depends on many factors. In the first place are socio-economic factors: the development of modern civilization, which has dramatically restructured the way of life of people due to the increase in the population of cities, the introduction of electricity and household chemicals, the intensification of labor processes, the complication of curricula, information overload, transport difficulties, changed nutrition and other psychosocial stress. Hereditary predisposition to diseases of the circulatory organs is also important, but it cannot be considered as the main cause, since a sharp increase in morbidity and mortality from these diseases occurred in such a short period of time during which genetic changes are impossible in humans [4,5]. These hazards affect the personality and body of the child and adolescent. Due to difficult everyday circumstances, the activity of the nervous system, its autonomic department, which is responsible for the joint, coordinated activity of organs and systems of the whole organism, is often upset in children. Violation of autonomic regulation can manifest itself in the form of vegetative-vascular dystonia (VVD). The essence of VVD is that the primary

pathological changes do not occur in the “target organ”, but in the apparatus of its nervous regulation. Psychosomatic relations are violated - the connection of mental phenomena, the adaptive activity of the autonomic nervous and humoral systems with the functional activity of the cardiovascular system.

According to the literature, among children with non-communicable diseases who visit a doctor, 50-75% are patients with VVD [6–8]. The relevance of studying the personality characteristics of children with VVD is dictated by the fact that many psychosomatic disorders (ischemic and hypertension diseases, bronchial asthma, gastric ulcer and 12 p.c., neurodermatitis, etc.) originate in childhood and their primary manifestations are vegetative disorders.

Neurocirculatory dystonia (NCD) is a variant of VVD, manifested mainly by disorders of the cardiovascular system. In some cases, an increase predominates, in others - a decrease in blood pressure, and thirdly - the regulation of the activity of the heart is disturbed. Purpose of the study. Study of the influence of the mental state and personality characteristics of patients on the manifestations and development of NCD in children and adolescents of the Uzbek population. Material and methods. We studied 43 patients with NCD (18 boys and 25 girls) aged 7 to 16 years with hypotonic, hypertensive and cardiac types. In the examined group of patients with NCD, children with hypertensive (46.5%) type prevailed. Patients (39.5%) were diagnosed with hypotonic NCD, and in 14 patients with cardiac type. For the study of individual - typological and personal characteristics of children, in addition to clinical and pedagogical observations, traditional experimental - psychological methods were used, allowing the most differentiated approach to the analysis of the personality of a sick child: 1. Examination and observation of the behavior of children in the experimental situation in order to identify the features of the emotional-volitional sphere; 2. Schwanzler's partially standardized diagnostic interview - conversation;

3. Pathocharacterological diagnostic questionnaire (PDO) - for children and adolescents from 10 to 18 years old;

4. Study of self-esteem by the Dembo-Rubinstein method;

5. Children's version of the Cattell personality questionnaire for children from 8 to 12 years old;

6. Children's version of the Eysenck personality questionnaire for children;

7. Projective methods of personality research;

a) Rosenzweig picture frustration (stress) test for children and adolescents; b) Rorschach tests;

8. Standard questionnaire-characteristics for a child (filled out by a teacher and parents);

9. Identification of the characteristics of the microsocial environment - families and schools;

10. Carrying out an ECG study (in 12 standard leads), echoencephalography, rheoencephalography, etc.;

11. Measurement of blood pressure, diastolic blood pressure, counting the pulse rate;

12. Study of vegetative homeostasis (vegetative tone, reactivity, security). In addition to these studies, generally accepted clinical methods were used (general blood count, urine, feces, chest and skull radiography), biochemical methods with the determination of total protein, residual nitrogen, urea, potassium and calcium in blood serum, rheumatic tests. Specialist consultations were held (psychiatrist, psychoneurologist, endocrinologist, cardiorheumatologist, traumatologist). An objective study of children was carried out in a children's hospital using generally accepted methods - examination, palpation, percussion, auscultation.

The results of the study were subjected to variational-statistical processing: mean values (X), standard deviation (T) and its errors (+m), testing hypotheses from the normal distribution were tested by Student's t-test. Conducted correlation and dispersion analysis according to the program. The centile distribution of personal factors indicators was calculated using a mathematical algorithm.

Results. From the data presented in table No. 1, it follows that patients with NCD in general are significantly extraverted (17.3 ± 0.6 and 16.7 ± 0.4 , $P < 0.001$), which makes it possible to characterize them as more sociable, active and prone to leadership. For hypotonic and cardiac types, the increase in sociability was not significant ($P > 0.05$). Patients with NCD of the hypotonic type are characterized by depressed mood or

apathy. Most children are disturbed by obsessive fears for somatic health, they consider themselves seriously ill. A high degree of anxiety is characteristic of both children with hypertonic, hypotonic, and cardiac types of NCD. Patients with the cardiac type of NCD were characterized by a sharp weakening of physical and intellectual performance, as well as phobias related to confined spaces, driving in transport, crowds, and heights. Among the psychopathological manifestations, cardialgia and other unpleasant sensations in the region of the heart occurred constantly ($P < 0.05$) and were the most significant for a patient with a cardiac type of NCD.

Table-1
Average scores of indicators (in points) according to the Eysenck questionnaire in children of the control group and patients with NCD

Indicators	Standardization data		Neurocirculatory dystonia		Hypertonic type	Hypotonic type	Cardiac type
	M	D	M	D			
Extraversion - Introversion	15,1 ± 0,4	14,3 ± 0,4	17,3 ± 0,6*	16,7 ± 0,4*	17,6 ± 0,4*	16,4 ± 0,7	15,6 ± 0,9
Neuroticism	12,6 ± 0,5	13,3 ± 0,5	15 ± 0,8*	16,6 ± 0,6*	17,0 ± 0,7*	15,7 ± 1,5	15,8 ± 1,4
The data are statistically significant ($P < 0.05 - 0.001$) compared with healthy children.							

A high rate of psycho-emotional instability in patients (15 ± 0.8 and 16.6 ± 0.6 $P < 0.001$ in boys and girls) indicates an increased level of anxiety and neuroticism. Patients with NCD are irritable or tense. Often dissatisfied with their surroundings. The hypertonic type is characterized by a high sense of responsibility and intensity. More than half of the patients show signs of neuropathy. The current mental state of children with NCD determined by the Kettell method as a whole manifests itself as a personality of a highly neurotic response, which confirms the connection of NCD with personality traits. Table. 2. In the group of patients with NCD, the most characteristic were mild and frequent occurrence of unmotivated anxiety, mood swings, subdepressive episodes in premorbidity. Mild vulnerability and sensitivity are indicated by a decrease in factor C (3.2 ± 0.5 and 2.7 ± 0.4 ; $P < 0.001$). They are also distinguished by pronounced incredulity, resentment, aggressiveness, persistence in achieving the goal and ambitious aspirations (the rise of the "E" factor 6.1 ± 0.3 and 6.6 ± 0.4 , $P < 0.05$). A decrease in the "H" factor (3.2 ± 0.3 and 1.6 ± 0.4 in boys and girls, $P < 0.001$) reflects the presence of high self-doubt, a tendency to constant doubts when making decisions, to the formation of obsession, a decrease entrepreneurial spirit and energy.

Dissatisfaction with the situation, one's behavior in it, and a high intensity of unreacted urges were reflected in the rise of Q and Q3 factors (6.8 ± 0.3 and 7.04 ± 0.15 ; $P < 0.001$ 6.8 ± 0.4 and 6.9 ± 0.3 ; $P < 0.001$ in boys and girls, respectively). In general, patients with NCD are characterized by a pronounced increase in emotional stress, difficulty in making interpersonal contacts and contributing to the disruption of the psycho-vegetative regulation of the individual. The predominance of the desire for well-mannered forms of behavior in combination with conscious self-control (increased factors I and Q3 (7.1 ± 0.6 and 7.0 ± 0.5) prevents the response of negative emotions, which contributed to the long-term preservation of emotional stress and further difficulties in adaptation. Patients with NCD usually had combinations of disharmonious personality traits, which led to the appearance of intrapsychic conflicts between dominant and mutually exclusive types of needs. These intrapsychic conflicts underlay violations of social adaptation in the school and family spheres, and also prevented psycho-vegetative adaptation, which manifested itself in psychopathological and vegetative-somatic disorders in this disease. Comparison of the average profile of individuals with NCD and the control group revealed significant differences. The average profile (Fig. 1.) of the group of people with NCD differs from the average profile of the control group in features that reflect higher anxiety (factor «Q 6.8 ± 0.3 and 7.04 ± 0.15 ; $P < 0.01$), which is accompanied by a tendency to the emergence of unpleasant somatic sensations, a more pessimistic coloring of perspective and great rigidity. According to F.B. Berezin et al (18), due to this rigidity, once the affect of anxiety has arisen, it does not fade for a long time. Apparently, this circumstance can contribute to the repetition of anxious reactions. The above profile features were combined with signs indicating a relatively high level of tension, irritability and frustration (high Q4

6.8 ± 0.4 and 6.9 ± 0.3 ; $P < 0.001$. Decreased mood and anxious affect in NCD patients were significantly to a greater extent than in healthy people, could disrupt adaptation to the immediate social environment, which is reflected by deep "dips" of the curve (factors "H" 3.2 ± 0.3 and 1.6 ± 0.4 ; "C" 3.2 ± 0.5 and 3.3 ± 0.4 $P > 0.05$) profile.

An increase in activity and readiness for action is reflected to a greater extent on the profile curve by «peaks» (factors «E» and «F».) Thus, in patients with NCD, conflicts between the need to be in the center of attention of others (rising factors (A, E, E, F), the desire to focus on non-conformal, special internal criteria of behavior, conflicts between selfish and altruistic motives, emotional immaturity (factors «H» and «I»)), demonstrativeness, weakness of mental «delays» and ambitious attitudes that are especially significant for the individual («E», «G»). The peculiarity of the reaction to frustration depends on the nature of the individual development of the subject, which in turn is based on a combination of certain genetic premises and social factors. This reaction seems to be based on two factors. On the one hand, these are the features of mental response associated with the personal characteristics of the subject, on the other hand, there are special relationships between two aspects of response: mental and vegetative. Finally, it is possible that a combination of both of these moments is necessary for the emergence of NCD. We conducted a study of the considered possibilities of reaction to frustration in sick children with NCD. Variants of psycho-emotional response to frustration in patients with NCD and healthy people significantly differed (Table 3).

In children with NCD, the extrapunitive reaction «E» was significantly reduced (9.05 ± 0.8 and 8.8 ± 0.5 in boys and girls). Decreased mood and anxious affect in sick children with NCD to a much greater extent than in healthy children could disrupt adaptation to the immediate social environment, more often causing the need for help «IP» (13.2 ± 0.5 and 13.0 ± 0.6 ; $P < 0.05$ in boys and girls) and could disrupt behavior control to a somewhat greater extent, however, as can be seen from Table 5.17, there was no extrapunitive reaction that was quite typical for the control group. Violation of behavior control was accompanied by the restriction of social contacts and the severity of schizotimism «M» (12.1% and 14.2% vs. control 34.2 and 34.7%; $P < 0.05$ in boys and girls). The given data give grounds to believe that persons with NCD are characterized both by peculiar personality traits that cause a tendency to certain types of mental reactions, and by peculiar relationships between the mental and vegetative aspects of the response, which determine the originality of the autonomic reaction. Data on the study of patients with NCD by the Rorschach method are presented in Table 4. and compared with the results obtained in the examination of healthy children. As a result of the analysis of Table 4, sharp differences were found in the quality of shaping. In patients with NCD, color responses prevailed (3.5 ± 0.5 and 2.7 ± 0.4 in boys and girls, $P < 0.05$) with a slight decrease in the number of kinesthetic ones (0.2 ± 0.06 and 0.3 ± 0.05 in boys and girls), which indicates the predominance of general neurotic symptoms. For them, according to Rorschach, reproductive rather than creative thinking, labile affectivity and superficial contacts with other people are more characteristic. In patients with NCD, color shock is quite pronounced. A decrease in interpretations (5.3 ± 0.5 and 5.7 ± 0.6 in boys and girls) and a significant increase in «D» responses indicate a decrease in the ability to synthesize. A decrease in kinesthetic interpretation, according to Rickers-Ovsiankina, is a sign of the attenuation of emotional reactions (Fig. 2.). Along with this, when studying the protocols of patients with NCD, other features were found that distinguish patients from healthy people: frequent refusals, especially for tables IV, VIII, IX, X, an indication of symmetry, an increase in CF-responses, an increase in A + Ad, interpretation of stimulus material in the form of questions, an increase in the percentage of answers in terms of content PI, a decrease in original answers. (Table 5). As can be seen from Table 6. and Fig. 3., the type of experience in NCD is, on the whole, extra-intense. In contrast to the healthy population of schoolchildren, in the group of NCD patients there is a significant increase in the mixed type of extratension. The ambiguous personality variant was not registered. The use of the objective assessment scale of the pathocharacterological diagnostic questionnaire (PDO), (112) showed that the number of adolescents with character accentuations significantly differed ($P < 0.001$) among healthy ones (52.35%). In contrast to healthy adolescents, the following types of character accentuation were significantly more common in patients with NCD: cycloid ($P < 0.05$), labile ($P < 0.001$), sensitive ($P < 0.001$). Psychoasthenic, hysteroid and epileptoid types of accentuation were also more often observed in adolescents with NCD, but this difference was not statistically significant ($P > 0.05$). The severity of accentuation was not the same in adolescents with different types of NCD. (Table 7.) In

NCD of the hypertensive type, unstable, labile and cycloid types of accentuation were diagnosed significantly more often ($P < 0.01$), and sensitive, labile and cycloid types were characteristic of the hypotonic type of NCD. A significant predominance of individuals with character accentuations among patients with NCD can be considered in terms of the pathogenetic role of emotional stress and other psychological factors in the development of NCD of the hypertensive type. According to A.E. Lichko, with unstable, epileptoid and asthenoneurotic types of character accentuation, psychological conflict is especially characteristic. Thus, the results of the studies presented by us suggest that personality factors play a certain role in the development of hypotonic, hypertonic, and cardiac types of NCD in children. Recently, much attention has been paid to the study of the role of psychosocial factors in the genesis of NCD. The lack of clear ideas about the mechanism of the pathogenic influence of psychosocial factors in childhood severely limits the possibilities for the prevention and treatment of functional psychosomatic disorders. In order to study the etiological role of psychotraumatic factors and their participation in the formation of the clinical picture of NCD, we examined the micro-social environments of the family and school of children with NCD. For this purpose, we used the questionnaire developed by us «Studying the influence of the microsocial environment on the formation of a pathological personality» [rational proposal adopted for implementation in AndGosMi No. 1288 of 12.06.99]. An in-depth survey of parents of children and adolescents with NCD and their families revealed data of practical interest both for pediatricians and specialists in related disciplines. 6.8% of married couples had short-term disagreements. More than half of the families of children with NCD (59%) had frequent and lengthy quarrels that turned into scandals (22.7%). In general, 88.5% of families were diagnosed with destructive relationships. A significant share in the hierarchy of causes of frequent conflicts between spouses is occupied by the temper of a husband or wife (20.7%). As for the destructive relations between parents and children, they are to some extent a consequence of the conflict of marital relations. Most conflicts between parents and children arise due to irritability and fatigue of parents (19.2%), low academic performance of schoolchildren (19.2%), their unwillingness to participate in homework (11.5%), bad behavior (30.7%). Some idea of the level of pedagogical culture of parents is given by our survey of parents of children with NCD on the methods used in raising children. On the whole, orders and demands (23.4%), prohibitions without special explanations (29.8%), and physical punishment (21.2%) took the first place in the family's pedagogical arsenal. Thus, it was possible to obtain information about the features of the participation of psychotraumatic factors in the etiology of NCD. The influence of a negative family environment was revealed. In families of children with NCD there is a chronic neuro-psychic overstrain. The latter turns out to be against the background of external well-being in the family and school. Stress is not associated with strong and one-time shocks, resentment, disappointment. It is a reflection of the objectively existing difficulties in the life and study of the child, the overcoming of which exceeds his adaptive capabilities.

According to our data, such conditions are most often created as a result of excessive demands on him in the family and school. Parents force their child to succeed in any way. They, as a rule, overestimate the capabilities of their son or daughter, use authoritarian methods to achieve their goals (order, demand, physical punishment, prohibition without special reasons).

Findings. Thus, in the families of children with NCD, upbringing is typical of the type of «hyper-custody». Increased hypersocial attitudes, insufficient emotional contact between parents and children, pedagogical illiteracy of parents in children developed a high level of neuroticism, a sense of internal tension, irritability, attention distraction, depressed mood or apathy, decreased physical and intellectual performance, phobias, desire for leadership. Another group of pathogenic microsocial factors is acute conflict situations. The most typical conditions for the emergence of acute conflicts were quarrels with parents and teachers, situations of clashes with peers (when striving for leadership, worries about relationships between parents.) In these children, personality manifestations were unstable. Clinically, NCD was not limited to disorders of vascular tone. Often there were complaints of headaches, nausea, pain in the chest and abdomen, heaviness and pain in the region of the heart, etc. The majority of the children examined by us 40 (93%) with NCD had unfavorable factors of the microsocial environment, which, to one degree or another, participated in the formation of psychosomatic disorders. The identified acute and chronic types of psychotraumatic situations play a different role in the formation of the clinical picture of NCD.

According to D. N. Isaev, acute and severe injuries most contribute to the emergence of secondary neuropsychic syndromes. Repeatedly repeated mental stresses are related to the vegetative-vascular level of response, and by causing long-term pressor reactions of blood vessels, they are directly involved in the formation of a pre-hypertensive state. Psychogenic stresses of greater depth, arising against the background of prolonged nervous overstrain, contribute to the development of more detailed pictures of psychovegetative disorders.

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THE ROLE OF IL-4 AND TLR6 GENE POLYMORPHISM IN PATIENTS WITH BRONCHIAL ASTHMA WITH ALLERGIC RHINITIS

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Abstract. Relevance. As is known, the occurrence of chronic diseases, such as bronchial asthma, requires a combined effect of genetic and environmental factors. At the same time, the influence of genetic predictors on the course of recurrent bronchitis in children is not excluded. The aim of the study was to study the role of IL-4 and TLR6 gene polymorphisms in patients with bronchial asthma with allergic rhinitis. Material and methods. We have studied the clinical course of bronchial asthma occurring in patients with allergic rhinitis. The observation was carried out in 130 children aged 7 to 14 years. The main group consisted of 105 people. The comparison group consisted of 45 children with allergic rhinitis with bronchial asthma and 45 children of the Republic of Belarus with biofeedback + AR. The studies were carried out on a contractual basis in the laboratory «Genotexnologiya» and at the Institute of Immunology and Human Genomics of the Academy of Sciences of the Republic of Uzbekistan; cyto-immunological study of immunological parameters (levels of IgA, IgM, IgG, IL-4, TNF- α) in induced sputum (MI), was determined by ELISA (Russia) in the laboratory «Genotexnologiya». Results. The frequency of the unfavorable allele G, determined in the main and control groups, does not statistically significantly differ from each other $\chi^2 = 5.754$; $p=0.017$; OR=2.98; 95% CI 1.19-7.49). As can be seen from the presented data, a significant predominance of the C/T genotype of the C-590T polymorphism of the IL-4 gene in BA children with AR was established (22.2%, respectively, compared to 11.1% in the RB group with BOS + AR; $\chi^2 = 1.31$; $p=0.4$; OR=2.0; 95% CI 0.62-6.45). According to the data of statistical analysis, the association of the T/T genotype with the development of BA with AR in children was proven ($\chi^2 = 2.39$; $p=0.56$; OR=4.87; 95%CI 0.54-43.64). Conclusions: as a result, it can be emphasized that the carriage of the polymorphic marker TLR6 745T is a genetic risk factor for the development of RB with BOS and AR, while the presence of a homozygous genotype for the minor allele 745C reduces the risk of developing BA and has protective properties.

Key words. bronchial asthma, allergy, rhinitis, genotype, inflammation, interleukini, inflammatory mediator, endocrine regulator.

Актуальность. Как известно, для возникновения хронических заболеваний, таких как бронхиальная астма, необходимо сочетанное воздействие генетических и средовых факторов. В то же время не исключается влияние генетических предикторов на течение рекуррентного бронхита у детей. Для уточнения роли генов модификаторов воспалительного процесса как на течение хронического аллергического воспаления, так и рецидивирующее поражение нижних дыхательных путей, нами проведено следующее исследование. В ходе работы была проанализирована мутационная изменчивость в ассоциации с фенотипическими признаками заболеваний у детей обследованных групп. Нами проведена оценка диагностической значимости полиморфизма генов IL-4 (C-590T), TLR6 (C745T), TNF α (-308 G/A) в крови у детей с бронхиальной астмой, как вероятные генетические.

По данным обзора литературы [1–5], генетические предикторы бронхообструкции, гиперреактивности, атопии или бронхиальной астмы в целом еще в полной мере не изучены. Большой интерес представляет исследование полиморфизма C-590T гена ИЛ-4 при различных бронхообструктивных заболеваниях как у детей, а именно доказано влияние данного полиморфизма на течение бронхиальной астмы. Это связано с тем, что он регулирует продукцию В-клетками иммуноглобулина Е, и помимо всего, влияет на дифференцировку Т-лимфоцитов хелперов 2 типа.

При анализе распределения аллелей по полиморфизму C-590T гена ИЛ-4 среди условно здоровых детей отмечалось преобладание аллеля С, а также ассоциированных с ним генотипов, а именно генотипов, С/С и С/Т (85,0% и 15,0% соответственно).

Целью исследования явилось, изучить роль полиморфизма генов IL-4 и TLR6 у больных бронхиальной астмой с аллергическим ринитом

Материал и методы. Нами было изучено клиническое течение бронхиальной астмы, протекающей у больных с аллергическим ринитом. Наблюдение проведено у 130 детей в возрасте от 7 до 14 лет. Основную группу составили 105 человек. Группу сравнения составили дети с аллергическим ринитом с бронхиальной астмой 45 детей и 45 детей РБ с БОС +АР. Прежде всего, интерес представляли данные аллергологического анамнеза. Молекулярно-генетические методы: исследование полиморфизма С-590Т гена IL-4, полиморфизма гена TLR6 С745Т и полиморфизма 308 G/A гена TNF- α методом ПЦР анализа, которые являются специфическими диагностическими маркерами развития БА и АР у детей. Исследования проводились на договорной основе в лаборатории «Genotехnologiya» и в Институте иммунологии и геномики человека АН РУз; цито-иммунологическое исследование иммунологических показателей (уровни IgA, IgM, IgG, IL-4, TNF- α) в индуцированной мокроте (ИМ), определяли методом ИФА (Россия) в лаборатории «Genotехnologiya».

Статистическая обработка. Результаты проведенных исследований обработаны программой, разработанной в пакете Microsoft Office Excel-2010. Использовались методы вариационной статистики с вычислением средних арифметических значений (M), их стандартных ошибок (m) и достоверных различий по критерию Фишера - Стьюдента.

Результаты и обсуждение. Наблюдаемое распределение частот генотипов не отличалось от теоретически ожидаемого по уравнению Харди-Вайнберга. Подобное распределение генотипов было отмечено и в исследуемых группах. А именно, у детей как БА с АР и РБ с БОС наблюдалось преобладание генотипов С/С и С/Т над Т/Т (таб-1).

Таблица-1

Частота распределения аллелей и генотипов полиморфизма С-590Т гена IL-4 среди обследуемых групп детей

Группы	Частота аллелей				Частота распределения генотипов					
	Т, %		С, %		С/С, %		С/Т, %		Т/Т, %	
	n	%	n	%	N	%	n	%	n	%
Контрольная группа, (n=40)	7	8,75	73	91,2	34	85,0	5	15,0	1	2,2
РБ с БОС +АР (n= 45)	13	14,4	77	85,5	35	87,5	7	15,5	3	6,6
БА с АР (n=45)	20	22,2	70	77,7	30	66,6	10	22,2	5	11,1

Примечание: * - достоверность данных к контрольной группе (* - $P < 0,05$; ** - $P < 0,01$); ^ - достоверность данных к показателям детей РБ с БОС +АР (^ - $P < 0,05$); а - достоверность данных к показателям детей БА с АР (а - $P < 0,05$).

Гетерозиготный генотип С/С также встречался чаще в этой же подгруппе больных (30,0% против 34,0% в контроле).

Согласно таблице 2, частота неблагоприятной аллели G, определенная в основной и контрольной группах статистически значимо не отличается друг от друга $\chi^2 = 5,754$; $p = 0,017$; $OR = 2,98$; $95\%CI 1,19-7,49$). Как видно из представленных данных установлено достоверное преобладание генотипа С/Т полиморфизма С-590Т гена IL-4 у детей БА с АР (22,2% соответственно по отношению к 11,1% в группе РБ с БОС +АР; $\chi^2 = 1,31$; $p = 0,4$; $OR = 2,0$; $95\%CI 0,62-6,45$). Согласно данным статистического анализа, доказана ассоциация генотипа Т/Т с развитием БА с АР у детей ($\chi^2 = 2,39$; $p = 0,56$; $OR = 4,87$; $95\%CI 0,54-43,64$).

Таким образом, данный полиморфизм является предрасполагающим к развитию заболевания. При анализе распределения частот аллелей и генотипов полиморфизма С-590Т гена ИЛ-4 в зависимости от скоростных показателей ФВД отмечено преобладание гетерозиготного генотипа С/Т в общей группе пациентов при более легких нарушениях, что определяет его протективное действие в отношении степени выраженности обструкции дыхательных путей (таб-2).

Таблица-2

Различия в частоте распределения аллелей и генотипов полиморфного локуса С-590Т гена IL-4 среди обследуемых групп детей

Аллели и генотипы	Количество обследованных аллелей и генотипов		Статистическое различие
	Основная группа БА с АР	Контроль	

Аллель Т	20	7	$\chi^2 = 5,754; p=0,017; OR=2,98; 95\%CI 1,19-7,49$
Аллель С	70	73	
Генотип С/С	30	34	$\chi^2 = 3,826; p=0,051; OR=0,353; 95\%CI 0,12-1,03$
Генотип С/Т	10	5	$\chi^2 = 1,37; p=0,4; OR=2,0; 95\%CI 0,62-6,45$
Генотип Т/Т	5	1	$\chi^2 = 2,39; p=0,56; OR=4,87; 95\%CI 0,54-43,64$

Частота распределения патологического генотипа G/G в подгруппе недоношенных новорожденных в 5 раз выше, по сравнению с подгруппой доношенных новорожденных ($\chi^2 = 2,51; p=0,50; OR=5,0; 95\%CI 0,68-36,48$), но они статистически незначимы, однако имеется тенденция к статистическому различию.

Возможно, что при расширении численности группы обследуемых детей различия достигнут статистической значимости и данный генотип будет являться генетическим фактором развития БА (таб-3).

Перспективными для изучения при бронхиальной астме являются рецепторы врожденного иммунитета (TLR), реализующие свое действие на начальных этапах иммунного ответа и во многом определяющие интенсивность иммунных реакций на микробные и немикробные аллергены.

Таблица-3

Различия в частоте распределения аллелей и генотипов полиморфного локуса C-590T гена IL-4 между подгруппами обследуемых групп детей

Аллели и генотипы	Количество обследованных аллелей и генотипов		Статистическое различие
	Основная группа БА с АР	РБ с БОС +АР	
Аллель Т	20	13	$\chi^2 = 1,82; p=0,18; OR=1,7; 95\%CI 0,78-3,65$
Аллель С	70	77	
Генотип С/С	30	35	$\chi^2 = 1,38; p=0,24; OR=0,29; 95\%CI 0,22-1,46$
Генотип С/Т	10	7	$\chi^2 = 0,65; p=0,42; OR=1,55; 95\%CI 0,5-4,52$
Генотип Т/Т	5	3	$\chi^2 = 0,55; p=0,46; OR=1,75; 95\%CI 0,39-7,81$

Установлено, что TLR участвуют в распознавании аллергенов в дыхательных путях, регулируют активность и поляризацию адаптивного Th1, Th2, Th17 – иммунного ответа, играя важную патогенетическую роль в развитии БА. Как видно из таблицы 18 у детей из контрольной группы превалирует встречаемость аллелей С полиморфизма С745Т гена TLR6, которая встречалась у 95% детей, по сравнению с Т аллелей – 5% (таб-4).

У детей с БА с АР отмечается преобладание Т аллелей по отношению к показателям контрольной группы в 5,5 раз ($P < 0,001$). В контрольной группе в 90,0% случаев отмечается генотип С/С полиморфизма С745Т гена TLR6, гетерозиготный С/Т встречался в 10% случаях. При развитии РБ с БОС и АР у детей установлено преобладание гетерозиготных генотипов полиморфизма С745Т гена TLR6 на фоне сниженной встречаемости гомозиготного варианта С/С. Также хочется заметить, что гетерозиготный генотип ТТ полиморфизма С745Т гена TLR6 встречается только у больных детей, у практически здоровых детей данный генотип отсутствует.

Таблица-4

Частота распределения аллелей и генотипов полиморфизма С745Т гена TLR6 среди обследуемых групп детей

№	Группы	Частота аллелей				Частота распределения генотипов					
		Т, %		С, %		С/С, %		С/Т, %		Т/Т, %	
		п	%	п	%	п	%	п	%	п	%
1	Контрольная группа (n=40)	6	7,5	74	92,5	35	87,5	4	10,0	1	2,5
2	РБ с БОС+АР (n= 45)	21	23,3	69	76,7	30	66,6	9	20,0	6	15,0
3	БА с АР (n=45)	33	36,7	57	63,3	21	46,6	15	33,3	9	20,0

Примечание: * - достоверность данных к контрольной группе (* - $P < 0,05$; ** - $P < 0,01$); ^ - достоверность данных к показателям детей с ОБ РТ (^ - $P < 0,05$); а - достоверность данных к показателям детей с БА (а - $P < 0,05$).

Гомозиготный тип С/С полиморфизма С745Т гена TLR6 ассоциирован со сни-

женным риском развития ОБ с РТ и БА. Доказана ассоциация генотипа Т/Т с развитием БА с АР и РБ с БОС и АР у детей (χ^2 с поправкой Йейтса = 3,859, $p=0,038$, $df=1$, $OR=2,985$ (ДИ 1,085 – 6,989) (таб-5)).

Таблица-5

Различия в частоте распределения аллелей и генотипов полиморфного локуса С745Т гена TLR6 между подгруппами обследуемых групп детей

Аллели и генотипы	Количество обследованных аллелей и генотипов		Статистическое различие
	Основная группа БА с АР	РБ с БОС +АР	
Аллель Т	33	21	$\chi^2 = 3,8$; $p=0,05$; $OR=1,9$; 95%CI 0,99-3,64
Аллель С	57	69	
Генотип С/С	21	30	$\chi^2 = 3,66$; $p=0,05$; $OR=0,44$; 95%CI 0,19-1,03
Генотип С/Т	15	9	$\chi^2 = 2,05$; $p=0,15$; $OR=2,0$; 95%CI 0,77-5,21
Генотип Т/Т	9	6	$\chi^2 = 0,72$; $p=0,4$; $OR=1,62$; 95%CI 0,53-5,02

Таким образом, данный полиморфизм является предрасполагающим к развитию БА с АР и РБ с БОС и АР. Относительный риск развития БА с АР у детей с мажорным аллеля Т составляет 1,62 (95% CI:1, 0,53-5,02).

Выводы: в итоге можно подчеркнуть, что носительство полиморфного маркера TLR6 745Т является генетическим фактором риска развития РБ с БОС и АР, в то время как наличие гомозиготного генотипа по минорному аллелю 745С уменьшает риск развития БА и обладает протективными свойствами.

Таким образом, можно предполагать, что носительство полиморфного маркера TLR6 745Т является генетическим фактором риска развития РБ с БОС и АР, в то время как наличие гомозиготного генотипа по минорному аллелю 745С уменьшает риск развития БА с АР и обладает протективными свойствами. Интерлейкин-6 является цитокином, который функционирует как воспалительный медиатор и эндокринный регулятор. Кроме того, он играет важную роль в механизмах защиты хозяев в качестве посланника между врожденными и адаптивными системами. IL-6 как ключевой медиатор воспалительного ответа, продуцируемый в основном активированными макрофагами, может играть важную роль в совокупных процессах воспаления

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CLINICAL AND IMMUNOLOGICAL FEATURES OF BRONCHOBSTRUCTIVE SYNDROME IN CHILDREN

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Abstract. In the last decade, an increase in the proportion of obstructive bronchitis has been observed in the structure of respiratory organs damage, which is associated with an increase in the number of frequently ill children and exposure to adverse environmental factors. The aim of the study was: to identify the clinical and immunological features of broncho-obstructive syndrome in children. Materials and methods. Under our supervision were 120 children aged 1 to 15 years. Of these, 58.3% (70) of patients were diagnosed with OOB, 41.7% (50) of patients with RB with biofeedback. The control group consisted of 20 practically healthy children of the same age. Conclusions. To predict the risk of developing bronchial asthma, the relative risk coefficients (RR) and odds ratios (OR) were determined. In OOB, regardless of nasology, there is a longer manifestation of dyspnea, oral rales, moist cough and moist rales in the lungs.

Key words. broncho-obstructive syndrome, risk factors, retrospective analysis, pneumonia, acute obstructive bronchitis, recurrent bronchitis.

Актуальность. В последнее десятилетие в структуре поражения органов дыхания отмечается увеличение удельного веса обструктивных бронхитов (ОБ) [1,2], что связано с увеличением числа часто болеющих детей и воздействием неблагоприятных факторов окружающей среды. Синдром бронхиальной обструкции достаточно часто встречается у детей, особенно первых трех лет жизни. До настоящего времени нет четких данных о распространенности БОС при различной бронхолегочной патологии у детей. Частота бронхиальной обструкции, развившейся на фоне инфекционных заболеваний нижних дыхательных путей у детей раннего возраста, составляет, по данным разных авторов, от 5 до 40%. У детей с отягощенным семейным анамнезом по аллергии БОС, как правило, развивается чаще, в 30-40% случаев, такая же тенденция имеется и у детей, которые часто, более 6 раз в году, болеют респираторными инфекциями [3]. Бронхообструктивный синдром (БОС) - актуальная проблема педиатрии, занимающая одно из первых мест в структуре заболеваний органов дыхания у детей [4-6].

Таким образом, возникает необходимость раннего выявления и выделения групп риска по формированию БА.

Целью исследования: выявление клинических и иммунологических особенностей бронхообструктивного синдрома у детей.

Материалы и методы. Под нашим наблюдением находились 120 детей в возрасте от 1 до 15 лет. Из них у 58,3% (70) больных диагностирован ООБ, у 41,7% (50) больных – РБ с БОС. Контрольную группу составили 20 практически здоровых детей того же возраста.

Проведен анализ анамнестических данных, в том числе наличие отягощенного семейного анамнеза, пол, возраст начала заболевания, характер питания на первом году жизни, частоту и особенности течения острых респираторных инфекций (ОРИ), бытовые условия, наличие у родителей вредных привычек. Проанализированы данные ante-, перинатального анамнеза, течение неонатального периода, особенности заболеваний в раннем возрасте, наличие других аллергических заболеваний, кроме БА - атопического дерматита (АД) и аллергического ринита (АР).

Статистическую обработку полученных результатов проведено с помощью пакета программ Statistica, 6.0.

Важными факторами, определяющими состояние здоровья ребенка и его развитие, являются особенности акушерского статуса, состояние ребенка при рождении и его развитие до наступления настоящего заболевания. Результаты анамнестических данных представлены в таблице 1.

Были проведены обследования детей в возрастной группе от 1 до 15 лет (табл. 1). Распределение детей по возрасту показало, что внебольничной пневмонией с

обструктивным синдромом чаще встречается 1-3 лет 48(63%), у детей в возрасте 4-6 зарегистрированно 17(23%), 7-11 лет 9(12%), тогда как у детей 12-18 лет составила 2(2%).

Таблица-1

Распределение обследованных детей по группам и возрасту

Возраст	Внебольничная пневмония с явлениями БО n=76		ООБ n=72		РБ с БОС n=150	
	абс	%	абс	%	абс	%
1-3 лет	48	63	32	44	35	24
4-6 лет	17	23	17	24	46	30,5
7-11 лет	9	12	18	25	46	30,5
12-18 лет	2	2	5	7	23	15
Всего	76	100	72	100	150	100

У 1-3 лет детей с ООБ и РБ с БОС 32(44%) – 35(24%) , у детей в возрасте 4-6 зарегистрированно 17(24%) – 46(30,5%), 7-11 лет 18(25%) - 46(30,5%), тогда как у детей 12-18 лет составила 5 (7%) - 23(15%).

На тяжесть течения и исходы ООБ, РБ с БОС существенное влияние оказывает своевременность госпитализации и оказание врачебной помощи. Следует отметить, что больные поступали на лечение и обследование в различные сроки от начала заболевания (таб-2).

Таблица-2

Сроки госпитализации больных с БОС

Сроки поступления	ООБ n=120		ВП с БОС n=211		РБ с БОС n=50	
	абс	%	абс	%	абс	%
1-2е сутки	11	10,0	62	29,4	8	16,0
3-5 день	74	67,3	96	45,5	18	36,0
5-7 день	25	22,7	53	25,1	24	48,0
Всего:	110	100,0	211	100,0	50	100,0

Анализируя эти показатели, мы выявили, что при ООБ больные в основном поступали на 3-5 день заболевания 74 (67,3%); при РБ с БОС с рекуррентным течением поступали дети в основном на 5-7 день болезни - 24 (48,0%) детей; при ВП с БОС в основном поступали на 3-5 день заболевания 96 (45,5%) после безуспешного лечения на дому.

На тяжесть обследованных больных существенное влияние оказывает неблагоприятный преморбидный фон и сопутствующая патология (таб-3). Анализируя данную таблицу можно констатировать, что во всех трех группах наблюдения наиболее часто встречались такие фоновые состояния, как анемия I-II степени, остаточные явления рахита и аллергический диатез. В группе больных ООБ у детей вышеуказанные состояния имели большее значение. Из сопутствующей патологии заболевания ЛОР органов установлены у 14 (23,3%) больных с ООБ, у 20 (33,3%) больных ООБ с рекуррентным течением. У больных РБ с БОС у 54 (83,1%) обследуемых наблюдались заболевания ЛОР органов.

Таблица-3

Характеристика фонового состояния и сопутствующей патологии у обследованных больных

Фоновые заболевания	ООБ n=60		РБ с БОС n=60		P	P1
	абс	%	абс	%		
Анемия I-II	48	80,0	51	85,0	>0,01	>0,01
Остаточные явления рахита	15	25,0	28	46,6	>0,01	>0,01
Атопический дерматит	6	10,0	20	33,3	>0,01	>0,01
Избыточный вес	13	21,6	16	26,6	>0,01	>0,01
БЭНП	11	18,3	19	31,6	>0,01	>0,01
Заболевания ЛОР органов	14	23,3	20	33,3	>0,01	>0,01

Примечание: P - достоверность различий показателей между I и II группами больных;

P1 - достоверность различий показателей между II и III группами больных;

Факторный анализ фонового состояния и сопутствующей патологии показал, что наиболее высокий риск возникновения БА возможен при наличии остаточных явлений рахита (RR=1,8; OR=2,6), атопического дерматита (RR=2,04; OR=8,6), заболеваний ЛОР-органов (RR=1,5; OR=2,9).

Таким образом, представленные данные еще раз подтверждают, что дети с различной степенью выраженности фоновых состояний и сопутствующей патологии являются группой риска по развитию заболеваний.

Основными жалобами родителей больных детей были кашель 120 (100,0%), одышка 120 (100,0%) повышение температуры тела у 74 (61,5%) детей, снижение аппетита 108 (90,3%), слабость 92 (76,6%), нарушение сна 113 (93,8%). Клиническая оценка основывалась на совокупности симптомов интоксикации, дыхательной и сердечной недостаточности, аускультативных, перкуторных данных и рентгенологических изменений.

При поступлении в отделение детей с ООБ ведущим клиническим проявлением заболевания была дыхательная недостаточность.

Такое состояние как слабость отмечалась у 39 (55,4%) больных, аппетит был сниженным у 57 (81,8%) больных. Нарушение сна, бледность кожных покровов и одышка отмечались в 70 (100,0%) случаев. Цианоз носогубного треугольника наблюдался у 22 (31,8%) детей. Температура тела при поступлении была фебрильной у 13 (19,1%) больного. Характер кашля был сухим у 57 (81,8%) больных, влажным - у 13 (18,2%) больных. При аускультации легких на фоне жесткого дыхания выслушивались сухие хрипы у 55 (78,2%) больных, у 15 (21,8%) выслушивались влажные хрипы.

При перкуссии грудной клетки определялся коробочный оттенок перкуторного звука у 62 (88,2%). Перкуторные изменения в легких у 59 (83,9%) имели локальный характер в виде укорочения легочного звука, у 53 (75,8%) наблюдался коробочный оттенок перкуторного звука, который характерен для бронхиальной обструкции. Если локальные перкуторные изменения были идентичными в сравниваемых группах больных, то коробочный оттенок перкуторного звука был характерен для больных с ООБ.

При наблюдении больных РБ с БОС нами выделены фазы обострения и клинической ремиссии.

Обострение РБ с БОС характеризовалось острым (подострым) началом, кашлем, вначале сухим – у 46 (92,0%), влажным – у 4 (8,0%) больных. Сухой кашель при поступлении по характеру приступообразный, больше в ночное время, на 5-6 сутки лечения трансформировался во влажный.

Цианоз носогубного треугольника наблюдался у 12 (24,0%), со стороны кожных покровов - сухость – у 36 (72,0%) больных. Аускультативные признаки были разнообразны и в основном зависели от уровня поражения слизистых бронхов. Сухие хрипы определялись у 6 (12,0%) детей, влажные проводные хрипы у 44 (88,0%) детей. Признаки гипоксии в виде цианоза носогубного треугольника у больных с ООБ держались в течение $2,3 \pm 0,8$ суток, а у больных РБ с ОБ этот показатель составил $3,4 \pm 0,3$ суток.

При аускультации продолжительность жесткого и ослабленного дыхания у больных с пневмонией составила $11,2 \pm 0,3$ и $7,8 \pm 0,5$ суток соответственно, что достоверно длительнее, чем у больных ОБРТ.

При рентгенологическом обследовании у 70 (100%) больных с ООБ отмечалась эмфизема легочной ткани, усиление бронхосудистого рисунка.

При рентгенологическом обследовании у 50 (100,0%) больных ОБРТ отмечались признаки бронхиальной обструкции – вздутие легочной ткани, повышение ее прозрачности, горизонтальное расположение ребер, широкие межреберные промежутки, уплощение и низкое стояние легочного рисунка.

Результаты изучения иммунного статуса представлены в таблице-1. Как видно из таблицы, у детей при ОБ определяется достоверное ($p < 0,01$) снижение содержания CD3+-лимфоцитов до $50,9 \pm 0,7\%$ по сравнению с практически здоровыми детьми. Содержание CD4+ и CD8+-лимфоцитов также достоверно отличались от нормальных величин. Содержание CD20+ - лимфоцитов у больных ОБ было достоверно ($p < 0,001$) выше, чем у практически здоровых детей и составило $20,8 \pm 0,6\%$. По - видимому, прогрессирующее снижение активности Т-супрессоров создает возможность активации В-системы иммунитета, которая является ключевым этапом

в реализации аллергических реакций. Большое значение в реализации иммунных функций играют клеточные факторы резистентности – натуральные киллеры, которые обладают цитопатической активностью. Активация натуральных киллеров происходит в результате их контакта с антигеном, следствием чего является цитотоксическое поражение инфицируемой клетки. Относительное число CD16+ - лимфоцитов в группе больных ОБ было достоверно повышено относительно нормальных величин и составило $12,4 \pm 1,2\%$ ($p < 0,01$). Анализ работы неспецифического звена иммунитета фагоцитоза, показал достоверное подавление ФАН по сравнению с контролем в группе больных ОБ ($p < 0,01$). У больных при ОБ с рекуррентным течением относительное количество CD3+ и CD4+ - лимфоцитов достоверно ($p < 0,01$) снижалось по сравнению с практически здоровыми детьми в 1,3 и 1,4 раза соответственно. Отмечалось достоверное снижение CD8+ - лимфоцитов ($p < 0,01$) по сравнению с практически здоровыми детьми. Содержание CD20+ - лимфоцитов у больных ОБ с рекуррентным течением было достоверно ($p < 0,01$) выше, чем у практически здоровых детей.

У больных с ОБ с рекуррентным течением относительное число CD16+ - лимфоцитов было достоверно ($p < 0,01$) снижено до $15,8 \pm 0,5\%$. Уровень фагоцитарной активности нейтрофилов у больных ОБ с рекуррентным течением был достоверно снижен по сравнению с показателями практически здоровых детей ($p < 0,01$) и составило $36,1 \pm 1,2\%$. (таб-4).

Результаты иммунологических исследований детей, больных РБ с БОС указывает на глубокие нарушения: определяется достоверное снижение содержания CD3+-лимфоцитов до $38,5 \pm 0,7\%$ ($p < 0,01$), включая иммунорегуляторные субпопуляции, CD4+ - лимфоцитов до $25,8 \pm 1,3\%$ ($p < 0,01$) и CD8+ - лимфоцитов до $13,9 \pm 0,6\%$ ($p < 0,01$) по сравнению с показателями ООБ. Содержание CD20+ - лимфоцитов у больных РБ с БОС было достоверно ($p < 0,01$) выше и составило $34,7 \pm 0,5\%$, чем у детей с ООБ. По - видимому, прогрессирующее снижение активности Т-супрессоров создает возможность активации В-системы иммунитета, которая является ключевым этапом в реализации аллергических реакций.

Таблица-4

Показатели клеточного иммунитета у обследованных детей, (M±m)

Показатели	Практически здоровые дети (n=20)	ООБ (n=120)	РБ с БОС (n=42)	P	P1
Лейкоциты, абс.	6677,8±167,9	6200±0,41	6600,22±0,33	>0,05	<0,01
Лимфоциты, %	33,51±0,50	35,26±0,56	38,35±0,66	<0,01	<0,01
CD3+-лимф., %	61,52±2,21	36,17±0,21	38,55±0,54	<0,01	<0,01
CD4+-лимф., %	39,11±2,11	20,31±0,44	25,87±1,56	<0,01	<0,01
CD8+-лимф., %	19,50±1,83	12,45±0,61	13,92±0,33	<0,01	<0,001
(CD4+/CD8+) ИРИ	2,0±0,2	1,59±0,03	1,86±0,05	<0,05	<0,05
CD16+-лимф., %	10,17±1,28	14,20±0,07	17,83±0,37	<0,05	<0,01
CD20+-лимф., %	16,36±0,47	33,91±0,42	34,74±0,36	<0,01	<0,001
ФАН, %	58,54±2,35	34,31±0,17	36,94±0,43	<0,01	<0,01

Примечание: P - достоверность различий показателей между I и II группами больных; P1 - достоверность различий показателей между II и III группами больных;

Анализ показателей фагоцитоза характеризующего неспецифическое звено иммунитета, в группе больных РБ с БОС, показал достоверное ФАН до $36,9 \pm 0,92$ мг/%, что в два раза ниже чем у детей ООБ ($p < 0,01$).

Выводы. 1. Для прогнозирования риска формирования бронхиальной астмы определены коэффициенты относительного риска (RR) и отношения шансов (OR). При ООБ, независимо от назологии, наблюдается более длительное проявление одышки, пероральных хрипов, влажного кашля и влажных хрипов в легких. На рентгенограммах больных всех групп, как правило, отмечается эмфизематозное расширение легких с обеих сторон с горизонтальным стоянием ребер, которые характерны для синдрома ООБ. При наличии бронхиальной обструкции более выражены симптомы интоксикации, дыхательной недостаточности, что более длительно проявляется клиническими признаками заболевания.

2. Для больных ООБ с РБ с БОС характерен дисбаланс клеточного звена иммунитета, за счет снижения CD3+, CD4+, CD8+, CD16+-лимфоцитов, на фоне активации гуморального звена (повышения CD20+-лимфоцитов в 1,5–1,6 раза), снижения фагоцитарной активности нейтрофилов в 1,4–1,6 раза.

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COMPARATIVE AGE FEATURES OF CLINIC AND PATHOGENETIC ASPECTS OF SCHOOL DISADAPTATION

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Abstract. Intensive processes of maturation of certain biological systems of the body in conjunction with an increase in the level of socio-psychological requirements for students, increase the possibility of psihotraumatik personality. The clinic manifestations and the main factors of pathogenesis of school disadaptation in the comparative-age aspect (7-11 years old, n = 950) and (12-17 years old, n = 550). More significant factors of risk together with the psycho - social ones (conditions of micro social sphere of family and school) are genetic and cerebral organic. The feature of found out by children and teenagers disadaptation is its massive somatisation, which charactrised by polymorph vegetative and visceral disorders in different organs and systems (digestive, skin, respiratory, moving, heart-vessel,secretory,endocrine) and painful manifestation. Results. Thus, clinical and population-based studies conducted among

healthy schoolchildren, revealed a greater incidence of children and adolescents with adjustment disorders (72%), among which is dominated by Grade III - a relative maladjustment. The most significant risk factors, along with psycho-social (micro social status of the family and school environment) are genetic and cerebro-organic. A feature of the identified children and adolescents maladjustment was its massive somatic, which was characterized by polymorphic vegetative-visceral disorders in various organs and systems (digestive, skin, respiratory, locomotor, cardiovascular, excretory, endocrine) and algic manifestations.

Key words. school disadaptation, factors of risk, somatisation.

School period of life is considered by most authors as a very special, very important period of human life, have a great influence on the formation of the body [1–4]. Intensive processes of maturation of certain biological systems of the body in conjunction with an increase in the level of socio-psychological requirements for students, increase the possibility of psihotraumatik personality. These biological and psychological characteristics of a certain effect on the prevalence and clinical manifestations disadaptation (crisis) disorders in this age group. All this creates conditions for a possible formation and manifestation of abnormally personal characteristics, which does not rule out further genesis clinic border states and increases the likelihood of neuropsychiatric and somatic diseases [5,6]. «School maladjustment» - a violation of the individual student adaptation to the school environment, which acts as a private phenomenon of disorder in the child's overall ability to adapt in connection with any pathological factors.

Purpose a comparative study of age-related clinical manifestations and pathogenesis of the main factors of school exclusion [SE].

Material and methods

The main methods of investigation were clinical-epidemiological and psychological. Additionally used psychopathological, paraclinic and catamnesis methods. Observation of children with impaired adaptation we carried out in conditions of children's clinics and psycho-neurological clinic (7-11 years, n=950) and (12-17 years, and n=550).

Results and discussion

Fully taped maladjustment in children 12-17 years of 29,6 ± 3,58%; P> 0,05 (22,4 and 36,0% of boys and girls) than in younger schoolboys 22 ± 3,38% (16,5 and 28,1% respectively in girls and boys). This ratio is celebrated and II degree maladjustment (14.5 and 25.6%, 10.4 and 19.4%, P> 0.05, respectively, in girls and boys) in the age periods 12-17 and 7-11 years. In 72.7% of girls and 52.5% of boys aged 7-11 years and 63.1% of girls and 38.4% of boys aged 12-17 with maladjustment infringements of only one of the 3 parameters.

Thus, much more often than in children (15,7 ± 1,18%), among school-age adolescents (29,4 ± 1,9%; P <0,001) found violations of adaptation.

The degree of response and the quality of mental and emotional changes Profile depend on the age of the subjects. So, boys and girls aged 7-11 years of mental and emotional changes in the background significantly marked decrease in impu-nitive «M» orientation reaction (20,4 ± 5,11; P <0,01). In general, the observed increase in reduction

of tolerance to frustration, which is manifested by increased ekstrapunitive indicator «E» reactions ($48,65 \pm 6,34$) and the reaction needs to continue, «1-R» ($44,45 \pm 6,31$; $P < 0,05$). In adolescents, students with maladjustment reaction ratio between the types of reactions and their direction abruptly broken.

It is stated significant increase ekstrapunitive «E» self-protective reactions of the type ($58,25 \pm 3,5$; $P < 0,05$) when compared with the children of 7-11 years and compared to children 12-17 years of healthy population. It is also a marked trend of increasing demand indicator reaction continued, «1-R» ($21,75 \pm 2,98$; $P < 0.001$). Reactions on the «O-D» type ($21,95 \pm 2,99$; $P < 0.01$) - domination of the obstacle is reduced in comparison with the healthy population. The findings suggest that a stressful situation with students maladjustment likely to respond to the aggression of others, excessive self-defense, and their emotional reactions differ inadequate. Low «On-D» in both age groups ($19,2 \pm 5,0$ and $21,95 \pm 2,99$; $P < 0,001$) 7-11 and 12-17 years shows a decline in severity and self-esteem. Obstacles caused by frustration, children assessed as having significant value or children looking for the source of conflict outside of yourself. Significantly less than normal, the answers impunitive-oriented and slightly more intrapunitive ($23,8 \pm 3,08$; $P < 0.05$).

Neurotic disorders were found in 20.1% of all surveyed and represented mainly asthenia, hysterical and obsession-but-phobic disorders. Asthenic disorders of psychogenic origin characterized by symptoms of «irritable weakness» in combination with mood fluctuations, vascular disorders: nervousness, anxiety, irritability, etc. These few students participated in public affairs classes. As a rule, they performance was low, which led to conflicts with the teachers. Hysteria, neurotic disorders presented acute affective demonstrative behavior problems, a variety of complaints, mainly of asthenic and hypochondriac nature; impulsivity, aggression, lack of physical feeling, unpleasant pain, etc. These teens were characterized by partial maladjustment in a team that was caused by systematic conflicts with teachers and classmates, sharp fluctuations in performance indicators. Obsessive-fobic disorders encountered in the ground rated as obsessive fear of hypochondric nature, compulsive actions, fear of illness and death, Onychophagia three-hotillomanii etc. In this group, the relative maladjustment arose because of poor performance. The expressed disturbances of behavior and conflicts with his classmates have been noted. Analysis of the frequency of neurological disorders shows that children aged 7-11 years with impaired adaptation of the most common symptoms of motor disinhibition syndrome or hyperactivity or restlessness intensively manifested ($28,0 \pm 3,61$ and $44,6 \pm 4,0\%$), disinhibition ($31,5 \pm 3,7$ and $29,3 \pm 3,66\%$), lack of focus and impulsive action ($39,7 \pm 3,94$ and $27,5 \pm 3,59\%$), violation of concentration ($17,6 \pm 3,06$ and $15,5 \pm 2,91\%$), restlessness ($27,5 \pm 3,59$ and $39,3 \pm 3,93\%$ respectively for girls and boys). Adolescents 12-17 years manifestations syndrome, primarily motor excitability ($21,0 \pm 3,20$ and $27,0 \pm 3,48\%$) and motor disinhibition ($12,4 \pm 2,58$ and $18,5 \pm 3,05\%$), restlessness ($13,5 \pm 2,68$ and $22,0 \pm 3,25\%$ respectively for girls and boys) are gradually smoothed out. It was found that premature birth with the birth of a premature baby were observed in 11 (12.08%) women, children with congenital malnutrition - in 15 (16.5%), post-term baby - in 7 (7.69%), which is significantly different from the proportion of children in the general population (2,99; 2,32%, $P < 0,001$). The average weight of girls body with adjustment disorder at birth (3235 ± 8.9 g) did not differ from the mass of the girls in the control group (3320 ± 294 g, $P < 0.05$), and the average body mass of boys with TTTD (3057 ± 84.9 g) was significantly lower than control group newborn males ($3372 \pm 33,4$ g, $P < 0,01$).

It should be noted that in children with impaired adaptation dominated children at birth have both reduced (< 2.5 kg) of body weight - 14 (15.4%, $P < 0.01$) and increased (> 4.0 kg) body weight - 15 (16.3%), which significantly reduces the percentage of children having an average body weight (3100-3500 g), respectively, in females (36.7% $P < 0.01$) and 37.4 boys ($P < 0.01$) as compared with the control group (55,5-54,9%). In the group of children with maladjustment high proportion of occurrence of pre - and perinatal ($P < 0.05 - 0.001$) disease than in the control group, which were based on the microcirculatory disorders hypoxic and hypoxic-traumatic nature.

The results of experimental studies of psychological maladjustment in children with perinatal CNS, indicate mental disorders health, manifested in violation of pace, the inertia of mental processes, exhaustion and violation of affective-personal sphere (reduction of cognitive activity, indecision in action, disruption of activities at difficulties). A significant part of the intellectual functions they seemed intact, however, noted the weakening of

mnemonic processes, which led to a reduction of the storage material and the strength of its hold.

A special place among the neurotic symptoms of the surveyed children and adolescents with SE occupy the thoughts and concerns about their appearance and structure of the body. These symptoms are significantly higher in adolescents 12-17 years than in children 7-11 years old ($36,0 \pm 3,77$ and $44,0 \pm 3,89\%$ against $14,0 \pm 2,79$ and $12,7 \pm 2,68\%$; $P < 0.001$), respectively, in girls and boys. The results of the study of personality characteristics of children and adolescents with SM show that overall detection of types of character accentuations significantly different from population ($B < 0.001$). Large group of gipertimnye and gipertim-but-mixed ($24,5 \pm 4,72$ and $13,7 \pm 3,34\%$; $P < 0.05$, respectively, for boys and girls), hysteroid ($4,1 \pm 2,20$ and $4,7 \pm 2,35\%$), astenonevrotic ($4,5 \pm 2,30$ and $5,5 \pm 2,53\%$, $P < 0.05$) the types of character accentuations. Indicators of the other types did not differ from those of the population. An analysis of the family situation in the group of children with SE showed in most cases the presence of frequent conflicts between the parents (87.7% , $P < 0.001$). Almost half of the surveyed were raised in a single-parent families (37% , $P < 0.001$), - absence of one or both parents, often the father, the presence in the family of his stepfather, stepmother, and others, as well as in the atmosphere of constant scandals and conflicts of family relationships.. Normal conditions of education are much rarer (7.7% , $P < 0.001$) than in children and adolescents without behavioral disorders (control group). Among the forms of improper upbringing often detected gip-opek (35.7%), neglect (36.0%). The situation of «idol» family more common (18.9%) than «Cinderella.» Quite often revealed mixed variants of improper upbringing. It is characteristic that in the majority of households surveyed (86.8%) of the material and living conditions were favorable. Hence, the emergence of deviant behavior among adolescents depended not so much on material well-being, but on the negative climate.

Conclusion. Thus, clinical and population-based studies conducted among healthy schoolchildren, revealed a greater incidence of children and adolescents with adjustment disorders (72%), among which is dominated by Grade III - a relative maladjustment. The most significant risk factors, along with psycho-social (micro social status of the family and school environment) are genetic and cerebro-organic. A feature of the identified children and adolescents maladjustment was its massive somatic, which was characterized by polymorphic vegetative-visceral disorders in various organs and systems (digestive, skin, respiratory, locomotor, cardiovascular, excretory, endocrine) and algic manifestations. Neurotic disorders occur among children and adolescents in a relatively large percent of cases, and usually leads to severe violations of students to adapt to the team.

Neurological examination of school-age children with pre- and perinatal pathology identifies risk with SE, determined on the basis of minimum functional deviations forecast further psychomotor development of the child, to ensure the timely correction of these deviations. Situation and behavioral disorders due to occur more frequently on a background of accentuations nature, lead to a full school maladjustment.

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